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Primary Analysis of the Pivotal IGNYTE-ESO Trial of Lete-cel in Patients With Synovial Sarcoma or Myxoid/Round Cell Liposarcoma

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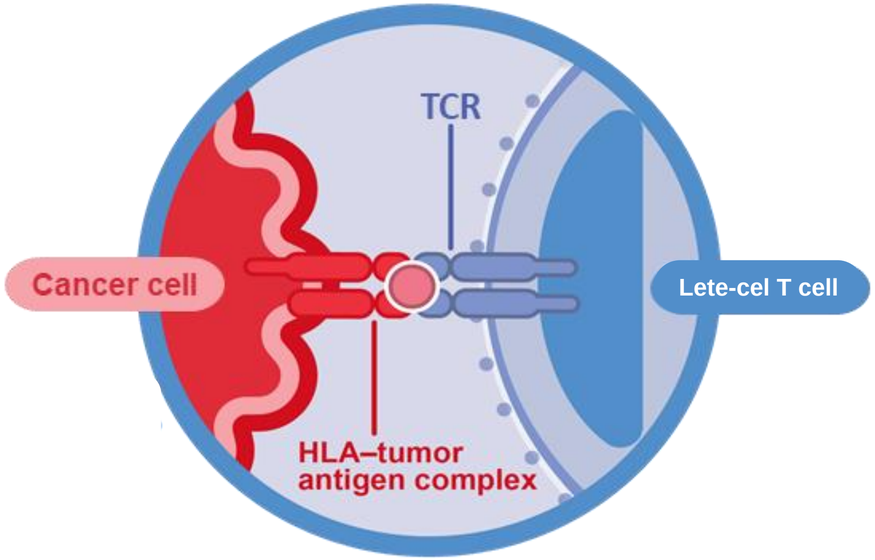
2024 ANNUAL MEETING

November 13-16 • San Diego, CA

Letetresgene Autoleucel: Promising Efficacy in Earlier Studies

- Lete-cel: Autologous CD4+ and CD8+ T cells genetically modified to express a TCR recognizing the NY-ESO-1 peptide presented by HLA-A*02:01, A*02:05, or A*02:06
- Lete-cel has >12-fold greater binding to an NY-ESO-1:HLA complex than naturally occurring TCRs
- Lete-cel was infused following lymphodepletion into patients with advanced/metastatic SyS or MRCLS expressing NY-ESO-1:



Pilot trial in patients with SyS[1]: 20–50% ORRs across cohorts

Pilot trial in patients with MRCLS[2]: 20–40% ORR across cohorts

Substudy 1 of IGNYTE-ESO Phase 2 trial in patients with treatment-naïve SyS[3]: 80% ORR

Substudy 2 planned interim analysis of IGNYTE-ESO Phase 2 trial in patients with previously treated SyS or MRCLS[4]: 40% ORR = primary endpoint success criterion met

1. D'Angelo SP, et al. *J Immunother Cancer.* 2020;8(suppl 3):A182. 2. D'Angelo SP, et al. *J Clin Oncol*. 2022;40(16 suppl):Abs 11500. 3. Burgess M, et al. Abstract ID: 1548396 presented at: CTOS 2023; Dublin, Ireland.
4. D'Angelo SP, et al. *J Clin Oncol*. 2024;42(16 suppl):Abs 2500.

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HLA, human leukocyte antigen; lete-cel, letetresgene autoleucel; MRCLS, myxoid/round cell liposarcoma; NY-ESO-1, New York esophageal squamous cell carcinoma 1; ORR, overall response rate; SyS, synovial sarcoma; TCR, T-cell receptor.

