

# Imneskibart + Low-Dose Subcutaneous IL-2 ± Nivolumab in Patients With CPI-Refractory Cutaneous Melanoma: Promising Results From an Ongoing Phase 1/2 Study

Poster 242  
Abstract 9526  
NCT05267626  
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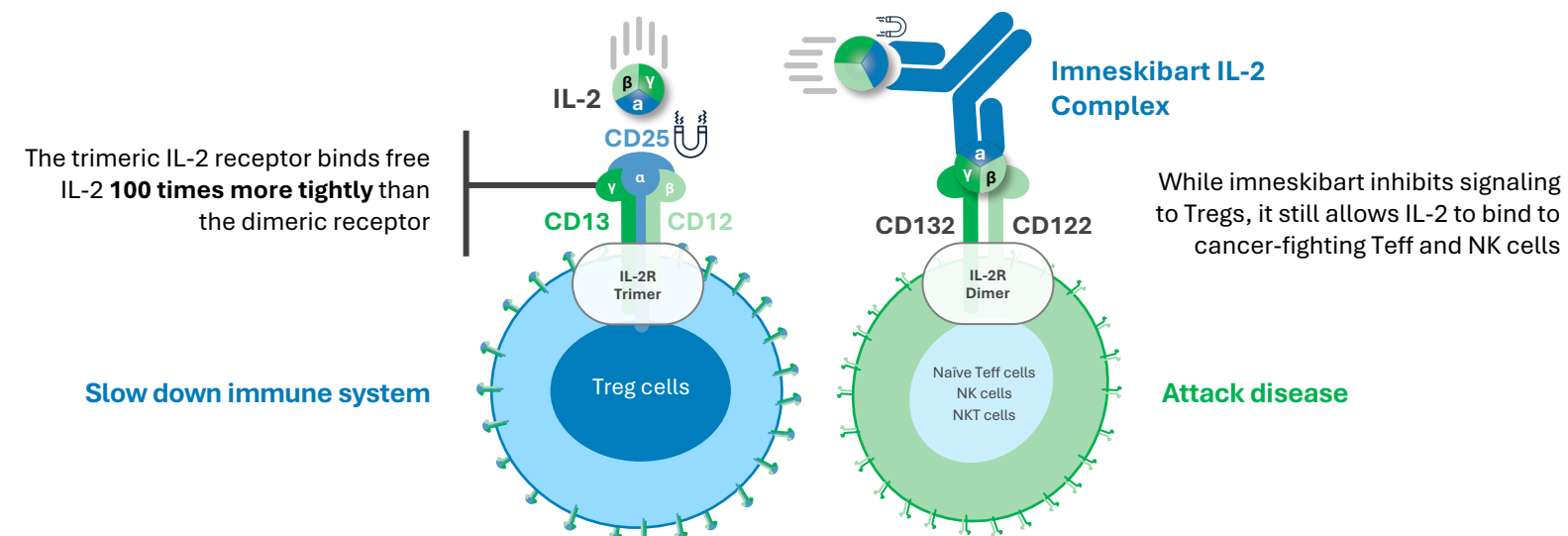
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## Imneskibart Background

**Redirects IL-2 to Effector T Cells (Teff) / Natural Killer Cells (NK) and Away From Regulatory T Cells (Tregs) and Vascular Endothelium**

- Imneskibart is a human IgG1 monoclonal antibody designed by leveraging artificial intelligence (Biolojic Design).
- Imneskibart binds interleukin-2 (IL-2) with pM affinity and completely inhibits its binding to CD25, without hindering its binding to CD122/CD132.

## Redirected IL-2 Signaling on Binding to Imneskibart



### Unique MOA Addresses the IL-2 Negative Feedback Loop

- Treatments activating effector cells against tumors are undermined by an autoinhibitory loop caused by endogenous IL-2 secreted from activated Teffs.
- Imneskibart can transform the IL-2 negative feedback loop into a positive feedback loop.
- Re-engineered IL-2 therapeutics cannot address the negative feedback loop, resulting in endogenous IL-2 stimulating Treg expansion, and limiting efficacy.
- Estimated human half-life is ~19.5 days.

## Study Design and Study Status

This is a Phase 1/2 open label dose escalation and expansion study. Enrollment is ongoing in Phase 2 evaluating imneskibart 9 mg/kg every two weeks (Q2W) intravenously (IV) + low-dose, subcutaneous (SC) aldesleukin (IL-2) loading dose of 135K IU/kg ± checkpoint inhibitor (CPI) in patients with cutaneous melanoma and non-small cell lung cancer (NSCLC).

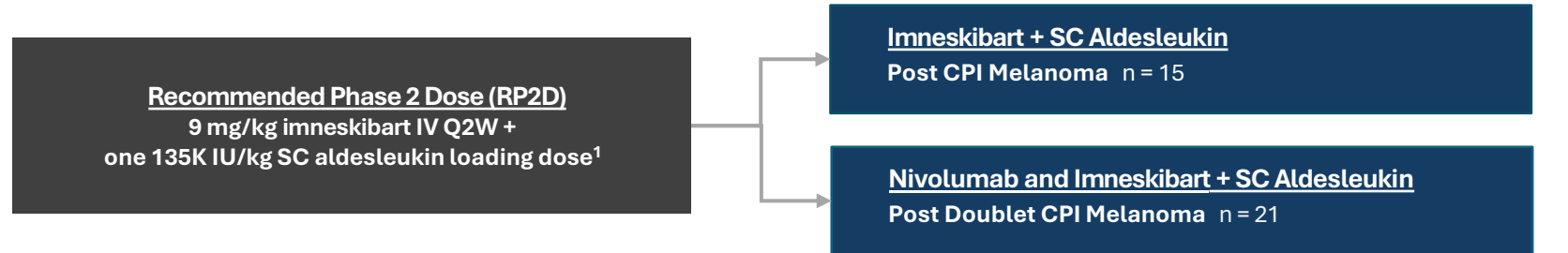
**Ongoing melanoma cohort** evaluates imneskibart + loading dose SC aldesleukin as defined above and nivolumab 480 mg every 4 weeks (Q4W).

