

POSTER SESSION 13: Other topics (WIN Symposium related)

P13.1

The impact of clinicians' perceptions and experiences of lenvatinib for differentiated thyroid cancer on adherence

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Lenvatinib is an oral tyrosine kinase inhibitor used when differentiated thyroid cancer no longer responds to radioactive iodine treatment and continues to progress. Clinical trials have demonstrated that lenvatinib reduces tumour size in c. 65% of patients and increases median progression-free survival. The efficacy of lenvatinib, however, is significantly compromised by non-persistence when patients experience side effects at the start of treatment.

This study aimed to understand clinicians' experiences of managing patients on lenvatinib and the impact of their beliefs about lenvatinib on adherence to inform the development of a patient support programme which increases efficacy outcomes.

A focus group and five telephone interviews were conducted with clinicians which investigated their experiences prescribing lenvatinib; their patients' concerns and their thoughts around support materials. Clinicians did not consider adherence a problem because many patients have high necessity beliefs because lenvatinib is perceived as their last treatment option. Side effects were the main concern but clinicians assumed patients would raise these during consultations. They believed lenvatinib was effective but did not understand the rationale behind the recommended dose and adjusted it, or allowed medication breaks, in cases of severe side-effects. They thought family, carers and GPs play an important support role. Practical barriers included overwhelming patients with information and older patients accessing resources online. Clinicians' misconception that adherence is not an issue and patients will openly discuss side effects suggests a lack of effective communication. Clinicians should highlight to patients that side effects will diminish and the treatment will improve their quality of life. Clinicians need to be provided with clear scientific evidence for the recommended dose to convey the importance of adhering to it. Providing patients with access to clear information in the form of concise materials on disease, treatment, side effects and how to manage them is key to improving adherence. To improve adherence, patient support programmes must understand and address both practical and perceived barriers which are tailored to clinician and patients' needs.

P13.2

Individualised Molecular Profiling for Allocation to Clinical Trials (IMPACT) and Molecular Tumour Board- an Asian tertiary cancer centre

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Background: The primary aim of tumour molecular profiling (MP) is to identify clinically relevant genomic alterations that may be amenable to targeted therapeutics – either in the context of trials or existing approved agents. Here, we describe our single-centre multidisciplinary MP experience, culminating with a monthly molecular tumour board (MTB). We also describe the barriers to trial enrolment.

Methods: Following consent, archival or new tissue samples of patients (pts) with advanced cancers were obtained and submitted for testing. A panel of assays across multiple platforms were performed including immunohistochemistry (IHC), multiple allele specific PCR and mass spectrometry or targeted next generation sequencing (NGS) panels (29 gene and 143 genes). Results were discussed at monthly MTB (held from 5/13 to 4/17) and matched to available trials/therapeutics.

Results: A total of 738 samples were processed under IMPACT, involving 710 pts. Median age at consent was 58 (Range 18-83), 44% were female. Ethnic characteristics: Chinese (n=605, 82%), Malay (n=42, 6%), Indian (16, 2%) and others (75, 10%). Tumour types profiled: Lung (31%), Gastrointestinal including hepatobiliary (31%), Breast (11%) and others (27%). 34% of samples were fresh tissue biopsies. IHC was performed on 70% of samples, FISH on 23% and sequencing on 68%. 57% (n=417) of samples had actionable alterations. Common discovered mutations include: p53 mutant (n=236, 32%), EGFR (n=178, 24%), KRAS (n=96, 13%), PIK3CA (n=71, 10%). 58% (n=427) were found to be actionable.

6% (n=45) profiling events led to biomarker matched trial enrolment whilst 22% (n=161) were enrolled in other phase I trials without matched aberrations. 534 (72%) profiling events did not lead to trial enrolment. Common reasons include 38% (n = 201) when standard treatment was still effective, 19% (n = 100) progressive metastatic disease, 13% (n = 70) no trial slots available, 9% (n=47) pt declined MTB recommendations and 2% (n = 7) did not meet trial entry criteria.

Conclusions: It is feasible to perform MP and institute a MTB for allocation to trials. 6% of all MP events lead to enrolment onto molecularly matched trials. Pt education and timely application of broad, customized MP panels could improve clinical trials enrolment.

P13.3

Modulation of hepatic cancer stem cells markers following the induction of extrinsic apoptosis pathway by CD95: a preliminary study

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Background: Hepatocellular carcinoma (HCC) remains one of the lethal malignancies that have a poor prognosis and high recurrence rate. Although HCC is a heterogeneous disease, dysregulation of molecular profiling related to apoptosis also contributes to the disease progression. This study reports on a relevant function of CD95 death receptor that can induce apoptosis via modulation of apoptosis genes and cancer stem cell markers in HCC.

Materials and Methods: For the in vivo study, genes CD90, CD95, and CD95L from 47 samples (14 HCC, 9 peri-HCC, 13 cirrhosis, and 11 normal) from patients undergoing liver resection without any prior treatments were analyzed. For the in vitro study, HCC the human cell lines HepG2, JHH6, and HUH7 were used representing high to low basal CD95 expression. Apoptosis-induction was performed by using anti-CD95 (DX2) at a concentration of 250 ng/ml and 500 ng/ml for 24 hours. Flow cytometry and quantitative real-time PCR were performed to analyze the data.

Results: The expressions of CD95 and CD95 genes were highly variable in human tissues. A significant increase for CD95L was noticed in HCC as compared to normal tissues, as observed for CD90. After in vitro treatment of anti-CD95, genes TNF- α and TRAIL2R were upregulated in all cell lines in a dose-dependent manner, as well as pro-apoptotic gene Puma and BAX. Cancer stem cell marker CD24 was highly upregulated in HepG2 and to a lower extent in JHH6, while CD13 was slightly increased in all cell lines. There was a decrease of CD133 in HepG2 and no significant changes for EpCAM, CD44, and CD90.

Conclusions: We observed a modulation of apoptotic genes Puma, BAX, TNF- α , and TRAIL2R and cancer stem cell markers CD24, CD13, and CD133 after induction by CD95 antibody in acute phase treatment.

Keywords: Apoptosis, HCC, CD95, CSC, apoptotic genes

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