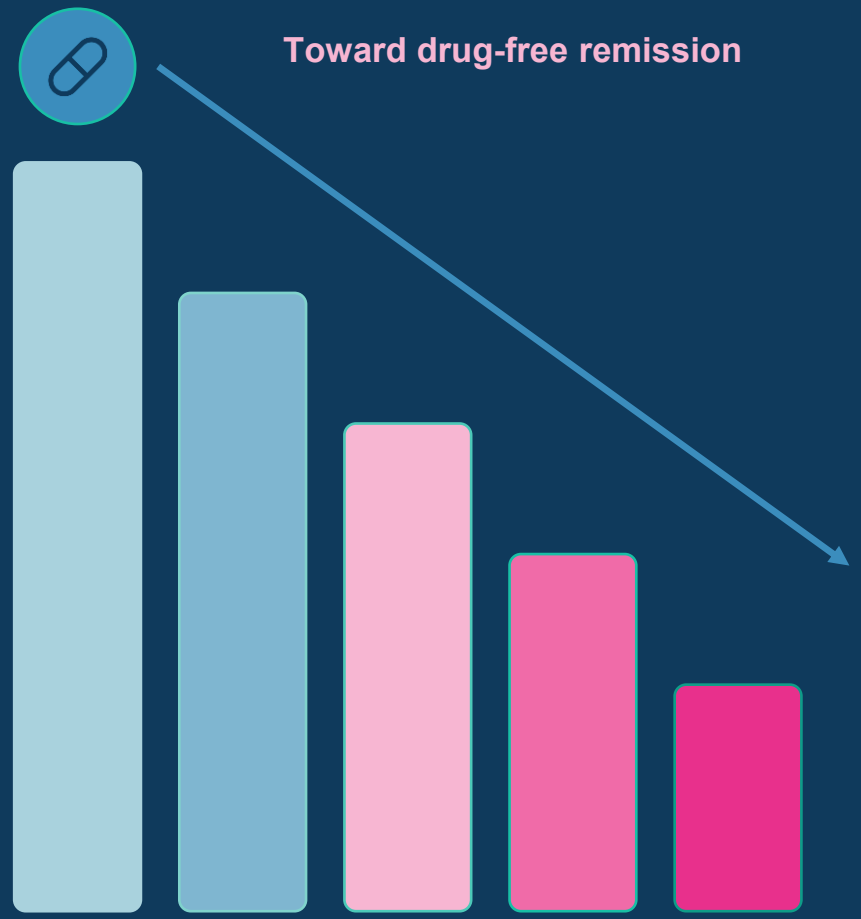
PEDIATRIC RHEUMATOLOGY

CAR-T cell therapy for juvenile-onset autoimmune diseases: a promising future?



Pediatric evidence, safety caveats and the road to trials

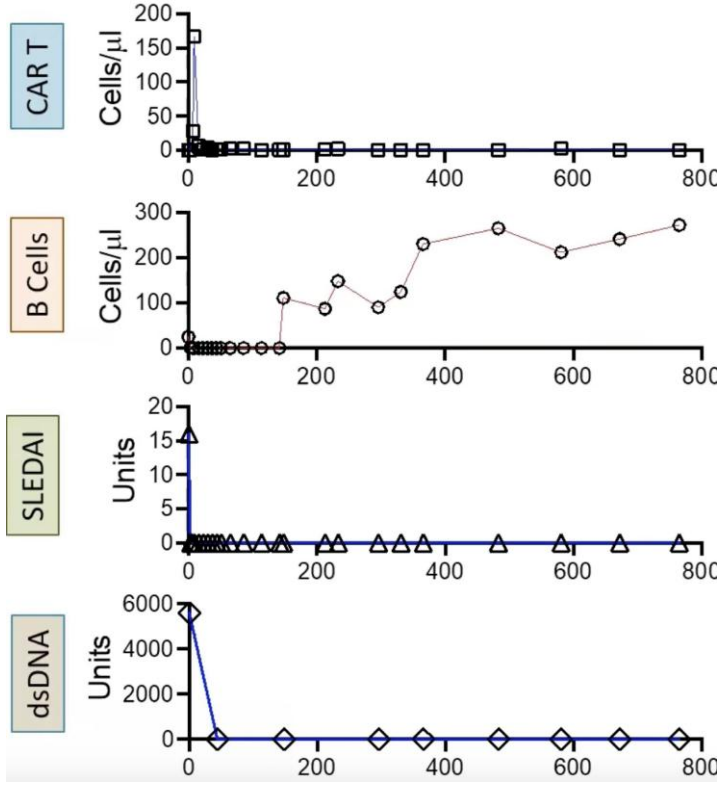
Maurine JOURET Pediatric rheumatology, Hospices Civils de Lyon

