Imneskibart (AU-007) + Low-Dose SC IL-2 + Avelumab: Phase 2 Activity in CPI-Refractory Advanced Adenocarcinoma NSCLC

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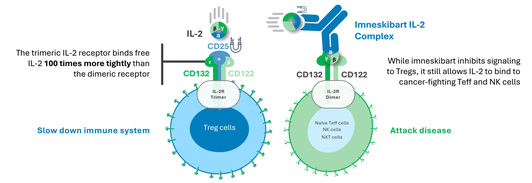
Abstract 6280
Presentation Number 2573P
NCT05267626

Imneskibart Background

Imneskibart binds to IL-2 and redirects it 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

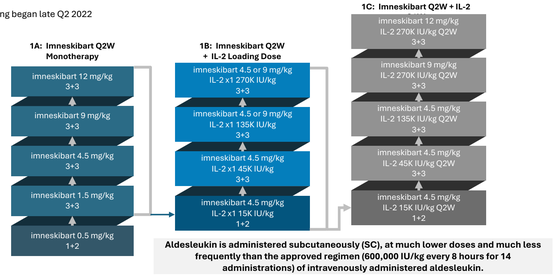


Unique MOA Addresses the IL-2 Negative Feedback Loop

- 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.

Phase 1 Dose Escalation – Enrollment Complete

Dosing began late Q2 2022



Aldesleukin is administered subcutaneously (SC), at much lower doses and much less frequently than the approved regimen (600,000 IU/kg every 8 hours for 14 administrations) of intravenously administered aldesleukin.

Phase 2 Cohort Expansion – Enrollment Complete

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

Phase 2 Expansion Cohorts
- Melanoma, Non-Small Cell Lung Cancer, Renal Cell Carcinoma[2]

Recommended Phase 2 Dose (RP2D)
9 mg/kg imneskibart IV Q2W
+
One 135K IU/kg SC aldesleukin loading dose[1]
(NOTE: In the absence of imneskibart, this low dose level of aldesleukin would be immune suppressing as most of it would be consumed by Tregs.)

- **RP2D imneskibart + SC aldesleukin (N = 24)** — 2L melanoma and 2/3L RCC
- **Nivolumab + RP2D imneskibart + SC aldesleukin (N = 20)** — 2L melanoma
- **RP2D imneskibart + SC aldesleukin (N = 10)** — 2L PD-L1+ NSCLC
- **Avelumab + RP2D imneskibart + SC aldesleukin (N = 26)** — 2L PD-L1+ NSCLC

[1]Boost IL-2 dosing on Day 1 of each Cycle (Q8W) allowed if tumor volume unchanged or increasing
[2]Initially enrolled RCC but has paused

Clinical Activity Across Tumor Types in Phase 1 and 2

Phase 1 Dose Escalation

Tumor	Imneskibart Dose (mg/kg)	Dose / Regimen Aldesleukin (IU/kg)	Best Objective Response (% Decrease)
HNSCC	4.5	45K Q2W	-100%
CRC (MSS)	9.0	135K Q2W	-27%
Bladder	4.5	45K loading dose	Metabolic CR
Bladder	4.5	270K loading dose	-13%
NSCLC	4.5	15K loading dose	-14%

Phase 2 Cohort Expansion
RP2D: 9 mg/kg Imneskibart + 135K SC IL-2 Loading Dose

Cohort	Response Evaluable (n)	Summary of Responses
Melanoma RP2D	14	4 PR (29%) 9 SD (64%)
Melanoma RP2D + Nivolumab (ongoing)	18	1 CR (6%) 4 PR (22%) 8 SD (44%)
RCC RP2D	9	1 PR (11%) 4 SD (44%)

HNSCC: head & neck squamous cell carcinoma; CRC: colorectal cancer; MSS: microsatellite stable
CR: complete response; PR: partial response; SD: stable disease

Study Design and Study Status

This is a Phase 1/2 open label dose escalation and expansion study. Phase 2 evaluates imneskibart 9 mg/kg every two weeks (Q2W) intravenously (IV) + SC aldesleukin loading dose of 135K IU/kg in patients with non-small cell lung cancer (NSCLC), cutaneous melanoma, and renal cell carcinoma (RCC).

- NSCLC cohorts evaluate imneskibart 9 mg/kg IV Q2W + single loading dose SC aldesleukin 135K IU/kg ± 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 checkpoint inhibitor therapy ± chemotherapy.
- Efficacy is based on pharmacodynamic (PD) markers of immune stimulation and objective response; tumor assessments occur at end of each 8-week cycle. Patients can receive an additional SC aldesleukin dose at 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.

