



GITMO *1000***miglia**

**IL TRAPIANTO E LE TERAPIE
CELLULARI: PRESENTE E FUTURO**

Istituto Oncologico Veneto IOV-IRCCS, Castelfranco Veneto

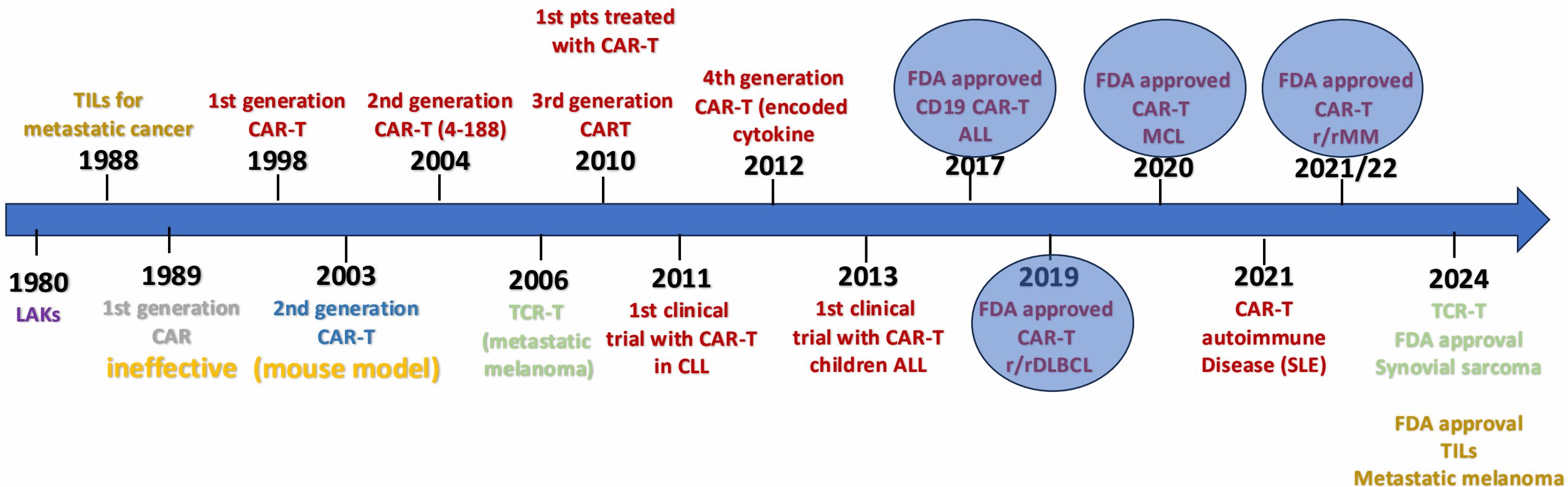
Sala Convegni dell'Ospedale S. Giacomo Apostolo

19 OTTOBRE 2026

Applicazioni presenti e future delle terapie cellulari

**Alessandra SPEROTTO
UOSD Terapie Cellulari
UOC Oncoematologia
IOV – IRCCS Castelfranco Veneto**

Cell therapy



CAR-T approvals and indications

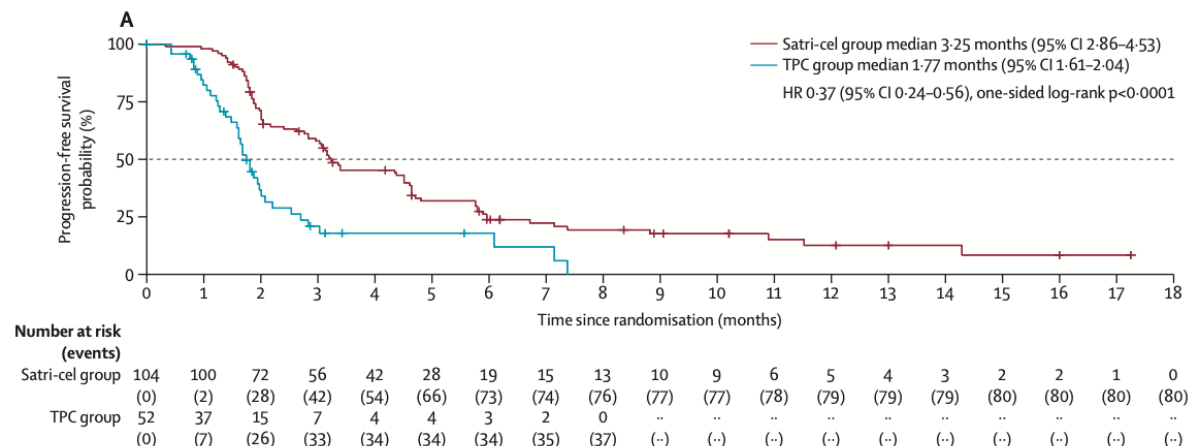
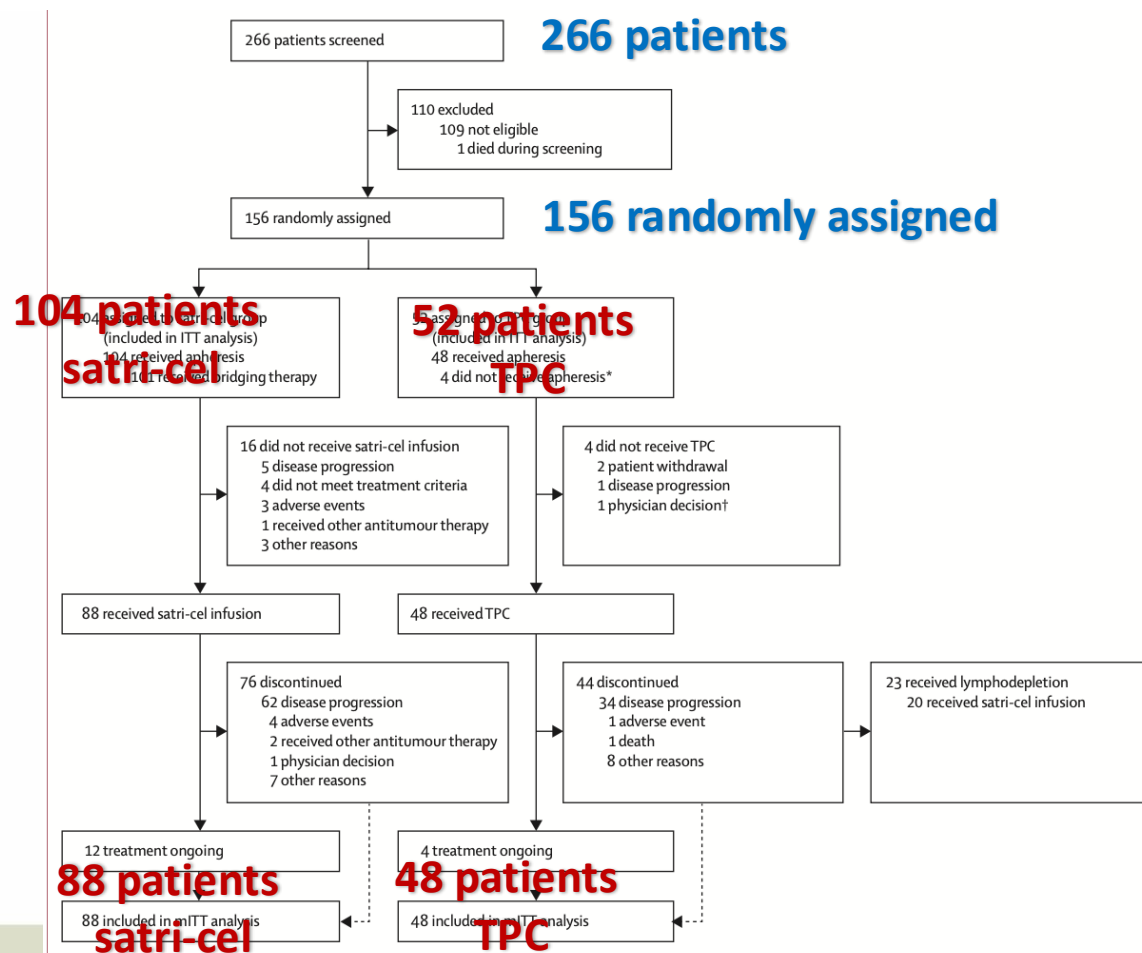
First approval / reimbursement dates, ordered by FDA approval. Indication overview as of 8 October 2026.

Product	FDA	EU (EMA/EC)	AIFA / SSN	Indications: FDA/EU summary, not SSN coverage
tisagenlecleucel	Aug 2017	Aug 2018	Aug 2019	B-ALL ≤25 years (refractory / specified relapses). Adult LBCL (FDA) / DLBCL (EU) and FL after ≥2 prior lines.
axicabtagene ciloleucel	Oct 2017	Aug 2018	Nov 2019	Adult LBCL, including DLBCL and PMBCL. FL: ≥2 prior lines (FDA), ≥3 (EU). Selected LBCL: 2nd-line use.
brexucabtagene autoleucel	Jul 2020	Dec 2020	Mar 2022	Adult MCL. EU: ≥2 prior lines, including a BTK inhibitor. B-ALL: adults (FDA), ≥26 years (EU).
lisocabtagene maraleucel	Feb 2021	Apr 2022	Feb 2024	Adult LBCL (selected 2nd-line use), FL and MCL. FDA also: CLL/SLL and MZL. Eligibility differs by indication.
idecabtagene vicleucel	Mar 2021	Aug 2021	Feb 2024	Adult MM after ≥2 prior lines, including an IMiD, a proteasome inhibitor and an anti-CD38 antibody (FDA/EU).
ciltacabtagene autoleucel	Feb 2022	May 2022	Apr 2026	Adult MM after ≥1 prior line including an IMiD and a proteasome inhibitor, lenalidomide-refractory (FDA/EU).
obecabtagene autoleucel	Nov 2024	Jul 2025	Not verified*	B-ALL: adults (FDA), ≥26 years (EU).

Claudin-18 isoform 2-specific CAR T-cell therapy (satri-cel) versus treatment of physician's choice for previously treated advanced gastric or gastro-oesophageal junction cancer (CT041-ST-01): a randomised, open-label, phase 2 trial

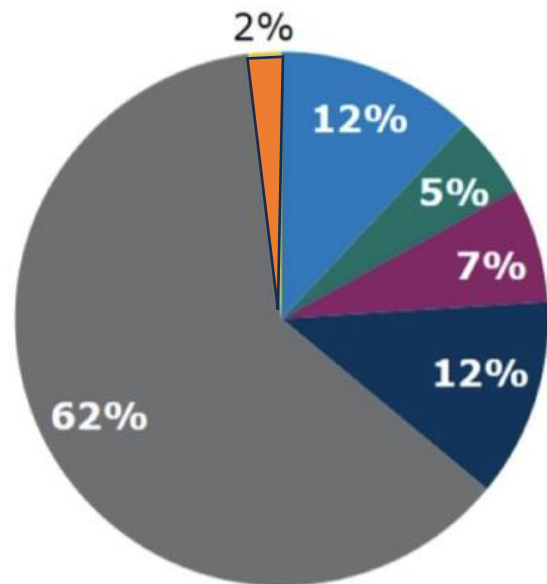
Approved by
National Medical
Products Administration

Lancet 2025; 405: 2049-60



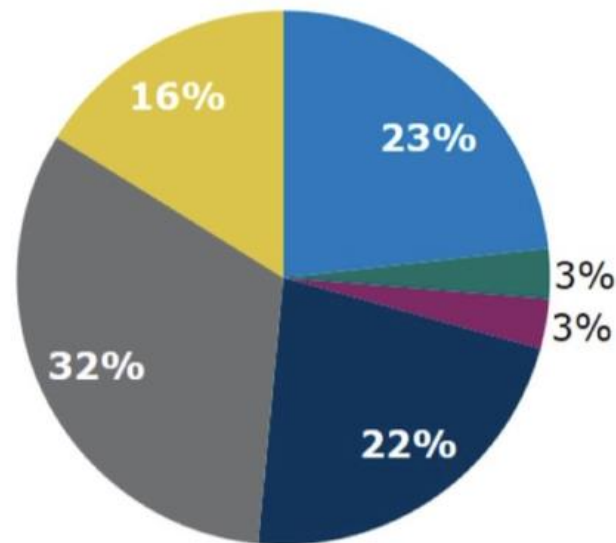
- Improvement in PFS
- Manageable safety profile
- Third line treatment (advanced gastric or gastro-oesophageal cancers)

