# Pharmacokinetic Analyses and Immunophenotyping of Patients Treated With Nelmastobart (hSTC810), A Novel Immune Checkpoint Inhibitor

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## Background

- A Phase I clinical trial is currently underway to evaluate Nelmastobart (hSTC810), an antibody targeting Butyrophilin 1A1 (BTN1A1), a novel immune checkpoint protein.
- This trial is a standard 3 + 3 dose escalation design to (i) explore the safety, tolerability, and pharmacokinetics, (ii) define a recommended Phase II dose (RP2D), and (iii) evaluate preliminary efficacy in patients with advanced solid tumors.
- Nelmastobart is administered intravenously every 2 weeks (Q2W) across 6 dose levels from 0.3 mg/kg to 15 mg/kg.
- As of March 31, 2023, a total of 44 patients were enrolled.
- No dose-limiting toxicities (DLTs) were observed, and the maximum administered dose (MAD) was 15 mg/kg Q2W.
- Most common TRAEs reported were grade 1-2 fatigue, headache, and nausea.
- Here, we provide an update on the clinical trial data previously presented, with a focus on the results of the pharmacokinetic, anti-drug antibody, cytokine, and immunophenotyping analyses.

## Methods

**Pharmacokinetics (PK) Analysis**

- Blood PK samples for all subjects were collected on Day 1 of Cycles 1-5 (within 30 minutes pre-dose and within 30 minutes from the end of infusion), and starting from Cycle 6 until Cycle 24, on Day 1 of every 3 cycles thereafter (within 30 minutes pre-dose). For steady state investigation, PK samples were collected on C1D2, C1D5, C1D8, C2D8, C5D2, C5D5, C5D8.
- PK samples were evaluated using a validated ELISA sandwich method.
- We provide the results of the pharmacokinetics study of these patients for the selected doses and dosing intervals, including the peak plasma concentration (Cmax), the time to reach Cmax (Tmax), and the average plasma concentration of hSTC810 over the dosing interval in steady state (Cavg).

**Anti-drug antibody (ADA) Analysis**

- Serum samples for anti-drug antibodies (ADA) were collected pre-dose on C1D1, C2D1, C3D1, C6D1, C12D1 , C24D1.
- PK samples were evaluated using a validated ECL Bridge Method.

**Pharmacodynamics Analysis**

- Samples for cytokine and immunophenotype analyses were collected at pre-dose C1D1, C1D8, C2D1, and C3D1.
- For cytokine analysis, a panel of cytokines was measured including IFN- γ, IL-2, IL-4, IL-6, IL-10,TNF-α, MCP-1, and TGF- β.
- For immunophenotyping analysis, flow cytometry was used to detect a panel of immunological marker proteins including CD3, CD4, CD8, CD19, CD14, CD16, CD56, CD25, CD45

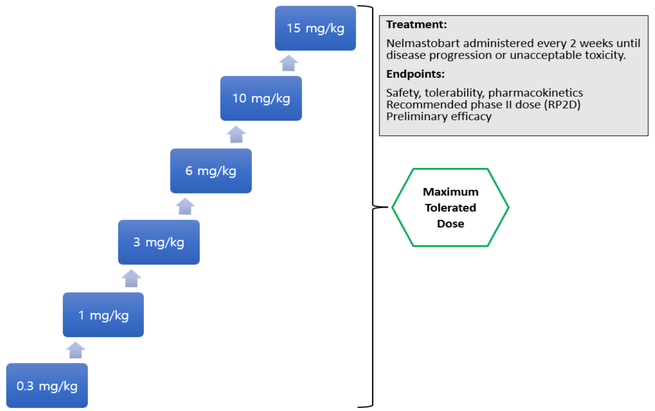


Figure 1. Study Design

## Results: Pharmacokinetics

- Increase in exposure was dose proportional to Nelmastobart over the dose range of 0.3 – 10 mg/kg following single and multiple dose.
- Following intravenous infusion, maximum concentrations were reached shortly after the end of infusion with Median Tmax ranging from 1.5 hours. Median Tmax remained the same across different dose levels in cycle 1.
- The half life ranged from 275 – 385 hours following single dose and 382 – 461 hours following multiple dose. Half life was similar over the doe range of 0.3 – 10 mg/kg.

| Dose (mg/kg) | Cycle | Mean C max (ng/mL) | T max (h) | Half-life (h) |
|---|---|---|---|---|
| 0.3 | 1 | 7490.00 | 1.50 | 308.26 |
| 1 | 1 | 17510.00 | 1.50 | 317.14 |
| | 5 | 29666.66 | N/A | 291.99 (n=2) |
| 3 | 1 | 47100.00 | 1.50 | 385.41 |
| | 5 | 80520.00 | N/A | 423.30 (n=3) |
| 6 | 1 | 89144.44 | 1.50 | 276.61 |
| | 5 | 16133.33 | N/A | 382.81 (n=1) |
| 10 | 1 | 160800.00 | 1.50 | 275.32 |
| | 5 | 213000.00 | N/A | 416.66 (n=1) |

