Conference Abstracts

Genomic characterization of patients (pts) with de-novo high-volume metastatic castration-sensitive prostate cancer (dn-hv-mCSPC) compared to those without dn-hv-mCSPC.

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BACKGROUND

Dn-hv-mCSPC have the poorest survival outcomes among various subsets pts with mCSPC (Fizazi, Lancet Oncol 2019). However, the molecular underpinnings behind the poor prognosis is not entirely understood. In this study, we aimed to assess the tumoral genomic characteristics in pts with dn-hv-mCSPC.

METHODS

In this IRB-approved study, patient-level data were collected retrospectively. Eligibility: patients with mCSPC with availability of tumor comprehensive genomic profiling (CGP) from a CLIA-certified lab before start of ADT. Clinically relevant genes previously reported to be associated with prognosis in metastatic prostate cancer were included: TP53, PTEN, RB1, BRCA2, CDK12, MYC, PIK3CA, SPOP, APC, CTNNB1, and, ATM. Variants of unknown significance and genomic aberrations present in < 5% pts were excluded. High-volume disease was defined per CHAARTED criteria. Genomic aberration prevalence was compared using a Chi-square test and was adjusted for false discovery (Benjamini-Hochberg).

RESULTS

304 pts were eligible: dn-hv-mCSPC (N = 100) vs non-dn-hv-mCSPC (N = 204); median age 67 vs 63 years, median PSA at baseline 35 vs 14 ng/mL, median Gleason score 9 vs 9, visceral metastases 15% vs 3%. 41% and 27% of pts had ≥2 mutations in the dn-hv-mCSPC and non-dn-hv-mCSPC respectively (P = 0.01). Overall, most commonly mutated genes were TP53, TMPRSS2, and PTEN. Pts with dn-hv-mCSPC had higher frequency of TP53 (P = 0.016) and BRCA2 (P = 0.05) mutations.

CONCLUSIONS

In this real-world patient population, dn-hv-mCSPC pts were shown to have a greater number of clinically relevant genomic aberrations. Detailed genomic landscape of these pts will be presented in the meeting. These hypotheses-generating data need external validation.