# #75P - Efficacy and Updated Safety Results from Pivotal Phase II Trial 201 of Naxitamab (Hu3F8), a Humanized GD2 Targeted Immunotherapy for the Treatment of Refractory/Relapsed (R/R) High-Risk (HR) Neuroblastoma (NB)

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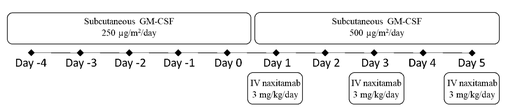
## Background/Aim

- NB represents the most common extracranial solid tumor of childhood.
- HR-NB typically includes metastases in bones and/or bone marrow (BM).
- Naxitamab is a humanized monoclonal antibody targeting GD2 abundantly expressed in NB.
- A phase 1 trial with naxitamab and granulocyte-macrophage colony-stimulating factor (GM-CSF) showed encouraging results (JAMA Oncol 2018; 4:1729).
- We evaluated naxitamab in HR-NB patients who had disease ONLY in bones and/or BM that was refractory to initial treatment(s) or who had insufficient response to therapy for relapsed/progressive disease.

## Methods

In Trial 201, naxitamab was administered IV in the outpatient setting. Dosing was 9 mg/kg/cycle divided into 3 doses (Days 1, 3, 5) administered over a minimum of 30 minutes with cycles repeated every 4 weeks.
GM-CSF was administered subcutaneously daily for 10 days starting 5 days prior to naxitamab: 250 µg/m$^2$ per day from Day -4 to Day 0 and 500 µg/m$^2$ per day at Day 1 to Day 5. GM-CSF were provided for administration at home after patient/parents were trained on how to administer the drug.
Patients were eligible if disease was limited to bone and/or BM.
Patients with relapse NB were eligible following salvage therapy and with no progressive disease at trial entry.

Treatment cycle:




Treatment cycles were repeated every 4 weeks (±1 week) until response followed by 5 additional cycles. Subsequent cycles could be repeated every 8 weeks (±2 weeks) through 101 weeks from first infusion at the discretion of the investigator.

Centralized response assessment was done according to the revised INRC (JCO 2017;35:2580).

We report interim efficacy data from 22 patients and safety data on the first 36 patients enrolled. Patients were recruited from April 2018 with a data cut-off 23 July 2020 (efficacy) and 27 November 2019 (safety).

## Statistical Methodology

Overall response rate (ORR) and CR rate: 95% confidence intervals (CIs) were calculated using exact methodology. The duration of response (DoR) was calculated from response either to progression or the time of the last evaluable assessment.

## Conclusions:

- In R/R HR-NB patients with residual disease only in the bone/BM compartment, an area of high unmet need, naxitamab + GM-CSF can achieve **major clinical responses.**
- **CR was achieved in 13 of 22 evaluable patients** as per independent review assessments.
- In the efficacy analysis the **ORR was 68%.**
- Naxitamab offers a **unique option** for treatment of patients in the **outpatient setting** (see abstract #353 /poster #74P for details on naxitamab administration).
- Adverse events were generally manageable with timely recognition and intervention.

## Results

**Table 1: Demographics (Efficacy Population)**

| Demographics | Category | N=22 |
|---|---|---|
| Age, years | Mean<br>SD<br>Median<br>Min, Max | 5.6<br>2.0<br>5.0<br>3, 10 |
| Sex, n (%) | Female<br>Male | 9 (41%)<br>13 (59%) |
| Race, n (%) | White<br>Asian<br>Other | 10 (45%)<br>11 (50%)<br>1 (5%) |

**Table 2: Baseline Disease Characteristics (Efficacy Population)**

| Baseline disease characteristics | Group | N=22<br>n (%) |
|---|---|---|
| *MYCN* amplification status | Amplification<br>Gain<br>Neither gain nor amplification<br>Unknown | 3 (14%)<br>1 (5%)<br>13 (59%)<br>5 (23%) |
| INSS stage at diagnosis | Stage 3<br>Stage 4<br>Unknown | 1 (6%)<br>19 (86%)<br>2 (9%) |
| Histology per INPC | Favorable histology<br>Unfavorable histology<br>Unknown | 1 (5%)<br>14 (64%)<br>7 (32%) |
| Neuroblastoma location[a] | Bone<br>Bone marrow<br>Both bone and bone marrow | 13 (59%)<br>2 (9%)<br>7 (32%) |
| Disease-status | Primary refractory<br>Relapsed patients | 14 (64%)<br>8 (36%) |

