AU-007, a Human Monoclonal Antibody (mAb) That Binds to IL-2 and Inhibits CD25 Binding, Plus Low-Dose Aldesleukin, in Advanced Solid Tumors: Phase 2 Update

Meredith McKean[1], Sophia Frentzas[2], Drew Rasco[3], John Powderly[4], Andrew Weickhardt[5], Alison Hiong[6], Paul de Souza[7], George R. Blumenschein[8], Vinod Ganju[9], Siwen Hu-Lieskovan[10], Ganessan Kichenadasse[11], Catherine Oakman[12], Nehal Lakhani[13], Timothy Wyant[14,15], Jenny Tang[14], Lori Richards[14], Aron Knickerbocker[14], Inbar Amit[15], Yanay Ofran[14,15], James Vasselli[14]

[1]Sarah Cannon Research Institute, Tennessee Oncology, Nashville, TN; [2]Department of Medical Oncology, Monash Health and Faculty of Medicine, Nursing and Health Sciences, Monash University, Clayton, Australia; [3]START Center for Cancer Care, San Antonio, TX; [4]Carolina BioOncology Institute, Huntersville, NC; [5]Austin Health, Heidelberg, Australia; [6]The Alfred Hospital, Melbourne, Australia; [7]Western Sydney University, Sydney, Australia; [8]Department of Thoracic-Head & Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; [9]Peninsula and South East Oncology, Frankston, Australia; [10]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; [11]Southern Oncology Clinical Research Unit, Bedford Park, Australia; [12]Western Health, Sunshine Hospital, St Albans, Australia; [13]The START Center for Cancer Research, Grand Rapids, MI; [14]Aulos Bioscience, Larkspur, CA; [15]Biolojic Design, Rehovot, Israel

aulos™

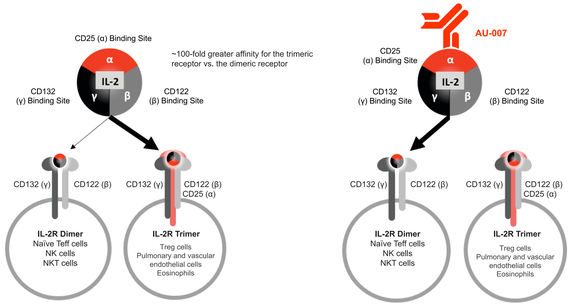
Abstract ID
CT178
NCT05267626

AU-007 Background

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

- AU-007 is a human IgG1 monoclonal antibody designed by leveraging artificial intelligence (Biolojic Design).
- AU-007 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 AU-007



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.
- AU-007 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 Status

- This is a Phase 1/2 open label dose escalation and expansion study.
- Phase 1 dose escalation is complete. AU-007 was evaluated as monotherapy; in combination with a single loading dose of low-dose, subcutaneous (SQ) aldesleukin given with the initial AU-007 dose; and with both AU-007 and low-dose, SQ aldesleukin given every 2 weeks in patients with unresectable locally advanced or metastatic solid cancers (19 tumor histologies).
- AU-007 is administered intravenously (IV) every 2 weeks (Q2W) in all cohorts and aldesleukin is administered SQ at much lower doses and much less frequently than the approved aldesleukin IV regimen.
- The recommended Phase 2 dose (RP2D) of AU-007 and SQ aldesleukin is being evaluated in Phase 2 expansion:
  - AU-007 (9 mg/kg) + a single SQ aldesleukin loading dose (135K IU/kg) in patients with cutaneous melanoma and renal cell carcinoma (RCC).
  - Two additional expansion cohorts enroll PD-L1+ non-small cell lung cancer (NSCLC) patients who have failed prior checkpoint inhibitor (CPI) therapy. One cohort enrolls patients evaluating the RP2D regimen of AU-007 + SQ aldesleukin. The second cohort enrolls patients evaluating the combination of avelumab + the RP2D regimen of AU-007 + SQ aldesleukin with a safety run-in followed by cohort expansion.
  - A cohort in second-line (2L) cutaneous melanoma therapy evaluating the combination of nivolumab + the RP2D regimen of AU-007 + SQ aldesleukin, with a safety run-in followed by cohort expansion, is now enrolling patients.
- 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 end of each 8-week cycle based on tumor growth kinetics observed on end-of-cycle scans.

