A New Prognostic Model of Overall Survival (OS) in Patients (pts) with Metastatic Hormone Sensitive Prostate Cancer (mHSPC)

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Background
Research on prognostic factors in patients with metastatic hormone-sensitive prostate cancer (mHSPC) remains limited. Previous studies have identified disease volume and metastatic diagnosis status as key indicators of overall survival (OS). This study aimed to develop and validate a prognostic model for OS specifically in de novo mHSPC patients.

Methods
Data were pooled from four randomized phase III trials comparing androgen deprivation therapy (ADT) alone to ADT plus docetaxel. OS was defined as the time from randomization to death or last follow-up. Variables considered in the analysis included age, ECOG performance status (PS), Gleason score, metastatic site, number of bone metastases, opioid use, disease volume, M1 metastatic diagnosis, hemoglobin, albumin, PSA, and alkaline phosphatase. Multiple imputation was applied for missing data. The model was developed using proportional hazards modeling with data from the CHAARTED and GETUG-15 trials. Validation was performed using two comparisons from the STAMPEDE trial: ADT vs. ADT + docetaxel (A vs. C) and ADT vs. ADT + zoledronic acid + docetaxel (A vs. E). Model discrimination was assessed using the time-dependent area under the ROC curve (tAUC).

Results
The analysis included 2,234 patients, of whom 1,419 died, with a median follow-up of 72.6 months. The median age was 64.6 years; 71.2% of patients had an ECOG PS of 0, and 63.3% had high disease volume. Key prognostic factors for OS were disease volume, PS, alkaline phosphatase, and hemoglobin. Patients with high disease volume had a hazard ratio of 1.86 (95% CI: 1.49-2.33) compared to those with low disease volume. The tAUCs for the STAMPEDE comparisons (A vs. C, A vs. E) and in the control arm (ADT) were 0.72 (95% CI: 0.69-0.76), 0.70 (95% CI: 0.67-0.72), and 0.72 (95% CI: 0.69-0.76), respectively. Median OS in low-, intermediate-, and poor -risk groups was 75.5 months (95% CI: 69.3-82.2), 40.4 months (95% CI: 36.9-43.7), and 29.1 months (95% CI: 24.1-34.4), respectively.

Conclusions
High disease volume was identified as the most important prognostic factor for OS in de novo mHSPC patients. While the model demonstrated moderate discriminative ability, its applicability is limited to de novo mHSPC. Three distinct prognostic risk groups were identified. External validation in contemporary patients treated with ADT and androgen receptor pathway inhibitors (ARPI) is needed.

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