TPS10075 Poster Session

Phase 1/2 study of zilovertamab vedotin in pediatric and young adult hematologic malignancies or solid tumors (LIGHTBEAM-U01A).

Hyoung Jin Kang, Pablo Berlanga, Quentin Campbell-Hewson, Steven G. DuBois, Kyung-Nam Koh, Christine Mauz-Körholz, Michael James Sullivan, David Mangum, Rachael Windsor, David S. Dickens, Alexandre Duarte, Farzana D. Pashankar, Shifra Ash, Andrew Joseph Bellantoni, Scott J. Diede, Rohini Singh, Yulia Sidi, Michal Yalon; Seoul National University College of Medicine, Seoul National University Cancer Research Institute, Seoul National University Children's Hospital, Seoul, South Korea; Department of Pediatric and Adolescent Oncology, Gustave Roussy Cancer Campus, Villejuif, France; Great North Children's Hospital, Newcastle upon Tyne, United Kingdom; Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, MA; Asan Medical Center Children's Hospital, University of Ulsan College of Medicine, Seoul, South Korea; Martin Luther University of Halle-Wittenberg, Justus-Liebig University of Giessen, Giessen, Germany; Children's Cancer Centre, Royal Children's Hospital, Melbourne, Australia; Intermountain - Primary Children's Hospital, Salt Lake City, UT; University College London Hospital, London, United Kingdom; University of Iowa- Holden Comprehensive Cancer Center, Iowa City, IA; Fundação Faculdade Regional de Medicina de São José do Rio Preto-Centro Integrado de Pesquisa, São José Do Rio Preto, Brazil; Yale-New Haven Hospital, New Haven, CT; Department of Pediatric Hematology-Oncology, Ruth Rappaport Children's Hospital, Rambam Health Care Campus, Technion - Israel Institute of Technology, Rappaport Faculty of Medicine, Haifa, Israel; New York Medical College, Valhalla, NY; Merck & Co., Inc., Rahway, NJ; Sheba Medical Center–Tel HaShomer, Ramat Gan, Israel

Background: ROR1 is an oncofetal protein expressed in various blood and solid cancers. Zilovertamab vedotin (ZV) is an antibody-drug conjugate comprising a monoclonal antibody against ROR1, a proteolytically cleavable linker, and monomethyl auristatin E. LIGHTBEAM-U01A (NCT06395103) is a single-arm, open-label, phase 1/2 basket study designed to evaluate ZV in 4 disease cohorts: pediatric B-cell acute lymphoblastic leukemia (B-ALL), pediatric diffuse large B-cell lymphoma (DLBCL)/Burkitt lymphoma, pediatric neuroblastoma, and pediatric or young adult Ewing sarcoma. **Methods:** Pediatric participants (pts) are aged 0 to < 18 years; young adults are aged 18-25 years. Pts must have a confirmed diagnosis of B-ALL or DLBCL/Burkitt lymphoma per WHO criteria that has relapsed after ≥2 prior lines of therapy, or histologically confirmed neuroblastoma or Ewing Sarcoma that is refractory to frontline therapy. Pts with B-ALL must have ≥5% bone marrow blasts (M2 or M3), pts with DLBCL/Burkitt lymphoma must have radiographically measurable disease per IPNHL response criteria, and pts with neuroblastoma or Ewing sarcoma must have measurable disease per RECIST v1.1 (or MIBG-avid evaluable neuroblastoma). Pts aged ≤16 years must have a Lansky play-performance scale ≥50, pts aged > 16 to < 18 years must have a Karnofsky performance status of ≥50, and pts aged ≥18 years must have an ECOG performance status of 0 or 1. The study consists of 2 parts: dose escalation and confirmation (part 1) and efficacy expansion (part 2). Part 1 will enroll 3-12 pts per dose level. Also, ≥3 pts will be enrolled in 2 age groups: 1 to < 6 years and 6 to < 18 years. Pts will receive ZV at a starting dose of 2 mg/kg IV Q3W, escalating to 2.25 and 2.5 mg/kg or de-escalating to 1.75 mg/kg per a modified toxicity probability interval design-2. In part 2, eligibility will be expanded to ≥6 months for all cohorts and ≤25 years for Ewing sarcoma (if adequate safety and tolerability are shown, eligibility will expand to age 0 to < 6 months). In part 2, 10 pts will be enrolled in each cohort and will receive ZV at the preliminary RP2D determined in part 1. Disease assessments for pts with DLBCL/Burkitt lymphoma, neuroblastoma, or Ewing sarcoma will be performed Q8W for 6 months, then Q12W through 24 months, then Q24W through 5 years, then annually. Disease assessments for B-ALL will be performed at the end of each treatment cycle, at 6 months, at 1 year, then annually. Adverse events (AEs) will be monitored ≤30 days after last dose of study treatment (90 days for serious AEs; 30 days if new anticancer therapy is initiated) and will be graded per NCI CTCAE v5.0. Primary end points are safety and objective response rate. Secondary end points are pharmacokinetics, immunogenicity, duration of response, and eligibility for transplant/CAR-T therapy for pts with B-ALL or DLBCL/Burkitt lymphoma. Approximately 50-90 pts will be enrolled. Recruitment is underway. Clinical trial information: NCT06395103. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.