OBX-115 (amsokigene autoleucel; amsoki-cel) TIL cell therapy in ICI-resistant advanced melanoma: Pooled safety and updated efficacy with minimally invasive tumor tissue procurement, low-dose lymphodepletion, and IL2-free regimen

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PHari@ObsidianTx.com

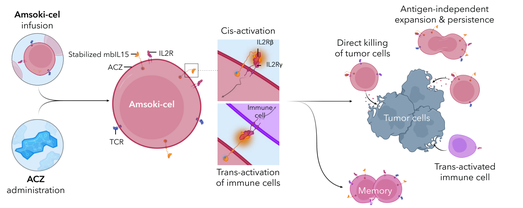
Rodabe N Amaria,[1] Allison S Betof,[2] Gino K In,[3] Alexander N Shoushtari,[4,5] Yazan Samhouri,[6] Tirrell T Johnson,[7] Omid Hamid,[8] Georgina V Long,[9] Michael A Davies,[1] Hussein A Tawbi,[1] Isabella C Glitza Oliva,[1] Jennifer McQuade,[1] Parameswaran Hari,[10] Giridharan Ramsingh,[10] Giri Sulur,[10] Raina Duan,[10] Ricky Rudraraju,[10] Jason A Chesney[11]

1. The University of Texas MD Anderson Cancer Center, Houston, TX, USA; 2. Stanford University School of Medicine, Stanford, CA, USA; 3. Norris Comprehensive Cancer Center, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA; 4. Memorial Sloan Kettering Cancer Center, New York, NY, USA; 5. Weill Cornell Medical College, New York, NY, USA; 6. Banner MD Anderson Cancer Center, Gilbert, AZ, USA; 7. Orlando Health Cancer Institute, Orlando, FL, USA; 8. The Angeles Clinic and Research Institute, A Cedars-Sinai Affiliate, Los Angeles, CA, USA; 9. Melanoma Institute Australia, The University of Sydney, and Royal North Shore and Mater Hospitals, Sydney, Australia; 10. Obsidian Therapeutics, Cambridge, MA, USA; 11. Department of Medicine, UofL Health – Brown Cancer Center, Louisville, KY, USA

Introduction

- Patients with immune checkpoint inhibitor (ICI)-resistant advanced (unresectable or metastatic) melanoma have limited effective treatment options, and an unmet medical need exists for novel therapeutics in this setting
- Amsokigene autoleucel (amsoki-cel; OBX-115) is a tumor-infiltrating lymphocyte (TIL) cell therapy that is engineered to express acetazolamide (ACZ)-regulatable membrane-bound IL15 (mbIL15; **Figure 1**)
- Regulatable mbIL15 abrogates the need for systemic high-dose IL2, which is an essential component of the non-engineered TIL cell therapy regimen and can lead to substantial toxicity that may limit patient eligibility
- Amsoki-cel has been investigated in patients with ICI-resistant advanced melanoma in a single-center phase 1 first-in-human study (FIH, NCT05470283) and a multicenter phase 1/2 study (Agni-01, NCT06060613) and early clinical data indicate a favorable safety profile and promising efficacy[1–3]
- Herein, we report pooled safety across the FIH and Agni-01 studies and an updated efficacy analysis of patients treated at the RP2D

Figure 1. Amsoki-cel Mechanism of Action



Amsoki-cel expresses functionally inducible mbIL15. When ACZ is administered, the mbIL15 protein is stabilized, enabling cell membrane expression. Without ACZ, the protein is unstable and degraded intracellularly.[4,5] mbIL15 can activate the IL2 receptor in both cis (same cell) and trans (other immune cells), regulating amsoki-cel tumor killing, generation of memory TIL, and antigen-independent expansion and persistence.[6]

