



Administration of Letetresgene Autoleucel (Lete-cel)

ICD-10 Coordination & Maintenance Committee Update
Spring 2025



Disclaimer

This presentation contains “forward-looking statements,” as that term is defined under the Private Securities Litigation Reform Act of 1995 (PSLRA), which statements may be identified by words such as “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect” and other words of similar meaning. These forward-looking statements involve certain risks and uncertainties. Such risks and uncertainties could cause our actual results to differ materially from those indicated by such forward-looking statements, and include, without limitation: the success, cost and timing of our product development activities and clinical trials; our ability to submit an IND and successfully advance our technology platform to improve the safety and effectiveness of our existing TCR therapeutic candidates; the rate and degree of market acceptance of T-cell therapy generally and of our TCR therapeutic candidates; government regulation and approval, including, but not limited to, the expected regulatory approval timelines for TCR therapeutic candidates; and our ability to protect our proprietary technology and enforce our intellectual property rights; amongst others. For a further description of the risks and uncertainties that could cause our actual results to differ materially from those expressed in these forward-looking statements, as well as risks relating to our business in general, we refer you to our Annual Report on Form 10-K filed with the Securities and Exchange Commission filed for the year ended December 31, 2022, our Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the Securities and Exchange Commission. The forward-looking statements contained in this presentation speak only as of the date the statements were made and we do not undertake any obligation to update such forward- looking statements to reflect subsequent events or circumstances.

We urge you to consider these factors carefully in evaluating the forward-looking statements herein and you are cautioned not to place undue reliance on such forward-looking statements, which are qualified in their entirety by this cautionary statement. The forward-looking statements contained in this presentation speak only as of the date the statements were made and we do not undertake any obligation to update such forward-looking statements to reflect subsequent events or circumstances.

We intend that all forward-looking statements be subject to the safe-harbor provisions of the PSLRA.

Letetresgene Autoleucel (Lete-cel): A Personalized T-Cell Therapy With Improved Recognition of Cancer Cells

- Lete-cel is an 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
- BLA submission for the treatment of advanced or metastatic synovial sarcoma (SyS) and myxoid round cell liposarcoma (MRCLS) is anticipated in 2025
 - Granted Breakthrough Designation for Synovial Sarcoma (February 2016) and MRCLS (January 2025)
 - US Orphan Drug Designation for Soft Tissue Sarcoma (March 2016)
- Adaptimmune intends to submit a New Technology Add-on Payment (NTAP) application for FY 2027

Unmet Medical Need for SyS and MRCLS Patients With Limited Treatment Options and Poor Prognoses

SyS and MRCLS Overview

- SyS and MRCLS represents **5-10% of all soft tissue sarcomas**, with ~1000 cases per year in each (~2,000 total) in the United States¹
- Both are characterized by chromosomal translocations, with **median age at presentation in the 40's**²
- **30–50% of patients will develop metastases**^{3,4}
- Despite initial sensitivity to chemotherapy, these aggressive tumours tend to have **very poor outcomes once they metastasize**

Limited Treatment options

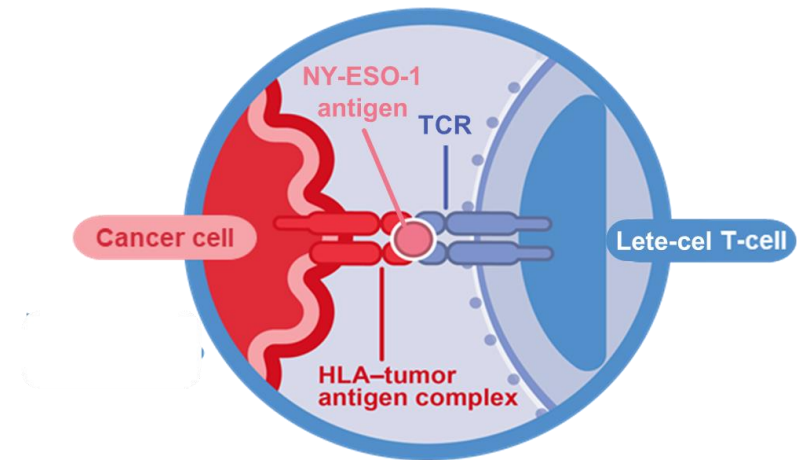
	SyS	MRCLS
Overall response to second-line therapy and beyond ²	4.2% - 14.7%	10.0% - 18.2%
Retrospective real-world median OS from start of second line ⁵	16 months	26 months
Retrospective real-world median PFS from start of second line ⁵	3.9 months	3.5 months

