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SUPRAME: A Phase 3 trial evaluating IMA203 T-cell receptor (TCR) T-cell therapy vs investigator's choice in previously treated advanced cutaneous melanoma

Martin Wermke[1], Dirk Schadendorf[2], Caroline Robert[3], Winfried Alsdorf[4], Rodabe N. Amaria[5], Allison Betof Warner[6], Antonia Busse[7], Christoffer Gebhardt[4], John Haanen[8], Jessica Hassel[9], Tobias A.W. Holderried[10], Sebastian Klobuch[8], Suanna C. DeVane[11], Silvana Hengler[12], Delfi Krishna[11], Andrea Mayer-Mokler[12], Dmitry Pankov[11], Cedrik M. Britten[12], Jason J. Luke[13]

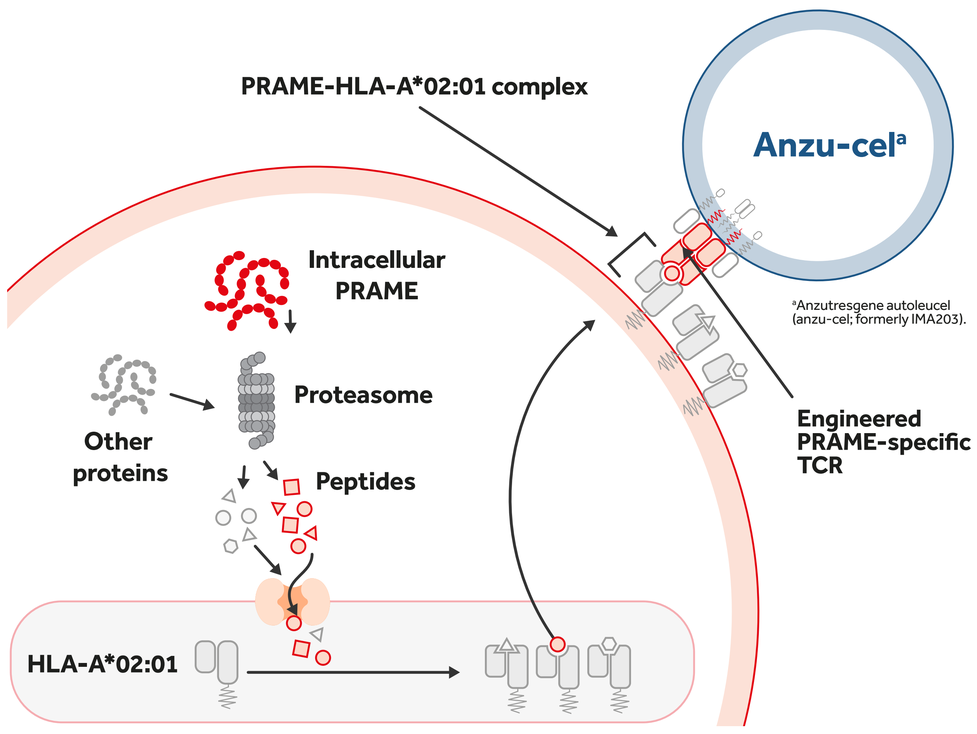
[1]University Hospital Dresden, Dresden, Germany; [2]University Hospital Essen, Essen, Germany; [3]Gustave Roussy, Villejuif, France; [4]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [5]University of Texas MD Anderson Center, Houston, TX; [6]Stanford Cancer Center, Stanford, CA; [7]Charité University Medicine Berlin, Berlin, Germany; [8]The Netherlands Cancer Institute, Amsterdam, Netherlands; [9]University Hospital Heidelberg, Heidelberg, Germany; [10]University Hospital Bonn, Bonn, Germany; [11]Immatics US Inc, Houston, TX; [12]Immatics Biotechnologies GmbH, Tuebingen, Germany; [13]University of Pittsburgh, Pittsburgh, PA

Anzutresgene autoleucel (anzu-cel; formerly IMA203) is a PRAME-directed engineered autologous TCR T-cell therapy

