

Uzatresgene autoleucel autologous T-cell monotherapy for advanced solid tumors: SURPASS, a phase 1, open-label trial

Victor Moreno

victor.moreno@startmadrid.com

Hospital Fundación Jiménez Díaz <https://orcid.org/0000-0001-6099-4236>

Victor Moreno

Hospital Fundación Jiménez Díaz

Kathleen Moore

OUHSC

Adam Asch

University of Oklahoma Health Sciences Center

Brian Van Tine

Washington University in St. Louis <https://orcid.org/0000-0003-4572-6668>

John Charlson

Medical College of Wisconsin

Marcus Butler

Princess Margaret Cancer Centre <https://orcid.org/0000-0002-9840-7057>

Andres Cervantes

Hospital Clínico de Valencia, University of Valencia, Biomedical Research Institute INCLIVA , CIBERONC
Instituto de Salud Carlos III <https://orcid.org/0000-0003-3806-3691>

Jeffrey Clarke

Duke University

Jon Zugazagoitia

Hospital Universitario 12 de Octubre

Emiliano Calvo

START Madrid-CIOCC <https://orcid.org/0000-0003-4921-829X>

Donald Lawrence

Massachusetts General Hospital Cancer Center

David Aggen

Memorial Sloan Kettering Cancer Center

Elena Garralda

VHIO - Vall d'Hebron Institute of Oncology <https://orcid.org/0000-0002-4412-7842>

Ana Oaknin

Vall d'Hebron Institute of Oncology, Vall d'Hebron Barcelona Hospital Campus <https://orcid.org/0000-0002-3592-7194>

Melissa Johnson

Sarah Cannon Research Institute <https://orcid.org/0000-0001-9874-1314>

Bernard Doger

START Madrid-FJD-Hospital Universitario Fundacion Jimenez Diaz

Angelina Petrichenko

University of Pennsylvania <https://orcid.org/0000-0003-0600-0709>

Emma Cook

Perelman School of Medicine University of Pennsylvania <https://orcid.org/0009-0006-9073-6194>

Aoife Roche

University of Pennsylvania

Frederic Bushman

Perelman School of Medicine University of Pennsylvania <https://orcid.org/0000-0003-4740-4056>

Francine Brophy

Adaptimmune

Alejandro Garcia-Consuegra

Adaptimmune

Amy Sauer

Adaptimmune

Marisa Rosenberg

Adaptimmune

Darren Jolliffe

Adaptimmune

Laura Boxall

Adaptimmune

Chris Evans

Adaptimmune

Alex Tipping

Adaptimmune

Martin Isabelle

Adaptimmune

Robyn Broad

Adaptimmune

Bhavna Paratala

Arbutus Biopharma

Molly McNickle

Adaptimmune

Elliot Norry

Adaptimmune

Karen Chagin

Adaptimmune

David Hong

The University of Texas MD Anderson Cancer Center <https://orcid.org/0000-0001-8721-1609>

Article

Keywords: Autologous T-cell therapy, TCR-T cell therapy, Cell therapy for Solid Tumors

Posted Date: April 3rd, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-9238113/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: **Yes** there is potential Competing Interest. Competing interests V.M. reports consulting fees from AbbVie, Roche, Bayer, BMS, Janssen, Syneos, Affimed, Astra Zeneca, and Merck; Principal Investigator – Institutional Funding from Abbvie, Achilles, Adaptimmune, Adc Therapeutics, Ascendis Pharma, Astra Zeneca, Bayer, Beigene, Bicycle Tx, Bioinvent, Biomea Fusion, Biontech, Bristol Myers Squibb, Boehringer, C4 Therapeutics, Calico Life Sciences LLC, Celgene, Constellation, Crescendo Biologics, Cullinan, Daiichi Sankyo, Debiopharm, Dragonfly, Enliven Therapeutics, Epizyme, Exelixis, Famewave, F-Star Beta Limited, Genentech, Genmab, Gilead, Grey Wolf Therapeutics, GlaxoSmithKline, Hexal Ag & Sandoz, Hifibio, Hookipa Biotech, Hutchmed, Igm Biosciences, Imcheck Therapeutics, Immunocore, Immunetp, Incyte lomx Therapeutics, lovance, Italfarmaco, Iteos, Janssen, Light Chain Bioscience, Lilly, Loxo Oncology, Merck, Merus, Miltenyi Biomedicine, Monta Biosciences, MSD, Mythic Therapeutics, Ningbo Newbay, Novartis, Oxford Biotherapeutics, Pfizer, PharmaMar, Pmv Pharma, Prelude Therapeutics Inc., Pyxis Oncology, Regeneron, Relay Therapeutics, Repare Therapeutics, Revolution, Roche, Schrödinger, Scorpion Therapeutics, Seagen, Shattucks, Synthorx, Takeda, Tango Therapeutics, Tesaro, Totus Medicines, Turning Point Therapeutics, and Vividion Therapeutics. K.M. reports research grants from Clovis Oncology, Genentech, GlaxoSmithKline, Lilly, Merck, PTC Therapeutics, and Verastem Oncology; honoraria or consultation fees from Aadi, Alkermes, Aravive, AstraZeneca, Blueprint Medicines, Caris Life Sciences, Clovis Oncology, DualityBio, Eisai, Genentech/Roche, and GlaxoSmithKline. A.A. B.V.T. reports speaker's bureau for Iterion Therapeutics, Inc. and Total Health Conference; consultancy for Cytokinetics Inc., Bayer, Deciphera Pharmaceuticals, Daiichi Sankyo Inc., EcoR1, Advenchen, Putnam, Salaris Pharmaceuticals, Inc., Boxer Capital LLC, and Acuta Capital Partners, LLC; grants/research support and Board membership for Polaris; licenses/patents for Accuronix Therapeutics; and membership of Data Advisory Boards for Bayer US Medical Affairs Oncology, PTC Therapeutics, Aadi Biosciences, Boehringer Ingelheim, Agenus,

Regeneron Pharmaceuticals, Advenchen, EcoR1 Capital, LLC, and Curis. J.C. reports speaker's bureau for Deciphera; consultancy for Adaptimmune, Deciphera and Ipsen; and honoraria from Adaptimmune. J.Z. reports consultancy for Sanofi, Astra Zeneca, BMS, Roche, Pfizer, Novartis, and Guardant Health; speakers' honoraria from Sanofi, Takeda, BMS, Pfizer, Roche, Astra Zeneca, NanoString and Guardant Health; travel honoraria from Sanofi, Takeda, BMS, Pfizer, Roche, Astra Zeneca, and NanoString; and research support/funds from BMS, Astra Zeneca, and Roche. E.C. reports leadership roles at START, PharmaMar, EORTC, Sanofi, BeiGene, Novartis, and Merus NV; stock or other ownership interests at START and Oncoart Associated; honoraria from HM Hospitales Group; consulting or advisory roles for Nanobiotix, Janssen-Cilag, Roche/Genentech, TargImmune Therapeutics, Servier, Bristol Myers Squibb, Amunix, Adcendo, Anaveon, AstraZeneca/MedImmune, Chugai Pharma, MonTa, MSD Oncology, Nouscom, Novartis, OncoDNA, T-Knife, Elevation Oncology, PharmaMar, Ellipses Pharma, Syneos Health, Genmab, and Diaccurate; research funding from START; is President and founder of Foundation INTHEOS, and member of the non-for-profits Foundation PharmaMar and CRIS Cancer Foundation. D.L. D.A. reports consultancy for Bristol Myers Squibb, Seattle Genetics, and Astellas, grants from Astellas, and drug for clinical trials from Merck. E.G. A.O. reports honoraria or consultancy for Agenus, AstraZeneca, Clovis Oncology, Corcept Therapeutics, Deciphera Pharmaceuticals, Eisai, EMD Serono, F. Hoffmann-La Roche, Genmab, GSK, ImmunoGen, Itheos, Merck Sharps & Dohme de España, SA, Mersana Therapeutics, Novocure, PharmaMar, Sattucklabs, Seagen and Sutro Biopharma; and travel/accommodation from AstraZeneca, PharmaMar and Roche. M.J. reports institutional research funding from AbbVie, Acerta, Adaptimmune, Amgen, Apexigen, Arcus Biosciences, Array BioPharma, Artios Pharma, AstraZeneca, Atreca, BeiGene, BerGenBio, BioAtla, Black Diamond, Boehringer Ingelheim, Bristol-Myers Squibb, Calithera Biosciences, Carisma Therapeutics, Checkpoint Therapeutics, City of Hope National Medical Center, Corvus Pharmaceuticals, Curis, CytomX, Daiichi Sankyo, Dracen Pharmaceuticals, Dynavax, Lilly, Elicio Therapeutics, EMD Serono, EQRx, Erasca, Exelixis, Fate Therapeutics, Genentech/Roche, Genmab, Genocera Biosciences, GlaxoSmithKline, Gritstone Oncology, Guardant Health, Harpoon, Helsinn Healthcare SA, Hengrui Therapeutics, Hutchison MediPharma, IDEAYA Biosciences, IGM Biosciences, Immunitas Therapeutics, Immunocore, Incyte, Janssen, Jounce Therapeutics, Kadmon Pharmaceuticals, Kartos Therapeutics, Loxo Oncology, Lycera, Memorial Sloan-Kettering, Merck, Merus, Mirati Therapeutics, Mythic Therapeutics, NeoImmune Tech, Neovia Oncology, Novartis, Numab Therapeutics, Nuvalent, OncoMed Pharmaceuticals, Palleon Pharmaceuticals, Pfizer, PMV Pharmaceuticals, Rain Therapeutics, RasCal Therapeutics, Regeneron Pharmaceuticals, Relay Therapeutics, Revolution Medicines, Ribon Therapeutics, Rubius Therapeutics, Sanofi, Seven and Eight Biopharmaceuticals / Birdie Biopharmaceuticals, Shattuck Labs, Silicon Therapeutics, Stem CentRx, Syndax Pharmaceuticals, Takeda Pharmaceuticals, Tarveda, TCR2 Therapeutics, Tempest Therapeutics, Tizona Therapeutics, TMUNITY Therapeutics, Turning Point Therapeutics, University of Michigan, Vyriad, WindMIL Therapeutics, Y-mAbs Therapeutics; and consulting/advisory role payments made to institution from AbbVie, Amgen, Arcus Biosciences, Arrivent, Astellas, AstraZeneca, Axelia Oncology, Black Diamond, Calithera Biosciences, Daiichi Sankyo, EcoR1, Genentech / Roche, Genmab, Genocera Biosciences, GlaxoSmithKline, Gritstone Oncology, Ideaya Biosciences, Immunocore, iTeos, Janssen, Jazz Pharmaceuticals, Merck, Mirati Therapeutics, Molecular Axion, Novartis, Oncorus, Pyramid