- Unresectable locally advanced or metastatic cutaneous melanoma (including acral melanoma).
- Must have objective progression after receiving at least two cycles of prior doublet therapy (anti-PD-1 + anti-CTLA-4 or anti-PD-1 + anti-LAG-3).
- Confirmation of radiographic progression ≥ 4 weeks prior to the first dose of study drug to rule out late response to most recent therapy.
- Patients with BRAF mutations must either be ineligible for or have refused a BRAF + MEK inhibitor.
- Efficacy is based on pharmacodynamic (PD) markers of immune stimulation and objective response; tumor assessments occur at the end of each cycle. Patients can receive an additional SC aldesleukin boost dose at the end of each cycle based on tumor growth kinetics observed on end-of-cycle scans.
- Patients are treated in 8-week cycles and may continue additional cycles until discontinuation criteria are met.

**Ongoing NSCLC cohort** evaluates imneskibart + loading dose SC aldesleukin as defined above + avelumab (anti-PD-L1 with Fc effector function for ADCC) 800 mg Q2W.

- PD-L1+ (tumor proportion score ≥ 1%) NSCLC patients who have failed prior CPI therapy ± chemotherapy.

NSCLC data to be presented at a future meeting.



<sup>1</sup>Boost IL-2 dosing on Day 1 of each Cycle (Q8W) allowed if tumor size is unchanged or increasing or if objective response not yet attained

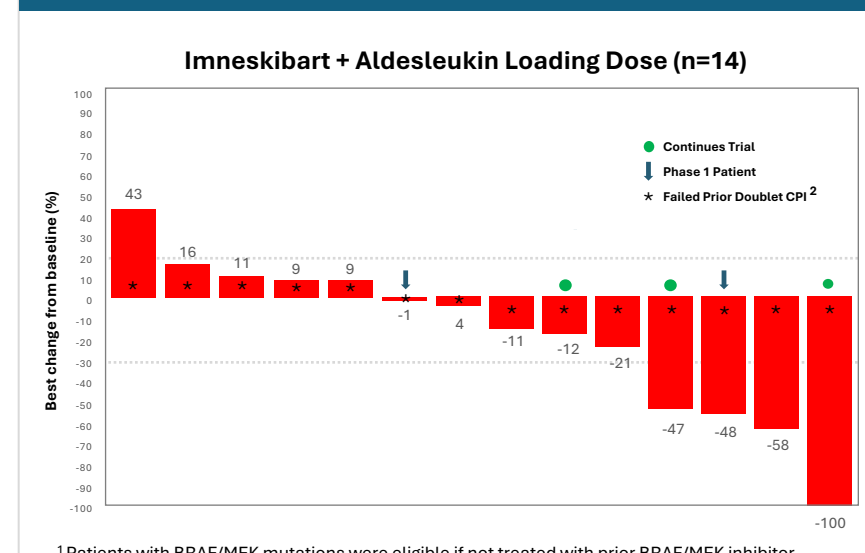
## Melanoma Patient Characteristics

Patient Characteristics	Imneskibart + IL-2 N = 31*	Nivolumab Combo N = 17	Total N = 48
Mean age, years (range)	64.1 (34-89)	64.3 (28-86)	64.2 (28-89)
Gender, n (%)			
Male	15 (48.4)	15 (88.2)	30 (62.5)
Female	16 (51.6)	2 (11.8)	18 (37.5)
Race, n (%)			
White	29 (94)	15 (88)	44 (92)
Black	1 (3)	0	1 (2)
Asian	0	0	0
American Indian/Alaska native	1 (3)	0	1 (2)
Other	0	1	1 (2)
Not reported/missing	0	1	1 (2)
ECOG performance status, n (%)			
0	12 (38.7)	10 (58.8)	22 (45.8)
1	19 (61.3)	7 (41.2)	26 (54.2)
Mean number of prior therapies n (range)	2.5 (1-7)	2.7 (1-6)	2.5 (1-7)