Commercial CAR-T Cells Indications 2025



- Multiple Myeloma
- Follicular Lymphoma
- Mantle Cell Lymphoma
- Autoimmune disease

Non Commercial CAR-T Cells Indications 2025



- Acute Lymphoblastic Leukemia
- Large B Cell Lymphoma
- Other

Other= tumori solidi

Autologous CAR-T trials in solid tumors - 2026

CAR-T product	Clinical Trial	Targeted antigen	Disease	Cell source	Phase
MSLN-CAR-T	NCT05531708	MSLN	Mesothelin+ advanced refractory solid tumors	Autologous T cells	Phase I
MSLN-CAR-T	NCT05373147	MSLN	Mesothelin+ solid tumor	Autologous T cells	Early Phase I
MSLN-CAR-T	NCT04480852	MSLN	Non-small cell lung cancer Mesothelioma	Autologous T cells	Early Phase I
MSLN-CAR-T	NCT06141293	MSLN	MSLN+ positive solid tumor	RD133 autologous T cells	Early Phase I
MSLN-CAR-T	NCT06166070	MSLN	Solid tumor	RD133 autologous T cells	Early Phase I
MSLN-CAR-T secreting PD-1 nanobodies	NCT04480852	MSLN	Non-small cell lung cancer Mesothelioma	Autologous T cells	Early Phase I
PD-1 antibody expressing MSLN CAR-T cells	NCT03615313	MSLN	MSLN+ advanced recurrent/refractory solid tumor	Autologous T cells	Phase I Phase II
MSLN CAR-T	NCT02158716	MSLN	Metastatic pancreatic adenocarcinoma Epithelial ovarian cancer Mesothelioma	Autologous T cells	Phase I
aPD1-MSLN-CAR-T	NCT04503980	MSLN	Colorectal cancer Ovarian cancer	Autologous T cells	Early Phase I
CTLA-4/PD-1 antibodies expressing MSLN CAR-T	NCT03182693	MSLN	Advanced solid tumor	Autologous T cells	Phase I Phase II
PD-1 antibody expressing MSLN CAR-T	NCT03030001	MSLN	Advanced solid tumor	Autologous T cells	Phase I Phase II
MSLN CAR-T	NCT03545815	MSLN	MSLN+ multiple solid tumor	Autologous T cells	Phase I
GD2/PSMA bi-specific CAR-T	NCT06437315	GD2/PSMA	GD2 and PSMA+ tumors	Autologous T cells	Phase I Phase II

GD2 CAR-T

NCT02107953

GD2 CAR-T01

NCT03373097

GD2 CAR-T

NCT04196413

GD2 CAR-T

NCT00385930

CLDN18.2 CAR-T

NCT04467853

CLDN18.2 CAR-T

NCT06472857

CLDN18.2 CAR-T

NCT03374897

CLDN18.2 CAR-T

NCT04581473

CLDN18.2 CAR-T

NCT06195619

CLDN18.2 CAR-T

NCT06520732

CLDN18.2 CAR-T

NCT06472857

CLDN18 CAR-T

NCT04503278

CEA CAR-T

NCT06415474

CEA CAR-T

NCT05538195

CEA CAR-T

NCT04348643

CEA CAR-T

NCT05396330

CEA CAR-T

NCT02349724

CEA CAR-T

NCT02415496

CEA CAR-T

NCT02855636

ROR1 CAR-T

NCT06274451

Fase

Early Phase I

Phase I

Phase I-II

Totale

CEA CAR-T	NCT02349724	CEA	Colorectal cancer Breast cancer Pancreatic cancer Lung cancer Gastric cancer	Autologous T cells	Phase 1
CEA CAR-T	NCT02415496	CEA	Liver metastatic	Autologous T cells	Phase 1
CEA CAR-T	NCT02855636	CEA	Liver metastatic	Autologous T cells	Phase 1b
ROR1 CAR-T	NCT05274451	ROR1	Triple negative breast cancer Non-small cell lung cancer Metastatic non-small cell lung cancer Breast cancer Advanced lung cancer	LYL787 autologous T cells	Phase 1

Numero totale studi in corso

10

62

24

96

CEA CAR-T	NCT05538195		Gastric cancer Pancreatic cancer Rectal cancer Esophageal cancer		Phase 2
CEA CAR-T	NCT04348643	CEA	Colorectal cancer Gastric cancer Pancreatic cancer Liver cancer Breast cancer Lung cancer Solid tumor	Autologous T cells	Phase 1 Phase 2
CEA CAR-T	NCT05396330	CEA	Colorectal cancer Esophageal cancer Stomach cancer Pancreatic cancer Metastatic tumor Recurrent cancer	Autologous T cells	Phase 1
CEA CAR-T	NCT02349724	CEA	Colorectal cancer Breast cancer Pancreatic cancer Lung cancer Gastric cancer	Autologous T cells	Phase 1
CEA CAR-T	NCT02415496	CEA	Liver metastatic	Autologous T cells	Phase 1
CEA CAR-T	NCT02855636	CEA	Liver metastatic	Autologous T cells	Phase 1b
ROR1 CAR-T	NCT06274451	ROR1	Triple negative breast cancer Non-small cell lung cancer Metastatic non-small cell lung cancer Breast cancer	LYL787 autologous T cells	Phase 1

HER2 CAR-T	NCT03500991	HER2	HER2+ recurrent/refractory pediatric CNS tumor	Autologous T cells	Phase 1
EGFR-TGFB-R-KO CAR-T	NCT04976218	EGFR	EGFR+ solid tumor	Autologous T cells	Phase 1
Anti-CTLA-4/PD-1 expressing EGFR CAR-T	NCT03182816	EGFR	EGFR-positive advanced solid tumor	Autologous T cells	Phase 1 Phase 2
EGFR CAR-T	NCT01869166	EGFR	EGFR+ advanced solid tumors	Autologous T cells	Phase 1 Phase 2
EGFRvIII CART-T	NCT02209376	EGFRvIII	Residual/recurrent EGFRvIII + glioma	Autologous T cells	Phase 1
PD-1 antibody expressing EGFR CAR-T	NCT02873390	EGFR	EGFR+ advanced solid tumors	Autologous T cells	Phase 1 Phase 2
PD-1 antibody expressing EGFR CAR-T	NCT02862028	EGFR	EGFR+ advanced solid tumors	Autologous T cells	Phase 1 Phase 2
VEGFR1/PD-L1 CAR-T	NCT05477927	VEGFR1 and PD-L1	Malignant peritoneal effusion Malignant ascites Serous cavity metastases	Autologous T cells	Phase 1
EGFR/B7-H3 CART-T	NCT05341492	EGFR and B7-HE	Advanced lung cancer Advanced triple negative breast cancer	Autologous T cells	Early Phase 1
B7-H3 CAR-T	NCT05190185	B7-H3	Malignant melanoma Lung cancer Colorectal cancer	Autologous T cells	Phase 1
CD276 CAR-T	NCT04691713	CD276	Solid tumor	Autologous T cells	N/A
CTLA-4 and PD-1 antibodies expressing MUC1-CAR-T	NCT03179007	MUC1	MUC1+ advanced/recurrent/refractory solid tumors	Autologous T cells	Phase 1 Phase 2
PD-1 knockout MUC1 CAR-T	NCT03706326	MUC1	Advanced esophageal cancer	Autologous T cells	Phase 1 Phase 2

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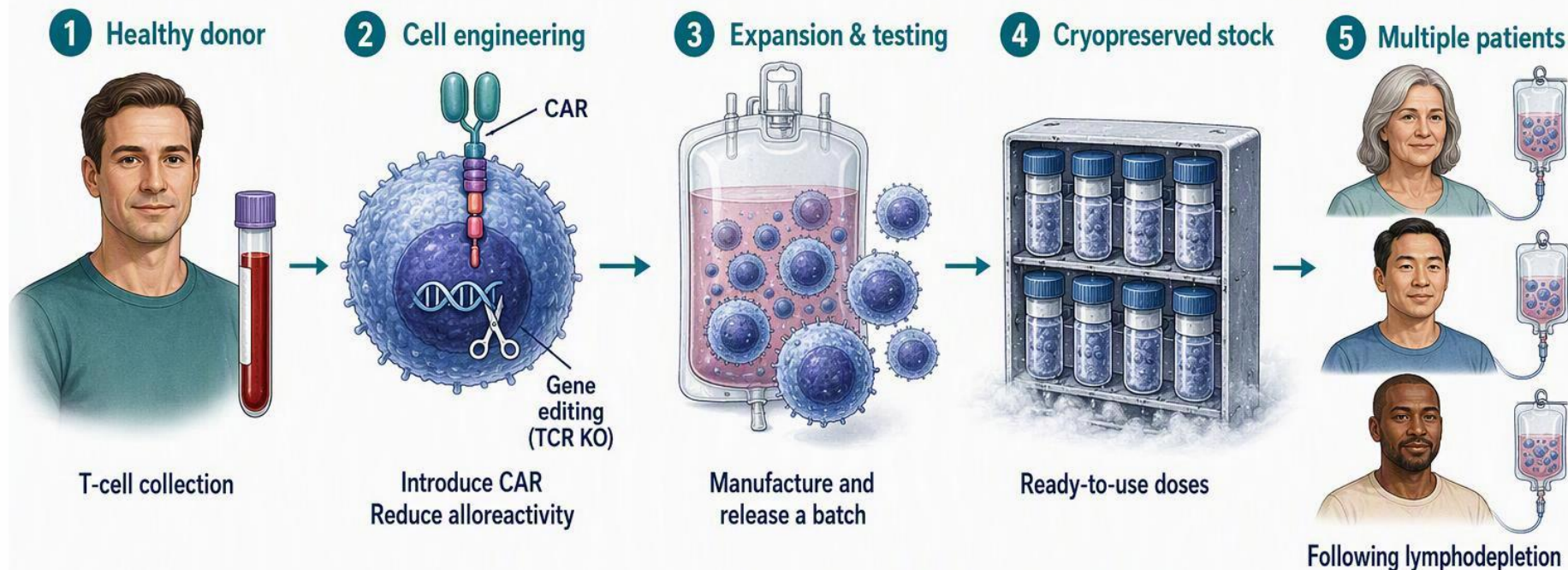
CAR-T therapies closer FDA approval

Orphan drugs

- MB-101: auto CAR-T (antigen IL13RA2) – glioblastoma.
- MB-109: auto CAR-T (antigen IL13RA2 + oncolytic virus) - glioblastoma.
- Multi-target CAR-T: (antigens EGFR – IL13RA2) – glioblastoma
- **MT027: allogeneic CAR-T («off the shelf»)** – antigen B7-H3 – glioblastoma:
FDA fast trak designation: GLIOMAX-101
Phase II study (intracranial administration)

Allogeneic CAR-T cells

The donor-derived off-the-shelf concept



Potential advantages

- Faster access
- Scalable batch production
- No patient-specific apheresis

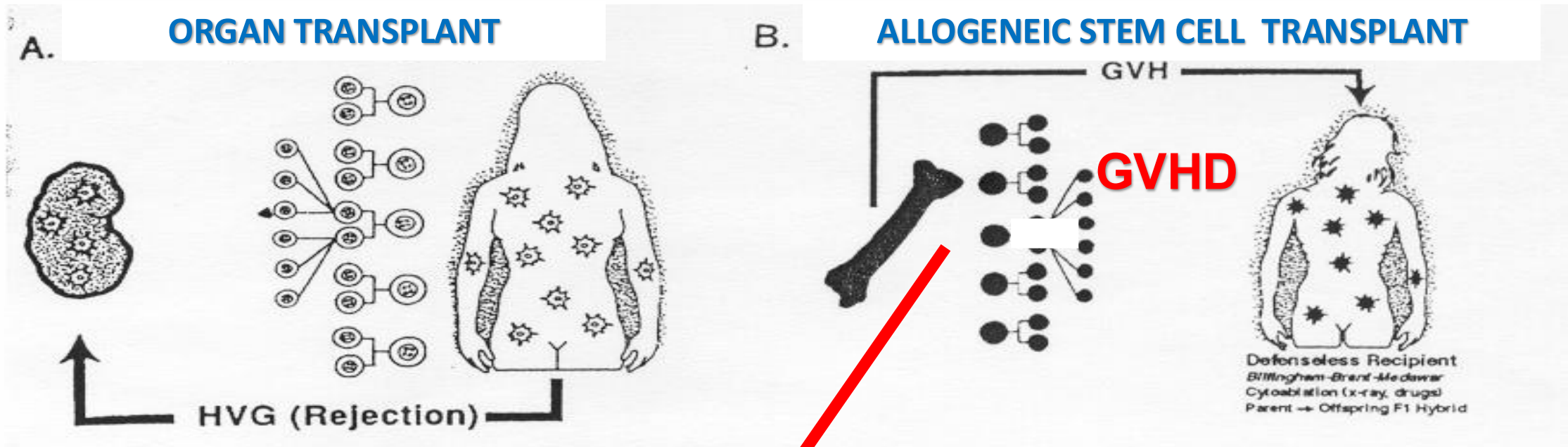
Key challenges

- Graft-versus-host disease
- Host immune rejection
- Limited persistence and treatment toxicity