We report on adenocarcinoma patients enrolled in the avelumab combination cohort.

- 6 of 8 patients in non-avelumab arm were squamous cell carcinoma (SCC) histology. One patient with SCC continues in Cycle 10 with stable disease.

Patient Characteristics

Patient Characteristics	Avelumab Combo (N = 26)
Mean age, years (range)	67 (37-77)
Gender, n (%) Male Female	 15 (58) 11 (42)
Race, n (%) White Black Asian American Indian/Alaska native Other Not reported/missing	 21 (81) 3 (11) 1 (4) 0 1 (4) 0
ECOG performance status, n (%) 0 1 Missing	 4 (15) 21 (81) 1 (4)
Mean number of prior therapies n (range)	2.6 (1-6)
Histology Adenocarcinoma Squamous cell carcinoma Other/unknown	 16 8 2

Data cutoff as of September 18, 2026

Adverse Event Summary: Mild and Tolerable Profile

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

Event (n, %)	Imneskibart + IL-2[1] N = 83	Avelumab Combo[2] N = 26
Any AE	**79 (95)**	**25 (96)**
Drug-Related AEs	**68 (82)**	**22 (85)**
Drug-Related SAEs	**5 (6)**	**6 (23)**
CRS	3	2
Infusion-related reaction	1	1
Pyrexia	1	0
Injection site rash	1	0
Adrenal insufficiency	0	1
Cardiac failure	0	1
Confusional state	0	1
Decreased appetite	0	1
QT prolongation	0	1
Pneumonia	0	1

Event (n, %)	Imneskibart + IL-2[1] N = 83	Avelumab Combo[2] N = 26
Drug-Related Grade 3 or 4 AEs	**12 (15)**	**7 (27)**
Lymphopenia	7	1
Anemia	2	1
CRS	1	1
Fatigue	1	0
Lipase increased	1	0
Neutropenia	1	1
Maculopapular rash	1	0
Autoimmune encephalitis	1	0
Adrenal insufficiency	0	2
Hypertension	0	1
Cardiac failure	0	1
Cellulitis	0	1
Decrease appetite	0	1
Diverticulitis	0	1
QT prolongation	0	1
Pneumonia	0	1

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

Most Drug-Related AEs Tolerable and Easily Managed

Drug-Related Adverse Events in > 10% of Patients

Adverse Event (n, %)	Imneskibart + IL-2[1] N = 83	Avelumab Combo[2] N = 26
Pyrexia	21 (25)	4 (15)
Fatigue	20 (24)	7 (27)
Chills	18 (22)	6 (23)
Nausea	12 (15)	6 (23)
Infusion-related reaction	11 (13)	6 (23)
Injection site reaction	11 (13)	4 (15)
Injection site erythema	9 (11)	3 (11)
CRS	9 (11)	3 (11)
Anemia	5 (6)	4 (15)
Vomiting	3 (4)	4 (15)
Decrease appetite	2 (2)	3 (11)
Diarrhea	3 (4)	3 (11)
Hypotension	2 (2)	3 (11)

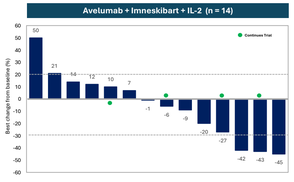
[1]Imneskibart Q2W + IL-2 loading dose or IL-2 Q2W
[2]Imneskibart Q2W + IL-2 loading dose + avelumab

- Most drug-related adverse events (AEs) were mild, Grade 1 or 2, with imneskibart + SC loading dose aldesleukin alone or in combination with avelumab.
- In the avelumab cohort, two patients experienced Grade 3 adrenal insufficiency that resolved in 4 and 5 days, respectively. One patient experienced Grade 4 transient lymphopenia and one experienced Grade 4 cardiac failure that resolved in one month.
- No capillary leak syndrome observed.
- The most common Grade 3 or 4 AE with imneskibart + SC aldesleukin 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.

