The Christie
School of Oncology

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Abstract Booklet

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Application No.	**ABSTR002**
Title	Extending the scope of TEM – Effect of radiotherapy on outcome in locally excised T2 rectal cancer
Presenting Author	Henry Wu, University of Manchester
Other Authors	
Subsection	Surgical Oncology
Consider for	

Contents

Background: Local excision by Endoscopic Microsurgery (TEM) has remained controversial in rectal carcinomas stage T2 and above due to higher rates of local recurrence principally from occult nodal metastases. There has been considerable interest in the use of TEM combined with radiotherapy as an alternative to radical resection.

Aim: Evaluate the efficacy of TEM and radiotherapy as an alternative to radical resection in stage T2 rectal carcinomas.

Method: Records of 12 patients who underwent TEM for stage T2 rectal carcinoma at the Royal Preston Hospital were reviewed. Their treatments and outcomes were recorded.

Results: 6 patients received radiotherapy and 6 did not because they either elected for subsequent radical surgery (3 patients) or were unfit for further treatment and underwent follow-up (3 patients). Median follow-up was 20 months. In the no-radiotherapy group, 1 patient who underwent subsequent radical surgery had involved mesorectal lymph nodes and 1 patient undergoing follow-up without radical surgery developed mesorectal nodal recurrence. In the radiotherapy group, all 6 patients underwent follow-up with no recurrences to date. There was no 90 day surgical mortality.

Discussion and Conclusion: Whilst the numbers in the study were not sufficient for valid statistical comparison, the lack of tumour recurrences in the group receiving radiotherapy does support the use of TEM with radiotherapy as a promising alternative treatment modality for stage T2 rectal carcinoma particularly in patients who are at high risk for radical surgery, have a near complete response to pre-op radiotherapy or are keen to avoid a permanent stoma.

REFERENCES:

1) Bach, S.P., Hill, J., Monson, J.R.T., Simson, J.N.L., Lane, L., Merrie, A., Warren, B. and Mortensen, N.J.M. (2009) ‘A predictive model for local recurrence after transanal endoscopic microsurgery for rectal cancer’, British Journal of Surgery, 96(3), pp. 280–290. doi: 10.1002/bjs.6456.

2) Lezoche, E., Guerrieri, M., Paganini, A.M., D’Ambrosio, G., Baldarelli, M., Lezoche, G., Feliciotti, F. and De Sanctis, A. (2005) ‘Transanal endoscopic versus total mesorectal laparoscopic resections of T2–N0 low rectal cancers after neoadjuvant treatment: A prospective randomized trial with a 3-years minimum follow-up period’, Surgical Endoscopy And Other Interventional Techniques, 19(6), pp. 751–756. doi: 10.1007/s00464-004-8930-x.

3) Bujko, K., Richter, P., Kołodziejczyk, M., Nowacki, M.P., Kulig, J., Popiela, T., Gach, T., Olędzki, J., Sopyło, R., Meissner, W., Wierzbicki, R., Polkowski, W., Kowalska, T., Stryczyńska, G. and Paprota, K. (2009) ‘Preoperative radiotherapy and local excision of rectal cancer with immediate radical re-operation for poor responders’, Radiotherapy and Oncology, 92(2), pp. 195–201. doi: 10.1016/j.radonc.2009.02.013.

Application No. **ABSTR003**
Title How trastuzumab's mechanism of action provides insights in future drug development
Presenting Author Rory Tinker, University of Manchester
Subsection Medical Oncology/Haematology
Consider for Poster & Oral

Contents

Breast Cancer is a major clinical problem . Around 20% of the UK's 50,000 annual cases of breast cancer have over amplification of HER2 receptors, leading to such tumours being classified as HER2 positive. HER2 is a membrane tyrosine kinase and oncogene. Herceptin® (trastuzumab) is a humanised monoclonal antibody that binds to the extracellular domain of HER2 and is a targeted cancer therapy for HER2 positive cancers. This presentation aims to present a literature review, summarising the scientific consensus of trastuzumab's mechanisms of action, how resistance develops, its side effects and to consider future advances in the drug class. I argue that trastuzumab uses the immune system to create antibody dependent cellular cytotoxicity directed against malignant cells, inhibits intracellular pathways, prevents dimerization of receptors and angiogenesis. Resistance develops through mutations in the HER2 receptor and its corresponding pathways preventing trastuzumab from functioning effectively. One in five patients experience reversible cardiotoxicity. Second generation monoclonal antibodies utilizing the same principal as trastuzumab offer an exciting future for targeted cancer therapy. To conclude, more research is needed around resistance, cardiotoxicity and mechanisms of action. Better understanding of such processes could result in future generations of trastuzumab delivering improved efficacy, fewer side effects and longer therapeutic windows before resistance develops. In addition, the lessons learned from the development of trastuzumab as a monoclonal antibody can be further applied to development of new targeted therapies in oncology and other medical areas.

Application No. **ABSTR005**
Title A multicentre cohort study to redefine and validate pathological assessment of response to neoadjuvant therapy in treated oesophagogastric adenocarcinoma
Presenting Author Megan Lloyd, University of Southampton
Subsection
Consider for

Contents

Background and Aims: A universally accepted measure of significant response to neoadjuvant therapy in oesophageal adenocarcinoma (OAC) is required to stratify patients for precision treatment. Our study aimed to define the utility of Mandard tumour regression grade (TRG) in UK clinical practice, assess its reliability, and validate a clinically meaningful endpoint of significant pathological response.

Methods: A questionnaire assessed current clinical use of TRG in 11 UK centres. 7 centres provided prospectively collected clinicopathological data from patients with treated OAC (2001-2016). Pathological primary tumour response to neoadjuvant therapy was assessed using TRG, with blinded validation of scoring. Lymph node downstaging (LDS) was assessed by comparing clinical and pathological staging (cN+ to ypN0).

Results: TRG was recorded by 73% of centres with 63% using TRG 1-3 to define a significant response to therapy. Of 1258 patients studied, a significant overall survival advantage was seen with TRG 1-2 (responders, n=189) compared to TRG 3-5 (non-responders, n=1069) (mean overall survival; TRG 1-2: 10.4 years, 95% CI: 9.4-11.3 vs TRG 3-5: 4.8 years, 95% CI: 4.3-5.2, $p<0.0001$). A subset of non-responders demonstrated LDS with a subsequent survival advantage (mean overall survival; TRG 3-5 with LDS, n=155: 7.9 years, 95% CI: 7.0-8.7 vs TRG 3-5 without LDS, n=581: 3.2 years, 95% CI: 2.9-3.6, $p<0.0001$).

Discussion and Conclusion: This multi-centre study validates responders to neoadjuvant therapy with overall survival double that of non-responders. Assessment of response should not be confined to the primary tumour as a cohort of apparent non-responders gain a survival advantage by lymph node down staging.

Application No.	**ABSTR006**
Title	Inhibition of Nrf2 in a Mouse Model of Colorectal Cancer: Effect on Protein Quantification and Gene Expression in the Colon
Presenting Author	Amy Cash, University of Liverpool
Other Authors	Neil Kitteringham and Jonathan Evans, University of Liverpool
Subsection	Translational Oncology/Basic Science
Consider for	Poster & Oral

Contents

Background: Nrf2 upregulates the transcription of detoxifying genes to minimise harm caused by oxidative and chemical stress. Nrf2 is over-expressed in a various cancers and may confer a survival advantage to these cells. Inhibition of Nrf2 could, therefore, be of therapeutic value. Brusatol has previously been investigated as an inhibitor of Nrf2 in vitro and has been shown to inhibit tumour growth in a CRC mouse model by researchers at The University of Liverpool. We explored the ability of brusatol to inhibit Nrf2, and the subsequent impact on NQO1, at the protein and genetic level in tissue taken from the CRC mouse model.

Methods: Using liver and colon tissue from the CRC mouse model, western blotting and qPCR was performed.

Results: For Nrf2 protein quantification, there was a statistically significant decrease in brusatol-treated samples compared with control of 94.4% ($p = 0.0225$) and 94.6% ($p = 0.008$) for liver and colon samples respectively. No results for NQO1 were obtained. There was a small reduction in mRNA expression for both Nrf2 and NQO1 however these results did not reach significance.

Conclusion: The results indicate that brusatol is an excellent inhibitor of Nrf2 at the post-translational level in vivo. This suggests that there is potential for brusatol to act as a therapeutic agent against a variety of tumours over-expressing Nrf2.

Application No. **ABSTR007**
Title Correlation of MGMT promoter methylation status and levels with survival benefit and sensitivity to Temozolomide in the GBM (Glioblastoma Multiforme) patient population of NHS Tayside
Presenting Author Zhong Wei Khor
, University of Dundee
Other Authors Hannah Lord, NHS Tayside
Subsection Clinical Oncology
Consider for Poster

Contents

BACKGROUND:

Previous studies have identified that the silencing of O6-methylguanine-DNA methyltransferase (MGMT) via methylation of its promoter region renders Glioblastoma Multiforme (GBM) more sensitive to Temozolomide, improving patients' prognoses.

AIM:

This study aims to confirm the above relationship in the NHS Tayside patient population.

METHODS:

A retrospective study involving 27 patients with GBM treated at NHS Tayside between 2012 and 2016 was carried out. Data collected using patients' case notes and electronic data bases: MGMT methylation status and percentage expression; treatment received; overall survival; progression free survival.

RESULTS:

14 patients out of 27 patients were MGMT methylation positive (defined as 8.7% methylation and above).

All patients were commenced on TMZ chemotherapy with the exception of 4 due to palliative reasons.

The average overall survival time for patients with positive MGMT methylation was 17 months 24 days as compared to 8 months 23 days for MGMT unmethylated patients.

Average progression free survival was also significantly longer for MGMT methylation positive patients (15 months 13 days) compared to methylation negative patients (7 months and 6 days).

Above the threshold for positive MGMT methylation (8.7%), there was no correlation between higher MGMT percentage levels with patient overall survival and progression free survival.

DISCUSSION:

In this study, a clear benefit is shown between positive MGMT methylation status and patient outcome. This further validates the application of MGMT methylation as a prognostic factor in real world, non-trial patients with GBM.

CONCLUSIONS:

MGMT methylation status should be consistently investigated in all GBM patients to predict response to TMZ and for patient prognostication.

Application No. **ABSTR009**
Title The association between breastfeeding and breast cancer risk: a review of findings
Presenting Author Swabirah Rassool, University of Manchester
Subsection Public health, prevention & screening
Consider for Poster

Contents

Background: Breastfeeding is hypothesised to decrease breast cancer risk. If this association holds true, breastfeeding – being a potentially modifiable behaviour – could be used to reduce the incidence of breast cancer. This is paramount as breast cancer is currently the most common cancer in the UK.

Aims: This poster aims to review some previous epidemiological findings to determine whether there is evidence or not of the protective benefit of lactation.

Methods: A Medline search was carried out to identify eligible systematic reviews and/or meta-analyses.

Results: The collective epidemiologic evidence is largely inconsistent. An inverse association between lifetime duration of breastfeeding and breast cancer risk looks likely, although the protective benefit has not been consistently incremental. Ever breastfeeding appears to have no or a slight effect on overall risk of breast cancer, but was associated with a significant decrease in risk of hormone receptor-negative (HR-) breast cancers.

Discussion: Investigating the protective effect of breastfeeding against breast cancers in general may have underestimated the risk reduction reported by previous studies. Since HR- breast cancers are more common in younger women and have a poor prognosis, the protective effect of lactation against this subtype has major public health implications. The biological basis is still unclear though.

Conclusion: Once the mechanism of action of the protective effect of breastfeeding is established, at-risk women should be encouraged to breastfeed to reduce the incidence of HR- breast cancers.

Application No. **ABSTR010**
Title Turning up the heat: Can heat sensitisation prior to radiation treatment decrease the survival of HPV negative head and neck cancer cells
Presenting Author Katherine Deasy, University of Liverpool
Other Authors Leah Evans, Emma Scott and Dr James Wilson
Subsection
Consider for

Contents

Background: Annually there are over 500,000 instances of head and neck squamous cell carcinoma (HNSCC) worldwide1. Research demonstrates that response of HNSCC to treatment is associated with high risk types of human papilloma virus (HPV)2. HPV positive HNSCC responds better to radiotherapy than HPV negative HNSCC3. Can this be improved in cell lines by heat sensitisation?

Aims:

- Do HPV positive cell lines (HPVPCL) and HPV negative cell lines (HPVNCL) differ in % survival after radiation exposure

- Does heat sensitisation reduce %cell survival of HPVNCL when exposed to radiation

- Are there increased chromosome aberrations in HPVNCL exposed to heat and radiation treatment compared with controls

Methods: Chlonogenic, heat and radiation treatment and chromosome analysis were undertaken to determine the effect HPV status had on cell survival and how this was affected by heat sensitisation.

Results: HPVPCL decreased in %survival when exposed to radiation from 100% to 12.75%, compared to 100% to 32.23% for HPVNCL. Using heat sensitisation the %survival of HPVNCL to radiation treatment decreased to 17.4% and % of chromosome aberrations increased by 217% compared to controls

Discussion: HPVNCL showed an improved cell survival to radiation exposure compared to HPVPCL. However, heat sensitisation and radiation treatment together reduced this survival by 54% on average in HPVNCL. Heat and radiation treatment together also increased the percentage of chromosome aberrations seen in HPVNCL.

Conclusion: heat sensitisation prior to radiation treatment on in vitro cell lines has been shown to decrease the %survival and increase the % of DNA damage in HPV negative HNSCC cell lines.

References:

1) Stenson, K. (2016). Epidemiology and risk factors for head and neck cancer. [online] Uptodate.com. Available at: http://www.uptodate.com/contents/epidemiology-and-risk-factors-for-head-and-neck-cancer [Accessed 1 Jul. 2016].

2) Macmillan.org.uk. (2016). Risk factors and causes of head and neck cancer - Cancer information - Macmillan Cancer Support. [online] Available at: http://www.macmillan.org.uk/cancerinformation/cancertypes/headneck/aboutheadneckcancers/causes.aspx [Accessed 1 Jul. 2016].

3) Lassen, P., Eriksen, J., Hamilton-Dutoit, S., Tramm, T., Alsner, J. and Overgaard, J. (2009). Effect of HPV-Associated p16INK4A Expression on Response to Radiotherapy and Survival in Squamous Cell Carcinoma of the Head and Neck. Journal of Clinical Oncology, 27(12), pp.1992-1998.

Application No.	**ABSTR011**
Title	Metastatic melanoma: prognostic factors and survival in patients with brain metastases
Presenting Author	Emily Frinton, University of Manchester
Other Authors	Dr Ruth Board (Consultant Medical Oncologist, Rosemere Cancer Centre, Lancashire Teaching Hospitals NHS Foundation Trust)
Subsection	Medical Oncology/Haematology
Consider for	

Contents

Background: Brain metastases from malignant melanoma carry a poor prognosis. Novel systemic agents have improved overall survival (OS), but the value of whole-brain radiotherapy (WBRT) and stereotactic radiosurgery (SRS) remains uncertain (Dyer et al 2014). The melanoma-specific graded prognostic assessment (msGPA) provides useful prognostic information, but the relevance to the modern-day population has not been validated (Wilkins et al 2015).

Aims: Validation of the msGPA and the role of SRS combined with other treatment versus WBRT alone.

Methods: Since 2011, 48 patients received treatment for brain metastases from malignant melanoma at the Rosemere Cancer Centre medical oncology clinic. Data were collated on demographic factors and survival. Survival analyses were performed using Kaplan-Meier methods. Cox regression was used to identify prognostic factors on univariate and multivariate analysis.

Results: OS from the date of diagnosis of brain metastases was 6.07 months (95% CI 2.13-10.0). On univariate analysis, BRAF, performance status and msGPA were significant prognostic indicators for OS (p=0.0086, p=0.0014 and p=0.0001 respectively), and remained significant on multivariate analysis. OS for BRAF-positive treated patients (n=21) was 8.2 months, versus 3.7 months for BRAF-negative patients (n=23). SRS combined with systemic agents (n=16) produced an OS of 13.5 months. Patients receiving WBRT alone (n=12) had a poor prognosis (1.6 months).

Discussion and Conclusions: The msGPA remains a valid prognostic indicator in the era of novel systemic treatments for melanoma. Incorporation of BRAF-status may produce a model with even greater prognostic discrimination. WBRT alone has no role in the active management of melanoma brain metastases.

References:

Dyer MA, Arvold ND, Chen YH, Pinnell NE, Mitin T, Lee EQ, Hodi FS, Ibrahim N, Weiss SE, Kelly PJ, Floyd SR, Mahadevan A, Alexander BM [2014]. The role of whole brain radiation therapy in the management of melanoma brain metastases. Radiate Oncol. Jun 22;9:143.

Wilkins A, Furness A, Corbett RW, Bloomfield A, Porta N, Morris S, Ali Z, Larkin J, Harrington K [2015]. The melanoma-specific graded prognostic assessment does not adequately discriminate prognosis in a modern population with brain metastases from malignant melanoma. Br J Cancer. Nov 3;113(9):1275-81

Application No.	**ABSTR014**
Title	A retrospective analysis of the demographics, biology and outcomes in elderly patients with diffuse large B-cell lymphoma
Presenting Author	William Oakley, University of Southampton
Subsection	Medical Oncology/Haematology
Consider for	Poster & Oral

Contents

Background: Diffuse large B-cell lymphoma (DLBCL) is the most common high-grade non-Hodgkin lymphoma. Sixty-three percent of cases of DLBCL are in those aged 65 years and over. Comorbidities, physiological decline and geriatric symptoms complicate the management of DLBCL in elderly patients.

Aims: The aims were to describe the demographic profile; gain a better insight into the biology; evaluate the role of prognostic screening; correlate baseline parameters with outcomes; and assess immunochemotherapy delivery in elderly patients with DLBCL.

Methods: A retrospective study that included all patents aged 60 years and over who were diagnosed with de novo DLBCL at University Hospital Southampton from 2010 to 2012. Paper and electronic medicals records were reviewed in all cases. Clinical and pathological variables were assessed.

Results: Sixty-eight patients were eligible. Median age was 74 years (range 60-90). 3-year overall survival (OS) was 50% (95% confidence interval: 38.1-61.9). Multivariate analysis revealed that age over 80 years (hazard ratio [HR]: 2.9, p=0.044); Ann Arbor stage III or IV disease (HR: 3.2, p=0.021); ECOG performance score of 2, 3 or 4 (HR: 3.7, p=0.021); elevated white blood cell count (HR: 0.1, p=0.015) and elevated neutrophil count (HR: 0.08, p=0.023) were associated with a reduction in 3-year OS. The age-adjusted International Prognostic Index effectively stratified elderly patients.

Discussion: The study highlighted the importance of clinical and haematological parameters but indicated that immunohistochemical markers are not useful in prognostication.

Conclusion: A better understanding of the factors associated with poorer outcome in elderly patients will assist clinical decision making.

