Abstract: PB2956

Title: WAVELINE-006: A PHASE 2 STUDY OF ZILOVERTAMAB VEDOTIN (ZV) ALONE OR IN COMBINATION WITH NEMTABRUTINIB AS SUBSEQUENT-LINE THERAPY IN AGGRESSIVE AND INDOLENT B-CELL MALIGNANCIES

Abstract Type: Publication Only

Topic: Aggressive Non-Hodgkin lymphoma - Clinical

Background:

Despite significant advances in treatment for malignant neoplasms, resistance and relapse to front-line therapy remain common. The transmembrane protein ROR1 and Bruton tyrosine kinase (BTK) are overexpressed in several hematologic cancers. The antibody-drug conjugate ZV comprises a humanized IgG1 monoclonal anti-ROR1 antibody, a proteolytically cleavable linker, and the antimicrotubule agent monomethyl auristatin E. Nemtabrutinib is a reversible BTK inhibitor. Combining ZV and nemtabrutinib can potentially improve response to therapy in patients (pts) with B-cell malignancies. waveLINE-006 is a phase 2 study (NCT05458297) designed to evaluate safety and efficacy of ZV as monotherapy or in combination with nemtabrutinib in pts with relapsed or refractory (R/R) B-cell malignancies.

Aims:

To present the methodology of the phase 2 waveLINE-006 study to educate physicians on the potential role of ZV alone and with nemtabrutinib in R/R B-cell malignancies.

Methods:

Eligible pts are aged ≥18 years with biopsy-proven and/or histologically confirmed B-cell malignancies (mantle cell lymphoma [MCL], Richter transformation [RT], chronic lymphocytic leukemia [CLL], or follicular lymphoma [FL]), R/R disease, and an ECOG PS of 0 to 2. Approximately 275 pts will be enrolled in 1 of 6 cohorts (A-F). In cohorts A (n=40; R/R MCL; ≥2 prior therapies including a BTK inhibitor and either received or was ineligible for chimeric antigen receptor T-cell therapy) and B (n=50; R/R RT; ≥1 prior therapy), pts will receive ZV 2.5 mg/kg IV Q3W. In cohort C (R/R MCL; ≥1 prior therapy and no prior exposure to noncovalent BTK inhibitors), a safety run-in phase will be conducted in 30 pts to evaluate ZV 2.0 to 2.5 mg/kg IV Q3W plus nemtabrutinib 65 mg orally once daily, followed by enrollment of 15 additional pts who will receive the recommended phase 2 dose (RP2D) of the combination. Pts in cohort D (ZV schedule optimization; n=80; R/R CLL or FL; ≥2 prior therapies) will be randomly assigned 1:1 to receive ZV 2.5 mg/kg IV Q3W (arm 1) or ZV 2.0 mg/kg IV Q2/3W (arm 2). Pts in the efficacy expansion cohorts E (n=30; R/R FL; ≥2 prior therapies) and F (n=30; R/R CLL; ≥2 prior therapies) will receive the dose and schedule of ZV determined in cohort D. Pts enrolled in each cohort will receive treatment until disease progression, unacceptable toxicity, or other discontinuation criteria are met. Response will be assessed by CT or PET at baseline, Q12W up to week 108, then Q24W thereafter. Adverse events will be monitored and graded per NCI CTCAE v5.0. The primary end points are safety and tolerability of ZV alone in pts with CLL or FL (cohort D) and in combination with nemtabrutinib in pts with MCL (cohort C), and ORR of ZV alone in pts with MCL (cohort A), RT (cohort B), FL (cohorts D and E), and CLL (cohort F) and in combination with nemtabrutinib in pts with MCL (cohort C). Secondary end points include DOR of ZV alone (cohorts A, B, D, E, and F) and in combination with nemtabrutinib (cohort C) and the safety and tolerability of ZV alone (cohorts A, B, E, and F).**

Results:

Recruitment is ongoing in Brazil, Canada, Chile, China, Czechia, Estonia, Germany, Ireland, Israel, Italy, Japan, Republic of Korea, Poland, Portugal, Singapore, Spain, Sweden, Türkiye, the United Kingdom, and the United States.

Summary/Conclusion:

The results of waveLINE-006 will provide clarity on the efficacy and safety of ZV alone and with nemtabrutinib in R/R B-cell malignancies.

Keywords: Phase II, Targeted therapy, Bruton’s tyrosine kinase inhibitor (BTKi), B cell lymphoma