

Dinutuximab beta-based first-line maintenance therapy for newly diagnosed high-risk neuroblastoma following a COG-based pathway: a single-center real-world study in China

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Abstract

Background: This study delineates the feasibility, cycle-stratified safety profile, and relapse pattern of dinutuximab beta-based first-line maintenance for children with newly diagnosed high-risk neuroblastoma managed under a Children's Oncology Group (COG)-based pathway at a single Chinese center.

Methods: We retrospectively included 13 children treated between January 2021 and December 2024 who received dinutuximab beta maintenance after a COG-framework regimen; a contemporaneous cohort of 43 newly diagnosed high-risk patients (including 30 who did not receive dinutuximab beta) provided treatment-pathway and drug-accessibility background. Post-maintenance event-free survival (EFS) and safety were the primary observations; given the small sample, survival is reported descriptively, as is post-treatment response. Adverse events were graded by CTCAE v5.0 and classified per actual treatment cycle as immunotherapy-only or combined chemotherapy-immunotherapy.

Results: Before maintenance, 10 of 13 patients were in complete remission (CR) and 3 in partial remission (PR; all marrow residual), and 10 underwent autologous stem cell transplantation (ASCT). At the end of immunotherapy, 11 patients were in CR and 2 had progressive disease (PD; PL6 and PL7). With a median follow-up of 28.6 months, 3-year EFS from first infusion was 69.2% (95% CI 44.1–94.3), with a single overall survival (OS) event. Across 65 cycles (41 immunotherapy-only, 24 combined), pain was $\leq$ grade 2 and cytokine release and capillary leak were mostly low grade; grade $\geq$ 3 myelosuppression, neutropenia, infection, and fever were numerically higher in combined cycles (83.3%, 58.3%, 37.5%, 37.5%) than in immunotherapy-only cycles (34.1%, 9.8%, 19.5%, 26.8%). Four EFS events occurred: two CNS (intracranial) relapses, one skull-base/parameningeal relapse, and one abdominal nodal progression with death. There was no treatment-related death.

Conclusions: A COG-framework high-risk pre-maintenance pathway can be completed under real-world conditions and bridged to dinutuximab beta maintenance. This cohort entered maintenance with low residual burden, so the observed response and survival should not be attributed to dinutuximab beta monotherapy; cycle-based stratification helps separate anti-GD2-related toxicity from combined-chemotherapy background toxicity. CNS and skull-base events comprised a high proportion of relapses, which can inform follow-up but does not imply an increased CNS relapse rate in the immunotherapy era or a dinutuximab beta-altered relapse spectrum.

Background

Neuroblastoma is the most common extracranial solid tumor of childhood, accounting for approximately 8–10% of all pediatric malignancies and 15% of cancer-related deaths in children[1]; high-risk patients exhibit a particularly high relapse rate and account for a substantial share of childhood cancer-related mortality.[2] Current high-risk treatment is a multidisciplinary sequential framework comprising dose-intensive induction chemotherapy, maximal safe resection of the primary tumor, high-dose chemotherapy with autologous hematopoietic stem cell transplantation (ASCT), primary-site

radiotherapy, isotretinoin, and anti-GD2 immunotherapy.[3–6] The COG ANBL0032 and HR-NBL1/SIOPEN trials established that anti-GD2 antibodies (including dinutuximab beta) significantly improve EFS and OS in high-risk patients and drove their adoption as standard first-line maintenance therapy.[4–9, 19]

In China, the implementation of anti-GD2 maintenance is still shaped by multiple practical constraints, including drug cost, transplant accessibility, the use of concurrent chemotherapy during maintenance, and completeness of follow-up. A 2021 national expert consensus issued detailed recommendations on the administration and adverse-event management of dinutuximab beta,[10] and Chinese first-line maintenance cohorts have since been reported,[11–12] but real-world data derived from patients who completed a full COG pathway, with safety characterized systematically at the level of the individual treatment cycle, remain limited.

This study describes the feasibility, cycle-stratified safety profile, and relapse pattern of 13 patients at our center who were bridged to dinutuximab beta maintenance after completing a full COG pathway; the contemporaneous 43-patient high-risk cohort provides essential treatment-pathway and drug-accessibility background. This study is explicitly not designed to establish efficacy causally in such a small sample.

