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cell infiltration, whereas NRG3/ERBB4 axis was specifically expressed and activated in pre-treatedhigh-risk neuroblastoma, along with moderate upregulation in effector cell cytotoxicity. Moreover, chemotherapy-inhibited NRG3 and ERBB4 expression levels were reversely elevated by 3F8 (Naxitamab, CI cohort) in the induction phase, and positively correlated with NB-reactive immune response. Subsequent functional studies verified NB cells exposing to CI induced NRG3/ERBB4 activation, further promoted GZMB and GNLY expressions in CD8T and NK cells. Integrating bulk-RNA with lipidomic data revealed NRG3/ERBB4 activation in NB cells orchestrated ganglioside metabolism to avoid intra-tumor accumulation, in order to restore tumor-reactive immune response.

Conclusions: Collectively, we generated detailed NB-associated secrete patterns under different risks, and clarified their possible network with immune effector cells in pre-treatment, chemotherapy and chemo-immunotherapy of NB. These data elucidate a novel mechanism of 3F8, and an important step forward in understanding tumor-effector cell interaction, specifically in chemo-immunotherapy NB patients. Further, we also provide candidates beneficial for the development of adjuvant treatments, and inform more refined combination strategies to overcome immune resistance.

PO309 / #2449 | *AS05 - SIOP Scientific Program / AS05e. Neuroblastoma*

Safety and Feasibility of GD2 Immunotherapy in Neuroblastoma Following Autologous Versus Allogeneic Transplantation: A Retrospective Study

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Background and Aims: GD2 immunotherapy for neuroblastoma, which combines granulocyte-colony stimulating factor (G-CSF) with recombinant interleukin-2 (IL-2, teceleukin), was introduced in Japan in September 2021. This includes its use in patients who have undergone prior allo-HSCT. However, data regarding its safety and feasibility, particularly for post-allo-HSCT, are scarce. This study aimed to assess the safety and feasibility of GD2 immunotherapy in patients with neuroblastoma, compare patients with and without prior allo-HSCT, and evaluate the impact of previous treatments on treatment feasibility, tolerability, and safety.

Methods: We retrospectively reviewed the medical records of patients with newly diagnosed high-risk or relapsed/refractory neuroblastoma who started GD2 immunotherapy between September 2021 and December 2022.

Results: GD2 immunotherapy was initiated within 1 year of autologous transplantation in 41 patients (Auto group) and allogeneic transplantation in 11 patients (Allo group). The six-course completion rate was significantly lower in the Allo (45.5%) than in the Auto group (84.3%; $p = 0.0115$). Discontinuation due to disease progression was more frequent in the Allo than in the Auto group (36.4% vs. 9.8%), showing a large difference compared to discontinuation due to adverse events (18.2% vs. 5.9%). Planned treatment modifications, including G-CSF and IL-2 dose reductions, were more common in the Allo than in the Auto group (60.5% vs 3.2%). Regarding grade 3 or higher adverse events per course, the Allo group showed a trend towards more frequent AST (20.9% vs 10.9%) and significantly more frequent ALT (27.9% vs 8.9%) elevations than the Auto group, whereas the Auto group showed more frequent neutropenia than the Allo group (16.7% vs 7.0%).

Conclusions: The completion rate of GD2 immunotherapy was lower after allo-HSCT than after auto-HSCT for neuroblastoma. However, discontinuation of allo-HSCT was primarily due to disease progression. Considering the observed safety profile, planned modifications are recommended to ensure safety when administering GD2 immunotherapy after allogeneic transplantation.

PO310 / #1426 | *AS05 - SIOP Scientific Program / AS05e. Neuroblastoma*

Tpog Nb 2020 Protocol Intermediate-Risk Group: Current Results

Deniz Kizmazoglu, Nilgun Kurucu, Refik Cecen, Serhan Kupeli, Sibel Tekgunduz, Ali Varan, Nursah Eker, Begum Sahin, Ayse Erbay, Neriman Sari, Eda Ataseven, Handan Dincarslan, Birsen Baysal, Suheyla Ocak, Betul Sevinir, Arzu Okur, Ebru Yilmaz, Derya Özyörük, Ayhan Dagdemir, Murat Elli, Deniz Tugcu, Sule Yesil, Elif Güler, Bahar Genc, Zuhal Sıvıs, Bengu Demirag, Asli Yilmaz, Canan Ozdemir, Fatih Erbey, Volkan Hazar, Yavuz Koksal, Sultan Aydin, Aykan Ozguven, Tezer Kutluk, Zekiye Altun, Safiye Aktas, Ahmet Celik, Dilek Ince, Nur Olgun

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Background and Aims: To evaluate intermediate-risk group (IRG) patients enrolled in the TPOG NB 2020 protocol.

Methods: Clinical characteristics, treatment outcomes and survival rate were analyzed.

Results: A total of 108 patients were classified in IRG. The median age at diagnosis was 11 months (0–11 years), M/F:1.16. 67.6% of the patients were younger than 18 months. The primary tumor location:surrenal (51%), paravertebral (30.5%), midline (14.8%), multifocal (2.8%), and other (0.9%). Opsoclonus-myoclonus syndrome was present in two patients, and life-threatening symptoms were observed in 10 patients. Stage distribution: Stage L2 (59.3%), Stage M (32.4%), and Stage MS (8.3%). The most common metastatic sites included liver ($n = 23$), bone ($n = 22$), bone marrow ($n = 15$), distant lymph nodes ($n = 10$), lungs ($n = 7$), and skin ($n = 5$). Tumor histopathology revealed neuroblastoma in 91.7% ($n = 99$) of patients, and among those with available differentiation data, 67% were classified as undifferentiated or poorly differentiated.11q deletion was detected in 45% of tested patients. Primary surgery was performed in 26% ($n = 28$) of patients, with complete resection in 14 patients, microscopic residual disease in 5 patients, and macroscopic residual disease