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IGNYTE-ESO Substudy 2 Study Design

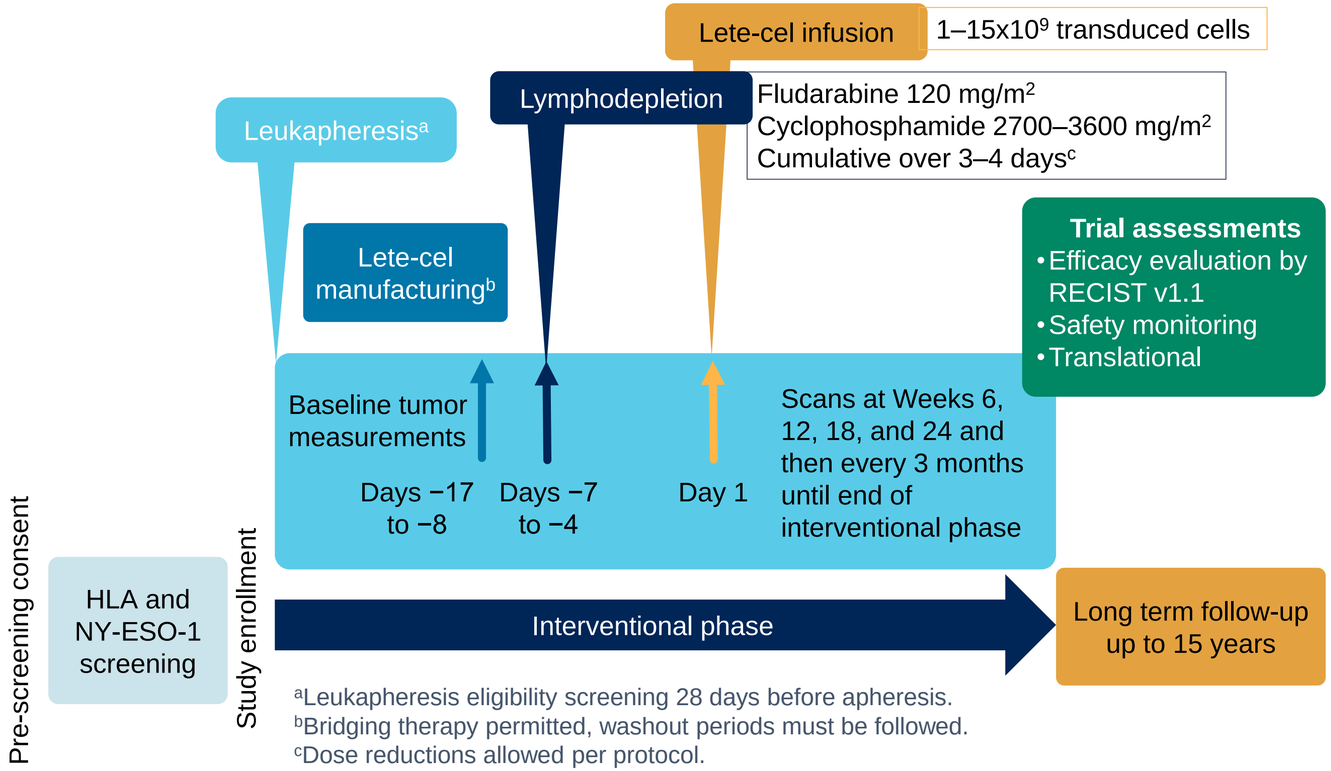
Eligibility

- HLA-A*02:01, *02:05, or *02:06 positive
- Aged ≥10 years
- NY-ESO-1–expressing (≥30% staining at 2+/3+ per IHC) metastatic or unresectable SyS or MRCLS
- ECOG PS 0–1
- Must have started/received anthracycline-based chemotherapy before apheresis
- Must have progression on their last prior line of therapy (bridging therapy excluded) and measurable disease per RECIST v1.1 before lymphodepletion

Endpoints

- Primary: ORR per RECIST v1.1 by central independent review
- Secondary include: Safety (AEs, serious AEs, AEs of special interest), ORR by investigators, time to response, duration of response, disease control rate, PFS, OS

Ongoing, international, open-label Phase 2 trial (NCT03967223)



[a]Leukapheresis eligibility screening 28 days before apheresis.
[b]Bridging therapy permitted, washout periods must be followed.
[c]Dose reductions allowed per protocol.