Methods

Study design and participants

This was a single-center, retrospective, real-world study with a follow-up cutoff of May 31, 2026. The primary analysis population comprised 13 children with newly diagnosed high-risk neuroblastoma diagnosed at Shenzhen Children's Hospital between January 2021 and December 2024, treated along a COG framework, and given dinutuximab beta maintenance; patients first exposed in the relapsed or refractory setting were excluded. Reporting follows the STROBE statement.

High-risk classification was based on the International Neuroblastoma Risk Group (INRG) staging system (INRGSS) and integrated age, MYCN status, histology, and imaging/nuclear-medicine assessment, with final assignment by the institutional multidisciplinary team (MDT). One patient was INRGSS stage L2 with non-amplified MYCN and negative marrow pathology, marrow smear, and flow-cytometric minimal residual disease (MRD); however, PET/CT showed diffusely increased metabolic activity in the spine, sternum, and pelvis that could not fully exclude bone/marrow involvement. Considering age > 5 years at onset, unfavorable histology, and persistent imaging uncertainty, this patient was treated along the high-risk pathway after thorough solid-tumor MDT discussion. This case was not handled as confirmed metastatic (stage M) disease and was separately excluded in a sensitivity analysis. The background cohort comprised all 43 contemporaneous newly diagnosed high-risk patients (13 who received and 30 who did not receive dinutuximab beta); it was used only to depict contemporaneous treatment-pathway and drug-accessibility background and was not designed as an antibody-exposure control.

Treatment

Patients in the dinutuximab beta group received comprehensive treatment along a pathway based on the COG ANBL0531/ANBL0532 framework (autologous stem-cell harvest, maximal safe resection of the primary tumor, single or tandem ASCT[3]) and completed primary-site radiotherapy before immunotherapy (performed at outside institutions; dose/target-volume records were incomplete, so local control was not analyzed). Dinutuximab beta was given by long-term continuous intravenous infusion:[10, 13] immunotherapy-only cycles were 35 days, with 100 mg/m² per cycle (10 mg/m²/day × 10 days, 240 h total); cycles combined with chemotherapy were 28 days. All patients received GM-CSF during infusion; the 7 patients who received concurrent chemotherapy were treated mainly with vincristine-irinotecan-temozolomide (VIT)-based regimens (1–5 cycles). Maintenance use of isotretinoin (13-cis-retinoic acid) varied by era and was inconsistent across this cohort, and it is therefore not evaluated for efficacy. Analgesia was based on gabapentin, non-opioid analgesics, and morphine[14]; morphine was given mainly by continuous intravenous infusion and supplemented with oral immediate-release morphine tablets (used in some patients when pain was prominent after intravenous morphine was stopped).

Assessments and endpoints

The primary observations were post-maintenance EFS and safety; post-treatment response status and overall response rate (ORR) are reported descriptively only. Disease assessment before and at the end of maintenance included conventional imaging (CT/MRI), PET/CT, metaiodobenzylguanidine (MIBG) or meta-fluorobenzylguanidine (MFBG) scanning, and bone-marrow smear, biopsy, and flow-cytometric MRD. CNS (intracranial) relapse was defined as tumor involving the brain parenchyma, meninges, cerebrospinal fluid, or cranial-nerve sheath/dura, diagnosed by contrast-enhanced MRI and, where available, pathological or CSF evidence; skull-base/parameningeal bone involvement was recorded separately as a skeletal/extradural site and was not counted as CNS relapse. EFS and OS used the first infusion as time zero for the dinutuximab beta cohort and diagnosis as time zero for the background cohort. Adverse events were graded by CTCAE v5.0[15] and classified per cycle as immunotherapy-only or combined chemotherapy-immunotherapy for descriptive analysis; infection-related events included clinically diagnosed pneumonia, intestinal infection, bloodstream infection/sepsis, and catheter-related infection. Response was determined from the disease assessment at the end of maintenance; patients who did not achieve a durable remission and showed progression confirmed by imaging or pathology shortly after the last infusion were classified as treatment failure (PD).

Statistical analysis

Categorical variables are presented as counts and percentages and continuous variables as medians with ranges. EFS and OS were estimated by the Kaplan-Meier method with 95% CIs; patients without an event or death were censored at May 31, 2026. Exploratory between-group comparisons used the log-

rank test and univariable Cox regression (hazard ratios and 95% CIs; Supplementary Table S3). Because patients in the dinutuximab beta group had to survive and complete prior therapy before entering maintenance, this comparison is subject to immortal time bias and supports no causal inference. The cycle-level safety analysis was descriptive and not adjusted for within-patient correlation. Analyses used R 4.6 (survival, survminer).