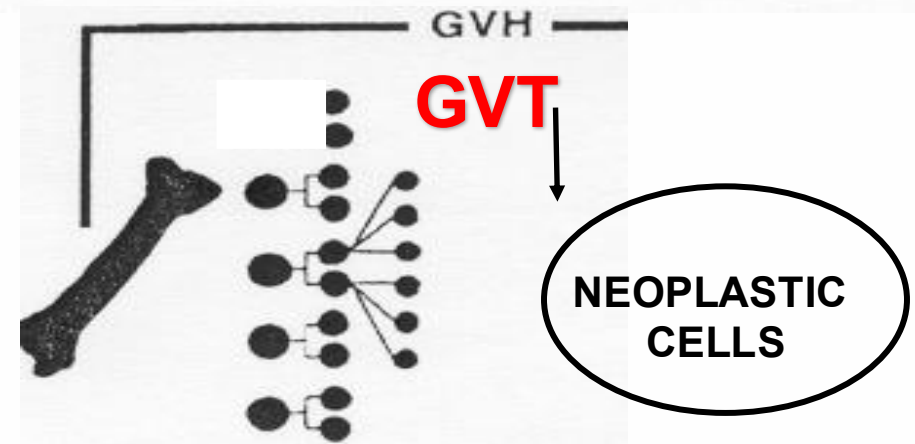
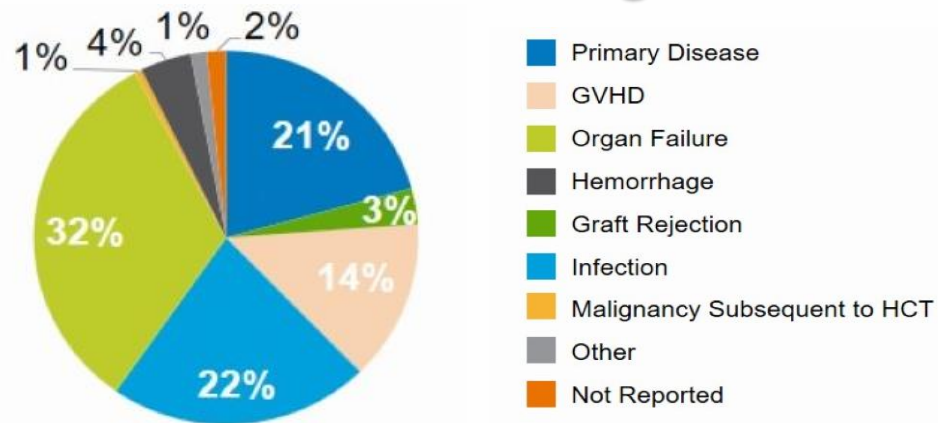
Engineering strategies vary by platform. TCR disruption is one approach to reduce graft-versus-host disease.

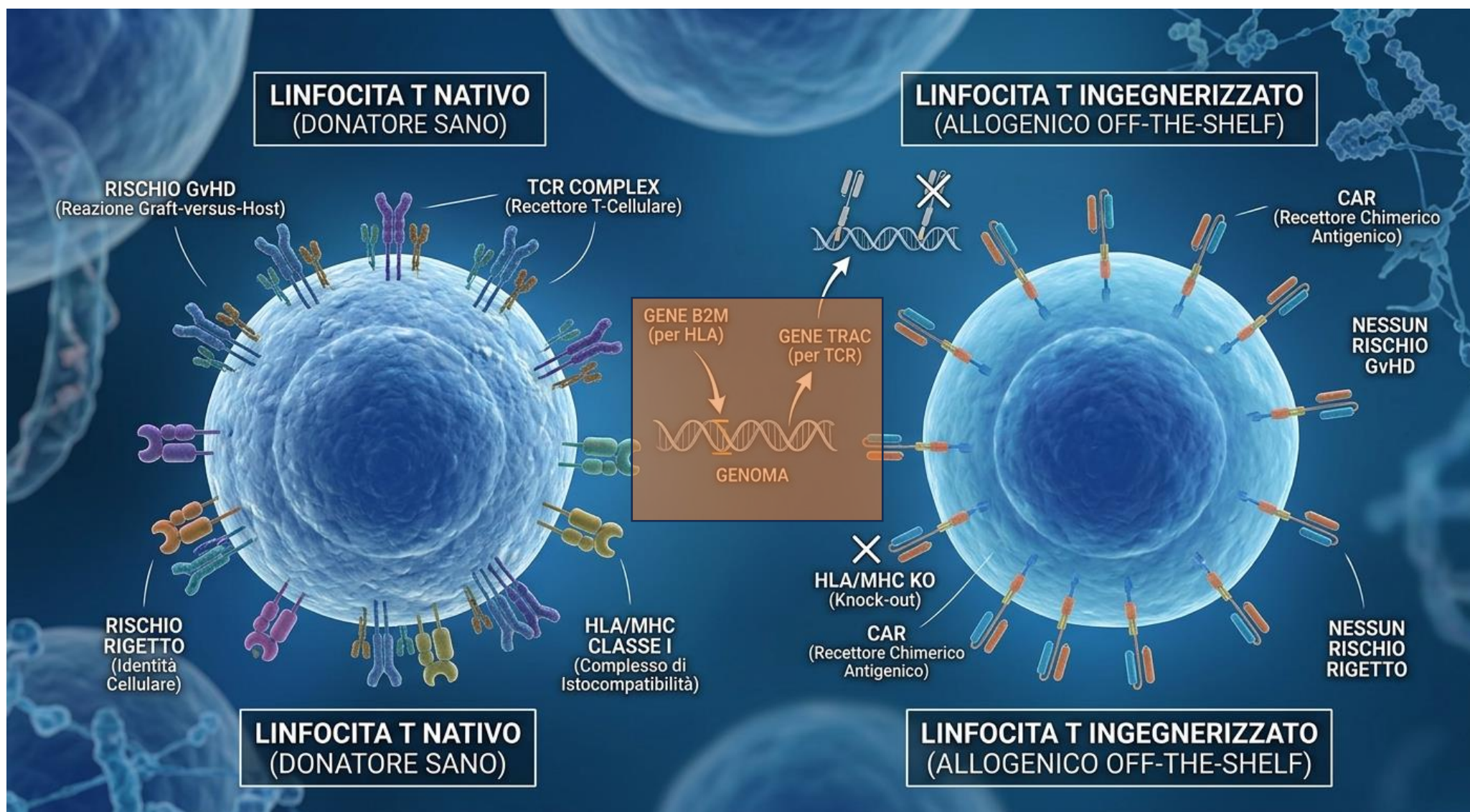
Conceptual donor T-cell platform. Compatibility and efficacy are not guaranteed.