\*Includes Phase 1 melanoma patients  
Data cutoff as of April 6, 2026

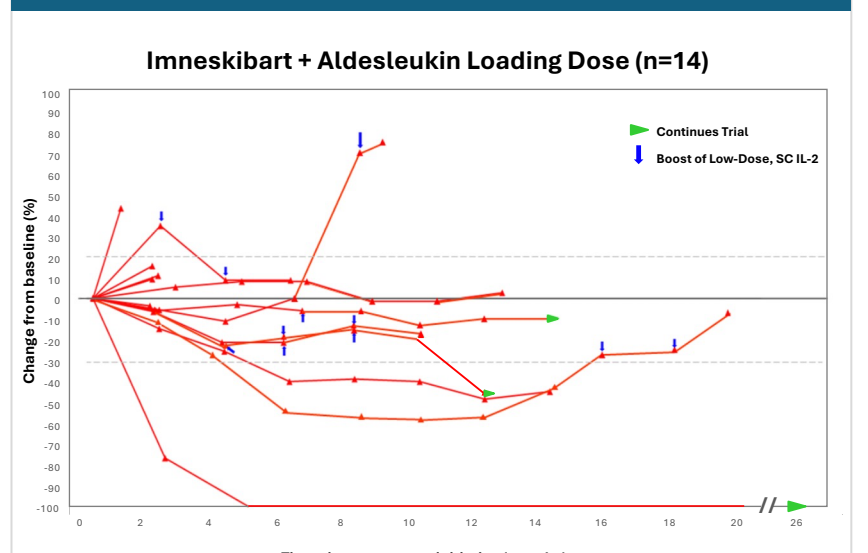
## Clear Activity in Melanoma With Imneskibart + Low-Dose IL-2 Without Nivolumab in Phase 1 and 2

**Best Response in the Target Lesions of Melanoma Patients<sup>1</sup>**



<sup>1</sup>Patients with BRAF/MEK mutations were eligible if not treated with prior BRAF/MEK inhibitor  
<sup>2</sup>Patients who progressed on prior doublet checkpoint inhibitors: anti-CTLA-4 + anti-PD-1 and/or anti-PD-1 + anti-LAG-3

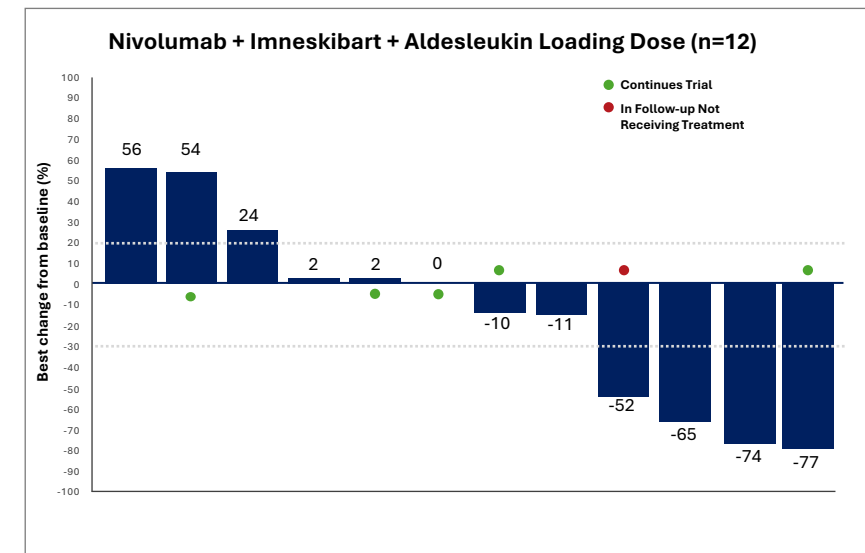
**Percentage Change Over Time vs. Baseline in the Target Lesions of Melanoma Patients<sup>1</sup>**



- Given the ability to slow or reverse tumor growth with boost IL-2, we have implemented boost IL-2 every 8 weeks (Q8W) until at least RECIST PR (~30% reduction) is achieved. We may evaluate every 8-week IL-2 dosing in future trials.

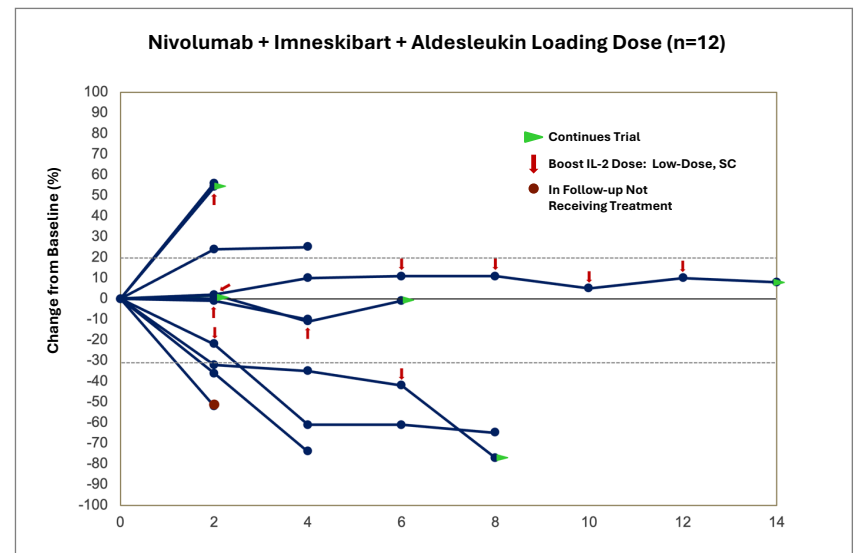
## Clear Activity in Melanoma Patients Who Progressed on Prior Doublet CPI Therapy Treated With Nivolumab + Imneskibart + Low-Dose, SC IL-2

**Best Response in the Target Lesions of Melanoma Patients<sup>1</sup>**



<sup>1</sup>Patients with BRAF/MEK mutations were eligible if not treated with prior BRAF/MEK inhibitor

**Percentage Change Over Time vs. Baseline in Target Lesions of Melanoma Patients<sup>1</sup>**



- Given the ability to slow or reverse tumor growth with boost IL-2, we have implemented boost IL-2 Q8W until at least RECIST PR (~30% reduction) is achieved. We may evaluate every 8-week IL-2 dosing in future trials.