Application No.	**ABSTR015**
Title	PSA monitoring in patients discharged from urology to primary care: an audit of GP compliance with local PSA protocol
Presenting Author	Shahab Haghollahi, University of Warwick
Other Authors	Aimee McCreedy and Sophie Walford, University of Warwick
Subsection	Primary Care
Consider for	Poster & Oral

Contents

Background: Patients with high PSA are referred to urology in accordance with NICE guidelines (NG12, 2015). Upon discharge, GPs should provide follow-up PSA testing according to recommended schedules in urology discharge letters. Aims: This audit examines primary care compliance with Locally Enhanced Service Monitoring of Patients with Stable Prostate Cancer in Primary Care (2013) guidance on follow-up PSA testing and the GP practice standard of offering annual follow-up for 5 years following a high PSA test result. Method: We audited 241 patients who had a PSA test in the last 5 years and identified those referred to urology. We assessed whether, upon discharge back to primary care, PSA follow-up was conducted according to local guidelines. Results: The GP practice achieved full compliance with local guidelines on PSA follow-ups for patients with stable prostate cancer, and good compliance with urology recommendations for other discharged patients. Discussion: PSA is useful for monitoring recurrence of prostate disease. Timely testing in at-risk individuals allows early detection and reduction in prostate cancer mortality (Schröder FH, et al., 2014). Urology discharge instructions were sometimes less well-defined, and in such cases a clinical decision by the GP on appropriate alert schedule may be needed. Conclusion: This practice could achieve 100% compliance with urology discharge recommended monitoring schedules by implementing a manual alert system.

References:

Locally Enhanced Service Monitoring of Patients with Stable Prostate Cancer in Primary Care. 31st March 2013. South and Warwickshire practices.

NICE (June 2015). Suspected Cancer: Recognition and Referral Guidelines. NG12, 1.6 Urological Cancers

Schröder FH, et al., 2014. Screening and prostate cancer mortality: results of the Europeans Randomised Study of Screening for Prostate Cancer (ERSPC) at 13 years of follow- up. The Lancet. Volume 384, No.9959, p2027-2035

Application No.	**ABSTR016**
Title	Are Asian women more prone to less favourable subtypes of breast cancer?
Presenting Author	Joseph Wan, University of Manchester
Other Authors	Jaanika Molderson, Phil Foden, Julie Morris and Anil Jain, University Hospitals of South Manchester
Subsection	Clinical Oncology
Consider for	Poster & Oral

Contents

Introduction

Breast cancers present with differential expression levels of hormone receptors (ER, PR, HER2), which modern chemotherapy targets, resulting in 8 different subtypes. Research has shown that each subtype presents with different histopathological features, thus affecting survival. We aim to investigate the prevalence of breast cancer receptor subtypes between Asian and Caucasian women; and to compare their prognostic indices.

METHODS

231 Asian patients with invasive breast carcinoma (IBC), age-matched with equal numbers of Caucasian patients; were included in this retrospective cohort study (n=462). Receptor profiles and histopathological features were extracted from medical records; Nottingham Prognostic Index (NPI) was calculated.

RESULTS

Across all receptor subtypes, Asian patients presented with higher NPI; lymph node status; invasive grade; and larger tumour sizes ($p<0.005$); and had higher prevalence of HER2-positive subtypes (30.3%, $p=0.002$); whereas Caucasian patients have a higher proportion of ER+/PR+/HER2- subtype ($p=0.030$), which is associated with favourable prognostic indices. TNBC prevalence is similar in both groups, demonstrating the highest proportion of grade 3 tumours, while HER2-positive subtypes demonstrated the highest NPI. Furthermore, prognostic indices were worse in younger patients.

CONCLUSION

Consistent with recent literature, our study had provided evidence that Asian patients were more prone to HER2-overexpressing breast cancer, but not TNBC subtypes, Also, poor clinico-pathological features were associated with these 2 subtypes, correlating to a poor prognosis. Given the poor prognostic indices they presented with and high treatment costs involved with these subtypes, our results have implications for clinical care and future research.

Application No.	**ABSTR017**
Title	Outcomes of Autologous Stem Cell Transplants in Patients with Multiple Myeloma
Presenting Author	Lorne Thomson, University of Manchester
Other Authors	Fiona DIgnan, Sarah Burns, Muhammad Saif, Chiari Lobetti Bodoni, Eleni Tholouli and Alberto Rocci, Manchester Royal Infirmary
Subsection	Medical Oncology/Haematology
Consider for	Poster & Oral

Contents

Multiple myeloma is a blood cancer originated from the plasma cells. Autologous stem cell transplants form the standard of treatment for younger patients but are less common in those over the aged 65. Given that the median age at diagnosis of multiple myeloma patients is 70 many older patients may benefit from such transplants. In this study we look at how patient's aged 65 and over vary from their younger counterparts across a variety of outcomes. We compare 31 patients younger than 65 with 11 patients aged 65 and over. Across a range of measures few differences were observed between the older and younger patient groups, although more research is required into the effects of staging of disease and fitness on outcomes from transplants.

Application No.	**ABSTR018**
Title	Overexpression of Phosphorylated AKT (pAKT) is not Correlated with the Presence of a KRAS Mutation in Patients with Advanced Colorectal Cancer
Presenting Author	Gayatri Raghuram, Basildon University Hospital
Other Authors	Dr S Richman and Professor P Quirke
Subsection	Translational Oncology/Basic Science
Consider for	

Contents

Background

Developments in advanced colorectal cancer treatment have seen the introduction of drugs targeting the epidermal growth factor receptor (EGFr). KRAS mutation status has been shown to be a prognostic biomarker of response to such therapies.

Aims

This study aims to establish whether there is a correlation between expression of phosphorylated AKT (pAKT), a protein downstream to KRAS, and KRAS mutation status, potentially resulting in an additional biomarker of response to anti-EGFr therapy.

Methods

Colorectal cancer tissue from patients with advanced colorectal cancer was collected and sequenced to determine patients' KRAS mutational status. Immunohistochemistry was performed on tissue microarrays using a pAKT monoclonal antibody and staining intensity was scored.

Results

KRAS mutation status was available for 163 patients. Of these, 76 (46.6%) were KRAS mutant and 87 (53.4%) were KRAS wildtype. Staining was nuclear and/or cytoplasmic for p-AKT, so cores were given two scores. There was no significant difference between the distribution of either nuclear (46% v 42.5%, p=0.75) or cytoplasmic (44.7% v 34%, p=0.30) pAKT overexpression in the KRAS-mutant versus KRAS-wildtype populations respectively.

Discussion

Determination of pAKT protein expression appears not to discriminate between tumours with KRAS mutations, and those without. Although one previous study found a correlation between p-AKT expression and KRAS status (Davies, 2011), our study supports the results of a few existing studies conducted in colon and rectal cancer (Davies 2010, Kato 2007).

Conclusions

Based on this study, we suggest that the use of pAKT expression levels as a biomarker of potential response to anti-EGFr therapy is not at this time justified.

References

1. Davies JM, Deal AM, Funkhouser WK, Calvo BF, et al. (2011). Phospho-ERK and AKT status, but not KRAS mutation status, are associated with outcomes in rectal cancer treated with chemoradiotherapy. Radiation Oncology, Volume 12(6), p.114.

2. Davies JM, Deal AM, Funkhouser WK, Calvo BF, et al. (2010) Relationship between k-ras status with pAKT, pERK, and outcomes in patients with rectal cancer (RC). American Society of Clinical Oncology.

3. Kato S, Higuchi T, Ishikawa T, et al. (2007) PIK3CA mutation is predictive of poor survival in patients with colorectal cancer. International Journal of Cancer, Volume 212, p.1771 - 1778.

Application No. **ABSTR019**
Title What is the effect of age on treatment decision in patients with invasive breast cancer?
Presenting Author Sargam Vohra, University of Manchester
Other Authors Dr. Sacha Howell and Dr. Vivek Misra, The Christie

Subsection Medical Oncology/Haematology
Consider for Oral

Contents

Background

Breast cancer is the most common malignancy in women in UK. Incidence of breast cancer increases with age with approximately 46% of the breast cancer cases diagnosed in females over the age of 65 years(Dixon, 2012). Literature suggests that older patients are less likely to receive standard management for breast cancer(Lavelle et al., 2007).

Aim

To investigate the effect of age on treatment delivery in patients with invasive breast cancer.

Method

Data was collected retrospectively from 500 patients over 2012-2014. This included details regarding tumour characteristics such as staging, hormone receptor status, functional status and comorbidities. Logistic regression was employed to adjust for these variables to explore the effect of age on delivery of chemotherapy, radiotherapy and endocrine treatment.

Results and Discussion

Elderly patients are less likely to receive chemotherapy when tumour characteristics, functional status and comorbidities are accounted for. Compared to much younger patients(20-40 years), the odds of receiving chemotherapy is significantly lower in patients aged 71-80 years(OR=0.06,95% CI:0.01-0.31). Patients aged above 70 years are more likely to undergo dosage reductions and fewer chemotherapy cycles due to treatment toxicities(Lyman et al., 2013). Therefore, fewer patients diagnosed at 70 years or above accept chemotherapy when offered by clinicians. The likelihood of patients receiving radiotherapy increases with age when the same variables are accounted for. Compared to patients aged 20-40 years, patients aged 71-80 years have increased odds of receiving radiotherapy(OR=2.54,95% CI:0.39- 16.5). No substantial change is observed in endocrine treatment delivery with increasing age.

Conclusion

There is need to implement changes in current practice to decrease treatment discrepancies between older and younger patients.

References

Dixon, J.M. (2012) ABC of breast diseases. Edited by Michael J. Dixon. 4th edn. United Kingdom: Wiley-Blackwell (an imprint of John Wiley & Sons Ltd).

Lavelle K, Moran A, Howell A. Non-standard management of breast cancer increases with age in the UK: A population based cohort of women > or =65 years. British journal of cancer. 2007 Mar 28 [cited 14th Jul 2016];96(8):1197–203. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17387342.

Lyman, G., Dale, D., Tomita, D., Whittaker, S. and Crawford, J. (2013) 'A retrospective evaluation of chemotherapy dose intensity and supportive care for early-stage breast cancer in a curative setting', Breast cancer research and treatment., 139(3), pp. 863–72.

Application No.	**ABSTR020**
Title	The Use of Wearable Technology to monitor patients receiving Chemotherapy
Presenting Author	Harris Trainer, University of Manchester
Other Authors	Umair Gondal, University of Manchester and Omer Aziz, Mike Braun and Mark Saunders, The Christie
Subsection	Clinical Oncology
Consider for	Poster & Oral

Contents

Introduction: Chemotherapy causes complications that occur in an out-of-hospital environment. This study aims to investigate the potential of wearable technology for remote monitoring of patients, enabling earlier detection of complications, such as neutropaenic sepsis, thereby reducing admissions, reducing costs and increasing patients QoL.

Method: Questionnaires were developed for chemotherapy patients and their carers to determine opinions on overall care and follow-up, desire for further monitoring and levels of anxiety and depression. Following a review of commercial fitness monitors, three devices (Fitbit Charge-HR, Jawbone Up-3 and Pulse-Ox) were chosen for head-to-head comparison, which resulted in selection of the Fitbit. Subsequently, 11 healthy volunteers wore the device for 1 week, while keeping a diary of activities and completing a questionnaire.

Results: 39 patients (average age=62 years, 24 men), and 29 carers (average age=59 years, 7 men) completed the questionnaire. Responses confirmed a desire for remote outpatient monitoring and, interestingly, greater levels of treatment-related anxiety in carers than patients (P=0.0004).

Studies in volunteers demonstrated the Fitbit's ability to accurately capture data on heart rate, activity levels and sleep, however there were problems with remotely accessing the data.

Conclusion: This study has demonstrated a clear enthusiasm among patients and carers for wearable technology, and furthermore shown the capability of existing monitors to capture accurate and reliable data. Challenges regarding software and the ability to measure temperature and oxygen saturation are likely to be resolved in the near future, with this technology offering a significant advancement in out-of-hospital monitoring in oncology.

Application No.	**ABSTR021**
Title	Pre-pectparallel presentation implant placement with total acellular dermal matrix cover – a new technique for implant-based breast reconstruction
Presenting Author	Valerie Wong, University of Manchester
Other Authors	Lyndsey Highton and John Murphy, University Hospital of South Manchester NHS Foundation Trust
Subsection	Surgical Oncology
Consider for	Poster & Oral

Contents

Background

Breast reconstruction is recommended for women undergoing therapeutic or prophylactic mastectomy1. While the conventional approach of sub-pectparallel presentation implant-based breast reconstruction confers good cosmesis, pectparallel presentationis muscle detachment is associated with some potential disadvantages, including post-operative pain, disruption of muscle function and animation deformity. The development of acellular dermal matrices (ADMs) has facilitated implant-based breast reconstruction.

Aims

Our aim was to assess the feasibility of the novel technique of pre-pectparallel presentation implant-based breast reconstruction with total ADM cover.

Methods

This approach was adopted in 68 patients (100 breasts) between June 2013 and June 2016. The cohort included patients undergoing immediate and delayed breast reconstruction as well as those requiring revision breast reconstruction. Patient demographics, surgical complications and outcomes were analysed.

Results

Minor and major complications occurred in fourteen breasts (14%), including seroma in six, skin necrosis and cellulitis in two, and delayed wound healing, rippling, wound dehiscence, and stitch abscess in one breast. No patient required more than a one-night inpatient stay with no delays to adjuvant treatment. To date, patient satisfaction and cosmetic outcomes have been excellent.

Discussion

The use of ADM in breast reconstruction allows immediate breast reconstruction with accurate implant positioning without compromising the pectparallel presentationis muscle. This has psychological benefits in terms of preservation of body image and less stress in the post-operative period2.

Conclusion

This novel technique offers an adequate cosmetic outcome for patients wanting a quick recovery without potential compromise of pectparallel presentation muscle function. Whilst our cohort showed promising initial results, longer-term outcomes and studies are awaited.

References

1. Sbitany, H., Sandeen, S.N., Amalfi, A.N., Davenport, M.S. and Langstein, H.N., 2009. Acellular dermis–assisted prosthetic breast reconstruction versus complete submuscular coverage: A head-to-head comparison of outcomes.Plastic and reconstructive surgery, 124(6), pp.1735-1740.

2. Salzberg, C.A., 2006. Nonexpansive immediate breast reconstruction using human acellular tissue matrix graft (AlloDerm). Annals of plastic surgery,57(1), pp.1-5.

Application No. **ABSTR022**
Title Chemotherapy-Induced Peripheral Neuropathy: Incidence and Effect on Quality of Life
Presenting Author Jianlin Cheney Wong, University of Manchester
Subsection Clinical Oncology
Consider for Poster & Oral

Contents

Background: Due to advancements in cancer treatment and higher survival rates, chemotherapy-induced peripheral neuropathy (CIPN) has become an increasingly important side effect. CIPN mainly affects sensory nerves, resulting in neuropathic symptoms that can negatively impact quality of life (QoL).

Aims: To investigate the incidence of CIPN in patients receiving neurotoxic drugs and the impact of neurotoxicity on QoL.

Methods: Thirty-eight patients receiving treatment with either carboplatin, cisplatin, paclitaxel or docetaxel were enrolled into this prospective observational study. Neurotoxicity was evaluated using the NCI-CTC neuropathy score while the impact of CIPN on QoL was assessed using the EORTC QLQ-C30, EORTC QLQ-CIPN20, FACT-G and FACT/GOG-Ntx questionnaires. CIPN and QoL assessments were performed at baseline and at every subsequent chemotherapy cycle.

Results: CIPN presented as a predominantly sensory neuropathy. Eighteen patients developed CIPN over a median of 4 chemotherapy cycles. FACT-G and FACT/GOG-Ntx assessments demonstrated CIPN to have a negative impact on QoL, especially on the domains of physical, social/family and functional well-being.

Discussion: As the incidence of CIPN and its negative impact on QoL has been shown to be significant, CIPN and QoL assessments should be incorporated into routine cancer care. This is especially important since clinical decision-making regarding chemotherapy is based on a fine balance between the benefits and side effects of treatment.

Conclusions: CIPN is a common side effect that negatively impacts QoL. As such, evaluation of CIPN and QoL should be integrated into cancer management so as to improve clinical outcomes and QoL.

Application No.	**ABSTR023**
Title	How stringently can endometrial hyperplasia management guidelines be followed whilst retaining patient autonomy?
Presenting Author	James Ashcroft, University of Manchester
Other Authors	Ghada Mohiyddeen
Subsection	Surgical Oncology
Consider for	

Contents

Background: Endometrial cancer is the most common gynaecological malignancy in the UK. Endometrial hyperplasia is an irregular proliferation of endometrial glands which presents as irregular menstrual/postmenopausal bleeding with or without polyp involvement. Endometrial hyperplasia with atypia can progress to endometrial cancer whilst hyperplasia without atypia is not considered premalignant.

Aims: This audit aimed to investigate outcomes of the Lancashire Teaching Hospital NHS Foundation Trust's management of endometrial hyperplasia in premenopausal and postmenopausal patients compared to the Royal College of Obstetricians and Gynaecologist's management of endometrial hyperplasia guideline (February 2016).

Methods: 68 patients diagnosed with endometrial hyperplasia were audited. 19 were premenopausal (13 without atypia, 6 with atypia) and 49 were postmenopausal (18 without atypia, 31 with atypia). 55 patients had polyp involvement.

Results: 71.0% of patients without atypia, 63.3% of patients with atypia and 94.5% of patients with polyp involvement were managed correctly. Incorrect management in those without atypia was due to patient choice with regards to management and incomplete treatment length prescriptions. Incorrect management in those with atypia was due to refusal of surgery, surgical technical difficulty and inappropriate medical management.

Discussion: Autonomy must be respected in patient management especially when recommended treatments influence wellbeing and fertility. Surgical operations may be unsuitable for those at high risk and preferable for others at low risk.

Conclusions: This audit has found results which fall short of current management guidelines. Local guidelines should ensure correct treatment lengths are prescribed and that medical management is not a routine first line treatment of atypia.

References

No, RCOG Green Top Guideline, 2016. 67. Management of Endometrial Hyperplasia. London (UK).

Application No.	**ABSTR024**
Title	Retrospective Analysis of Sperm Banking for Oncology Patients
Presenting Author	Lisa Jachertz, University of Manchester
Other Authors	Natalie Croghan, University of Manchester
Subsection	Medical Oncology/Haematology
Consider for	Poster & Oral

Contents

Background

The combination of increased cancer incidence and increased survival has shifted the focus of cancer treatment from survival alone to survival and post-treatment quality of life. Ability to father a family is a concern amongst oncology patients and sperm banking is essential to preserve fertility against gonadotoxic treatments.

Aims

To identify: referral patterns of oncology patients to St Mary's, effects of cancer on sperm quality, sample usage rate, sample disposal rate and long term outcomes from sample use.

Methods

The database was analysed retrospectively, and information was compiled into a suitable excel spreadsheet.

Results

From 1976 to 2016 4,341 men between the ages of 12 and 67 were referred with cancer, of these 4,194 attended and 3,756 successfully banked a sample. 20% of men that could need sperm banking in the North West of England were referred. Referral rates are increasing year on year. Testicular cancer was the most common referral. Sperm concentration was significantly lower in testicular cancer. Usage rate was 9.7% and disposal rate was 9.5%. 75% of samples are still in storage. Most disposals and usages occurred within 5 years of banking.

Conclusion

Referrals for sperm banking are low - further work with oncologists is needed to increase this. Testicular cancer is the most common referral and most likely to have abnormal sperm quality before treatment. Measures to increase disposal, or usage rates should be implemented. Inviting patients for semen analysis at 5 years after banking may help them make a decision regarding their banked sperm.

Application No.	**ABSTR025**
Title	Mortality within 30 days following systemic anti-cancer therapy in patients with a diagnosis of a Hepatopancreaticobiliary (HPB) or Neuroendocrine (NET) Malignancy – A Single Centre Experience
Presenting Author	Anthony Beard, University of Manchester
Other Authors	Antony McGurk, Angela Lamarca, Jurjees Hasan, Wasat Mansoor, Richard A Hubner, Juan W Valle and Mairéad G McNamara
Subsection	Medical Oncology/Haematology
Consider for	Poster & Oral

Contents

Background: In 2015, The Christie published a report of 30-day mortality after treatment with systemic anti-cancer therapy (SACT) in response to benchmarks set out by the National Confidential Enquiry into Patient Outcomes and Death (NCEPOD).