Table 1. Summary of PK Parameters for Single-dose and Multiple-dose

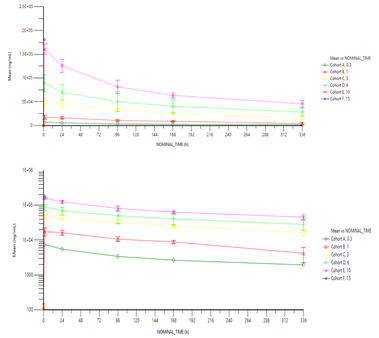

Figure 2. PK Profile for Single-dose

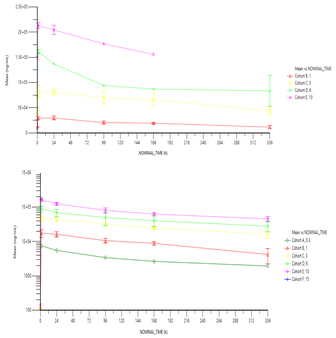

Figure 3. PK Profile for Multiple-dose

## Results: Anti-drug antibody

- Positive ADA screen was detected at C1D1 pre-dose (1 subjects) and C2D1 pre-dose (2 subject). 2 subjects were found to have a negative ADA screen in all subsequent cycles.
- In a single subject, a positive ADA screen was consistently detected starting from C2D1pre-dose to end of treatment.

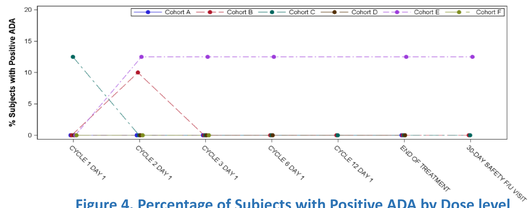


Figure 4. Percentage of Subjects with Positive ADA by Dose level

## Results: Pharmacodynamics

**Cytokines**

- Preliminary analyses show an increase in serum IFN-γ and TNF-a levels in individual subjects. Continuous follow-up is required to observe a correlation with Nelmastobart.
- Overall, there are no major changes in the cytokine profile of Nelmastobart and no cytokine-mediated toxicities.

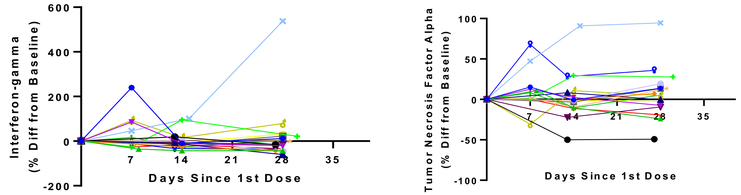


Figure 5. Cytokine Results

**Immunophenotype**

- Preliminary analyses show a trend towards a decrease in CD4+CD25+ cells and an increase in CD8+CD25+ cells, CD19+CD25+ cells, and CD25+ NK T cells.
- Further analyses is required to correlate these changes with patient responses.

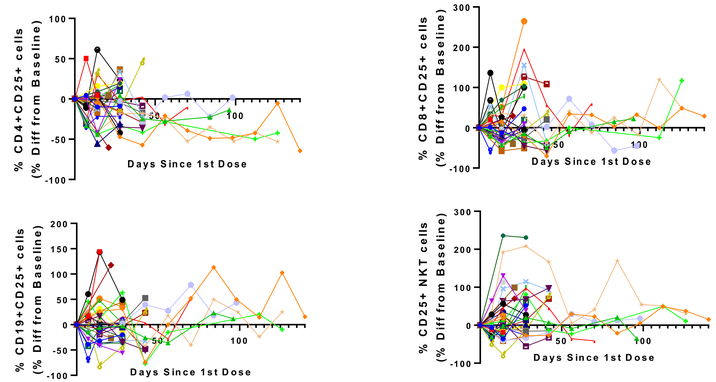


Figure 6. Immunophenotyping Results

## Conclusion

- The interim results of the current Phase 1 clinical trial suggest the usefulness of Nelmastobart in treating patients with advanced solid tumors.
- Interpretation of the pharmacokinetic, pharmacodynamic, and anti-drug antibody analyses indicate that Nelmastobart is a highly stable antibody with minimal to no toxicity.
- With respect to the pharmacokinetic properties, the dose-proportional increase and consistent Tmax values indicate that Nelmastobart is a highly stable antibody.
- Further ADA, cytokine, and immunophenotype analyses is required to observe any correlations with Nelmastobart.