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Comparison of abiraterone acetate and prednisolone (AAP) or combination enzalutamide (ENZ) + AAP for metastatic hormone sensitive prostate cancer (mHSPC) starting androgen deprivation therapy (ADT): Overall survival (OS) results of 2 randomised phase III trials from the STAMPEDE protocol


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Background
AAP or ENZ added to ADT improves outcomes for mHSPC. Any benefit of combining ENZ & AAP in this disease setting is uncertain.

Methods
STAMPEDE is a multi-arm, multi-stage (MAMS), platform protocol conducted at 117 sites in the UK & Switzerland. 2 trials with no overlapping controls randomised mHSPC patients (pts) 1:1 to ADT +/- AAP (1000mg od AA + 5mg od P) or AAP + ENZ (160mg od). Treatment was continued to progression. From Jan 2016 docetaxel 75mg/m 2 3-weekly with P 10mg od was permitted + ADT. Using meta-analysis methods, we tested for evidence of a difference in OS and secondary outcomes (as described previously: failure-free, metastatic progression-free, progression-free & prostate cancer specific survival) across the 2 trials using data frozen 3 Jul 2022. All confidence intervals (CI) 95%. Restricted mean survival times (RMST) restricted to 84 months (m).

Results
Between Nov 2011 & Jan 2014, 1003 pts were randomised ADT +/- AAP & between Jul 2014 & Mar 2016, 916 pts were randomised ADT +/- AAP + ENZ. Randomised groups were well balanced across both trials. Pt cohort: age, median 68 years (yr), IQR 63, 72; PSA prior to ADT, median 95.7 ng/ml, IQR 26.5, 346; de novo 94%, relapsed after radical treatment, 6%. In AAP + ENZ trial, 9% had docetaxel + ADT. OS benefit in AAP + ENZ trial, HR 0.65 (CI 0.55 - 0.77) p = 1.4×10^-6; in AAP trial, HR 0.62 (0.53, 0.73) p = 1.6×10^-9. No evidence of a difference in treatment effect (interaction HR 1.05 CI 0.83–1.32, p = 0.71) or between-trial heterogeneity (I^2 p = 0.70). Same for secondary end-points. % (CI) of pts reporting grade 3-5 toxicity in 1st 5 yr: AAP trial, ADT: 38.5 (34.2-42.8), + AAP: 54.4 (50.0-58.8); AAP + ENZ trial, ADT: 45.2 (40.6 - 49.8), + AAP + ENZ: 67.9 (63.5 – 72.2); most frequently increased with AAP or AAP + ENZ = liver derangement, hypertension. At 7 yr in AAP trial (median follow-up: 95.8m), % (CI) pts alive with ADT: 30 (26, 34) versus with ADT + AAP: 48 (43, 52); RMST: ADT: 50.4m, ADT + AAP: 60.6m, p = 6.6 x 10^-5.

Conclusions
ENZ + AAP need not be combined for mHSPC. Clinically important improvements in OS when adding AAP to ADT are maintained at 7 yr.

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NCT00268476.

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Disclosure


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