Aims: The number of treatment-related deaths within 30-days following SACT in HPB/NET malignancies was audited.

Methods: Electronic records of patients who died within 30 days of starting a cycle of SACT from 2009-2015 were assessed retrospectively to determine: (1) number of SACT-related deaths, (2) clinical characteristics, (3) causes of death and (4) standard of care received using NCEPOD benchmarks.

Results: Within this period, 48,421 received SACT; 1853 died (4%) within 30 days. Of these, 101 (5%) were treated for HPB/NET malignancies (98 [97%] in advanced setting); majority (67%) had pancreatic cancer; median age was 65 years (range 39-85). Eastern Co-operative Oncology Group Performance Score (PS) was not systematically recorded throughout treatment, but was available initially; 0 for 21 patients, 1 for 47, 2 for 27 and 3 for six. Decision to treat was deemed appropriate in 95%. Standard-of-care received preceding death was available in 99/101 patients; 80% received “good care”, 18% had “insufficient information”. Three deaths in HPB/NET patients (3%) were SACT-attributable; one “definitely”, two “probably”. One patient received adjuvant treatment, two palliative chemotherapy and received “good care” prior to death.

Discussion/Conclusion: Percentage of patients with a HPB/NET diagnosis dying within 30 days of SACT was low and standard-of-care was appropriate antecedent to death. Information regarding PS was incomplete; thorough documentation of PS is recommended.

Application No.	**ABSTR026**
Title	Radiation Therapy Treatment Planning of Prostate Cancer using Automatic Contouring and Magnetic Resonance Imaging
Presenting Author	Andrew Chia, University of Manchester
Other Authors	Dr Alan McWilliam, Dr Lucy Kershaw, Professor Marcel Van Herk and Dr Ananya Choudhury, The Christie NHS Foundation Trust
Subsection	Clinical Oncology
Consider for	Poster & Oral

Contents

Background - Treatment planning for prostate cancer radiotherapy (RT) uses imaging to calculate a tumoricidal radiation dose to the prostate. Accurate RT planning limits toxicity to surrounding structures, such as the bladder and rectum. Current treatment planning involves a computed tomography (CT) planning scan, on which clinicians delineate pelvic organs manually, generating contours.

Aims – To investigate alternative methods of RT planning. Comparing the use of magnetic resonance imaging (MRI) with existing CT imaging. Analysing the accuracy of contours automatically generated by computer software using atlas data from different patients (inter-patient contouring) and the same patient (intra-patient contouring).

Methods - MRI images of 15 patients undergoing radical RT for prostate cancer were manually contoured for comparison purposes. Automatic-contours were propagated using ADMIRE atlas-based auto-segmentation software for inter-patient data. Intra-patient data was generated for second-visit MRI scans of 6 patients. Structure delineation performed by 5 clinicians was compared between MRI and CT images for 3 patients.

Results - Visual evaluation of automatic-contours revealed inaccuracies for bladder, rectum and superior and inferior poles of prostate for inter-patient and intra-patient data. Intra-patient prostate contouring was superior (DICE 0.830 vs 0.767). No significant difference was observed for clinician contour variation (inter-observer variation) between MRI and CT imaging.

Discussion and Conclusions – Supplementary manual editing by clinicians would be required for automatic-contouring using atlas-based propagation to generate feasible treatment planning contours. MRI provided improved contour accuracy of the superior and inferior prostate. Further studies with additional clinician contours may display benefits for MRI use in treatment planning.

Application No.	**ABSTR027**
Title	Predicting fertility in children with cancer: Is AMH the missing link?
Presenting Author	Rebecca Luckett, University of Sheffield
Other Authors	WH Wallace and TW Kelsey
Subsection	Paediatric Oncology
Consider for	

Contents

Background: Whilst the five-year survival rates of children with cancer continue to improve, research in the adverse long term effects, such as premature ovarian insufficiency (POI), is deficient. Current markers of ovarian reserve, follicle stimulating hormone (FSH), anti-Müllerian hormone (AMH) and antral follicle count (AFC), show predictive capacity in assessing time until menopause and thus risk of POI, but have not been fully investigated. This ability to accurately predict the risk of POI would lead to more appropriate clinical counselling with increased awareness of interventions.

Aims: To compare data on the aforementioned ovarian reserve markers, and use this information to create a preliminary quantitative model to assess time until menopause and hence, risk of POI.

Methods: A review of the literature was conducted; using this data and values from Hansen et al in 2012, a preliminary quantitative model to predict time until menopause was created.

Results: AMH shows the greatest relative importance to predict ovarian reserve, however is of ultimate use in conjunction with antral follicle count. The multiclass AUC for the preliminary quantitative model using AMH and AFC was 95%.

Discussion: The data used in the study was based upon the normal population, leading to an incongruence when to applying to childhood cancer survivors, it illustrated the potential role of AMH to assess ovarian reserve and thus determine risk of POI.

Conclusions: AMH appears to be the greatest marker to assess risk of premature ovarian insufficiency, therefore shows the greatest need for further investigation to assess its clinical use.

Reference:

Hansen, K.R., Craig, L.B., Zavy, M.T., Klein, N.A. and Soules, M.R., 2012. Ovarian primordial and non-growing follicle counts according to the Stages of Reproductive Aging Workshop (STRAW) staging system. Menopause (New York, NY), 19(2), p.164.

Application No.	**ABSTR028**
Title	Outcomes following second-line chemotherapy for patients with advanced pancreatic adenocarcinoma: A single centre experience
Presenting Author	Katie Connors, University of Manchester
Other Authors	Christina Rigby, Rob Morgan, Richard Hubner, Juan Valle and Mairéad McNamara, The Christie
Subsection	Medical Oncology/Haematology
Consider for	Poster & Oral

Contents

Introduction: The prognosis for patients with pancreatic adenocarcinoma is poor and only 15-20% of patients are suitable for potentially-curative surgery at time of diagnosis. In advanced disease, gemcitabine +/- nab-paclitaxel or 5-fluorouracil (5-FU)-based triple combination chemotherapy are first-line options. For patients progressing on first-line treatment, there are few accepted second-line chemotherapy options; median overall survival (OS) of approximately 6 months.

Aims: To assess progression-free (PFS) and OS in patients with inoperable pancreatic adenocarcinoma who received second-line chemotherapy at The Christie NHS Foundation Trust and compare outcomes to historical controls.

Methods: Case notes of consecutive patients with advanced pancreas cancer receiving second-line chemotherapy treated from January 2012-April 2016 were reviewed retrospectively. Reasons why patients did not receive second-line treatment were documented. The Kaplan-Meier method was used to determine survival outcomes.

Results: One-hundred and ninety-five patients of 414 seen (47%) received first-line chemotherapy. Thirty-five patients (15%) received second-line chemotherapy; these patients had a median age of 62 years (range 46-78), 54% were female and 97% had an Eastern Cooperative Oncology Group Performance Score (PS) of 0-1. The most common reasons for non-receipt of second-line chemotherapy were patient death (33%) and poor PS (31%). The median OS from starting second-line treatment was 7.4 months (95%-Confidence Interval 5.5-10); 5.7 months, 6.9 months and 11.5 months for those receiving Oxaliplatin/5-FU (N=15), Gemcitabine (N=7) and Gemcitabine/Capecitabine (N=6) respectively.

Discussion/conclusion: Few patients with pancreatic adenocarcinoma were fit enough to receive second-line chemotherapy. Survival outcomes in those receiving second-line chemotherapy at The Christie were comparable to historical data.

Application No.	**ABSTR029**
Title	Evaluating Foscan® mediated photodynamic therapy in 2D and 3D colorectal cancer models
Presenting Author	Drew Goodchild, University of Leeds
Other Authors	Thomas Maisey, Sarah Perry, Mohammed Ibrahim Khot and David Jayne, Leeds Institute of Biomedical & Clinical Sciences (LIBACS)
Subsection	Surgical Oncology
Consider for	Poster

Contents

Background: Colorectal cancer (CRC) is a major cause of death worldwide, with current therapeutic interventions offering limited success in treatment. Photodynamic therapy (PDT) is a promising alternative strategy that involves light mediated activation of a photosensitising agent, such as the second-generation photosensitiser Foscan; resulting in phototoxic cell death. Simple in-vitro tumour models play vital roles in facilitating this research.

Aims: Assess the cytotoxic effect of Foscan-PDT in CRC cell lines and to investigate differences in Foscan-PDT between 2D and 3D in-vitro culture platforms.

Methods: Foscan-PDT was assessed in 2D monolayer (HT-29, SW-480) and 3D spheroid (HT-29) models of CRC. A light dose of 1J/cm2 was administered and cytotoxicity in monolayers was determined, using a dye exclusion based viability assay. Qualitative images were taken of spheroids.

Results: Significant light and Foscan® dependant relationships were observed in HT-29 and SW-480 monolayers: (p=0.004) and (p=0.003) respectively. In 2D, HT-29 demonstrated greater resistance than SW-480. In 3D, the effects of PDT were only observed at the highest concentration of Foscan®

Discussion: Foscan-PDT might offer advantages to conventional chemotherapy in the treatment of CRC. Different cell responses were observed between cell lines and culture models, with spheroids bring more resistant to PDT than 2D cultures. This indicates that the 3D structure and physiological gradients influence response to treatment, highlighting the importance of effective pre-clinical models for clinical translation.

Conclusions: Foscan-PDT induces cytotoxicity in 2D and 3D CRC cultures. 3D multicellular spheroids appear more resistant than 2D cultures.

Application No.	**ABSTR031**
Title	Investigating the Impact of Small Molecule Inhibitors on Anti-CD20 Monoclonal Antibody Therapy in B-Cell Malignancies
Presenting Author	Victoria Stokes, University of Manchester
Other Authors	Eleanor Cheadle and Tim Illidge, Paterson Institute
Subsection	Medical Oncology/Haematology
Consider for	Poster & Oral

Contents

Background: The introduction of anti-CD20 monoclonal antibodies revolutionised the treatment of B-cell malignancies. Despite promising results, patients still relapse and many gain resistance to therapy. Research is now focused on enhancing their efficacy. Therapies such as farnesyltransferase inhibitors (FTIs) up-regulate CD20 expression on B-cells are predicted to synergistically enhance anti-CD20 monoclonal antibody mechanisms of cell death.

Aims: This study aimed to further investigate the effect of FTIs (L-744,832) on anti-CD20 monoclonal antibody induced cell death.

Method: The effect of L-744,832 on CD20 expression in vitro on Raji and Daudi cells at 24 hours was investigated. Pre-treated tumour cells and/or neutrophils were cultured together for 4 hours to assess if L-744,832 enhances anti-CD20 monoclonal antibody mediated antibody-dependent cellular phagocytosis.

Results: L-744,832 pre-treatment of tumour cells and/or neutrophils did not enhance anti-CD20 monoclonal antibody dependent phagocytosis. L-744,832 did not activate neutrophils. L-744,832 treatment produced a reduction in tumour cell number, with preliminary data suggesting L-744,832 has an anti-proliferative role on tumour cells.

Discussion: Further preliminary data suggests L-744,832 was not able to up-regulate CD20 expression in B-chronic lymphoblastic leukaemia cells, and recent studies suggest this may be due to an insufficiency in PU.1. Macrophages are another effector cell that induce phagocytosis and should be investigated as a potential mediator.

Conclusion: L-744,832 does not act via neutrophils. Future work should analyse other mechanisms of anti-CD20 monoclonal antibody cell death in vitro and in vivo and further explore the effect of FTIs on CD20 expression and cell death in other B-cell malignancies.

Application No.	**ABSTR032**
Title	Development of a prognostic index to predict tolerance to chemotoxicity in the treatment of Breast Cancer
Presenting Author	Talvinder Bhogal, University of Manchester
Other Authors	Dr. Lisa Barraclough, The Christie Hospital
Subsection	Clinical Oncology
Consider for	Poster & Oral

Contents

Background: One in eight women will be diagnosed with Breast Cancer during their lifetime. The majority of these patients will undergo adjuvant chemotherapy. In some patients, this is fraught with severe and life-threatening side-effects.

It has been shown that in assessing certain variables it may be possible to highlight those susceptible to severe chemotoxicity. If correctly identified these patients may be offered a reduced chemotherapy-dose to optimise safety. Current practice deploys a very subject method in which age and a few other factors are quickly assessed in the clinician's mind. It is therefore vital that a concrete scoring system is developed provides accurate guidelines.

Methods: Review of literature identified two scoring systems that have been developed in prognosticating chemotherapy side-effects. With aid from these we produced our own tool; The Prognostic Index. Retrospective analysis of 100 breast cancer patients was conducted in order to test it.

Results: The Prognostic Index showed promise in assessing risk of chemotoxicity. We then analysed individual parameters and found that performance status, comorbidity and evidence of metastases strongly correlated to adverse events. Interestingly, age (extensively used in current protocol), was a poor marker of toxicity.

Discussion: We find that The Prognostic Index aids in pre-empting chemotoxicity. We have proven that it is possible to design a tool which can aid clinicians. Further prospective work on a large cohort is now required to increase the accuracy of this tool. In doing so we hope it will replace current practice which is deemed out-dated and inaccurate.

Application No. **ABSTR033**
Title Screening and managing brain metastases in NSCLC
Presenting Author Mariya Mehdi, University of Manchester
Other Authors Dr Margaret Harris, The Christie NHS Foundation Trust
Subsection
Consider for

Contents

Background: Over 30% of patients with non-small cell lung cancer (NSCLC) develop brain metastases during the course of their illness (Langley et al., 2013). Brain metastases signify poor prognosis measured in a matter of months even with optimal treatment. The NICE (2011) guidelines recommend considering a brain scan at diagnosis in those selected for curative treatment to allow aggressive management of brain metastases and prevent futile treatment to the lung.

Aims: To conduct an audit to see whether these NICE guidelines are being followed at the Christie. In addition, we wanted to identify which patients developed brain metastases, how brain metastases were diagnosed and treated, and also, the outcome of these patients, post-diagnosis.

Method: I carried out an audit using data from electronic patient records and the PACS system.

Results: 156 patients included. 9 patients out of 56 who were treated with curative intent had a brain scan at diagnosis, representing only 16% of patients who fulfilled the criteria. No intracranial metastases were diagnosed on screening. From the whole cohort audited, 17 patients developed brain metastases. All of these patients presented with either stage III or stage IV disease and 12 out of the 17 were adenocarcinomas. Median survival after diagnosis of brain metastases was 40 days.

Conclusion: The majority of patients undergoing curative treatment were not screened at diagnosis. Those diagnosed with brain metastases had brain scans after experiencing neurological symptoms. The recommendation is to screen patients who present with stage III disease and are receiving intensive curative treatment.

References

Langley, R.E., Stephens, R.J., Nankivell, M., Pugh, C., Moore, B., Navani, N., Wilson, P., Faivre-Finn, C., Barton, R., Parmar, M.K.B. and Mulvenna, P.M. (2013) ‘Interim data from the medical research council QUARTZ trial: Does whole brain Radiotherapy affect the survival and quality of life of patients with brain Metastases from non-small cell lung cancer?’, Clinical Oncology, 25(3), pp. e23–e30

National Institute for Health and Care Excellence (NICE), 2011. Lung cancer: diagnosis and management. NICE guideline CG121

Application No.	**ABSTR034**
Title	Adjuvant chemotherapy for breast cancer in Lancashire: current practice and patient experiences
Presenting Author	Philip Wright, University of Manchester
Other Authors	Elaine Young, Lancashire Teaching Hospitals
Subsection	Medical Oncology/Haematology
Consider for	Poster & Oral

Contents

BACKGROUND – Adjuvant chemotherapy is often an important component of breast cancer management, reducing the risk of disease recurrence following local treatment. A large number of drugs are available, in a growing number of combination regimens, with no single best or standard regimen agreed or identified. Within the Lancashire and South Cumbria Cancer Network, five regimens are routinely used, with local guidelines providing some guidance in selection.

AIMS – To audit current practice of adjuvant chemotherapy use within the network, focussing on choice of regimen and tolerance. To explore patient experiences of chemotherapy treatment, including any variation between regimens.

METHODS – Audit of 359 patients who commenced adjuvant chemotherapy in the twelve months prior to May 2016. 88 of these also completed questionnaires, describing the impact of treatment on their health and quality of life, and experiences of side-effects.

RESULTS – Significant variation in regimen selection between clinicians and treatment locations was identified. All questionnaire respondents reported impacts from chemotherapy on their health and quality of life, particularly on social and employment activity. There was no evidence of a superior regimen in terms of tolerability. Patient experiences suggest areas for improvement in the management of some side-effects.

DISCUSSION – Regimen selection may reflect clinicians' own interpretation of the evidence, or local population comorbidity. This data will be used to inform future local guidelines. Protocol changes could reduce the incidence and severity of side-effects for some patients. Treatment experiences provided by questionnaire respondents can be used to create information resources for future patients.

Application No.	**ABSTR036**
Title	Exploring the relationship between mutational class and clinical severity in Neurofibromatosis type 2 (NF2)
Presenting Author	Jonathan Wong, University of Manchester
Other Authors	Simon Freeman and Gareth Evans, Central Manchester Foundation Trust and Manchester NF2 Research Group
Subsection Consider for	Clinical Oncology

Contents

Background

Neurofibromatosis type 2 (NF2) is an autosomal dominant tumour predisposition syndrome that leads to the formation of multiple meningiomas, schwannomas and ependymomas along the cranio-spinal axis and hallmark feature of bilateral vestibular schwannomas (VS). It is inherited in half of patients and other half occur de novo. Previous studies have analysed severity with regard to meningioma count, mortality rates, and age at diagnosis and presenting symptoms.

Aim

To determine the relationship between genotype and clinical severity by looking at baseline age, cranial nerve schwannoma size and growth rates.

Method

MRI scans and data from patients registered with the Manchester NF2 centre were used in this study, dating back to 2006. Schwannomas that had treatment before baseline scans were excluded, and patients with 2 or more scans were used to calculate growth rate.

Results

153 patients met the inclusion criteria and 378 schwannomas were identified: 150 VSs, 93 Trigeminal nerve (CNV), 86 Lower cranial nerve complex (CN9-12), 9 Occulomotor nerve (CN3) and 2 Abducens nerve (CN6). 92 schwannomas were excluded: 89VSs, 1 CN5, 2 CN9-12 due to treatment prior to baseline scan. There was a strong correlation between genotype and genetic severity classification rt=.981, p=.001. Genetic severity was negatively correlated to age for VS, CN5 and CN9-12 schwannomas ($p<.001$), and positively correlated to baseline size and growth rate for VS and CN5 schwannomas ($p<.05$).

Conclusion

Genotype is an important factor influencing clinical severity of the NF2 condition. This was most significant seen in VS and CN5 schwannomas.

Application No.	**ABSTR037**
Title	Functional Outcomes of Salvage Surgery in Laryngeal and Hypopharyngeal Carcinoma
Presenting Author	Joshua Caplan, University of Manchester
Other Authors	Jarrod Homer, Manchester Royal Infirmary/University of Manchester and Rohit Verma, Manchester Royal Infirmary
Subsection	Surgical Oncology
Consider for	Poster & Oral

Contents

Aims – The aim of this study was to quantify the risk of adverse functional outcomes in patients undergoing salvage laryngectomy and pharyngolaryngectomy for the treatment of laryngeal and hypopharyngeal squamous cell carcinoma. This will also enable comparison of the risks and will show whether one type of surgery has more favourable outcomes than another. This will give centre specific information when consenting patients for surgery, and also aids in planning surgery.

