Imneskibart (AU-007), a Human Monoclonal Antibody (mAb) That Binds IL-2 and Prevents CD25 Binding, + Low-Dose Subcutaneous IL-2: Phase 2 Update on CPI-Refractory Melanoma and Non-Small Cell Lung Cancer (NSCLC)

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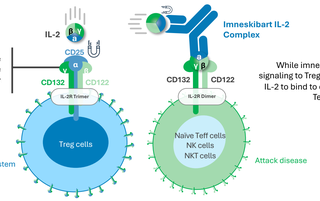
Imneskibart Background

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.

Study Design and Study Status

- This is a Phase 1/2 open label dose escalation and expansion study – Phase 1 is complete.
- The recommended Phase 2 dose (RP2D) of imneskibart and low-dose, subcutaneous (SQ) aldesleukin (IL-2), imneskibart 9 mg/kg every two weeks (Q2W) intravenously (IV) + SQ aldesleukin loading dose of 135K IU/kg, is currently being evaluated in Phase 2 expansion in patients with cutaneous melanoma and non-small cell lung cancer (NSCLC).

Cutaneous melanoma cohorts evaluate the RP2D regimen of imneskibart + SQ aldesleukin and the RP2D regimen plus nivolumab 480 mg every four weeks (Q4W) with a safety run-in (RP2D -1, aldesleukin 45K IU/kg) followed by cohort expansion.
- 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.

NSCLC cohorts evaluate the RP2D regimen of imneskibart + SQ aldesleukin and the RP2D regimen plus avelumab (anti-PD-L1 with Fc effector function for ADCC) 800 mg Q2W with a safety run-in (RP2D -1, aldesleukin 45K IU/kg) followed by cohort expansion.
- PD-L1+ (tumor proportion score ≥ 1%) NSCLC patients who have failed prior checkpoint inhibitor (CPI) therapy ± chemotherapy.

- Efficacy is based on pharmacodynamic (PD) markers of immune stimulation and objective response; tumor assessments occur at the end of each 8-week cycle. Patients can receive an additional SQ aldesleukin dose at the beginning of each 8-week cycle based on tumor growth kinetics observed on end-of-cycle scans.

Enrolling Phase 2 in Post-CPI-Doublet Failed Melanoma, and Post-CPI +/- Chemo-Failed, PD-L1 Positive Non-Small Cell Lung Cancer

Phase 1 Dose Escalation
19 different solid tumor types
Completed without dose-limiting toxicity

Phase 2 Expansion Cohorts
Melanoma, NSCLC, Renal Cell Carcinoma (RCC)

Recommended Phase 2 Dose (RP2D)

9 mg/kg imneskibart IV Q2W
+
One 135K IU/kg SQ aldesleukin loading dose[1]

[1]Boost IL-2 dosing on Day 1 of each Cycle (Q8W) allowed if tumor volume unchanged or increasing

Aselumab is provided by the healthcare business of Merck KGaA, Darmstadt, Germany (CrossRef Funder ID: 10.13039/100009945).

RP2D Imneskibart + SQ Aldesleukin
Post CPI Melanoma n=20
- 13 patients enrolled / 6 ongoing

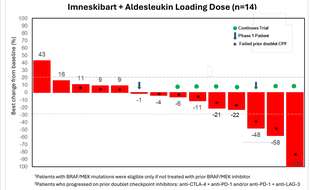
Nivolumab + RP2D Imneskibart + SQ Aldesleukin
Post Doublet CPI Melanoma n=20
- 3 patient safety run-in with 45K IU/kg aldesleukin completed
- 3 patients enrolled at the RP2D: single loading dose 135K IU/kg aldesleukin
- 3 patients ongoing

RP2D Imneskibart + SQ Aldesleukin
Post PD-L1+ NSCLC n=10
- 4 patients enrolled / 1 ongoing

Avelumab + RP2D Imneskibart + SQ Aldesleukin
Post PD-L1+ NSCLC n=20
- 5 patients received 45K IU/kg aldesleukin in the completed safety run-in
- 10 patients enrolled at the RP2D: single loading dose 135K IU/kg aldesleukin
- 15 total patients enrolled / 6 ongoing

