TPS5119 Poster Session

A phase 3 trial of the androgen receptor ligand-directed degrader, BMS-986365, versus investigator's choice in patients with metastatic castration-resistant prostate cancer (CA071-1000 - rechARge).

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Background: Prostate cancer relies on the androgen receptor (AR) pathway as a key oncogenic driver. BMS-986365 is a heterobifunctional, orally bioavailable ligand-directed degrader targeting the AR via a first-in-class dual mechanism of AR degradation and antagonism. Results from the first-in-human phase 1 study showed that BMS-986365 was well tolerated with a manageable safety profile and demonstrated antitumor activity in heavily pretreated patients with metastatic castration resistant prostate cancer (mCRPC) regardless of AR gene alterations (Rathkopf et al. *Ann Oncol* 2025;36:76–88). Here, we present the study design of rechARge (NCT06764485), a phase 3, 2-part, randomized, open-label trial evaluating the efficacy and safety of BMS-986365 versus investigator's choice of AR pathway inhibitor (ARPI) or docetaxel, in patients with mCRPC who have failed treatment with 1 prior ARPI. **Methods:** Approximately 960 patients will be randomized in this phase 3, 2-part study. In Part 1 (dose selection), patients will be randomized 1:1:1 to receive either BMS-986365 400 or 300 mg BID Q28D, or investigator's choice comprising ARPI (enzalutamide [160 mg QD] or abiraterone [1000 mg QD + prednisone] Q28D); or docetaxel 75 mg/m^2 + prednisone Q21D up to a maximum of 10 cycles. In Part 2, patients will be randomized 1:1 to receive either BMS-986365 (dose determined from Part 1) or investigator's choice treatment (same as Part 1). Randomization is stratified by prior type of ARPI and investigator's choice (2nd ARPI vs docetaxel). Patients will be treated until radiographic progressive disease by blinded independent central review (BICR) or unacceptable toxicity; all patients must continue androgen deprivation therapy as part of the standard of care. Key inclusion criteria include no more than 1 previous ARPI, confirmed progressive mCRPC defined by having ≥1 of the following: prostate-specific antigen (PSA) progression or radiographic disease progression in soft tissue based on RECIST 1.1 criteria or bone defined as the appearance of ≥2 new lesions on a bone scan; ECOG PS of 0–1, asymptomatic or mildly symptomatic from prostate cancer (Brief Pain Inventory-Short Form, worst pain in last 24 hr <4), no liver metastases, and no prior chemotherapy in the mCRPC setting (docetaxel permitted for mCSPC if >12 months since completion). The primary endpoint is radiographic progression-free survival by BICR using RECIST 1.1 (soft tissue) and PCWG3 (bone) criteria. The key secondary endpoint is overall survival. Other secondary endpoints include safety, overall response rate, confirmed PSA response rate (PSA30 and PSA50), and patient reported outcomes. The study is recruiting at 230 sites in 24 countries/territories across North America, Europe, Latin America, and East Asia. Clinical trial information: NCT06764485. Research Sponsor: Bristol Myers Squibb.