# GLIMMER-01: Phase 1/2 Trial of a First-in-class Bi-sialidase (E-602) in Combination with Cemiplimab in Patients with PD-(L)1-resistant Solid Tumors

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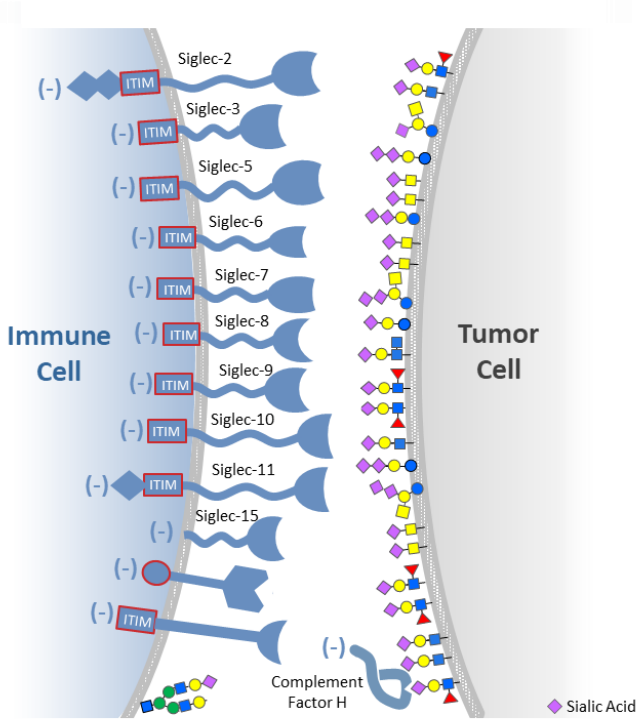
*Presented at the Society for Immunotherapy of Cancer (SITC) Annual Meeting, November 6-10, 2024, Houston, TX, USA*

# Desialylation of Tumors to Relieve Sialoglycan-Mediated Suppression and Reinvigorate the Anti-Cancer Immune Response

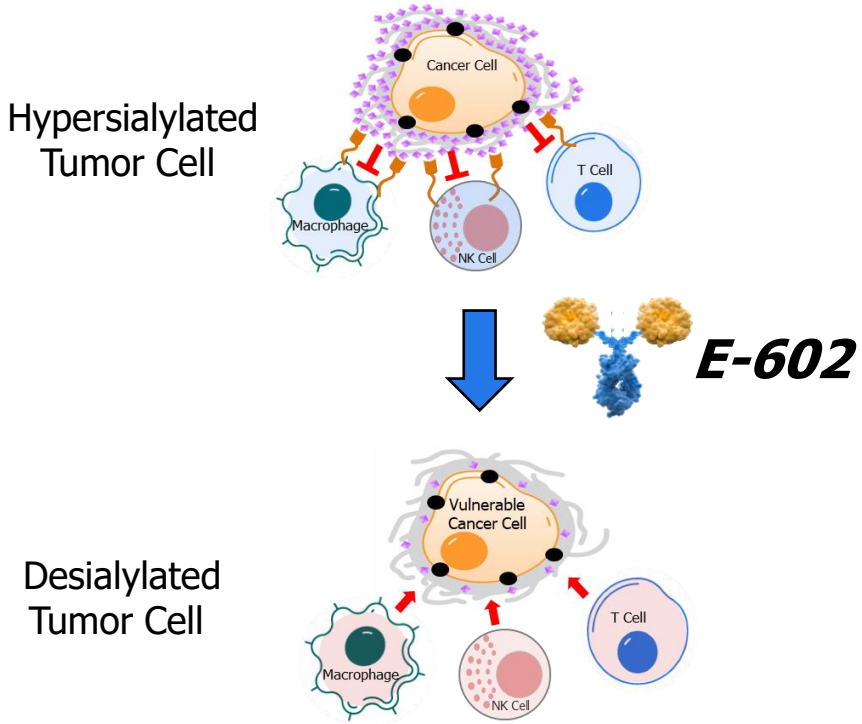
## Tumor Cell Sialoglycans Suppress Innate and Adaptive Antitumor Immunity