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in 9 patients. Induction therapy response was evaluated in 100 out of 108 patients, with a complete or partial response rate of 86%. Delayed surgery was performed in 65 patients, resulting in complete resection in 37 patients (34%), microscopic residual disease in 16 patients, and macroscopic residual disease in 12 patients. The 3-year event-free survival rate was 84%, with 8 cases of relapse (6 primary, 2 systemic) and 5 cases of refractory or progressive disease. The 3-year overall survival rate was 96%, with three reported deaths. Two deaths were due to disease progression, while one occurred at 7 months post-surgery due to surgical complications. The median follow-up duration was 24 months (1–55 months).

Conclusions: The intermediate-risk group comprises approximately 20% of all patients. Based on our current findings, the rate of relapse, refractoriness, or progression is 12%. Survival rates are consistent with the literature and show a similar trend to the TPOG NB 2009 protocol.

PO311 / #1626 | *AS05 - SIOP Scientific Program / AS05e. Neuroblastoma*

Evaluation of Neuroblastoma Cases Younger Than 18 Months: Dokuz Eylül University Experience

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Background and Aims: To evaluate the clinical characteristics, treatment responses, and survival rates of neuroblastoma (NB) cases diagnosed under 18 months of age.

Methods: A retrospective analysis was conducted on 72 patients younger than 18 months who were diagnosed and followed for NB at our center between 1987 and 2024. Treatment responses and survival rates were assessed.

Results: Among all NB patients, 39% were younger than 18 months at diagnosis. M/F:1.0, and the median age at diagnosis was 6.2 months (0–18 months). At diagnosis, 50% (n = 36) of patients were younger than 6 months, 27.8% (n = 20) were between 6–12 months, and 22.2% (n = 16) were older than 12 months. The stage distribution: Stage 1:9.8% (n = 5), Stage 2:19.6% (n = 5), Stage 3: 31.2% (n = 16), Stage 4: 31.2% (n = 16), and Stage 4S:18% (n = 9). Patients treated with TPOG-NB-2020 protocol: L1 (n = 5), L2 (n = 4), M (n = 10), and MS (n = 2). The risk groups: LRG:29.2% (n = 21), IRG:50% (n = 36), and HRG: 20.8% (n = 15). In the LRG;5-and 10-year event-free survival (EFS) rates were 90%, while the overall survival (OS) rates were 95%. In the IRG, the 5- and 10-year EFS rates were 83%, while the OS rates were 97%. In the HRG, the stage distribution was Stage 1 (n = 1), Stage 2 (n = 2), Stage 3 (n = 3), and Stage 4 (n = 9). Among the six deceased patients, all were MYCN-positive, 5/6 died due to progressive disease. The 5- and 10-year EFS rates were 33%, and the OS rates were 56%. For all patients, the median follow-up duration was 79 months (4 months–18 years), and the median time to event development was 6 months (3–13 months). In the <18-month-old group, the 1-, 5-, and 10-year EFS rates were 76%, 74%, and 74%, while the OS rates were 90%, 88%, and 88%, respectively.

Conclusions: The treatment outcomes of our infant neuroblastoma patients were found to be successful and consistent with global literature. Survival rates were significantly lower in patients with MYCN amplification compared to those without amplification.

PO312 / #803 | *AS05 - SIOP Scientific Program / AS05e. Neuroblastoma*

Veno-Occlusive Disease in Children With Neuroblastoma Following Busulphan-Melphalan High-Dose Chemotherapy

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Background and Aims: Children with high risk neuroblastoma generally undergo autologous stem cell transplant (SCT) with busulfan/melphalan (Bu/Mel) conditioning as part of their standard treatment. Veno-occlusive disease (VOD) remains a leading cause of morbidity and mortality in Bu/Mel autologous SCT. Our study aimed to review factors which may impact on incidence of VOD.

Methods: An audit of all children diagnosed with high risk neuroblastoma who underwent Bu/Mel autologous SCT over an 11 year period (January 2013 to December 2023) in a single national paediatric oncology referral centre was performed. Data of children who were diagnosed with VOD were compared with those who did not have a diagnosis of VOD (non-VOD). Statistical analysis was performed using SPSS.

Results: Forty-nine children underwent Bu/Mel autologous SCT. 35% (17/49) developed VOD. Mean age at transplant: VOD: 3.6 years, non-VOD: 4.2 years (p value 0.448). Of those who got VOD 59% (10/17) were female versus 47% (15/32) female in non-VOD group. MYC-N amplification was higher in VOD cohort (VOD: 71% (12/17) vs non-VOD: 41% (13/32), p value 0.046). 24% (4/17) VOD group had tandem transplant versus 28% (9/32) in non-VOD (p value 0.729). Mean GFR was lower in VOD group (VOD: 86.9 mL/min/1.73m^2, non-VOD: 107.3 mL/min/1.73m^2, p value 0.014). Children with one kidney higher in VOD cohort (VOD: 29% (5/17), non-VOD: 9% (3/32), p value 0.071). 5-year overall survival (OS) was 51% in VOD cohort vs 46% in non-VOD cohort (p value 0.677).

Conclusions: Our study demonstrates statistical significance of lower GFR and MYC-N amplification in VOD incidence. Having one kidney at time of transplant trended towards, but did not reach, significance. There was no significant difference in VOD incidence in children who underwent tandem transplant, nor any differences in age nor gender. There was no difference In 5-year OS in those that had VOD at time of transplant.

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