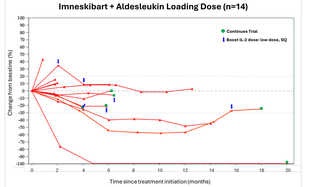
Clear Activity in Melanoma With Imneskibart + Low-Dose IL-2 Without CPI in Phase 1 and 2

Best Response in the Target Lesions of Melanoma Patients[1] Treated With Imneskibart + Low-Dose, SQ IL-2 Who Progressed on Prior CPI Therapy



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

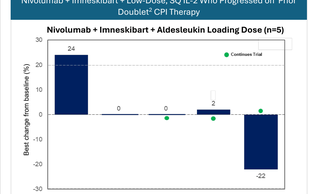
Percentage Change Over Time vs. Baseline in the Target Lesions of Melanoma Patients Treated With Imneskibart + Low-Dose, SQ IL-2 Who Progressed on Prior CPI Therapy



- Strong signal of anti-tumor activity with imneskibart + SQ loading dose aldesleukin with ongoing deep and durable tumor reductions in patients who progressed after receiving doublet checkpoint inhibitor therapy.
- Three patients with the deepest tumor reductions in target lesions continued treatment beyond one year: -48% reduction (on study for 14 months), -58% reduction (continues on study for 18+ months), and a complete response (-100% reduction; continues on study for 21+ months).

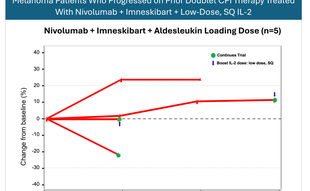
Early Signs of Anti-Tumor Activity in Melanoma Patients Who Progressed on Prior Doublet CPI Therapy Treated With Nivolumab + Imneskibart + Low-Dose, SQ IL-2

Best Response in the Target Lesions of Melanoma[1] Patients Treated With Nivolumab + Imneskibart + Low-Dose, SQ IL-2 Who Progressed on Prior Doublet[2] CPI Therapy



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

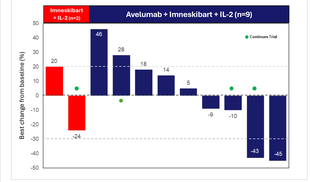
Percentage Change Over Time vs. Baseline in the Target Lesions of Melanoma Patients Who Progressed on Prior Doublet CPI Therapy Treated With Nivolumab + Imneskibart + Low-Dose, SQ IL-2



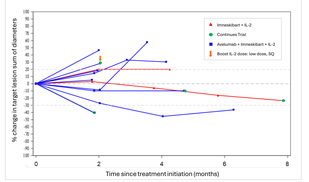
An initial safety run-in evaluating a lower IL-2 loading dose of 45K IU/kg aldesleukin + 480 mg Q4W nivolumab + 9 mg/kg Q2W imneskibart is completed and the RP2D imneskibart + aldesleukin dose of 135K IU/kg will now be administered in combination with nivolumab and imneskibart to all newly enrolled patients.
- No dose-limiting toxicity (DLT) in the safety run-in.
- Initial signs of anti-tumor activity in very early clinical data in the safety run-in with the lower aldesleukin dose (45K IU/kg).
- Eligible patients must have:
  - Objective progression after receiving at least two cycles of prior doublet CPI therapy (anti-PD-1 + anti-CTLA-4 and/or anti-PD-1 + anti-LAG-3).
  - Radiographic progression must be demonstrated ≥ 4 weeks prior to the first dose of study drug to rule out late response to most recent therapy.

Preliminary Activity With Imneskibart + Low-Dose, SQ IL-2 ± Avelumab in Phase 2 in NSCLC Patients Who Failed Prior CPI ± Chemotherapy

Best Response in NSCLC Patients Treated With Imneskibart + Low-Dose, SQ IL-2 ± Avelumab

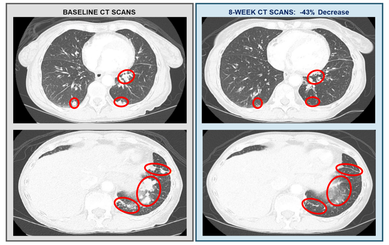


Percentage Change Over Time vs. Baseline in NSCLC Patients Treated With Imneskibart + Low-Dose, SQ IL-2 ± Avelumab



- Initial signal of anti-tumor activity with imneskibart + SQ loading dose of aldesleukin alone and in combination with avelumab in patients with NSCLC who failed prior CPI therapy ± chemotherapy.