14 Siglecs in humans

Hundreds of Sialoglycans

## Desialylation of Tumor Cells Enhances Innate and Adaptive Antitumor Immunity



# E-602 in Combination with Cemiplimab in PD-(L)1 Resistant NSCLC and Melanoma Patients

## E-602 Monotherapy Dose Escalation* (GLIMMER-01 Part 1)

- Dose escalation: 1, 3, 10, 20, 30 mg/kg
- Established safety (well tolerated, no MTD)
- PK half-life: 18-26 hours
- Established proof-of-mechanism
  - Desialylation increased T cell activation in blood
  - Desialylation led to a dose-dependent increase in peripheral cytokines IP-10, TNF-α, and MIP-1β
- Determined RP2D 20mg/kg
  - Based on PD of T cell activation

* Luke, *et al*, AACR 2023 annual meeting, abstract #9654

## E-602 + Cemiplimab Combination (GLIMMER-01 Part 2)

- Primary endpoints
  - Safety and tolerability of the combination
  - Objective response rate
- Dose and schedule
  - E-602: 20mg/kg, Q1W
  - Cemiplimab: 350mg, Q3W
- PD-(L)1 resistant cancer patients (n=21)
  - NSCLC (n=12); melanoma (n=8); EGJ (n=1)
  - Median Age: 66 years (Range 42 - 82)
  - Female: 11 / 21 (52%)
  - ECOG PS of 1 at screening: 14/21 (67%)
  - Tumor biopsies before and during treatment
  - Frequency of Baseline Tumor Hypersialylation: 15/20 (75%)

# Safety Summary: E-602 in Combination with Cemiplimab

No DLTs at 20 mg/kg E-602 in combination with cemiplimab

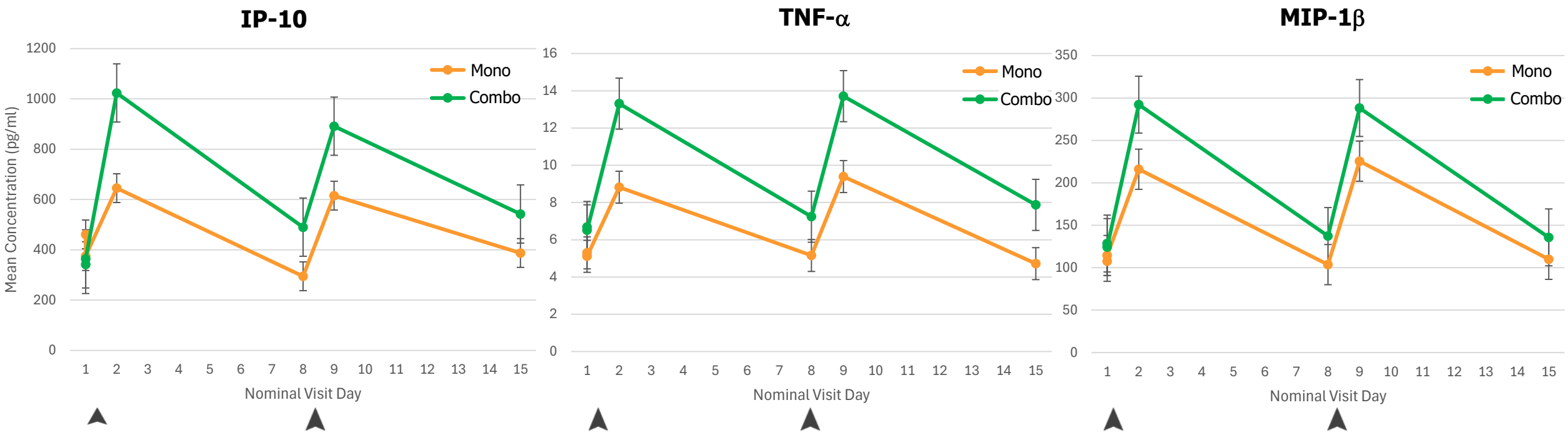
One Treatment Related SAE of Grade 3 infusion related reaction

## Frequency of Treatment-Related AEs Occurring in > 1 Patient

| Adverse Event N=21 participants | Grade 1 n (%) | Grade 2 n (%) | Grade 3 n (%) | Grade 4 n (%) |
|---|---|---|---|---|
| Infusion related reaction | | 8 (38%) | 1 (5%) | |
| Fatigue | 1 (5%) | 2 (10%) | | |
| Chills | 2 (10%) | | | |
| Nausea | 2 (10%) | | | |

