

**45P** Circulating tumour associated cells in esophageal cancers are resistance educated per previous chemo treatments

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**Background:** Innate and acquired chemoresistance to anticancer therapies are a well-known phenomenon in Esophageal Squamous Cell Carcinomas (ESCC). There are presently no viable approaches for real-time monitoring of resistance in ESCC. We used a novel method for chemo-interrogation (CI) by harvesting sufficient number of Circulating-Tumor Associated Cells (C-TACs) which are defined as apoptosis-resistant cells of tumorigenic origin and are positive for Epithelial Cell Adhesion Molecule (EpCAM) and pan-cytokeratins (pan-CK) irrespective of CD45 status.

**Methods:** Peripheral blood was collected from 80 patients with confirmed diagnosis of ESCC, among whom 52 were recently diagnosed therapy-naïve, while 28 were pre-treated patients. Peripheral blood mononuclear cells (PBMCs) were harvested by centrifugation and treated with commercially available stabilizing agents, by a proprietary protocol, to stabilize apoptosis resistant C-TACs. Surviving C-TACs were confirmed by immunostaining for EpCAM, pan-CK and CD45. Harvested C-TACs were treated in vitro with a panel of conventional cytotoxic anticancer agents and fraction of surviving cells were estimated to determine resistance profiles.

**Results:** Among the 52 cases of recently diagnosed therapy naïve ESCC, innate chemoresistance was observed towards platinum agents in 40.8% samples (unique patient-drug combinations), taxanes in 34.6% samples, topoisomerase inhibitors in 42.9% samples and antimetabolites in 34.6% samples. Among the 28 cases of previously treated ESCC, resistance towards previously administered systemic agents was observed in 87% of all samples, which included resistance towards platinum agents in 87.5% samples, taxanes in 82.1% samples, topoisomerase inhibitors in 100% samples and antimetabolites in 85.7% samples, respectively.

**Conclusions:** We show for the first time that sufficient C-TACs can be harvested for meaningful CI in newly diagnosed treatment naïve ESCC as well as refractory ESCCs. Post-treatment chemoresistance being an order of magnitude higher than the untreated cohort, indicates that C-TACs in ESCC are resistance-educated by previous treatments and can guide treatment strategy in ESCC.

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