AE, adverse event; ECOG PS, Eastern Cooperative Oncology Group performance status; HLA, human leukocyte antigen; IHC, immunohistochemistry; lete-cel, letetresgene autoleucel; MRCLS, myxoid/round cell liposarcoma; NY-ESO-1, New York esophageal squamous cell carcinoma 1; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; SyS, synovial sarcoma.

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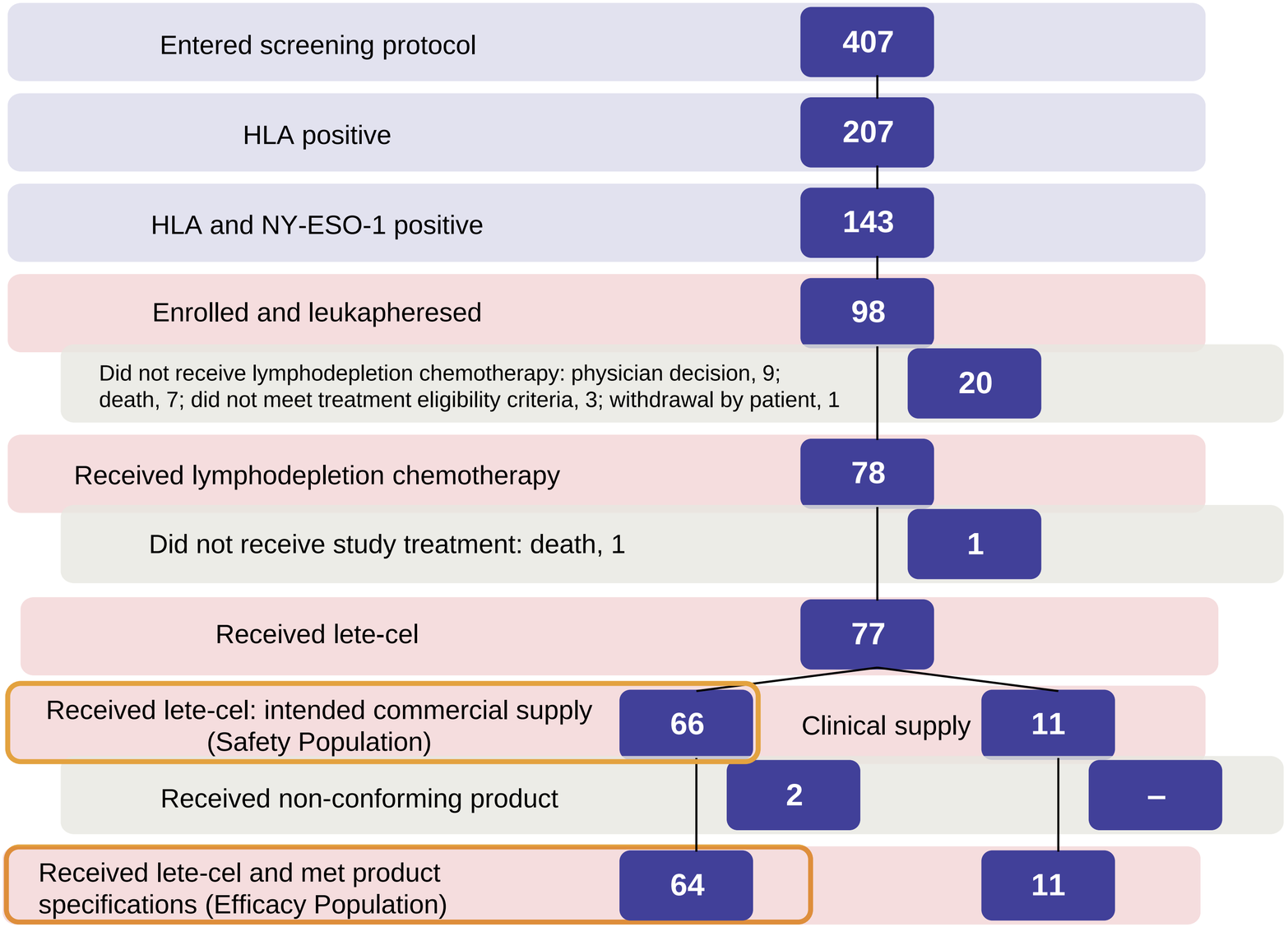
Participants