MRCLS, myxoid round cell liposarcoma; OS, overall survival; PFS, progression free survival; SyS, synovial sarcoma

1. De Vita A, et al. *Onco Targets Ther.* 2016;9:6233–46. 2. D'Angelo SP, et al. *Lancet.* 2024;403:1460–71. 3. Hoffman A, et al. *Cancer.* 2013;119:1868–77. 4. Pokras S, et al. *Future Oncol.* 2022;18:3637–50. 5. Pollack SM, et al. *Cancer Med.* 2020;9:4593–4602.

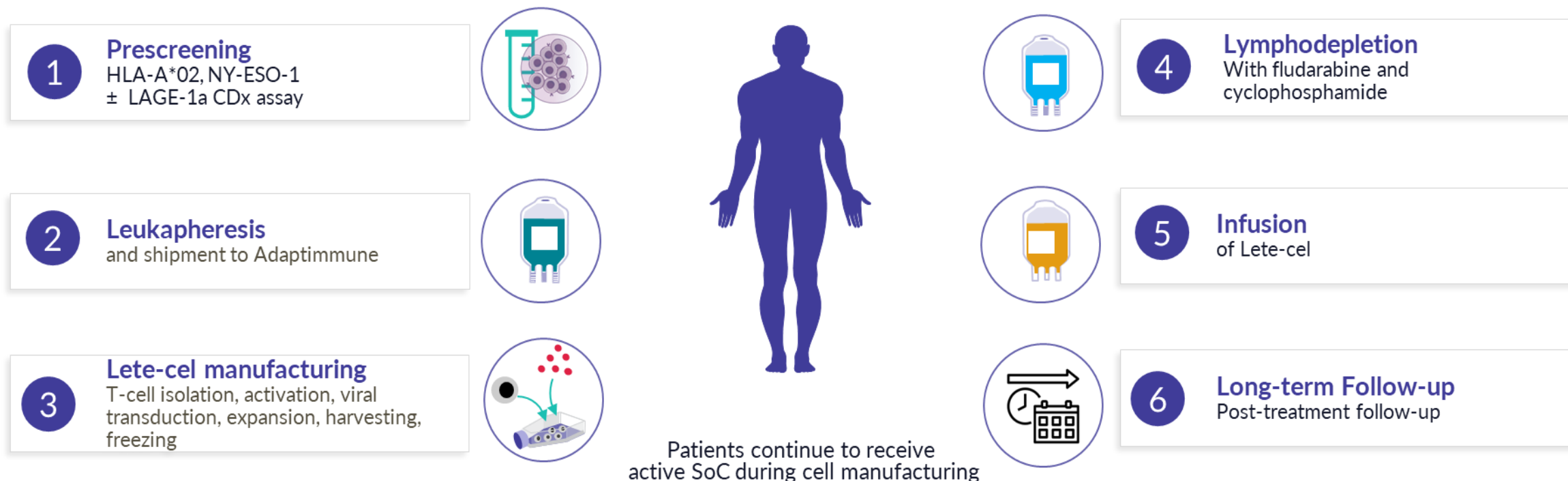
Letetresgene Autoleucel (Lete-cel) Product Overview

- Lete-cel is anticipated to be indicated for the treatment of advanced or metastatic synovial sarcoma (SyS) and myxoid round cell liposarcoma (MRCLS)
- Lete-cel is an 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 is comprised of T-cells that express affinity-enhanced TCRs that recognize a specific HLA-A*02 restricted NY-ESO-1 peptide
 - By recognizing the cancer cell's HLA-peptide complex, lete-cel can target SyS and MRCLS cancer cells expressing NY-ESO-1/HLA-A*02 and eliminate them