Study Cohorts and Enrollment Status

AU-007 Phase 1 Dose Escalation
19 different solid tumor types were eligible
Completed without dose-limiting toxicity

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

RP2D
9 mg/kg AU-007 IV Q2W + One 135K IU/kg SQ Aldesleukin Loading Dose

- **RP2D AU-007 + SQ Aldesleukin**
  2L Melanoma and 2nd/3rd L RCC n=20-25
  - Now enrolling only melanoma patients
  - 22 patients enrolled
- **Nivolumab + RP2D AU-007 + SQ Aldesleukin**
  2L Melanoma n=20
  - Now open for enrollment as of April 2025
  - Initial 3 patient safety run-in using 45K IU/kg aldesleukin
- **RP2D AU-007 + SQ Aldesleukin**
  2L PD-L1+ NSCLC n=10
  - 4 patients enrolled
- **Avelumab + RP2D AU-007 + SQ Aldesleukin**
  2L PD-L1+ NSCLC n=20
  - 3 patient safety run-in using 45K IU/kg aldesleukin completed
  - 5 patients enrolled

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

Results

Patient Demographics

Patient Characteristics	N=95
Mean age, years (range)	64.3 (33-89)
Gender, n (%) Male Female	 53 (56) 42 (44)
Race, n (%) White Black Asian American Indian/Alaska native Other	 84 (88) 4 (4) 4 (4) 1 (1) 2 (2)
ECOG performance status, n (%) 0 1	 38 (40) 57 (60)
Mean number of prior therapies n (range)	3.1 (1-10)

Tumor Histologies Evaluated in the Trial

Cancer Diagnosis (n, %)	N=95
Melanoma (includes 2 uveal/2 acral)	29 (30)
Clear cell renal cell carcinoma	19 (20)
Non-small cell lung cancer	12 (13)
Pancreatic cancer (escalation only)	8 (8)
Colorectal cancer (escalation only)	6 (6)
Head and neck squamous cell carcinoma	5 (5)
Other cancer (escalation only): Urothelial, cervical, endometrial, thyroid, gall bladder, nasopharyngeal, Merkel cell carcinoma, cutaneous squamous cell carcinoma, anal squamous cell carcinoma, hepatocellular carcinoma, leiomyosarcoma, intrahepatic bile duct carcinoma	16 (17)

Data cutoff as of March 20, 2025

Safety

Event (n, %)	AU-007 Monotherapy N=15	AU-007 + IL-2 N=75
Any AE	**14 (93)**	**69 (92)**
Drug-Related AEs	**4 (27)**	**56 (75)**
Drug-Related SAEs	**0**	**5 (7)**
Cytokine release syndrome (CRS)	0	3
Infusion-related reaction	0	1
Fever	0	1
Drug-Related Grade 3 or 4 AEs	**0**	**11 (15)[1]**
Lymphopenia	0	6
CRS	0	1
Anemia	0	1
Lipase elevation	0	1
Neutropenia	0	1
Maculopapular rash	0	1

[1] One patient had 2 Grade 3/4 AEs: lymphopenia and anemia

Drug-Related Adverse Events in > 5% of Patients (AU-007 + IL-2) N=75

Adverse Event	Grade 1 or 2 N (%)	Grade 3 or 4 N (%)
Fatigue	16 (21)	0
Pyrexia	16 (21)	0
Chills	14 (19)	0
Infusion-related reaction	11 (15)	0
Nausea	10 (13)	0
Injection site reaction	8 (11)	0
Injection site erythema	6 (8)	0
CRS	6 (8)	1 (1)
Lymphopenia	0	6 (8)
AST elevation	5 (7)	0
Headache	5 (7)	0
Influenza-like illness	5 (7)	0
Anemia	4 (5)	2 (3)
ALT elevation	4 (5)	0

- No dose-limiting toxicity (DLT) occurred through Phase 1 dose escalation.
- Most drug-related adverse events (AEs) were Grade 1 or 2 except for:
  - Grade 3 anemia in one patient who entered study with Grade 2 anemia and had rapid disease progression, receiving only 2 doses of study drug.
  - Grade 4 CRS in one patient. 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.
  - Grade 3 transiently elevated lipase without clinical symptoms in one patient; resolved without intervention.
  - Grade 3 maculopapular rash in one patient that occurred after 6 months on study that resolved with oral prednisone and then topical steroids. The patient continues on trial.
  - Grade 3 or 4 transient (3-7 days) lymphopenias that were not associated with adverse outcomes in 6 patients. Transient lymphopenia is a known effect of IL-2 treatment as lymphocytes traffic out of blood and into tissue.