BACKGROUND

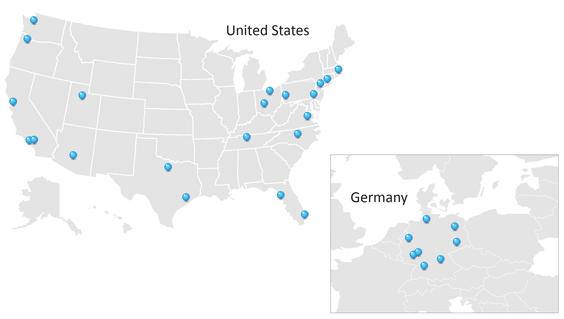
- Outcomes in metastatic melanoma after failure of ICI are poor, with limited long-term survival; there is an urgent need for therapies delivering more durable survival[1,2]
- Anzu-cel is an autologous engineered TCR T-cell therapy targeting PRAME, an intracellular protein displayed as peptide antigen at high density on the surface of multiple solid tumors, including melanoma (**Fig. 1**)[3]
- Anzu-cel TCR T demonstrated a favorable tolerability profile and durable objective responses in heavily pretreated patients with various tumor types[3]:
  - In melanoma, anzu-cel showed 56% (18/32) confirmed ORR, 12.1-month mDOR, 6.1-month mPFS, and 15.9-month mOS at median follow-up of 14.4 months[4]
  - The most frequent TEAEs were LD-related cytopenias in 97%[4]
  - CRS was mostly lower grade (82% grade 1/2; 18% grade 3; no grade ≥4) and ICANS was infrequent (12% grades 1-3)[4]

Figure 1. Anzu-cel Mechanism of Action[3]



ENROLLMENT

- The trial will be conducted in approximately 65 sites across North America and Europe
- Refer to clinicaltrials.gov for the most up-to-date list of activated sites



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METHODS

Study Overview

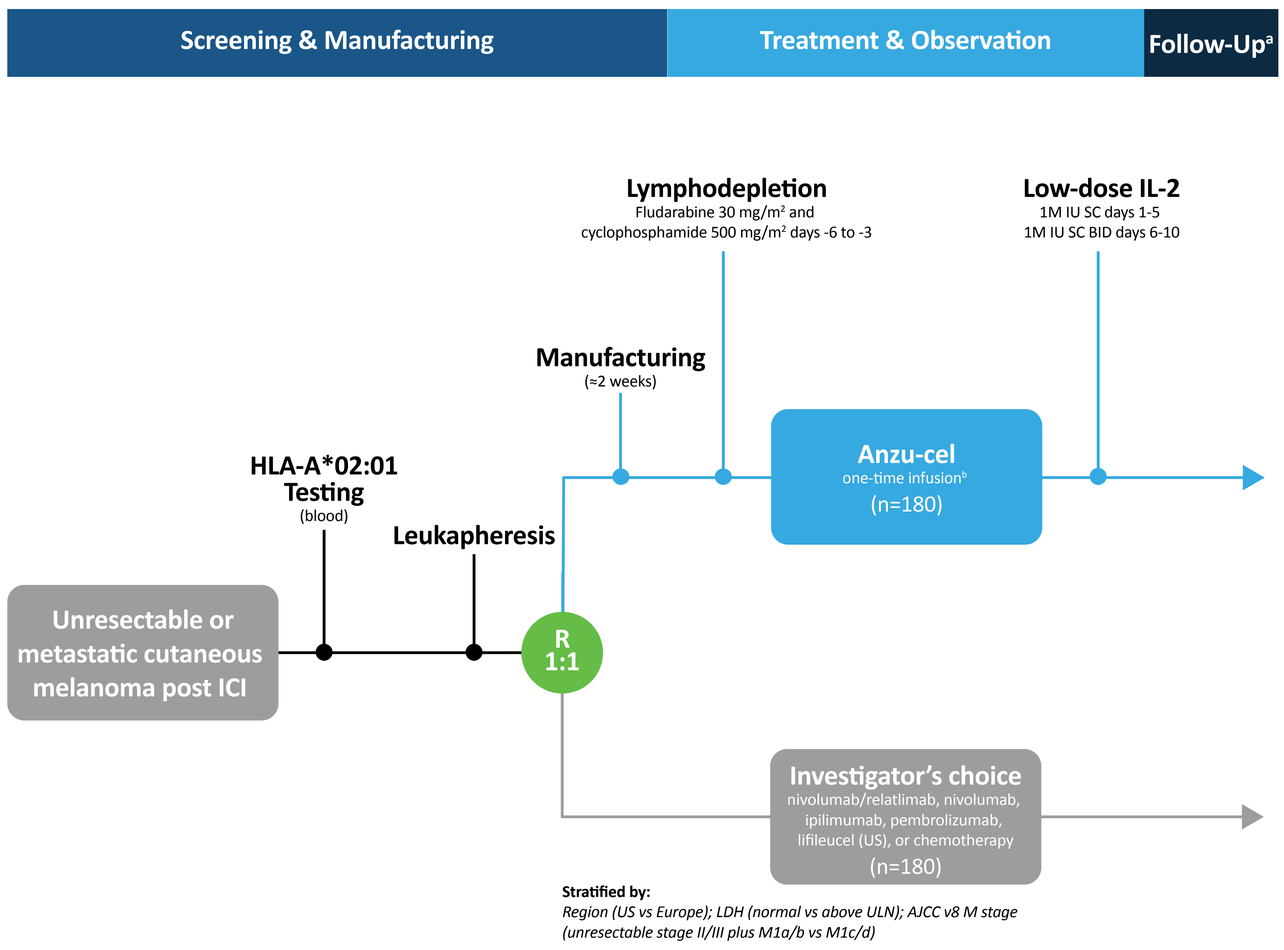
- SUPRAME (NCT06743126) is a phase 3, multicenter, open-label, randomized, actively controlled trial that will evaluate the efficacy, safety, and tolerability of anzu-cel compared to investigator's choice in patients with previously treated unresectable or metastatic cutaneous melanoma, including acral melanoma (**Fig. 2**)

