Safety and pharmacokinetic profile from a phase 1 trial of BGB dinutuximab beta-101 as maintenance therapy in pediatric patients with high-risk neuroblastoma in China

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ABSTRACT

Background and Aims: Neuroblastoma is the most common extracranial pediatric solid tumor, representing 8%–10% of childhood tumors and ~15% of pediatric malignancy-related deaths. Disialoganglioside 2 (GD2) is overexpressed on neuroblastoma cells; dinutuximab beta is a chimeric anti-GD2 monoclonal antibody approved in China and Europe for patients ≥12 months with high-risk neuroblastoma who achieved at least partial response after standard-of-care therapy. We present safety and pharmacokinetic results from an open-label, multi-center, single-arm, phase 1 trial of dinutuximab beta + 13-cis-retinoic acid (13-cis-RA) as maintenance therapy in pediatric patients with high-risk neuroblastoma in China.

Methods: Eligible patients (≥12 months) had high-risk neuroblastoma and achieved at least partial response after standard-of-care therapy. Intravenous dinutuximab beta (100 mg/m^2/cycle; day 1–11) was given with oral 13-cis-RA (160 mg/m^2/day; day 12-25) for up to five 35-day cycles. Primary objectives were to assess safety and tolerability of dinutuximab beta + 13-cis-RA, and to characterize the pharmacokinetics of dinutuximab beta in pediatric patients in China.

Results: As of July 19, 2023, 8 patients (median age 5.0 years) were enrolled. All completed treatment and had no disease progression at trial discontinuation. Median follow-up was 205.0 days. All patients experienced ≥1 treatment-related adverse event (TRAE). The most common TRAEs were abdominal pain (87.5%), diarrhea, rash, and decreased appetite (all 75.0%). Grade ≥3 and serious TRAEs were recorded for 87.5% and 12.5% of patients, respectively. Following 10-day consecutive infusion at 10 mg/m^2/day, the geometric mean (geometric CV%) area under the curve and maximum serum concentration for dinutuximab beta were 3,956.3 h*µg/mL (33.1) and 13.5 µg/mL (32.7), respectively. The geometric mean (minimum, maximum) half-life for dinutuximab beta was 254 hours (200, 332).

Conclusions: This study demonstrates an acceptable and manageable safety profile for dinutuximab beta plus 13-cis-RA. The pharmacokinetic data supports this regimen for further development as maintenance therapy in pediatric patients with high-risk neuroblastoma in China.