Lete-cel: Patient Care Pathway

Patient T cells are isolated and transduced with a lentivirus to express a genetically modified TCR with improved recognition of **NY-ESO-1**



Average prescreening assay: 14 days¹

Lete-cel enriching, activating, transducing, expanding, harvesting and release testing: 28 to 35 days²

Follow-up: up to 15 years

HLA, human leukocyte antigen; LAGE-1a, L antigen family member 1 isoform a; NY-ESO-1, New York esophageal squamous cell carcinoma 1; SoC, standard of care; TCR, T-cell receptor.
1. D'Angelo SP, et al. Poster presented at SITC 2019; Poster P453 (Image adapted). 2. D'Angelo SP, et al. Cancer Discov. 2018;8:944-957.

Lete-cel: Inpatient Administration

- **Inpatient Administration:**
 - Lete-cel may be administered in the inpatient setting (similar to CAR-T, TCR-T and TIL therapies)
 - Once admitted to the hospital, the patient receives a dose range of 1×10^9 to 15×10^9 total transduced T cells as a single intravenous infusion administered through a central or peripheral vein
- **Medical Record Documentation:**
 - Information regarding lete-cel and its associated administration procedure will be documented in the medical record and identifiable from multiple perspectives (e.g., Medication Administration Record [MAR], physician orders, pharmacy notes, treatment summary, progress notes, etc.)

Lete-cel: Pivotal IGNYTE-ESO Trial in patients with SyS and MRCLS Cell Liposarcoma

Eligibility

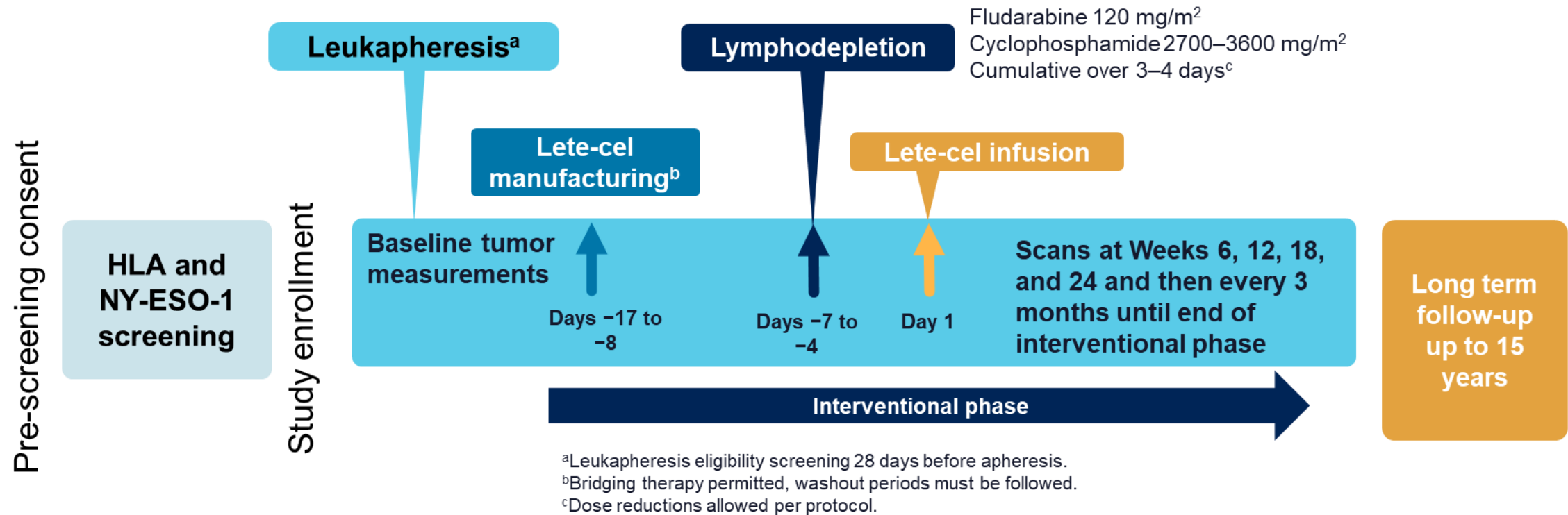
- HLA-A*02:01, *02:05, or *02:06 positive
- Aged ≥10 years
- NY-ESO-1–expressing (≥30% staining at 2+/3+ per IHC) metastatic or unresectable SyS or MRCLS
- ECOG PS 0–1
- Must have started/received anthracycline-based chemotherapy before apheresis
- Must have progression on their last prior line of therapy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

Endpoints

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

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.