# E-602 + Cemiplimab Resulted in a Greater Increase of Peripheral Cytokines than E-602 Monotherapy

## Mean Concentrations of Peripheral Cytokines




▲ E-602 Administration

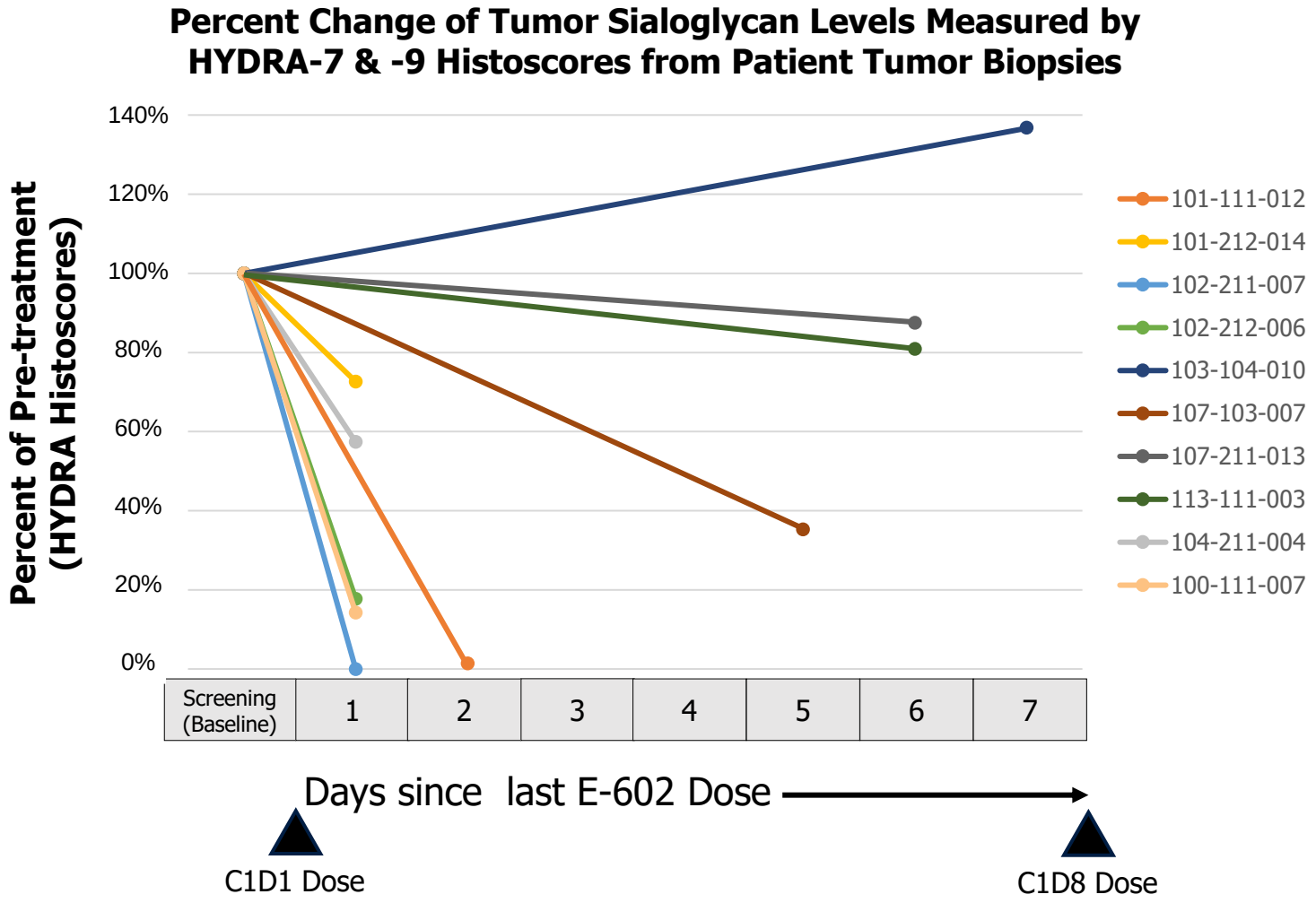
Mono: E-602 (20mg/kg, Q1W) (E-602 has demonstrated a dose-dependent increase in peripheral cytokine levels during dose escalation.)