Pharmacokinetics

- AU-007 pharmacokinetic (PK) exposures were comparable from 4.5-12 mg/kg, administered alone or in combination with SQ aldesleukin.
- The calculated human half-life is approximately 21 days.

Early Signals of Strong Anti-Tumor Activity in Phase 1 Dose Escalation

Durable Objective Tumor Reductions Observed in Phase 1 Dose Escalation in Melanoma, Bladder, Head and Neck (Nasopharyngeal), NSCLC, RCC, and Colorectal Cancer

Case Report 1: Bladder Cancer Metabolic Complete Response

- 67-year-old man with metastatic bladder cancer who had progressed on an anti-PD-L1 treatment March 2023.
- The patient has non-measurable disease only (2 non-target lesions): bladder wall thickening and small pelvic lymph node. Both lesions strongly PET scan positive at baseline.
- April 2023, initial AU-007 (4.5 mg/kg) + one SQ 45K IU/kg IL-2 dose.
- March 2024, PET imaging negative, pelvic lymph node absent, and bladder thickening hard to define on CT scan.
- The response is considered an ongoing metabolic complete response (CR) for one year.
- The patient continues on treatment now for 2 years tolerating the study therapy well with only Grade 1 toxicity.

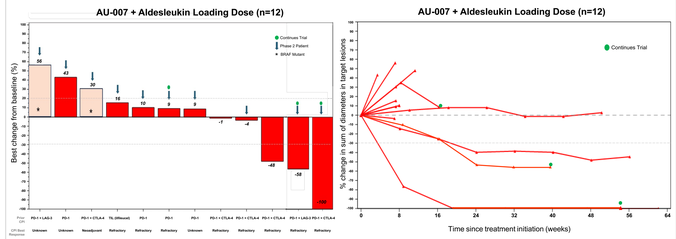
Case Report 2: Nasopharyngeal Cancer Unconfirmed Complete Response

- 55-year-old man with metastatic nasopharyngeal head and neck cancer who had progressed on 5 prior systemic therapies: cisplatin, carboplatin, paclitaxel + carboplatin, nivolumab + carboplatin [initial partial response (PR) followed by progression], and gemcitabine + carboplatin.
- The patient had a cervical spine target lesion that caused significant arm pain and loss of hand function.
- August 2023, initial AU-007 (4.5 mg/kg) + SQ 45K Q2W IU/kg IL-2 dose. After 4 months on study, the AU-007 dose was increased to 9 mg/kg (the AU-007 RP2D).
- The cervical spine lesion initially grew 12% after one cycle (2 months) but then decreased in size to 31% below baseline by the end of Cycle 2 and was a confirmed PR by Cycle 3 (-31% decrease). The lesion continued to gradually decrease in size until the lesion resolved (-100% decease) at the end of Cycle 10 after 20 months of study treatment.
- The patient's arm pain gradually resolved and he was able to regain hand function.
- The patient continues on treatment now for 20 months and is tolerating the study therapy well with only Grade 1 drug-related toxicity.

Efficacy in Melanoma

Best Response in Melanoma Patients in Phase 1 and Phase 2: Clear Evidence of Activity Observed With AU-007 Q2W + Single SQ Loading Dose of IL-2

Percentage Change Over Time vs. Baseline in Melanoma Patients in Phase 1 and Phase 2 Receiving AU-007 Q2W + Single SQ Aldesleukin Loading Dose: Clear Evidence of Durable Tumor Response

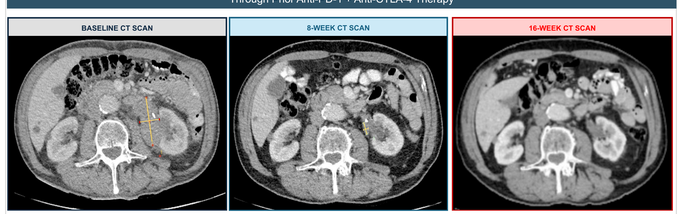


* Lighter columns represent the only BRAF-mut patients who received prior BRAF/MEK inhibitor therapy (both patients progressed on prior therapy)

- Three melanoma patients whose tumors were refractory to either prior anti-CTLA-4 + anti-PD-1 or anti-PD-1 + anti-LAG-3 therapy had deep and durable tumor shrinkages: -48% reduction (on study for 13 months), -58% reduction (continues on study for 10+ months), and a complete response (-100% reduction) in target lesions (continues on study for 13+ months).
- A patient with rapidly progressing acral melanoma who progressed on prior anti-PD-1 therapy received the AU-007 + single low-dose, SQ aldesleukin loading dose regimen for 11 months in dose escalation (4.5 mg/kg AU-007 + 135K IU/kg SQ aldesleukin) and had initial tumor growth followed by tumor reduction to below baseline tumor size.

