PROPOSAL OF TREATMENT OF HIGH-RISK NEUROBLASTOMA WITH IMMUNOTHERAPY AND CHEMOTHERAPY

Patient: VLADIMIR ATAIANTS
BUDGET nº: 26PS00697
Department: Oncology
Specialist: Dr. Jaume Mora
Diagnosis: High-risk neuroblastoma

Vladimir Ataiants is a 5-year-old boy diagnosed with relapsed/refractory high-risk neuroblastoma.

He was initially diagnosed in 2023 in Russia with stage 4 neuroblastoma originating in the left adrenal gland, with bone and bone marrow metastases. Molecular studies showed MYCN gain and 11q23 deletion in 50% of nuclei, without MYCN amplification, ALK alteration, or 1p36 deletion. He was classified as high-risk under the NB-2004 protocol.

Initial treatment included chemotherapy and dinutuximab, achieving a very good partial response. In December 2024, disease progression was documented with bone and lymph node involvement. He subsequently received irinotecan/temozolomide (I/T) chemotherapy with good response after six cycles and continued on I/T plus dinutuximab.A biopsy of a left supraclavicular lymph node was performed in December 2024. From April to September 2025, he received immunochemotherapy.

A MIBG scan in June 2025 showed persistent uptake in the skull and left femur, consistent with refractory bone disease. Continuation of chemo-immunotherapy with the addition of radiotherapy was planned.

A second-opinion teleconsultation was held on July 7, 2025, confirming the primary refractory nature of the disease. At that time, the patient was clinically stable and receiving appropriate rescue therapy. Further evaluation was recommended.

Treatment ended in September 2025. Disease evaluation in November 2025 showed stable disease.

On February 10, 2026, a follow-up second-opinion consultation was conducted. Given the history of prolonged refractory disease, the poor prognosis was emphasized. Evaluation for possible central nervous system (CNS) involvement was recommended through brain MRI. In the absence of CNS disease, chemo-immunotherapy with naxitamab was proposed as a potential option. Other therapies such as MIBG and CAR-T were discussed but not recommended.

The most recent 18F-DOPA PET scan (February 2, 2026) demonstrated progression, with increased size and intensity of previously identified bone lesions, appearance of multiple new bone lesions, new uptake in the

parieto-occipital region of the left cerebral hemisphere, and increased uptake in cervical lymph nodes. Correlation with MRI was recommended to assess possible intracranial involvement.

Recently, the patient has developed bone pain. The local medical team has proposed initiating treatment with cyclophosphamide and topotecan.

The clinical reports from patient (Federal State Budgetary Institution National Medical Research Center of Children's Hematology, Oncology, and Immunology- Dr Elena Dmitrievna Kireeva 3rd February 2026) has been evaluated by Dr. Jaume Mora, Scientific Director of the Department of Pediatric Oncology of our hospital.

After reviewing the medical information, Dr. Mora indicates that the recommended treatment consists of 7 cycles of chemo-immunotherapy with Naxitamab. We are currently awaiting the report of the CNS MRI in order to rule out any involvement of the central nervous system.
. The specialist recommends undergoing a complete diagnostic evaluation at our hospital to confirm the clinical status and treatment plan.

For refractory disease: Patients with high-risk neuroblastoma who do not achieve a complete response to induction chemotherapy are classified as primary refractory, with generally poor prognoses. For these patients, anti-GD2 chemoimmunotherapy offers promising potential for salvage. When administered promptly following induction failure, this approach has demonstrated a 3-year overall survival (OS) rate of 84.8% and an event-free survival (EFS) rate of 54.4% (Muñoz et al., *Cancers*, 2023).
The proposal includes:

1. Stage of extent of disease evaluation and patient's general condition

During this stage the patient may or may not be admitted in the inpatient unit and includes:

- First consultation with the referral oncologist and final consultation to evaluate the results of the tests and information of the treatment plan.
- Consultation with cardiologist.
- Laboratory test (Oncology profile).
- Imaging tests (MRI with anesthesia; CT, PET-CT and MIBG)
- Bone marrow aspiration with bone marrow examination
- Port - a - Cath placement if needed.
- Appointment with the Neurosurgery Department (Dr. Hinojosa).
- Histopathological and molecular review. **It is imperative that the family brings the tumor's paraffin blocks from the initial biopsy to confirm the diagnosis and perform molecular analysis.**

The complete diagnostic evaluation will be performed on an outpatient basis and will require 7-10 business days.

It is very important that the parents bring the paraffin blocks to repeat the pathological anatomy study.

2. Chemo-immunotherapy

Chemoimmunotherapy refers to the combination of an anti-GD2 monoclonal antibody and chemotherapy. The treatment regimen is consistent for both approaches, with the following common parameters:

- Seven treatment cycles administered every four weeks.
- Disease evaluations, including bone marrow studies and MIBG scans, performed every two cycles.

