TPS5131 Poster Session

Darolutamide plus androgen deprivation therapy (ADT) in patients with high-risk biochemical recurrence (BCR) of prostate cancer: A phase 3, randomized, double-blind, placebo-controlled study (ARASTEP).

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Background: Patients with prostate cancer treated with radiotherapy (RT) or radical prostatectomy (RP) as primary therapy may develop BCR – a prostate-specific antigen (PSA) increase with no evidence of metastases on conventional imaging (e.g. magnetic resonance imaging/computed tomography). Prostate-specific membrane antigen positron emission tomography/computed tomography (PSMA PET/CT) is more sensitive than conventional imaging and may detect lesions in patients with BCR that conventional imaging cannot. BCR is an indicator of disease progression and warrants effective treatment to delay further progression, particularly if lesions are detected by PSMA PET/CT. The androgen receptor inhibitor darolutamide is structurally different by design to deliver robust clinical efficacy with a differentiated tolerability profile. In the phase 3 ARAMIS trial, darolutamide significantly improved metastasis-free survival (MFS) and overall survival (OS) in patients with nonmetastatic castration-resistant prostate cancer (nmCRPC). ARASTEP is a phase 3 trial (NCT05794906) evaluating whether darolutamide plus ADT improves radiological progression-free survival (rPFS) by PSMA PET/CT vs placebo plus ADT in patients with high-risk BCR and PSMA PET/CT-positive lesions following primary therapy. **Methods:** Key eligibility criteria included: prior primary RT or RP ± adjuvant RT (ART) or salvage RT (SRT), with high-risk BCR (PSA doubling time [PSADT] <12 months and PSA ≥0.2 ng/mL after primary RP [± ART/SRT] or PSA ≥2 ng/mL above nadir after primary RT only), ≥1 PSMA PET/CT-positive prostate cancer lesion with no visible lesions on conventional imaging, and serum testosterone ≥150 ng/dL. ARASTEP is planned for 750 patients from 23 countries to be randomized 1:1 to oral darolutamide 600 mg twice daily or placebo, both with ADT, for 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent. During the 24-month treatment period, patients will be monitored for safety every 12 weeks, and every 24 weeks for PSMA PET/CT and conventional imaging events. After 24 months, patients with PSA values ≥0.2 ng/mL will continue study treatment as part of active follow-up until PSMA PET/CT progression is confirmed by blinded independent central review (BICR), followed by long-term follow-up for conventional imaging progression. Patient stratification factors are PSADT (<6 vs ≥6–<12 months), intent to treat baseline PSMA PET/CT lesions with image-guided RT/surgery (Yes vs No), and distant ± locoregional vs locoregional-only lesions. The primary endpoint is rPFS by PSMA PET/CT assessed by BICR. Secondary endpoints include MFS on conventional imaging by BICR, time to CRPC, OS, quality of life, and safety. As of January 2025, 458 patients have been randomized from 220 sites. Clinical trial information: NCT05794906. Research Sponsor: Bayer.