Method – This was a cohort study of 46 patients who had undergone either a salvage total laryngectomy (TL), circumferential pharyngolaryngectomy (cPL), or partial pharyngolaryngectomy (pPL) over 14 years at Manchester Royal Infirmary (MRI). The data was collected using computerised and paper patient records and The Christie and MRI hospitals.

Results – There is significant risk of patients losing the ability to swallow solid food and also to lose their ability to communicate through speech. The risk of swallowing ($p=0.005$) and voice ($p=<0.001$) complications are variable depending on the type of operation. Fistula appears to play a significant role in increasing the risks of swallowing ($p=0.003$) and voice ($p=<0.001$) complications. Fistula formation also increases the length of hospital stay ($p=0.001$).

Conclusions – The risks of these surgical procedures are fistulation formation, increased hospital stay, swallowing and voice complications. These centre specific risks can now be quantified for patients. The outcomes of these procedures vary somewhat. The highest fistula rates occur in the cPL group. This association suggests that if oncologically possible a pPL will result in better functional outcomes than a cPL.

Application No.	**ABSTR038**
Title	Image Guided Adaptive Brachytherapy for Cervical Cancer: Impact of Dose and Size of High Risk Clinical Target Volume
Presenting Author	Chloe Sherrington, University of Manchester
Subsection	Clinical Oncology
Consider for	Oral

Contents

Background and Aims

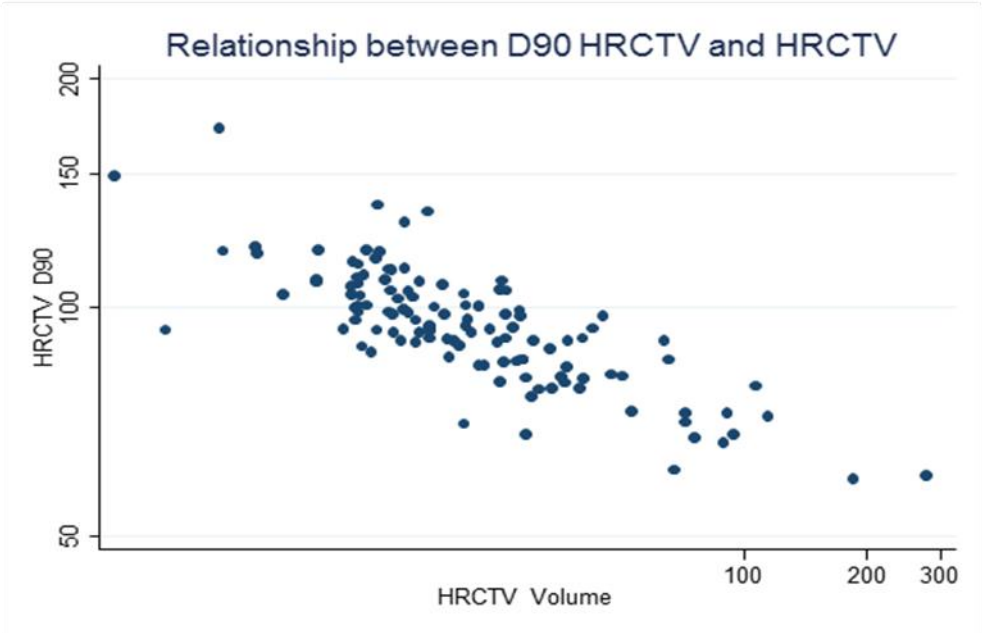
Brachytherapy is a well-recognised cervical cancer treatment. Evidence states effectiveness of this intervention is dependent on the (1) relationship between HRCTV and D90 HRCTV1, (2) rate of local control with respect to HRCTV2 and D90 HRCTV3, and (3) association between D2cc and toxicity to surrounding pelvic organs2. All three determinants will be assessed throughout this study.

Methods

147 patients that received brachytherapy for primary cervical cancer were identified. Patient parameters surrounding demographics, disease stage and treatment were noted. HRCTV, D90 HRCTV and D2cc to the bowel, rectum and bladder were outlined from IGABT treatment plans. CTCAE v4.0 grades of toxicity were recorded. Comparative variables were analysed using Stata® software. Follow up for local control was documented from initial consultation until death, disease recurrence or most recent outpatient appointment.

Results

A negative correlation was identified between HRCTV and D90 HRCTV. From 140 patients with recorded HRCTV values, a 10% local recurrence was observed. Four and ten patient recurrences had HRCTV values of ≥30cm3 and <30cm3, respectively. D90 HRCTV values from 122 patients highlighted that incidence of local recurrence occurred more frequently within individuals receiving ≥90Gy compared to <90Gy. Furthermore, a positive correlation was noted between increasing D2cc and severity of toxicity to pelvic organs.



Discussion

Predicted observations were confirmed regarding both dose-volume relationship and organ toxicity. Expectations that larger HRCTV and D90 HRCTV values result in increased and decreased disease recurrence, respectively were contradicted.

Conclusion

Advances in interstitial brachytherapy techniques intend to improve patient outcomes further.

Application No.	**ABSTR039**
Title	Bone Health and Tolerability of Aromatase Inhibitors as Adjuvant Treatment of Early Breast Cancer in Postmenopausal Women
Presenting Author	Bethan Thomas, University of Manchester
Other Authors	Elaine Young, Lancashire Teaching Hospitals Trust
Subsection	Medical Oncology/Haematology
Consider for	Poster & Oral

Contents

Background: Aromatase inhibitors (AIs) are used as adjuvant treatment in oestrogen-sensitive breast cancers. Recent evidence supports extending length of treatment from five years to ten years.[1] Guidelines are in place to reduce the risk of treatment-induced osteoporosis.[2]

Aims: This study aimed to evaluate the effect on quality of life caused by side effects of letrozole, as well as two-year outcomes of bone mineral density (BMD) monitoring within Lancashire Teaching Hospitals Trust (LTHTR).

Methods: Forty patients were interviewed using a structured questionnaire to explore their experiences of AIs. A retrospective audit was conducted to assess whether bone management guidelines were being followed.

Results: Eighty-three percent of patients reported experiencing side effects, with 5% rated severely. Although quality of life had been affected in 21% of patients, 89% would extend their treatment to 10 years, with high tolerability reported. Vitamin D deficiency and low BMD were found in 49% of patients checked at baseline. Vitamin D measurements were not carried out in 63% of patients already taking supplementation, despite deficiency being found in half of those checked. DEXA scans were omitted in 9% of patients at baseline and 16% at follow-up. Low BMD was found in 48% of patients at follow-up.

Conclusions: The majority of patients would be happy to extend the length of their AI treatment. Bone health remained stable across the cohort over two years, presumably through appropriate use of lifestyle advice, Vitamin D supplementation, and bisphosphonates. Further staff and patient education could help improve compliance with guidelines to 100%.

References:

1) HSP News Service. (2016) ASCO 2016: 10 years of Aromatase inhibitor therapy reduces breast cancer recurrence without compromising quality of life in Postmenopausal patients - the ASCO post. Available at: http://www.ascopost.com/News/41622 (Accessed: 26 July 2016).

2) Greater Manchester, Lancashire & South Cumbria Strategic Clinical Network & Senate. (2014) Lancs & South Cumbria Breast NSSG Reference Manual for the Management of Breast Cancer.

Application No.	**ABSTR040**
Title	Serious Adverse Events (SAEs) in Phase I oncology trials within the Experimental Cancer Medicine Team (ECMT) at The Christie NHS Foundation Trust
Presenting Author	Marianna Christodoulou, Salford Royal NHS Foundation Trust
Other Authors	Shaun Villa, Carla Siswick, Matt Krebs, Natalie Cook, Fiona Thistlethwaite, Andrew Hughes, Sreeja Aruketty, Louise Carter, Jaseela Chiramel, Robert Metcalf, Alison White, Deborah Jowle, Victoria Sheard, Anisah Mehmood, Helen Shekelton, Rick Boton, Claire
Subsection	Medical Oncology/Haematology
Consider for	Poster & Oral

Contents

Background

SAEs in clinical trials can significantly impact patients' morbidity and mortality. In Phase I trials in healthy volunteers, SAE rates of less than 0.5% have been reported. SAE rates among Phase I oncology trials are poorly defined.

Aims

We aimed to identify the SAE rate in Phase I oncology trials within the ECMT.

Methods

SAEs occurring between 04/05/2014 and 08/03/2016 were identified and retrospectively interrogated using clinical trial site files, trial workbooks, case report forms and electronic patient records.

Results

Of 136 patients enrolled in 25 Phase I trials, 42 (30%) patients experienced an SAE (some experienced multiple SAEs). Overall, 68 SAEs were reported across 13 trials (no SAEs in 12 trials). Hospitalisation was the most frequent outcome reported in 93% of SAEs (each SAE may have multiple outcomes) with no deaths reported. Most SAEs (42%) were defined as Grade 2, 38% Grade 3, 13% Grade 1 and 8% Grade 4 as per the Common Terminology Criteria for AEs. Causes of SAE were investigational medicinal product (IMP)-related, disease-related and unrelated to IMP/disease (38%, 31% and 31% respectively). The average SAE duration was 5.5 days. Following the SAE, the IMP was continued on the same dose in 43% of cases followed by interruption, dose reduction and discontinuation in 21%, 4% and 25% of cases respectively.

Discussion

SAEs were more prevalent in patients on Phase I oncology trials compared to healthy volunteers.

Conclusions

There is need for active SAE monitoring in Phase I oncology trials and subsequently an 'SAE tracker' has been established within the ECMT.

Application No.	**ABSTR042**
Title	Characterising the early response to immunotherapy in the CT26 murine cancer model
Presenting Author	David Prossor, University of Southampton
Other Authors	Edd James, University of Southampton
Subsection	Translational Oncology/Basic Science
Consider for	Poster & Oral

Contents

Background

Cytotoxic T lymphocytes (CTLs) recognise and eliminate neoplastic cells, however, tumours are able to evade the immune response. One of these immune-evasion mechanisms involves regulatory T cells (Treg) which prevent protective anti-tumour CTL responses. Treg depletion in the CT26 mouse tumour model revealed the emergence of potent anti-tumour CTL, highlighting the importance of priming in this response (James et al., 2010). In addition, checkpoint inhibition immunotherapy induces protective anti-tumour responses in ~30% of mice. Why immunotherapy only works in a minority of mice is unknown, but it is likely to alter the anti-tumour T cell repertoire.

Aims

1) To investigate whether tumour cells migrate to draining lymph nodes

2) To characterise the effects of immunotherapy on anti-tumour T cell repertoires

Methods

PCR techniques were used to detect cancer specific genome changes in tumour challenged draining lymph nodes. The Vβ composition of tumour antigen GSW11-specific TCRs were analysed by flow cytometry at different time points in anti-PD1 treated and control tumour challenged mice.

Results

Tumour cells were detected in draining lymph nodes of challenged mice. Anti-PD1 treated mice show a much more diverse TCR repertoire with more oligoclonal expansion compared to the control group.

Discussion and conclusions

These findings support recent studies that suggest tumours restrict TCR repertoires and that immunotherapy acts to broaden the TCR composition to enhance antitumour potency (Luo et al., 2014, Jia et al., 2015). These changes may therefore allow the prediction of response signatures following immunotherapy.

References:

JAMES, E., YEH, A., KING, C., KORANGY, F., BAILEY, I., BOULANGER, D. S., VAN DEN EYNDE, B. J., MURRAY, N. & ELLIOTT, T. J. 2010. Differential suppression of tumor-specific CD8+ T cells by regulatory T cells. J Immunol, 185, 5048-55.

JIA, Q., ZHOU, J., CHEN, G., SHI, Y., YU, H., GUAN, P., LIN, R., JIANG, N., YU, P., LI, Q. J. & WAN, Y. 2015. Diversity index of mucosal resident T lymphocyte repertoire predicts clinical prognosis in gastric cancer. Oncoimmunology.

LUO, W., HE, W. T., WEN, Q., CHEN, S., WU, J., CHEN, X. P. & MA, L. 2014. Changes of TCR repertoire diversity in colorectal cancer after Erbitux (cetuximab) in combination with chemotherapy. Am J Cancer Res, 4, 924-33.

Application No.	**ABSTR043**
Title	Use of the Mirena Levonorgestrel-Releasing Intrauterine System (LNG-IUS) for Grade 1 Endometrial Carcinoma in Obese Women
Presenting Author	Teicia Ho, University of Dundee
Other Authors	Ian Sanders and Michelle Ferguson, Department of Oncology, Ninewells Hospital and Medical School, Dundee
Subsection	Medical Oncology/Haematology
Consider for	Poster & Oral

Contents

Background:

Obesity, which multiples the risk of endometrial cancer (EC) by 5-fold1 contributes to the annual 1% incidence rise amongst young, premenopausal women2 who may decline the current standard and definitive intervention, total (laparoscopic) hysterectomy (TLH) ± bilateral salpingo-oophrectomy (BSO). Furthermore, obesity and its associated co-morbidities complicate the feasibility of TLH–BSO. Presently, the Mirena levonorgestrel-releasing intrauterine system (LNG-IUS) is an off-license non-surgical, fertility-sparing alternative, but robust data demonstrating its efficacy and place in treatment is lacking.

Aim:

To assess LNG-IUS performance in terms of disease control, patient experience, and cost-effectiveness in women with Grade 1 EC and BMI ≥30 km/m2.

Methods:

Clinical and histopathological progress of obese women diagnosed with Grade 1 EC who were primarily treated using LNG-IUS at our centre from 2013–2016 were retrospectively analysed. Women unsuitable for LNG-IUS or who underwent radical surgery ± adjuvant therapy for endometrial disease were excluded.

Results:

Symptoms, regardless of histological features, persisted in 67 of 143 (46.85%, 95% CI, 45-48%) person-months of follow-up (range 2-35 months). Of eight women, two achieved histological and symptom remission. Half the cohort ultimately received additional progesterone or TLH–BSO despite initial contraindications.

Discussion:

Abandonment of examination secondary to patients' physique and inconsistent institutional monitoring in the absence of recognised protocol compromises optimal management. New guidelines recommend regular surveillance until hysterectomy is performed.3

Conclusion:

Response to LNG-IUS was variable and unpredictable. Despite symptom relief and/or histological regression in certain women, radical surgery remains first-line.

Lacking long term outcomes limit calculation of cost-effectiveness versus hysterectomy.

References:

1. Fader A., Arriba H., Frasure H. et al. 2009. Endometrial cancer and obesity: Epidemiology, biomarkers, prevention, and survivorship. Gynaecology Oncology, 114(1), pp. 121-127.

2. Baker J., Obermair A., Gebeski V., Janda M. 2012. Efficacy of parallel presentation or intrauterine device-delivered progestin in patients with complex endometrial hyperplasia with atypia or early endometrial adenocarcinoma: A meta-analysis and systematic review of the literature. Gynaecology Oncology, 125(1), pp. 263-270.

3. Royal College of Obstetricians and Gynaecologists, 2016. Green-top Guideline No. 67: Management of Endometrial Hyperplasia. London: Royal College of Obstetricians and Gynaecologists.

Application No. **ABSTR044**
Title Audit in management of neutropenic sepsis: Reducing the door to needle time in giving antibiotics within one hour of presentation using a clinical proforma

Presenting Author Hanis Hanafi, Aberdeen Royal Infirmary
Subsection Medical Oncology/Haematology
Consider for Poster & Oral

Contents

Background

Neutropenic sepsis is a potentially fatal complication of chemotherapy requiring treatment with intravenous antibiotics. Recovery is dependent on prompt treatment as delay in giving treatment can result in septic shock and potentially death. NICE Guidelines recommend door to needle time for first dose of antibiotics within one hour of presentation.

Aim

To investigate the compliance in giving antibiotics within one hour of presentation to patients in Aberdeen Royal Infirmary with suspected neutropenic sepsis and the effectiveness of reducing door to needle time for antibiotics using a clinical proforma.

Method

Case notes of 60 patients presenting to the acute medical ward with suspected neutropenic sepsis were assessed over two month period. Patient arrival time and time of antibiotics given were documented. The same data were then collected prospectively over another two month period after the clinical proforma was implemented.

Results

Initially only 30% of suspected neutropenic patients received IV antibiotics within one hour of presentation. Results showed that 95% of suspected neutropenic patients received IV antibiotics within one hour of presentation after the clinical proforma has been implemented.

Discussion

It is well known that expeditious use of antibiotics in patients with suspected neutropenic sepsis has reduced mortality and morbidity rates. The changes implemented from the clinical proforma have resulted in a positive outcome for patients with a reduction in morbidity and mortality from neutropenic sepsis through the use of a dedicated clinical proforma.

Conclusion

Implementation of a clinical proforma has resulted in reduction in morbidity and mortality from neutropenic sepsis.

Application No.	**ABSTR045**
Title	Childhood cancer survivorship: an exploration of awareness and information needs among healthcare professionals in primary and secondary care in the United Kingdom
Presenting Author	Victoria Wilson, University of Bristol
Other Authors	Rachel Cox and Rachel Dommett, Bristol Royal Hospital for Children
Subsection	Paediatric Oncology
Consider for	Poster & Oral

Contents

Background/Aims

The incidence rate of childhood cancer, coupled with the concept of increased survival, has established an ageing population who are a specific at-risk group. This group is susceptible to a range of late effects requiring specialised healthcare.

Late effects are somewhat unknown outside the paediatric oncology setting.

Raised clinical suspicion and awareness regarding late effects amongst all healthcare professionals would ideally enable efficient monitoring and recognition of complications.

Methods

Recent case histories, where professionals failed to recognise links between the current problem and past childhood cancer treatment, were examined.

Questionnaires to both primary and secondary care practitioners were used to ascertain individuals' experience and understanding of late effects and how they would seek further information.

Results

In primary care all practitioners had experience of caring for childhood cancer survivors, compared to 17% in the secondary care study. Only one practitioner in secondary care was able to correctly identify recurrence or progression as the leading cause of mortality amongst survivors. 71% of respondents noted that survivors may face risks of recurrence, yet consensus regarding any other late effects varied (Cardiac 35%, Respiratory 17%, Infertility 29%).

Discussion/Conclusion

The necessity and potential to improve patient care by increasing awareness of late effects has been identified by this initial study.

A mnemonic known as CE-RISK has been developed with each letter representing a late effect-

C-cardiovascular

E-endocrine

R-relapse or secondary neoplasm

I-infertility

S-syndromes-metabolic

K-kidney function

Further work aims to co-create patient held alerts using CE-RISK that health professionals would also find beneficial.

Application No. **ABSTR046**
Title Using communication experiences of teenage and young adult cancer patients in order to shape undergraduate medical education communication skills teaching
Presenting Author James Adams, University of Manchester
Other Authors Sarah Shepherd, University of Manchester
Subsection Clinical Oncology
Consider for Poster & Oral

Contents

Background: Every day 7 teenagers and young adults (TYA's), between the ages of 16-24 are diagnosed with cancer. Many of them present to GP's or A+E departments which are unaccustomed to dealing with young cancer patients, and it is common for them to have poor communication experiences from medical professionals.

Aims: To take the experiences of TYA who have received a cancer diagnosis and combine them in order to create materials that can be used to improve communication skills of the next generation of doctors.

Methods: Following a literature review, patients were interviewed using a specifically designed interview schedule. Two assessors then collated the interviews and analysed the key themes which emerged. These themes, along with quotations were taken and used to form a document, written in first person, aimed at providing guidance to all professionals.

Discussion: It was that many patients had experience of poor communication from professionals. A European study of over 300 patients (1) showed TYA's endorsed communication research as their 2nd highest priority in cancer care. Evidence from another large study (2), suggests that medical professionals who receive communication skills training based on patient experience and preference are better able to meet patients' needs vs. those who don't.