<sup>1</sup>Patients with BRAF/MEK mutations were eligible if not treated with prior BRAF/MEK inhibitor

## Adverse Event Summary: Mild and Tolerable Profile

**Low Rate of Drug-Related SAEs and Grade 3/4 AEs**

Event (n, %)	Imneskibart + IL-2 <sup>1</sup> N = 83	Nivolumab Combo <sup>2</sup> N = 17
<b>Any AE</b>	<b>79 (95)</b>	<b>16 (94)</b>
<b>Drug-Related AEs</b>	<b>68 (82)</b>	<b>11 (65)</b>
<b>Drug-Related SAEs</b>	<b>5 (6)</b>	<b>4 (24)</b>
CRS	3	2
Infusion-related reaction	1	1
Pyrexia	1	0
Adrenal insufficiency	0	0
Injection site rash	1	0
Pneumonitis	0	1
<b>Drug-Related Grade 3 or 4 AEs</b>	<b>12 (15)</b>	<b>1 (6)</b>
Lymphopenia	7	0
Anemia	2	0
CRS	1	0
Fatigue	1	0
Lipase elevation	1	0
Neutropenia	1	0
Maculopapular rash	1	0
Autoimmune encephalitis	1	0
Pneumonitis	0	1

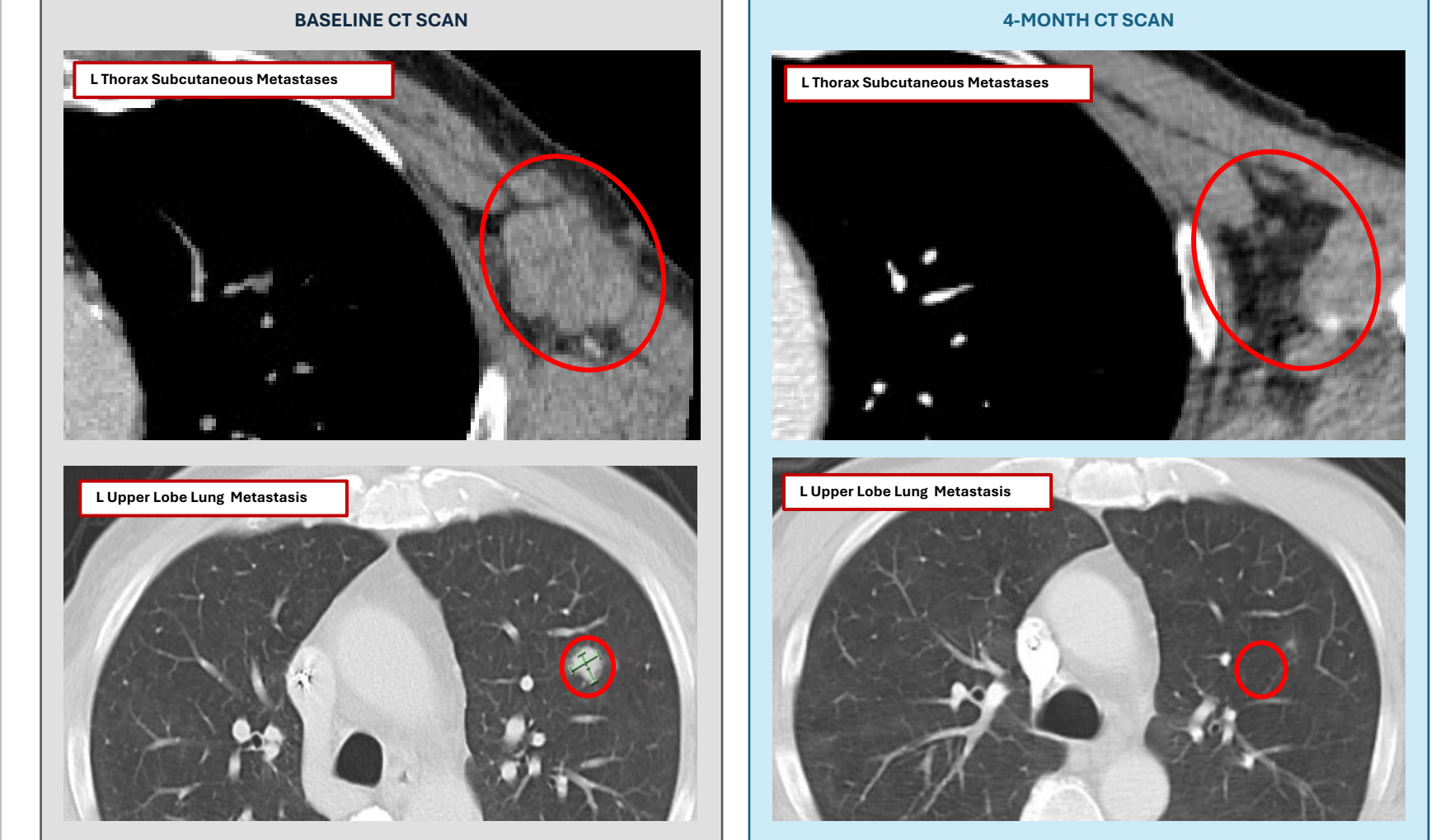
**Most Drug-Related AEs Tolerable and Easily Managed**

