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A Phase 2 Study (GOG-3084) of ADP-A2M4CD8 TCR T-Cell Therapy, Alone or in Combination With Nivolumab, in Patients With Recurrent Ovarian Cancers

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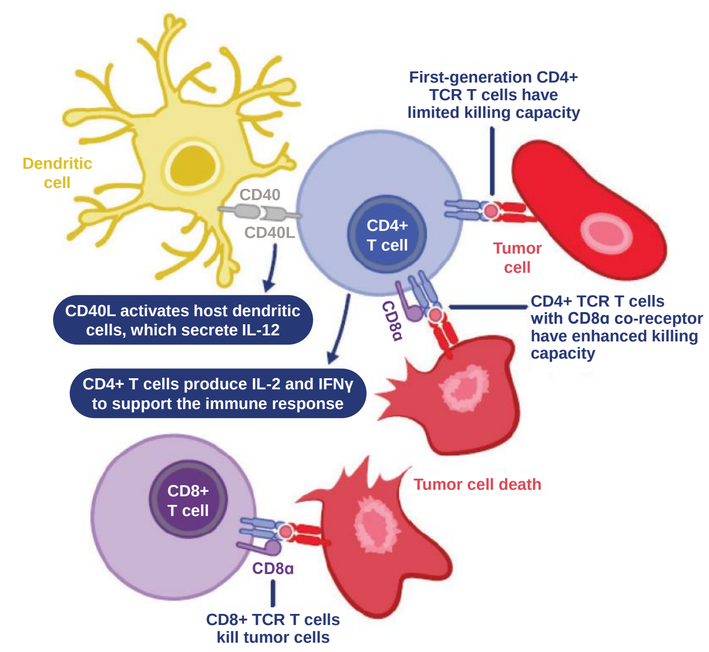
INTRODUCTION

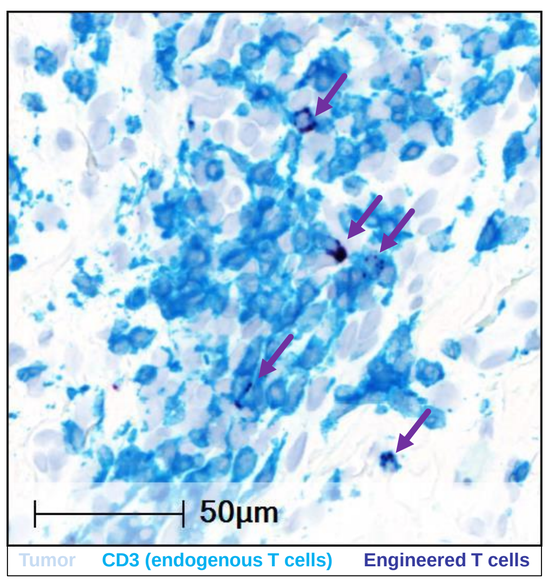
- ADP-A2M4CD8, an autologous mixed CD4+ and CD8+ T-cell receptor (TCR) T-cell therapy, targets melanoma-associated antigen A4 (MAGE-A4) in a human leukocyte antigen (HLA) A*02–restricted manner and expresses a CD8α co-receptor (**Figure 1**)
- The CD8α co-receptor confers additional functionality to the CD4+ cells, leading to activation of T-helper as well as T-cytotoxic cells, allowing both endogenous and engineered T cells to infiltrate the tumor (**Figure 2**)
- MAGE-A4 is expressed (≥30% tumor cells at ≥2+ intensity by immunohistochemistry) in ~25% of ovarian cancers, and ~45% of the US/European population expresses the relevant HLA-A*02 alleles[1]
- The ongoing Phase 1 SURPASS trial (NCT04044859) of ADP-A2M4CD8 in HLA-A*02–eligible participants demonstrated an acceptable benefit-to-risk profile, with responses across multiple MAGE-A4+ solid tumors, including platinum-resistant ovarian cancer, with an overall response rate on March 9, 2023, of 40% (6/15; 95% CI: 16.34–67.71; **Figure 3**)
- Consequently, an open-label non-comparative Phase 2 trial (SURPASS-3; NCT05601752 [**Figure 4**]; partnered with the GOG Foundation, GOG-3084) will investigate ADP-A2M4CD8 for platinum-resistant ovarian cancer, including a combination cohort with nivolumab exploring the potential to increase ADP-A2M4CD8 efficacy by overcoming immunosuppressive pathways