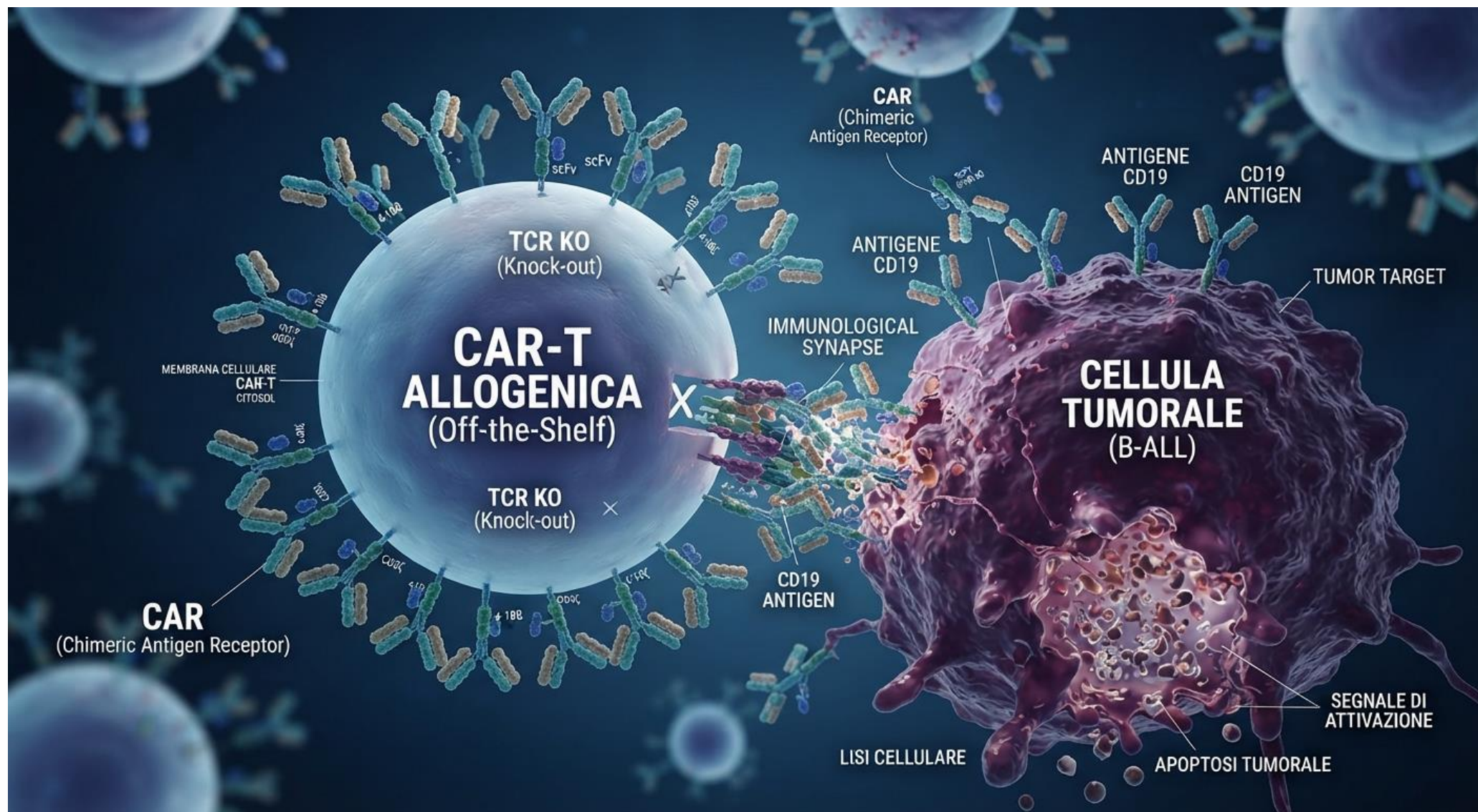
TRAPIANTO ALLOGENICO DI CELLULE STAMINALI - BARRIERA IMMUNOLOGICA



Cause of death after allogeneic transplant







Allogeneic CAR-T trials in solid tumors - 2026

Clinicaltrials.gov

CAR-T product	Clinical Trial	Targeted antigen	Disease	Cell source	Phase
MSLN-CAR-T	NCT05531708	MSLN	Mesothelin+ advanced refractory solid tumors	Autologous T cells	Phase I
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MSLN-CAR-T	NCT05141293	MSLN	MSLN+ positive solid tumor	PD133 autologous T cells	Early Phase I
MSLN-CAR-T	NCT05166070	MSLN	Solid tumor	PD133 autologous T cells	Early Phase I
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PD-1 antibody expressing MSLN CAR-T cells	NCT03615313	MSLN	MSLN+ advanced recurrent/refractory solid tumor	Autologous T cells	Phase I
MSLN-CAR-T	NCT02159716	MSLN	Metastatic pancreatic adenocarcinoma Epithelial ovarian cancer Mesothelioma	Autologous T cells	Phase II
aPD1-MSLN-CAR-T	NCT04503990	MSLN	Colorectal cancer Ovarian cancer	Autologous T cells	Early Phase I
CTLA-4/PD-1 antibodies expressing MSLN CAR-T	NCT03182993	MSLN	Advanced solid tumor	Autologous T cells	Phase I
PD-1 antibody expressing MSLN CAR-T	NCT03030001	MSLN	Advanced solid tumor	Autologous T cells	Phase II
MSLN CAR-T	NCT03545815	MSLN	MSLN+ multiple solid tumor	Autologous T cells	Phase II
GD2/PSMA bi-specific CAR-T	NCT05437315	GD2/PSMA	GD2 and PSMA+ tumors	Autologous T cells	Phase I
GD2 CAR-T	NCT02107993	GD2	Sarcoma Osteosarcoma Neuroblastoma Melanoma	Autologous T cells	Phase II
GD2 CAR-T01	NCT0373097	GD2	Neuroblastoma GD2+ tumors Osteosarcoma Ewing sarcoma	Autologous T cells	Phase I
GD2 CAR-T	NCT04196413	GD2	Glioma spinal cord Glioma Brainstem	Autologous T cells	Phase I
GD2 CAR-T	NCT00985930	GD2	Neuroblastoma	Autologous T cells	
CLDN18.2 CAR-T	NCT04467853	CLDN18.2	Claudin 18.2+ advanced tumor	LCAR-C185 cells	
CLDN18.2 CAR-T	NCT05472857	CLDN18.2	Gastric cancer Pancreatic cancer Advanced ovarian cancer Gastroesophageal junction cancer	Autologous T cells	
CLDN18.2 CAR-T	NCT03874897	CLDN18.2	Advanced solid tumor	Autologous T cells	
CLDN18.2 CAR-T	NCT04581473	CLDN18.2	Gastric adenocarcinoma Pancreatic cancer Gastroesophageal junction cancer	CID41 autologous T cell	
CLDN18.2 CAR-T	NCT05195619	CLDN18.2	Solid tumor	Autologous T cells	
CLDN18.2 CAR-T	NCT05620732	CLDN18.2	Advanced pancreatic and gastric carcinoma	Autologous T cells	
CLDN18.2 CAR-T	NCT05472857	CLDN18.2	Gastric cancer Pancreatic cancer Advanced ovarian carcinoma Gastroesophageal junction cancer	Autologous T cells	
CLDN6 CAR-T	NCT04503278	CLDN6	Solid tumor	Autologous T cells	
CEA CAR-T	NCT05415474	CEA	Colorectal cancer Esophageal cancer Stomach cancer Pancreatic cancer Metastatic tumor Recurrent cancer	Autologous T cells	
CEA CAR-T	NCT05538195	CEA	Colon cancer Gastric cancer Pancreatic cancer Rectal cancer Esophageal cancer	Autologous T cells	
CEA CAR-T	NCT04348643	CEA	Colorectal cancer Gastric cancer Pancreatic cancer Liver cancer Breast cancer Lung cancer Solid tumor	Autologous T cells	Phase 1 Phase 2
CEA CAR-T	NCT05396300	CEA	Colorectal cancer Esophageal cancer Stomach cancer Pancreatic cancer Metastatic tumor Recurrent cancer	Autologous T cells	Phase 1
CEA CAR-T	NCT02349724	CEA	Colorectal cancer Breast cancer Pancreatic cancer Lung cancer Gastric cancer	Autologous T cells	Phase 1
CEA CAR-T	NCT02416486	CEA	Liver metastatic	Autologous T cells	Phase 1
CEA CAR-T	NCT02850536	CEA	Liver metastatic	Autologous T cells	Phase 1b
ROR1 CAR-T	NCT05274651	ROR1	Triple negative breast cancer Non-small cell lung cancer Metastatic non-small cell lung cancer Breast cancer	LYL787 autologous T cells	Phase 1

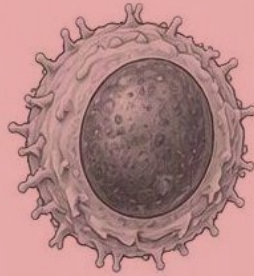
Fase	N. Totale studi in corso
Early Phase I	5
Phase I	15
Phase I-II	8
Totale	28

Development of T-cell therapies

Selected milestones, 1988–2024

TIL

Tumor-infiltrating
lymphocytes



1988

Clinical responses
in melanoma

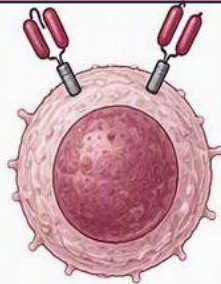
Rosenberg et al.

2024*

First FDA-approved TIL therapy
Lifileucel (Amtagvi)
Advanced melanoma

CAR-T

Chimeric antigen
receptor T cells



1989

Chimeric receptor
proof of concept

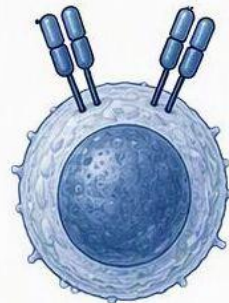
Gross, Waks & Eshhar

2017

First FDA-approved CAR-T therapy
Tisagenlecleucel (Kymriah)
Pediatric and young adult B-ALL

TCR-T

T-cell receptor-
engineered T cells



2006

Tumor regression
with engineered TCRs

Morgan et al.

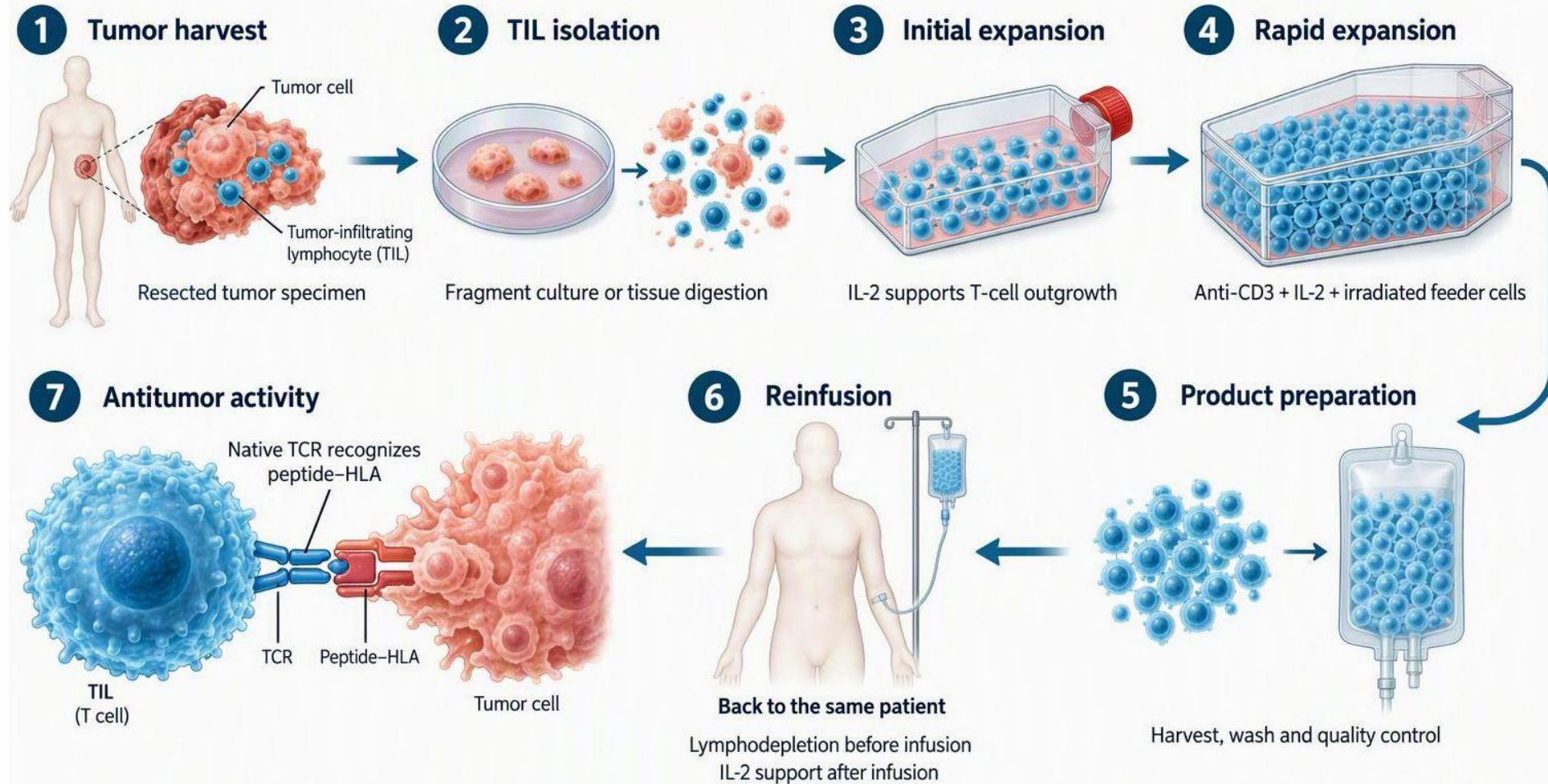
2024*

First FDA-approved TCR-T therapy
Afamitresgene autoleucel (Tecelra)
Selected patients with synovial sarcoma

* Accelerated FDA approval in 2024

TIL therapy: manufacturing and reinfusion

Autologous tumor-infiltrating lymphocytes



Conventional TILs retain their native receptors; genetic engineering is not required.

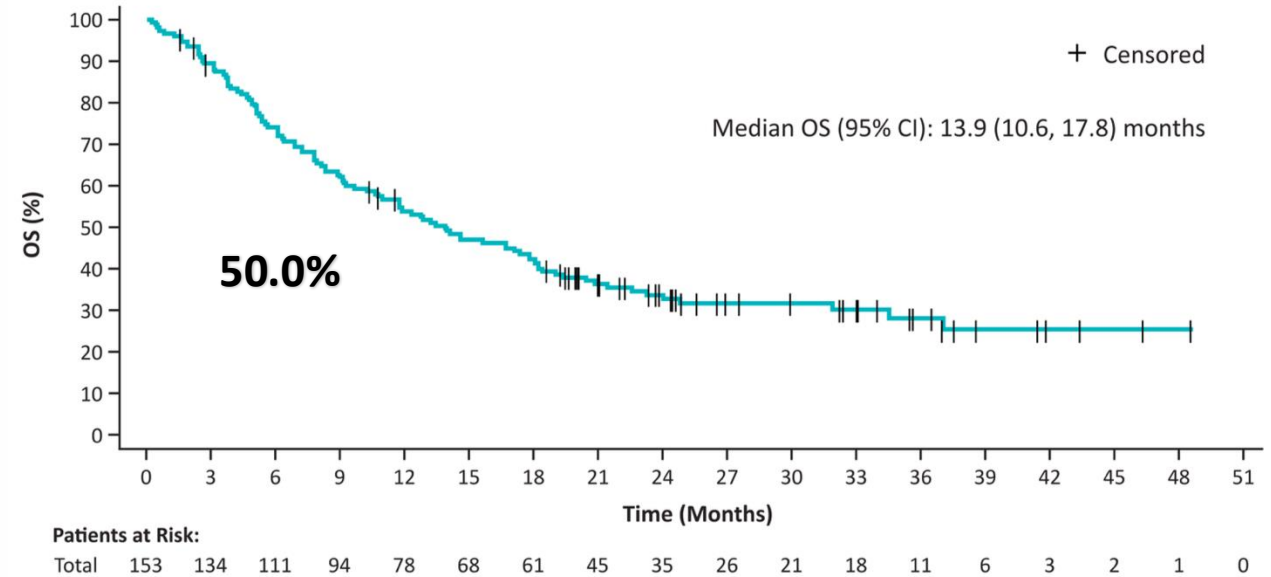
Simplified conventional workflow. Details vary by protocol.