Methods

- The FIH and Agni-01 single-arm open-label trials are exploring dosing, safety, and efficacy of the investigational amsoki-cel regimen in patients with ICI-resistant advanced melanoma
  - The primary objectives of FIH and Agni-01 phase 1 were safety, tolerability, and recommended phase 2 dose (RP2D), and of Agni-01 phase 2 was objective response rate (ORR; RECIST v1.1) at the RP2D
- Patients underwent tumor tissue procurement (TTP) by core needle biopsy (CNB) with an 18-gauge needle (≥4-cm cumulative length) or by surgical excision, followed by low- or standard-dose lymphodepletion, amsoki-cel infusion (per-protocol escalating maximum cell dose), and oral ACZ (per-protocol escalating doses and schedules); no IL2 was administered (**Figure 2**)

Figure 2. Agni-01 Study Design*



*Study design evolved over several protocol amendments from FIH to Agni-01. †May be administered in the inpatient or outpatient setting, per institutional standard. Standard-dose LD (7 day regimen: Cy 60 mg/kg × 2 days, Flu 25 mg/m² × 5 days). ‡ACZ is administered at cohort-defined doses once daily starting day of amsoki-cel infusion for ≤14 days; at Dose Level 3, initial ACZ dosing was split into two ≤7-day periods within 28 days (Day 0–6 or until ALC ≥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.

Disclosures

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- As of the 05 May 2026 data cutoff, 37 patients were treated across studies and dose levels (Safety Set); 15 patients treated at dose level 3 (DL3) / RP2D comprise the Key Efficacy Set (**Figure 3**; **Table 1**)
- An efficacy update as of 25 Sep 2026 is reported

Figure 3. FIH and Agni-01 Combined Patient Disposition



Table 1. Baseline Patient and Disease Characteristics

	Key Efficacy Set (N=15)	Safety Set (N=37)
Age, median (range), years	55.0 (41–78)	52.0 (27–78)
Female, n (%)	6 (40.0)	19 (51.4)
ECOG PS, n (%)		
0	12 (80.0)	28 (75.7)
1	3 (20.0)	9 (24.3)
LDH >ULN, n (%)	6 (40.0)	19 (51.4)
Melanoma subtype, n (%)		
Cutaneous	9 (60.0)	27 (73.0)
Mucosal	3 (20.0)	4 (10.8)
Acral	3 (20.0)	3 (8.1)
Uveal mutation/origin*	0	3 (8.1)
Mutation status, n (%)		
BRAF-mutant	8 (53.3)	15 (40.5)
NRAS-mutant	3 (20.0)	9 (24.3)
Brain and/or liver lesions, n (%)	3 (20.0)	12 (32.4)
Lines of prior systemic therapy, median (range)	2.0 (1–5)	3.0 (1–6)
Lines of prior ICI therapy	2.0 (1–5)	2.0 (1–5)
Prior systemic therapy, n (%)	15 (100.0)	37 (100.0)
Anti-PD-1 monotherapy only†	1 (6.7)	1 (2.7)
Anti-PD-1 combination‡	14 (93.3)	36 (97.3)
Anti-PD-1 + anti-CTLA-4	11 (73.3)	32 (86.5)
Anti-PD-1 + anti-LAG-3	8 (53.3)	14 (37.8)
BRAF ± MEK inhibitor, n/N (%)	6/8 (75.0)	12/15 (80.0)
Primary-resistant (SITC criteria), n/N (%)	12/15 (80.0)	32/37 (86.5)
Anti-PD-1 monotherapy[7]	1/9 (11.1)	6/20 (30.0)
Anti-PD-1 combination[8]	12/14 (85.7)	31/36 (86.1)
Target lesion SOD, median (range), mm	58.0 (14.2–213.0)	58.0 (11.7–213.0)

*Clinically or genetically defined uveal melanoma. †Excludes patients who also had combination therapy. ‡Patients may have received >1 combination therapy.