🌀 Lete-cel: Pivotal IGNYTE-ESO Trial (NCT03967223) Design



Lete-cel: IGNYTE-ESO Baseline Characteristics

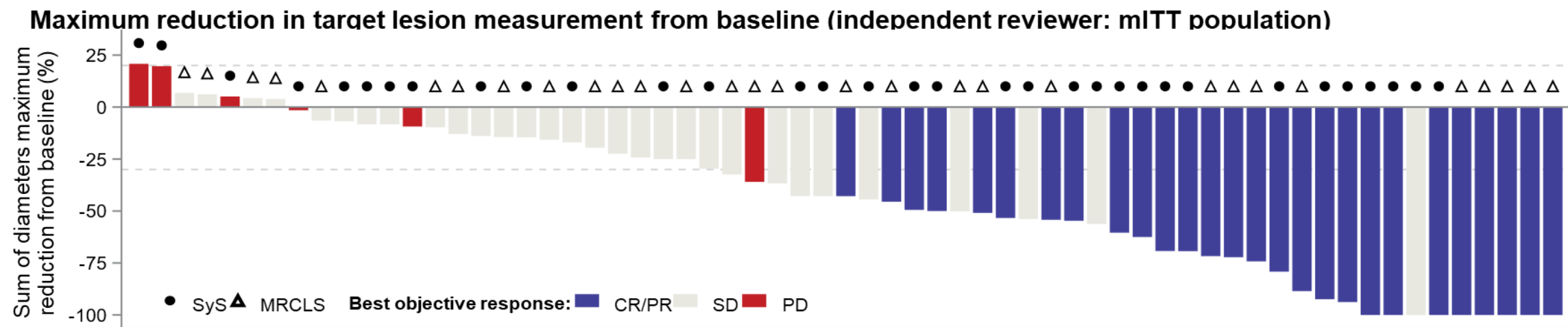
Characteristic	N=64
SyS, n (%)	34 (53)
MRCLS, n (%)	30 (47)
Male, n (%)	36 (56)
Female, n (%)	28 (44)
Race, n (%)	
White	62 (97)
American Indian or Alaska Native	1 (2)
Asian	1 (2)
Age, years, median (min, max)	46 (18, 70)
Extent of disease at screening, n (%)	
Local unresectable	1 (2)
Metastatic	63 (98)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