Efficacy and safety of lifileucel, a one-time autologous tumor-infiltrating lymphocyte (TIL) cell therapy, in patients with advanced melanoma after progression on immune checkpoint inhibitors and targeted therapies: pooled analysis of consecutive cohorts of the C-144-01 study

Chesney J et al, '22

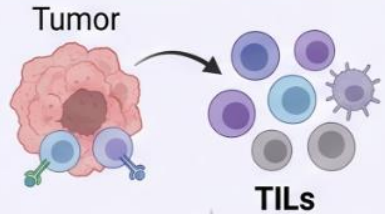
Studio Registrativo – approvazione FDA

Characteristic	Cohort 2+4 (N=153)
Median age, years (range)	56.0 (20–79)
Sex, n (%)	
Male	83 (54.2)
Female	70 (45.8)
Prior systemic therapies, n (%)	
Median number of therapies (range)	3.0 (1–9)
Anti-PD-1/PD-L1	153 (100)
Anti-CTLA-4	125 (81.7)
Anti-PD-1 plus anti-CTLA-4 combination	82 (53.6)
BRAF±MEK inhibitor	39 (25.5)
IL-2	13 (8.5)
Primary refractory to anti-PD-1/PD-L1,§ n (%)	83 (54.2)

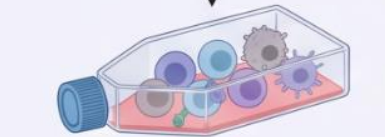


A: Selection Strategies

Current TILs (Bulk Selection)



Bulk Expansion

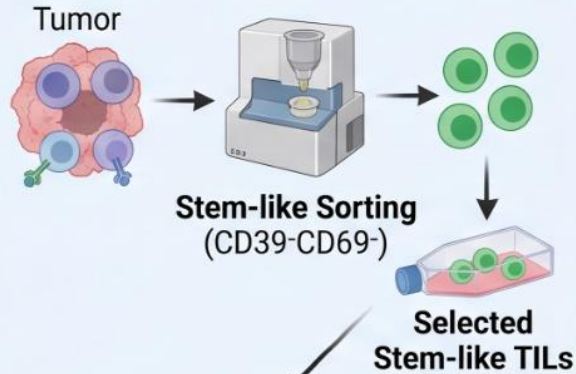


Expanded Bulk TILs (Heterogeneous Population, Variable Efficacy)

Selection based on total growth, often includes exhausted and less effective cells.

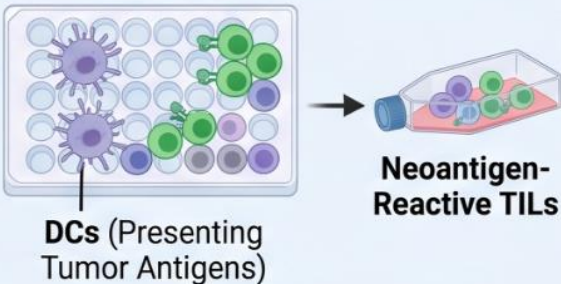
vs.

Next-Gen Strategies (Phenotypic & Functional Selection)



vs.

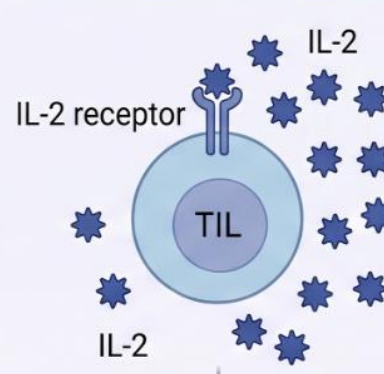
Neoantigen-Reactivity Screening



Selection for potent phenotypes (e.g., stem-like) or tumor specificity via co-culture, improving efficacy.

B: Cytokine Enhancement

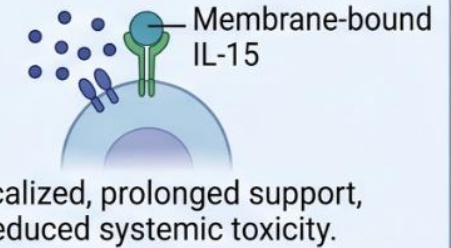
Current (Exogenous High-Dose IL-2)



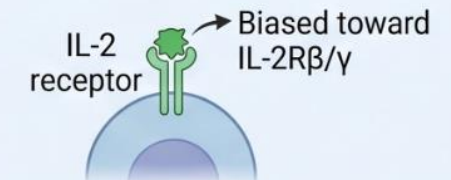
High Toxicity
(Vascular Leak Syndrome,
Systemic Inflammation)

vs.

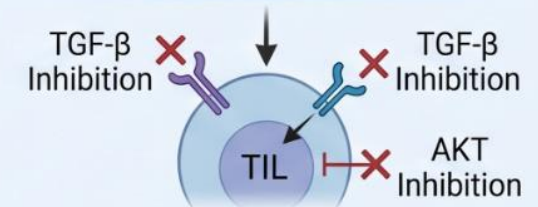
Next-Gen Strategies (Targeted & Engineered Cytokines)



vs.



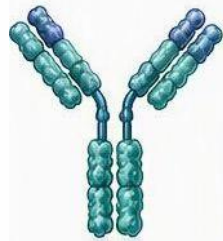
Engineered IL-2: Improved specificity for TILs, reduced Treg stimulation.



Concurrent Inhibition: Blocks immunosuppression, enhances expansion & persistence.

TIL therapy: combination strategies

Investigational combinations in solid tumors

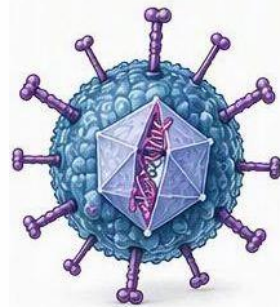


Checkpoint blockade

Pembrolizumab or nivolumab

Rationale: reduce T-cell inhibition

Clinical studies, including phase III

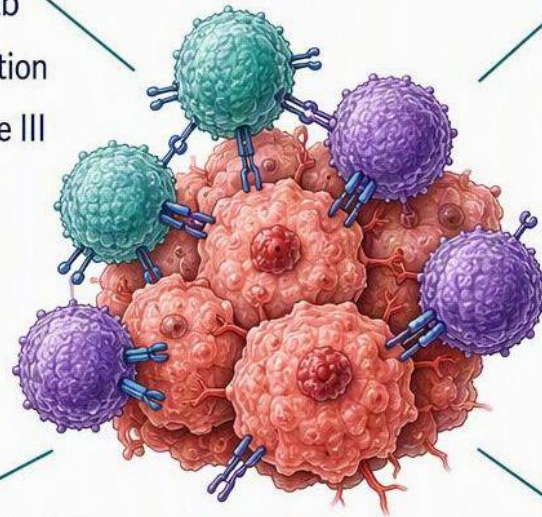


Oncolytic viruses

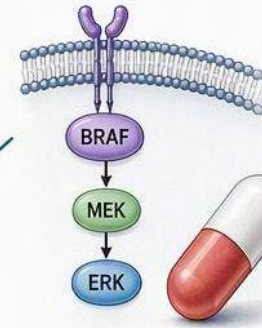
TILT-123

Rationale: local immune activation

Phase I clinical evidence



TILs



Targeted therapy

BRAF inhibition, e.g. vemurafenib

BRAF V600-mutant melanoma

Pilot clinical evidence



Radiotherapy

Local irradiation

Rationale: tumor priming /
local control

Exploratory integration

Established lifileucel regimen components

Lymphodepleting chemotherapy before infusion + IL-2 support after infusion

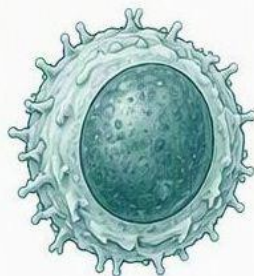
Selected strategies. Combination benefit and optimal sequencing remain under study.

Development of T-cell therapies

Selected milestones, 1988–2024

TIL

Tumor-infiltrating lymphocytes



1988

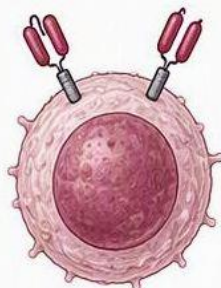
Clinical responses in melanoma
Rosenberg et al.

2024*

First FDA-approved TIL therapy
Lifileucel (Amtagvi)
Advanced melanoma

CAR-T

Chimeric antigen receptor T cells



1989

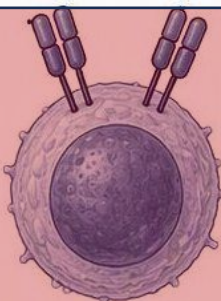
Chimeric receptor proof of concept
Gross, Waks & Eshhar

2017

First FDA-approved CAR-T therapy
Tisagenlecleucel (Kymriah)
Pediatric and young adult B-ALL

TCR-T

T-cell receptor-engineered T cells



2006

Tumor regression with engineered TCRs
Morgan et al.

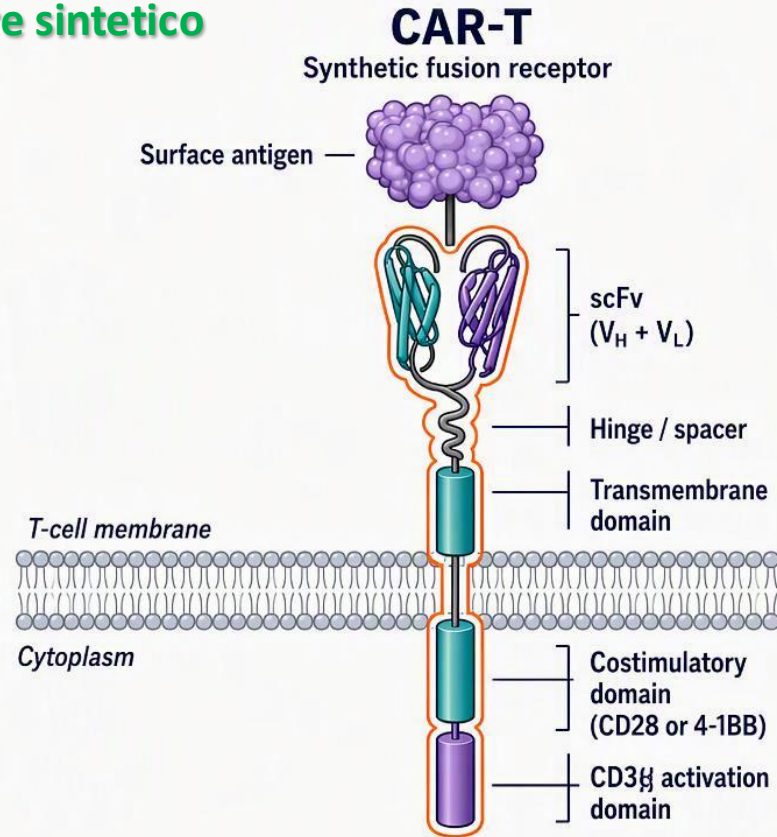
2024*

First FDA-approved TCR-T therapy
Afamitresgene autoleucel (Tecelra)
Selected patients with synovial sarcoma

* Accelerated FDA approval in 2024

CAR-T versus TCR-T: receptor structure

Recettore sintetico



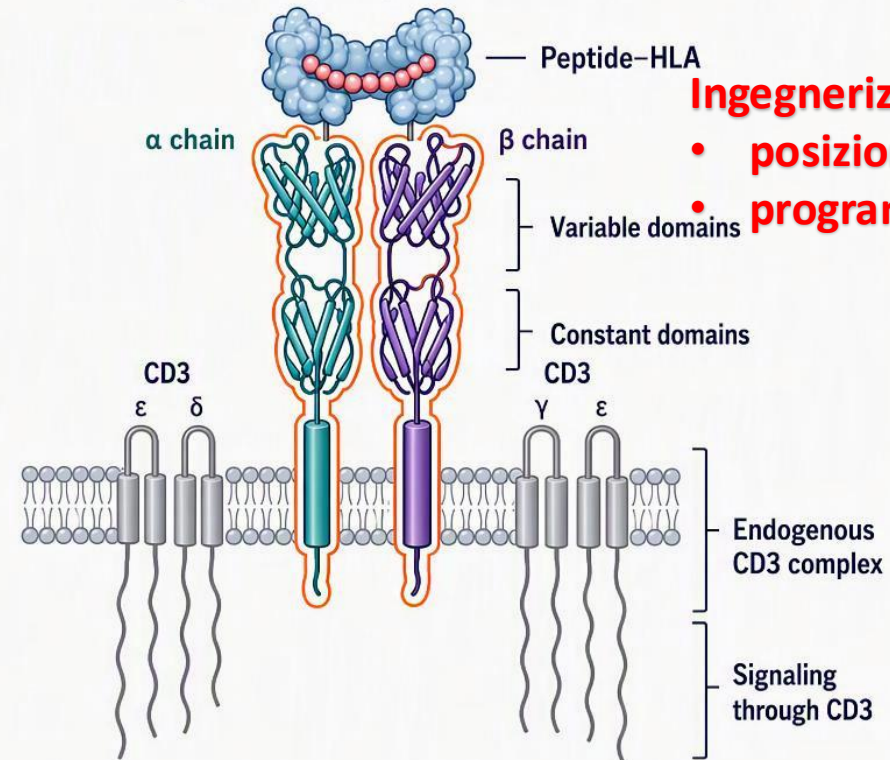
CAR: engineered fusion of selected domains

 Orange outline: genetically introduced receptor

TCR chains retain natural architecture; sequence optimization is optional.

