94P Encyclopedic tumour analysis guided treatments with conventional drugs outperform available alternatives in refractory cancers

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Background: Refractory cancers pose formidable management challenges. We hypothesized that such malignancies have unexplored vulnerabilities that can be identi-fied using Encyclopedic Tumor Analysis (ETA) and effectively targeted using conven-tional agents in a label- and organ-agnostic manner to yield treatment benefit. The pan-cancer RESILIENT trial addressed patients with advanced refractory malignancies who were treated with ETA guided treatments regimens without any restrictive eligibil-ity criteria.

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. Synergistic integration of MP, IHC and CRR datasets (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 as well as Objective Response Rate (ORR), Disease Control Rate (DCR) and Progression Free Survival (PFS).

Results: Among the 200 patients who were screened, 110 patients received ETA-guided treatments and were evaluable for response per protocol. PR was observed in 47 patients (ORR = 42.7%) and 99 patients continued to exhibit PR or SD at study termi-nation (DCR = 90%). Median PFS was 125 days. Median PFS rate at 90 days was 94.0%. No significant therapy related adverse events (AEs) were noted – there were no grade IV AEs or treatment related deaths. Most patients reported stable to improved Quality of Life (QoL) in terms of disease-related symptoms and functional status.

Conclusions: ETA-guided treatments offer meaningful survival benefits and outper-formed available alternatives including checkpoint inhibitors in this heavily pretreated pan-cancer population.

Legal entity responsible for the study: The authors.

Funding: Datar Cancer Genetics Limited.

Disclosure: D. Patil: Full / Part-time employment: Datar Cancer Genetics Limited. D. Akolkar: Full / Part-time employment: Datar Cancer Genetics Limited. V. Datta: Full / Part-time employment: Datar Cancer Genetics Limited. A. Ghaisas: Full / Part-time employment: Datar Cancer Genetics Limited. R. Patil: Full / Part-time employment: Datar Cancer Genetics Limited. H. Singh: Full / Part-time employment: Datar Cancer Genetics Limited. A. Srinivasan: Full / Part-time employment: Datar Cancer Genetics Limited. S. Apurwa: Full / Part-time employment: Datar Cancer Genetics Limited. R. Datar: Shareholder / Stockholder / Stock options, Licensing / Royalties, Officer / Board of Directors: Datar Cancer Genetics Limited. All other authors have declared no conflicts of interest.