enteral therapeutic Genomic alterations in Desmoplastic Small Round Tumor

Joanne Xiù1, Ajaz Bulbul1, Sadaf Rashad1, Andrea Hamrick2, Erik La Quaglia1, Lorraine S. Katz3, Phoenix, AZ; Kymera Independent Physicians, Carlsbad, NM; All Saints School of Medicine, Chicago, Department of Pediatric Surgical Oncology, University of Texas MD Anderson, USA.

Abstract

Background: Desmoplastic Small Round Cell Tumor (DSRCT) originates from a cell with multilineage potential. A molecular hallmark of DSRCT is the EWS-WT1 translocation. Ewing’s and DSRCT are treated similarly due to similar oncogene activation pathways and DSRCT has been represented in very limited numbers in sarcoma studies.

Methods: Thirty-five DSRCT tumors were tested with a multiplatform profiling service (Caris Life Sciences, Phoenix, AZ). Specific tests performed included sequencing (NextGen), protein expression (IHC) and gene amplification (CISH or FISH). Tumor mutational load was calculated as nonsynonymous missense mutations sequenced with a 592 gene panel. Molecular alterations were compared to 88 Ewing sarcomas (ES). Chi-square tests were used for comparison and statistical significance was determined as p < 0.05.

Results: In the 35 DSRCT tumors, high expression of TOP2A were seen in 63%, TOP3 in 63%, P63 in 62%, androgen receptor (AR) expression in 59% of AR positive tumors. Low expression of TUBB3 was seen in 44%, MGMT in 45%, T5 in 48%, RRM1 in 57% and ERCC1 in 76% of tumors. When compared to ES, no significant difference was seen among herceptin (Her2), ROS1, RAS, and ALK status. Among hormone receptors, androgen receptor shows the highest expression frequency. PD-L1 expression on tumor cells is absent in ES; PD-1 expression on TIL was seen in 25% tumors tested (2 of 8) and PD-L1 expression on TIL was seen in 32% (6 of 19) ES tumors. Among hormone receptors, androgen receptor shows the highest expression frequency. PD-L1 expression on tumor cells is absent in ES; PD-1 expression on TIL was seen in 25% tumors tested (2 of 8) and PD-L1 expression on TIL was seen in 32% (6 of 19) ES tumors.

Conclusions: We investigated 31 tumors of the extremely rare and highly aggressive tumors of DSRCT for molecular alterations. We identified high expression of topoisomerase expression including TOP2A and TOP1, high expression of androgen receptor expression as well as low expression of PD-L1 expression. This supports the use of topoisomerase inhibitors including anthracyclines and etoposide in DSRCT treatment. Induction neoadjuvant HD Alkylator and Anthracycline based chemotherapy followed by Maximal resection and consolidation with chemotherapy leads to better outcomes and is supported by biomarker data presented in the study. Our molecular results on PD-L1 expression and tumor mutational load analysis have important implications for therapeutic intervention in DSRCT, however the low patient number precludes a conclusion. Small molecular TKI's have shown clinical results so far and have not been represented in trials including Pazopanib approval in the PALETTE trial [7].

References