[a] Independent review (IR) assessments

INPC = International Neuroblastoma Pathology Committee; INSS = International Neuroblastoma Staging System

**Table 3: Prior medication/treatment for NB (Efficacy Population)**

| Prior medication/treatment | N=22<br>n (%) |
|---|---|
| Prior surgery | 20 (91%) |
| Prior chemotherapy | 21 (95%) |
| Prior radiation | 8 (36%) |
| Prior anti-GD2 therapy | 4 (18%) |

### Efficacy

**Table 4: Overall response rate (ORR) and complete response (CR) rate - IR assessments**

| Group | Endpoint | n (%) | 95% CI Lower limit | 95% CI Upper limit |
|---|---|---|---|---|
| Overall (N=22) | ORR | 15 (68%) | 45% | 86% |
| | CR rate | 13 (59%) | 36% | 79% |
| Refractory (N=14) | ORR | 10 (71%) | 42% | 92% |
| | CR rate | 9 (64%) | 35% | 87% |
| Relapsed (N=8) | ORR | 5 (63%) | 24% | 91% |
| | CR rate | 4 (50%) | 16% | 84% |

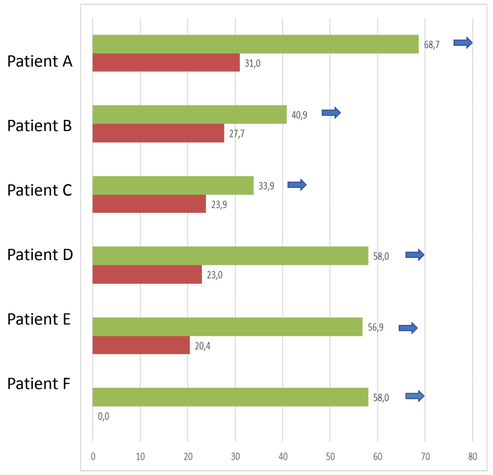
The median number of treatment cycles to onset of response was 2 (range: 2-5).

Progressive disease was reported for 3/22 patients (14%), comprising 2/14 (14%) refractory and 1/8 (12.5%) relapsed. Stable disease and minor response were reported for 3/22 patients (14%) comprising 1/14 (7%) and 2/8 (25%) for refractory and relapsed patients.

BM clearance in patients with positive BM at trial start (IR): CR in BM was observed in 7 of 9 patients. The median DoR (IR assessments) was 25 weeks (95% CI [19, not estimable]).

For the 15 responders confirmed by IR (**Table 4**), the DoR assessment was supplemented with available response data (investigator assessments) recorded during long-term follow-up (LTFU). The median DoR (IR+LTFU) was 27 weeks (95% CI [19, not estimable]).
All 6 patients with available LTFU information were still in remission at the last investigator response assessment indicated by blue arrows in **Figure 1**.

**Figure 1:** DoR for patients with an ongoing response at the end of the IR assessments only [red horizontal bars] and supplemented with LTFU response data (Investigator assessments) [green horizontal bars] (weeks)




### Safety

Grade 1 or 2 (CTCAE v4.0) naxitamab-related Treatment Emergent Adverse Events (TEAEs) reported by at least 30% of patients included urticaria, tachycardia, pain, pyrexia, hypotension, bronchospasm, cough, vomiting, nausea, pruritus, hypertension, diarrhea, abdominal pain, and pain in extremity.

Grade 3 and 4 naxitamab-related TEAEs are sumarised in **Table 5**.

**Table 5: Summary of TEAEs Grade 3 or 4 reported by at least 10% of patients**

| Preferred Term | N=36<br>n (%) | | |
|---|---|---|---|
| | Grade 3 | Grade 4 | Grade 3 or 4 |
| Patients with at least one naxitamab-related TEAE | 30 (83%) | 5 (14%) | 31 (86%) |
| Pain | 24 (67%) | - | 24 (67%) |
| Hypotension | 21 (58%) | 1 (3%) | 22 (61%) |
| Urticaria | 13 (36%) | - | 13 (36%) |
| Bronchospasm | 8 (22%) | - | 8 (22%) |
| Abdominal pain | 5 (14%) | - | 5 (14%) |

Eight (22%) patients reported 9 naxitamab-related SAEs:
4 anaphylactic reaction, 2 hypotension, 1 laryngeal oedema, 1 pyrexia, 1 respiratory depression.

Three (8%) patients discontinued treatment due to naxitamab-related Grade 4 TEAE: 2 anaphylactic reaction, 1 respiratory depression; all were SAEs.

No fatal events were reported.

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