Winning Abstracts from the Christie International Student Cancer Conference 2016

Introduction

In this edition of Anticancer Research, we present selected abstracts from the 6th International Student Cancer Conference held at the Christie School of Oncology, Manchester UK, on September 24th and 25th 2016. Emily Frinton, from the University of Manchester, UK, presented an updated evaluation of the melanoma-specific graded prognostic assessment (msGPA) since the clinical development of BRAF inhibitors, to a modern-day population of 48 patients with brain metastases from melanoma treated with radiotherapy. This study found that the msGPA still has prognostic utility and that incorporation of BRAF status may improve the prognostic utility of this approach. Jolanda Schoon, from the University of Sheffield, UK, presented an analysis of the effect of 12 single nucleotide polymorphisms in DNA damage repair genes (XRCC2 and XRCC3) on survival in 1,076 patients with metastatic colorectal cancer treated within the FOCUS clinical trial. This study found that an XRCC2 heterozygote and homozygote genotypes of SNP rs3218408 were associated improved survival in this group of patients. Finally, Sheba Macheka of the University of Newcastle, UK, presented the development of a novel immunofluorescent assay for the detection of circulating tumour cells (CTCs) from patients with hepatocellular carcinoma (HCC), exploiting the expression of the HCC specific marker asialoglycoprotein receptor-1 by CTCs. CTCs identified with this approach expressed both epithelial and mesenchymal markers. All the student presentations were of high quality and we anticipate the next International Student Cancer Conference will be equally successful.

ABSTR011
METASTATIC MELANOMA: PROGNOSTIC FACTORS AND SURVIVAL IN PATIENTS WITH BRAIN METASTASES

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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 (1). *Aims:* Validation of the msGPA and the role of SRS combined with other treatment *versus* WBRT alone. *Patients and 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 Conclusion:* 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.

1 Wilkins A, Furness A, Corbett RW, Bloomfield A, Porta N, Morris S, Ali Z, Larkin J and Harrington K: The melanoma-specific graded prognostic assessment does not adequately discriminate prognosis in a modern population with brain metastases from malignant melanoma. Br J Cancer *113(9)*: 1275-1281, 2015.
2 Dyer MA, Arvold ND, Chen YH, Pinnell NE, Mitin T, Lee EQ, Hodi FS, Ibrahim N, Weiss SE, Kelly PJ, Floyd SR, Mahadevan A and Alexander BM: The role of whole brain radiation therapy in the management of melanoma brain metastases. Radiat Oncol *9*: 143, 2014.

Key Words: Metastatic melanoma, prognostic factors, brain metastases.

ABSTR055
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

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Background: The FOCUS study aimed to determine the most effective use of chemotherapeutics Irinotecan and Oxaliplatin. The 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 with 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 1,076 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; P_{trend}=0.036. These effects remained significant after controlling for treatment group (P_{trend}=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.

Key Words: Fluorouracil, oxaliplatin, irinotecan, metastatic colorectal cancer.

ABSTR064
THE ISOLATION AND CHARACTERISATION OF CIRCULATING TUMOUR CELLS FROM PATIENTS WITH HEPATOCELLULAR CARCINOMA

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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 that may help 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. *Aims:* To detect CTCs in blood samples from patients with HCC, by targeting cells expressing ASGPR1 or Vimentin using imagestreamX flow cytometry. *Materials and Methods:* Blood samples were obtained from 8 consenting patients with HCC. Red blood cells and leucocytes were depleted, in order to enrich for CTCs. Following this, patient samples were stained with a panel of antibodies conjugated with fluorochromes, in order to identify Vimentin, Cytokeratin or ASGPR1 positive CTCs using ImagestreamX. Furthermore, CTC detection was based on additional parameters such as surface area (>200 μm^2), the absence of $CD45^+$ expression and a large nuclear content. *Results:* ASGPR1 and Cytokeratin were the most common biomarkers expressed by CTCs detected in 5 out of 8 of patients. A greater number of CTCs detected, expressed only vimentin compared to cytokeratin. This confirmed that CTCs down-regulated the expression of epithelial biomarkers such as cytokeratin, due to EMT. *Discussion:* We designed a novel sensitive panel of antibodies that detected biomarker positive CTCs which expressed ASGPR1, vimentin and cytokeratin from peripheral blood samples, using imagestreamX.

1 Dent BM, Ogle LF, O'Donnell RL, Hayes N, Malik U, Curtin NJ, Boddy AV, Plummer ER, Edmondson RJ, Reeves HL, May FEB and Jamieson D: High-resolution imaging for the detection and characterisation of circulating tumour cells from patients with oesophageal, hepatocellular, thyroid and ovarian cancers. Int J Cancer *138(1)*: 206-216, 2016.
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: Detection of Circulating Tumor Cells in Hepatocellular Carcinoma Using Antibodies against Asialoglycoprotein Receptor, Carbamoyl Phosphate Synthetase 1 and Pan-Cytokeratin'. PLoS ONE *9(4)*: e96185, 2014.
3 Ogle LF, Orr JG, Willoughby CE, Hutton C, McPherson S, Plummer R, Boddy AV, Curtin NJ, Jamieson D and Reeves HL: Imagestream detection and characterisation of circulating tumour cells – a liquid biopsy for Hepatocellular Carcinoma? J Hepatol *65(2)*: 305-313, 2016.

Key Words: Circulating tumour cells, hepatocellular carcinoma.

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