Adverse Event (n, %)	Imneskibart + IL-2 <sup>1</sup> N = 83	Nivolumab Combo <sup>2</sup> N = 17
Pyrexia	21 (25)	1 (6)
Fatigue	20 (24)	2 (12)
Chills	18 (21)	2 (12)
Nausea	12 (15)	2 (12)
Infusion-related reaction	11 (13)	1 (6)
Injection site reaction	11 (13)	4 (24)
CRS	7 (9)	5 (29)

<sup>1</sup>Imneskibart Q2W + IL-2 loading dose or IL-2 Q2W - all tumor types  
<sup>2</sup>Imneskibart Q2W + IL-2 loading dose and nivolumab - melanoma

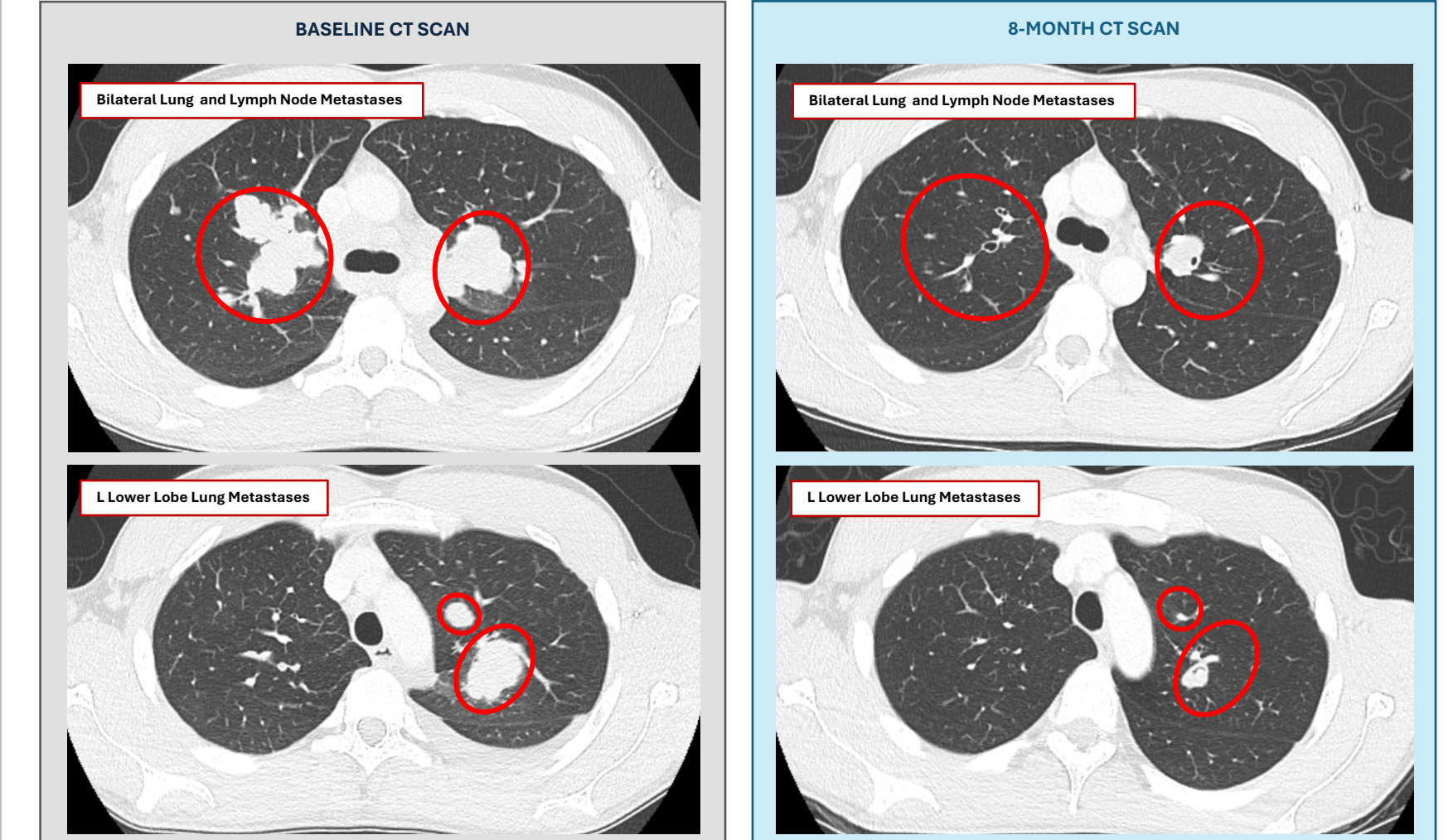
- Most drug-related adverse events (AEs) were mild, Grade 1 or 2, with imneskibart + SC loading dose aldesleukin alone or in combination with nivolumab.
- The addition of nivolumab to imneskibart + SC loading dose aldesleukin does not increase the rate of drug-related Grade 3/4 AEs in the emerging data.
- The most common Grade 3 or 4 AE was transient (3-7 days) lymphopenia that was not associated with adverse outcomes in any patient. Transient lymphopenia is a known effect of IL-2 treatment as lymphocytes traffic out of blood and into tissue.
- One patient receiving imneskibart + SC loading dose aldesleukin experienced Grade 4 cytokine release syndrome (CRS). It resolved without tocilizumab using steroids, IV fluids, and brief vascular pressor support. This patient was noted retrospectively to have subclinical elevated IL-6 (5x) serum levels likely due to an active case of gout at baseline.