Biosciences, Regeneron Pharmaceuticals, Revolution Medicines, Sanofi-Aventis, SeaGen, SyntheKine, Takeda Pharmaceuticals, Turning Point Therapeutics, and VBL Therapeutics. B.D. D.S.H. reports research/grant Funding to institution from AbbVie, Adaptimmune, Adlai-Nortye, Amgen, Astra-Zeneca, Bayer, Biomea, Bristol-Myers Squibb, Daiichi-Sankyo, Deciphera, Eisai, Eli Lilly, Endeavor, Erasca, F. Hoffmann-LaRoche, Fate Therapeutics, Genentech, Genmab, Immunogenesis, Infinity, Mirati, Navier, NCI-CTEP, Novartis, Numab, Pfizer, Pyramid Bio, Revolution Medicine, SeaGen, STCube, TCR2, Turning Point Therapeutics, and VM Oncology; travel, accommodations, expenses from AACR, ASCO, CLCC, Bayer, SITC, and Telperian; consulting, speaker, or advisory role for 28Bio, Aadi Subsidiary, Abbvie, Acuta, Adaptimmune, Alkermes, Alpha Insights, Amgen, Affini-T, Astellas, Aumbiosciences, Axiom, Baxter, Bayer, Boxer Capital, BridgeBio, CARSGen, CDR-life, CLCC, COG, COR2ed, Cowen, Ecor1, Erasca, Fate Therapeutics, F.Hoffmann-La Roche, Fortress Biotech, Genentech, Gennao Bio, Gilead, GLG, Group H, Guidepoint, HCW Precision Oncology, Immunogenesis, InduPro, iwCAR-T speaking, Janssen, Kumquat, Liberium, MedaCorp, Medscape, Numab, Oncologia Brasil, ORI Capital, Pfizer, Pharma Intelligence, POET Congress, Prime Oncology, Projects in Knowledge, Quanta, RAIN, Ridgeline, SeaGen, Stanford, STCube, Takeda, Tavistock, Trieza Therapeutics, Turning Point Therapeutics, WebMD, YingLing Pharma, and Ziopharm; other ownership interests in Molecular Match (Advisor), OncoResponse (Founder, Advisor), and Telperian (Founder, Advisor). A.P. E.C. declares no conflicts. A.R. F. Bushman F. Brophy, A.G-C., A.S., M.R., D.J., L.B, C.E., A.T., M.I., R.B., B.P., M.M., E.N., and K.C. are employees of Adaptimmune, or were at the time of study, and may hold stock/options in Adaptimmune.

Abstract

Uzatresgene autoleucel (uza-cel), a next-generation engineered T-cell receptor autologous T-cell therapy, targets melanoma-associated antigen (MAGE) A4 widely presented by human leukocyte antigens (HLA) on solid tumors. This phase 1, open-label trial evaluated uza-cel in adult HLA-eligible patients with advanced, previously treated MAGE-A4–positive solid tumors. In the monotherapy cohort, patients with ovarian (n=15), esophagogastric junction, esophageal, or gastric (n=14), urothelial (n=8), head and neck cancers (n=4), non-small cell lung cancer or melanoma (n=2 each), and synovial sarcoma or myxoid/round cell liposarcoma (n=1 each) received lymphodepleting chemotherapy (fludarabine 30 mg/m²x4 days, cyclophosphamide 600 mg/m²x3 days) then a single uza-cel intravenous infusion. Most common adverse events were neutropenia (80.9%), cytokine release syndrome (78.7%), anemia and lymphopenia (70.2% each), mostly transient. Overall response rate per RECIST v1.1 was 16/47 (34.0%; 95% CI 20.9–49.3), including 2 complete responses (in ovarian and urothelial) and 14 partial responses, with evidence of broad immune engagement.

ClinicalTrials.gov identifier: NCT04044859

Introduction

Adoptive cell therapy using autologous T cells engineered to express modified T-cell receptors (TCRs) specifically targeting cancer antigens is emerging as a promising option for a range of solid tumors. Given TCRs recognize antigens presented on the cell surface by the human leukocyte antigen (HLA) complex, TCR T-cell therapy can recognize and target intracellular antigens. This contrasts with chimeric antigen receptor (CAR) T-cell therapies, which typically recognize cell surface antigens. Various CAR T-cell therapies are approved for treatment of several hematologic malignancies; however, there has been a lack of efficacy in solid tumors to date.

Cancer/testis antigens (CTAs) are a family of intracellular proteins widely expressed across a range of solid tumors and, consequently, of significant interest in the development of TCR T-cell therapies. Melanoma-associated antigen A4 (MAGE-A4) is a CTA expressed across various tumor types, with restricted expression in healthy adult tissues, mainly in the testis¹. In a recent analysis, MAGE-A4 expression was assessed by immunohistochemistry in samples from HLA-eligible patients and was positive (defined as $\geq 30\%$ of tumor cells staining at 2+ or 3+ intensities) in 22% of head and neck, 24% of ovarian, 16% of melanoma, 14% of non-small cell lung cancer (NSCLC), 9% of gastric, 21% of esophageal, 26% of esophagogastric junction (EGJ), 40% of myxoid/round cell liposarcoma (MRCLS), 70% of synovial sarcoma (SyS), and 32% of urothelial cancers². This prevalence in a range of solid tumors and limited expression in healthy adult tissues, along with its immunogenicity, means MAGE-A4 is a prime target for TCR T-cell therapy¹.

Afami-cel (afamitresgene autoleucel) is a first-in-class autologous T-cell therapy engineered to express an affinity-enhanced TCR targeting a MAGE-A4 antigen presented on the cancer cell surface by specific

HLA-A*02 alleles. The phase 1 trial of afami-cel achieved an overall response rate of 24%, with responses in 9 of 38 patients with relapsed/refractory metastatic solid tumors expressing MAGE-A4. Manageable cytokine release syndrome was seen in 55% of patients and grade ≥ 3 hematologic toxicities in all participants³.

