Trial in progress: Agni-01 phase 2 cohort of OBX-115 (amsokigene autoleucel; amsoki-cel) tumor-infiltrating lymphocyte (TIL) cell therapy in patients with ICI-resistant advanced melanoma

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Introduction

- Immune checkpoint inhibitors (ICI) have improved treatment outcomes for patients with melanoma; however, most patients do not achieve long-term survival
- Non-engineered TIL cell therapies require high-dose interleukin 2 (IL2), which has well-described high-grade toxicity,[1,2,3] limiting patient eligibility and frequently requiring specialized management
- Lifileucel, a non-engineered tumor-derived autologous T-cell immunotherapy (tumor-infiltrating lymphocyte [TIL] cell therapy), is FDA-approved for anti-PD-1–exposed unresectable or metastatic melanoma[4] and has shown activity in this setting (ORR, 31.5%; mDOR, NR), but is associated with a treatment-related mortality rate of 7.5%[1]
- OBX-115 (amsokigene autoleucel; amsoki-cel) expresses functionally inducible membrane-bound IL15 (mbIL15). When ACZ is administered, the mbIL15 protein is stabilized, enabling cell membrane expression; without ACZ, the protein is unstable and degraded intracellularly. mbIL15 can activate the IL2 receptor in both cis (on the same cell) and trans (other immune cells), regulating amsoki-cel tumor killing, generation of memory TIL, and antigen-independent expansion and persistence (**Figure 1**)
- In preclinical studies, cytoTIL15™ TIL (amsoki-cel) in the presence of ACZ demonstrated enhanced proliferation, persistence, and antitumor activity compared with non-engineered TIL + IL2[5,6] as well as the ability to re-expand upon ACZ redosing
- Amsoki-cel has favorable characteristics for response, with a high proportion of CD8+ T cells, an effector-memory and stem-like–progenitor phenotype, with low levels of immune checkpoint / exhaustion markers[7]
- In Cohort 1 of the Agni-01 trial, amsoki-cel demonstrated promising activity (ORR, 66.7%; 8 of 10 responses ongoing at ~4.3-month median study follow-up) and a favorable safety profile in patients with ICI-resistant advanced melanoma (**Figure 2**)[8]
- A registration-enabling Cohort 3 has been added to the Agni-01 trial (NCT06060613) and is enrolling patients with ICI-resistant advanced melanoma at multiple US and ex-US sites using centralized manufacturing (**Figure 3**)

Figure 1. Amsoki-cel Mechanism of Action

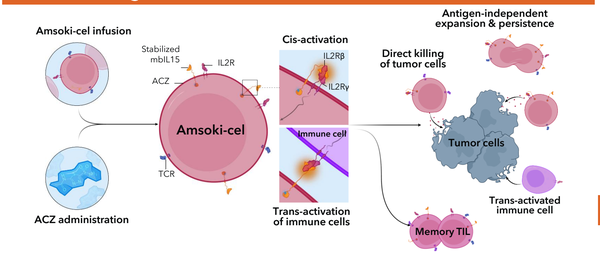
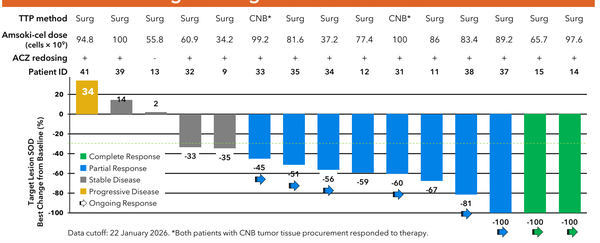
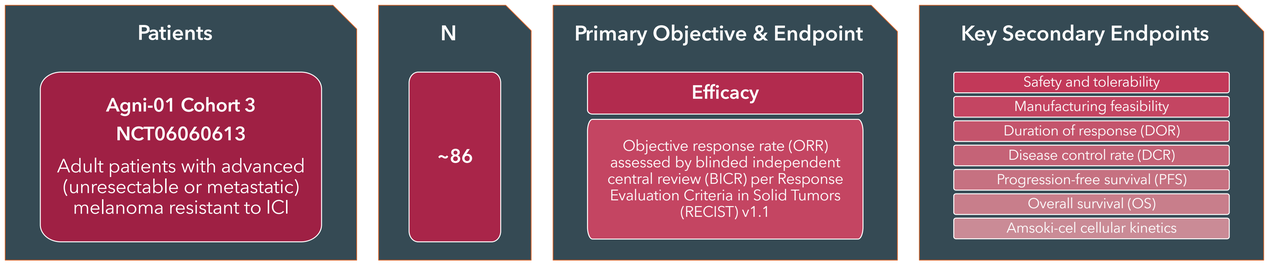