Combo: E-602 (20mg/kg, Q1W) + Cemiplimab (350mg, Q3W)

# E-602 + Cemiplimab Led to Tumor Desialylation Lasting 2-5 Days, Despite Its Rapid Clearance With a Half-life of ~1 Day

HYDRA

Proprietary IHC reagents for measuring sialoglycans

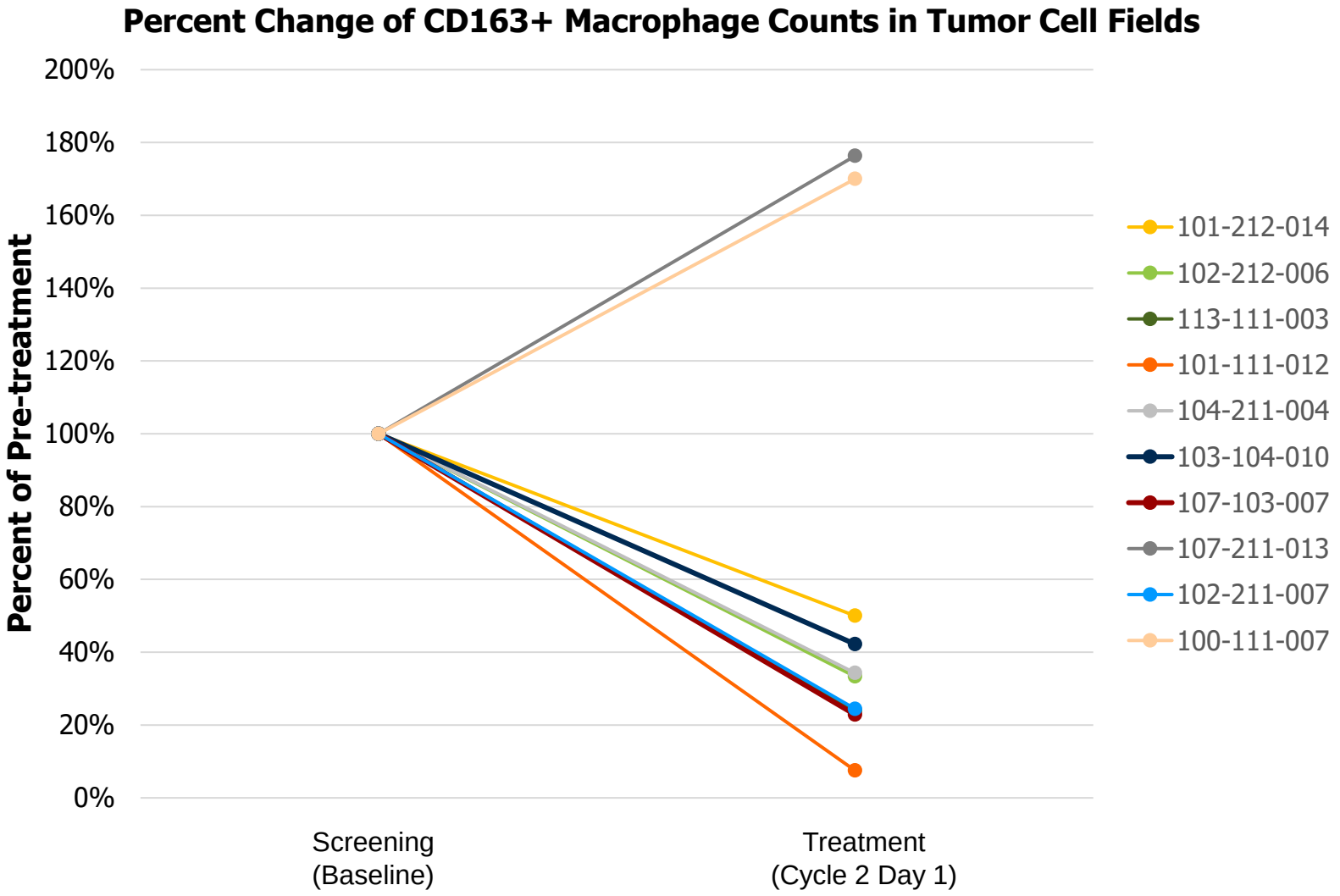



**9/10 patients showed tumor desialylation**

(Excluding patients with baseline HYDRA histoscore ≤ 20)

**Tumor Desialylation Duration Can be Increased to Improve Efficacy by Extending Half-life**

# E-602 + Cemiplimab Decreased CD163+ Tumor-Associated Macrophages Within Tumors




**8/10 patients showed a decrease in tumor-associated macrophages in tumors**

(Excluding patients with baseline HYDRA histoscore ≤ 20)

# Patients With Hypersialylation at Baseline Trended toward Better Clinical Outcomes than Patients Lacking Hypersialylation

