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Perioperative apalutamide (APA) plus androgen-deprivation therapy (ADT) with radical prostatectomy plus pelvic lymph node dissection (RP + PLND) vs RP + PLND alone in patients (pts) with high-risk localized or locally advanced prostate cancer (HR LPC/LAPC): PROTEUS substudy

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Background

Radical prostatectomy (RP) is a standard of care (SOC) with curative intent for HR LPC/LAPC. In the blinded PROTEUS main study, 1 y perioperative APA + ADT vs placebo + ADT significantly improved the dual primary end points of pathological response and metastasis-free survival (MFS) following RP + PLND in pts with HR LPC/LAPC. Because the PROTEUS main study did not include an immediate RP control arm, this prespecified substudy compared perioperative APA + ADT vs immediate RP + PLND (henceforth RP alone).

Methods

Pts with M0 HR LPC/LAPC who were candidates for RP were randomized 1:3 to open-label APA (240 mg/d) + ADT for 6 cycles before and after RP vs RP alone. Primary end point was event-free survival (EFS), defined as time to first event of biochemical failure, local/regional recurrence, distant metastasis, or death. Secondary/exploratory end points were consistent with the PROTEUS main study.

Results

Of 408 randomized pts (perioperative APA + ADT [102] or RP alone [306]), median (range) age was 66.0 (45-84) y; PSA, 14.1 (1.4-422.6) ng/mL; GS ≥8, 97.1%; cT3/cT4, 28.7%; cN1, 7.1%; median follow-up was 37.8 mo. The primary end point was met: median EFS not reached (APA + ADT) vs 19.1 mo (RP alone); HR 0.38 (95% CI 0.26-0.55; p<0.0001). MFS by conventional or PSMA PET imaging favored APA + ADT (HR 0.49; 95% CI 0.26-0.90). Rates of subsequent therapy (tx) at 3 y were 35% (APA + ADT) vs 68% (RP alone). Risk of needing subsequent tx was reduced by 71% with APA + ADT (HR 0.29; 95% CI 0.20-0.43); rates of adjuvant and salvage radiotherapy were 3.9% and 15.7% (APA + ADT) vs 14.4% and 27.8% (RP alone). Grade 3/4 adverse events were 30.7% (APA + ADT) vs 21.7% (RP alone).

Conclusions

Perioperative APA + ADT significantly improved EFS, MFS, and time to subsequent tx vs RP alone. These results reinforce the clinical benefit of perioperative APA + ADT, with 62% lower risk of recurrence or death, 51% lower risk of metastasis or death, and approximately 50% fewer pts needing subsequent tx at 3 y. By providing a direct comparison with RP alone, this substudy supports perioperative APA + ADT as a tx of choice for HR LPC/LAPC.

Clinical trial identification

NCT03767244.

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Legal entity responsible for the study

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Disclosure

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