## 74% Reduction at 4 Months in the Target Lesions of a Patient Whose Tumor Previously Progressed Through Prior Anti-PD-1 + Anti-LAG-3 Doublet Therapy



- 69-year-old man with melanoma metastatic to the left upper lobe of the lung, L subcutaneous thorax, colon, and peritoneum.
- The patient received prior ipilimumab, nivolumab + relatlimab, TIL therapy, and talimogene laherparepvec (T-VEC) therapy.
- December 2025, the patient began treatment with the RP2D imneskibart + aldesleukin in combination with nivolumab 480 mg Q4W.
- Confirmed partial response with 36% and 74% tumor size decrease at end of Cycles 1 and 2, respectively.

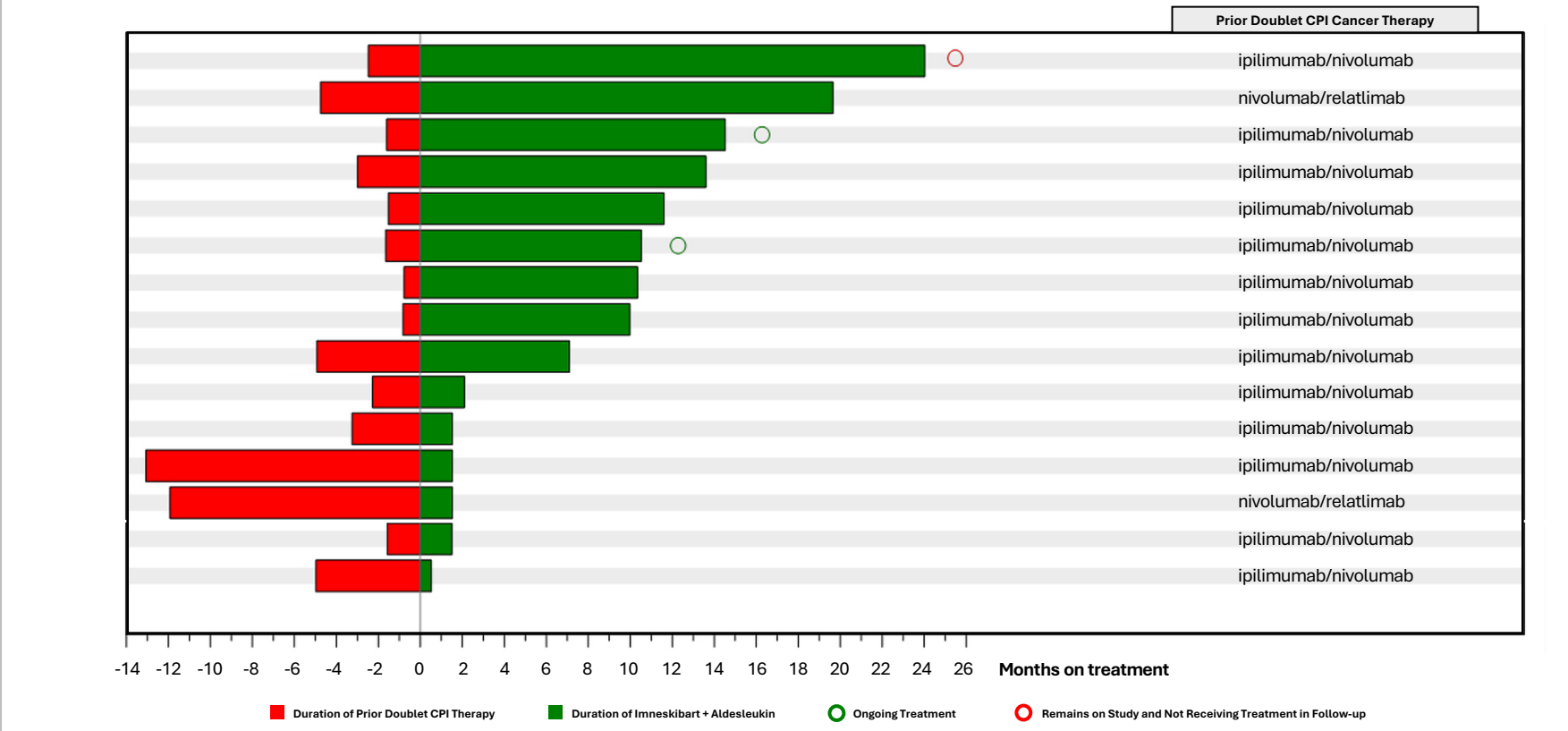
## 77% Reduction at 8 Months in the Target Lesions of a Patient Whose Tumor Previously Progressed Through Prior Anti-PD-1 + Anti-CTLA-4 Doublet Therapy



- 28-year-old man with melanoma metastatic to the mediastinal lymph nodes and lung.
- The patient received prior neoadjuvant and then adjuvant pembrolizumab followed by ipilimumab + nivolumab.
- September 2025, the patient began treatment with the RP2D imneskibart + aldesleukin in combination with nivolumab 480 mg Q4W.
- Confirmed partial response with 32%, 35%, 42%, and 77% tumor size decrease at end of Cycles 1, 2, 3, and 4, respectively.