Results

Baseline characteristics

Among the 13 patients, the median age at diagnosis was 3.8 (0.6–9.0) years and the median age at first infusion was 4.7 (1.5–10.0) years; 8 were male and 5 female. At diagnosis, 12 were INRGSS stage M and 1 was stage L2 (the high-risk rationale for the L2 case is detailed in Methods 2.1 and Supplementary Table S4). MYCN was amplified in 6, non-amplified in 6, and unknown in 1; the primary site was retroperitoneal in 11 and posterior mediastinal in 2. Before maintenance, 10 patients were in CR and 3 in PR (all with marrow residual) (Table 1).

Table 1
Baseline characteristics, prior treatment, and immunotherapy exposure

Characteristic	Value
Age at diagnosis, median (range), years	3.8 (0.6-9.0)
Age at first infusion, median (range), years	4.7 (1.5–10.0)
Male/female	8/5
INRGSS stage M / L2	12 (92.3%) / 1 (7.7%)
MYCN amplified / non-amplified / unknown	6 (46.2%) / 6 (46.2%) / 1 (7.7%)
Primary site: retroperitoneal / posterior mediastinal	11 / 2
CR before immunotherapy	10 (76.9%)
PR before immunotherapy (marrow residual)	3 (23.1%)
COG-based induction	13 (100.0%)
ASCT	10 (76.9%); tandem/single 6/4
Primary-site radiotherapy before immunotherapy	13 (100.0%)
GM-CSF during maintenance	13 (100.0%)
No. of dinutuximab beta cycles, median (range)	5 (4–7)
Patient level: concurrent chemotherapy / none	7 (53.8%) / 6 (46.2%)
Cycle level: immunotherapy-only / combined	41 / 24
Dinutuximab beta dosing	100 mg/m ² per cycle; 10 mg/m ² /day × 10 d, continuous infusion 240 h
<i>Treatment cycles are classified by the actual treatment combination of each cycle; one patient may contribute both immunotherapy-only and combined cycles. The 7 patients with concurrent chemotherapy received mainly VIT-based regimens (1 VIT + IT, 1 a single VIT cycle), 1–5 cycles. The single INRGSS L2 patient was treated along the high-risk pathway after solid-tumor MDT judgment and not on the basis of confirmed metastatic disease (rationale in Supplementary Table S4). All patients completed primary-site radiotherapy before immunotherapy; dose, target volume, and radiotherapy toxicity were not analyzed.</i>	

Treatment exposure and response

Ten patients underwent ASCT (tandem 6, single 4); all completed COG induction and primary-site radiotherapy and all received GM-CSF, with a median of 5 (4–7) dinutuximab beta cycles. At the patient

level, 7 received concurrent chemotherapy and 6 did not; at the cycle level there were 41 immunotherapy-only and 24 combined cycles. At the end of immunotherapy, 11 patients were in CR and 2 had PD (descriptive ORR 11/13, 84.6%): PL7 had PD at the end of treatment and subsequently progressed in abdominal lymph nodes and died; PL6 did not achieve a durable complete remission and, presenting as peripheral facial palsy, had skull-base/parameningeal progression confirmed by imaging and surgery less than 2 months after the last infusion, classified as treatment failure (PD) and an EFS event. Of the 10 patients in CR before treatment, 8 were in CR and 2 had PD after treatment (PL6, PL7); all 3 patients in PR before treatment (all marrow residual) achieved CR.

Relapse pattern and survival

The median follow-up was 28.6 (18.6–46.9) months. There were 4 EFS events and 1 OS event: 2 CNS (intracranial) relapses (PL3, PL12), 1 skull-base/parameningeal relapse (PL6), and 1 abdominal nodal progression with death (PL7). Median EFS and OS were not reached; 1-, 2-, and 3-year EFS were 84.6% (95% CI 65.0–100), 69.2% (44.1–94.3), and 69.2% (44.1–94.3), and 1-, 2-, and 3-year OS were 100%, 100%, and 83.3% (53.5–100) (Fig. 1, Table 2). With only one OS event, the 3-year OS estimate rests on a small risk set and should be interpreted cautiously. Excluding this single OS event (the INRGSS L2 patient PL7), the 3-year EFS and OS of the remaining 12 patients were 75.0% and 100% (sensitivity analysis).