Primary Endpoint	Secondary Endpoints
• PFS	• OS, ORR, safety, QoL (EORTC QLQ-C30, EQ-5D-5L)

Eligibility Criteria

Key Inclusion Criteria	Key Exclusion Criteria
• Cutaneous melanoma (including acral) with unresectable or metastatic disease • Aged ≥18 years • HLA-A*02:01 positive • Measurable disease (RECIST v1.1) • ECOG PS 0 or 1 • Disease progression on or after ≥1 PD-1 inhibitor as monotherapy or in combination • Patients with *BRAF* mutation previously treated with 1 prior line of BRAF-directed therapy (± MEK inhibitor) per investigator discretion	• Primary mucosal melanoma, uveal melanoma, and melanoma of unknown primary • Active brain metastases or leptomeningeal disease • LDH >2.0 × ULN

Figure 2. SUPRAME Trial Design (NCT06743126)



[a]Follow-up visits occur every 12 weeks for all patients until withdrawal of consent, loss to follow-up, death, or end of treatment, whichever occurs first.
[b]Cell dose: 1.0 to 10.0 × 10^9 TCR T-cells.

ABBREVIATIONS: AJCC, American Joint Committee on Cancer; BID, twice daily; CRS, cytokine release syndrome; ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; EQ-5D-5L, EuroQol 5-Dimension 5-Level; HLA, human leukocyte antigen; ICANS, immune effector cell-associated neurotoxicity syndrome; ICI, immune checkpoint inhibitor; IL-2, interleukin-2; LD, lymphodepletion; LDH, lactate dehydrogenase; mDOR, median duration of response; mOS, median overall survival; mPFS, median progression-free survival; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PFS, progression-free survival; PRAME, preferentially expressed antigen in melanoma; QoL, quality of life; R, randomized; RECIST, Response Evaluation Criteria in Solid Tumors; SC, subcutaneous; TEAE, treatment-emergent adverse event; ULN, upper limit of normal.

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Please contact medinfo@immatics.com for additional information

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