Winning Abstracts from the International Cancer Careers Conference 2015

Introduction: In this edition of Anticancer Research we are pleased to present selected abstracts from the International Cancer Careers Conference held at The Christie School of Oncology, Manchester UK, on September 19th 2015.

The highlights included the work of Federico Nichetti *et al*., from the Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, who presented data on the association between thrombophilia-related genetic polymorphisms and the incidence of thromboembolic events in 179 patients with metastatic colorectal cancer. These pilot data are significant as thrombosis is known to affect approximately 10% of cancer patients and improved risk stratification will enable for better patient selection for prophylactic anti-coagulation.

In addition, Bianca San Juan *et al*. from the University of Leeds, UK, presented their pre-clinical work evaluating dichloroacetate to exploit the Warburg effect to augment the effects of radiotherapy in colorectal cancer.

Finally, we report the work of Lucy Millar *et al*. from the University of Nottingham, UK, who carried out a clinical study evaluating the impact of the use of ultrasound assessment to evaluate response to endocrine therapy as a primary treatment for operable breast cancer. As ever, the standard of all student presentations was very high and we anticipate the 2016 meeting will be equally successful.

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ABSTR018
VARIANT ALLELES IN FACTOR V LEIDEN (FVL), PROTHROMBIN, PLASMINOGEN ACTIVATOR INHIBITOR-1 (PAI-1), METHYLENETETRAHYDROFOLATE REDUCTASE (MTHFR) AND RISK OF THROMBOEMBOLIC EVENTS (TEE) IN METASTATIC COLORECTAL CANCER (MCRC) PATIENTS

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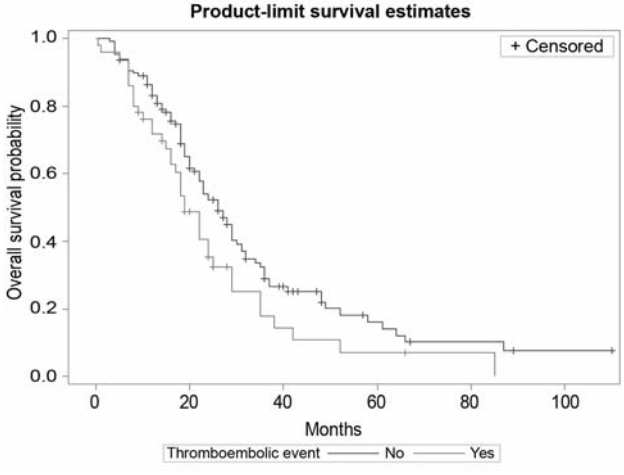
Background/Aim: TEE are a common complication in cancer patients, and represent the second cause of cancer-related deaths. The aim of this study was to analyze the effect of five thrombophilia-related polymorphisms on TEE's risk in a cohort of mCRC patients. *Patients and Methods:* 179 mCRC patients treated with first-line chemotherapy plus bevacizumab were included. The presence of mutations (Factor V Leiden G1691A, prothrombin G20210A) and polymorphisms (methylenetetrahydrofolate reductase [MTHFR] C677T and A1298C and plasminogen activator inhibitor [PAI-1] 4G/5G) was analyzed. *Results:* TEE occurred in 52 (29%) patients. FVL was found only in heterozygosis in 4 patients, and all developed TEE. TEE prevalence was higher in prothrombin G20210A carriers *vs*. non-carriers (71% *vs*. 27%; OR=6.65; 95%CI, 1.24-35.45; p=0.027), as well as in MTHFR C677T homozygous "TT" carriers *vs*. "TC"/"CC" (55% *vs*. 24%; OR=3.9; 95%CI, 1.71-8.87; p=0.001). MTHFR A1298C was not associated with TEE risk (p=0.445), while a trend was observed for the presence of PAI-1 "4G" allele (p=0.031). The multivariate analysis including age, sex, obesity and platelets count confirmed both MTHFR C677T and PAI-1 as significantly associated with TEE's risk (p=0.019 and p=0.038,



respectively). At an exploratory analysis, a median 7 months lower OS was observed in patients who developed TEE (p=0.031). *Conclusion:* Given the low prevalence of FVL and prothrombin G20210A as well as the preliminary association with TEE of MTHFR and PAI-1 in our series, larger studies are needed to validate our results. A prospective study on TEE prophylaxis in carriers of risk SNPs would be very useful.