Table 2

Response, survival outcomes, and relapse pattern of the dinutuximab beta cohort (from first infusion)

Item	Value
Disease status at end of immunotherapy (descriptive)	CR 11; PD 2 (PL6, PL7)
ORR (descriptive)	11/13 (84.6%)
Status at last follow-up	CR 9; alive after relapse 3; death 1
EFS events	4/13 (30.8%)
OS events	1/13 (7.7%)
Median follow-up, months	28.6 (18.6–46.9)
1-, 2-, 3-year EFS	84.6% (65.0–100), 69.2% (44.1–94.3), 69.2% (44.1–94.3)
1-, 2-, 3-year OS	100%, 100%, 83.3% (53.5–100)
Sensitivity analysis (excluding PL7)	3-year EFS 75.0%, OS 100% (n = 12)
EFS event composition	CNS (intracranial) relapse 2 (PL3, PL12); skull-base/parameningeal relapse 1 (PL6); abdominal nodal progression then death 1 (PL7)
<i>Response and ORR are descriptive. PL6 did not achieve a durable complete remission and had skull-base/parameningeal progression confirmed by imaging and surgery less than 2 months after the last infusion, recorded as treatment failure and an EFS event. With a single OS event the 3-year OS estimate rests on a very small risk set. Sites and evidence of the cranial-region relapses are in Supplementary Table S4.</i>	

Two relapses were CNS (intracranial): PL3, a left temporal parenchymal metastasis (surgically confirmed), and PL12, a small left occipital lesion (diagnosed on contrast-enhanced MRI, not biopsied). The third cranial-region event, PL6, was a skull-base/parameningeal bone relapse (mastoid/sigmoid-sinus/jugular-foramen involvement, surgically confirmed and N-MYC amplified) occurring less than 2 months after maintenance, and is classified as a skeletal/extradural rather than a CNS event (Supplementary Table S4). Survival of the contemporaneous 43-patient cohort and the 30-patient non-dinutuximab beta group from diagnosis is shown in Supplementary Table S5; the exploratory between-group comparison (Supplementary Table S3, Supplementary Figures S1–S2) is background only and does not support a drug-effect inference.

Safety

Across 65 evaluable cycles (41 immunotherapy-only, 24 combined), typical anti-GD2-related adverse events were predominantly low grade: pain occurred in 39/65 (60.0%) cycles and was uniformly $\leq$ grade 2, cytokine release syndrome in 22/65 (33.8%) with grade 3 in only 1 cycle, and capillary leak syndrome in 5/65 (7.7%) with grade 3 in only 1 cycle. Severe events were numerically more frequent in combined cycles: grade $\geq$ 3 myelosuppression, neutropenia, infection, and fever were 83.3%, 58.3%, 37.5%, and

37.5%, versus 34.1%, 9.8%, 19.5%, and 26.8% in immunotherapy-only cycles (Table 3). Because the same patient contributes multiple cycles and combined cycles often correspond to patients with higher residual burden, this comparison is descriptive. Any morphine support was used in 51/65 (78.5%) cycles and continuous intravenous morphine in 45/65 (69.2%; median infusion 96 h, range 24–264), reaching 100% in combined cycles. There was no treatment-related death.

Table 3
Main adverse events by treatment-cycle type (cycle-level descriptive analysis)