A 44% (7 of 16) response rate in patients with SyS in the phase 1 trial³ led to the initiation of the phase 2 SPEARHEAD-1 trial of afami-cel in pre-treated HLA-A*02-eligible patients with MAGE-A4-expressing advanced SyS or MRCLS. SPEARHEAD-1 achieved its primary efficacy endpoint, with cohort 1 demonstrating a 37% overall response rate, with the most common grade ≥ 3 adverse events (AEs) being cytopenias⁴. Afami-cel is the first TCR T-cell therapy approved by the FDA for solid tumors, highlighting the potential of TCR T-cell therapy in solid tumors. The other two responses in the phase 1 trial of afami-cel were in 1 of 3 patients with head and neck cancer and 1 of 2 patients with NSCLC.³ This, the overall disease control rate (percentage of patients with a response or stable disease [SD]) of 74%, and the observed infiltration of afami-cel into the solid tumors suggested that the rationale for targeting MAGE-A4-expressing tumors with TCR T-cell therapy was sound but highlighted the need for additional potency in solid tumors other than SyS and MRCLS.

Uzatresgene autoleucel (uza-cel; formerly ADP-A2M4CD8) is a next-generation TCR T-cell therapy, expressing the same MAGE-A4-targeting TCR as afami-cel but augmented with a CD8 α co-receptor that improves the polyfunctional response of T cells against MAGE-A4-positive tumors without altering the TCR's specificity. In preclinical studies, uza-cel has shown a clear improvement in T-cell activation and function over afami-cel, indicating significant potential for enhanced clinical efficacy in the treatment of MAGE-A4 expressing tumors⁵. Given the limited response rates to current therapies for advanced tumors expressing MAGE-A4, there is a compelling need for innovative treatments such as uza-cel, which is being evaluated in this phase 1 study. Here we report baseline, safety, efficacy, and translational findings of patients treated in the dose escalation and expansion uza-cel monotherapy cohort.

Patients and Methods

Trial design and oversight

SURPASS (NCT04044859) is a phase 1 open-label trial. Eligible patients were enrolled from a multicenter screening protocol study (NCT02636855). Patients were screened for HLA eligibility (positive for HLA-A*02:01, HLA-A*02:02, HLA-A*02:03, or HLA-A*02:06 allele or having the same protein sequence in the peptide binding domains [P group]) and tumor MAGE-A4 expression ($\geq 30\%$ of tumor cells staining at $\geq 2+$ intensity by immunohistochemistry). Patients aged 18–75 years with a diagnosis of advanced (metastatic or inoperable) urothelial, head and neck, esophageal (squamous and adenocarcinoma), EGJ, or gastric cancers, NSCLC (squamous, adenocarcinoma, adenosquamous, or large cell), melanoma, endometrial carcinoma, or ovarian carcinoma were eligible. Patients with SyS or MRCLS were also eligible at the beginning of the trial. Patients were ineligible based on positivity for any HLA-A*02:05P in

either allele; a history of chronic or recurrent autoimmune or immune-mediated disease requiring steroids or other immunosuppressive treatments, or unstable central nervous system disease (see Methods for full criteria and trial design).

SURPASS utilized a modified 3+3 design, with uza-cel dose escalation across Groups 1–2 and an expansion group. Planned dose ranges (total transduced cell number) were $0.8\text{--}1.2 \times 10^9$ (Group 1), $1.2\text{--}6 \times 10^9$ (Group 2), and $1.0\text{--}10 \times 10^9$ (expansion group) uza-cel T cells. Prior to each dose escalation, dose-limiting toxicities (DLTs) were assessed. Trial design is shown in Extended Data Fig. 1.

Leukapheresis was advised as soon as possible after enrollment, and patient eligibility was reconfirmed and baseline assessments made prior to lymphodepleting chemotherapy of fludarabine 30 mg/m^2 on days -7 to -4 and cyclophosphamide 600 mg/m^2 on days -7 to -5 . Uza-cel was administered via intravenous infusion on day 1. Patients remained in the interventional phase until disease progression, death, or withdrawal, and where applicable then transferred to long-term follow-up for monitoring for delayed AEs.

This trial was conducted in compliance with International Council for Harmonisation (ICH) Good Clinical practice, all applicable patient privacy requirements, and the guiding principles of the Declaration of Helsinki, and in accordance with local legal and regulatory requirements. Written informed consent was obtained prior to performing any procedures.

Patients

Patients were pre-screened for HLA-A2 and MAGE-A4 eligibility through a separate screening study (NCT02636855); further screening preceded enrollment into SURPASS and leukapheresis to collect autologous cells for manufacturing into uza-cel. Eligible patients were aged 18–75 years with a diagnosis of advanced (metastatic or inoperable) urothelial, head and neck, esophageal (squamous and adenocarcinoma), EGJ, or gastric cancers, NSCLC (squamous, adenocarcinoma, adenosquamous, or large cell), melanoma, endometrial carcinoma, or ovarian carcinoma were eligible. Patients with SyS or MRCLS were also eligible at the beginning of the trial. Patients were excluded based on positivity for any HLA-A*02:05 in either allele, or any HLA-A*02 alleles with the same protein sequence in the peptide binding domains; a history of chronic or recurrent autoimmune or immune-mediated disease requiring steroids or other immunosuppressive treatments, or unstable central nervous system disease. Full inclusion and exclusion criteria are available in the Supplement.

T-cell manufacturing

Uza-cel is autologous CD4 and CD8 T cells engineered with an affinity-enhanced TCR to target the tumor antigen MAGE-A4. Autologous T cells are obtained via leukapheresis from eligible participants who have antigen positive tumors and who have appropriate HLA-A. The CD4 and CD8 T cells are transduced with a self-inactivating lentivirus vector expressing the CD8 α _MAGE-A4 (affinity-enhanced clone c1032) under

good manufacturing practice conditions and expanded *in vitro*. For 40 of the 47 monotherapy patients, an AKT inhibitor was included (once this had been approved by the regulators). The product of this transduction is polyclonal T cells that are designed to target MAGE-A4 in tissue. The transfer lentiviral vector has been meticulously designed to contain only the minimal genetic elements required for function and no vector proteins for maximum biosafety.¹⁶ Cell product was typically ready to be returned to the site ~1 month after the start of manufacturing. Receipt of the T-cell product at the clinical site was required before the start of lymphodepleting chemotherapy.

Dosing/Procedures

A modified 3+3 dose escalation design was used comprising staggered uza-cel administration to 3 patients each in Groups 1 and 2 at dose ranges of $0.8-1.2 \times 10^9$ and $1.2-6 \times 10^9$ transduced cells, respectively, followed by the expansion group who received $1.0-10.0 \times 10^9$ transduced cells. Uza-cel was administered on day 1 following lymphodepleting chemotherapy of fludarabine 30 mg/m² on days -7 to -4 and cyclophosphamide 600 mg/m² on days -7 to -5 (dose reductions allowed per protocol). Bridging therapy was permitted, subject to specific washout periods, prior to the administration of lymphodepleting chemotherapy. Following chemotherapy, participants received the uza-cel infusion. Baseline and post-infusion biopsies from tumor lesions were performed for translational analysis. Full description in the Data Supplement (Methods). A DLT was defined as any clinical toxicity of grade 3 or higher regardless of the investigator's assessment of relationship to the T-cell infusion during the first 30 days following infusion for each patient in all groups.

Outcomes

The primary endpoints were to evaluate the safety and tolerability of uza-cel through the incidence of AEs, SAEs, dose-limiting toxicities and optimally tolerated dose range, as well as the determination of replication-competent lentivirus, T-cell persistence, and insertional oncogenesis.

Secondary endpoints were to evaluate the anti-tumor efficacy of uza-cel through objective response by RECIST v1.1 per investigator assessment, best overall response, time to response, duration of response, durable response, progression-free survival, and OS.

Exploratory objectives were to characterize the tumor and tumor microenvironment pre and post T-cell infusion, and to assess peripheral blood biomarkers.

Statistical analyses

This phase 1 study was not statistically powered, and no formal hypothesis testing was planned, therefore the data were summarized descriptively. Data were summarized by dose group and across

groups (all monotherapy recipients). Continuous data were summarized using means, medians, standard deviations, and ranges; categorical data were summarized using frequency counts and percentages. Adverse events were summarized and coded by the Medical Dictionary for Regulatory Activities (MedDRA v23.0 or higher). ORRs were summarized by two-sided 95% Wilson and Clopper-Pearson CIs for all monotherapy patients and by each tumor type. A full description of the statistical analyses is provided in the Data Supplement (Methods).