The administration protocol differs depending on whether the monoclonal antibody used is dinutuximab-beta or naxitamab:

- Dinutuximab-beta: Each cycle consists of a 5-day course of irinotecan and temozolomide and the administration of dinutuximab-beta. The treatment is administered on an inpatient basis over 7 days.
- Naxitamab: Each cycle includes a 5-day course of irinotecan and temozolomide, with naxitamab administered over 4 days. This regimen is delivered over 2 weeks on an outpatient basis.

Please note that in this document, the quoted price corresponds to 7 cycles. The rule to decide how many cycles each patient should undergo is as follows: **from the moment the patient has started chemoimmunotherapy treatment and reached complete remission, six cycles of immunotherapy will be conducted**

3. **Surgery-Radiotherapy** on refractory lesions IF NEEDED.

The estimated duration of all 7 cycles is 8-10 months.

In summary, the proposal of treatment at this time includes:

- Chemotherapy immunotherapy and adjuvant medication in accordance with protocol.
- Baseline imaging tests and follow up to monitor the treatment.
- Hospital stay of maximum 16 days in case of potential complications.
- Follow-up blood tests in accordance with the protocol and if medically required.
- Oncology day hospital sessions (Special procedures Unit) to administer the treatment and following check-ups, up to a maximum of 56 sessions over the 7 cycles.
- Medical consultations including control and monitoring visits at the inpatient unit and day hospital (Special Procedures Unit).

Recent publications from our team relevant in neuroblastoma:

1. Mora J., Castañeda A., Gorostegui M., Varo A., Perez-Jaume S., Simao M., Muñoz J.P., Garraus M., Larrosa C., Salvador N., Lavarino C., Krauel L., Mañe S., "Naxitamab Combined with Granulocyte Macrophage Colony Stimulating Factor as Consolidation for High Risk Neuroblastoma Patients in First

Complete Remission under Compassionate Use Updated Outcome Report". Cancers (Basel). 2023 Apr 28; 15(9):2535. doi: 10.3390/cancers15092535. PMID: 37174002; PMCID: PMC10177429

2. Mora J., "Autologous Stem Cell Transplantation for High Risk Neuroblastoma: Historical and Critical Review". Cancers (Basel). 2022 May 24; 14(11):2572. doi: 10.3390/cancers14112572. PMID: 35681553; PMCID: PMC9179268.
3. Mora J., Castañeda A., Gorostegui M., Santa María V., Garraus M., Muñoz J.P., Varo A., Perez-Jaume S., Mañe S., "Naxitamab combined with granulocyte macrophage colony stimulating factor as consolidation for high risk neuroblastoma patients in complete remission". Pediatric Blood Cancer. 2021 Oct; 68(1 0):e29121. doi: 10.1002/pbc.29121. Epub 2021 May 22. PMID: 34022112.
4. Mora J., Modak S., Kinsey J., Ragsdale C.E., Lazarus H.M., "GM-CSF, G-CSF or no cytokine therapy with anti-GD2 immunotherapy for high risk Neuroblastoma". Int J Cancer. 2024 Apr 15;154(8):1340 136 4. doi: 10.1002/ijc.34815. Epub 2023 Dec 18. PMID: 38108214.
5. Castañeda A., Gorostegui M., Miralles S.L., Chamizo A., Patiño S.C., Flores M.A., Garraus M., Lazaro J.J., Santa-Maria V., Varo A., Muñoz J.P., Mora J., "How we approach the treatment of patients with high risk neuroblastoma with naxitamab: experience from the Hospital Sant Joan de Déu in Barcelona, Spain". ESMO Open. 2022 Apr;7(2):100462. doi: 10.1016/j.esmoop.2022.100462. Epub 2022 Apr 6. Erratum in: ESMO Open. 2022 Jun;7(3):100504. doi: 10.1016/j.esmoop.2022.1005 04. PMID: 35397431; PMCID: PMC9006652.
6. Mora J., Castañeda A., Flores M.A., Santa-María V., Garraus M., Gorostegui M., Simao M., Perez-Jaume S., Mañe S., "The Role of Autologous Stem-Cell Transplantation in High--Risk Neuroblastoma Consolidated by antiby anti-GD2 Immunotherapy. Results of Two Consecutive Studies". Front Pharmacol. 2020 Oct 30; 11:575009. doi: 10.3389/fphar.2020.575009. PMID: 33324208; PMCID: PMC7723438.
7. Gorostegui M., Muñoz J.P., Perez-Jaume S., Simao-Rafael M., Larrosa C., Garraus M., Salvador N., Lavarino C., Krauel L., Mañe S., Castañeda A., Mora J., "Management of High-Risk Neuroblastoma with Soft-Tissue-Only Disease in the Era of Anti-GD2 Immunotherapy". Cancers (Basel). 2024 Apr 29; 16(9):1735. doi: 10.3390/cancers16091735. PMID: 38730688; PMCID: PMC11083939.
8. Muñoz J.P., Larrosa C., Chamorro S., Perez-Jaume S., Simao M., Sanchez-Sierra N., Varo A., Gorostegui M., Castañeda A., Garraus M., Lopez-Miralles S., Mora J., "Early Salvage Chemo-Immunotherapy with Irinotecan, Temozolomide and Naxitamab Plus GM-CSF (HITS) for Patients with Primary Refractory High-Risk Neuroblastoma Provide the Best Chance for Long-Term Outcomes". Cancers (Basel). 2023 Oct 3; 15(19):4837. doi: 10.3390/cancers15194837. PMID: 37835531; PMCID: PMC10571514.
9. Larrosa C., Mora J., Cheung N.K., "Global Impact of Monoclonal Antibodies (mAbs) in Children: A Focus on Anti-GD2". Cancers (Basel). 2023 Jul 22; 15(14):3729. doi: 10.3390/cancers15143729. PMID: 37509390; PMCID: PMC10378537.