Adverse event / supportive care	Overall (n = 65)	Immunotherapy-only (n = 41)	Combined (n = 24)
Fever	Any 54/65 (83.1%); G3-4 20/65 (30.8%)	G3-4 11/41 (26.8%)	G3-4 9/24 (37.5%)
Pain-related symptoms	Any 39/65 (60.0%); G3-4 0	G3-4 0	G3-4 0
Cytokine release syndrome	Any 22/65 (33.8%); G3-4 1/65 (1.5%)	G3-4 0	G3-4 1/24 (4.2%)
Capillary leak syndrome	Any 5/65 (7.7%); G3-4 1/65 (1.5%)	G3-4 0	G3-4 1/24 (4.2%)
Diarrhea	Any 26/65 (40.0%); G3 5/65 (7.7%)	G3 2/41 (4.9%)	G3 3/24 (12.5%)
Hematologic toxicity/myelosuppression	Any 65/65 (100.0%); G3-4 34/65 (52.3%)	G3-4 14/41 (34.1%)	G3-4 20/24 (83.3%)
Neutropenia	Any 34/65 (52.3%); G3-4 18/65 (27.7%)	G3-4 4/41 (9.8%)	G3-4 14/24 (58.3%)
Infection-related events	Any 24/65 (36.9%); G3 17/65 (26.2%)	G3 8/41 (19.5%)	G3 9/24 (37.5%)
Hepatic enzyme elevation	Any 10/65 (15.4%); G3 3/65 (4.6%)	G3 0	G3 3/24 (12.5%)
Any morphine analgesic support	51/65 (78.5%)	27/41 (65.9%)	24/24 (100.0%)
Continuous intravenous morphine	45/65 (69.2%)	25/41 (61.0%)	20/24 (83.3%)
<i>Cycle-level descriptive analysis, not adjusted for within-patient correlation; denominators are treatment cycles. G, grade. Pain-related symptoms include abdominal pain, headache, limb pain, musculoskeletal pain, arthralgia, chest pain, and recorded facial, periauricular, or perineal pain. Continuous intravenous morphine duration was a median of 96 h (range 24–264). No grade 5 (fatal) event occurred. Full grade distributions are in Supplementary Tables S1–S2.</i>			

Discussion

A central finding of this study is that, under real-world conditions, our center delivered the COG-framework high-risk multidisciplinary sequential regimen relatively completely and achieved a high rate of complete remission before immunotherapy. All 13 patients completed induction chemotherapy and

primary-site radiotherapy, 76.9% completed ASCT (including 6 tandem transplants), and the CR rate before the anti-GD2 phase reached 76.9%, with the remaining 3 patients in PR and all marrow-restricted residual disease. This degree of prior-therapy completion and pre-maintenance CR is clearly higher than in a recent Chinese real-world cohort (pre-dinutuximab beta CR 50.0%, ASCT completion 21.4%[12]) and approaches that of European cohorts with more complete prior therapy (pre-maintenance CR 81.1% in a three-center Polish series[18]). Against a Chinese backdrop of uneven anti-GD2 drug accessibility and cross-institutional radiotherapy and transplant resources, this result has practical significance in itself: a standardized, complete induction-surgery-transplant-radiotherapy chain is the prerequisite for entering anti-GD2 maintenance with low residual burden and largely determines the starting point and comparability of maintenance in the real world.

This high-CR, low-residual starting point also bounds the interpretation of efficacy. With 10 patients already in CR before maintenance, post-treatment remission is largely attributable to prior therapy; combined with concurrent IT/VIT chemotherapy in 7 patients, the specific contribution of single-agent dinutuximab beta cannot be isolated. International evidence likewise supports interpreting outcomes by disease burden at the start of maintenance: in ANBL0032, high-risk patients who completed prior therapy had 2-year EFS rise from 46% to 66% and OS from 75% to 86%;[4] HR-NBL1/SIOPEN identified failure to achieve CR before maintenance as an independent risk factor for relapse or progression (HR 1.494, $P = 0.0043$);[9] and COG induction-response analyses show that better end-induction response predicts superior EFS and OS.[16–17] Accordingly, the end-of-immunotherapy CR (11/13) and 3-year EFS (69.2%) in this cohort should be read as maintenance-phase outcomes against a background of a complete treatment chain and low residual burden, rather than as evidence of dinutuximab beta efficacy. Response adjudication is also assessment-dependent: although we incorporated CT/MRI, PET/CT, MIBG or MFBG, and marrow smear, biopsy, and flow MRD, centrally reviewed Curie/SIOPEN scoring and quantitative molecular MRD were not available,[12, 16] and future work should report remission in a stratified manner across imaging, morphologic, flow, and molecular levels.

