Prostate cancer (PC) and homologous recombination repair genes mutations (HRRm): a retrospective, monocentric, observational study aimed at recording histopathological and clinical data and their associations with oncological outcomes.

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Objective:

This study aimed to evaluate histopathological and baseline clinical characteristics in PC patients with HRRm, their prevalence, and clinical outcomes.

Methods:

From 2019 to 2023, we screened 400 patients with metastatic PC for HRR alterations. HRRm were identified using archival primary or metastatic tumor samples and/or circulating tumor DNA (ctDNA). We retrospectively analysed clinical and tumor characteristics in 45 patients with HRRm, recording histopathological and clinical data and their association with Progression-Free Survival (PFS) in metastatic hormone-sensitive PC (mHSPC) setting as oncological outcome

Results:

Out of the 400 screened patients, 45 (11%) had at least one mutation, with BRCA2 being the most commonly altered gene (46.7%), followed by BRCA1 (11.1%) and ATM (11.1%). Other rare HRRm were found in 5 patients (11.1%). Median age was 70 years. HRRm were associated with poorly differentiated PC: about 72% of patients had Gleason score = 8 and, among these, 22.7% had a Gleason score of 10. 58% of patients had metastatic disease at diagnosis, with 40% having High Volume disease. The most common sites of metastasis were bones and lymph nodes, with only 13% having visceral metastasis. In patients with non-metastatic disease at diagnosis, advanced stage (T3-T4) and nodal involvement were frequent, 53% and 35% respectively. 43 patients received medical treatment for mHSPC with androgen deprivation therapy (ADT) alone (37.8%), ADT plus androgen receptor targeting agents (42.2%), or ADT plus chemotherapy (15.5%). 29 patients had disease progression with a median PFS of 16.8 months, regardless of the therapy.

Conclusions:

PC with HRRm had more frequently Gleason ≥ 8, T3/T4 stage, nodal involvement, and metastases at diagnosis, confirming the need to early search for mutations in patients with advanced disease and these characteristics. mHSPC patients had significantly lower PFS compared to the literature, with a median PFS of 16.8 months, suggesting HRRm disease could have worse prognosis. These data support the need for tailoring a specific clinical management of these patients.

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