Post CPI +/- Chemotherapy Failed Adenocarcinoma NSCLC : Evidence of Activity With Avelumab + Imneskibart + Loading Dose IL-2

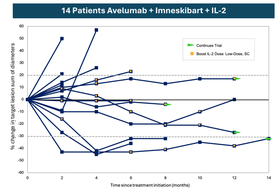
Best Response in Adenocarcinoma NSCLC in Phase 2 With Imneskibart Q2W + Single SC Loading Dose of IL-2

Avelumab + Imneskibart + IL-2 (n = 14)



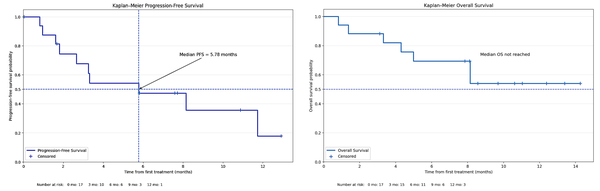
Percentage Change Over Time vs. Baseline in Adenocarcinoma NSCLC in Phase 2 With Imneskibart Q2W + Single SC Loading Dose of IL-2

14 Patients Avelumab + Imneskibart + IL-2



- Three patients who progressed on prior anti-PD-1 + chemotherapy had deep and durable tumor shrinkages: -42% reduction (refractory to 3 prior lines of therapy, on study for 8 months), -43% reduction (progressed after 3 prior lines of therapy, continues study for 12+ months), and 45% reduction in target lesions (refractory to 4 prior lines of therapy, on study for 6 months).
- Stable disease in 9/14 (64%).
- Disease control rate of 86%.
- Confirmed objective responses in 3/14 (21%) response-evaluable patients.

Median PFS and OS in Adenocarcinoma NSCLC Patients Treated With Avelumab + Imneskibart + Low-Dose, SC IL-2



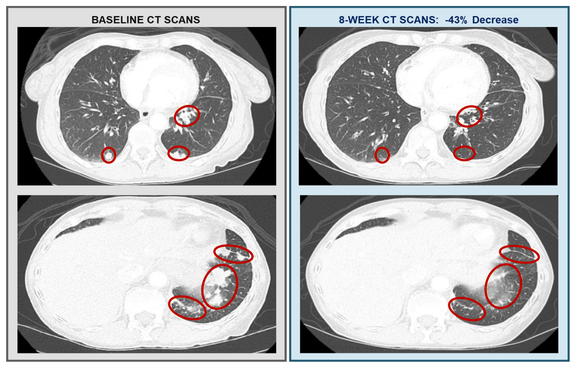
Progression-Free Survival (PFS)

- **Median PFS: 5.8 months** (95% CI, 1.8–11.7)
- **11/17 patients (64.7%)** had a PFS event
- **3-month PFS:** 69.7%
- **6-month PFS:** 44.3%

Overall Survival (OS)

- **Median OS: Not reached** (95% CI, 4.3–NE)
- **Median follow-up: 10.6 months**; **7/17 patients (41.2%)** have died
- **6-month OS:** 69.3%
- **12-month OS:** 53.9%

14-Month Ongoing Partial Response in an NSCLC Patient Who Previously Progressed Through Prior Anti-PD-1 + Chemotherapy. The Partial Response Began at 8 Weeks (1 Cycle) With 43% Tumor Reduction.

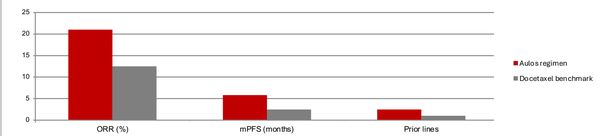


- 68-year-old woman with NSCLC (adenocarcinoma) with tumor lesions in lung, adrenal, and bone.
- The patient progressed on prior anti-PD-1 + carboplatin + pemetrexed and docetaxel + gemcitabine.
- July 2025, the patient began treatment with the RP2D imneskibart + aldesleukin in combination with avelumab 800 mg Q2W.
- 43% decrease in target lesion size noted at end of Cycle 1, after receiving 8 weeks of therapy.
- Partial response continues after 14 months (7 cycles) of study treatment.

Imneskibart Data (Second-Line or Later) vs. Docetaxel in 2L Metastatic NSCLC

In more heavily pretreated adenocarcinoma patients, the avelumab + imneskibart + IL-2 immunotherapy triplet regimen compares favorably to 2L docetaxel benchmarks

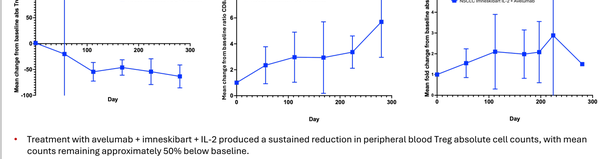
Confirmed ORR	Median PFS	Mean prior lines	Docetaxel benchmark in adenocarcinoma
21% **Avelumab + imneskibart + IL-2 (n = 14)**	**5.8 mo**	**2.6** **More heavily pretreated**	**4–15% ORR** **mPFS ~3–4 mo after 1 prior line** *Based on LUME-Lung 1 & REVEL adenocarcinoma subgroups*



Pharmacodynamic Profile: Durable Increases in CD8 T Cells and CD8/Treg Ratios, and Corresponding Decrease in Tregs

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

Mean Percent Changes in ABS Tregs | **Mean Fold Change in CD8/Treg Ratio** | **Mean Fold Change NSCLC NK Cell**



- Treatment with avelumab + imneskibart + IL-2 produced a sustained reduction in peripheral blood Treg absolute cell counts, with mean counts remaining approximately 50% below baseline.
- Peripheral blood CD8/Treg ratios and NK cell absolute counts increased following treatment, with median increases exceeding 3-fold and 2-fold over baseline, respectively.