Simplified schematic. Conventional second-generation CAR and αβ TCR shown.

TCR-T
Engineered αβ receptor with native CD3



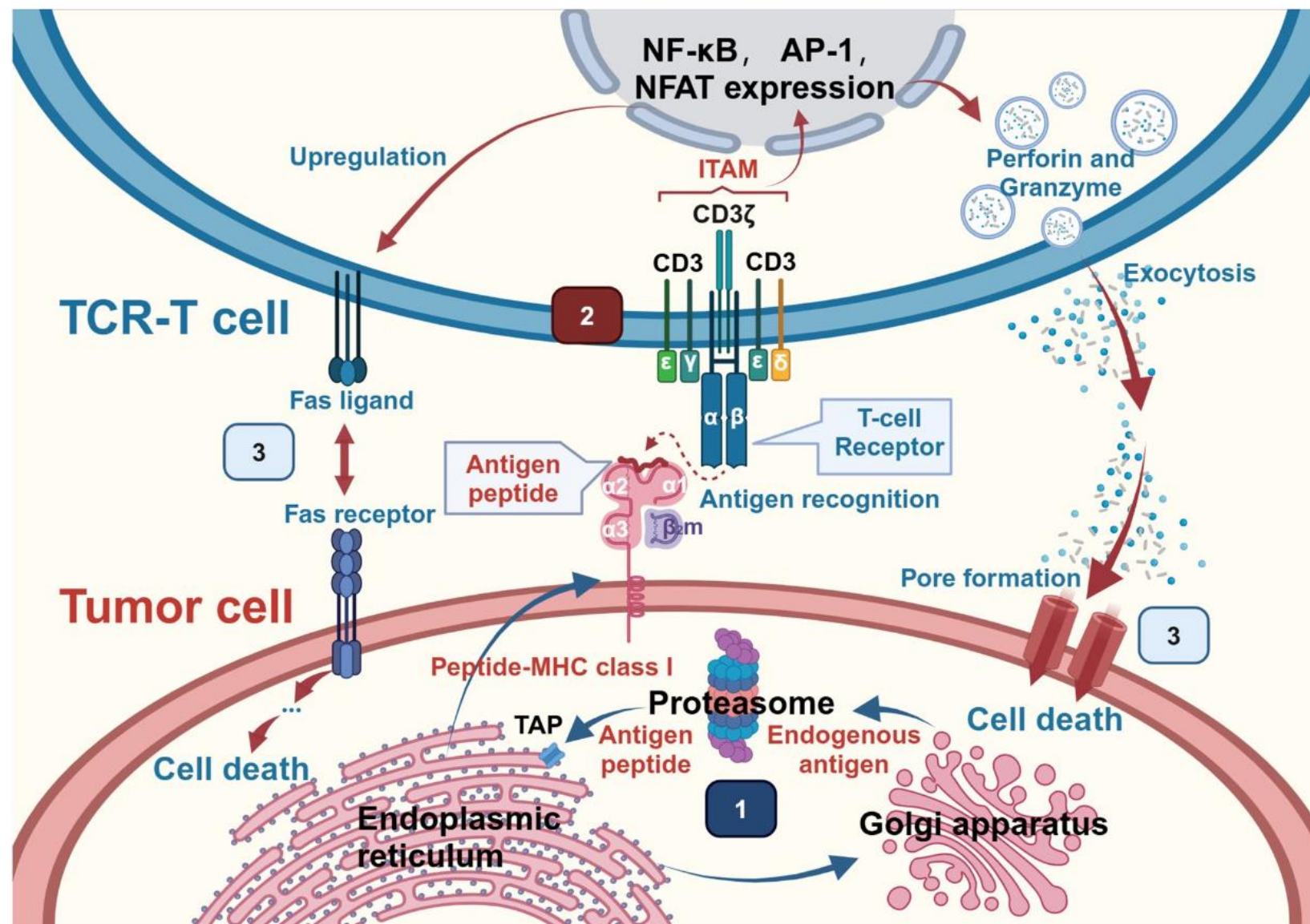
TCR: genetically introduced α and β chains

Biologicamente naturale

Ingegnerizzato

- posizionamento
- programmazione genetica

1. TCR-T + MHC
- ↓
2. Sinapsi immunologica
- ↓
3. Perforine e granzimi
- ↓
4. apoptosi

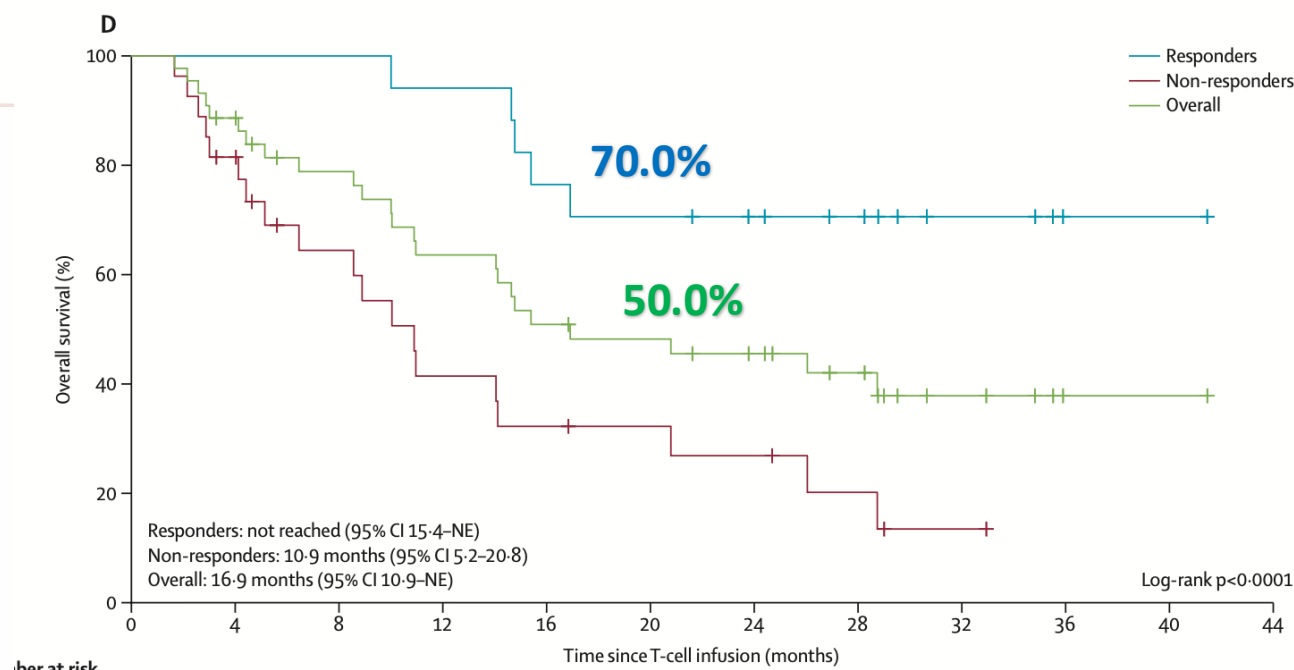


Afamitresgene autoleucel for advanced synovial sarcoma and myxoid round cell liposarcoma (SPEARHEAD-1): an international, open-label, phase 2 trial

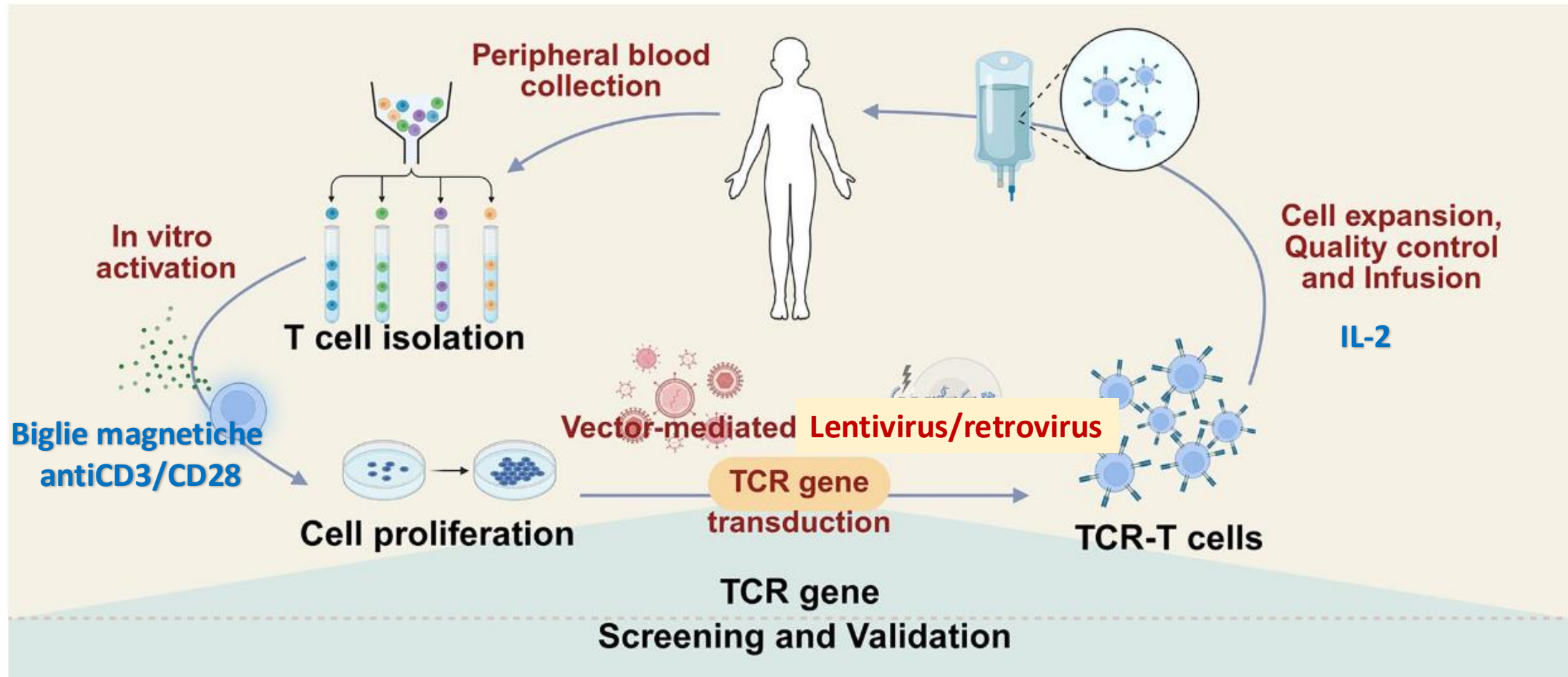
Lancet 2024; 403: 1460-71

Studio Registrativo – approvazione FDA

	Patients with synovial sarcoma (n=44)	Patients with myxoid round cell liposarcoma (n=8)	All patients (n=52)
Age at consent, years	40.5 (31.0–46.0)	43.5 (32.5–54.5)	41.0 (31.0–46.5)
Sex			
Female	22 (50%)	2 (25%)	24 (46%)
Male	22 (50%)	6 (75%)	28 (54%)
Previous lines of systemic therapy			
1	7 (16%)	3 (38%)	10 (19%)
2	14 (32%)	1 (13%)	15 (29%)
3	9 (20%)	0	9 (17%)
≥4	14 (32%)	4 (50%)	18 (35%)

