TPS5111 Poster Session

Phase 1, open-label, first-in-human study of ABBV-969, a dual variable antibody-drug conjugate, in patients with metastatic castration-resistant prostate cancer.

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Background: Metastatic castration-resistant prostate cancer (mCRPC) is an incurable disease with high unmet need. Six-transmembrane epithelial antigen of prostate 1 (STEAP1) is highly enriched in > 85% of prostate cancer (PC),[1] and prostate-specific membrane antigen (PSMA) expression is > 100-fold higher in patients (pts) with mCRPC.[2] These are well-established and actionable targets in mCRPC. ABBV-969, a dual variable domain IgG1 drug conjugate, targets STEAP1 and PSMA and includes a topoisomerase-1 inhibitor (Top1i) payload. Based on preclinical data, ABBV-969 is expected to have greater efficacy and wider activity than targeting either antigen alone. We describe a first-in-human study of ABBV-969 in pts with mCRPC. **Methods:** This phase 1 open-label study (NCT06318273) of ABBV-969 monotherapy evaluates safety, pharmacokinetics (PK), pharmacodynamics (PD), and efficacy. Eligible pts, ≥ 18 years of age, have mCRPC treated with and progressed on ≥ 1 prior novel hormonal agent for mPC/CRPC and ≥ 1 taxane for PC (or have refused, are intolerant to, or unable to access taxanes). Pts must have a life expectancy > 6 months, serum testosterone levels ≤ 50 ng/dL, ≥ 1 metastatic lesion at baseline, and serum prostate-specific antigen (PSA) levels ≥ 1.0 ng/mL. Part 1 (dose escalation) of the study will enroll up to ~80 pts and is guided by the Bayesian optimal interval design primarily based on the dose-limiting toxicity rate. Part 2 (dose expansion) will randomize up to 60 pts in 2 (1:1) or 3 (1:1:1) dose levels (determined in part 1). Part 1 will enroll pts in US, Israel, Japan, and Australia with Canada, France, and Spain added in part 2. Optimal (recommended phase 2) dose will be determined by the totality of PK, PD, safety, and efficacy data. Pts will receive intravenous ABBV-969 until disease progression, intolerable toxicity, or other study discontinuation criteria are met. The study objectives and endpoints are shown in the Table. 1. Xu M, et al. Cancers 2022;14:4034. 2. Sweat SD, et al. Urology 1998;52:637–40. Clinical trial information: NCT06318273. Research Sponsor: AbbVie Inc.

Objectives and endpoints.

Objective	Endpoint
Primary	
Safety and tolerability	Adverse events and dose-limiting toxicities Clinical laboratory parameters, vital signs, ECG
Secondary	
Preliminary efficacy	**Primary** ≥ 50% prostate-specific antigen (PSA) decrease from baseline **Secondary** Confirmed complete response(CR)/partial response (PR) per RECIST v1.1 PSA response duration Duration of response for pts with CR or PR Overall survival Progression-free survival
Pharmacokinetic (PK) characterization	PK parameters including C_{max}, T_{max}, $t_{1/2}$, and area under the curve using noncompartmental methods Determination of antidrug antibodies
Dose optimization	Recommended phase 2 dose determined using all available information

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