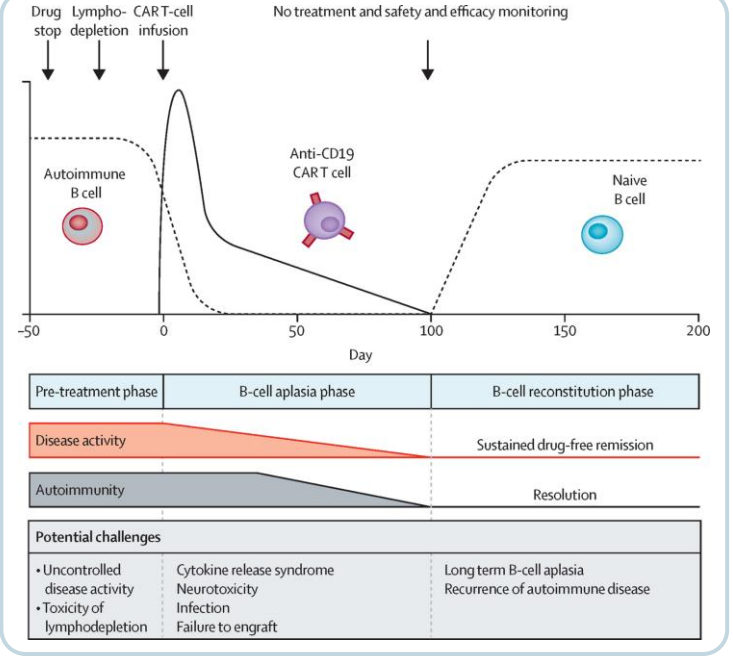
SFI-SPI 2026 · 5 November 2026 · Literature to August 2026 · Trial registry checked 19 October 2026

One infusion, lasting remission: the first patient, 2021

20-year-old woman, refractory lupus

- Class III nephritis, nephrotic syndrome, pericarditis
- Failed 7 drugs, incl. cyclophosphamide, belimumab and rituximab
- Anti-dsDNA 8,000–12,000 U/mL; proteinuria 4–6 g/day





2.5 years later

No treatment, no sign of autoimmunity, normal life (congress)

One infusion, drug-free remission in one patient

Confidence: very low

Could CAR T-cell therapy be offered earlier, during adolescence, before irreversible damage accumulates?

We reviewed published patients, case by case

QUESTION

What is the evidence for CAR T cells in juvenile-onset autoimmune disease, and how cautious should we be?

Search
PubMed, publishers, congresses

Extract
Patient by patient, incl. supplements

Deduplicate
Each child counted once

Cohort A	Infused before 18 y
Cohort B	Adult infusion, onset < 18 y
Onset unknown	Age at onset not reported

How to read the confidence gauge

Confidence: high	Several randomized trials or meta-analyses that agree
Confidence: moderate	One randomized trial, or many concordant cohorts
Confidence: low	Heterogeneous observational studies
Confidence: very low	Small numbers, single cases, unreplicated or unpublished data

A qualitative judgment on study design, not a GRADE score. Registry facts are rated on how they were verified.

patient-level review, not a systematic review

Adults now reach drug-free remission; children need it most

The pediatric problem

Lifelong disease

cSLE, JDM and jSSc start in childhood and last decades

Cumulative toxicity

Glucocorticoids and immunosuppressants from an early age

Rare drug-free remission

Most patients remain on treatment into adulthood

What CD19 CAR T cells achieved in adults

15/15 off immunosuppression; all 8 SLE in DORIS remission [3]
DORIS = definition of remission in SLE

22/24 met efficacy endpoints at 24 weeks, CASTLE phase 1/2 [4]

96% off drugs among 50 patients, 72.5 patient-years; 0 deaths (congress) [30]

Efficacy endpoints met in 22/24; all 24 off immunosuppressants — Confidence: moderate