The main clinical value of this study is the characterization of dinutuximab beta maintenance safety at the level of the treatment cycle. Anti-GD2-related pain, cytokine release, and capillary leak arise from on-target effects of the antibody on GD2 and peripheral nerve fibers and are mostly low grade and manageable with analgesia and supportive care, whereas myelosuppression, infection, and fever are driven mainly by the concurrent chemotherapy used during maintenance. Across 65 cycles this distinction is quantitatively visible: anti-GD2-related grade ≥ 3 events were only 0/65 (pain), 1/65 (cytokine release), and 1/65 (capillary leak), whereas grade ≥ 3 myelosuppression, neutropenia, and infection in combined cycles (83.3%, 58.3%, 37.5%) were far higher than in immunotherapy-only cycles (34.1%, 9.8%, 19.5%), concordant in direction with the Chinese cohort of Zhao et al.[12] The clinical value of this stratification is that, when assessing the safety of anti-GD2 maintenance, failure to distinguish cycle type readily misattributes the marrow and infectious toxicity of concurrent chemotherapy to the antibody, overstating single-agent anti-GD2 toxicity and potentially affecting dose-reduction or discontinuation decisions. Morphine use was relatively high (any support in 51/65 cycles; median continuous intravenous infusion 96 h; 100% in combined cycles), related to young age, prolonged

continuous infusion, early-period prescribing practice, and the absence of a standardized daily pain score; a structured pain-scoring and opioid-management pathway (including transition from intravenous to oral immediate-release morphine) could optimize analgesia and reduce overuse. These 65 cycles derive from the same 13 patients, are not independent between cycles, and combined cycles often correspond to patients with higher residual burden with confounding by indication, so these comparisons remain descriptive.

The relapse pattern provides a second observation of clinical value for follow-up strategy. Two of the four EFS events were CNS (intracranial parenchymal) relapses — PL3, a pathology-confirmed left temporal metastasis, and PL12, an MRI-diagnosed left occipital lesion; CNS relapse in neuroblastoma is conventionally diagnosed by MRI and does not require histology. The third cranial-region event, PL6, was a skull-base bone metastasis with parameningeal extension — a skeletal/extradural site that does not meet the definition of CNS relapse. Prior HR-NBL1/SIOPEN data indicate that CNS relapse is overall uncommon but carries a poor prognosis and is associated with MYCN amplification, multifocal metastasis, and skull/intracranial involvement.[21–22] With only 13 patients and no systematic CNS screening, we cannot infer an increased CNS relapse rate in the immunotherapy era, nor that dinutuximab beta alters the relapse spectrum. A more cautious clinical takeaway is to lower the threshold for cranial MRI surveillance in patients with cranial/intracranial involvement at diagnosis, MYCN amplification, multifocal metastasis, or persistent marrow residual before maintenance. Because dinutuximab beta is a large IgG that poorly crosses an intact blood-brain barrier, drug exposure within the CNS is low; lesions there are less affected by systemic immunotherapy and may become an important source of relapse once systemic disease is cleared, which offers a biological explanation for CNS relapse and supports exploring CNS-directed strategies such as intrathecal/intraventricular radioimmunotherapy (targeting GD2 or B7H3).[24] PL7 had PD at the end of immunotherapy, representing systemic treatment failure; patients with active disease at the end of maintenance should be considered early for salvage chemoimmunotherapy or clinical trials.[20]

The principal limitation is the very small sample (13 patients, 4 EFS events, 1 OS event); survival estimates, especially OS, are immature and the analyses are mainly descriptive. The contemporaneous non-dinutuximab beta cohort is treatment-pathway and drug-accessibility background rather than a drug-effect control (7 of them received naxitamab, also an anti-GD2 antibody), and with immortal time bias it cannot estimate a drug effect. The cycle-level safety analysis is not adjusted for within-patient correlation, and concurrent chemotherapy carries confounding by indication. One INRGSS L2 patient was assigned to the high-risk pathway by MDT judgment; this classification was not based on confirmed metastatic disease, and although a sensitivity analysis excluding the case was performed, it may still affect the OS estimate. Future work should use multicenter designs with a common landmark or time-dependent/propensity-score methods,[23] with harmonized definitions of pre-maintenance disease burden and of CNS versus skull-base relapse, to prospectively assess the efficacy and cycle-stratified safety of anti-GD2 maintenance.

Conclusions

After comprehensive treatment within a COG-based framework, dinutuximab beta maintenance can be implemented in children with newly diagnosed high-risk neuroblastoma at our center. This cohort entered maintenance with a high CR rate, a high ASCT completion rate, and low residual burden, so the observed response and 3-year EFS cannot be attributed to single-agent dinutuximab beta. The main, generalizable findings are a cycle-stratified safety profile (anti-GD2-related toxicity is mostly low grade, and grade ≥ 3 myelosuppression/infection/fever cluster in combined chemotherapy cycles) and a relapse pattern dominated by CNS and skull-base events. These observations require validation in larger samples.