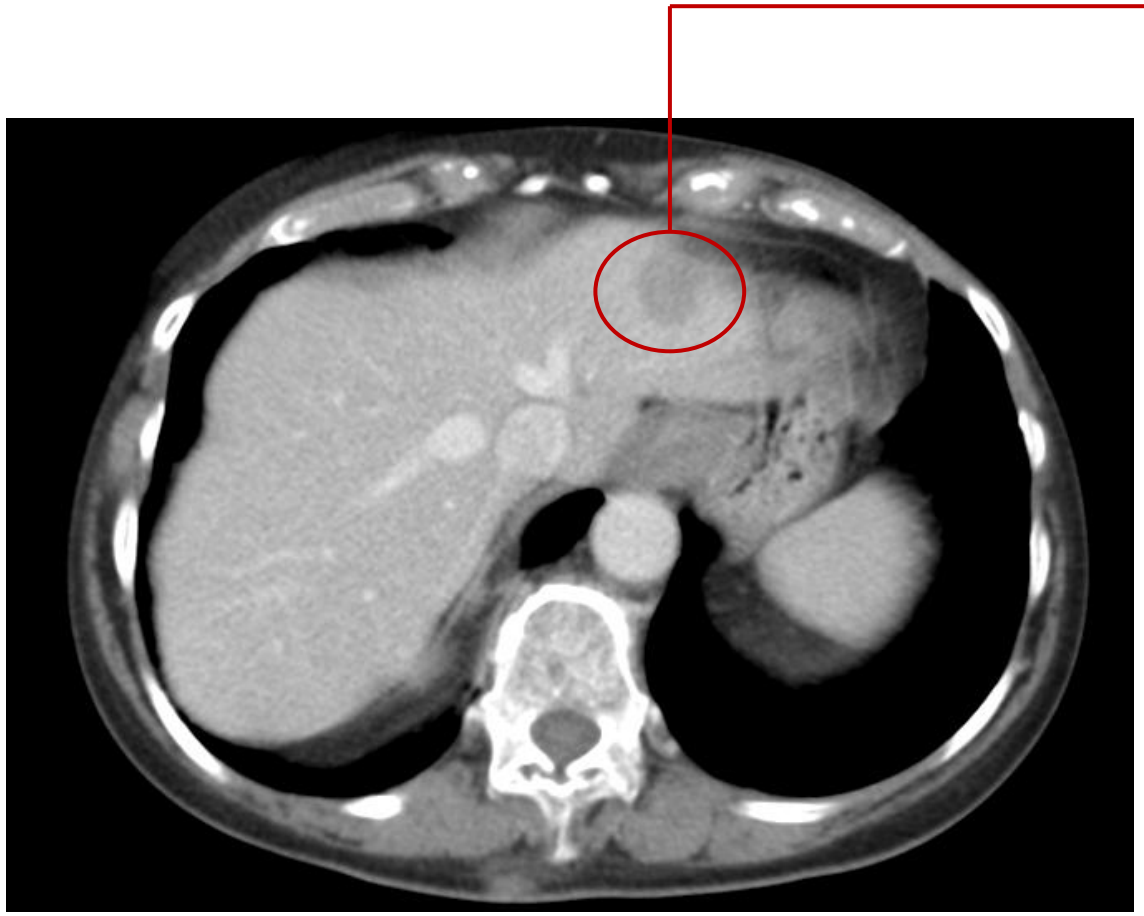
**These Data Support Desialylation of Tumor Cells with Hypersialylation as a Promising Therapeutic Strategy**

| Best Overall Response by Hypersialylation Status in PD-(L)1 Resistant Patients | | | | |
|---|---|---|---|---|
| **Patients** (PD-(L)1 resistant melanoma and NSCLC) | | **PR** | **SD** | **PD** |
| Patients with **Hypersialylation** (*HYDRA* ≥20) | n=15 | 1* (7%) | 6** (40%) | 8 (53%) |
| Patients **Lacking Hypersialylation** (*HYDRA* <20) | n=5 | 0 (0%) | 0 (0%) | 5 (100%) |