Conclusion: There is a very clear need to improve communications teaching within the medical profession. Evidence suggests basing material on patient experience improves doctor's abilities to meet patient needs. Therefore, documents like those created by this study should be used in the context of undergraduate medical education.

References

(1) Jones LJ, Pini SA, Morgan SJ, Birk GK, Stark DP. How do teenagers and young adults with cancer experience their care? A European survey. J Adolesc Young Adult Oncology. 2016. PMID: 27314907.

(2) Fuljimori M, Shirai Y, Asai M, Kubota K, Katsumata N, Uchitomi Y. Effect of communication skills training program for oncologists based on patient preferences for communication when receiving bad news; a randomised control trial. Journal clinical oncology. 2014. 32(20):2166-72. PMID: 24912901

Application No.	**ABSTR048**
Title	Investigations into the Role of the Fanconi Anaemia FANCD2 L153S Gene Mutation in Leukaemogenesis
Presenting Author	Talya Sumray, University of Manchester
Other Authors	Roberto Paredes and Stefan Meyer, University of Manchester
Subsection	Translational Oncology/Basic Science
Consider for	Poster & Oral

Contents

Background: Fanconi Anaemia (FA) is a rare inherited condition associated with congenital and developmental abnormalities. FA confers an extreme risk for the development of acute myeloid leukaemia, however a few cases of T-cell lymphoblastic leukaemia have also been associated with FA. Two of these are associated with mutations in FANCD2, which included the L153S mutation in both cases.

Aim: This project aimed to investigate aspects of a possible role of the L153S mutated FANCD2 protein in the development of T-cell leukaemia.

Methods: Effects of the L153S mutation on the FANCD2 protein was analysed in silico and experimentally. Patient-derived cells with the mutated and wildtype cells were cultured with and without MMC-induced DNA damage and analysed for FANCD2 by immunofluorescence and Western blot on cell lysates and after immunoprecipitation.

Results: In silico analysis predicted a strong destabilising effect of the L153S mutation on the FANCD2 structure. By immunofluorescence, FANCD2 was detected in L153S mutated cells, but not by Western Blot. Detection of FANCD2 in wildtype cells may be improved by immunoprecipitation.

Discussion: The L153S mutation of FANCD2 may have a destabilising effect on the protein. Discrepancy between FANCD2 signals by Western Blot and immunofluorescence could result from low levels of mutated protein below detection levels by Western blot. Further optimisation of the immunoprecipitation is needed before it can be used in mutated cells to increase the signal of FANCD2, and together with immunofluorescence might allow specific investigation of the L153S mutated protein for haematopoietic lineage commitment and T-cell leukaemogenesis.

Application No.	**ABSTR049**
Title	Defining incidence and use of radiotherapy in bulk disease in Diffuse Large B-cell Lymphoma
Presenting Author	Simon Gray, University of Manchester
Other Authors	Ben Taylor, Richard Cowan, Maggie Harris, Kim Linton, John Radford, Ed Smith and Tim Illidge, The Christie
Subsection	Medical Oncology/Haematology
Consider for	Poster & Oral

Contents

Background

Diffuse large B-cell lymphoma (DLBCL) is an aggressive disease that represents 30-40% of new diagnoses of non-Hodgkin lymphoma. Large tumour bulk is a recognised adverse prognostic factor in DLBCL and has previously been recorded using an `X modifier` to clinical staging for maximum tumour diameter (MTD) ≥10cm, with a view to applying consolidation radiotherapy to sites of bulk. Significant evidence now commends consolidation radiotherapy to sites with MTD≥7.5cm.

Aims

We audited recording of bulk disease and proposal of radiotherapy at MDT, and assessed which patients subsequently received radiotherapy. Our audit standards were:

Only patients with MTD≥10cm should receive an X modifier at clinical staging.

Where an X modifier is given and radiotherapy not proposed, a discussion about the use of radiotherapy should be documented at MDT.

Methods

MDT outcomes forms were used to assess recording of bulk; all other data was collected using these forms alongside other patient records, including clinic letters and imaging results.

Results

68% of patients given an X modifier at had MTD≥10cm on pre-MDT scan; 8% had MTD<7.5cm. 93% of patients without X modifiers had MTD<7.5cm; 4% had MTD≥10cm. 64% of patients with X modifiers subsequently received radiotherapy.

Discussion and Conclusions

Current recording of bulk disease using the X modifier with MTD≥10cm does not reflect current literature; instead, MTD should be quantitatively recorded and all MTD≥7.5cm considered for radiotherapy. If bulk disease is documented, the current standard should be radiotherapy and if radiotherapy is not proposed, reasons for this should be recorded at the discussion.

Application No. **ABSTR050**
Title An audit of the management of vitamin D deficiency in children treated for acute lymphoblastic leukaemia
Presenting Author Jessica Farnan, University of Liverpool
Subsection Paediatric Oncology
Consider for Poster

Contents

Background

Acute lymphoblastic leukaemia (ALL) in paediatrics has a high cure rate; therefore particular care is taken in reducing long-term complications such as osteoporosis. Osteoporosis can negatively affect quality of life but its diagnosis is difficult in children. Vitamin D plays an important role in the maintenance of bone mineral density, with vitamin D deficiency contributing to the risk of osteoporosis (Haddy et al., 2001).

Aim

To assess the diagnosis and management of vitamin D deficiency in ALL patients at Alder Hey Children's Hospital, to provide recommendations for change based on current guidelines.

Method

A retrospective audit of patients included in the UKALL 2003 trial.

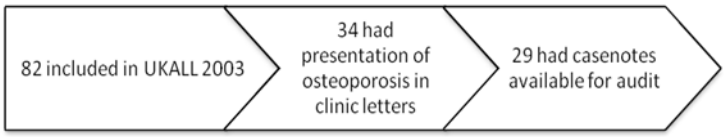


Figure 1 Selection of patients included in the audit

Standards are based on 'Interim guidelines for oncology patients with osteopenia/osteoporosis' set by Alder Hey's Oncology Department.

Results

Mean age at diagnosis of ALL was 8.1 years and the mean age at first presentation of osteoporosis was 11.1 years.

Figure 2 shows initial investigations.

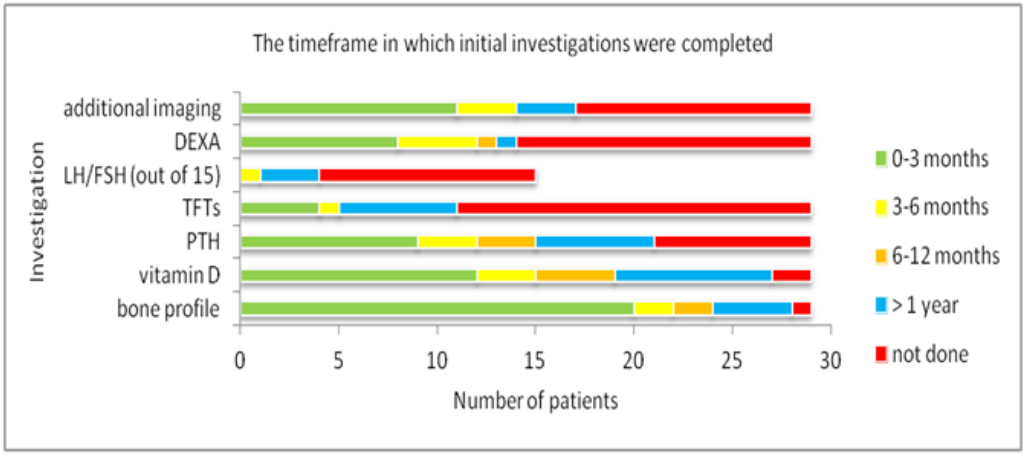


Figure 2 Graph showing the completion of initial investigations

27 patients (93.1%) had their vitamin D measured, results shown in figure 3.

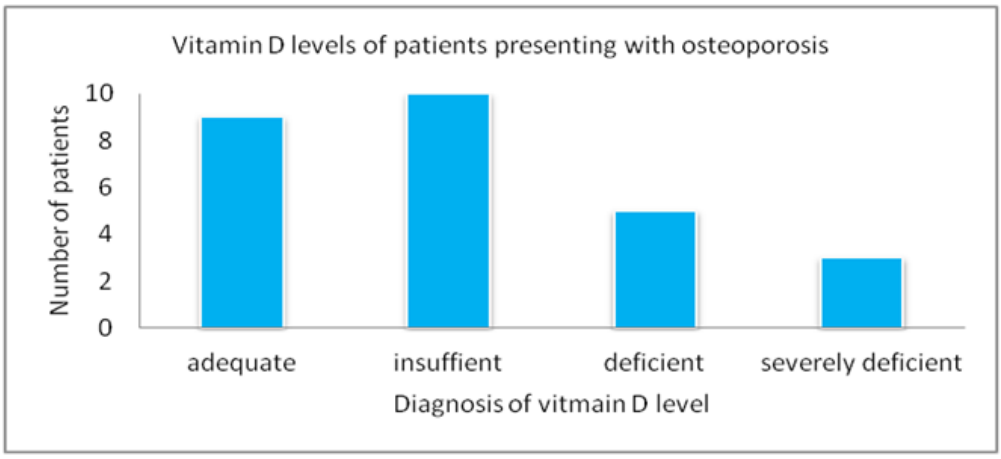


Figure 3 Graph showing results of vitamin levels

Of 18 patients with inadequate levels, 13 (72.2%) received replacement therapy – 9 (69.2%) with Ergocalciferol.

Discussion

Data shows inconsistencies in the investigation of osteoporosis and vitamin D deficiency, most evident in the measurement of TFTs and LH/FSH.

Replacement therapy was initiated in those with deficiency as per the guidelines.

Conclusion

Musculoskeletal pain can be a manifestation of ALL or a side effect of treatment so knowing when to investigate can be difficult (Riccio et al., 2013).

Measuring vitamin D routinely from diagnosis of ALL could allow identification and treatment of low levels to reduce the risk of deficiency and subsequent osteoporosis.

References

HADDY, T. B., MOSHER, R. B. & REAMAN, G. H. 2001. Osteoporosis in survivors of acute lymphoblastic leukemia. Oncologist, 6, 278-85.

RICCIO, I., MARCARELLI, M., DEL REGNO, N., FUSCO, C., DI MARTINO, M., SAVARESE, R., GUALDIERO, G., ORESTE, M., INDOLFI, C., PORPORA, G., ESPOSITO, M., CASALE, F. & RICCARDI, G. 2013. Musculoskeletal problems in pediatric acute leukemia. J Pediatr Orthop B, 22, 264-9.

Application No.	**ABSTR051**
Title	Breast Cancer in Myanmar: Exploring the Knowledge, Awareness and Sources of Information of a Group of Women in Hlaingthaya Township, Yangon
Presenting Author	Caroline Apsey, University of Leeds
Other Authors	Mahua Das, University of Leeds
Subsection	Public health, prevention & screening
Consider for	Oral

Contents

Background

Breast cancer is the most common form of cancer in women in Myanmar(1). Lack of awareness of breast cancer is resulting in late diagnosis and poor health outcomes (2, 3). Exploration of breast cancer awareness in women in Myanmar is necessary to make recommendations for how to improve health education thus improve health outcomes.

Aim

To explore the knowledge and awareness of breast cancer amongst a group of women in Hlaingthaya, Yangon and to explore their sources of health information in order to provide recommendations to improve existing health education services in Myanmar.

Method

Primary qualitative data was collected in June 2016 via semi-structured interviews with 10 women. Participants within the inclusion criteria were recruited and interviewed within their local area. Data was analysed using thematic coding.

Results

While there was awareness about the prevalence of breast cancer among women, there was little knowledge about the causes, symptoms, screening and treatment. Discussion with friends and TV programmes formed the core sources of health information.

Discussion

All women demonstrated an interest in greater education on breast cancer, specifically on prevention and screening using most popular methods such as education days and distribution of leaflets. These were deemed to be the most accessible, effective and cost-effective methods of health education.

Conclusion

This project offers an insight into awareness of breast cancer among women in Hlaingthaya Myanmar. The Ministry of Health must work with NGOs to provide community health education days to raise awareness about screening for breast cancer.

References

(1) World Health Organisation (2014). Cancer Country Profiles. [Online]. WHO. Available at: http://www.who.int/cancer/country-profiles/mmr_en.pdf [Accessed 02 Jul. 2016]

(2) World Health Organisation, (2007). Cancer Control knowledge into actions: early detection. [Online] WHO. Available at: http://www.who.int/cancer/modules/Early%20Detection%20Module%203.pdf [Accessed 07 Jul. 2016]

(3) Sein, T., Myint, P., Tin, N.,Win, H., Aye, S.S. and Sein, T. (2014). The Republic of the Union of Myanmar Health System Review. Health Systems in Transition. Volume 4(3) p. Not Available

Application No.	**ABSTR052**
Title	AZD1775 Kills Colorectal Cancer Cells Through Nucleotide Exhaustion and Double-Stranded DNA Breaks Independent of p53 Status
Presenting Author	Anna Littlejohns, University of Leeds
Other Authors	Peter Webster, University of Leeds, Dermot Burke, St. James's University Hospital and David Beech, University of Leeds
Subsection	Translational Oncology/Basic Science
Consider for	Poster & Oral

Contents

Background WEE1 is a protein kinase that regulates DNA synthesis through cyclin-dependent kinase 1 (CDK1) phosphorylation. AZD1775, a WEE1 inhibitor, has been shown to be an effective anticancer therapy in pre-clinical studies by impairing DNA synthesis through nucleotide exhaustion. However, there is limited evidence for its efficacy in colorectal cancer and the importance of p53 status is unclear.

Aims To determine the anticancer effects and mechanism of action of AZD1775 on two colorectal cancer cell lines with differing p53 status.

Methods HT29 (p53 mutated) and HCT116 (p53 wild type) colorectal cancer cells were investigated. Proliferation was assessed using a 48 hour WST-1 assay and apoptosis was measured using a caspase-3 assay. Flow cytometry was used to detect levels of double-stranded DNA breaks.

Results AZD1775 (1 μM) significantly inhibited proliferation of HT29 and HCT116 cells by 59.6% ($p=0.001$) and 62.0% ($p<0.001$) respectively. It caused increased double-stranded DNA breaks (HT29: 0.6% vs 43% $p<0.001$, HCT116: 1% vs. 25% $p<0.001$) and increased apoptosis (HT29: 0.8% vs 8.1% $p=0.02$, HCT116: 2.1% vs. 9.3% $p<0.02$) in both cell lines compared to vehicle control. Double-stranded DNA breaks could be partially reversed in both cell lines when co-treated with either a CDK1 inhibitor or exogenous nucleoside addition.

Discussion and Conclusions AZD1775 triggers nucleotide shortage promoting double-stranded DNA breaks and apoptotic cell death in colorectal cancer cell lines. These effects appear to occur independently of p53 status.

Application No.	**ABSTR053**
Title	Does the Combination of Gemcitabine and Nab-Paclitaxel Exhibit Synergism in the Treatment of Pancreatic Cancer?
Presenting Author	Mishal Din, University of Manchester
Other Authors	Peter Mullen, University of St Andrews
Subsection	Medical Oncology/Haematology
Consider for	Poster & Oral

Contents

Background

Pancreatic cancer is notoriously difficult to treat. This is partly due to cancer stem cells (CSCs), a highly tumorigenic sub-population of cells. Gemcitabine is a first line chemotherapeutic for locally advanced pancreatic cancer. Nab-Paclitaxel is a novel formulation of Paclitaxel used to treat a variety of cancers.

Aim

To investigate any evidence of synergy when combining Gemcitabine and Nab-Paclitaxel in the treatment of pancreatic cancer and its effects on CSC survival.

Method

Samples of the pancreatic cancer cell line MiaPaCa2 were treated with each drug individually, and then in a series of combinations. Treatment efficacy was determined using cell count analysis and calculation of IC50 values. CSC survival was investigated using the expression of 'Nanog' as an indicator of stem-ness.

Results

The inhibitory effects of drug combination on the growth of MiaPaCa2 cells was superior to both individual drug treatments. Cell growth remained inhibited when using combinations with low dose Nab-Paclitaxel. There was some evidence of this combination specifically targeting CSC populations, though this is inconclusive.

Discussion

This drug combination may elicit greater therapeutic effects at lower doses than either drug monotherapy. The possibility of CSC-focussed treatment could slow metastasis leading to better long-term prognosis.

Conclusion

The combination of Gemcitabine and Nab-Paclitaxel may provide a novel treatment for pancreatic cancer with fewer side-effects and delayed development of chemo-resistance. Further investigation is required to elucidate the mechanism of this drug combination and its effect on CSC survival.

Application No. **ABSTR054**
Title What are Colorectal Cancer Tumour Buds?
Presenting Author Yen June Lau
, University of Manchester
Other Authors Peter David Caie, University of St Andrews and David James Harrison, University of St Andrews, University of Edinburgh

Subsection Translational Oncology/Basic Science
Consider for Poster & Oral

Contents

Background:

Tumour budding has shown promise as a prognostic factor in colorectal cancer. However, the molecular profiles of tumour buds have only been investigated in relation to their ability to migrate (Epithelial-Mesenchymal-Transition). Since much literature has linked EMT to stem-cell abilities, it is only natural to inquire about the relationship between these two parameters and tumour budding.

Aims:

To investigate EMT and the expression of stem cell biomarkers in tumour buds and correlate subsequent findings to disease-specific-death.

Methods:

Immunofluorescence analysis was carried out for four putative stem-cell markers (CD133, Lgr5, Nanog, SOX2) and two EMT markers (Ki67, E-Cad). The analysis was carried out on a tissue microarray containing multiple tissue samples from 51 high-budding stage II colorectal cancer patients. The intensity of biomarkers was scored by eye, and correlations between the biomarkers and survival were made.

Results:

Most tumour buds did not express Ki67 or E-Cad, and only a small subset expressed SOX2. Univariate analysis revealed that expression of SOX2 within tumour buds was significantly associated with disease specific death ($p= 0.0058$).

Discussion:

The data suggested that the presence of EMT in tumour buds alone was insufficient to affect prognosis; it was in fact the presence of stem-like ability that seemed to accurately predict disease-specific-death.

Conclusion:

The presence of SOX2 in tumour buds has proved to be an accurate parameter of prognosis in this study. The novel combination of these two characteristics in prognostication may also shed light onto the underlying mechanism of metastases. Further research is necessary to further validate the prognostic value of this parameter.

Application No. **ABSTR055**

Title The Effect of Single Nucleotide Polymorphisms on Clinical Outcome and Survival in the FOCUS (Fluorouracil, Oxaliplatin and Irinotecan: Use and Sequencing) Clinical Trial of Metastatic Colorectal Cancer

Presenting Author Jolanda Schoon
, University of Sheffield

Other Authors Ian W. Brock and Angela Cox, University of Sheffield, Susan D. Richman, Matthew T. Seymour and Philip Quirke, University of Leeds, Lindsay Thompson, Angela Meade and Mahesh K.B. Parmar, Medical Research Council Clinical Trials Unit at UCL and Maria Marp

Subsection Translational Oncology/Basic Science

Consider for Poster

Contents

Background

The FOCUS study aimed to determine most effective use of chemotherapeutics Irinotecan and Oxaliplatin. Genetic factors influencing response to these drugs are complex. Of particular interest are DNA damage repair genes. This project explores common variants within two such genes: XRCC2 and XRCC3.

Aims

To test the hypothesis that 12 inherited genetic variants (single nucleotide polymorphisms; SNP) in XRCC2 and XRCC3 are associated with survival in patients with metastatic colorectal cancer.

