#74P - Pivotal Trial 201 Data on Outpatient Administration of Naxitamab (Hu3F8), a Humanized GD2 Targeted Immunotherapy for the Treatment of Refractory/ Relapsed (R/R) High-Risk (HR) Neuroblastoma (NB)

Daniel A Morgenstern[1], Jaume Mora[2], Godfrey CF Chan[23], Karsten Nysom[4], Melissa K Bear[5], Lene Worsaae Dalby[6], Steen Lisby[6], Brian H Kushner[7]

[1]The Hospital for Sick Children, Toronto, Canada, [2]Pediatric Cancer Center Barcelona, Hospital Sant Joan de Déu. Spain, [3]Queen Mary Hospital, University of Hong Kong, Hong Kong, [4]Rigshospitalet, Copenhagen, Denmark, [5]Riley Hospital for Children, Indianapolis, USA, [6]Y-mAbs A/S, Hoersholm, Denmark, [7]Memorial Sloan Kettering Cancer Center, New York, USA

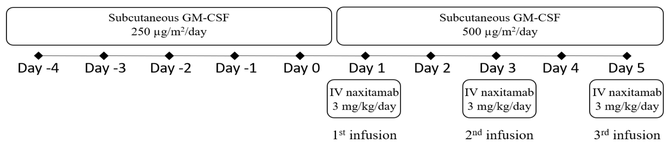
Background/Aim

- For patients with R/R HR NB, the prognosis is poor and there is no standard of care.
- One possible treatment for this population is immunotherapy targeting GD2, a disialoganglioside overexpressed in most NB cells.
- The currently available anti-GD2 chimeric antibody requires inpatient treatment with an infusion of 8-20 hours for 4-5 consecutive days or 10 days continuous infusion usually started and often completed as an inpatient.
- Naxitamab, a humanized GD2 receptor antibody with high affinity, is administered over a minimum of 30 minutes in the outpatient setting.
- Here we describe the outpatient experience from Trial 201 patients with R/R HR NB with residual disease in the bone or bone marrow (BM) who have demonstrated a partial response, minor response, or stable disease to prior therapy.

Methods

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. Naxitamab was given in combination with GM-CSF.
In Trial 201, naxitamab was administered IV in the outpatient setting. Dosing was 9 mg/kg/cycle divided into 3 doses administered (Days 1, 3, 5) with cycles repeated every 4 weeks until response followed by 5 additional cycles. Subsequent cycles could be repeated every 8 weeks through 101 weeks from first infusion at the discretion of the investigator.

Treatment cycle:



Statistical Methodology:

Two-sided 95% confidence intervals (CI) for proportions were calculated using the exact method for the binomial distribution.

Premedication and supportive therapies/medication per Trial 201 protocol:

The trial protocol includes defined mitigations for toxicities and when to pause, restart and decrease infusion speed.

Premedication: reduce risk of infusion-related reactions and nausea/vomiting

Prior to Cycle 1 Day 1 (C1D1) i.v. corticosteroids:
- methylprednisolone 2 mg/kg, max 80 mg or equivalent
- ½ to 2 hours prior to infusion of naxitamab
- In case of Grade 3 anaphylaxis or bronchospasm at C1D1, corticosteroids should be repeated C2D1 and C1D3

Prior to each naxitamab infusion:
- antihistamine
- acetaminophen
- antiemetic

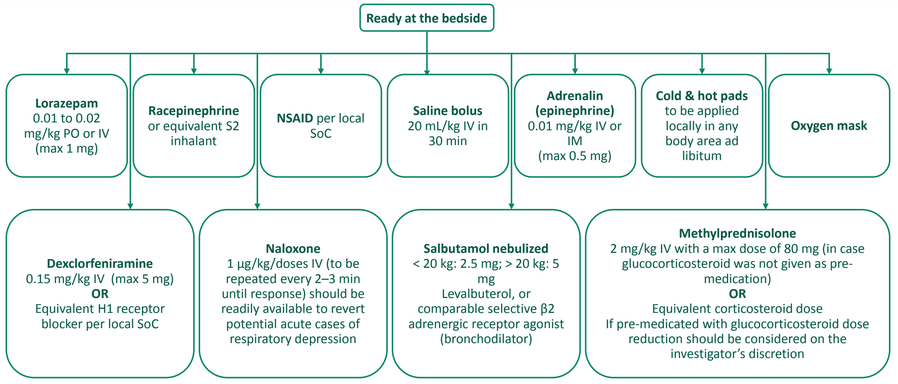
Pain management prior to and during infusion

Gabapentin:
- Initiation 5 days prior to the first infusion of naxitamab in each cycle (Day -4)
- Dose titration to full dose at Day -2 through to Day 7

Opioids:
Prior to infusion:
- Oral opioids (e.g. oxycodone 0.1-0.2 mg/kg max 5 mg)
- 45–60 minutes prior to initiation of each naxitamab infusion

During - for breakthrough pain:
- i.v. opioids (e.g. hydromorphone 0.00375-0.015 mg/kg)
- Can be repeated every 5 minutes for a max of 4 times

Ketamine:
Consider use of ketamine for pain that is not adequately controlled by opioids



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Conclusions:

- The vast majority (95%) of naxitamab infusions in Trial 201 were administered in the outpatient setting.
- The duration of infusion was short, at a median of 37 minutes and all infusions were <2hours.
- Naxitamab + GM-CSF have achieved major responses in R/R HR-NB with manageable adverse reactions (see abstract #341/poster #75P for details).
- With a short-duration, outpatient infusion, naxitamab provides an alternative option from current therapies for patients with R/R HR-NB.