Results

Patient disposition/characteristics

4,284 patients were screened and 1,916 (45%) were HLA-eligible. 1,588 were screened for tumor MAGE-A4 expression. 305 (7% of all screened) were HLA- and MAGE-A4 eligible. Beginning 20 Aug 2019, 47 patients were enrolled at 17 sites across the United States, Canada, and Spain into the monotherapy cohort, 3 patients each in Groups 1 and 2, and 41 patients in the expansion group. Data cutoff for this analysis is 24 May 2024 unless otherwise stated. Patient disposition is illustrated in Extended Data Fig. 2. All patients in this monotherapy group underwent leukapheresis, received lymphodepleting chemotherapy, and received uza-cel.

Patient and treatment characteristics are shown in **Table 1**. In the overall monotherapy group, 15 (31.9%) patients had ovarian cancer; 14 (29.8%) EGJ, esophageal, or gastric cancer; 8 (17.0%) urothelial cancer; 4 (8.5%) head and neck cancer; 2 (4.3%) each had NSCLC or melanoma; and 1 (2.1%) each had SyS or MRCLS. HLA-A2 types and baseline MAGE-A4 tumor antigen scores in the monotherapy group are shown in Extended Data Table 1.

Safety

AEs of any causality occurred during the interventional phase in all 47 patients receiving uza-cel monotherapy: 44 (93.6%) experienced grade ≥ 3 AEs (**Table 2**). Cytopenias and cytokine release syndrome (CRS) were the most common AEs.

AEs and grade ≥ 3 AEs deemed related to either T-cell infusion or lymphodepletion occurred in 47 (100.0%) and 42 (89.4%) of patients receiving uza-cel monotherapy, respectively (Extended Data Table 2). The most common AEs of any grade deemed, probably, or possibly related to T-cell infusion were CRS in 37 (78.7%), neutropenia in 15 (31.9%), fatigue in 11 (23.4%), anemia in 10 (21.3%), and thrombocytopenia in 9 (19.1%) patients.

No DLTs were reported with uza-cel. Grade 1 and 2 CRS were reported in 16 (34.0%) and 14 (29.8%) patients, respectively; 4 (8.5%) experienced grade 3 CRS, 2 (4.3%) grade 4, and 1 (2.1%) grade 5. First CRS occurred a median (range) of 3 (1–15) days after T-cell infusion and resolved in a median (range) of 5 (1–15) days. A total of 31 (66.0%) patients received tocilizumab and 8 (17.0%) received corticosteroids

for CRS. Grade 1 immune effector cell-associated neurotoxicity syndrome (ICANS) occurred in 5 (10.6%) patients, grade 2 in 1 (2.1%), and grade 3 in 2 (4.3%). Prolonged cytopenia occurred in 13 (27.7%) of patients at week 4 post T-cell infusion, 9 (19.2%) at week 8, and 3 (6.4%) at week 12. SAEs occurred in 32 (68.1%) of patients (Extended Data Table 2). There were SAEs with a fatal outcome in 3 (6.4%) patients during the interventional phase: CRS, which was deemed by the investigator definitely related to T-cell infusion, in a 60-year-old with ovarian cancer who had a large tumor burden in the lungs and previous lung radiotherapy; myositis in a 68-year-old with ovarian cancer with a history of myositis with prior cancer immunotherapy, who developed myositis > 8 months post T-cell infusion following a major dental procedure and concurrent with influenza infection; and multi-organ dysfunction in a 64-year-old male with metastatic EGJ cancer. There was one additional fatal SAE in the long-term follow-up phase of pancytopenia which was deemed probably or possibly related to study treatment in a 71-year-old man with esophageal cancer.

Median peak persistence of uza-cel T cells was 111,912 (range, 10,956–387,571) copies/μg DNA and occurred at a median of 15 days (range, 2–54) post infusion in the 47 patients receiving uza-cel monotherapy. Persistence was observed up to > 1,150 days post infusion in some patients (Fig. 1). There has been no evidence of replication-competent lentivirus as of the data cutoff.

Clinical activity

The overall response rate (ORR) per RECIST v1.1 by investigator assessment was 16 of 47 (34.0%, 95% confidence interval [CI] by exact Clopper-Pearson [binomial] method: 20.9–49.3). The ORR was 6 of 15 (40.0%, 95% CI 16.3–67.7) in ovarian, 2 of 14 (14.3%, 95% CI 1.8–42.8) in EGJ, esophageal, and gastric, 3 of 4 (75.0%, 95% CI 19.4–99.4) in head and neck, and 4 of 8 (50.0%, 95% CI 15.7–84.3) in urothelial cancers, with a response also observed in the 1 patient with SyS. Best overall responses for these monotherapy patients included 2 (4.3%) complete responses (1 each in ovarian and urothelial), 14 (29.8%) partial responses (PR), 22 (46.8%) SD, 6 (12.8%) progressive disease (PD), and 3 (6.4%) not evaluable (**Fig. 2**). Illustrative scans of a subset of 3 patients with responses are shown in Extended Data Fig. 4.

Median time to response for all cancer types was 4.3 weeks (range, 1.9–14.3 weeks); with medians (range) of 4.2 (1.9–13.0) weeks in ovarian, 9.9 (7.7–12.1) weeks in EGJ, esophageal and gastric, 4.3 (4.1–4.3) weeks in head and neck, and 6.1 (3.9–11.3) weeks in urothelial cancers. Median duration of response was 20.8 weeks (95% CI 11.6–37.7) in the overall monotherapy group; 16.9 weeks (95% CI 11.6–37.7) in ovarian, 8.7 weeks (95% CI 7.4–20.1) in head and neck, and 30.7 weeks (95% CI 11.0–42.4) in urothelial subgroups. Median progression-free survival was 12.6 weeks (95% CI 8.6–16.4) and median overall survival (OS) was 38.3 weeks (95% CI 26.3–46) in the overall monotherapy group.

A post-hoc analysis of ORR according to various subgroups suggested that patients who had received fewer lines of prior systemic therapy and had peak uza-cel persistence greater than the median had

higher response rates, although numbers were small and this analysis was not statistically powered, with responses occurring across all subgroups (Extended Data Fig. 5).

Translational analysis

Both engineered and endogenous T cells infiltrated solid tumors across the SURPASS indications after treatment with uza-cel (**Fig. 3a**). There was a trend towards greater infiltration of T cells in post-infusion biopsies compared to pre-infusion biopsies. In the subset of patients analyzed, those demonstrating tumor control (best overall response of PR or SD) tended to have higher tumor infiltration of proliferating, cytotoxic, and CD4 T cells (**Fig. 3b–d**); a variable proportion of these are the engineered cells. There was no direct correlation between infiltration of engineered T cells and either clinical response or tumor type, although there was an association between a greater percentage of CD4+ transduced cells in uza-cel manufactured product (that is, measured before infusion) and clinical response (**Fig. 3e**).

Pharmacodynamic signals demonstrated engagement of the broader immune system. Postinfusion, SURPASS patients saw induction of a range of serum proteins, including interferon gamma, achieved across solid tumor indications, including patients who received relatively low uza-cel doses (**Fig. 4a**). Induction of several proteins with origins outside the T-cell compartment were also observed, including interleukin 12 from dendritic cells and CXCL9/10/11 (**Fig. 4b**).

Multiplex immunofluorescence on post-infusion tumor biopsies showed a lower M2:cytotoxic T-cell (M1) ratio associated with tumor control (as indicated by best overall response of PR and SD, compared with PD), indicating a strong innate anti-tumor response (Extended Data Fig. 6). This reduced ratio suggests anti-tumor activation of the innate immune system since M2 macrophages are generally considered pro-tumorigenic, whereas M1 macrophages are considered pro-immunogenic.

Uza-cel reduced antigen positive tumor cells, with the greatest reduction observed in patients with a response (Extended Data Fig. 7). The decrease in MAGE-A4 expression was most probably due to tumor killing of MAGE A4-positive cells by engineered and endogenous T cells that have infiltrated the tumor.

Evidence of long-term persistence of the tumor killing potency of uza-cel in peripheral blood samples has been observed in 3 patients with ovarian cancer with samples taken at disease progression (after 80, 92, and 121 days respectively). In one patient killing capacity has been observed over 3 years post infusion.