Imneskibart Pharmacokinetics

- Imneskibart pharmacokinetics (PK) is approximately dose-proportional over the dose ranges tested.
- Comparable PK exposures were seen at 4.5, 9, and 12 mg/kg imneskibart administered alone or in combination with aldesleukin, **with or without avelumab**.
- Estimated human half life is ~19.5 days.

Conclusions

- The imneskibart + low-dose, SC IL-2 + avelumab immunotherapy triplet regimen demonstrated promising antitumor activity in heavily pretreated patients with checkpoint inhibitor (CPI)–refractory advanced adenocarcinoma NSCLC.
- Confirmed objective response rate (ORR) was 21% (3/14 response-evaluable patients), disease control was 86%, and median PFS was 5.8 months. These results compare very favorably with docetaxel outcomes reported in historical studies (ORR 4–15%, median PFS ~3–4 months, as second-line treatment), despite greater prior treatment exposure. Patients in this trial received a mean of 2.6 prior lines of therapy, compared with one prior line in the typical second-line docetaxel setting.
- Median OS was not reached at the data cutoff. Continued follow-up will further characterize survival outcomes.
- CD8/Treg ratios increased substantially from baseline, and greater increases were associated with longer PFS, supporting the biological rationale for redirecting IL-2 toward effector cells.
- NK cells increased from baseline, potentially enhancing avelumab-mediated antibody-dependent cellular cytotoxicity (ADCC). Avelumab is an IgG1 antibody with a wild-type Fc domain that enables NK cell-mediated tumor cell killing.
- The regimen demonstrated a manageable safety profile. Most treatment-related adverse events were Grade 1-2, with no capillary leak syndrome or treatment-related deaths.
- These findings support randomized evaluation of this immunotherapy triplet against standard therapy in patients with CPI-refractory advanced adenocarcinoma NSCLC.

Presented at the European Society for Medical Oncology (ESMO) Congress 2026, October 23-27, 2026

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George R. Blumenschein has received grants and/or contracts from Amgen, Bayer, Adaptimmune, Exelixis, Daiichi Sankyo, GlaxoSmithKline, Immatics, Immunocore, Incyte, Kite Pharma, Macrogenics, Tonix, AstraZeneca, Bristol-Myer Squib, Celgene, Genentech, Medimmune, Merck, Novartis, Roche, Sanofi, Xcovery, Tmunity Therapeutics, Regeneron, BeiGene, BeiOne Medicines, Repertoire immune Medicines, Verastem, Cytomx Therapeutics, Duality Biologics, Mythic Therapeutics, Takeda, Aulos Bioscience, Seagen, Pfizer, Nuvalent, Turning Point Therapeutics, Immutep, Boehringer Ingelheim, Daiichi Sankyo, Eisai, Elevation Oncology, Gilead, Ipsen, Janssen, Medimmune, Merck, Novartis, Roche, Sanofi, Tyme Oncology, Xcovery, Virogin Biotech, Bristol Myers Squibb, Celgene, Daiichi Sankyo, Hutti Bio, Genentech, Genzyme, Gilead, Lilly, Janssen, Medimmune, Merck, Novartis, Roche, Sanofi, Tyme Oncology, Xcovery, Virogin Biotech, Maverick Therapeutics, BeiGene, BeiOne Medicines, Regeneron, Cytomx Therapeutics, Intensen Biosciences, Oncorvus Therapeutics, Seagen, Scorpion Therapeutics, Immunocore, Full-life Technologies, GlaxoSmithKline, T-knife Therapeutics, and Oncotrust; has participated on a data safety monitoring board or advisory board for Virogin Biotech SAB, BeiOne Medicines, Immunocore, Regeneron, and Daiichi Sankyo; has an immediate family member who is employed by Johnson & Johnson/Janssen.

Avelumab was provided by the healthcare business of Merck KGaA, Darmstadt, Germany (www.emdgroup.com/ethics).

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