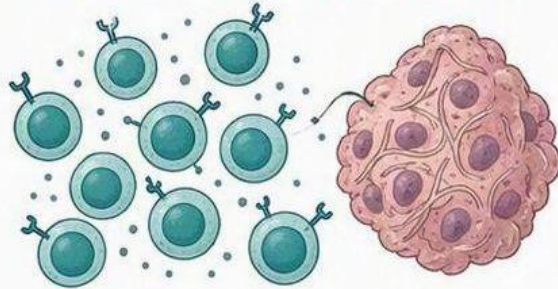


TCR-T production



TILs, CAR-T and TCR-T: limitations in solid tumors

TILs: mixed tumor-derived T cells



Production

Requires tumor harvest and successful cell expansion



Product variability

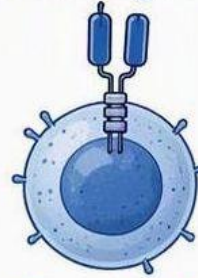
Tumor-reactive cell content and fitness vary



Treatment burden

Lymphodepletion and IL-2 drive much of the toxicity

CAR-T: engineered T cell with chimeric antigen receptor



Target selection

Conventional CARs access surface antigens only



Tumor escape

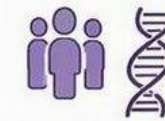
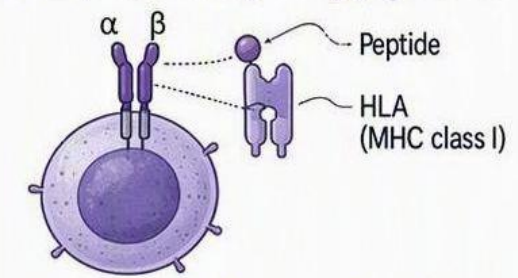
Low or lost target expression



Safety

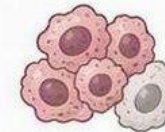
On-target injury to normal tissues, CRS and neurotoxicity

TCR-T: engineered T cell with alpha-beta TCR recognizing peptide-HLA



Patient selection

Requires the matching HLA allele



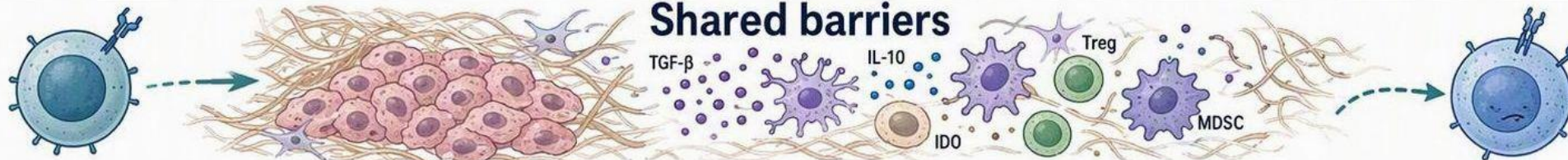
Tumor escape

Antigen loss or impaired HLA presentation



Safety

Peptide cross-reactivity, on-target toxicity and CRS



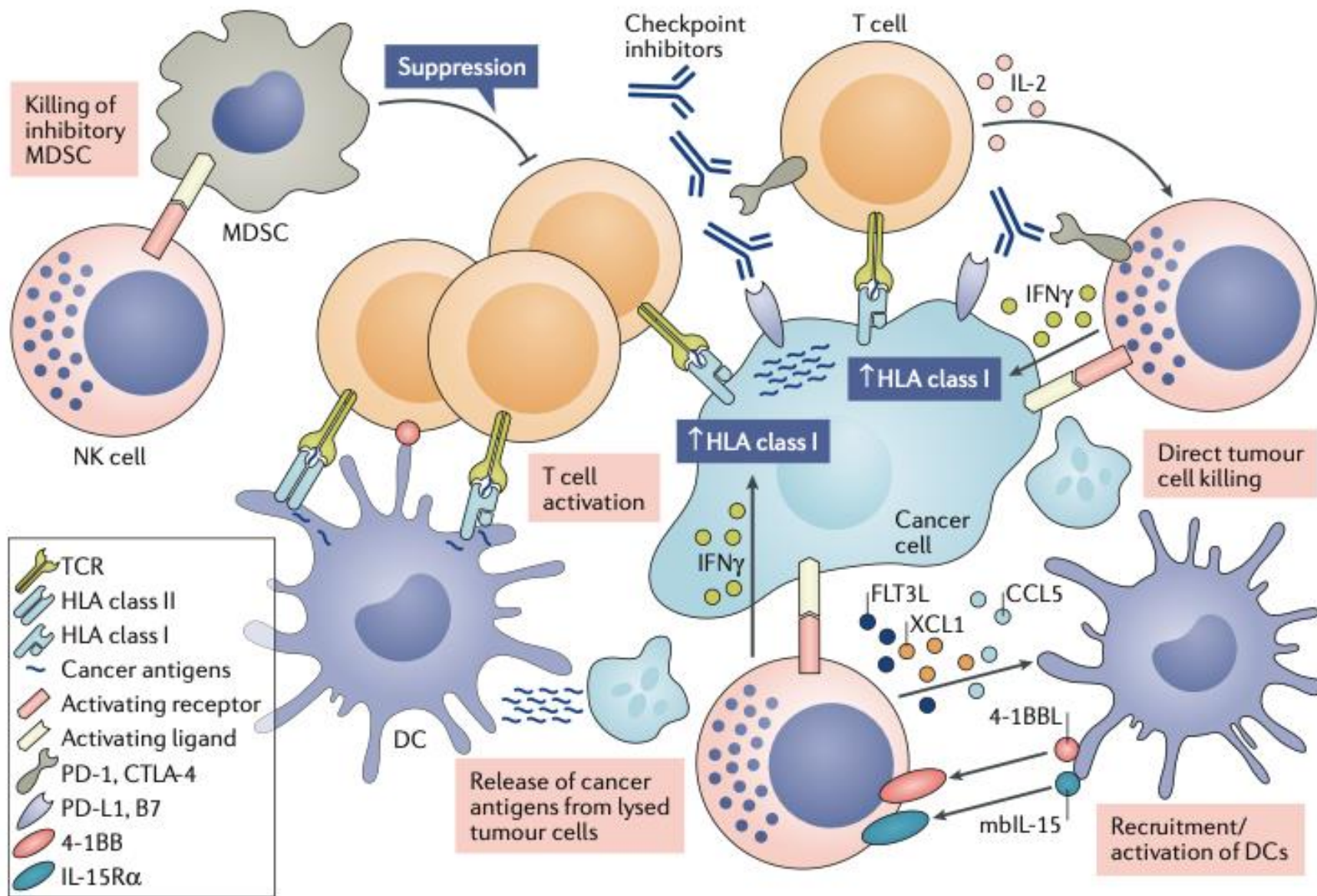
Poor tumor infiltration

Immunosuppressive microenvironment

Limited persistence and exhaustion

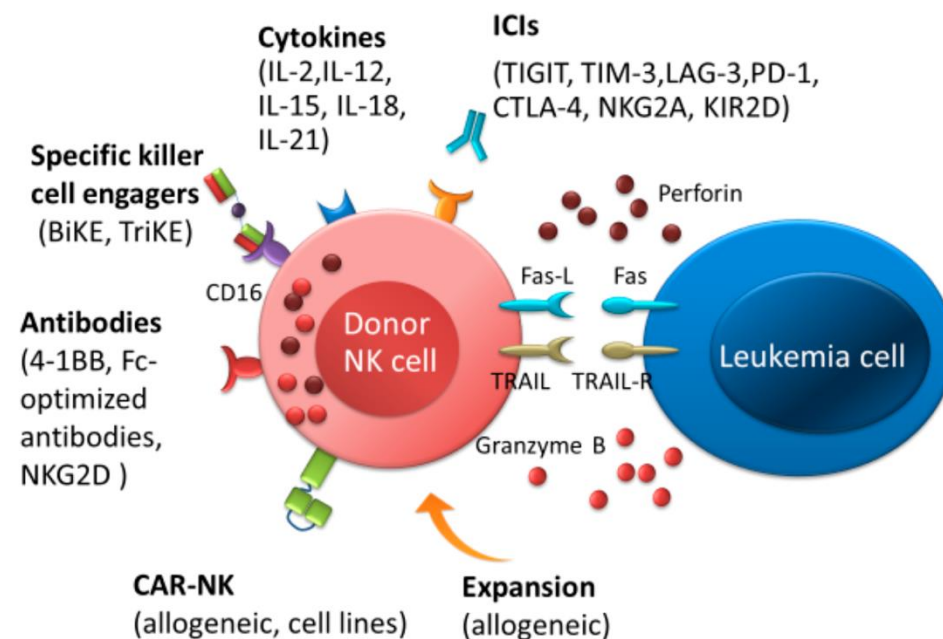
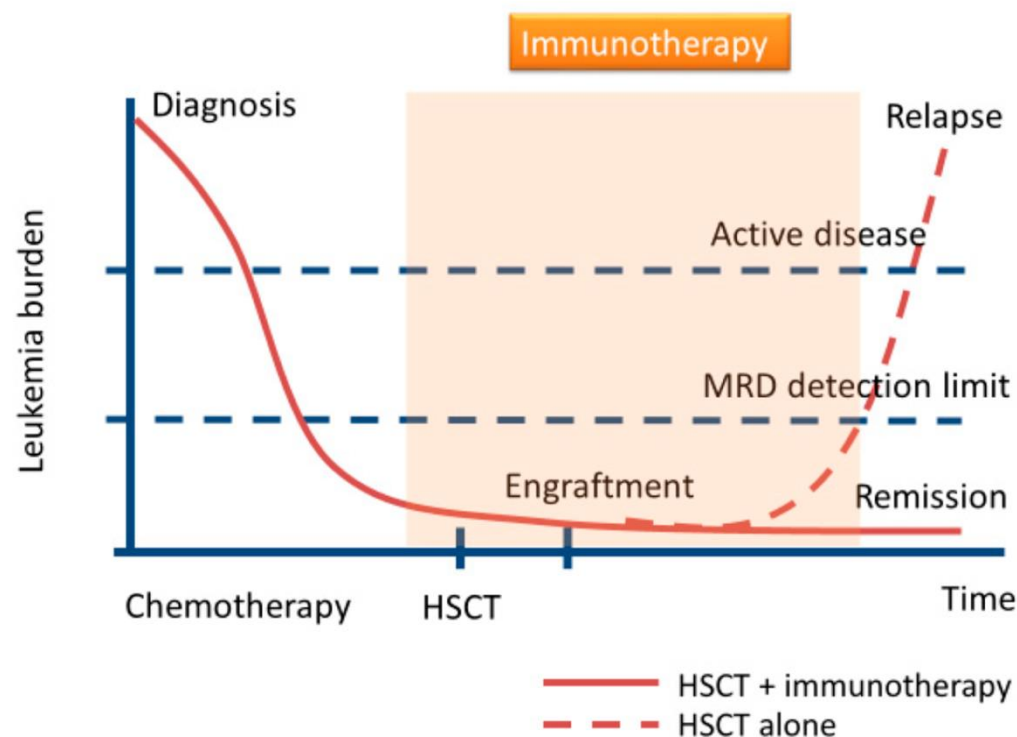
Risks vary by product and regimen. CRS = cytokine release syndrome. No head-to-head ranking implied.