Analysis of vector integration site distributions

Integration site analysis was used to evaluate clonality status in 9 patients with persistence of > 1% marked cells in peripheral blood mononuclear cells at 1 year after infusion (Extended Data Fig. 3). All samples yielded robust recovery of vector integration sites, and none showed clonal expansion of > 20%. However, patient 4 showed a clonal expansion of ~11% at month 12. The modestly expanded clone likely

harbored two integration sites of similar abundance, integrated within the transcription units of human *CBL* and *SCRIB*. Given that the two integration sites showed closely similar abundance, we inferred that both were integrated in the same cell clone. The vector copy number in patient 4 at the time of clonal expansion was only ~0.176 vector copies per cell, indicating that outgrowth of the clone was modest. Unfortunately, the patient passed away, so further monitoring was not possible. However, we tested the blood sample collected at month 9 post infusion to see if the same two cell clones (or single clone carrying both integration sites) had started to expand. Results were highly polyclonal and neither one of these integration sites were identified among the most frequent sites detected at month 9. Thus, no clearcut examples of insertional mutagenesis and malignancy were detected.

Discussion

Despite the development of targeted therapies including immunotherapeutics, there remains a need for novel treatment strategies for patients with advanced cancers of the types included in SURPASS. For example, in a phase 3 trial of previously treated patients with advanced NSCLC, ORRs to sitravatinib+nivolumab or docetaxel were 15.6% or 17.2%, respectively, and median OS was 12.2 months or 10.6 months, respectively.⁶ In separate studies of previously treated advanced urothelial carcinoma, response rates to enfortumab vedotin or chemotherapy were 40.6% or 17.9%, respectively,⁷ and 19.6% to nivolumab.⁸ In head and neck squamous cell carcinoma, response rates to nivolumab or standard therapy (methotrexate, docetaxel, or cetuximab) were 13.3% or 5.8%, respectively, in a phase 3 trial in patients with platinum-refractory disease,⁹ and 16% to pembrolizumab in a phase 2 trial in patients with platinum- and cetuximab-refractory disease.¹⁰ In platinum-resistant ovarian cancer, recent trials typically report ORRs of 4–29.6% to the cytotoxic therapies typically used, with addition of bevacizumab to chemotherapy increasing the ORR to 27.3% compared with 11.8% for chemotherapy alone in one trial.¹¹ In a phase 3 trial of patients with previously treated esophageal squamous cell carcinoma, ORR to tislelizumab was 20.3% compared with 9.8% to chemotherapy (paclitaxel, docetaxel, or irinotecan).¹² In a phase 2 trial for patients with metastatic esophageal or gastroesophageal junction cancers ORRs to paclitaxel or paclitaxel plus cixutumumab in the second line were 12% and 14%, respectively.¹³ The patients in SURPASS were mostly heavily pre-treated, with a median of three prior lines of therapy. The overall ORR of 34% and median OS of 38 weeks observed in the monotherapy cohort of SURPASS suggest a clinically meaningful impact of uza-cel treatment on HLA-eligible patients with advanced MAGE-A4-expressing tumors, particularly for patients with advanced ovarian, head and neck, and urothelial cancers. The small number of patients with either NSCLC or melanoma could contribute to responses to uza-cel not being observed in these patients, with as-yet undefined factors other than HLA type and target tumor MAGE-A4 antigen levels also likely to contribute. The HLA-restriction and MAGE-A4-targeted anti-tumor activity of uza-cel does mean that any efficacy will be restricted to a subset of patients who express those markers, highlighting the increasing importance of biomarker screening and encouraging addition of these markers to the typical screening panels.

Limitations of this study include the relatively small population of each of the tumor types, and the lack of a control arm for each. However, the safety profile observed suggests that uza-cel TCR T-cell therapy is tolerable for patients with a range of solid tumors. The safety profile is generally consistent with the expected results of lymphodepletion chemotherapy and TCR T-cell infusion. Incidence of CRS was similar in this trial compared with SPEARHEAD-1, the phase 2 trial of afami-cel in 52 patients with advanced SyS or MRCLS, however, grade ≥ 3 CRS occurred more frequently in SURPASS (15%) versus 2% in SPEARHEAD-1. Incidence of ICANS was also higher in SURPASS (17%) compared with SPEARHEAD-1 (2%). Conversely, incidence of grade ≥ 3 cytopenias was lower in SURPASS compared to SPEARHEAD-1 (lymphopenia 96%, neutropenia 85%, and leukopenia 81%).⁴ Long-term follow-up continues for patients treated in SURPASS, but the insertional oncogenesis data suggest that the risk of oncogenic transformation is low. Although we saw no unequivocal examples of insertional mutagenesis, we observed modest clonal expansion in 1 of the 9 patients analyzed and saw integration events in a proto-oncogene (*CBL*) and tumor suppressor (*SCRIB*), presumably leading to clonal expansion. Previously an expanded clone with a *CBL* integration site was described after CAR T-cell therapy;¹⁴ the expansion ultimately fell in abundance and was judged to be benign. As the number of investigational and approved T-cell therapies and associated treated patients increases more cases of integration events will likely be discovered, however, the safety profile of the current generation of lentiviral vectors is overwhelmingly positive.¹⁵

The extensive translational analysis of SURPASS illustrates that uza-cel not only infiltrates various solid tumors, but also activates endogenous innate and adaptive immune responses, influencing the tumor microenvironment. Further work is required to delineate the factors that contribute to experiencing durable responses to uza-cel. The association observed here in some SURPASS monotherapy patients between percent of CD4+ cells in the uza-cel manufactured product and clinical response could contribute to future developments in the production of uza-cel and other TCR T-cell therapies.

In conclusion, uza-cel showed a manageable safety profile in patients with MAGE-A4-expressing unresectable or metastatic solid tumors. CRS was frequent, tolerable, and manageable by tocilizumab and corticosteroids when indicated. The clinical responses seen are meaningful in the context of the advanced stage of these solid tumors. Clinical responses appear to be higher for participants with certain tumor types and fewer lines of therapy. Clinical responses are associated with strong evidence of uza-cel tumor infiltration, broad immune engagement, and anti-MAGE-A4-expressing tumor activity.

Declarations

Acknowledgements

This trial was funded by Adaptimmune. The authors would like to thank all the patients, their families, and caregivers and the trial teams at the participating sites. The authors would like to thank John Everett, Department of Microbiology, University of Pennsylvania Perelman School of Medicine, Philadelphia, for assistance generating the integration site analysis figure. Writing and editorial

assistance was provided by Christine Ingleby, DPhil, CMPP of Envision Pharma (Glasgow, UK), which was contracted and compensated by Adaptimmune for these services.

Author contributions

All authors critically reviewed the manuscript drafts and approved the final version; A.P., E.C., A.R., and F. Bushman performed integration site analysis and analyzed data; D.J. and L.B. performed statistical analysis; V.M., K.M., A.A., B.V.T., J.C., M.B., A.C., J.M.C., J.Z., E.C., D.L., D.A., E.G., A.O., M.J., B.D., D.S.H. were clinical investigators; F. Brophy, A.G-C., A.S., M.R., C.E., A.T., M.I., R.B., B.P., M.M., E.N., and K.C. analyzed and interpreted data.

References

1. Knafler, G. et al. Melanoma-associated antigen A4: a cancer/testis antigen as a target for adoptive T-cell receptor T-cell therapy. *Cancer Treat. Rev.* 134, 102891 (2025).
2. Wang, T. et al. Identifying MAGE-A4-positive tumors for TCR T cell therapies in HLA-A*02-eligible patients. *Mol. Ther. Methods Clin. Dev.* 32, 101265 (2024).
3. Hong, D. S. et al. Autologous T cell therapy for MAGE-A4(+) solid cancers in HLA-A*02(+) patients: a phase 1 trial. *Nat. Med.* 29, 104-114 (2023).
4. D'Angelo, S. P. et al. Afamitresgene autoleucel for advanced synovial sarcoma and myxoid round cell liposarcoma (SPEARHEAD-1): an international, open-label, phase 2 trial. *Lancet* 403, 1460-1471 (2024).
5. Anderson, V. E. et al. Enhancing efficacy of TCR-engineered CD4 + T cells via coexpression of CD8 α . *J. Immunother.* 46, 132-144 (2023).
6. Borghaei, H. et al. SAPPHIRE: phase III study of sitravatinib plus nivolumab versus docetaxel in advanced nonsquamous non-small-cell lung cancer. *Ann. Oncol.* 35, 66-76 (2024).
7. Powles, T. et al. Enfortumab vedotin in previously treated advanced urothelial carcinoma. *N. Engl. J. Med.* 384, 1125-1135 (2021).
8. Sharma, P. et al. Nivolumab in metastatic urothelial carcinoma after platinum therapy (CheckMate 275): a multicentre, single-arm, phase 2 trial. *Lancet Oncol.* 18, 312-322 (2017).
9. Ferris, R. L. et al. Nivolumab for recurrent squamous-cell carcinoma of the head and neck. *N. Engl. J. Med.* 375, 1856-1867 (2016).
10. Bauml, J. et al. Pembrolizumab for platinum- and cetuximab-refractory head and neck cancer: results from a single-arm, phase II study. *J. Clin. Oncol.* 35, 1542-1549 (2017).
11. Laurent, J. S. & Liu, J. F. Treatment approaches for platinum-resistant ovarian cancer. *J. Clin. Oncol.* 42, 127-133 (2024).
12. Shen, L. et al. Tislelizumab versus chemotherapy as second-line treatment for advanced or metastatic esophageal squamous cell carcinoma (RATIONALE-302): a randomized phase III study.