Figure 1. ADP-A2M4CD8 next-generation TCR T cells



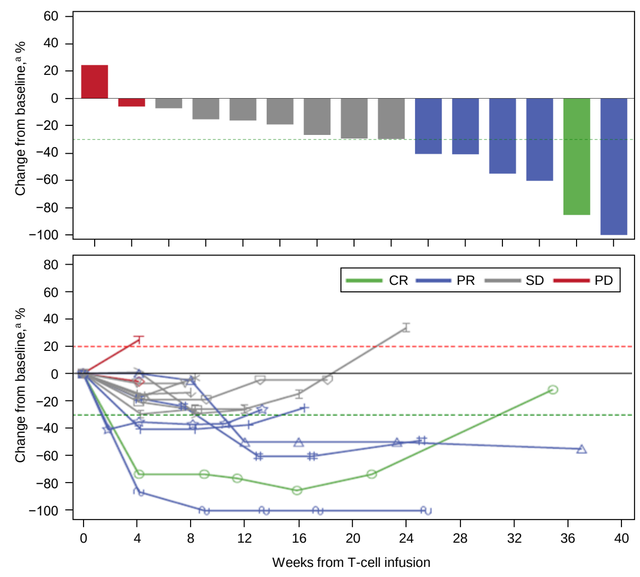
IFN, interferon; IL, interleukin; TCR, T-cell receptor

Figure 2. Engineered and endogenous T cells infiltrating the tumor of a patient in the SURPASS trial



Unscheduled skin bunch biopsy consistent with metastatic urothelial cancer, from a patient with urothelial cancer enrolled in SURPASS

Figure 3. Data in participants with ovarian cancer treated in the Phase 1 SURPASS trial support further development in the Phase 2 SURPASS-3 trial