- Amsoki-cel was successfully manufactured using CNB-acquired tumor tissue in 10 patients (27.0%) and surgically acquired tissue in 27 patients (73.0%)
  - Median (range) manufactured dose: 82.5 ×10⁹ cells (2.8–191 ×10⁹)
  - Median (range) infused dose: 74.5 ×10⁹ cells (1.4–150 ×10⁹)
- Median (range) cumulative initial ACZ dose (Day 0–28):
  - All dose levels: 2000 mg (625–10,250)
  - DL3/RP2D (Key Efficacy Set; optimized ACZ dosing): 7000 mg (2000–10,250)
- 30 patients (81.1%) received ≥1 ACZ redose (i.e., after Day 28; all outpatient), including 14/15 (93.3%) in the Key Efficacy Set
- 26 patients (70.3%) received low-dose lymphodepletion, including all patients in the Key Efficacy Set

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Results

Efficacy

- Among 15 patients treated at the RP2D, confirmed ORR was 66.7% (10/15), including 2 confirmed complete responses; target lesion sum of diameters (SOD) reduction was reported for 80.0% of patients (**Figure 5**)
  - 2 patients had CNB TTP, both with confirmed response
  - Deepening and durable responses were observed, with 33.3% of patients remaining in deep, ongoing responses at 12 months (**Figures 6–7**)
- At median (95% CI) study follow-up of 14.3 months (12.3, 25.0; reverse KM):
  - Median (95% CI) DOR was not reached (6.8 months, not estimable; **Figure 8**)
  - Median (95% CI) PFS was 8.3 months (3.9 months, not estimable) after infusion (**Figure 9**)

Safety and Tolerability

- No TTP-related treatment-emergent adverse events (TEAEs) were reported
- The amsoki-cel regimen, including lymphodepletion and ACZ, was well-tolerated (**Figure 4**)
  - 4 patients received low-dose lymphodepletion in the outpatient setting
- Lower rates and severity of hematologic TEAEs were reported for patients receiving low-dose lymphodepletion compared with those receiving standard-dose (comparisons are post-hoc and descriptive in nature)
  - All-grade: low-dose 69.2% vs standard-dose 100% (p=0.038)
  - Grade ≥3: low-dose 65.4% vs standard-dose 100% (p=0.025)
- ACZ-induced mbIL15 expression was not associated with ICANS, capillary leak, Grade >3 CRS or other Grade ≥3 immune-related TEAEs, or treatment-related mortality; no patient required ICU transfer
  - 6 patients reported CRS Grade 1–2; 1 event of CRS Grade 3 was reported

Figure 4. TEAEs reported in ≥30% of the Safety Set (N=37)

