Background Pseudoprogression and subsequent shrinkage of solid tumor foci are typical clinical processes and are seen in approximately 2–8% of cases during immune checkpoint inhibitor (ICI) treatment. Refractory/relapsed pediatric solid tumors including neuroblastoma (NB), however, are well-known to be highly resistant to ICI. In addition, in the case of NB, specific patterns of killer cell immunoglobulin-like receptor (KIR) mismatch between recipient and donor at hematopoietic stem cell transplantation showed a significant impact on their survival. We recently developed a cell therapeutic agent showing a unique natural killer (NK) cell-like phenotype, GAIA-102. GAIA-102 is generated from mixed allogeneic peripheral blood mononuclear cells, which are derived from three or more healthy donors with specific combinations of HLA-C allele and KIRs, and demonstrates highly active accumulation and adhesion to tumor foci in vitro and in vivo. In addition, GAIA-102 could lead animals to complete cures in an established peritoneal dissemination mouse model in preclinical studies, suggesting that GAIA-102 could induce tumor-specific acquired immunity.

The aims of this Phase I clinical study are to assess the safety and proof of concept (POC) for the potential efficacy of GAIA-102, suggesting a treatment-mediated acquired immune response.

Methods GAIA-102 has been prepared as 'off-the-shelf' agents and stocked in vials under liquid nitrogen in a gas phase. The single-agent cohort of basket trial in this Phase I study is a typical 3+3 design with increased frequencies of intravenous infusion (5x10^6 cells/kg/dose), one to 3 times a week (LEVEL 1–3), and 3 patients would be added at the recommended frequencies. The primary endpoint is the safety of repeated intravenous injection of GAIA-102. Ten patients (6 for NB, 2 for osteosarcoma, 1 for each, hepatoblastoma and rhabdomyosarcoma) have been completed to evaluate dose-limiting toxicity (DLT) at the time of this abstract submission. The antitumor response as a secondary endpoint is evaluated by RECIST version 1.1.

Results The first-patient-in was on October 24, 2022. No DLT has been observed, and all four patients in LEVEL 3 exhibited mild to moderate fever. Typical pseudoprogression followed by subsequent shrinkage has been observed in some tumor foci of two NB patients (LEVEL 1 and 3). The target lesion of rhabdomyosarcoma also showed central necrosis (LEVEL 3).

Conclusions Pseudoprogression and subsequent tumor shrinkage were observed in NB (2 of 6 patients, 33.3%) by sole treatment of GAIA-102, suggesting the potential POC indicating that GAIA-102 may induce antitumor acquired immunity in a clinical setting.

Trial Registration ClinicalTrials.gov ID: NCT05608148
Ethics Approval Approval No.2022306 (Institutional Review Board of Kyushu University Hospital)