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# A phase III trial with a 2x2 factorial design in men with de novo metastatic castration-sensitive prostate cancer: Overall survival with abiraterone acetate plus prednisone in PEACE-1

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### Background

Since 2015, combining androgen deprivation therapy (ADT) with either docetaxel, androgen signaling inhibitors (ASI), or radiotherapy to the primary tumor (RXT) (for low metastatic burden) was shown to improve overall survival (OS) and has thus become the new standard of care (SOC) in men with mCSPC. It is unknown whether combining those treatments on top of ADT could further increment outcomes. PEACE-1 is a phase 3 trial with a 2x2 factorial design of abiraterone acetate plus prednisone (abiraterone) and/or local radiotherapy. First results show that adding abiraterone to ADT+docetaxel significantly improves rPFS in men with mCSPC (HR: 0.50 (0.40-0.62), p<0.0001) (Fizazi, ASCO 2021).

### Methods

1173 men (57% high-, 43% low-volume) with *de novo* mCSPC were randomized to SOC, SOC+abiraterone, SOC+RXT or SOC+abiraterone+RXT (SOC was ADT+docetaxel for 710 pts). The overall type I error testing the abiraterone effect was 5% (4.9% for OS, 0.1% for rPFS). In the ADT+docetaxel population, 249 events were required to detect an HR of 0.70 for OS with 80% power.

### Results

The median follow-up is 4.4 yrs (n=273 death events in the ADT+docetaxel population). The effect of abiraterone on OS did not interact with the one of RXT (p=0.82) allowing to pool the abiraterone arms together for comparison. OS was improved by abiraterone both in the overall population (HR: 0.83, 95% CI: 0.69-0.99, p=0.034; medians: 5.7 vs 4.7 yrs) and in the ADT+docetaxel population (HR: 0.75, 95% CI: 0.59-0.96, p=0.021; medians: NR vs 4.4 yrs). Among the ADT+docetaxel pts who developed CRPC, 231/263 (88%) then received at least one life-prolonging therapy and 222/263 (84%) at least one ASI in the control arm, compared to 110/141 (78%) and 67/141 (48%) in the abiraterone arm, respectively. Grade 3-5 adverse events reported in >5% of pts in the ADT+docetaxel population included neutropenic fever (5% vs 5%), neutropenia (10% vs 9%), liver toxicity (6% vs 1%) and hypertension (21% vs 13%) in the abiraterone and control arms, respectively.

### Conclusions

Adding abiraterone to ADT plus docetaxel improves both rPFS and OS in mCSPC men, even when 84% of mCRPC men from the control arm receive an ASI.

### Clinical trial identification

NCT01957436.

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