Abbreviations

anti-GD2, anti-disialoganglioside GD2; ASCT, autologous stem cell transplantation; COG, Children's Oncology Group; CR, complete remission; CRS, cytokine release syndrome; CNS, central nervous system; CTCAE, Common Terminology Criteria for Adverse Events; EFS, event-free survival; GM-CSF, granulocyte-macrophage colony-stimulating factor; INRG/INRGSS, International Neuroblastoma Risk Group (Staging System); IT, irinotecan-temozolomide; MIBG, metaiodobenzylguanidine; MFBG, meta-fluorobenzylguanidine; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, progressive disease; PR, partial remission; VIT, vincristine-irinotecan-temozolomide.

Declarations

Ethics approval and consent to participate: This study was approved by the Ethics Committee of Shenzhen Children's Hospital (approval number 2024075) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from the guardians of all included children.

Consent for publication: Not applicable.

Availability of data and materials: The datasets generated and analysed during the current study are not publicly available because they involve minors, but de-identified aggregate data are available from the corresponding author on reasonable request after ethics approval.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: MY designed the study, curated the data, performed the statistical analysis, and wrote the manuscript. SC, HX, CL, and HL collected cases and performed follow-up. XY designed the study and supervised revision and quality control. All authors read and approved the final manuscript.

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Figures

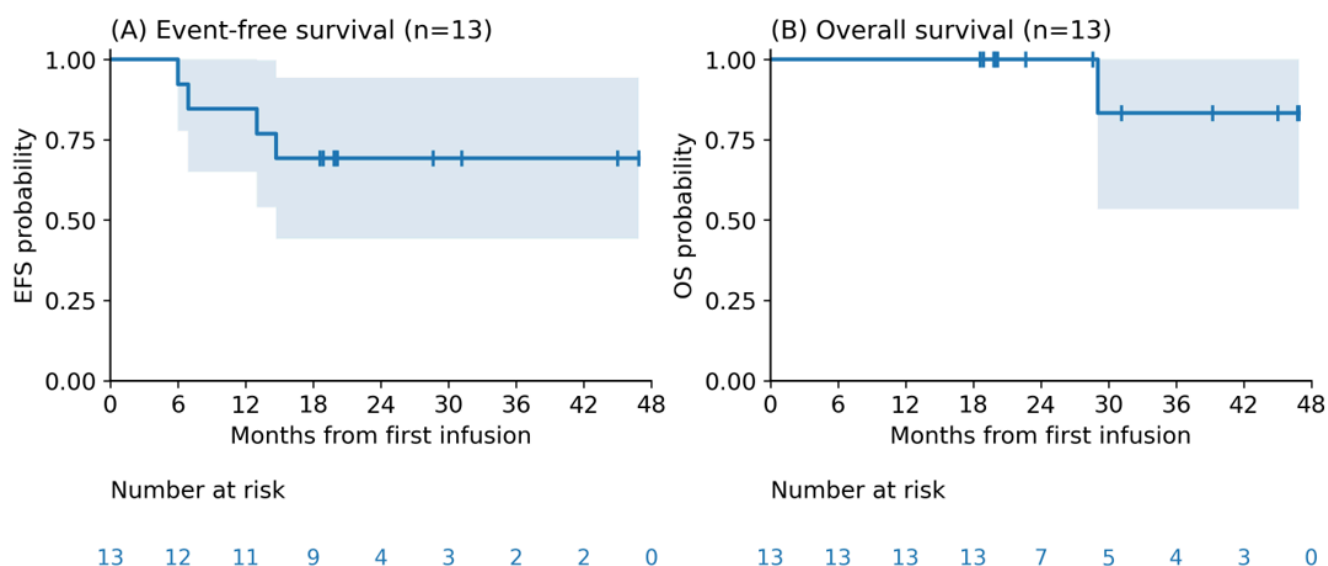


Figure 1

Event-free survival (A) and overall survival (B) of the 13-patient dinutuximab beta cohort, calculated from first infusion. Shaded bands denote 95% confidence intervals; vertical ticks denote censoring; numbers at risk are shown below each panel.

Supplementary Files

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