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late-breaking and deferred publication abstracts

LBA29 A phase 2 study of the aurora kinase A inhibitor alisertib for patients with neuroendocrine prostate cancer (NEPC)

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Background: NEPC is an aggressive androgen independent subtype of castration resistant prostate cancer. We previously showed that N-myc and Aurora A cooperate to drive the NEPC phenotype (Beltran et al, Cancer Discov 2011; Dardenne et al Cancer Cell in press). Targeting Aurora A with alisertib inhibits the allosteric interaction between Aurora A and N-myc and suppresses NEPC signaling and tumor growth in preclinical studies.

Methods: This is a multicenter Phase 2 study of alisertib 50mg BID x7d q21d for pts with metastatic prostate cancer and at least one: 1) NEPC morphology; 2) >50% NE marker IHC; 3) new liver metastases without PSA progression; 4) >3-5X serum NSE/CgA. Primary endpoint is 6-mo PFS, requiring 48 evaluable patients to detect > 30% PFS rate. Mandatory metastatic biopsy was assessed by whole exome/RNA-seq and pt-derived organoids were developed. Exploratory objectives are association of tumor molecular features and ctDNA with clinical features and response.

Results: 59 pts (41 (70%) pathologic criteria, 26 (44%) clinical) were treated. Median age was 67 yrs (45-87), median PSA 1.13 ng/ml (0.01-514.2), and # of prior therapies 4 (15% enza/abi, 30% docetaxel, 29% platinum). Metastatic sites were bone (78%,), lymph node (73%), lung (37%), and liver (61%). Of 56 evaluable pts, median PFS was 8.7 wks (8.0-10.4), 6 mo PFS 11.1% (16.3% for path NEPC; 5-31.6%), and median OS 38 wks (29.4-52.3). For those with scans SD/PR/CR at C3 (n = 17), median PFS was 20 wks (17-121) and 6 mo PFS was 35.8% (18.1% - 70.9%). Grade 3/4 toxicities identified in 5(9%) pts. 2 pts achieved exceptional response including complete resolution of liver metastases and a 3rd pt has stable disease at 39 mo follow-up. Correlation of molecular alterations (AURKA/MYCN, AR signaling, RB1/TP53) with clinicopathological features and characterization of exceptional responders including organoids will be presented.

Conclusions: A subset of patients with clinical/pathologically defined NEPC may benefit from single-agent alisertib. Integration of clinical, pathologic, and molecular features and characterization of exceptional response may improve patient selection. No new toxicity concerns were identified.

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