Methods

Analyses focused on effects of SNP genotype, and interaction between genotype and treatment, on failure-free survival during the trial, and overall survival, using Kaplan-Meier curves and a Cox proportional-hazards regression model. SNP data were available from 1076 subjects.

Results

Both the heterozygote and rare homozygote genotypes of SNP rs3218408 in the XRCC2 gene were associated with statistically significant improved survival in the trial, with hazard ratios (HR) and 95% confidence intervals (95% CI) of 0.86 (0.75-0.99) and 0.70 (0.53-0.93) respectively; Ptrend=0.036. These effects remained significant after controlling for treatment group (Ptrend=0.024). The heterozygote genotype for SNP rs861528 was associated with statistically significant poorer prognosis, but there was no effect of the rare homozygote genotype.

There was no evidence for interaction between SNPs and treatment group. SNPs rs3218454 and rs3218536 yielded statistically significant improved survival when the treatment was 5-Fluorouracil and Irinotecan and 5-Fluorouracil and Oxaliplatin respectively from the start.

Discussion

Results from these experiments show trends between genetic variants and overall survival from metastatic CRC. These results require validation in independent datasets.

Application No.	**ABSTR056**
Title	The effect of B-cell receptor signalling inhibitors on CXCR4 cross-talk in chronic lymphocytic leukaemia
Presenting Author	Alexander Wathen, University of Southampton
Other Authors	Nicola Weston Bell, Beatriz Valle Argos, Francesco Forconi, Graham Packham, University of Southampton
Subsection	Medical Oncology/Haematology
Consider for	

Contents

Background

Chronic lymphocytic leukaemia (CLL) is a B-cell malignancy in which antigenic stimulation of the B-cell receptor (BCR) drives pathogenesis/progression.1 Inhibitors of BCR-associated signalling kinases, such as the BTK and PI3K· inhibitors ibrutinib and idelalisib, have yielded dramatic clinical results associated with rapid re-localisation of malignant cells from protective tissue microenvironments to the blood.2,3 The mechanisms underlying redistribution are unknown but presumably involve effects on migration-controlling receptors. This study aimed to characterise the effects of kinase inhibitors on BCR-induced down-modulation of CXC-motif receptor-4 (CXCR4), a crucial determinant of CLL cell tissue homing/retention.

Methods

Primary peripheral blood mononuclear cells from 32 untreated CLL patients were stimulated in vitro using immobilised anti-IgM antibodies as surrogate antigen in the presence or absence of BCR-signalling inhibitors. CXCR4 expression was quantified using flow cytometry.

Results

BCR stimulation of CLL cells resulted in significant down-modulation of CXCR4 (mean 50% decrease). This BCR-induced receptor 'cross-talk' was effectively inhibited by idelalisib or tamatinib (SYK inhibitor). Receptor cross-talk was partially abrogated by ibrutinib, but not by the more selective BTK inhibitor acalabrutinib.

Discussion

These findings suggest that SYK and PI3K·, but not BTK, are required for BCR-CXCR4 crosstalk. Partial inhibition by ibrutinib is likely due to its off-target effects; its spectrum of interactions are likely to be key to its marked re-localisation effects.

Conclusions

These findings provide important insights into how BCR-associated kinase-inhibitors influence CXCR4. The data add to the characterisation of these exciting new therapies, supporting targeting of patient sub-populations based on laboratory parameters such as CXCR4 expression.

References

1. Packham G, Krysov S, Allen A, et al. The outcome of B-cell receptor signaling in chronic lymphocytic leukemia: proliferation or anergy. Haematologica 2014;99(7):1138-48.

2. Byrd JC, Furman RR, Coutre SE, et al. Targeting BTK with Ibrutinib in Relapsed Chronic Lymphocytic Leukemia. New England Journal of Medicine 2013;369(1):32-42.

3. Brown JR, Byrd JC, Coutre SE, et al. Idelalisib, an inhibitor of phosphatidylinositol 3-kinase p110delta, for relapsed/refractory chronic lymphocytic leukemia. Blood 2014;123(22):3390-7.

Application No.	**ABSTR058**
Title	Bone metastasis predict for shorter overall survival in metastatic adenoid cystic carcinoma
Presenting Author	Yonghan Li, University of Manchester
Other Authors	Nick Slevin, Catharine West, Andrew Sykes, Lip Wai Lee, Kate Garcez, David Thomson, Kathleen Mais, Jarrod J Homer, Guy Betts, Anshuman Chatuverdi and Robert L Metcalf, The Christie
Subsection	Clinical Oncology
Consider for	Poster & Oral

Contents

Background: Adenoid cystic carcinoma(ACC) are rare tumours (1% of all head and neck malignancies) arising most commonly the salivary glands. They are characterised by slow growth but a high propensity for local recurrence and metastatic spread. Coupled with a lack of established systemic therapies, they represent an unmet clinical need.

Objective: To identify a cohort of ACC patients treated at a tertiary care centre over a 34 year period and evaluate their clinical outcomes.

Method: A retrospective analysis was performed of 63 patients diagnosed with ACC from August 1982 to June 2016 at the Christie NHS Foundation Trust.

Results: 63 patients(20 male, and 43 female) were identified. Median follow-up duration was 9.9 years (range 1.5-31.7).

5-, 10- and 15-year survival rates were 87%, 63% and 45% respectively. Primary tumours of the major salivary glands versus other sites had better prognosis with 10-year survival rates of 85% versus 40% respectively (P=0.02). Metastases developed in the lungs (n=24, 65%), bone (n=10, 27%) and liver (n=10, 27%). Only 3(8%) patients were disease-free with a mean disease-free survival of 16.4 years.

After the appearance of distant metastases, 5- and 10-year survival rates were 55% and 11% respectively. Patients with bone versus lung metastases had a particularly poor prognosis with 4-year survival rates of 10% versus 74% respectively (P=0.01).

Discussion: Acknowledging the limitations of retrospective data collection, survival rates from diagnosis were comparable to previous reports. Survival after distant metastases were at the higher end of published data, which may reflect associated bias in patient selection in a tertiary cancer centre. An improved understanding of the molecular pathology of ACC is essential to improve treatments and outcomes and this is the subject of ongoing research.

Application No.	**ABSTR059**
Title	Risk factors for pancreatic cancer with a focus on inheritable pre-disposition: assessment of current referral practice to genetic counselling and outcomes of genetic screening
Presenting Author	Alexander Fulton, University of Manchester
Other Authors	Angela Lamarca, Christina Rigby, Lynne McCallum and Richard A Hubner, The Christie, Rille Pihlak, Mairéad G McNamara and Juan W Valle, The Christie/University of Manchester and Tara Clancy, Central Manchester University Hospitals NHS Foundation Trust
Subsection	Medical Oncology/Haematology
Consider for	Poster & Oral

Contents

BACKGROUND & AIMS: Approximately 1% of patients with pancreatic ductal adenocarcinoma (PDAC) have a germline predisposition for developing this malignancy. Mutation identification may enable the use of targeted therapies and guide family screening for carrier detection. The referral practice for genetic screening/counselling in patients diagnosed with PDAC was assessed.

METHODS: Electronic case records for consecutive patients with PDAC seen at The Christie between Aug-13 and Dec-15 were reviewed. Patients' demographic and cancer risk factor data were collected and analysed. The EUROPAC criteria(1) was utilised for identification of patients appropriate for genetic counselling referral. Univariate and multivariable logistic regression identified patients likely to fulfil the EUROPAC criteria.

RESULTS: A total of 400 patients were identified; 334 had the required personal/family history documented to assess whether EUROPAC criteria were met. Of 49 patients meeting the criteria, 8 (16.3%) were referred, 41.7% of patients referred attended their appointment; reason for non-attendance was primarily related to poor performance status or death. Three BRCA2 mutations were identified in the patient population (0.75%); one of these didn't fulfil the EUROPAC criteria (PDAC diagnosis at young age). The presence of any family history of malignancy was predictive of meeting EUROPAC criteria (multivariable analysis Odds Ratio 12.3 [95%-confidence interval 2.9-52.6]; p=0.01)

DISCUSSION & CONCLUSIONS: Of patients meeting referral criteria, few were referred. Earlier referral in the cancer pathway may enhance this. Consultation of EUROPAC criteria should be considered for patients with any family history of cancer. Expansion of criteria may be required to capture all relevant cases.

References

1. The European Registry of Hereditary Pancreatitis and Familial Pancreatic Cancer (EUROPAC). Familial Pancreatic Cancer Entry Criteria. [Available from: http://www.europac-org.eu/.

Application No.	**ABSTR061**
Title	Evaluation of PIM kinase as a novel opportunity to target c-Myc driven prostate cancer
Presenting Author	Nicholas Pearson, University of Manchester
Other Authors	Neil Smith, AstraZeneca, Dr Mick Brown and Professor Noel Clarke
Subsection	Translational Oncology/Basic Science
Consider for	Poster

Contents

Background: Prostate cancer (PCa) is the most common malignancy in men and is the cause of 1-2% of deaths in men (Attarrd et al, 2016). Biomarkers that stratify patients based on risk could improve PCa care and present new drug targets. One such biomarker is the transcription factor c-Myc, which is frequently amplified in human cancers and raised mRNA levels are seen in most PCa (Gurel et al, 2008). Yet c-Myc is considered “undruggable” having no active site and being required for normal proliferation. PIM family kinases have been shown to cooperate synergistically with c-Myc, driving tumourigenesis in in vivo tumour models (Wang et al, 2010). Current evidence supporting the relationship between c-Myc and PIM in PCa is derived from preclinical data.

Aims: Here we attempted to explore whether this translates to a clinical setting and further evaluate PIM as a target for c-Myc.

Methods: To achieve this we firstly validated immunohistochemistry assays for c-Myc and PIM, and then correlated the protein expression data from 284 PCa patient tissue samples, with their clinicopathological data.

Results: There was no strong correlation between the protein expressions of c-Myc or PIM and either Gleason grade or D’Amico score. From Kaplan-Meier plots the D’Amico score was superior to the Gleason grade and applications of prostate specific antigen serum levels at predicting prognosis. High nuclei c-Myc protein levels were associated with poor prognosis (overall survival).

Discussion: c-Myc and PIM appeared to have no synergistic relationship while PIM had minimal association with prognosis.

References:

1. Attard, G., Parker, C., Eeles, R. A., et al. (2016) Prostate cancer. Lancet, 387, 70-82.

2. Gurel, B., Iwata, T., Koh, C. M., et al. (2008) Nuclear MYC protein overexpression is an early alteration in human prostate carcinogenesis. Modern Pathology. 21, 1156-1167.

3. Wang, J., Roh, M., Franco, O. E., et al. (2010) Pim1 kinase synergizes with c-MYC to induce advanced prostate carcinoma. Oncogene. 29, 2477-2487.

Application No. **ABSTR062**
Title Applying novel analyses of cell interactions to describe effects of signal inhibitor therapy in CLL
Presenting Author Geraldine Hayes, University of Manchester
Subsection Medical Oncology/Haematology
Consider for Poster

Contents

Background and aims

It is recognised that small molecule inhibitors of intracellular signalling achieve clinical benefit (at least in part) by modifying dynamic interactions of chronic lymphocytic leukaemia (CLL) within the tumour microenvironment (TME). This project aimed to establish robust measures of interactive behaviour of live primary CLL lymphocytes that could describe, quantify and compare effects of signal inhibitor drugs.

Methods

CLL lymphocytes were cultured in vitro together with accessory cell types and exposed to different intracellular signal inhibitors. Fixed or live cultures were prepared and probed using microscopic and flow cytometric techniques before evaluation using objective morphometric (shape analysis) approaches to quantitatively describe and statistically evaluate behaviour.

Results

Cell shape and cell interaction were visualised using antibody or F-actin probes to demonstrate the formation of communicative F-actin structures (filopodia, lamellipodia and ruffles), cell groups and shape change, that were then quantified using novel analyses of binary image shape, antigen-co-localisation, and cell proximity, combined with live-cell analyses using skeletonised cell-groups and individual cell tracking. These analyses demonstrated that different dynamic interactions could be detected and evaluated to demonstrate objective statistical differences that reflected the cell-signal inhibitor used.

Discussion and conclusions

These approaches successfully demonstrated that different drug treatments profoundly altered interactive cytoskeletal structures in different ways, and showed that functional changes could be quantified and statistically evaluated. This approach may be combined with biochemical assays and measures of proliferation and survival to test new agents or combination therapies that may improve clinical outcomes in CLL.

Application No. **ABSTR063**
Title Bone marrow stromal cell mediated protection from oxidative stress, a putative mechanism of leukaemia cell survival in hypoxia

Presenting Author Musfira Shakeel, University of Manchester
Other Authors JiZhong Liu, University of Manchester and Vaskar Saha, University of Manchester/Tata Translational Cancer Research Centre, Kolkata, India

Subsection Paediatric Oncology
Consider for Poster & Oral

Contents

Background: Despite the high cure rates in newly diagnosed acute lymphoblastic leukaemia (ALL), 10-15% of the children relapse(1). Relapse is associated with poor outcome and cannot be explained by genetic heterogeneity alone. The bone marrow microenvironment also plays a role in disease recurrence(2).

Aim: To investigate bone marrow stromal cell (BMSC) mediated ALL cell survival in hypoxia.

Methods: ALL cells were cultured under normoxic (20% oxygen) and hypoxic (1% oxygen) conditions. Cell viability and cell count were checked using trypan blue. Western blot was utilised to analyse expression of the proteins of interest. Gene knockdown was carried out by lentivirus-mediated shRNA interference. For analysis of reactive oxygen species (ROS) flow cytometry was used.

Results: Cell survival was significantly better in normoxia compared to hypoxia while BMSC protected primary ALL cells in hypoxia. The addition of superoxide scavengers, tempol and tiron, significantly increased cell survival in hypoxia. Cells cultured in BMSC-derived conditioned medium had increased expression of the transcription factor forkhead box-O (FOXO)3a and the antioxidant manganese superoxide dismutase (MnSOD) compared to those cultured in normal medium. Knockdown of FOXO3a increased ROS levels and decreased survival in hypoxia. Increasing mitochondrial superoxide production by mitochondrial complex I (MCI) inhibitor BAY 87-2243 significantly decreased cell survival.

Conclusions: In hypoxia, high levels of superoxide cause cell death. BMSC support cell survival by up-regulating the expression of FOXO3a and MnSOD, which reduce superoxide levels. Increasing superoxide levels by interfering with MCI may be used as a therapeutic strategy in ALL to suppress BMSC mediated protection.

References:

(1) Raetz, E.A. and Bhatla, T. (2012). Where do we stand in the treatment of relapsed acute lymphoblastic leukemia? American Society of Haematology, 2012(1), 129-136.

(2) Manabe A, Smith E.C., Behm F.G., Raimondi S.C. and Campana D. (1992). Bone marrow-derived stromal cells prevent apoptotic cell death in B-lineage acute lymphoblastic leukaemia. Blood, 79(9), 2370-7.

Application No.	**ABSTR064**
Title	The isolation and characterisation of circulating tumour cells from patients with hepatocellular carcinoma
Presenting Author	Sheba Macheka, University of Newcastle
Other Authors	Dr David Jamieson, Dr Helen Reeves and Misti McCain
Subsection	
Consider for	

Contents

BACKGROUND: Hepatocellular carcinoma (HCC) is the second most common cause of cancer-related mortality. The characterization of circulating tumour cells (CTCs) from peripheral blood, may provide information which may help to predict prognosis or stratify patients for targeted therapies. Asialoglycoprotein receptor-1 (ASGPR1) is predominantly expressed by hepatocytes and this may be utilised as a biomarker to detect liver-specific CTCs. Some CTCs undergo the epithelial-to-mesenchymal-transition (EMT) and express Vimentin. This additional biomarker could aid with identifying CTCs.

AIM: To detect CTCs in blood samples from patients with HCC, by targeting cells expressing ASGPR1 or Vimentin using imagestreamX flow cytometry

METHODS: Blood samples were obtained from 8 consenting patients with HCC. Red blood cells and leucocytes were depleted, in order to enrich the CTCs. Following this, patient samples were stained with a panel of antibodies conjugated with fluorochromes, in order to identify Vimentin, Cytokeratin or ASGPR1 biomarker positive CTCs using ImagestreamX. Furthermore, CTC detection was based on additional parameters such as surface area (>200µm2), the absence of CD45+ expression and a large nuclear content.

RESULTS and DISCUSSION: ASGPR1 and Cytokeratin were the most common biomarkers expressed by CTCs detected in 62% (5/8) of patients. A greater number of CTCs detected expressed Vimentin alone (n=20), in comparison to Cytokeratin (n=5). This confirmed that CTCs downregulated the expression of epithelial biomarkers such as Cytokeratin, due to EMT.

CONCLUSIONS: We have designed a novel sensitive panel of antibodies that detected biomarker positive CTCs which expressed ASGPR1, Vimentin and Cytokeratin from peripheral blood samples, using imagestreamX.

REFERENCES

1. Dent, B.M., Ogle, L.F., O'Donnell, R.L., Hayes, N., Malik, U., Curtin, N.J., Boddy, A.V., Plummer, E.R., Edmondson, R.J., Reeves, H.L., May, F.E.B. and Jamieson, D. (2016) 'High-resolution imaging for the detection and characterisation of circulating tumour cells from patients with oesophageal, hepatocellular, thyroid and ovarian cancers', International Journal of Cancer, 138(1), pp. 206-216.

2. Li, J., Chen, L., Zhang, X., Zhang, Y., Liu, H., Sun, B., Zhao, L., Ge, N., Qian, H., Yang, Y., Wu, M. and Yin, Z. (2014) 'Detection of Circulating Tumor Cells in Hepatocellular Carcinoma Using Antibodies against Asialoglycoprotein Receptor, Carbamoyl Phosphate Synthetase 1 and Pan-Cytokeratin', PLoS ONE, 9(4), p. e96185.

3. Ogle, L.F., Orr, J.G., Willoughby, C.E., Hutton, C., McPherson, S., Plummer, R., Boddy, A.V., Curtin, N.J., Jamieson, D. and Reeves, H.L. (2016) 'Imagestream detection and characterisation of circulating tumour cells - a liquid biopsy for Hepatocellular Carcinoma?', J Hepatol.

Application No.	**ABSTR065**
Title	Optimising the delivery of a “Fit for surgery” Prehabilitation programme using Wearable Technology
Presenting Author	Umair Gondal, University of Manchester
Other Authors	H Trainer, University of Manchester, M Saunders and O Aziz, The Christie/University of Manchester
Subsection	Surgical Oncology
Consider for	

Contents

Background:

‘Prehabilitation’ is an effective concept for improving a patient’s pre-operative status to make them ‘fit for surgery’. Focusing on physical, nutritional and psychosocial aspects, these programmes are labour intensive to implement; thus requiring multiple home or clinic visits. Using Fitbit devices could be a potential avenue for delivering more efficient prehabilitation programme.

Aims:

This study aims to develop a technology based prehabilitation programme consisting of exercise, nutritional and psychological components. The feasibility of delivering this programme via a Fitbit device was also assessed.

Methods:

12 patients were recruited into a questionnaire based patient perception study following major abdominal surgery to evaluate compliance and perception towards wearable technology and prehabilitation. A further 6 healthy volunteers were recruited to wear a Fitbit device for 2 weeks and actively participate in the programme. The ability to perform 10,000 daily steps and the 6 minute walking test was assessed; along with comparison of completing manual vs digital nutritional diaries and monitoring of resting heart rate. Data was collected using the Fitbit Wellness Programme with subsequent qualitative analysis.

Results:

Patients responded positively towards a technology based prehabilitation programme and were happy to be actively monitored via a Fitbit. The device proved to be further efficacious through remote monitoring and the use of notification to encourage adherence.