Cut-off date: March 1, 2024

- Efficacy population: 64 patients treated with lete-cel conforming product (commercial supply)
- Safety population: 66 patients treated with lete-cel (commercial supply)
- 65% of HLA-eligible SyS patients[a] were NY-ESO-1 eligible, 100% of HLA-eligible MRCLS patients were NY-ESO-1 eligible

Commercial supply = lete-cel generated using the intended commercial vector supply and cell manufacturing processes



[a]With NY-ESO-1 data available

HLA, human leukocyte antigen; lete-cel, letetresgene autoleucel; mITT, modified intention-to-treat; NY-ESO-1, New York esophageal squamous cell carcinoma 1.

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Baseline Characteristics (Efficacy Population)

Characteristic	N=64
SyS, n (%)	34 (53)
MRCLS, n (%)	30 (47)
Male, n (%)	36 (56)
Female, n (%)	28 (44)
Race, n (%)	
White	62 (97)
American Indian or Alaska Native	1 (2)
Asian	1 (2)
Age, years, median (min, max)	46 (18, 70)
Extent of disease at screening, n (%)	
Local unresectable	1 (2)
Metastatic	63 (98)
Transduced cell dose x10^9, median (min, max)	6.7 (1.1, 11.4)

Characteristic	N=64
Systemic therapy regimens for advanced/metastatic disease prior to leukapheresis, n (%)	
0	7 (11)
1	19 (30)
2	26 (41)
≥3	12 (19)
Received chemotherapies prior to lymphodepletion, n (%)	
Anthracycline (ie, doxorubicin, epirubicin)	64 (100)
Ifosfamide	49 (77)
Anti-cancer therapy between leukapheresis and lymphodepletion, n (%)	
No	32 (50)
Yes	32 (50)
Radiotherapy between leukapheresis and lymphodepletion, n (%)	5 (8)

Cut-off date: March 1, 2024.
max, maximum; min, minimum; MRCLS, myxoid/round cell liposarcoma; SyS, synovial sarcoma.

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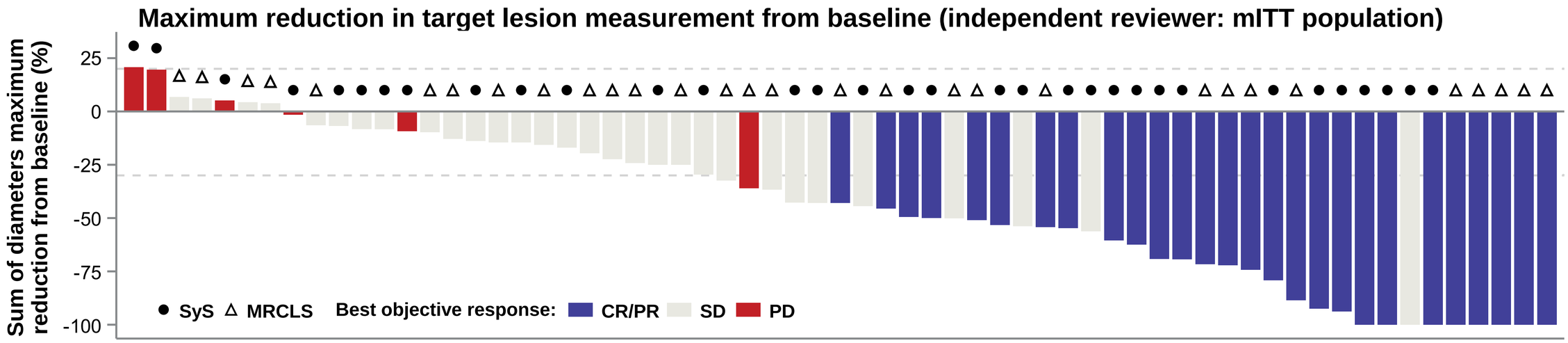
ORR at Primary Analysis: 42%



