

578MO

Phase Ib/II study of sabizabulin (VERU-111), an androgen receptor transport disruptor, in men with metastatic castration resistant prostate cancer (mCRPC) who failed an androgen receptor targeting agent (ARTA)

M.C. Markowski¹, M. Eisenberger², C.M. Pieczonka³, R.H. Getzenberg⁴, D. Rodriguez⁵, K.G. Barnette⁴, M.S. Steiner⁴, D.R. Saltzstein⁶, E.S. Antonarakis⁷, R. Tutrone⁸

¹ Oncology, Johns Hopkins Sidney Kimmel Cancer Center, Baltimore, MD, USA, ² Oncology Department, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, USA, ³ Department of Oncology, Associated Medical Professionals of NY, Syracuse, NY, USA, ⁴ Veru Inc, Miami, FL, USA, ⁵ Clinical Operations, Veru Inc, Miami, FL, USA, ⁶ Urology, Urology San Antonio, San Antonio, TX, USA, ⁷ Medical Oncology, Johns Hopkins University, Baltimore, MD, USA ⁸ Urology, Chesapeake Urology, Towson, MD, USA

Background

Sabizabulin is a novel oral agent that targets microtubules to disrupt transport of the AR. A phase Ib/II clinical study was conducted to assess safety, maximum tolerated dose and efficacy in men with mCRPC that progressed on an ARTA.

Methods

A phase Ib/II study was conducted in men with mCRPC who have failed an ARTA. The phase Ib portion (n=39) utilized a 3+3 design with escalating oral dosing of 4.5 mg to 81 mg for 7 days on /14 days off drug per 21-day cycle, then was expanded to continuous daily dosing. The phase II portion (n=41) evaluated the recommended phase II dose (63 mg PO daily). A PK study evaluating the phase II and phase III trial dosage forms was also conducted.

Results

Sabizabulin was well tolerated with the most common adverse events (>10% frequency) in patients that received 63 mg dose (n=54) including diarrhea, fatigue, ALT and AST increases which were mostly Grade 1 and 2. In the phase Ib portion, in men who were treated with 63 mg (n=14), the median duration on study was 10.8 m (2.3-24.7m). In the men with measurable disease (n=9), the ORR was 44% (n=4). For men ≥ 60mg dose (n=19), the estimated rPFS is 12.4 m (3 men still on study). The phase II is ongoing with evidence of PSA responses and objective responses. When combining phase Ib/II trials, in patients with measurable disease at baseline (n=29), the ORR (5PR +1CR observed) was 20.7%. In patients that received ≥ 63 mg (excluding baseline superscans) (n=55), the median rPFS is estimated to be 7.4 months with 10 men on study (Feb 2021). In the PK study, the phase III dose form had better oral bioavailability than the phase II dose form, thus the phase III recommended dose is 32mg PO qD.

Conclusions

In the phase Ib/II clinical trial, oral 63mg daily dosing has a favorable safety profile and chronic dosing is feasible. Efficacy was observed with PSA declines and long term durable responses. The phase III VERACITY study evaluating sabizabulin in chemotherapy naïve men with mCRPC who have failed an AR targeting agent is ongoing. Sabizabulin appears to be in a similar class of other FDA approved targeted cytostatic drugs that have shown to significantly prolong progression and survival.

Clinical trial identification

NCT03752099.

Legal entity responsible for the study

Veru Inc.

Funding

Veru Inc.

Disclosure

M.C. Markowski: Financial Interests, Institutional, Principal Investigator: Veru Inc. M. Eisenberger: Financial Interests, Personal, Member of the Board of Directors: Veru Inc. C.M. Pieczonka: Financial Interests, Institutional, Principal Investigator: Veru Inc. R.H. Getzenberg: Financial Interests, Personal, Full or part-time Employment: Veru Inc. D. Rodriguez: Financial Interests, Personal, Full or part-time Employment: Veru Inc. K.G. Barnette: Financial Interests, Personal, Leadership Role: Veru

Inc. M.S. Steiner: Financial Interests, Personal, Leadership Role: Veru Inc. D.R. Saltzstein: Financial Interests, Institutional, Principal Investigator: Veru Inc. E.S. Antonarakis: Financial Interests, Institutional, Member: Veru Inc. R. Tutrone: Financial Interests, Institutional, Principal Investigator: Veru Inc.

© *European Society for Medical Oncology*