Figure 2. Agni-01 Cohort 1 Data[8]



Study Design

Figure 3. This registration-enabling phase 2, single-arm, open-label, nonrandomized, multicenter cohort will assess the efficacy, safety, and tolerability of the autologous amsoki-cel engineered TIL cell therapy regimen in patients with ICI-resistant advanced melanoma



- Cryopreserved amsoki-cel is manufactured using the patient's own tumor tissue, procured by either minimally invasive core needle biopsy (CNB; 18-gauge needle, ≥4-cm cumulative length) or surgical excision (**Figure 4**)
- Patients receive low-dose lymphodepletion (4-day regimen: Cy 750 mg/m^2 ×3 days, Flu 30 mg/m^2 ×4 days), followed by amsoki-cel (maximum dose of 100 ×10^9 total viable cells), and ACZ 500 mg orally once daily starting day of infusion for ≤14 days (split into two ≤7-day periods within 28 days), with additional ACZ dosing for ≤7 days at periodic intervals until Week 24, and upon progression when new anticancer therapy is not immediately warranted (**Figures 4–5**)
- No IL2 is administered

Figure 4. Centralized Amsoki-cel Manufacturing and Outpatient-compatible Patient Journey

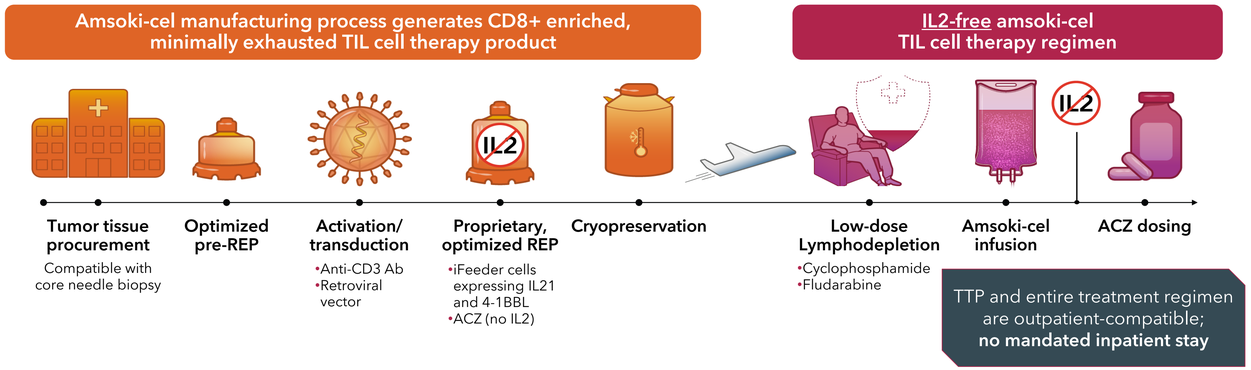
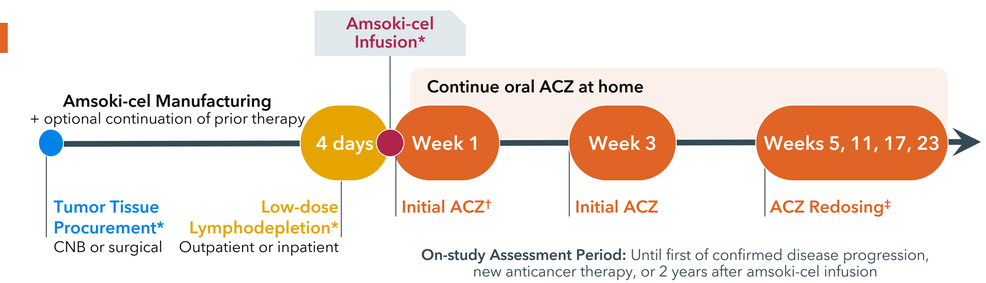


Figure 5. Agni-01 Cohort 3 Treatment Schema



*May be administered in the outpatient or inpatient setting, per institutional standard.

†ACZ is administered orally once daily starting day of amsoki-cel infusion for ≤14 days split into two ≤7-day periods within 28 days (Day 0–6 or until absolute lymphocyte count ≥5000 cells/μL whichever is earlier, and restarting between Day 14 and 21).

‡Additional ACZ dosing for ≤7 days at periodic intervals until Week 24, and upon progression when new anticancer therapy is not immediately warranted.