Best overall response, n (%)	Overall (N=64)	SyS (n=34)	MRCLS (n=30)
CR	6 (9)	3 (9)	3 (10)
PR	21 (33)	11 (32)	10 (33)
SD	30 (47)	14 (41)	16 (53)
PD	6 (9)	5 (15)	1 (3)
NE	1 (2)	1 (3)	0
ORR [95% CI]	27 (42) [29.9–55.2]	14 (41) [24.6–59.3]	13 (43) [25.5–62.6]

Patient(s) who had a best objective response of NE are not shown in the figure. Data displayed are restricted to patients receiving lete-cel intended commercial supply. Independent reviewer–assessed overall response rate and best response with confirmation (RECIST 1.1 criteria).

Cut-off date: March 1, 2024.

CI, confidence interval; CR, complete response; lete-cel, letetresgene autoleucel; mITT, modified intention-to-treat; MRCLS, myxoid/round cell liposarcoma; NE, not evaluable; ORR, overall response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SyS, synovial sarcoma.

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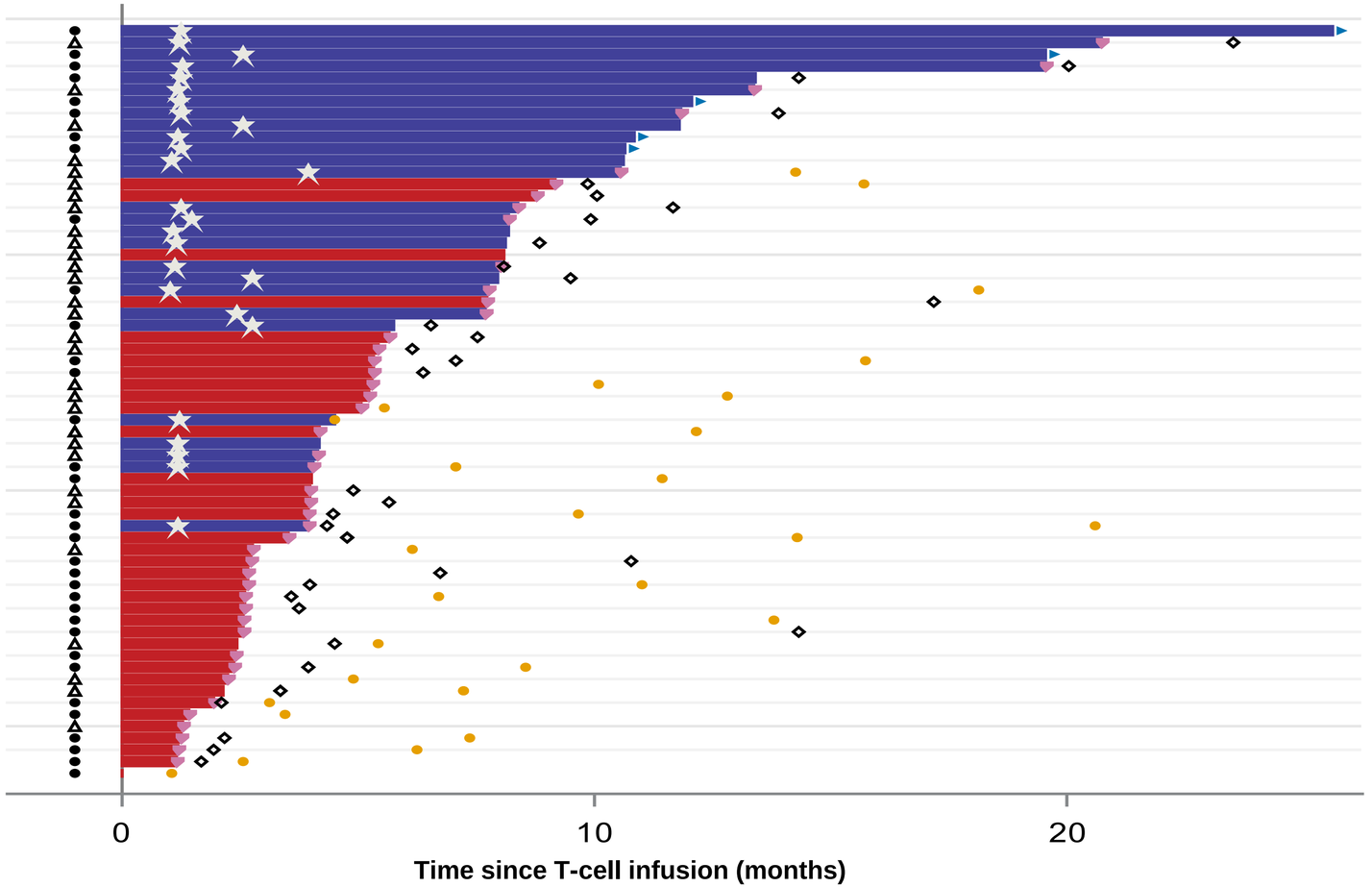
Responses Were Durable

