102P Encyclopedic tumour analysis (ETA) guided combination regimens of hormone receptor antagonists with other systemic agents for treatment of refractory cancers

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Background: Hormone and Growth Factor Receptors (HR) such as ER, PR, HER2 and AR are involved in the pathogenesis of various cancers and are commonly targeted in treatment regimens. HR antagonists Standard of Care (SoC) are often administered as monotherapy or as combinations with selected cytotoxic or targeted agents. In the SHIVA trial, monotherapy with HR antagonists based on molecular profiling was reported with dismal outcomes. We hypothesized that Encyclopedic Tumor Analysis (ETA)-informed novel combinations of HR and synergistic cytotoxic or targeted agents could be efficacious in multiple cancers.

Methods: Molecular Profiling (MP) of patients' fresh tumor tissue interrogated gene alterations and differentially regulated metabolic pathways to identify molecular targets of approved anticancer agents in a label-agnostic manner. Immunohistochemistry (IHC) identified hormone receptors (HR) that could be targeted with endocrine agents. Chemoresistance and response (CRR) profiling of viable tumor derived cells (TDCs) identified functional vulnerabilities of the tumor against a panel of systemic anticancer agents. Molecular indications linked to ER, PR, HER2 and AR as well as IHC findings were linked to selection of HR antagonists. Synergistic integration of MP, IHC and CRR data (i.e., ETA) generated patient-specific drug priority lists with projected efficacy and safety. Patients who received such ETA-guided treatments were evaluated by PET-CT scans to determine treatment response.

Results: 37 patients underwent ETA from the study sponsor and received ETA-guided combination treatments of HR antagonists with other agents. PR was seen in 17 patients (ORR = 45.9%). 32 patients showed PR or SD at most recent follow-up (DCR = 86.5%) and progression was seen in 5 patients. Median PFS was 147 days (range 31 to 410). No significant therapy related adverse events were observed in any of these patients. Most patients reported stable to improved Quality of Life (QoL).

Conclusions: ETA-guided combination treatment regimens with HR antagonists offer a viable and efficient strategy in advanced refractory malignancies and outperform monotherapy options.

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