MADRID 2026 ESMO congress

3715O

A phase 1/2 trial of zolucatetide, a first-in-class direct β-catenin:TCF inhibitor: Updated safety and efficacy in patients with desmoid tumors

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Background

Wnt pathway-activating mutations (WPAMs) occur in almost all of desmoid tumors (DT). Zolucatetide (formerly FOG-001) is a Helicon™ peptide that competitively inhibits the interaction between β-catenin and TCF transcription factors. This abstract presents updated data from the phase 1/2, multicenter study of zolucatetide in patients (pts) with WPAM+ solid tumors, including DT, enrolled in both the dose escalation phase and the ongoing dose optimization phase.

Methods

Pts with histologically confirmed DT who are either treatment naïve or have recurrent/refractory disease, including prior treatment with gamma-secretase inhibitor (GSI), are eligible for the study. Primary objectives include safety/tolerability of zolucatetide. Secondary objectives include anti-tumor activity.

Results

As of February 16, 2026, 38 DT pts had received zolucatetide at doses ranging from 150mg-900mg IV. Median age is 36.5 years and 71.1% are female. Disease control rate for all efficacy evaluable pts is 100%. Fourteen out of 19 pts with >1 post-baseline scan achieved an objective response (ORR; 74%) including 1 complete response (CR; 5.2%) with a median time to response of 3.8 months. The most common all-grade treatment-related adverse events (TRAE) were fatigue (42.1%), nausea (39.5%), alopecia (36.8%), AST increase (28.9%), hyperbilirubinemia (26.3%), ALT increase (23.7%), and hyponatremia (23.7%). The most common ≥G3 TRAE was hyperbilirubinemia (7.9%) with no other ≥G3 TRAE occurring in more than one pt. Overall, the most frequently reported TRAEs were low-grade and manageable or asymptomatic laboratory abnormalities that were reversible. No pts have discontinued study treatment due to an AE or had disease progression.

Conclusions

Updated results show that zolucatetide is well tolerated in pts with DT. Efficacy data demonstrate robust activity, with a rapid time to response and a high objective response rate observed in pts with DT who are treatment-naïve and those previously treated with a GSI. Dose optimization in a DT specific cohort is currently ongoing.

Clinical trial identification

NCT05919264.

Legal entity responsible for the study

Parabilis Medicines.

Funding

Parabilis Medicines.

Disclosure

M. Gounder: Financial Interests, Personal, Advisory Board: Avacta, Ikena Oncology, Immunome, Kura Oncology, Orion, Parabilis, Springwork Therapeutics; Financial Interests, Personal, Royalties: UpToDate; Financial Interests, Institutional, Advisory Board, GODDESS Patient Reported Outcomes Instrument in Desmoid Tumors: Memorial Sloan Kettering; Financial Interests, Institutional, Local PI, Research Grant for conduct of study: Bristol-Myers Squibb International, Neok Bio, Tango; Financial Interests, Institutional, Trial Chair, Research Grant for conduct of study: Erasca; Financial Interests, Institutional, Coordinating PI, Research Grant for conduct of study: Immunome; Financial Interests, Personal and Institutional, Coordinating PI, Research Grant for conduct of study: Kura Oncology, Springwork Therapeutics; Financial Interests, Personal and Institutional, Local PI, Research Grant for conduct of study: Orion, Parabilis, Vivace Therapeutics; Non-Financial Interests, Leadership Role, Scientific Director: Desmoid Tumor Research Foundation; Non-Financial Interests, Advisory Role: Chordoma Foundation, Liposarcoma Support Network. 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