Heavier lifetime burden in juvenile onset — Confidence: moderate

CD19 CAR T cells reset B cells deeper than rituximab

Targets along B-cell differentiation

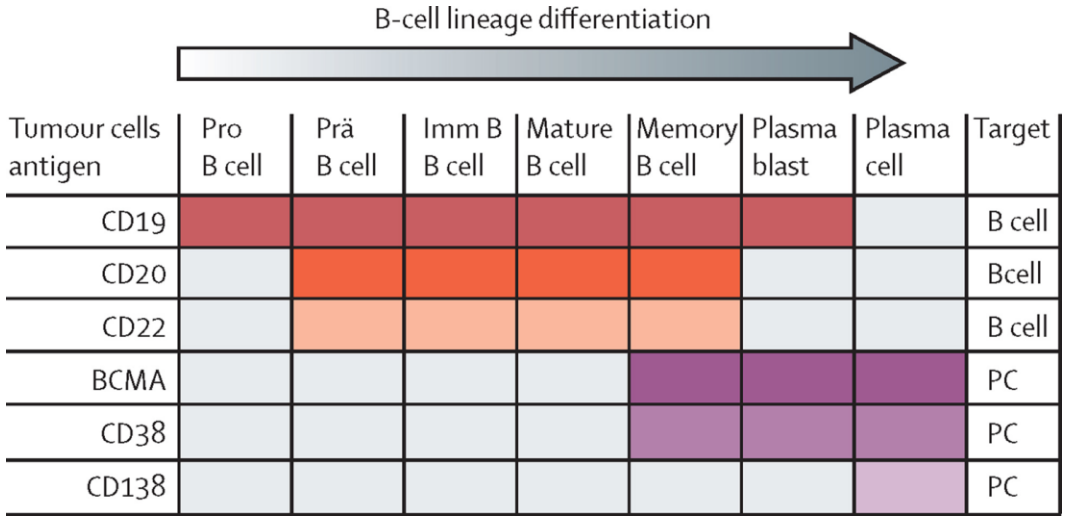


Figure: Schett G, Mackensen A, Mougiakakos D. CAR T-cell therapy in autoimmune diseases. The Lancet 2023; 402:2034–2044

Intensity of the immune reset

Rituximab

anti-CD20 antibody

Relapse risk

- Peripheral B-cell depletion
- B cells persist in lymph nodes [31]
- Plasmablasts and plasma cells spared

CD19 CAR T

reference approach

Best balance?

- Complete B-cell depletion in lymph nodes and organs [31]
- Plasmablasts and short-lived plasma cells hit
- Long-lived plasma cells spared: anti-dsDNA falls, vaccine antibodies persist [2, 3]

BCMA ± CD19 CAR T

deeper reset

Infection risk

- Also removes long-lived plasma cells
- Lupus phase 1: DORIS + LLDAS 12/15 at week 12 [33]
- Grade ≥ 3 neutropenia 15/15 [33]

CD19 CAR T clears tissue B cells, unlike rituximab — Confidence: low

CD19/BCMA co-infusion: grade ≥ 3 neutropenia in 15/15 — Confidence: low

26 pediatric patients identified, mostly in two series

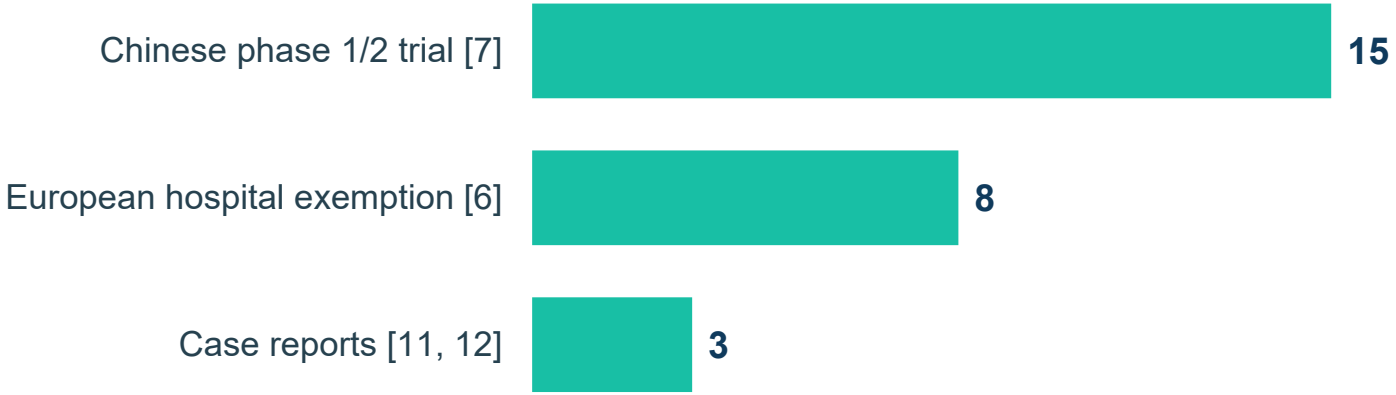
26

unique patients infused before 18 years (Cohort A)