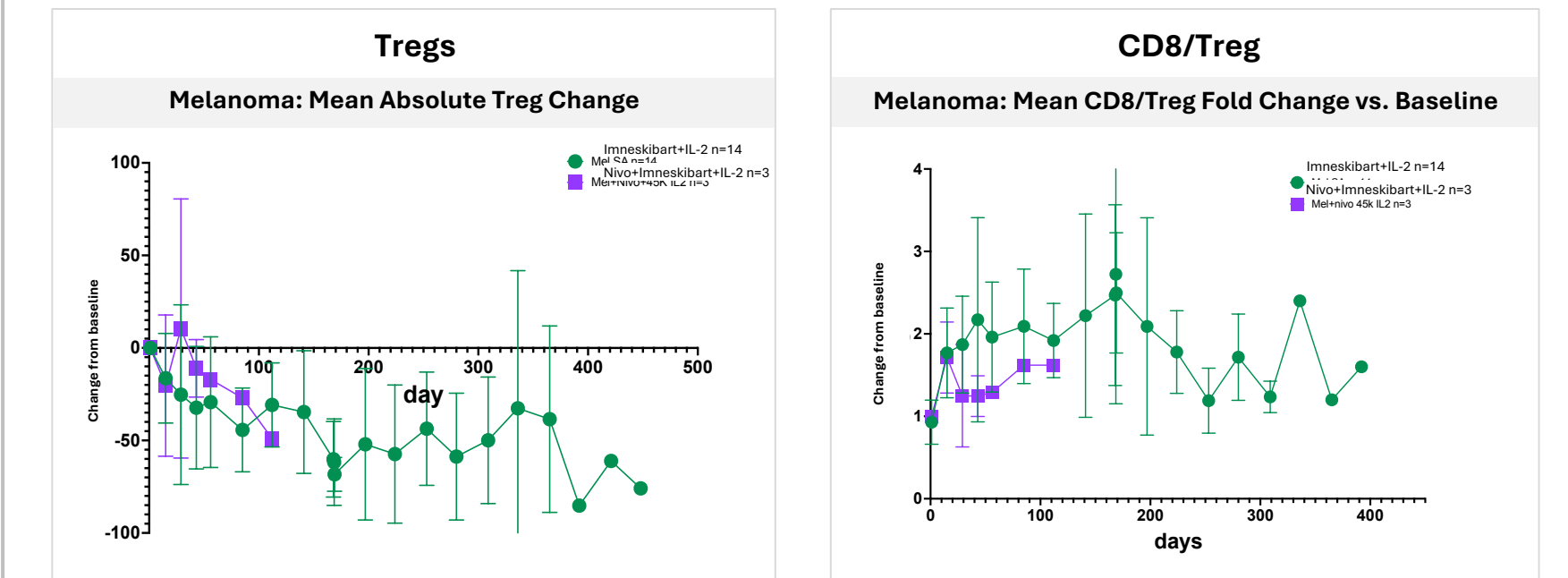
## Prior Doublet Checkpoint Inhibitor Cancer Therapy and Time on Imneskibart Study Treatment

**Imneskibart + Aldesleukin**



## Pharmacodynamic Profile: Durable Increases in the CD8/Treg Ratio With Corresponding Decreases in Tregs

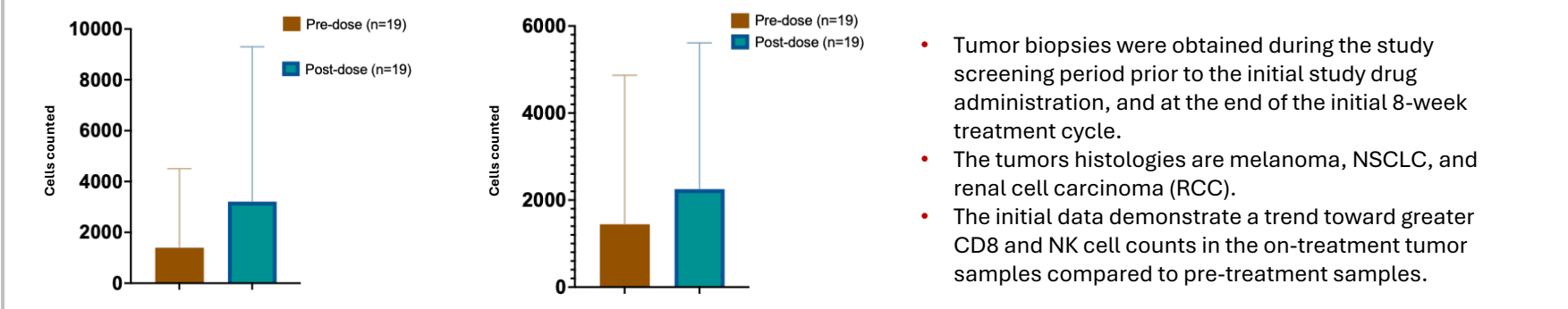
**Absolute change in cell count of Tregs per µl of blood and CD8/Treg ratio (based on ratio of counts per µl of blood)**



Day 1 through Day 3 omitted as all peripheral lymphocytes decrease over these days. This is considered an effect of IL-2 causing a brief redistribution of lymphocytes out of the peripheral blood. Imneskibart 9 mg/kg, IL-2 135K IU/kg (n=14), Nivo 480 mg, imneskibart 9 mg/kg, IL-2 45K IU/kg (n=2). Data on nivo+imneskibart+135K IL-2 not yet available.