Duration of follow-up for RECIST 1.1 assessment (independent reviewer: mITT population)



	Overall (N=64)	SyS (n=34)	MRCLS (n=30)
Duration of response, months, median (95% CI)	12.2 (6.8, 19.5)	18.3 (3.3, –)	12.2 (5.3, –)
Progression-free survival, months, median (95% CI)	5.3 (4.0, 8.0)	3.9 (2.6, 7.8)	7.7 (5.2, 9.2)

Data cut-off: March 1, 2024. Data displayed are restricted to patients receiving lete-cel intended commercial supply. Independent reviewer–assessed overall response rate and best response with confirmation (RECIST 1.1 criteria). Due to the small sample size and the pattern of censored patients who are ongoing in follow-up, median duration of response in SyS should be interpreted with caution.

CI, confidence interval; lete-cel, letetresgene autoleucel; mITT, modified intention-to-treat; MRCLS, myxoid/round cell liposarcoma; RECIST, Response Evaluation Criteria in Solid Tumors; SyS, synovial sarcoma.

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Treatment-Emergent Lymphodepletion-Related AEs

- There was one Grade 5 treatment-emergent lymphodepletion-related AE of pulmonary alveolar hemorrhage in the setting of pancytopenia, and a platelet count of 0 despite HLA-matched platelets and platelet-stimulating agents

Lymphodepletion-related AEs in >15% of patients, N=66

Adverse event, n (%)	Any grade	Grade ≥3
Any event	65 (98)	59 (89)
Neutropenia	48 (73)	48 (73)
Thrombocytopenia	42 (64)	32 (48)
Anemia	41 (62)	29 (44)
Leukopenia	32 (48)	31 (47)
Febrile neutropenia	19 (29)	18 (27)
Fatigue	14 (21)	0
Alopecia	13 (20)	0
Diarrhea	13 (20)	0
Decreased appetite	12 (18)	2 (3)
Nausea	12 (18)	0
Aspartate aminotransferase increased	11 (17)	6 (9)
Hypophosphatemia	11 (17)	2 (3)

AE, adverse event; HLA, human leukocyte antigen; lete-cel, letetresgene autoleucel.