10 publications
1.4 reports per patient

+ 5 juvenile-onset patients
treated within adult series (Cohort B)

Cohort A by source



Case reports: 2 children with refractory cSLE (China) [11]; 1 child with MDA5+ JDM and rapidly progressive ILD, no CRS, off immunosuppressants over 11 months (Spain) [12]

A consistent but uncontrolled pediatric signal

Confidence: very low

All 8 European children improved, with grade 1 toxicity only

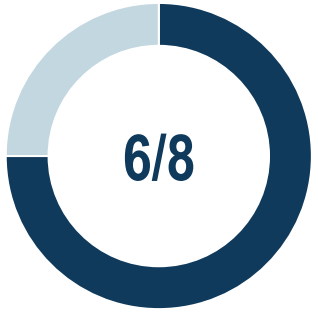
Patients

- 4 cSLE
- 3 JDM
- 1 jSSc

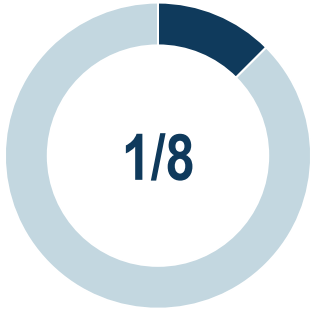
- Zorpocabtagene autoleucel, 1 × 10^6 cells/kg, made on site
- One infusion under the European hospital exemption
- Median follow-up 16.5 months (9–24)



substantial improvement or resolution



grade 1 CRS, no grade ≥ 2



grade 1 ICANS



severe infection

All improved; immunomodulators stopped durably

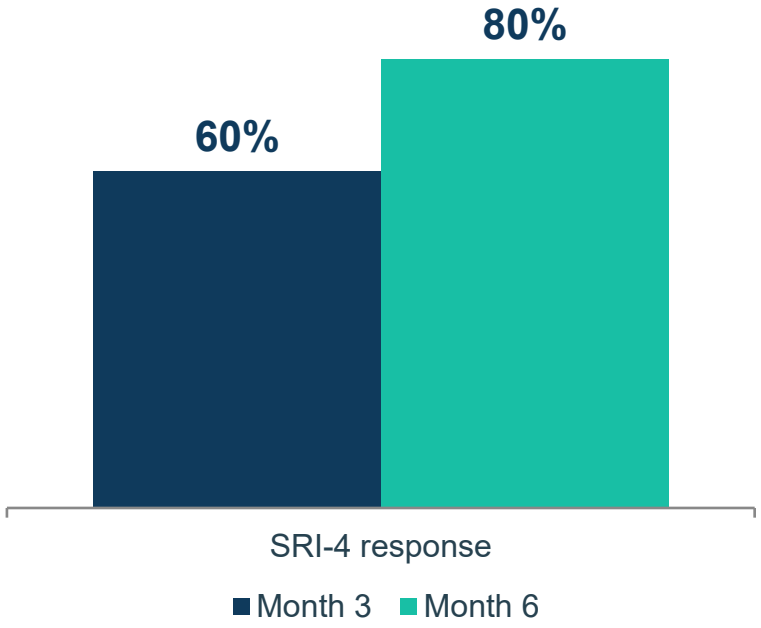
Confidence: very low

Toxicity limited to grade 1

Confidence: very low

Chinese trial: SRI-4 response in 12 of 15 at month 6

SRI-4 response, 15 patients with SLEDAI-2K ≥ 4



- 9/15 at month 3, 12/15 at month 6
- 1 low disease activity; 2 non-responders
- 3 low-activity patients met DORIS
- Median follow-up 10.2 months; 1 relapse off immunosuppressants
- *SRI-4 = SLE responder index: ≥ 4-point drop in SLEDAI-2K, no worsening elsewhere*

18
patients, 15 of them children

72%
grade 1 CRS

17%
neurotoxicity

0
dose-limiting toxicity

SRI-4 in 12/15 at month 6, off immunosuppressants — Confidence: low

Mostly grade 1 CRS (72%) — Confidence: low

Children are not small adults: genes, growth, fertility

Phenotype

- More aggressive disease, higher activity
- Greater cumulative glucocorticoid exposure