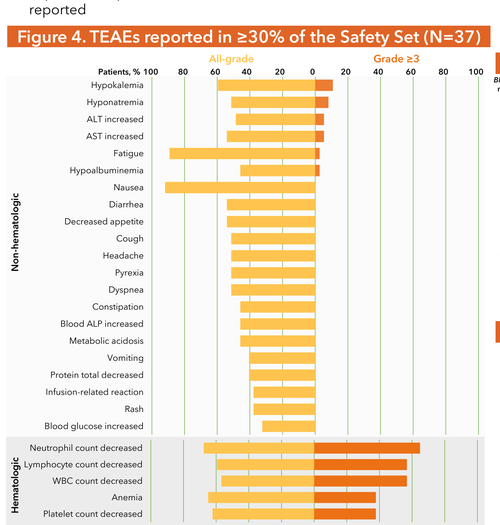


Figure 5. 66.7% ORR and SOD Reduction in 80% of Patients

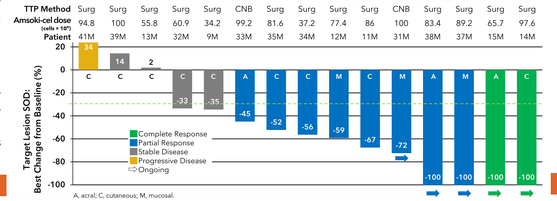


Figure 6. Deepening and Durable Responses

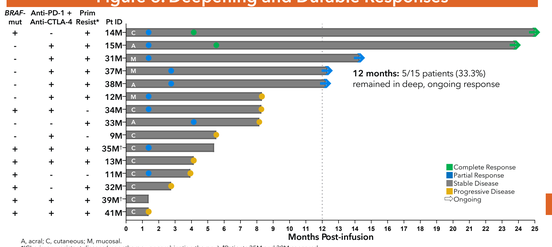


Figure 7. Continued Tumor Reduction over Time

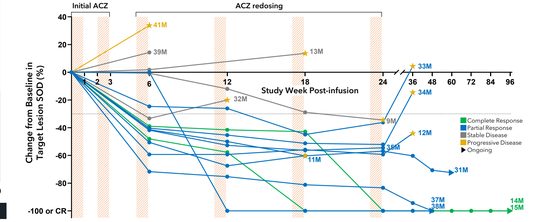


Figure 8. Median DOR Not Reached

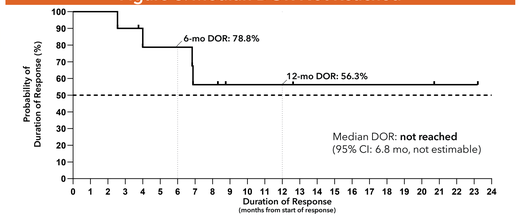


Figure 9. Median PFS 8.3 months

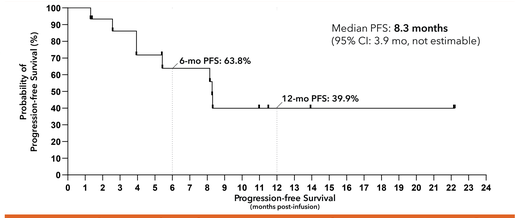
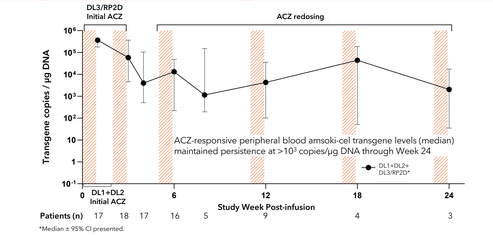


Figure 10. Amsoki-cel Transgene Levels Increase Post-ACZ



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Abbreviations

ACZ, acetazolamide; ALC, absolute lymphocyte count; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; CNB, core needle biopsy; CNS, central nervous system; CR, complete response; CRS, cytokine release syndrome; Cryo, cryopreserved; CTLA-4, cytotoxic T-lymphocyte-associated protein 4; Cy, cyclophosphamide; DL, dose level; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FIH, first-in-human; Flu, fludarabine; ICANS, immune effector cell-associated neurotoxicity syndrome; ICI, immune checkpoint inhibitor; ICU, intensive care unit; IL2, interleukin-2; IL2R, interleukin-2 receptor; KM, Kaplan Meier; LAG-3, lymphocyte activation gene 3; LD, lymphodepletion; LDH, lactate dehydrogenase; mbIL15, membrane-bound interleukin 15; mo, month; mut, mutant; ORR, objective response rate; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; PFS, progression-free survival; PR, partial response; Prim Resist, primary resistant; Pt ID, patient identification; RECIST, Response Evaluation Criteria in Solid Tumors; RP2D, recommended phase 2 dose; SITC, Society for Immunotherapy of Cancer; SOD, sum of diameters; Surg, surgical; TCR, T-cell receptor; TEAE, treatment-emergent adverse event; TIL, tumor-infiltrating lymphocytes; TTP, tumor tissue procurement; ULN, upper limit of normal; WBC, white blood cell.

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Conclusions

- In 37 patients with ICI-resistant advanced melanoma, the **investigational IL2-free amsoki-cel** regimen with **ACZ-regulatable mbIL15** was generally **well-tolerated**, with only 1 Grade 3 CRS, no ICU transfer, and no treatment-related mortality
  - Together with the **overall favorable safety profile**, **low-dose lymphodepletion** and **CNB-compatible** TTP may broaden patient eligibility and reduce treatment burden
- In 15 patients treated at the RP2D:
  - Encouraging clinical activity was observed, with **66.7% ORR** (including 2 CRs and 2 PRs with 100% SOD reduction), **deepening responses** over time, and durable responses with **median DOR not reached**
    - At the 12-month post-infusion landmark, 33.3% of all patients (5/15) remained in **deep, ongoing response** at 72%–100% SOD reduction

These findings suggest that investigational amsoki-cel may represent a meaningful advancement addressing the unmet medical need in ICI-resistant advanced melanoma and support continued evaluation of this regimen in the ongoing pivotal Agni-01 Cohort 3 (NCT06060613) and future studies

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