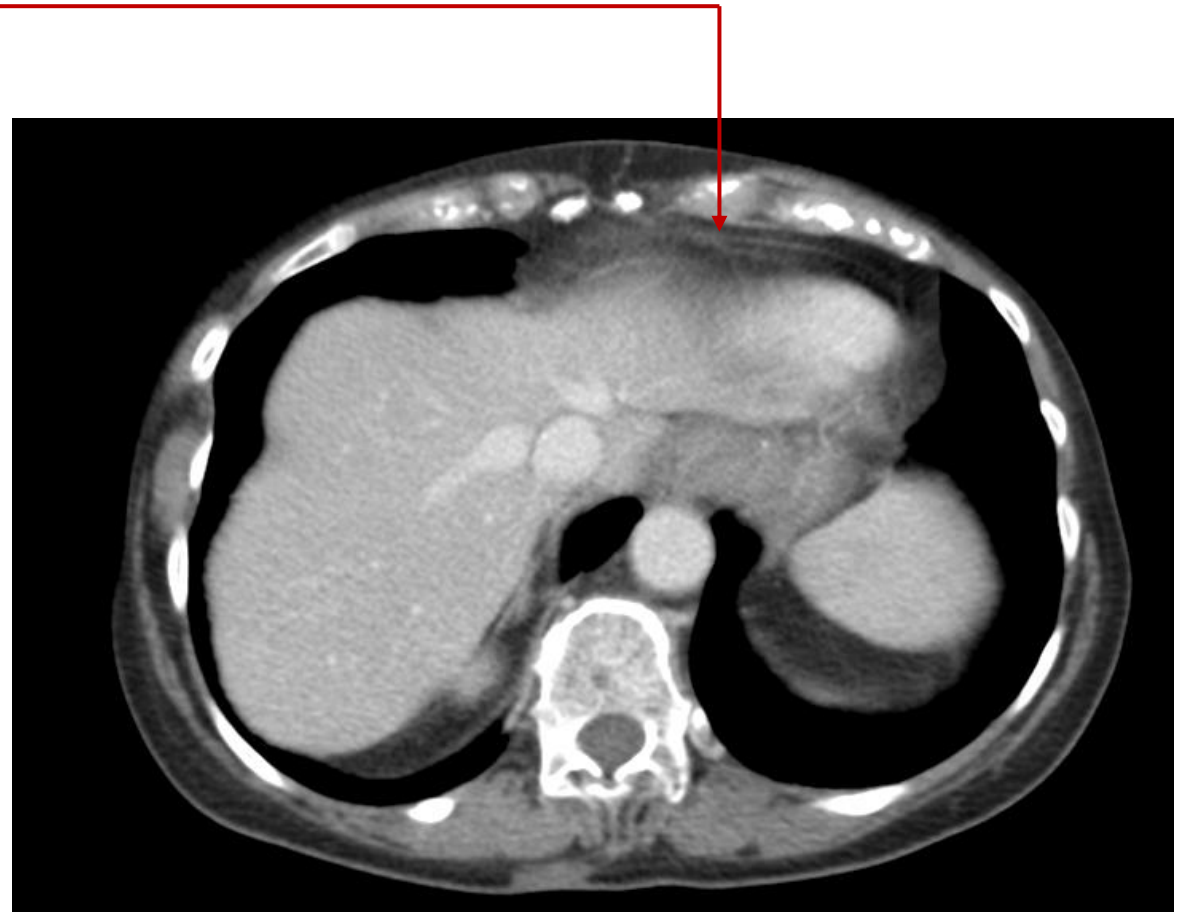
* Remains on therapy > **12 months** with complete resolution of liver mets, 80% reduction of other mets

** Duration of SD 3-6 months

# Confirmed Partial Response in Anti-PD-1 Resistant Melanoma Patient



09/27/2023 liver lesion 1.9 x 1.5 cm



11/15/2023 liver lesion resolved

The patient previously received adjuvant Ipilimumab and Nivolumab, and metastatic treatments with Nivolumab, Ipilimumab, Talimogene laherparepvec, and Binimetinib; all were discontinued due to complications or PD. Disease sites included the chest wall, liver, and left thigh, with non-target lesions in the ileum and breast. The last ICI treatment (Nivolumab) was given in November 2019, 3.9 years before starting E-602.

# Conclusions

1. Glycan editing (desialylation) of cell surface glycans offers a potential novel therapeutic approach to treat cancer.

2. E-602, a first-in-class engineered human sialidase Fc fusion, has demonstrated safety, proof-of-mechanism, and early antitumor activity in combination with cemiplimab for patients with PD-(L)1-resistant solid tumors.

3. Future goal: Increase tumor desialylation duration to improve antitumor activity

- Increase drug exposure by optimizing the human sialidase for extended half-life

- Enhance tumor targeting by incorporating a tumor targeting arm (TAA-targeted sialidase)

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# Acknowledgements

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The authors thank the participants, study sites, and investigators who participated in this clinical trial.

Palleon Pharmaceuticals funded this trial and participated in the trial design, research, analysis, data collection, interpretation of data, and the review and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship.