External validation of a digital pathology-based multimodal artificial intelligence (MMAI)-derived model in high-risk localized (M0)/metastatic (M1) prostate cancer (PCa) starting androgen deprivation therapy (ADT) in the docetaxel (Doc) or abiraterone (AAP) phase III STAMPEDE trials

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Background
Effective prognostication will allow better targeting of treatment (Rx) combinations for advanced PCa. A MMAI prognostic test (ArteraAI Prostate) was recently developed in localized PCa. We aimed to validate ArteraAI in advanced PCa using final data from 3 STAMPEDE trials (NCT00268476).

Methods
The MMAI model used digitized whole scan images from new H&E core prostate biopsies (PB), local Gleason score (GS), tumor stage (T), age and pre-ADT serum PSA. Fine-Gray/Cox regression adjusted for Rx allocation and cumulative incidence analyses were performed to evaluate associations with endpoints, as defined in STAMPEDE, for both continuous score (per standard deviation increase) and categorical (quartile, Q). PCa-specific mortality (PCSM) was the endpoint of primary interest. Death not from PCa was treated as a competing risk. HR, 95% CI, and p<0.001 (denoted by *) are reported.

Results
Of 3879 patients recruited Oct 2005 – Jan 2014 to ADT +/- radiotherapy (RT) alone or + Doc +/- zoledronic acid or + AAP, 3725 consented to tissue analysis, 2079 had H&E with sufficient tumor of which 1964 had all of GS, T, pre-ADT PSA (918 M0, 1046 M1, median follow-up: 7.8 years, yr). ArteraAI was strongly associated with PCSM (HR 1.67, 1.5-1.84*), overall survival (1.51, 1.4-1.63*), failure-free survival (1.48, 1.38-1.59*), and metastatic progression-free survival (1.59, 1.46-1.73*). ArteraAI Q4 v Q1-3 showed similar results for all endpoints, including PCSM (2.27, 1.95-2.65*). Of component clinical variables, p* for PCSM were PSA Q4 v Q1-3 (1.8, 1.54-2.11), Gleason 8-10 v <=7 (1.64, 1.36-1.98), and T4 v T1-2 (1.77, 1.36-2.32). ArteraAI Q4 v Q1-3 had more PCSM events at 5 yr: 16% (11-21) v 6% (4-8) in M0, 58% (52-64) v 40% (36-43) in M1 and notably for M0 treated with ADT +/- RT+ AAP: 18% (9-28) v 2% (0-4%).

Conclusions
ArteraAI successfully validated in STAMPEDE with stronger prognostic associations than individual clinical variables. The MMAI model identified poor prognostic features in PB from high-risk M0 and M1 PCa.

Clinical trial identification
NCT00268476.

Legal entity responsible for the study
University College London (UCL) - Professor Gerhardt Attard.

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Disclosure

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