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Special Interest and Treatment-Emergent T Cell–Related AEs

Cytokine release syndrome (CRS)[a]

- Median time of onset: 2 days (range 1 to 9)
- Median duration: 7 days (range 2 to 51)
- Among the patients with CRS, 79% required tocilizumab, 27% corticosteroids, and 6% anakinra

Rash (and associated terms)[a]

- “Rash maculopapular” was most common rash AE reported
- Median time of onset: 7 days (range: 2–332)
- Median duration: 22 days (range: 1–498)

Neurological

- ICANS occurred in four (6%) patients, all Grade 1

Grade 5 related AE

- There was one T cell-related AE of cardiac arrest, attributed primary pulmonary etiology

T cell–related AEs in ≥15% of patients, N=66

Adverse event, n (%)	Any grade	Grade ≥3
Any event	64 (97)	56 (85)
Cytokine release syndrome	61 (92)	8 (12)
Rash (and associated terms)	42 (64)	23 (35)
Neutropenia	30 (45)	28 (42)
Anemia	26 (39)	22 (33)
Thrombocytopenia	23 (35)	20 (30)
Alanine aminotransferase increased	21 (32)	11 (17)
Pyrexia	20 (30)	2 (3)
Aspartate aminotransferase increased	19 (29)	6 (9)
Diarrhea	16 (24)	0
Leukopenia	16 (24)	15 (23)
Nausea	16 (24)	0
Hypophosphatemia	13 (20)	0
Febrile neutropenia	12 (18)	11 (17)
Pruritus	12 (18)	0
Dyspnea	11 (17)	3 (5)
Headache	10 (15)	0

[a]CRS and rash attributes 1st occurrence and regardless of attribution Rash includes rash maculopapular, rash, erythema rash pruritic, dermatitis exfoliative, erythema multiforme, rash papular, skin mass, GVHD – skin.

AE, adverse event; ICANS, immune effector cell–associated neurotoxicity.

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Conclusions

- IGNYTE-ESO substudy 2 met the primary endpoint for efficacy
- At this primary analysis, lete-cel demonstrated 42% ORR (41% for SyS and 43% for MRCLS) by independent review
  - The median duration of response was 12.2 months overall, 18.3 months in SyS, and 12.2 months in MRCLS
  - The median PFS was 5.3 months overall, 3.9 months in SyS, and 7.7 months in MRCLS
- All patients experienced treatment-emergent AEs:
  - Cytopenias, CRS and rash were common and manageable
- These results support the advancement of lete-cel as a novel therapy for patients with unresectable or metastatic SyS and MRCLS; Biologics License Application to the FDA planned
- Further analyses of translational correlates are pending

AE, adverse event; CRS, cytokine release syndrome; FDA, US Food and Drug Administration; ICANS, immune effector cell–associated neurotoxicity; lete-cel, letetresgene autoleucel; MRCLS, myxoid/round cell liposarcoma; ORR, overall response rate; SyS, synovial sarcoma.

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Acknowledgments

- The authors would like to thank all the patients who took part in the trial, and all the additional investigators and their teams:
  - Farrukh Awan
  - Elizabeth Loggers
  - Antonio López Pousa
  - Michael Wagner
  - Jean-Yves Blay
  - John Charlson
  - Juan Jesus Martin Liberal
  - Steven Robinson

Disclosures

- Dr. Sandra D'Angelo reports consultancy fees and/or advisory board roles from Adaptimmune, EMD Serono, Amgen, Nektar, Immune Design, GlaxoSmithKline, Incyte, Merck, Immunocore, Pfizer, Servier, Rain Therapeutics, GI Innovations, and Aadi Biosciences.
- This study was funded by GlaxoSmithKline and is now funded by Adaptimmune
- Writing and editorial support was from Christine Ingleby, DPhil, CMPP, Envision Pharma Inc. (Glasgow, UK), funded by Adaptimmune