#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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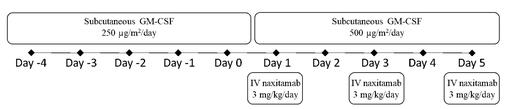
Background/Aim

- 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 SD Median Min, Max	5.6 2.0 5.0 3, 10
Sex, n (%)	Female Male	9 (41%) 13 (59%)
Race, n (%)	White Asian Other	10 (45%) 11 (50%) 1 (5%)

Table 2: Baseline Disease Characteristics (Efficacy Population)

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

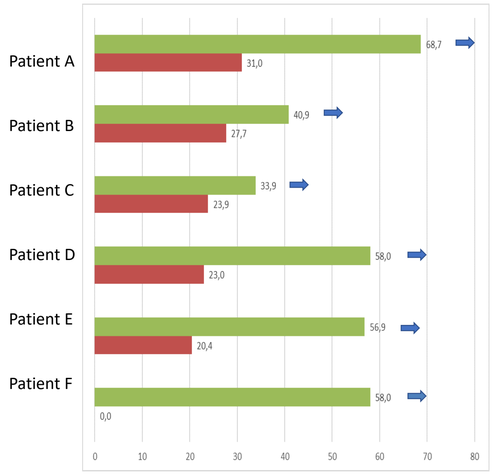
The median number of treatment cycles to onset of response was 2 (range: 2-5).

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 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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