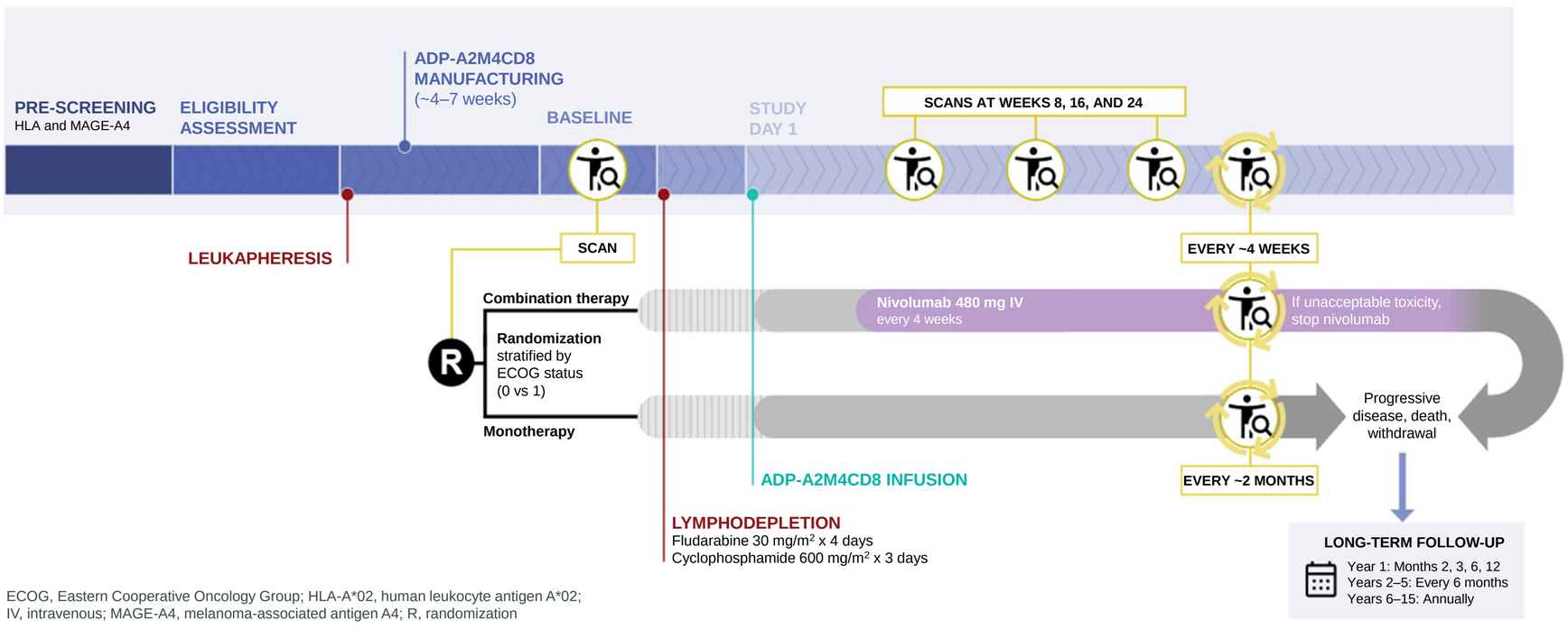


[a]Data represent maximal percentage changes from baseline in sum of diameters (sum of the long diameters for non-nodal lesions and short axis for nodal lesions) in target lesions through progression or before surgical resection; responses evaluated by RECIST v1.1 per investigator assessment. Data cut-off March 9, 2023. CR, complete response; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease

SURPASS-3 TRIAL (NCT05601752)

- Approximately 66 participants (**Table 1**) will be randomized 1:1 to receive ADP-A2M4CD8 or ADP-A2M4CD8 and nivolumab
- Autologous T cells will be collected by leukapheresis and transduced with a lentiviral vector
- Bridging therapies are permitted between leukapheresis and the start of lymphodepletion, with protocol-specified washout periods
- Lymphodepletion chemotherapy (fludarabine 30 mg/m^2/day for 4 days and cyclophosphamide 600 mg/m^2/day for 3 days) will be followed by infusion of 1–10x10^9 ADP-A2M4CD8 T cells
- From Week 4 post infusion, combination arm participants will receive nivolumab 480 mg every 4 weeks
- Imaging associated with key endpoints (**Table 2**) will be performed at baseline; Weeks 8, 16, and 24; and then every 2 months ± 28 days until disease progression
- SURPASS-3 is initiating in Q2 2023 (**Table 3**)

Figure 4. SURPASS-3 trial design



ECOG, Eastern Cooperative Oncology Group; HLA-A*02, human leukocyte antigen A*02; IV, intravenous; MAGE-A4, melanoma-associated antigen A4; R, randomization

Table 1. Key eligibility criteria

Inclusion criteria
Histologically confirmed high-grade serous or endometrioid recurrent/progressive platinum-resistant ovarian carcinoma
Must have received bevacizumab
Participants with a known BRCA mutation (germline or somatic) must have received a PARP inhibitor
May have received up to 4 prior regimens of combination or single-agent systemic treatment for recurrent or metastatic disease
HLA-A*02 and MAGE-A4 positive
Aged ≥18 years and ≤75 years
Measurable disease per RECIST v1.1
ECOG performance status of 0 or 1
Exclusion criteria
Active autoimmune or immune-mediated disease
Leptomeningeal disease, carcinomatous meningitis, or symptomatic CNS metastases

BRCA, breast cancer gene; CNS, central nervous system; ECOG, Eastern Cooperative Oncology Group; HLA-A*02, human leukocyte antigen A*02; MAGE-A4, melanoma-associated antigen A4; PARP, poly adenosine diphosphate-ribose polymerase; RECIST, Response Evaluation Criteria in Solid Tumors

