NEUROENDOCRINE PROSTATE CANCER (NEPC) IN PATIENTS (PTS) WITH METASTATIC CASTRATION RESISTANT PROSTATE CANCER (mCRPC) RESISTANT TO ABIRATERONE (ABI) OR ENZALUTAMIDE (ENZ): PRELIMINARY RESULTS FROM THE SU2C/PCF/AACR WEST COAST PROSTATE CANCER DREAM TEAM (WCDT)


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Aim: The mechanisms of resistance to androgen signaling inhibitors such as Abi or Enz are poorly understood. A growing proportion of these pts are developing treatment resistant NEPC. Progressive mCRPC has historically been challenging to biopsy and characterize on a molecular basis because of its bone tropism. As part of the WCDT project, which aims to identify genetic pathways underlying primary and acquired resistance to Abi and Enz, RNA sequencing (RNAseq) was used to develop a NEPC expression signature in mCRPC biopsies.

Methods: Following central radiologic review, eligible mCRPC pts underwent a metastasis (met) biopsy at one of 5 WCDT clinical sites, using a uniform biopsy protocol. Tissue was both frozen, and formalin fixed/paraffin embedded (FFPE). Frozen specimens underwent laser capture micro-dissection, RNA isolation, library preparation and RNAseq. Machine learning was used to derive NEPC markers from mCRPC adenocarcinoma and met NEPC RNAseq data. FFPE tissue was evaluated histologically, including NEPC markers.

Results: 85 of 300 planned mCRPC pts have undergone a met biopsy. To date, 53 specimens have been evaluated histologically. Histologically identified NEPC was present in 17 (32%) of biopsies overall, 12% of bone biopsies, 64% of lymph nodes, and 27% of liver biopsies. To date RNAseq data are available on 20 pts, including 6 with NEPC. A 106 gene signature for met NEPC was developed from this learning set.

Conclusions: Genomic sequencing and expression analysis can be accomplished in small bone and soft tissue mCRPC biopsies. The development of NEPC is a common event in mCRPC resistant to Abi or Enz. The majority of liver metastases are not NEPC. A 106 gene signature was derived from this met NEPC learning set and has identified a number of genes that provide insight into the biology and potential treatment of NEPC.

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