Conclusion:

Smart devices could potentially provide a useful method of delivering efficient prehabilitation programmes with improved patient compliance. Further development is recommended to improve the technological interface in order to collect data for certain vital parameters.

Application No.	**ABSTR066**
Title	KRAS mutation status as response predictor in colorectal cancer treatment with anti-EFGR
Presenting Author	Natalia Ramos Rueda, University of Navarra
Other Authors	Elena Martínez Noval, University of Navarra
Subsection	Medical Oncology/Haematology
Consider for	Poster & Oral

Contents

Background:

Colorectal cancer is one of the most prevalent malignant tumors in the world and it has high rates of mortality. A right election of a treatment could be a huge benefit for the patient.

Aims:

To assess the predictive value of the KRAS mutation status in order to choose the best treatment option for each patient.

Methods:

Literature review in different databases including articles related to the topic published from 2007 to the present.

Results:

The results of five studies are presented (OPUS, CRYSTAL, PRIME, CO-17 and the one of Amado et al.) and they have been evaluated efficacy and safety data related to anti-EGFR (Epidermal Growth Factor Receptor), as Cetuximab and Panitumumab, both when they are used alone or in combination with traditional chemotherapy drugs (FOLFOX y FOLFIRI).

Discussion and conclusions:

KRAS mutation status has a high predictive value in patients with mCRC (Metastatic Colorectal Cancer) in treatment with anti-EFGR, as monotherapy and in combination with chemotherapy. The use of monoclonal antibodies like Cmab and Pmab as frist line treatment in combination with chemotherapy in patients with Wild Type KRAS increase overall survival and the response to the treatment.

Studying the safety, it is observed that skin toxicity also have some predictive value in patients with anti-EFGR therapies.

Amado, R.G. et al., 2008. Wild-type KRAS is required for panitumumab efficacy in patients with metastatic colorectal cancer. Journal of Clinical Oncology, 26(10), pp.1626–1634.

Bokemeyer, C. et al., 2009. Fluorouracil, leucovorin, and oxaliplatin with and without cetuximab in the first-line treatment of metastatic colorectal cancer. Journal of Clinical Oncology, 27(5), pp.663–671.

Douillard, J.Y. et al., 2014. Final results from PRIME: randomized phase III study of panitumumab with FOLFOX4 for first-line treatment of metastatic colorectal cancer. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO, 25(7), pp.1346–55.

Eric Van Cutsem, Claus-Henning Köhne, Erika Hitre, , Jerzy Zaluski, Chung-Rong Chang Chien, Anatoly Makhson, Geert D'Haens, Tamás Pintér, Robert Lim, György Bodoky, Jae Kyung Roh, Gunnar Folprecht, Paul Ruff, Christopher Stroh, Sabine Tejpar, Michael Schl, J.N. and P.R., 2009. Cetuximab and Chemotherapy as Initial Treatment for Metastatic Colorectal Cancer. The New England Journal of Medicine, pp.1408–1417.

O'Callaghan, C.J. et al., 2011. The relationship between the development of rash and clinical and health-related quality of life outcomes by KRAS mutation status in patients with colorectal cancer treated with cetuximab in NCIC CTG CO.17. ASCO Meeting Abstracts , 29 (15_suppl), p.3588. Available at: http://meeting.ascopubs.org/cgi/content/abstract/29/15_suppl/3588.

Application No. **ABSTR067**
Title Supporting Oncology Support Workers
Presenting Author Aisling Armstrong, University of Sheffield
Other Authors Dr Joanne Thompson and Anna White, University of Sheffield

Subsection Medical Oncology/Haematology
Consider for Poster & Oral

Contents

Background

'Burnout' is one of the most common manifestations of distress amongst healthcare workers, with oncology health professionals cited as being at particular risk.

Aims

We aimed to (1) gain insight into the work experiences of oncology Support Staff (SS), focusing on the emotional impact of their work, relationships with patients and colleagues, and risk of burnout, and (2) gather data to shape the development of possible emotional support programs.

Methods

A qualitative Maslach Burnout Inventory Questionnaire (MBI) was used to explore the experiences of SS in addition to a focus group meeting.

Results

Eight staff members returned the questionnaire and six participated in the focus group. Results from the MBI demonstrated that SS were encountering a moderate to high level of burnout, particularly in the 'personal accomplishments' dimension. Thematic analysis of the focus group identified job satisfaction, patient needs, training needs, bereavement, peer support and feeling valued as an employee as areas of interest.

Discussion

Relationships with patients have a significant emotional impact on healthcare support workers in the oncology setting. The frequent experience of loss has emotional consequences such as burnout and impacts on other areas such as job satisfaction. Staff value the support gained from close team working in this setting, which is mostly informal.

Conclusion

Support workers were found to experience emotional distress and a moderate level of burnout. Although further research is needed to fully understand the causes and impact of work stress, improved staff support and training is recommended

Application No.	**ABSTR068**
Title	Investigating the need for education and training of primary care practitioners on the topic of lung cancer
Presenting Author	Thomas Hill, University of Manchester
Other Authors	Maria Neocleous and Bajinder Dhamrait, University of Manchester
Subsection	Primary Care
Consider for	Poster & Oral

Contents

ABSTRACT:

Background: 37,409 new cases of lung cancer were reported in the UK in 2014(Royal College of Physicians 2015); the large majority were detected at a late stage. Early diagnosis is pivotal in improving lung cancer prognosis.

Aims: This report aims to investigate the need for educational support for GPs in the Greater Manchester region in managing lung cancer patients.

Methods: Initially, phone interviews with several GPs aided in the formation of an online questionnaire, which was sent to GP practices and MacMillan GPs in the Greater Manchester region. The questionnaire explored their interest in training on lung cancer, use of guidelines for referral and identification of red flag symptoms.

Results: 48 GPs completed the survey, mainly from the Stockport and Wigan CCGs. Responses were poor from most other CCGs. Despite their confidence in spotting the signs and symptoms and making urgent referrals, only 10% of them received training on lung cancer in the last 12 months while 85% were interested in relevant training. Educational needs are apparent with a preference on the use of e-learning modules or a daytime event within their CCG.

Discussion: Results are not representative of CCGs in the region and further emailing or calling GP practices will hopefully increase questionnaire responses.

Conclusions: The lack of up to date training of primary healthcare practitioners with regard to lung cancer is evident. The formation of an e-learning package accessible to all GPs in Greater Manchester is likely to improve clinical knowledge, resulting in earlier detection and better prognoses.

Bibliography:

Royal College of Physicians, 2015. National Lung Cancer Audit Annual Report 2015 (for the audit period 2014)

Application No.	**ABSTR069**
Title	Building the Palliative Care Pyramid
Presenting Author	Adam Bhanji, University of Manchester
Other Authors	Sophie Williams, University of Manchester and Mike Tapley, Willow Wood Hospice
Subsection	Palliative Medicine
Consider for	Poster & Oral

Contents

Background: Challenges have been identified in approaching, discussing and communicating the transition into palliative care. Holistic support is an integrated part of the palliative care pyramid; clinicians should be able to treat patients as a whole, from medical and psychosocial point of view.

Aim: To identify the need for an integrated approach to palliative care to improve care in the last days of life.

Method: A critique of PubMed and an internet review of the literature with search terms 'the medical and holistic approach to palliative care' and 'communication with patients.'

Results: 'There are no precise ways of telling accurately when a patient is in the last days of life' 1 Clinical indicators, based on the gold standards framework2 can be used to identify the palliative needs of patients. Prognostic indicators can only assist clinicians in recognising dying patients; healthcare professionals need to get to know their patients and gain an understanding of their individual disease trajectory. There are no specific communication tools for discussing patient's prognosis, however the most important aspect to patients is to be realistic and have an individualised approach.3

Conclusion: Guidance on illness trajectories and prognostic indicators can only act as a rough guide in supporting patients, families and healthcare professionals at the end of life. The pyramid model of palliative care gives a visual tool to help clinician's approach both the medical and holistic aspects of palliative care and recognise the opportunities for flexibility in moving around the pyramid to offer individualised patient care.

References:

1. Review of the Liverpool care pathway https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/212450/Liverpool_Care_Pathway.pdf

2. Gold Standards Framework (GSF) http://www.goldstandardsframework.org.uk/cd-content/uploads/files/Library,%20Tools%20%26%20resources/A%20Full%20GSF%20Guidance%20Paper%20on%20Primary%20Palliative%20care%20for%20QOF.pdf

3. Hagerty RG, Butow PN, Ellis PM, Lobb EA, Pendlebury SC, Leighl N, Mac Leod C, Tattersall MH. Communicating with realism and hope: incurable cancer patients' views on the disclosure of prognosis. Journal of clinical oncology. 2005 Feb 20;23(6):1278-88.

Application No.	**ABSTR070**
Title	Audit of the cervical screening programme and uptake at Elliot Street GP Practice
Presenting Author	Dominic Rushton, University of Manchester
Subsection	Public health, prevention & screening
Consider for	Poster

Contents

An effective cervical screening programme is one which identifies problems in higher risk patients early so that they can be monitored for potentially harmful lesions and treated quickly. This audit aimed to assess the coverage of the cervical screening programme at Elliot Street Surgery, in order to create targeted recommendations towards specific age groups. Patients were randomly selected from a list of eligible women and data was collected via the GP patient data system. Checks for last cervical smear were made and data compiled from this. Analysis revealed low attendance in the 25-30 and 51-64 age ranges (68.2% and 68.4% age appropriate screening rate respectively), with increased attendance amongst those aged 31-40 and 41-50 (77.6% and 86.3% respectively). Drawing upon local CCG and national data allowed the efficacy of the practice's cervical screening programme as well as socioeconomic depravity to be assessed and compared comprehensively. The results from this audit reflected a national decline in the rate of cervical screening uptake[1]. Recommendations have been provided on how to increase uptake in low attending target populations.

[1] Screening and Immunisations team, Health and Social Information Centre. Cervical Screening Programme England Annual Statistics.; 2014. http://www.hscic.gov.uk/catalogue/PUB15968/cerv-scre-prog-eng-2013-14-rep.pdf (accessed 2nd-9th February 2016).

Application No.	**ABSTR071**
Title	Audit to assess treatment regimens and clinical outcomes for patients with recurrent or metastasised nasopharyngeal carcinoma
Presenting Author	Rohma Abrar, University of Manchester
Other Authors	Kathleen Mais, Nick Slevin, David Thomson, Lip Lee, Andrew Sykes, Kate Garcez and Robert Metcalf, The Christie
Subsection	Medical Oncology/Haematology
Consider for	

Contents

Background: Nasopharyngeal carcinoma (NPC) is a rare tumour arising from the epithelium of the nasopharynx. Locally recurrent NPC can be treated with salvage surgery and re-irradiation achieving long term control in selected subgroups. Although metastatic NPC is regarded as sensitive to many chemotherapy agents, there are no guidelines for the management of metastatic NPC.

Aims: To audit chemotherapy use and outcomes for patients with recurrent or metastatic NPC treated at The Christie NHSFT.

Methods: The management of recurrent or metastatic disease for 10 patients with NPC treated between 2007 and 2016, was audited.

Results: 6/10 patients had recurrent or metastatic NPC (male: female 6:0, median age 56 (range 50-71)). Median time to recurrence was 1.9 years.

Two patients received salvage surgery with 1 and 3 year disease free interval until further metastases/recurrences. One patient received TPF chemotherapy, followed by cetuximab, with radiological response. One patient achieved long term control with induction TPF chemotherapy (docataxel, cisplatin, fluorouracil) followed by concurrent cisplatin radiotherapy. Two patients received carboplatin and capecitabine chemotherapy – one had a radiological partial response and the other no measurable disease. One patient received docetaxel chemotherapy with radiological partial response. One patient received best supportive care alone.

Conclusion: Surgery and re-irradiation was used to good effect in locally recurrent NPC patients included in this audit. As expected, most patients had chemotherapy sensitive disease. Varied systemic chemotherapies were used to highlight a need to develop local guidelines for the systemic treatment of metastatic disease. Once this guideline is developed, this will be re-audited.

Application No.	**ABSTR072**
Title	A clinical audit of performance status in recurrent or metastatic HNSCC patients receiving palliative chemotherapy
Presenting Author	Kiran Nadeem, University of Manchester
Other Authors	Rizwana Rahman, University of Manchester, Kathleen Mais and Robert Metcalf, The Christie
Subsection	Clinical Oncology
Consider for	Poster & Oral

Contents

Background:

In recurrent or metastatic head and neck squamous cell carcinoma (HNSCC), palliative chemotherapy is recommended for patients with good performance status (PS). PS is a global measure of physical functioning. First-line chemotherapy for this cohort was defined as fluorouracil and cetuximab in combination with cisplatin or carboplatin in a study by Vermorken et al. (2008). This study only included patients with a Karnofsky PS of 70 or more, although survival benefit was primarily seen in patients of PS 80 or more.

Aims:

To assess whether performance status was recorded and was of a satisfactory level prior to chemotherapy commencement.

Methods:

Medical record review with a descriptive analysis in those with recurrent or metastatic HNSCC who began palliative chemotherapy between September 2015 and June 2016 (n=18).

Results:

89% (16/18) had PS recorded in at least one form before palliative chemotherapy commencement. All of these patients had WHO PS ≤2, KP >70 or ECOG ≤1. 93% were KP 80-100 (n=14); only one patient was KP 70 and WHO PS 2. PS was not recorded before starting chemotherapy in 11% (2/18), as they formed part of a clinical trial.

Discussion:

Performance status should be routinely assessed and recorded as it is a prognostic indicator. Overall, PS was well-documented; 89% had it recorded prior to commencing chemotherapy and in the remainder it was subsequently documented. All patients were KP 70-100, majority being KP 80-100, consistent with the group deriving greatest benefit from this treatment.

References:

Vermorken, J.B., Mesia, R., Rivera, F., Remenar, E., Kawecki, A., Rottey, S., Erfan, J., Zabolotnyy, D., Kienzer, H.-R., Cupissol, D., Peyrade, F., Benasso, M., Vynnychenko, I., De Raucourt, D., Bokemeyer, C., Schueler, A., Amellal, N. and Hitt, R. (2008) 'Platinum-based chemotherapy plus Cetuximab in head and neck cancer', New England Journal of Medicine, 359(11), pp. 1116–1127. doi: 10.1056/nejmoa0802656.

Application No.	**ABSTR073**
Title	Clinical audit assessing the time to medical assessment and antibiotic administration in paediatric oncology patients with febrile neutropenia
Presenting Author	Ruairi Wilson, University of Glasgow
Other Authors	Jairam Sastry, Katherine Longbottom, Dianna McIntosh and Joanne Stirling, Royal Hospital for Children, Queen Elizabeth University Hospital, Glasgow
Subsection	Paediatric Oncology
Consider for	Poster & Oral

Contents

Background:

Febrile neutropenia is an acute oncological emergency for paediatric patients on chemotherapy. Minimising the time to antibiotic administration in these patients is of central importance. Recent evidence has led to updated guidelines for antibiotic administration in this clinical setting. Currently there are two guidelines for treating febrile neutropenia at the Royal Hospital for Children (RHC), Glasgow: the national (MSN) guidelines and the local (RHC) guidelines. This audit evaluated compliance to both guidelines by examining time taken for medical assessment and time to first antibiotic administration.

Methods:

Over an 18-day period, attending medical and nursing staff completed a simple proforma, recording timing of events in the Emergency Department (ED), ward 2A and the Day Care Unit (DCU). Subsequent analysis of timings revealed compliance to both protocols. Patient outcomes at 72 hours were also recorded.

Results:

Data from 9 patients was collected and analysed. Based on mean timings: The Schiehallion unit (Ward 2A and DCU) complied with both protocols for time to medical assessment. The ED did not. The Schiehallion unit complied to the national (MSN) protocol of administering antibiotics within the first 60 minutes, but not the local (RHC) guideline of 30 minutes. The ED did not comply to either the local or the national guidelines.

Conclusions:

CEWS on presentation did not determine time to medical assessment. Lack of CVC line access on presentation was associated with reduced time to first antibiotic administration. Key improvements to the service should be targeted at the out-of-hours service for febrile neutropenia, particularly in the ED.

Application No.	**ABSTR074**
Title	Audit of use of platinum based chemotherapy in recurrent and metastatic head and neck squamous cell carcinoma (RM-HNSCC)
Presenting Author	Samuel Rack, University of Manchester
Other Authors	K Mais, N Slevin, L Lee, K Garcez, A Sykes, D Thomson and R Metcalf, The Christie
Subsection	Medical Oncology/Haematology
Consider for	

Contents

Background

The treatment of RM-HNSCC is with cetuximab, 5-FU plus either cisplatin or carboplatin (1). Although many studies included cisplatin and carboplatin in combination chemotherapy, no studies have conclusively shown a difference in overall survival between these agents. However, they have differing toxicity profiles.

Aim:

We aimed to audit the use of platinum chemotherapy before and after the introduction of a medical oncology RM-HNSCC clinic in September 2015.

Method

Records of the 29 patients receiving palliative chemotherapy were reviewed to determine which platinum agent was prescribed and documentation of the clinical reasoning.

Results

74% (14/19) of patients treated prior to September 2015 were commenced on cisplatin based palliative chemotherapy compared with 20% (2/10) of patients subsequently. Six of 14 patients treated prior to September 2015 with cisplatin were changed to carboplatin (due to renal impairment and nausea/vomiting). The two patients receiving cisplatin based chemotherapy subsequent to September 2015 were changed to carboplatin mid treatment due to toxicity. The rationale for choice of platinum agent was documented in the medical notes in 70% (7/10) of patients post September 2015 and in 11% (2/19) of patients prior to that. Subsequent to September 2015, reasons for use of carboplatin over cisplatin included; low baseline GFR, previous nephropathy, previous renal impairment caused by cisplatin in concurrent treatment, hearing loss and patient choice. The only documented reason for cisplatin post September 2015 was patient choice.

Conclusions

Since September 2015, the number of RM-HNSCC patients receiving carboplatin based chemotherapy has increased. Although the clinical reasoning is documented in 70% of patients, this can be improved upon and this will be the subject of a re-audit.

1. Vermorken JB, Mesia R, Rivera F, Remenar E, Kawecki A, Rottey S, et al. Platinum-based chemotherapy plus cetuximab in head and neck cancer. New England Journal of Medicine. 2008 Sep 11;359(11):1116-27. PubMed PMID: WOS:000259078200007.

Application No.	**ABSTR075**
Title	Predictive factors for occurrence of pancreatic cancer in diabetes patients: a meta-analysis
Presenting Author	Virginia Lam, University of Warwick
Other Authors	Dr Yen-fu Chen and Dr Sian Taylor Phillips
Subsection	Public health, prevention & screening
Consider for	

Contents

Background

Pancreatic cancer (PC) is one of the most lethal cancers but population screening is not feasible due to its low prevalence [1]. Recent studies showed that type two diabetes mellitus (T2DM) is an early manifestation of PC [2]. It is hoped to identity risk factors among patients with T2DM who later developed PC to allow more accurate risk stratification.

Aim

The aim of the study is to identify predictive factors of PC in patients with T2DM through systematically review of literature and to present the related adjusted or unadjusted risk estimates.

Method

Keyword search was performed in “Medline”, “Embase” and “Cochrane Database of Systematic Reviews” up to November 2015. Included studies were assessed using Quality in prognosis studies (QUIPS) tool.

Results

Thirteen studies were included. Out of thirteen predictive factors identified, age > 65 years old, smoking, hepatobiliary comorbidity were strong predictors of PC. Newly diagnosed T2DM and family history of PC are associated with increased risk. Weight loss and alcohol are less certain predictors.