Genetics

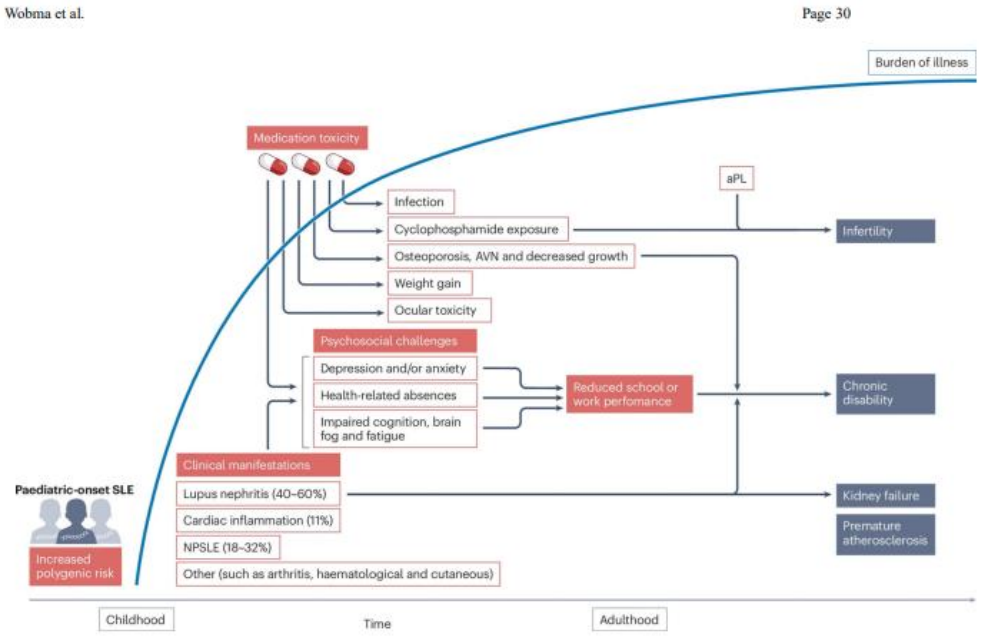
- Monogenic causes in 3.5–7% of cSLE [13–15]
- May modulate efficacy and relapse

Immune development

- Vaccine antibodies largely persist (long-lived plasma cells spared) [2, 3]
- Vaccination paused during B-cell aplasia; IgG monitoring

Life course

- Gonadotoxic lymphodepletion: fertility preservation
- Adult SLE women: no ovarian reserve signal [16]; NEJM
- 14 pregnancies, 8 healthy newborns, gonadal safety unproven [41]
- Growth, puberty, school, psychosocial burden



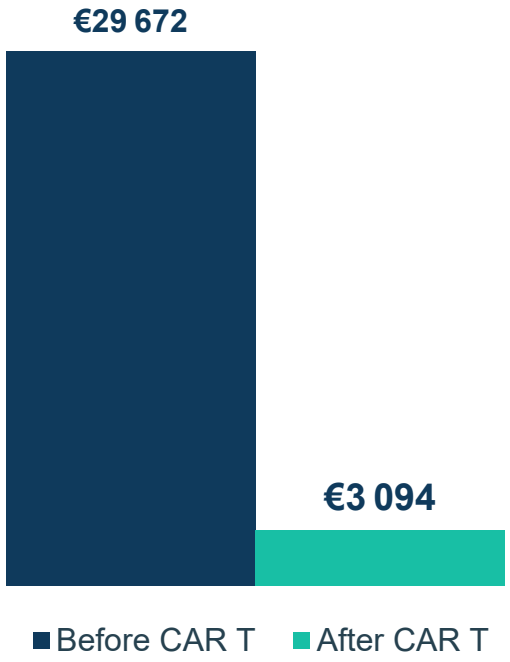
Burden of illness across the life course in pediatric-onset SLE. Source: Wobma et al. 2025 [29]

Monogenic causes in 3.5–7% of cSLE — Confidence: moderate

Vaccine antibodies persist; fertility data from adults only — Confidence: low

CAR T cut adult costs by about 90%; no pediatric data yet

Adults (Germany): annual direct costs per patient



≈ 90%

lower annual costs
€29,672 → €3,094

SF-36 physical
22.4% → 75.5%
SF-36 mental
24.7% → 63%
SF-36 = quality-of-life survey

Annual direct healthcare costs, before vs after; n = 8; manufacturing/administration not included [17]

Children (United States): cost of cSLE care

$14,944

direct cost/year (2001–04); excl. outpatient meds

$30,908

cost/QALY of cSLE care (not a CAR-T ICER)

"more costly" than adult SLE; no ratio reported [18]

Not yet modeled in children. A favorable cost per QALY is plausible given decades of avoided care, but remains a hypothesis.