J. Clin. Oncol. 40, 3065-3076 (2022).

13. Stockton, S. et al. Paclitaxel with or without cixutumumab as second-line treatment of metastatic esophageal or gastroesophageal junction cancer: a randomized phase II ECOG-ACRIN trial. *Oncologist* 28, 827-e822 (2023).
14. Shah, N. N. et al. Clonal expansion of CAR T cells harboring lentivector integration in the CBL gene following anti-CD22 CAR T-cell therapy. *Blood Adv.* 3, 2317-2322 (2019).
15. Jadowsky, J. K. et al. Long-term safety of lentiviral or gammaretroviral gene-modified T cell therapies. *Nat. Med.* 2025 Jan 20. [Epub ahead of print].
16. Dull, T. et al. A third-generation lentivirus vector with a conditional packaging system. *J. Virol.* 72, 8463-8471 (1998).
17. Berry, C. C. et al. INSPIRED: quantification and visualization tools for analyzing integration site distributions. *Mol. Ther. Methods Clin. Dev.* 4, 17-26 (2017).
18. Sherman, E. et al. INSPIRED: a pipeline for quantitative analysis of sites of new DNA integration in cellular genomes. *Mol. Ther. Methods Clin. Dev.* 4, 39-49 (2017).
19. Berry, C. C. et al. Estimating abundances of retroviral insertion sites from DNA fragment length data. *Bioinformatics* 28, 755-762 (2012).

Tables

Table 1 | Patient and treatment characteristics

Characteristic	Uza-cel monotherapy (<i>n</i> = 47)
Male, n (%)	25 (53.2)
Female, n (%)	22 (46.8)
Age, years, median (range)	60 (31–75)
Mean (standard deviation)	58.5 (10.95)
MAGE-A4 H score at screening, ^a median (range)	245 (90–300)
Transduced T cells infused, median (range)	4.95 (1.02–9.95) x10 ⁹
ECOG PS at baseline, n (%)	14 (29.8)
0	33 (70.2)
1	
Number of prior lines of therapy, median (range)	3.0 (1–8)
Received prior immunotherapeutic therapy, ^b n (%)	23 (48.9)
Received bridging therapy, n (%)	27 (57.4)
Race, n (%)	
White	47 (100)

^aH score of immunohistochemical staining strength calculated as: 1 x (% of 1+ cells) + 2 x (% of 2+ cells) + 3 x (% of 3+ cells).

^bImmunotherapeutics include atezolizumab, avelumab, budigalimab, durvalumab, nivolumab, pembrolizumab, tislelizumab.

ECOG PS, Eastern Cooperative Oncology Group Performance Status; MAGE-A4, melanoma-associated antigen A4; uza-cel, uzatresgene autoleucel.

Table 2 | AEs of any causality in ≥ 15%, or grade ≥ 3 AEs of any causality in ≥ 5%, of the 47 patients receiving uza-cel monotherapy in the interventional phase (start of lymphodepleting chemotherapy to end of interventional phase or 30 days post T-cell infusion, whichever is later)

AEs, n (%)	Any grade	Grade ≥ 3
Any AE	47 (100)	44 (93.6)
Neutropenia/neutrophil count decreased	38 (80.9)	36 (76.6)
Cytokine release syndrome	37 (78.7)	7 (14.9)
Anemia/red blood cell decreased	33 (70.2)	22 (46.8)
Lymphopenia/lymphocyte count decreased	33 (70.2)	33 (70.2)
Leukopenia/leukocyte count decreased	27 (57.4)	27 (57.4)
Nausea	24 (51.1)	2 (4.3)
Fatigue	23 (48.9)	5 (10.6)
Thrombocytopenia/platelet count decreased	21 (44.7)	13 (27.7)
Constipation	18 (38.3)	-
Diarrhea	17 (36.2)	1 (2.1)
Rash	17 (36.2)	4 (8.5)
Decreased appetite	16 (34.0)	4 (8.5)
Dyspnea	14 (29.8)	4 (8.5)
Hypophosphatemia	14 (29.8)	6 (12.8)
Pleural effusion	14 (29.8)	3 (6.4)
Pyrexia	14 (29.8)	-
Vomiting	14 (29.8)	2 (4.3)
Abdominal pain	13 (27.7)	3 (6.4)
Edema	13 (27.7)	1 (2.1)
Headache	12 (25.5)	-
Hypokalemia	12 (25.5)	2 (4.3)
Hypomagnesemia	12 (25.5)	-
Arthralgia	11 (23.4)	1 (2.1)
Hypocalcemia	10 (21.3)	3 (6.4)
Sinus tachycardia/tachycardia	10 (21.3)	-
Hypertension	9 (19.1)	7 (14.9)
Hypotension	9 (19.1)	-

Abdominal distension	8 (17.0)	-
Cough	8 (17.0)	-
Febrile neutropenia	8 (17.0)	8 (17.0)
Immune effector cell-associated neurotoxicity syndrome	8 (17.0)	2 (4.3)
Hyperglycemia	7 (14.9)	5 (10.6)
Hypoxia	7 (14.9)	6 (12.8)
Pneumonia	6 (12.8)	5 (10.6)
Blood fibrinogen decreased	6 (12.8)	4 (8.5)
Alanine aminotransferase increased	6 (12.8)	3 (6.4)
Acute kidney injury	5 (10.6)	4 (8.5)
Intestinal obstruction	4 (8.5)	4 (8.5)
Blood bilirubin increased	3 (6.4)	3 (6.4)

AE, adverse event.