Discussion

The strong predictors are similar to those of non-T2DM population. Exact smoking exposure has not been identified due to lack of standard definition. Given the diversity in risk estimates, pooling is not possible in most of the risk factors. A field-wide meta-analysis approach used in this study hopes to overcome the limitation.

Conclusion

Older T2DM patients who smokes and with hepatobiliary comorbidities are with higher risk of developing PC. This group of individuals could be ideal candidate to screen for PC.

Reference

1. Okano, K. and Y. Suzuki, Strategies for early detection of resectable pancreatic cancer. World journal of gastroenterology: WJG, 2014. 20(32): p. 11230.

2. Wang, F., et al., The relationship between diabetes and pancreatic cancer. Mol Cancer, 2003. 2: p. 4

Application No.	**ABSTR076**
Title	Improvement in 30-day mortality following systemic anti-cancer therapy in recurrent and metastatic head and neck cancer (HNC) following clinical service reconfiguration
Presenting Author	Yasmin Samir, University of Manchester
Other Authors	Robert Metcalf, Kathleen Mais, Tony McGurk, Nick Slevin, Lip Lee, Andrew Sykes, Kate Garcez and David Thomson, The Christie NHS Foundation Trust
Subsection	Medical Oncology/Haematology
Consider for	Poster

Contents

ABSTRACT

Background: The 2008 National Confidential Enquiry into Patient Outcome and Death reviewed 30-day mortality following systemic anti-cancer therapy (SACT). 30-day mortality is an indicator of the quality of services provided and has been the subject of ongoing national audit since 2008.

Aims: To review the 30-day mortality of patients with recurrent or metastatic head and neck cancer (RMHNC) treated at The Christie NHS Foundation Trust since 2008, before and after the establishment of a medical oncology clinic for the treatment of RMHNC patients in September 2015.

Methods: We evaluated the number of deaths within 30 days of receiving SACT for HNC between January 2008 and July 2016. Where available, we obtained data which may provide a profile of the circumstances surrounding death including SACT regimen, haematological results, performance status and comorbidities. Data was obtained from electronic patient records.

Results: 65 HNC patients treated at The Christie between January 2008 – July 2016 died within 30 days of SACT. 82% were male, with a median age of 58 (range 28 to 79 years). 48/65 deaths (74%) occurred in patients receiving palliative chemotherapy. Of these, 47/48 occurred prior to September 2015 (equivalent to an annual rate of 5.88 cases), with only a single case subsequent to September 2015.

Conclusion: In the palliative setting, 30-day mortality following SACT dropped from almost 6 cases per year to 1 per year following the introduction of a medical oncology clinic for the management of RMHNC patients. This is a clear patient benefit derived from this service reconfiguration.

References:

NCEPOD (2008). Systemic Anti-Cancer Therapy: For better, for worse? London, National Confidential Enquiry into Patient Outcome and Death. Available at: http://www.ncepod.org.uk/2008report3/Downloads/SACT_report.pdf [Accessed: 31st July 2016].

Application No.	**ABSTR077**
Title	Patient survey assessing holistic needs of patients during urgent referral process for suspected cancer
Presenting Author	Shehrazed Lounis, Barts and The London School of Medicine and Dentistry, QMUL
Other Authors	Connor Green, Barts and The London School of Medicine and Dentistry, QMUL, Mazlan Kamarudin and Krishnaswamy Madhavan, Southend University Hospital Foundation Trust
Subsection	Primary Care
Consider for	Poster & Oral

Contents

Background

Patients on urgent cancer referrals have seen improvements by way of prompt management initiated within national 2 week wait guidance. Support and information giving is an integral aspect of guidelines. Whilst extensive research has focused on clinical success of urgent referrals, the holistic needs and difficulties faced by patients have not been assessed.

The majority of patients in the '2 week wait' pathway are non-cancer. In this context, provision of information and support is a central element of care.

Aims

To assess whether national guidelines for support and information needs of patients with suspected cancer are being met.

Method

All patients urgently referred to gynaecology and urology were offered surveys. This included grading of 24 statements based on guidelines, assessing support needs of patients in both primary and secondary care.

Results

117 surveys were collected. 67.2% and 93.3% of patients in primary and secondary care, respectively, agreed with the statements, indicating the majority of their needs had been met. However, at the time of referral: 31.4% disagreed their GP had reassured them most referrals were found not to be malignant; 34% disagreed the referral had been discussed with them; 59% disagreed they had been explained how to seek further information; 46% felt the needs of their family were not considered.

Discussion and conclusions

Results showed significant lack of holistic support for all patients. Time constraints in primary care is one reason to explain this. Suggestions for improvement include focused consultation checklists to be used at the time of referral, and improved leaflets addressing specific patient concerns.

Application No.	**ABSTR078**
Title	The effects of ketamine on anxiety and depression in cancer patients with neuropathic pain - results from a double-blind randomised controlled trial
Presenting Author	Jonathan Gibb, University of St Andrews
Other Authors	Barry Laird and Marie Fallon, University of Edinburgh
Subsection	Palliative Medicine
Consider for	Poster & Oral

Contents

Background

Neuropathic pain is common among patients with cancer. Ketamine, a NMDA receptor antagonist, has been widely used in the treatment of cancer-related pain. In addition to the recognised role of ketamine in anaesthesia and pain management, there is now evidence to suggest that the administration of the drug is associated with acute, albeit temporary, antidepressant effects.

Aims

To assess the effect of parallel presentation ketamine versus placebo, in addition to best pain management for neuropathic pain, on anxiety and depression levels among cancer patients.

Methods

In this double-blind randomised controlled trial, 214 adult cancer patients with neuropathic pain were randomised into two groups receiving either parallel presentation ketamine or placebo. Patients were evaluated with the Hospital Anxiety and Depression Scale (HADS) at baseline, end of titration, and at days 4, 8, 12, and 16.

Results

There were no significant changes, between groups, in HADS-Anxiety (95% CI, -1.417 — 1.250) or HADS-Depression (95% CI, -0.500 — 0.173) scoring from baseline compared to trial end. However, on average, HADS scores between groups were not high at baseline.

Discussion

As patients with cancer and uncontrolled neuropathic pain often suffer with un-recognised anxiety and depressive disorders, it is highly important to consider how a pharmacological intervention may effect mood and quality-of-life. In this study no significant difference was seen overall in anxiety/depression levels. A subsequent study with participants with high baseline HADS scores is indicated.

Conclusions

The administration of parallel presentation ketamine did not significantly affect patients' self-reported anxiety and depression scores.

Application No.	**ABSTR079**
Title	LaNt α31 overexpression in human umbilical vein endothelial cells impairs cell migration; implications for angiogenesis
Presenting Author	Vishal Chohan, University of Liverpool
Subsection	Translational Oncology/Basic Science
Consider for	Poster

Contents

Background: The Laminin N-terminus proteins (LaNts) are a recently identified family of secreted proteins1. To date, they have been studied only in epidermal keratinocytes where they influence cell adhesion and migration through interaction with laminins in the extracellular matrix1. LaNtα31 is regulated by a promoter known to also be active in endothelial cells, however, the laminin matrix deposited by endothelial cells structurally differs from that of the epithelium1. These structural differences in microenvironment may result in LaNtα31 playing a context specific role and therefore be involved in regulating angiogenesis through modulating cell-matrix attachment.

Aim: LaNtα31 is expressed by endothelial cells and modifying its expression level influences cell spreading and motility.

Method: Cell extracts from primary human umbilical vein endothelial cells (HUVECs) were processed for western immunoblotting with antibodies against LaNtα31. Overexpression was induced through adenoviral infection with constructs encoding GFP tagged LaNtα31. Cell length, width, surface area and aspect ratio were calculated from phase contrast images. Cell speed and directionality were determined through analysis of phase contrast images taken every 2 minutes over 2 hours. LaNtα31 expression influence on the actin cytoskeleton was determined by phalloidin staining.

Results: LaNtα31 is expressed by HUVECs. HUVECs induced to overexpress LaNtα31 displayed decreased migration speed however, polarity of migration and cell morphology were unaffected. Migration rate differences were not due to gross differences in the arrangement of the actin cytoskeleton.

Conclusion: LaNt is present is in HUVEC cells and influences cell motility suggesting a putative role in the regulation of angiogenesis.

1. Hamill, K. J. (2009). Identification of a Novel Family of Laminin N-terminal Alternate Splice Isoforms. THE JOURNAL OF BIOLOGICAL CHEMISTRY.

Application No.	**ABSTR080**
Title	Analysis of SWI/SNF Catalytic Subunits Mutations and Drug Sensitivity in Colorectal Carcinoma
Presenting Author	Sarah EL-Zahab, University of Brighton and Sussex
Subsection	Translational Oncology/Basic Science
Consider for	Poster & Oral

Contents

Background: SWI/SNF (SWitch/Sucrose Non-fermentable) chromatin remodelling complexes are ATP-dependent complexes that alter chromatin structure regulating genetic expression and various biological processes within cells. SWI/SNF complex subunits are frequently mutated in a wide range of human cancers (Shain and Pollack, 2013).

Aims: This project explores the mutational frequencies of SWI/SNF and non-SWI/SNF mutant colorectal carcinoma cell lines. Analysis of relative sensitivities of SWI/SNF and non-SWI/SNF mutant colorectal cancer cell lines to anticancer therapy, is also discussed (Forbes et al., 2015).

Methods & Results: Detailed database search has revealed that approximately 44% of the colorectal cancer cell lines are associated with SWI/SNF mutations with high co-mutation rates in both catalytic subunits (SMARCA2 & SMARCA4). SWI/SNF (26%) mutant colorectal cancer cell lines are more sensitive to anticancer therapy compared to non-SWI/SNF (16.7%) mutant cell lines. SNF2-N and bromodomain are the 2 most highly mutated domains in both catalytic subunits.

Discussion & Conclusion: The effect of high co-mutation rates in both catalytic subunits on survival of tumour cells is dependent the functional specificity of SWI/SNF complex and the subsequent impact of its loss in different cell types. Moreover, the increased drug sensitivity of SWI/SNF compared to non-SWI/SNF mutant cell lines, is deduced to be related to the association of SWI/SNF complexes with DNA repair proteins. Inactivating mutations in the remodelling complex would result in the loss of the repair proteins, affecting the efficiency of DNA repair mechanisms making it more sensitive to anticancer therapy. Recent research revealed that SNF2-N and Bromodomain inhibitors are considered as potential therapeutic targets in the treatment SMARCA4-mutant cancer cells due to their critical role maintaining SWI/SNF function (Vangamudi et al., 2015).

References:

• Forbes SA, Beare D, Gunasekaran P, Leung K, Bindal N, Boutselakis H, Ding M, Bamford S, Cole C, Ward S, Kok CY. COSMIC: exploring the world's knowledge of somatic mutations in human cancer. Nucleic acids research. 2015 Jan 28;43(D1):D805-11. Doi: 10.1093/nar/gku1075

• Shain AH, Pollack JR. The spectrum of SWI/SNF mutations, ubiquitous in human cancers. PloS one. 2013 Jan 23;8(1):e55119. Doi: 10.1371/journal.pone.0055119

• Vangamudi B, Paul TA, Shah PK, Kost-Alimova M, Nottebaum L, Shi X, Zhan Y, Leo E, Mahadeshwar HS, Protopopov A, Futreal A. The SMARCA2/4 ATPase Domain Surpasses the Bromodomain as a Drug Target in SWI/SNF-Mutant Cancers: Insights from cDNA Rescue and PFI-3 Inhibitor Studies. Cancer research. 2015 Sep 15;75(18):3865-78. Doi: 10.1158/0008-5472.CAN-14-3798

Application No. **ABSTR081**
Title The Limitations of the Use of the Sternocleidomastoid Muscle as a Reconstructive Flap
Presenting Author Larissa Jones, University of Leeds
Other Authors James Moor, Leeds General Infirmary and David Roberts, University of Leeds

Subsection Surgical Oncology
Consider for Poster & Oral

Contents

Background: Use of the sternocleidomastoid (SCM) muscle as a flap was introduced in 1908. Its efficacy has since been continually questioned. It has been used to treat a wide range of malignant defects. In the past decade, novel uses for the SCM flap have appeared in the literature and its usage has been re-evaluated. There are possible disadvantages in using SCM, including potential variable blood supply, oncological safety and viability with radiation treatment. The SCM also has many benefits as a flap and its versatility means it can challenge free-tissue flaps in certain circumstances.

Aims: To determine, in light of these questions and emerging research, the utility of the SCM reconstructive flap.

Methods: Review of the literature, particularly focusing on the past 15 years following the most recent review of 2001 (Kierner et al., 2001).

Results: Recent anatomic studies provide a clearer image of the blood supply of the SCM; there are concerns about use of the SCM flap with nodal involvement; post-operative radiation is not contra-indicated; complication rates between studies vary considerably.

Discussion: The SCM remains an easy to use flap, in a convenient location, with a shorter operating time required. The SCM should be considered as an alternative for free-tissue flaps when the patient cannot tolerate a long operating period, when other flap sites are unsuitable or when there is a lack of microvascular equipment.

Conclusions: Under certain conditions, the SCM flap could provide an option for those patients with very few other options for reconstruction available to them.

Reference:

1) Kierner, A.C., Zelenka, I. and Gstoettner, W. 2001. The Sternocleidomastoid FlapIts Indications and Limitations. The Laryngoscope. [Online]. 111(12),pp.2201–2204. [Accessed 3 April 2016]. Available from: http://doi.wiley.com/10.1097/00005537-200112000-00025.

Application No.	**ABSTR082**
Title	An audit of myelosuppression in patients with Glioblastoma brain tumours receiving chemoradiotherapy at The Christie
Presenting Author	Ryan Hemming, University of Manchester
Other Authors	Gillian Whitfield, The Christie
Subsection	Clinical Oncology
Consider for	Poster & Oral

Contents

Background: Standard post-operative treatment for Glioblastoma involves 6 weeks' radiotherapy with concurrent temozolomide chemotherapy , followed by 6 adjuvant temozolomide cycles. Side effects include neutropenia and thrombocytopenia.

Aims: This audit was undertaken to measure our haematological toxicity and identify predictors.

Methods: We analysed haematological parameters from our electronic records for patients with Glioblastoma treated with this regime. We used statistical tests to investigate whether myelosuppression was independent of gender, comorbidity score, performance status or age.

Results: 111 consecutive patients were included. Ninety-six patients (86.5%) completed six weeks of concurrent temozolomide. Fifteen were recent without adjuvant data; of the remainder, 79.2% (76/96) proceeded to adjuvant temozolomide.

Fifteen patients (13.5%) became thrombocytopenic (≤100x10^9/L) concurrently; of the eight proceeding to adjuvant temozolomide, seven (87.5%) experienced thrombocytopenia adjuvantly. Overall 31.6% became thrombocytopenic adjuvantly.

Ten patients (9.0%) became neutropenic ≤1.0x10^9/L concurrently; of the five proceeding to adjuvant temozolomide, none experienced neutropenia adjuvantly, but two became thrombocytopenic. Overall 2.6% became neutropenic adjuvantly.

Twelve patients received platelet transfusions. There were no clinically significant haemorrhages and one non-fatal neutropenic sepsis due to myelosuppression.

Univariate analyses showed no statistically significant association between clinical factors and myelosuppression.

Discussion: Concurrent thrombocytopenia predicted for platelets ≤100x10^9/L in the adjuvant phase, but not for platelets ≤50x10^9/L, probably due to appropriate temozolomide dose reductions. Concurrent neutropenia did not predict adjuvant neutropenia.

Conclusions: The adjuvant phase had a much higher incidence of thrombocytopenia, but less neutropenia. . Concurrent thrombocytopenia predicted for increased risk of adjuvant thrombocytopenia. Clincal factors did not predict myelosuppression.

Application No.	**ABSTR084**
Title	New Insights into the Prognosis and Treatment of Pancreatic Cancer
Presenting Author	Catherine Donnelly, University of Manchester
Other Authors	Mark Dunne, University of Manchester
Subsection	Clinical Oncology
Consider for	Poster & Oral

Contents

Background: Pancreatic cancer is the 5th most common cause of cancer-related death in the UK and USA. Lack of symptoms until the latter stages of cancer progression, along with poor screening, have led to a 5-year survival rate of less than 5%1. The cancer has often metastasized to the liver, peritoneum and lung before it is detected.

Aims: To identify molecular targets for earlier screening, diagnosis and treatment by expanding on the proposed multi-step model of progression from normal ductal epithelium to invasive pancreatic ductal adenocarcinoma (PDA) to include more recent research.

Methods: Academic journal databases, such as Ovid and MEDLINE, were searched for relevant clinical articles, using relevant key phrases. Each article for use was critiqued and selected according to its objectives, study design, research methods and potential biases.

Results: Fascin, a novel tumour marker seen in intermediate-late step of the multi-step model2, MUC4 and MUC5AC, seen at high frequencies in later stages of progression to PDA3, are promising markers for diagnosis, detectable in pancreatic juice obtained by endoscopic retrograde cholangiopancreatography (ERCP). Fascin may be particularly promising for treatment of low grade lesions.

Conclusion: Newly defined tumour markers may prove invaluable for diagnosis and treatment. However, the complexity and risks associated with ERCP renders it an inappropriate tool for screening. Less invasive, cheap and efficacious screening methods must now be developed in order to take advantage of recent discoveries and increase pancreatic survival rates.

References:

1. Arumugam, T., Ramachandran, V., et al. (2009) Epithelial to mesenchymal transition contributes to drug resistance in pancreatic cancer. Cancer Research (14): pg 5820-8.

doi: 10.1158/0008-5472.CAN-08-2819

2. Li, A., Morton, JP., et al. (2014) Fascin is regulated by slug, promotes progression of pancreatic cancer in mice, and is associated with patient outcomes. Gastroenterology (5): 1386-96. doi: 10.1053/j.gastro.2014.01.046.

3. Kim, GE., Bae, HI., et al. (2002) Aberrant expression of MUC5AC and MUC6 gastric mucins and sialyl Tn antigen in intraepithelial neoplasms of the pancreas. Gastroenterology (123): 1052–60.

Application No.	**ABSTR085**
Title	Anti-TNF Therapy in Established Lung Cancer - A Clinical Dilemma to Withdraw or Continue Treatment: A Report of Two Cases
Presenting Author	Ruairi Wilson, University of Glasgow
Other Authors	Noelle O'Rourke, Beatson West of Scotland
Subsection	Clinical Oncology
Consider for	Poster & Oral

Contents

A 72 year-old man with rheumatoid arthritis (RA) and a 50 pack-year history of smoking and a 63-year old man with RA and a 40 pack-year history of smoking both developed non-small cell lung cancer (NSCLC) in close succession. Previously, both patients had obtained clinical remission of their RA after starting anti-TNF therapies.

There have been concerns in using anti-TNF therapies, regarding the potential to cause malignancy; however evidence has consistently shown that there is no increased risk of developing solid tumours in RA patients on anti-TNF therapies. Despite this, little evidence is available to guide the decision to withdraw or continue anti-TNF therapy in patients with established solid tumours. Clinical trials have demonstrated safety in using anti-TNF therapies in cohorts of patients with established malignancy; however it remains unclear as to the effects of these anti-TNF therapies on tumour progression or regression.

Ultimately, in these two cases, clinical deterioration and worsening quality of life as a result of exacerbating symptoms of RA warranted a return to these patients' anti-TNF therapies, particularly once symptom control and quality of life became more important to these individual patients, after it became apparent that their chemotherapy had failed to halt tumour progression.

These two cases raise an interesting clinical question and pose a dilemma to the treating oncologist. It further provides a good example of striking the balance between optimising therapy while maintaining quality of life in the treatment of cancer.