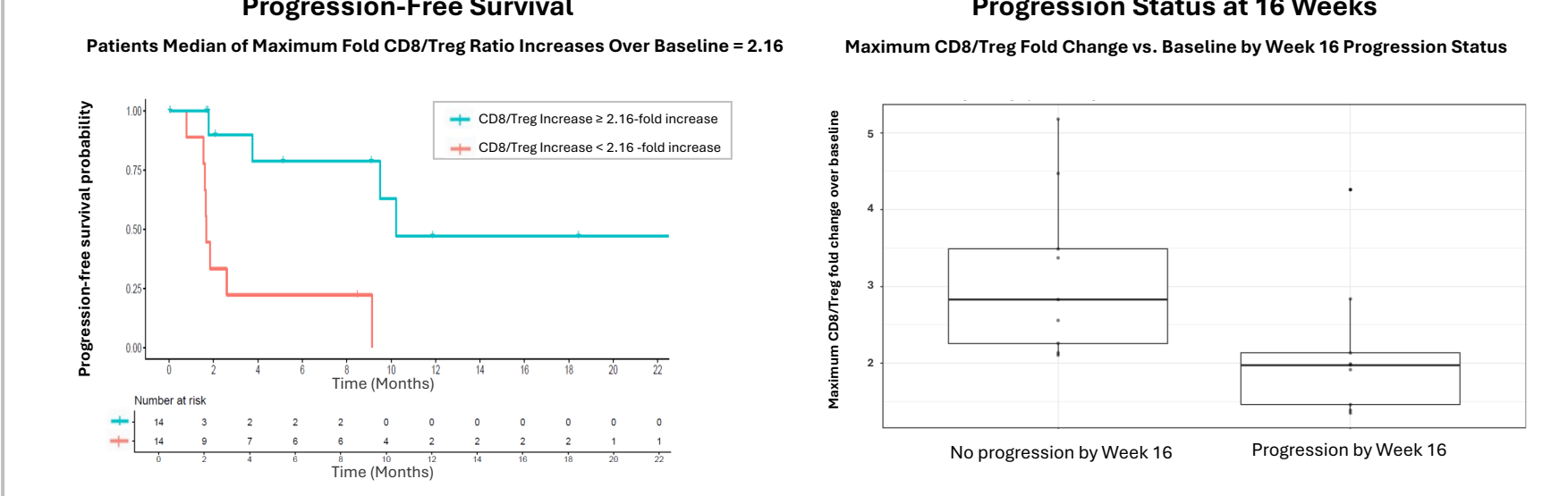
- Initial pharmacodynamic data demonstrate that decreases in Tregs and increases in the CD8+/Treg ratio observed with nivolumab in combination with imneskibart and aldesleukin are similar in magnitude to those observed with imneskibart and aldesleukin alone.

## Intratumoral Effector Cells Increase After One 8-Week Treatment Cycle



- Tumor biopsies were obtained during the study screening period prior to the initial study drug administration, and at the end of the initial 8-week treatment cycle.
- The tumors histologies are melanoma, NSCLC, and renal cell carcinoma (RCC).
- The initial data demonstrate a trend toward greater CD8 and NK cell counts in the on-treatment tumor samples compared to pre-treatment samples.

## Higher CD8/Treg Ratio Associated With Better Anti-Tumor Activity



- Longer durations of progression-free survival (PFS) were observed in melanoma patients who achieved a ≥ 2.16 -fold increase over their baseline CD8/Treg ratio.
- Results are calculated by deriving the median greatest Treg decrease across all patients (excluding the first 2 days on treatment) and dividing the patients who were ≤ the median or > than the median for CD8/Treg ratio fold change versus baseline.
- Patients divided by progression status after 16 weeks (2 Cycles) on treatment and the individual patient maximum CD8/Treg ratio fold increase over baseline plotted for each patient.
- Boxplots summarize maximum CD8/Treg ratio fold increase by progression status group showing median (line in each box) with lower and upper box boundaries corresponding to the 25th and 75th percentile.

## Conclusions

- Clinically meaningful activity in a high-bar setting:** 4/12 patients with partial responses (33%), 3 confirmed and 1 awaiting confirmation, and 67% disease control rate (DCR) with the triplet regimen of imneskibart + low-dose, SC aldesleukin and nivolumab in confirmed doublet CPI-refractory melanoma (post anti-PD-1 + anti-CTLA-4 or anti-PD-1 + anti-LAG-3), where late responses to prior therapy are effectively excluded. PFS and overall survival (OS) data are maturing.
- Compelling durability and depth emerging:** Responses are deepening and ongoing, consistent with de novo anti-tumor immunity and immune memory formation.
- Mechanism validated in patients:** Pharmacodynamic analyses demonstrated decreased peripheral Tregs, increased CD8+ T cells and NK cells, and increased CD8/Treg ratios, supporting selective immune effector cell expansion.
- Well-tolerated triplet regimen:** The emerging safety profile of the triplet regimen is consistent with the known safety profiles of nivolumab and imneskibart + aldesleukin, with no new toxicity signals observed.
- Differentiated IL-2 biology with drug-like properties:** Sustained, selective signaling (half-life >19 days) enables potent immune activation without Treg expansion or high-dose IL-2 toxicity, such as vascular leak syndrome.
- Strong foundation for combinations and expansion:** Biology supports broad combinability across immuno-oncology modalities, with observed synergy with anti-PD-1 and anti-PD-L1 agents, and a clear rationale for combinations with CPIs, antibody-drug conjugates (ADCs), CD3 bispecifics, and other T cell-engaging or antigen-releasing therapies that benefit from increased numbers and activation of effector cells.
- Future clinical development:** Data in this doublet CPI-refractory melanoma patient population strongly support continued clinical development with the triplet regimen of imneskibart + low-dose, SC aldesleukin and nivolumab. Potential registration paths are being evaluated.

Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting, May 29–June 2, 2026

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