43% Tumor Reduction at 8 Weeks in the Pulmonary Target Lesions of a NSCLC Patient Who Previously Progressed Through Prior Anti-PD-1 + Chemotherapy



- 68-year-old woman with NSCLC (adenocarcinoma) with tumor lesions in lung, adrenal, and bone.
- The patient progressed on prior anti-PD-1 + carboplatin + pemetrexed and docetaxel + gemcitabine.
- July 2025, the patient began treatment with the RP2D imneskibart + aldesleukin in combination with avelumab 800 mg Q2W.
- 43% decrease in target lesion size noted at end of Cycle 1, after receiving 8 weeks of therapy; patient continues in Cycle 2.

Patients With Target Tumor Reduction Other Than Melanoma and NSCLC

Tumor	Dose/Regimen Imneskibart (mg/kg)	Dose/Regimen Aldesleukin (IU/kg)	Best Response on Prior CPI	Number of Prior Cancer Regimens	Best Objective Response (% Decrease)	Time on Treatment (Months)
HNSCC[1]	4.5 Q2W	45K Q2W	PR (anti-PD-1)	4	-100% (Confirmed CR)	28.5+[3]
CRC (MSS)	9.0 Q2W	135K Q2W	Not applicable	3	-27%	3.3
Bladder	4.5 Q2W	45K loading dose	PD (anti-PD-L1)	1	Confirmed metabolic CR[2] and ctDNA negative	32.5+[3]
Bladder	4.5 Q2W	270K loading dose	PD (anti-PD-1)	4	-13%	4.7
RCC	9.0 Q2W	135K loading dose	PD (anti-PD-1)	2	-24%	20.5+[3]
RCC	9.0 Q2W	135K loading dose	PD (anti-PD-1)	6	-12%	14+[3]
RCC	9.0 Q2W	135K loading dose	Not applicable	0	-46%	16.5+[3]

[1]Head and neck nasopharyngeal histology
[2]Patient with non-target lesion disease only with highly metabolically active tumors at baseline on PET scan that became negative at Cycle 7 (14M on study)
[3]Patient continues on study therapy

Adverse Event Summary in Phase 1 and 2: Mild and Tolerable Profile

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

Safety Summary

Event (n, %)	Imneskibart + IL-2[1] N=77	Avelumab Combo N=11	Nivolumab Combo N=5
Any AE	**72 (93)**	**11 (100)**	**5 (100)**
Drug-Related AEs	**63 (82)**	**7 (64)**	**3 (60)**
Drug-Related SAEs	**5 (6)**	**2 (18)**	**1 (20)**
CRS	3	0	1
Infusion-related reaction	1	0	0
Pyrexia	1	1	0
Adrenal insufficiency	0	1	0
Injection site rash	1	0	0
Drug-Related Grade 3 or 4 AEs	**11 (15)**	**2 (18)**	**0**
Lymphopenia	6	1	0
CRS	1	1	0
Anemia	2	0	0
Lipase elevation	1	0	0
Neutropenia	1	0	0
Maculopapular rash	1	0	0
Hypertension	0	1	0
Autoimmune encephalitis	1	0	0

Data cutoff as of September 29, 2025

Most Drug-Related AEs Tolerable and Easily Managed

Drug-Related Adverse Events in > 10% of Patients

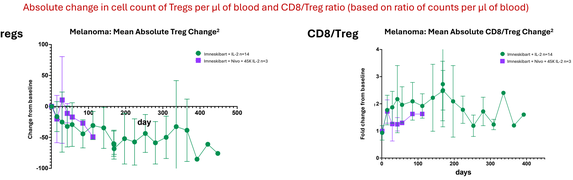
Adverse Event (n, %)	Imneskibart + IL-2[1] N=77	Avelumab Combo[2] N=11	Nivolumab Combo[2] N=5
Pyrexia	19 (25)	2 (18)	0
Fatigue	17 (22)	2 (18)	0
Chills	16 (21)	4 (36)	1 (20)
Infusion-related reaction	11 (14)	2 (18)	0
Nausea	10 (13)	2 (18)	1 (20)
Injection site reaction	9 (12)	0	2 (40)
CRS	7 (9)	1 (9)	2 (40)
Anemia	6 (8)	2 (18)	0
Diarrhea	2 (2)	2 (18)	0
Hypotension	1 (1)	2 (18)	0
Fall	0	0	1 (20)
Dermatitis acneiform	0	0	1 (20)