Table 2. Key endpoints

Primary endpoint
Objective response per RECIST v1.1 by IRAC
Secondary endpoints
AEs and serious AEs
AEs of special interest
Replication-competent lentivirus
T-cell clonality and insertional oncogenesis
DR, TTR, DoR, PFS per RECIST v1.1 by IRAC, and by investigator radiological assessment
Overall survival
Levels of serum cancer antigen (CA)125
Exploratory endpoint
Patient-reported outcomes using EQ-5D-3L

AE, adverse event; DoR, duration of response; DR, durable response; IRAC, independent radiological assessment committee; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response

Table 3. Trial sites and investigators

Site name	Investigator	Region
City of Hope Cancer Center	Lorna Rodríguez	US
Hospital Universitario 12 de Octubre	Ainhoa Madariaga	ES
University Health Network (UHN) Princess Margaret Cancer Centre	Neesha Dhani	CA
The Ohio State University James Cancer Centre	David O'Malley	US
University College London Hospitals NHS Foundation Trust, University College Hospital Macmillan Cancer Centre	Rowan Miller	GB
The Christie Hospital	Fiona Thistlethwaite	GB
Institut Gustave Roussy	Alexandra Leary	FR
Centre Léon Bérard	Isabelle Ray-Coquard	FR
Vall d'Hebrón University Hospital	Ana Oaknin	ES
Clínica Universidad de Navarra	Antonio Gonzalez-Martin	ES
HM Sanchinarro, CIOCC	Aranzazu Barquin	ES
Stephenson Cancer Center	Kathleen Moore	US
UC San Diego Moores Cancer Center	Ramez Eskander	US
Karmanos Cancer Institute	Robert Morris	US
Hospital Clínico de Valencia, INCLIVA Biomedical Research Institute	Andres Cervantes	ES
University of Texas Southwestern Medical Center	David Miller	US
The Royal Marsden	Andrew Furness	GB
Hospices Civils de Lyon	Benoit You	FR
Institut de Cancérologie de Strasbourg (ICANS)	Laurianne Eberst	FR
Georgia Cancer Center at Augusta University	Sharad Ghamande	US
Cleveland Clinic Foundation	Peter Rose	US
Honor Health	Justin Moser	US
Rutgers Cancer Institute of New Jersey	Eugenia Girda	US
Virginia Commonwealth University Massey Cancer Centre	Leslie Randall	US
Hospital Universitario Ramón y Cajal	Alfonso Cortes	ES
University of South Florida/ Tampa General Hospital	Matthew Anderson	US
Avera Cancer Institute	David Starks	US
Vidant Medical Center, East Carolina University	Darla Liles	US
L'Institut du Cancer de Montpellier	Michel Fabbro	FR
Swedish Cancer Institute	Fernanda Musa	US

CA, Canada; ES, Spain; FR, France; GB, Great Britain; US; United States

CONCLUSIONS

- SURPASS-3 is a Phase 2, open-label, randomized, non-comparative clinical trial to evaluate the clinical outcome of ADP-A2M4CD8 TCR T-cell therapy as monotherapy and in combination treatment with nivolumab in HLA-A*02–eligible participants with recurrent ovarian cancer positive for MAGE-A4
- SURPASS-3 is currently recruiting at ~30 sites across North America and Europe

REFERENCES 1. Wang T, et al. Poster (LB001) presented at AACR 2022; New Orleans, LA.

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- Kathleen Moore (email – Kathleen-Moore@ouhsc.edu)

FOOTNOTES AND ABBREVIATIONS USED IN TEXT AE, adverse event; BRCA, breast cancer gene; CA, Canada; CNS, central nervous system; CR, complete response; DoR, duration of response; DR, durable response; ECOG, Eastern Cooperative Oncology Group; ES, Spain; FR, France; GB, Great Britain; HLA-A*02, human leukocyte antigen A*02; IFN, interferon; IL, interleukin; IRAC, independent radiological assessment committee; MAGE-A4, melanoma-associated antigen A4; PARP, poly adenosine diphosphate-ribose polymerase; PD, progressive disease; PFS, progression-free survival; PR, partial response; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; TCR, T-cell receptor; TTR, time to response; US; United States