

Abiraterone acetate plus prednisolone (AAP) with or without enzalutamide (ENZ) added to androgen deprivation therapy (ADT) compared to ADT alone for men with high-risk nonmetastatic (M0) prostate cancer (PCa): Combined analysis from two comparisons in the STAMPEDE platform protocol

Background: Patients (pts) with high-risk M0 PCa are treated with ADT and when indicated, local radiotherapy (RT). Intensifying hormone treatment with AAP, ENZ or apalutamide continuous to progression improves outcomes of metastatic PCa but its efficacy in M0 PCa starting ADT is unknown.

Methods: STAMPEDE is a multi-arm, multi-stage trial that, as part of 2 separate comparisons randomised PCa pts with M0 node positive or high-risk node negative (>1 T3/4, PSA >40ng/ml, Gleason 8-10 or relapsing) 1:1 to ADT (control) vs ADT with AAP (1000mg AA + 5mg P od) or ADT vs ADT with AAP + ENZ (160mg od) for 2 years (y), unless RT was omitted when treatment could be to progression. The primary end-point was metastasis-free survival (MFS, time to death or distant metastases). The sub-group of pts who received ADT +/- AAP was partially reported with metastatic pts in 2017 so one-sided type 1 error rate was set to 1.25%. All analyses were pre-specified, pooled using meta-analyses methods and stratified as described previously. Data frozen 3rd August 2021. Results: 1974 M0 pts at 113 sites in UK & Switzerland were randomised, 914 (Nov 2011 to Jan 2014) to ADT +/- AAP & 1060 (Mar 2016 to Jul 2014) to ADT +/- AAP + ENZ. Groups were well balanced: median age 68 y, range 43-86; median PSA 34 ng/ml, range 0.4-2773; Gleason 8-10, 79%; node positive 39%; planned for RT 85%. Median months to stopping AAP, 23.7 (IQR: 17.6-24.1); AAP when given with ENZ, 20.7 (IQR: 4.4-24); ENZ, 23.2 (IQR: 6.3-24). 180 MFS events occurred in the research group and 306 in the control group. AAP-based therapy improved MFS (HR 0.53, 95% CI 0.44-0.64, P.2.9 10- 11) & survival (HR 0.60, 95% CI 0.48-0.73, P.9.3 10-7): 6-y MFS from 69% to 82%, 6-y survival from 77% to 86%. Treatment effect was consistent in major subgroups and between AAP & AAP + ENZ randomisation periods (MFS HR.0.54, 95% CI 0.43-0.68; HR.0.53, 95% CI 0.39-0.71 respectively; interaction HR . 1.02, 95% CI: 0.70-1.50, p.0.908).

Conclusions: 2 y of AAP-based therapy significantly improves MFS & survival of high risk M0 PCa starting ADT and should be considered a new standard of care.

Clinical trial identification: NCT00268476.