PUBLICATIONS

Title

Encyclopedic Tumor Analysis Guided Personalized Treatments: A Paradigm Shift in Clinical Management of Advanced Refractory Cancers.

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ABSTRACT

Background : Standard of Care (SoC) systemic regimens have limited and diminishing efficacy in advanced refractory solid organ malignancies. Though checkpoint inhibitors are finding increased clinical application in such disease settings, their benefit is restricted to populations with qualifying molecular features such as PD-L1 expression or mismatch repair deficiency (dMMR). We hypothesized that integrative molecular and cellular investigations (Encyclopedic Tumor Analysis, ETA) can reveal unexplored vulnerabilities in such malignancies which can be effectively targeted using conventional agents in a label-free and organ-agnostic combinations. In the pan-cancer RESILIENT trial, patients with advanced refractory malignancies were recruited without any restrictive eligibility criteria and treated with ETA-guided personalized treatments.

Methods : Fresh tumor tissue was obtained from 200 patients and used for ETA, which included gene alterations and differential gene expression as well as *in vitro* chemoresistance and response (CRR) profiling of viable tumor derived cells (TDCs) against a panel of approved anti-tumor agents. Patient-specific combination regimens included agents selected on the basis of molecular indications and *in vitro* drug efficacy against TDCs. In patients who received ETA-guided treatments, treatment response was evaluated radiologically to determine Objective Response Rate (ORR), Disease Control Rate (DCR) and Progression Free Survival (PFS).

Results : Among the 143 patients who received ETA-recommendations, 126 were evaluable for response *per protocol*. PR was observed in 54 patients (ORR = 42.9%) and 114 patients continued to exhibit PR or SD at study termination (DCR = 90.5%). Median PFS was 134 days. Median PFS rate at 90 day was 93.9%. 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.

Conclusion : ETA-guided treatments offered meaningful pan-cancer ORR and PFS benefits in this heavily pretreated population and thus outperformed the clinical benefits reported for checkpoint inhibitors as well as other systemic treatment options.