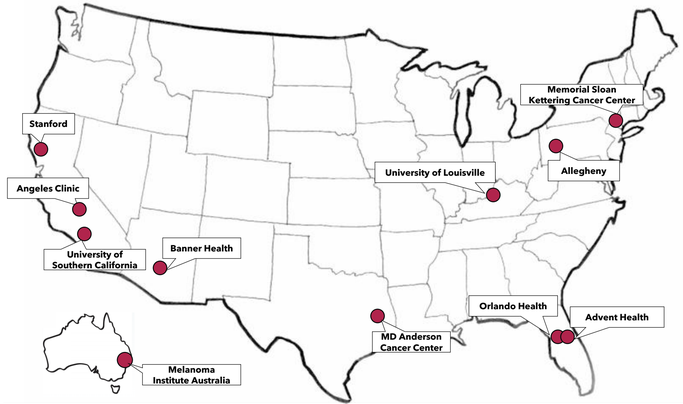
Key Inclusion Criteria

- Age ≥18 years
- Histologically confirmed diagnosis of advanced melanoma
  - Unresectable Stage IIIC, IIID, or Stage IV metastatic melanoma with documented radiographic disease progression after systemic therapy containing a PD-1– or PD-L1–blocking antibody
- ≤2 prior lines of systemic therapy
  - If (neo)adjuvant setting, progression during or within 12 weeks after the last dose
  - BRAFi/MEKi therapy was not required for patients with targetable *BRAF* mutations, but must not have progressed on BRAFi/MEKi if most recent prior therapy
- ≥1 lesion (or aggregate lesions) suitable for amsoki-cel manufacturing (surgical, ≥1.5-cm diameter; CNB, ≥4-cm cumulative length with 18-gauge needle)
- ≥1 RECIST v1.1-measurable lesion remaining after tumor tissue procurement
- ECOG performance status 0 or 1
- Estimated life expectancy >6 months

Key Exclusion Criteria

- Uveal melanoma
- Active autoimmune disease, including active uveitis or any other medical illness that would pose increased risks for study participation
- History of brain metastases or leptomeningeal disease; patients with ≤4 brain metastases that have been treated and are asymptomatic may be eligible
- Prior allogeneic organ transplant, allogeneic cell therapy, or genetically engineered cell therapy (not including autologous stem cell or non-engineered TIL cell therapy)
- Systemic steroid therapy >10 mg/day of prednisone or equivalent

Figure 6. Activated Study Locations



Abbreviations

Ab, antibody; ACZ, acetazolamide; AE, adverse event; BICR, blinded independent central review; CNB, core needle biopsy; ctDNA, circulating tumor DNA; DCR, disease control rate; DOR, duration of response; ECG, electrocardiogram; ECOG, Eastern Cooperative Oncology Group; ICI, immune checkpoint inhibitors; IL2, interleukin 2; IL2R, interleukin 2 receptor; mbIL15, membrane-bound interleukin 15; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein-1; PD-L1, programmed death ligand 1; PFS, progression-free survival; PR, partial response; QD, daily; RECIST, Response Evaluation Criteria in Solid Tumors; REP, rapid expansion protocol; TCR, T-cell receptor; TIL, tumor-infiltrating lymphocytes; TTP, tumor tissue procurement.

Disclosures

Allison S Betof reports consulting for Adaptimmune, Bristol-Myers Squibb, BluePath Solutions, cTRL Therapeutics, Delcath, GE Healthcare, Genmab, Immunocore, IO Biotech, Iovance Biotherapeutics, Novartis, Merck, Pfizer, and Replimune; and institutional research funding from Bristol-Myers Squibb, Immatics, Immunocore, Iovance Biotherapeutics, Lyell Immunopharma, Obsidian Therapeutics, and Replimune.

References

1. US Food and Drug Administration Center for Biologics Evaluation and Research (CBER). AMTAGVI Prescribing Information (https://www.fda.gov/media/176417/download).
2. Rohaan MW, et al. N Engl J Med 2022;387(23):2113-2125.
3. Chesney J, et al. J Immunother Cancer 2022;10(12).
4. US Food and Drug Administration Center for Biologics Evaluation and Research (CBER). AMTAGVI Accelerated BLA Approval (https://www.fda.gov/media/176418/download).
5. Burga R, et al. Emerging Cellular Therapies at the Forefront of Cancer Immunotherapy: Keystone Symposia 2023. Fairmont Banff Springs, Alberta, Canada.
6. Pedro K, et al. AACR Annual Meeting 2023. Orlando, FL: Cancer Research; 2023:LB096.
7. Bernatchez C et al. ISCT Annual Meeting 2024. Vancouver, Canada: 909.
8. Betof AS, et al. ASCO Annual Meeting 2026. Chicago, IL: 9507.

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