A clinically applicable strategy to concurrently profile prostate cancer (PCa) in circulation and bone using high-definition single cell analysis (HD-SCA)

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Introduction. The bone is the most appropriate organ site to characterize advanced PCa, but repeated bone biopsies are not feasible. Clinically relevant differences may exist between PCa clones in tissue and circulation, especially during therapy. To concurrently characterize tumor cells in blood (CTC) and bone in a clinically feasible manner, we adapted the HD-SCA platform to bone marrow aspirates (BMA).

Methods. Peripheral blood and BMAs were obtained from individual patients with biochemically recurrent (BRPC; n=52), metastatic hormone-naïve (mCSPC; n=26) and metastatic castration-resistant (mCRPC; n=63) PCa, before treatment or progressing on therapy. Eleven mCSPC and 59 mCRPC patients had bone metastasis. HD-SCA is a non-enrichment-based platform that allows for quantification of cell morphometry, protein expression and single cell genomic and proteomic analyses. Candidate tumor cells were defined as DAPI+/CK+/CD45-. Androgen receptor (AR) protein expression was also examined in single/clustered tumor cells. Clusters were defined as ≥2 tumor cells in direct contact, and their presence was correlated with survival outcomes. Whole genome copy number profiles (CNV) were obtained from single cancer cells.

Results. Tumor cells were detected in 26% mCSPC and 39% mCRPC BMAs, while all BMAs from BRPC patients were negative. BMA status was concordant with corresponding BM biopsies (per clinical pathology assessment), but detection in BMAs was 45% more sensitive. Tumor cell clusters were more frequent, abundant and bigger in BMAs than in blood, expressed higher levels of AR per tumor cell, and were prognostic in mCRPC (both for progression-free and overall survival). Analysis of CNV profiles revealed distinct clonal patterns and distribution in BMA/blood from 3 patients with tumor cells present in both compartments.

Conclusions. Our strategy allows for concurrent high-content profiling of CTCs and bone metastatic deposits in PCa patients. The simultaneous evaluation of the two liquid compartments resulted in novel insights into the prevalence and clinical significance of tumor cell clusters and clonal heterogeneity in advanced disease.

Conflict of Interest. None.

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