We are enrolling additional melanoma patients in the Phase 2 cohort receiving the loading dose schedule of IL-2. In addition, a Phase 2 combination cohort with anti-PD-1 nivolumab for 2L treatment of melanoma is now enrolling patients who have not received a prior BRAF/MEK inhibitor.

Durable 100% Shrinkage Beginning at 16 Weeks in the Single Target Lesion of a Melanoma Patient Who Had Previously Progressed Through Prior Anti-PD-1 + Anti-CTLA-4 Therapy

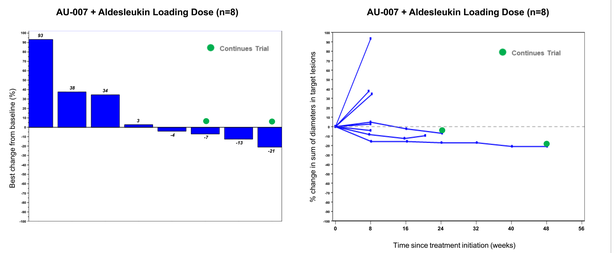


- 70-year-old man with large-volume metastatic disease in the retroperitoneum.
- The patient progressed on prior combination anti-PD-1 and anti-CTLA-4 treatment in December 2023.
- January 2024, the patient received AU-007 (9 mg/kg) + one 135K IU/kg IL-2 dose.
- The 100% tumor shrinkage continues through Cycle 7, 13+ months on treatment.

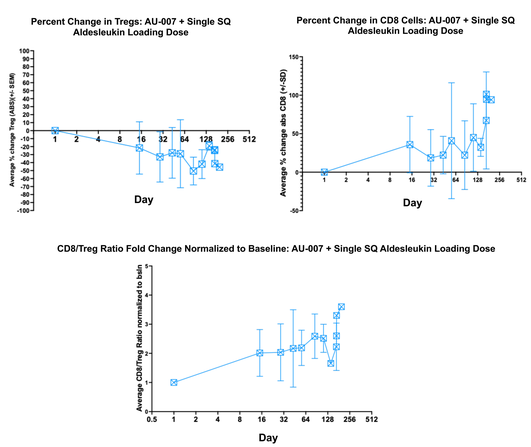
Durable Tumor Shrinkages Were Observed in Checkpoint Inhibitor-Resistant or Progressed RCC

Best Response in RCC Patients in Phase 2 Receiving AU-007 Q2W + Single SQ Aldesleukin Loading Dose

Percentage Change Over Time vs. Baseline in RCC Patients in Phase 2 Receiving AU-007 Q2W + Single SQ Aldesleukin Loading Dose



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



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.

- Treg cells decreased in the periphery in the presence of AU-007 at all dose levels.
- Data support the hypothesis that AU-007 can control and redirect the endogenously produced IL-2 and the exogenously administered IL-2 to reduce the Treg population and increase circulating CD8 effector T cell populations.

Conclusions

- AU-007 Q2W has a tolerable and manageable safety profile as monotherapy and in combination with low-dose, SQ aldesleukin.
- Strong evidence of anti-tumor activity observed in heavily pre-treated patients with tumors that progressed through prior checkpoint inhibitors, including melanoma (anti-PD-1/CTLA-4 and anti-PD-1/LAG-3), RCC (anti-PD-1), bladder cancer (anti-PD-L1), HNSCC (anti-PD-1), and NSCLC (anti-PD-L1).
- AU-007 + low-dose, SQ aldesleukin continues to demonstrate a unique pharmacodynamic profile in the IL-2 therapeutic class; decrease in Tregs appears to be a critical determinant of observed efficacy.
- Phase 2 expansion cohorts evaluating the AU-007 + SQ aldesleukin RP2D continue enrolling in cutaneous melanoma and NSCLC.
- An additional expansion cohort is evaluating the combination of AU-007 + a single SQ loading dose of aldesleukin + anti-PD-L1 avelumab in NSCLC.
- A new Phase 2 cohort is now open and enrolling patients with cutaneous melanoma who have not received a prior BRAF/MEK inhibitor. This cohort is evaluating AU-007 + a single SQ loading dose of aldesleukin combined with anti-PD-1 nivolumab as a second-line treatment.

Presented at the American Association for Cancer Research (AACR) Annual Meeting, April 25-30, 2025

Access this presentation via QR code