ABSTR021
EVALUATION OF THE USE OF RADIOLOGICAL ASSESSMENT ALONGSIDE CLINICAL ASSESSMENT IN PATIENTS WITH OPERABLE PRIMARY BREAST CANCER RECEIVING PRIMARY ENDOCRINE THERAPY

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Background/Aim: Some patients with oestrogen receptor-positive operable primary breast cancer receive endocrine therapy as their primary treatment. In the Derby Breast Unit there is a Primary Endocrine Therapy Clinic where these patients are followed-up on a regular basis by clinical and radiological assessment. Currently the decision whether to continue or change treatment is based on the clinical assessment. This study aimed to evaluate whether ultrasound assessment could aid in treatment decisions. *Patients and Methods:* A retrospective review of 67 patients seen in the Clinic over a 12-month period with full information available was carried out. These patients were assessed at 3, 6, 9 and 12 months following initiation of endocrine therapy, using UICC criteria. Chi-squared tests were used to compare responses in terms of progression *versus* non-progression at these time points based on clinical and radiological assessments. *Results:* There was a statistically significant (p<0.001) correlation between both assessments at all time points. Similar significant correlations were also observed between clinical assessment at 9 months and ultrasound assessment at 6 months and between clinical assessment at 12 months and ultrasound assessments at 6 and 9 months. *Conclusion:* These results show that both forms of assessments correlate with one another and response status based on ultrasound assessment could pre-date that of clinical assessment by 3 to 6 months. This suggests that ultrasound assessment could pick up changes earlier and be used to guide treatment decisions. Further work is needed to delineate the clinical relevance of these findings.

ABSTR045
EFFECT OF LOWER DOSES OF DICHLOROACETATE IN COMBINATION WITH RADIOTHERAPY ON COLORECTAL CANCER CELL LINES

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Background/Aim: Neoadjuvant radiotherapy confers a well-established benefit in locoregional recurrence for patients with locally invasive rectal cancer. However, only around 50% experience significant down-staging of their tumour. Radiation-associated toxicity renders dose escalation unachievable. Dichloroacetate (DCA) is a generic drug shown to modify tumour metabolism reversing the Warburg effect and inducing apoptosis and may potentially enhance the effect of radiation. This study aimed to investigate the effects of DCA at lower doses in combination with radiotherapy on the survival of CRC cell lines, and any possible synergistic DNA damage. *Materials and Methods:* CRC cells (LoVo) and control cells (HEK 293) were treated with DCA (2, 5, 10 mM) and radiation (0, 4, 8 Gy). Influences of the combination treatment on cell survival were analyzed using MTT assays and clonogenic assays, while the induction of DNA damage was analyzed by quantifying gamma-H2AX foci. Statistical analyses were performed using GraphPad; differences between DCA-treated and vehicle control groups were assessed using the Mann-Whitney *U*-test. *Results:* DCA (5 mM) significantly reduced the survival of CRC cells in combination with 4 Gy and 8 Gy (p=0.0244, 0.0078, respectively). DCA (10 mM) significantly reduced survival of CRC cells in combination with 4 Gy and 8 Gy (p<0.0001, <0.0001, respectively). DCA (5 mM) significantly increased the mean number of DNA double-strand breaks (DSB) per CRC cell in combination with 4 Gy and 8 Gy (p=0.0041, 0.023, respectively). In unirradiated CRC cells, all the DCA doses (2, 5, 10 mM) significantly increased the mean number of DSB per CRC cell (p<0.0014). In the control cell line DCA (5, 10 mM) significantly increased the mean number of DSB per cell induced at 4 Gy (p<0.0001). *Conclusion:* Lower doses of DCA may have an additive killing effect in combination with radiation in CRC cells. A similar picture of sensitivity was seen in normal cells demonstrating that DCA is not completely harmless. Increasing doses of DCA associated with increased levels of DSB's in CRC cells and it may be a potential mechanism behind DCA. Further research is warranted exploring the mechanism behind the effects of DCA and as a potential adjunct in the management of rectal cancers.

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