NK cells



Natural Killer Immunotherapy for Minimal Residual Disease Eradication Following Allogeneic Hematopoietic Stem Cell Transplantation in Acute Myeloid Leukemia

Norimichi Hattori *^{id} and Tsuyoshi Nakamaki 2019



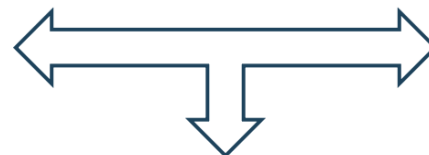
Infusione di cellule NK alloreattive come strategia di consolidamento per pazienti adulti affetti da leucemia mieloide acuta: studio multicentrico

NCT00799799 - Curti A – Università Bologna

Criteri inclusione:

- Età > 18 anni;
- ECOG ≤ 2
- FE ≥ 50
- LAM de novo e secondarie
- In prima remissione citologica
- ≥ 2 remissione anche molecolare

Fluda 25mg/mq x5 gg
Edx 2gr/mq 1gg



Criteri esclusione:

- ECOG > 2
- FE < 50
- Altre comorbidità
- LAM rischio favorevole
- LAM in prima remissione molecolare*
- Eleggibilità trapianto allogenico

Randomizzazione genetica:
braccio A: infusione NK Kir alloreattive vs braccio B: solo follow-up

Infusione di cellule NK alloreattive come strategia di consolidamento per pazienti adulti affetti da leucemia mieloide acuta: studio multicentrico

NCT00799799 - Curti A – Università Bologna

Transplant No.	Donor	Recipient	Donor KIR Ligand Missing in Recipient
1	A24, B35, Cw4 A24, B62, Cw3*	A24, B35, Cw4 A24, B35, Cw4	Group 2 HLA-C
2	A2, B35, Cw4 A24, B51, Cw-	A2, B35, Cw4 A1, B35, Cw-	HLA-Bw4
3	A33, B35, Cw4 A3, B44, Cw4	A33, B35, Cw4 A2, B60, Cw3	HLA-Bw4
4	A32, B44, Cw8 A3, B18, Cw6	A32, B44, Cw8 A3, B52, Cw8	
5	A3, B7, Cw7 A30, B18, Cw6	A3, B7, Cw7 A3, B7, Cw7	
6	A1, B7, Cw6 A3, B45, Cw7	A1, B7, Cw6 A30, B14, Cw4	
7	A25, B51, Cw1 A2, B44, Cw5	A25, B51, Cw1 A25, B51, Cw3	
8	A31, B39, Cw3 A3, B39, Cw4	A31, B39, Cw3 A2, B35, Cw3	
9	A1, B35, Cw4 A2, B51, Cw7	A1, B35, Cw4 A2, B41, Cw7	
10	A3, B18, Cw4 A2, B35, Cw3	A3, B18, Cw4 A10, B51, Cw5	
11	A1, B8, Cw7 A74, B18, Cw6	A1, B8, Cw7 A33, B14, Cw7	Group 1 HLA-C
12	A29, B35, Cw7 A32, B44, Cw5	A29, B35, Cw7 A3, B62, Cw7	Group 1 HLA-C + HLA-Bw4
13	A3, B44, Cw4 A29, B8, Cw7	A3, B44, Cw4 A24, B35, Cw4	Group 2 HLA-C
14	A30, B62, Cw3 A3, B52, Cw2	A30, B62, Cw3 A2, B27, Cw1	Group 1 HLA-C
15	A3, B7, Cw7 A-, B35, Cw4	A3, B7, Cw7 A24, B18, Cw8	Group 1 HLA-C
16	A2, B18, Cw7 A-, B51, Cw7	A2, B18, Cw7 A1, B8, Cw7	HLA-Bw4
17	A1, B49, Cw7 A31, B13, Cw6	A1, B49, Cw7 A11, B52, Cw7	Group 1 HLA-C
18	A3, B35, Cw4 A23, B17, Cw7	A3, B35, Cw4 A24, B38, Cw4	Group 2 HLA-C
19	A1, B27, Cw8 A3, B37, Cw6	A1, B27, Cw8 A3, B52, Cw3	Group 1 HLA-C
20	A24, B50, Cw6 A11, B51, Cw7	A24, B50, Cw6 A3, B35, Cw4	Group 2 HLA-C + HLA Bw4

Tre principali NK specificità

HLA - C gruppo 1 – Asn77 – Lys80

HLA - C gruppo 2 – Ser77 – Asn80

HLA - Bw4

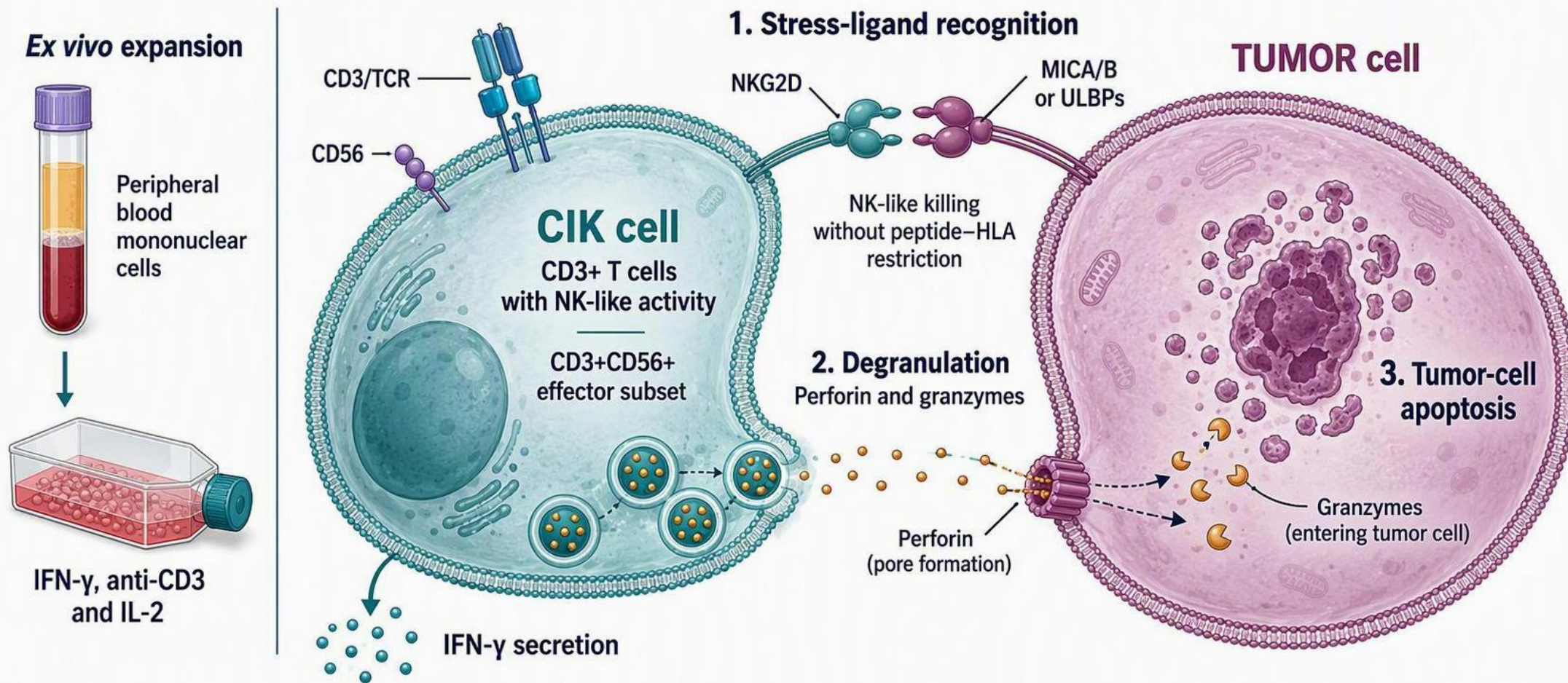
<30% pazienti

Tipizzazione HLA: 6 (72.0%)

- Dec post induzione 1**
- In attesa referto 2 (46.5%)**

No NK alloreattivi: 3 (23.0%)

Cytokine-induced killer (CIK) cells: mechanism of action



T-cell identity with NK-like cytotoxicity

NKG2D is a major pathway. TCR-dependent recognition and other receptors may also contribute.



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journal homepage: www.elsevier.com/locate/cytogfr

Short survey

Cytokines for the induction of antitumor effectors: The paradigm of Cytokine-Induced Killer (CIK) cells

Elisa Cappuzzello^{a,1}, Roberta Sommaggio^{a,1}, Paola Zanovello^{a,b}, Antonio Rosato^{a,b,*}



Innovative therapeutic strategy for B-cell malignancies that combines obinutuzumab and cytokine-induced killer cells

Anna Dalla Pietà^{a,1}, Elisa Cappuzzello^{a,1}, Pierangela Palmerini^{a,1}, Annavera Ventura^{a,1}, Andrea Visentin^{a,2}, Giuseppe Astori^{a,3}, Katia Chierogato^{a,3,4}, Valentina Mozzo^{a,5}, Omar Perbellini^{a,6}, Maria Chiara Tisi^{a,6}, Livio Trentin^{a,2}, Carlo Visco^{a,7}, Marco Ruggeri^{a,6}, Roberta Sommaggio^{a,5}, Antonio Rosato^{a,5}

LETTER TO THE EDITOR

A rescue approach in refractory diffuse large B-cell lymphoma with obinutuzumab-redirected cytokine-induced killer cells: a first-in-human case report

ONCOIMMUNOLOGY
2020, VOL. 9, NO. 1, 1–13
<https://doi.org/10.1080/2162402X.2020.1777046>

ORIGINAL RESEARCH

Adoptive cell therapy of triple negative breast cancer with redirected cytokine-induced killer cells

Roberta Sommaggio^a, Elisa Cappuzzello^b, Anna Dalla Pietà^b, Anna Tosi^b, Pierangela Palmerini^b, Debora Carpanese^a, Lorenzo Nicolè^c, and Antonio Rosato^{a,b}

ONCOIMMUNOLOGY
2016, VOL. 5, NO. 8, e1199311 (10 pages)
<http://dx.doi.org/10.1080/2162402X.2016.1199311>

ORIGINAL RESEARCH

Retargeting cytokine-induced killer cell activity by CD16 engagement with clinical-grade antibodies

Elisa Cappuzzello^a, Anna Tosi^a, Paola Zanovello^{a,b}, Roberta Sommaggio^{a,*}, and Antonio Rosato^{a,b,*}



Istituto
Oncologico
Veneto
IRCCS

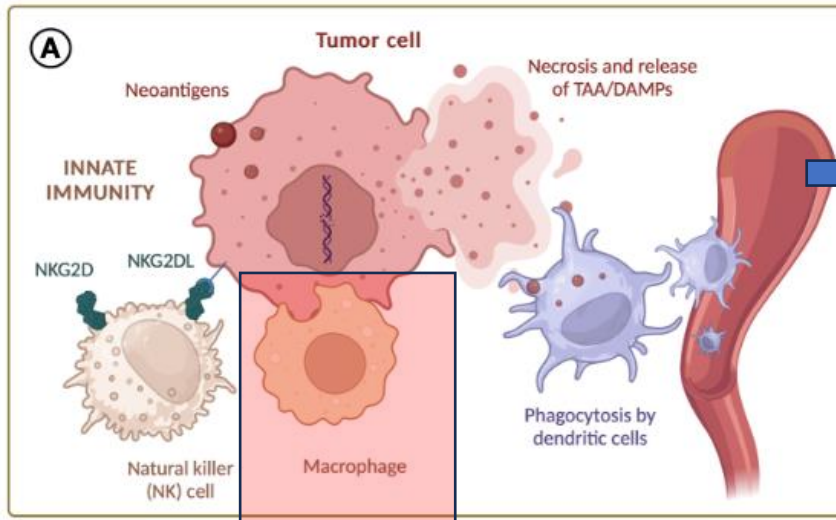
A Multicenter, Phase I Study to Evaluate the Feasibility and Safety of Autologous Cytokine-Induced Killer Cells (CIK_D332) in Combination with Tafasitamab and Lenalidomide in Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma (DLBCL): The FOCUS Study

Study Identifier: IOV-DLBCL-01-2026-FOCUS
EuCT n°: 2026-525494-39-00

IOV-IRCCS – Vicenza - Verona

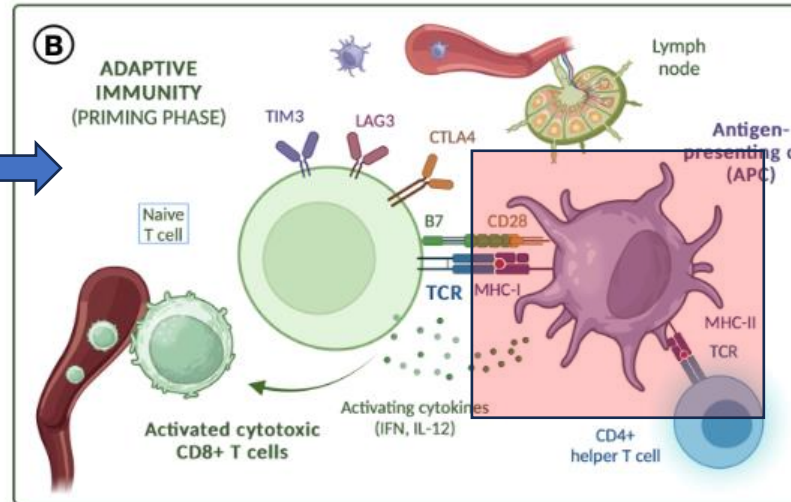
Grazie!

Innate immunity



Adaptive immunity

Priming phase



Effector phase