Figures

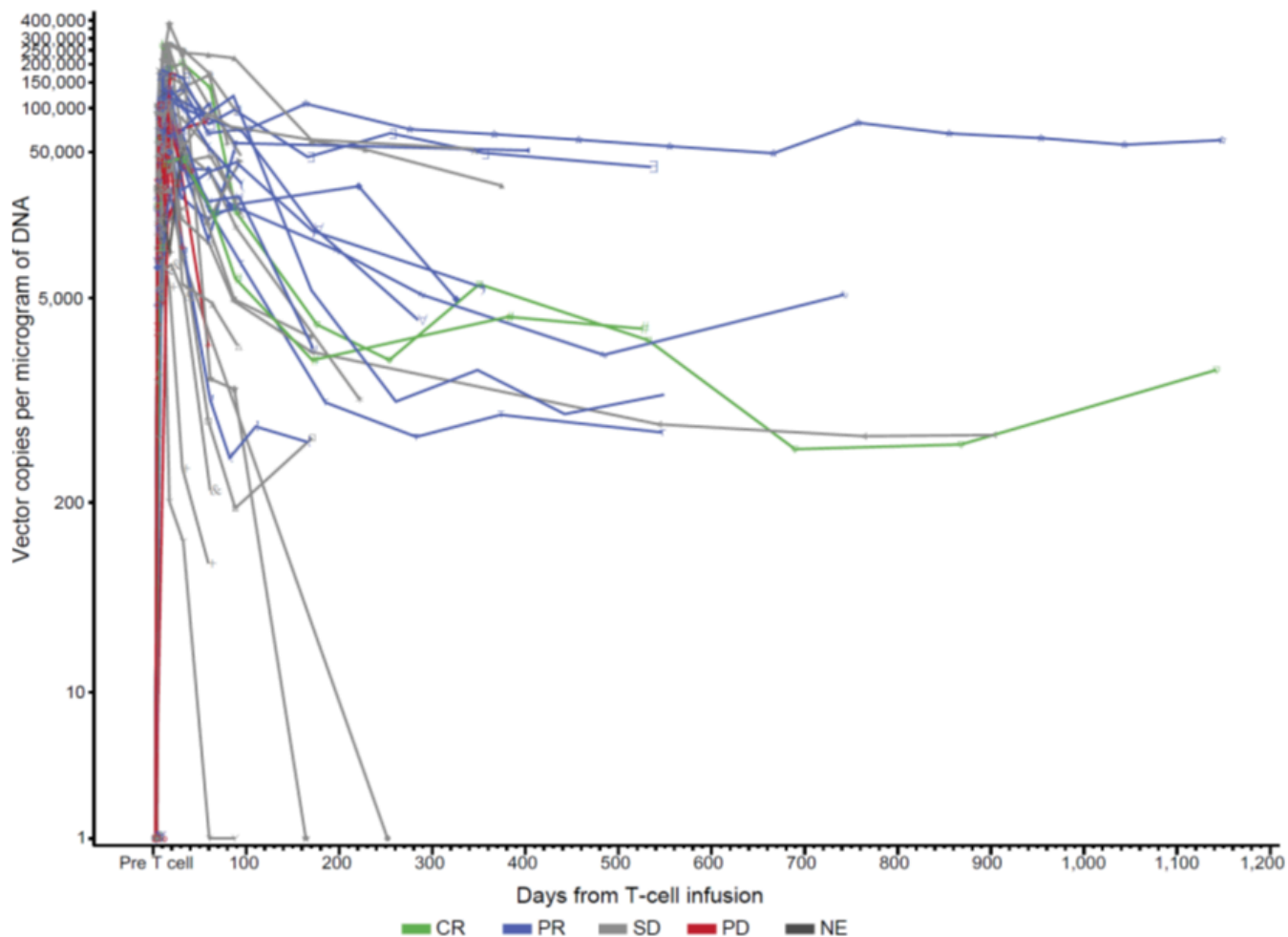


Figure 1

Uzatresgene autoleucel persistence over time in peripheral blood of 47 patients receiving monotherapy, colored by best overall response.

CR, complete response (green); NE, not evaluable (dark grey); PD, progressive disease (red); PR, partial response (blue); SD, stable disease (light grey).

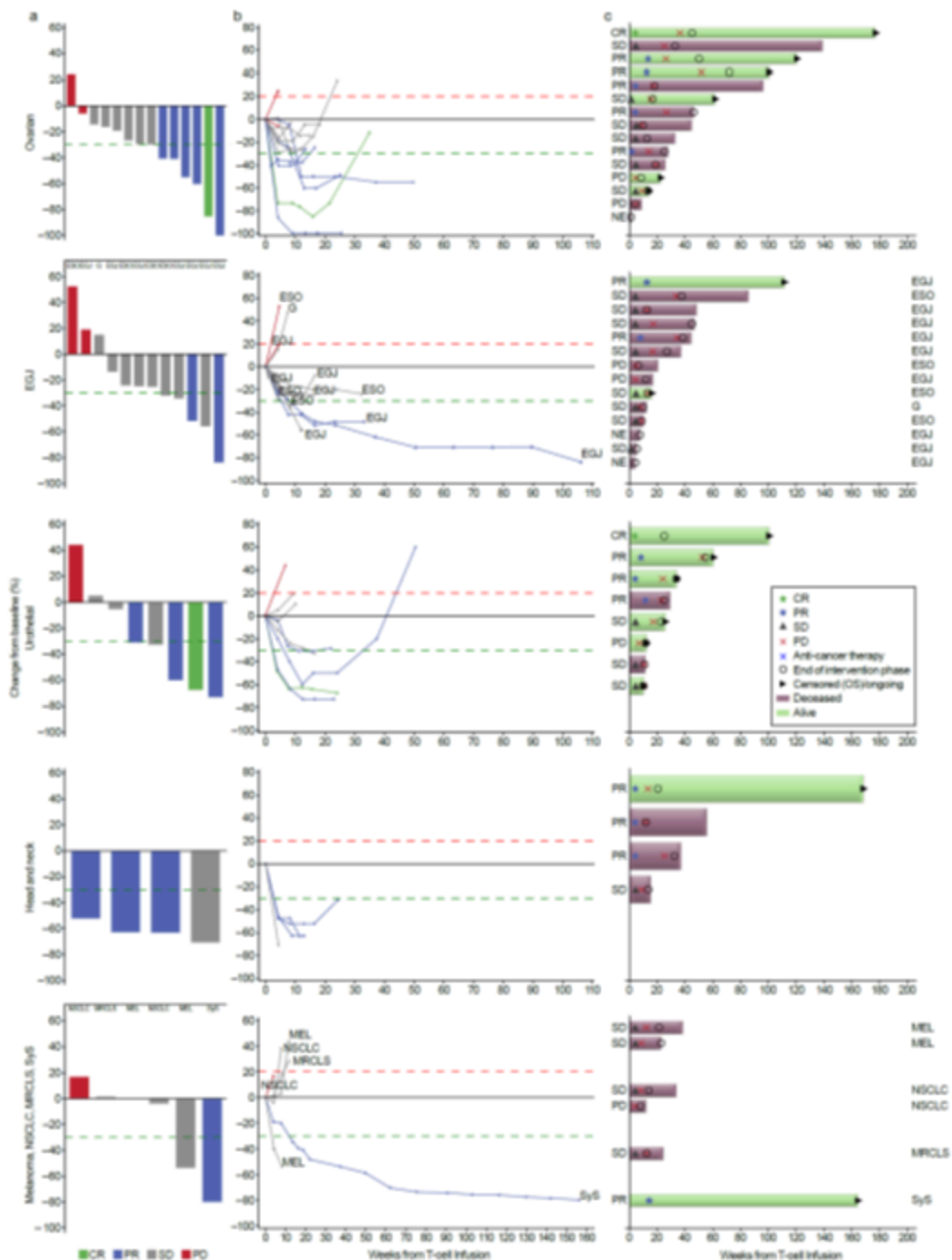


Figure 2

Best overall responses by cancer type for 47 patients receiving monotherapy.

a, Maximum percentage change from baseline in the sum of the lesion diameters colored by best overall response per RECIST v1.1 by investigator review. Three non-evaluable patients not shown. **b**, Change from baseline over time in the sum of the lesion diameters colored by best overall response per RECIST v1.1 by investigator review. **c**, Response characteristics per RECIST v1.1 and follow-up over time. CR, complete response (green); EGJ, esophagogastric junction; ESO, esophageal; G, gastric; MEL, melanoma, MRCLS, myxoid/round cell liposarcoma; NSCLC, non-small cell lung cancer; PD, progressive disease

(red); PR, partial response (blue); RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease (gray); SyS, synovial sarcoma.