Why SJD Barcelona Children's Hospital?

The Pediatric Cancer Center Barcelona is a new monographic center for the benefit of children and adolescents with cancer and their families. The facility will bring together the healthcare services aimed at patients with developmental cancer in one single place, as well as spaces dedicated to research. The aim is to treat a large volume of patients more effectively, efficiently and adequately, more than 400 new patients per year, with the highly specialized team of the SJD Barcelona Children's Hospital Oncology Department. The SJD Barcelona Children's Hospital's Oncology Department is a national and international reference center for the care and research of developmental cancer.

The accumulated experience and the personalized care offered, places SJD among the best international centers for the treatment of this childhood cancer. The management of patients with neuroblastoma is highly complex, especially when it is a high-risk case, more than 50% of all neuroblastomas at presentation. A multidisciplinary approach is required and few centers can provide all super-specialized disciplines that are required to aim for the best cure rates. SJD Barcelona Children's Hospital offers all treatment modalities that patients may need in order to find the best strategy based on a broad clinical experience and research that started more than 15 years ago.

Link to Oncology Department, Pediatric Cancer Center Barcelona and Doctor's CV:

https://www.sjdhospitalbarcelona.org/en/medical-services/oncology

https://www.sjdhospitalbarcelona.org/en/pediatric-cancer-center-barcelona

https://www.sjdhospitalbarcelona.org/en/news/sjd-barcelona-childrens-hospital-best-centers-world-treatment-neuroblastoma

https://www.sjdhospitalbarcelona.org/en/specialists/jaume-mora-graupera

Treatment cost considerations:

To begin the process of care in our center (that is, the diagnostic confirmation phase, evaluation of the extent of the disease, and evaluation of the state of the patient) an initial deposit of the full amount indicated in this proposal is needed.

If upon arrival at the hospital there is an available clinical trial addressing the type of cancer that the patient is diagnosed with and the patient is shown to meet the qualifying criteria of entry to the trial, the hospital will return part of the monetary deposit paid corresponding to the financial coverage of the clinical trial in accordance with current international regulations once the patient has been discharged from the pathology for which the patient came to the hospital.

Any other provision necessary or hospital stay required as a result of treatment complications that exceed the maximum number of inpatient stays in this proposal shall be invoiced separately. The treatment proposal and the budget do not include any admission or stay in the Pediatric Intensive Care Unit (not expected) that might be necessary in case of complications associated with the administration of immunotherapy.

The treatment costs are regarded as a closed package of services (forfait), which cannot be split (that means, the price of each service is not specified and only the total amount is provided). The budget does not include accommodation during the stay in Barcelona. To complete the treatment, the patient must remain in Barcelona during approximately xx months.

All the previous evaluations have been carried out without actually examining the patient in person, they are not binding and may be subject to change once the patient is seen by the specialists and the indicated complementary tests are performed. The current treatment plan may change depending on the results of the diagnostic evaluation and the patient's health status.

If you have any additional question, please do not hesitate to ask. We remain at your disposal and look forward to hearing from you.

Best regards,

Barcelona, 18 February 2026

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Pediatric Cancer Center
Barcelona Children's Hospital

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In accordance with the provisions of article 7 of Law 7/2012, transactions in which any of the intervening parties acts as a businessperson or professional, the amount of which is equal to or greater than 10,000 euros or its equivalent in foreign currency, may not be paid in cash.

This proposal is valid for 6 months.