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Long-Term Complications in Survivors of Neuroblastoma: Clinical Data of Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology

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Introduction: Survival of neuroblastoma patients has improved over recent decades, but there is a risk of chronic treatment-related health issues in survivors.

Methodology: The study included 120 patients with NB of the intermediate/high risk group, diagnosed for the period 01.2012-12.2019, who completed specific treatment according to the modified German NB-2004 protocol at the national pediatric oncology center. Median follow-up was 96 months (range: 40-167). Descriptive and univariate/ multivariate analyses identified risk factors for late toxicity

Results: The median age at neuroblastoma diagnosis was 15 months (range: 0.46-104), at the time of the survey – 118 months (range: 50-216). All had received chemotherapy; radiation (29%), isotretinoin (96%), anti-GD2 antibody therapy (4%%), MIBG (14%), and single ASCT (52%). ASCT conditioning included: Treosulfan/Melphalan (TreoMel) (83%), Carboplatin/Etoposide/Melphalan (CEM) (17%). Musculoskeletal diseases (including dental anomalies) were diagnosed in 78%, renal

disease in 46%, hearing loss in 45%, endocrine diseases in 35%, hepatic focal nodular hyperplasia (FNH) in 22%, cardiac disease in 14%, second benign tumors in 6%, second malignant tumors in 4%.In the multivariate regression analysis, exposure to MIBG (p<0.001) and ASCT (p=0.020) were potential risk factors for thyroid diseases. Univariate analysis identified a potential risk factor for hearing loss: cisplatin (cumulative dose ≥400 mg/m2) (p = 0.004). Univariate analysis identified ASCT as a potential risk factor for dental anomalies (p= 0.029), growth failure (height Z-score, -2) (p= 0.027). Radiation therapy was associated with an increased risk of growth failure (p= 0.042). Patients were at greater risk of developing spinal deformity with intraspinal extension of NB (p= 0.022) and after laminotomy (p= 0.028), thoracotomy (p= 0.023). ASCT and MIBG were not associated with an increased risk of ototoxicity, FNH, renal disease or second neoplasms.

Conclusion: Late complications occur frequently in survivors of NB. Long-term follow-up and screening of this population is essential.