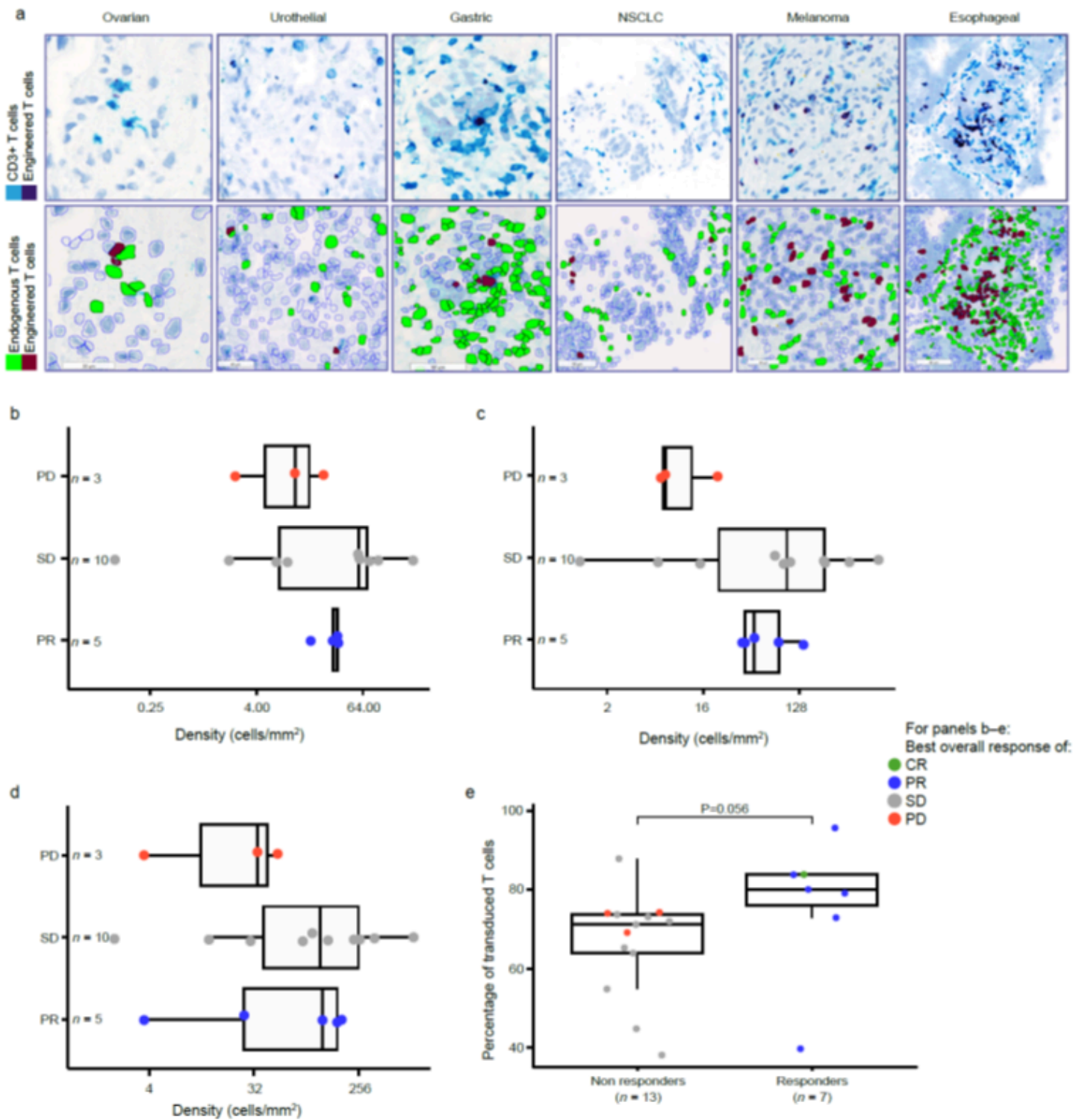


Figure 3

SURPASS tumor biopsies are infiltrated by uza-cel and endogenous T cells.

a, Top row shows examples of post-infusion biopsies stained with immunohistochemistry illustrating variable tumor infiltration by endogenous (pale blue) and engineered (purple) T cells across a range of solid tumor indications. Bottom row illustrates the same images with overlays quantifying the endogenous (lime green) and engineered (purple) T cells. The patients shown in these plots had variable amounts of engineered cells detectable in their peripheral blood, in each case showing some retention but significantly below their peak value by the time of biopsy. Quantification of **b**, proliferating, **c**, cytotoxic, and **d**, CD4+ tumor-infiltrating T cells according to the patients' best overall response as of 29 July 2024 data cutoff. **e**, Percentage of uza-cel manufactured product (engineered T cells prior to infusion) that are CD4+ is significantly greater for those patients that went on to have a best overall response of complete or partial response as of 29 July 2024 data cutoff (by Mann Whitney). Plots depict the median within the boxes denoting interquartile range, with whiskers ranging between the minimum and maximum values within 1.5 times the interquartile range below or above the first or third quartile. Dots represent individual data points. Note, samples were not available for all patients, the numbers included in each analysis are indicated in the respective panels. CR, complete response (green); NSCLC, non-small cell lung cancer; PD, progressive disease (red); PR, partial response (blue); SD, stable disease (grey); uza-cel, uzatresgene autoleucel.

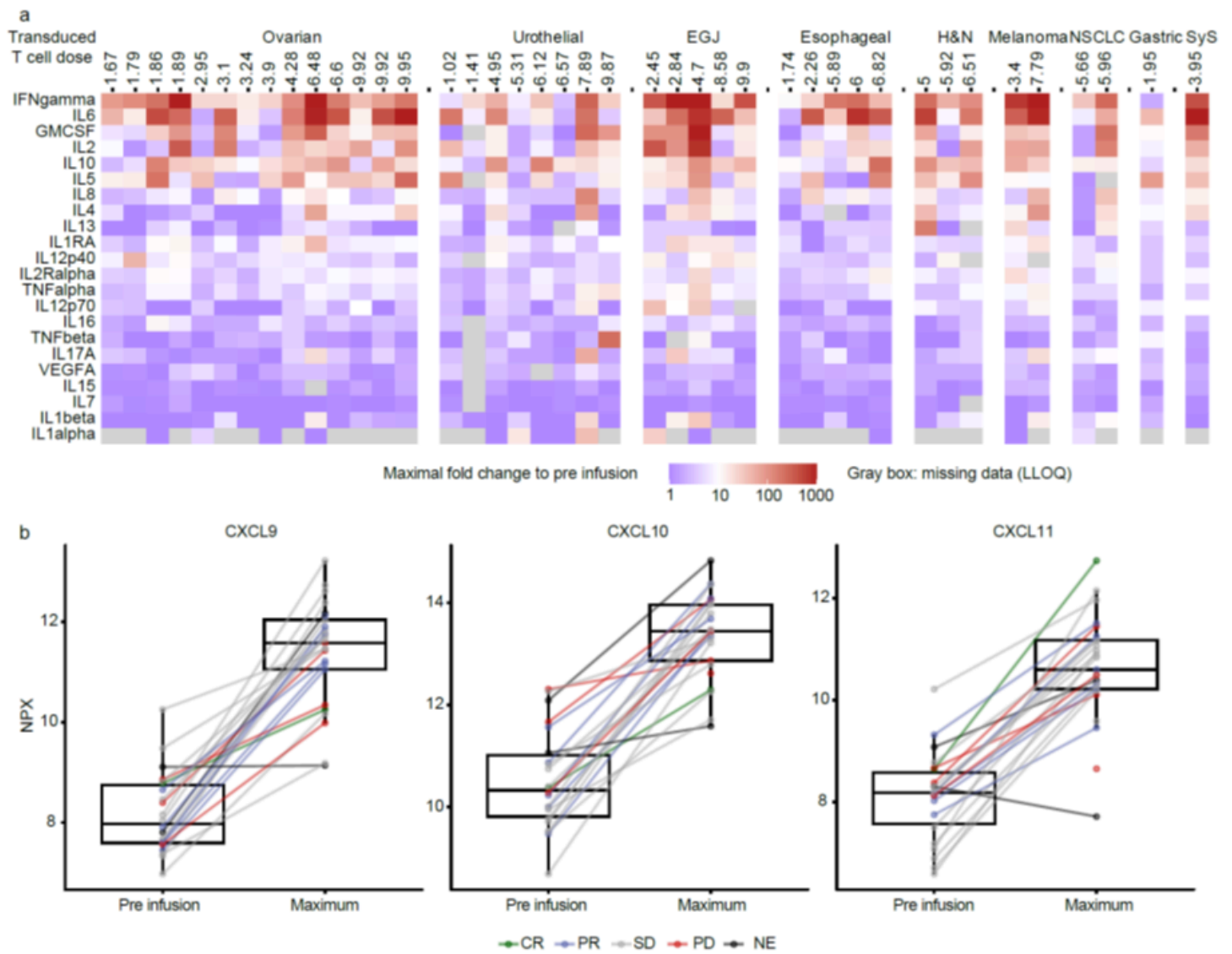


Figure 4

Broad engagement of the immune response.

a, Induction of serum responses across solid tumor indications, and at relatively low transduced T-cell doses. **b**, Examples of induction of non-T-cell serum proteins from baseline levels pre infusion to the maximum level observed in any post infusion timepoint for which data are available. Note the Y axes are plotted as log₂ so each increase by 1 is a doubling. Plots depict the median within the boxes denoting interquartile range, with whiskers ranging between the minimum and maximum values within 1.5 times the interquartile range below or above the first or third quartile. Dots represent individual data points. Note, samples were not available for all patients for all analyses. CR, complete response (green); CXCL, CXC chemokine ligand; EGJ, esophagogastric junction; H&N, head and neck; IFN, interferon; IL, interleukin; LLOQ, lower limit of quantification; NE, not evaluable; NPX, normalized protein expression value; NSCLC, non-small cell lung cancer; PD, progressive disease (red); PR, partial response (blue); SD, stable disease (gray); SyS, synovial sarcoma; TNF, tumor necrosis factor.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryMaterial.docx](#)
- [SurpassAo0SupplementalConsortStatement.docx](#)
- [TrialProtocolv1.pdf](#)
- [Extendeddata.docx](#)