[1]Imneskibart Q2W + IL-2 loading dose or IL-2 Q2W
[2]Imneskibart Q2W + IL-2 loading dose + CPI

- Most drug-related adverse events (AEs) were mild, Grade 1 or 2, with imneskibart + SQ loading dose aldesleukin alone or in combination with avelumab or nivolumab.
- The low rate of drug-related Grade 3 and 4 AEs previously observed with imneskibart + SQ loading dose aldesleukin continues with mature data.
- The addition of avelumab or nivolumab to imneskibart + SQ loading dose aldesleukin does not increase the rate of drug-related Grade 3 and 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 + SQ 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.

Pharmacodynamic Profile: Durable Decreases in Tregs and Corresponding Increases in CD8/Treg Ratios in Melanoma[1]

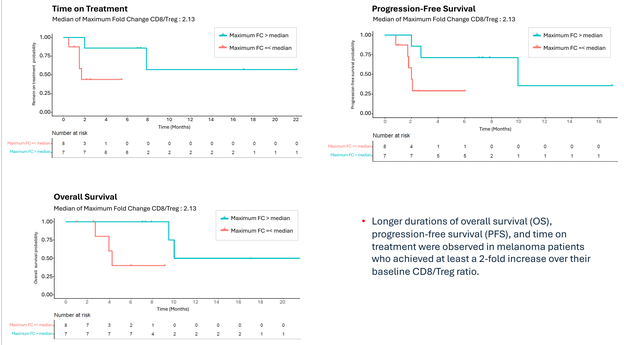
Absolute change in cell count of Tregs per µl of blood and CD8/Treg ratio (based on ratio of counts per µl of blood)



[1]NSCLC data is currently being collected; however, the data has not matured due to patient recruitment schedules
[2]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.

- The mean peripheral blood Treg absolute cell counts continues to decrease after dosing with imneskibart + aldesleukin. The addition of nivolumab to imneskibart and RP2D -1 SQ aldesleukin dose (45K IU/kg) does not affect the decrease in the peripheral Treg population in the emerging data.
- Increases in the peripheral blood CD8/Treg ratio are observed with the mean increases exceeding 2-fold over baseline with imneskibart + aldesleukin. Early data demonstrate that the addition of nivolumab to imneskibart and SQ aldesleukin (45K IU/kg) results in CD8/Treg ratios similar to those observed in patients who received imneskibart and SQ aldesleukin without nivolumab.

Higher Peripheral Blood CD8/Treg Ratio Associated With Better Efficacy vs. Low CD8/Treg Ratio



- Longer durations of overall survival (OS), progression-free survival (PFS), and time on treatment were observed in melanoma patients who achieved at least a 2-fold increase over their baseline CD8/Treg ratio.

Conclusions

- Imneskibart + low-dose, SQ aldesleukin possesses a unique mechanism of action by reducing Tregs while increasing NK and CD8 cells, thus increasing the Teff/Treg ratio, resulting in clinically meaningful tumor regressions with a manageable safety profile (low incidence of drug-related Grade 3/4 adverse events); therefore, treatment can be safely be administered in an outpatient setting.
- Melanoma patients with primary resistance to prior doublet immune checkpoint inhibitors had durable, deep tumor reductions when treated with imneskibart + low-dose, SQ IL-2 without a CPI.
- Emerging data in melanoma patients receiving imneskibart + low-dose aldesleukin and nivolumab demonstrate an early signal of activity and mild safety profile in melanoma patients who progressed on prior doublet CPI therapy.
- Early signal of activity is observed in NSCLC patients receiving imneskibart + low-dose aldesleukin and avelumab whose tumors progressed on prior anti-PD-1/L1 therapy ± chemotherapy.
- In addition to the activity observed in melanoma and NSCLC, two long-lasting complete responses were achieved in patients with bladder cancer and head and neck cancer whose tumors progressed on prior checkpoint inhibitors.
- Pharmacodynamic data demonstrate:
  - Continued durable peripheral Treg decreases with imneskibart + low-dose IL-2.
  - Higher CD8/Treg ratio associated with longer OS, PFS, and time on treatment.

Presented at the 40th Annual Meeting of the Society for Immunotherapy of Cancer (SITC), November 5-9, 2025

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