Lete-cel: Pivotal IGNYTE-ESO Primary Endpoint



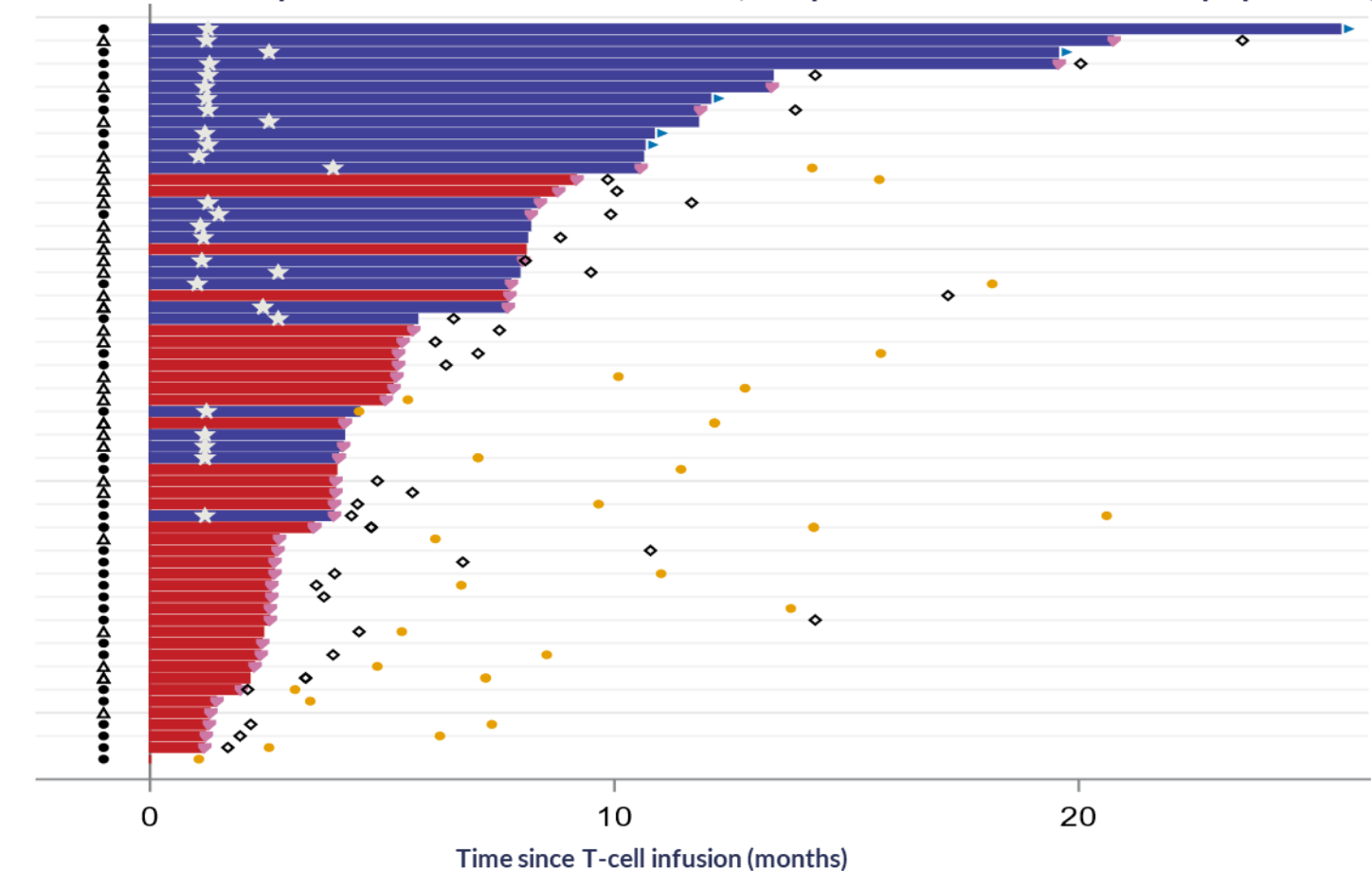
Best overall response, n (%)	Overall (N=64)	SyS (n=34)	MRCLS (n=30)
CR	6 (9)	3 (9)	3 (10)
PR	21 (33)	11 (32)	10 (33)
SD	30 (47)	14 (41)	16 (53)
PD	6 (9)	5 (15)	1 (3)
NE	1 (2)	1 (3)	0
ORR [95% CI]	27 (42) [29.9–55.2]	14 (41) [24.6–59.3]	13 (43) [25.5–62.6]

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.

Lete-cel: IGNYTE-ESO Demonstrated durable responses

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)

- Death
- ▴ Ongoing
- ▾ RECIST progression
- ★ First confirmed response
- ◆ Anti-cancer therapy
- SyS
- ▴ MRCLS
- Response
- Responder
- Non-responder

Data cut-off: March 1, 2024.

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.

Treatment-emergent lymphodepletion-related Adverse Events (AE)

- 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)

T-Cell Related Adverse Events and those of Special Interest

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

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

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

Summary

- Lete-cel is an 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 is anticipated to be a new treatment option indicated for the treatment of advanced or metastatic synovial sarcoma (Sys) and myxoid round cell liposarcoma (MRCLS)
 - There is an unmet medical need for SyS and MRCLS patients with limited treatment options and poor prognoses
- Lete-cel may be administered in the inpatient setting (similar to CAR-T, TCR-T and TIL therapies)