Results

We report data on the first 36 patients enrolled as per data cut-off date 27 November 2019.
The results below are grouped by infusion across cycles and patients meaning that 1st infusion represents first infusion in all cycles for all patients.

Administration (outpatient, dose)

- **Outpatient administration** for the 36 enrolled patients was achieved for **495/519 (95%) of all naxitamab infusions** with similar rates across and during cycles.

- **98% (508/519)** of the **infusions** provided the **complete dose**. Of the 11 infusions, which were not completed, all were reported to be due to adverse events and the PT reported (for 10 of 11 events) were: 5 hypotension (Grade 3), 3 anaphylaxis (2 Grade 4 and 1 Grade 3) , 1 respiratory depression (Grade 4), and 1 laryngeal oedema (Grade 3).

Infusion duration

- Overall, the **median (min; max) duration** of completed infusions was **37 minutes (17; 97min)**. The median duration of infusion was similar across cycles.
- The median duration of the 1st infusion of a cycle (46 min) was longer than the 2nd and 3rd (each 36 min) (**Table 1**).
- For the 95% of infusions administered in the outpatient setting, the infusion duration results were similar.

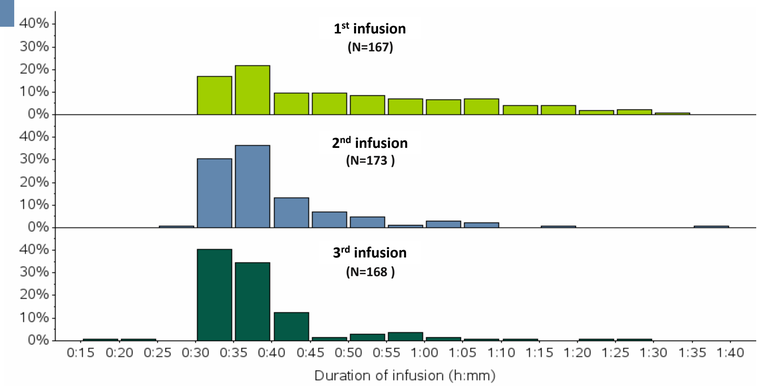
Table 1: The duration of completed infusions

Infusion (number of infusions)	Median duration of infusion (minutes)	Minimum (minutes)	Maximum (minutes)
Overall (N=508)[a]	37	17	97
1st infusion (N=167)	46	30	90
2nd infusion (N=173)	36	29	97
3rd infusion (N=168)	36	17	89

[a] Of the 11 infusions not completed, 9 were 1st infusion and 2 were 3rd infusion.

The distribution of infusion duration (**Figure 1**) shows that most completed infusions had a duration of 30 to 40 minutes. The distribution of duration differed between the 1st, 2nd and 3rd infusion of a cycle as only 50% of the 1st infusion of a cycle were completed within 45 minutes as compared to 2nd and 3rd infusion where it was 84% and 89%. Overall, **74% of the completed infusions lasted ≤45 minutes**.

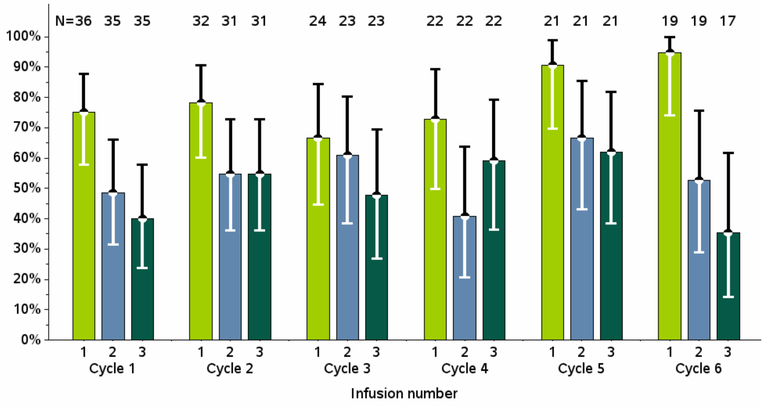
Figure 1: Distribution of duration of completed infusions



Infusion details (rate change/interruption)

- Overall, 204/519 (**39%**) naxitamab **infusions** were **without rate change or interruption**; the result for infusions done in an outpatient setting was similar (187/495 [38%]).
- The median (min; max) infusion interruption time was 15 minutes (3 min; 68 min).
- Across cycles, more infusion interruptions or rate changes were reported during 1st infusion compared to 2nd and 3rd infusion (**Figure 2**) and no improvement was observed over subsequent cycles.

Figure 2: Proportion (95% CI) of infusions with rate change or interruption, Cycles 1-6



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Author Contact Information: daniel.morgenstern@sickkids.ca