About 90% lower direct costs in 8 adults

Confidence: very low

In adults, CRS is mostly mild, but IEC-HS has proved fatal

Mostly grade 1

CRS

- Erlangen: 10/15 grade 1, 1/15 grade 2 [3]
- CASTLE: no CRS > grade 2, no ICANS (n = 24) [4]

New, organ-specific

LICATS

- ***Local immune effector cell-associated toxicity syndrome***
- 30/39 patients (77%), onset ~ day 10 [19]
- In organs already affected
- Mostly grade 1–2; all resolved

Oncology signal

Late risks

- Secondary T-cell malignancies: FDA class warning, 2024 [26]
- No autoimmune case data yet

Fatal, 2026

IEC-HS

- Novartis: 8 rap-cel trials halted after 3 deaths [20]
- BMS: zola-cel enrollment paused [20]
- Trade press only; causes under review

CRS mostly grade 1 in autoimmune disease — Confidence: moderate

Fatal IEC-HS in 2026 adult trials — Confidence: very low

Toxicity management is borrowed from oncology

Grade	CRS	ICANS	IEC-HS
G1	Supportive care; tocilizumab if fever > 3 days or high risk	ICE monitoring; supportive care ± levetiracetam	ASTCT consensus grading available (2023; updated 2026)
G2	Tocilizumab 8 mg/kg (max 800 mg); dexamethasone if no response at 24 h	Dexamethasone 10 mg IV q6h	High-dose corticosteroids + anakinra
G3	Tocilizumab + dexamethasone 10 mg q6h; ICU	High-dose corticosteroids, antiseizure drugs; ICU	Refractory: ruxolitinib, then etoposide
G4	Tocilizumab + methylprednisolone 1 g/day; anakinra if refractory	Methylprednisolone 1 g/day × 3 days	Track ferritin, fibrinogen, cytopenias

Children / developmental delay: use the Modified ICE (M-ICE), not the CAPD (ASTCT 2026) [22]

ICANS: tocilizumab only if CRS coexists. All regimens extrapolated from oncology; no autoimmune or pediatric protocol.

Regimens extrapolated from oncology guidelines

Confidence: low

IEC-HS looks like MAS, a syndrome we know well

IEC-HS after CAR T (ASTCT 2023)

- Elevated or rapidly rising ferritin (required)
- With cytopenias, low fibrinogen, transaminitis, hemophagocytosis
- Exclude infection and active CRS; often late after CRS
- Treated with corticosteroids + anakinra

≈

Macrophage activation syndrome

- Hyperferritinemia, cytopenias, low fibrinogen
- Liver injury, hemophagocytosis
- Complicates sJIA and cSLE
- Treated with corticosteroids + anakinra

Hypothesis: children with prior MAS, or an HLH-prone genetic background, may carry a higher IEC-HS risk. Untested.

Higher IEC-HS risk after prior MAS

Confidence: very low

Six reasons for caution in pediatric rheumatology

1

26 pediatric patients

No controlled trial; two series carry 23

2

Cohort-level safety only

CRS and ICANS rarely reported patient by patient

3

Age-dependent tools

ICE vs M-ICE: neurotoxicity not comparable across ages

4

Hyperinflammation-prone hosts

cSLE, prior MAS, inborn errors of immunity: IEC-HS risk unknown

5

Decades of follow-up needed

Growth, puberty and gonads in no series; malignancy surveillance

6

Adult signals unresolved

Causes of the 2026 IEC-HS deaths still under review

Pediatric safety profile not established

Confidence: very low

Treat children only in trials, expert centers and registries

1

Select

Trials or hospital exemption, in qualified centers pairing pediatric rheumatology and a CAR T team

2

Prepare

discuss fertility preservation, vaccination review, baseline growth and puberty

3

Grade and report

ASTCT 2026 criteria (M-ICE in children), patient-level toxicity data

4

Follow for years

registries: growth, puberty, fertility, IgG, secondary malignancy

EBMT-ISCT-JACIE 2026 consensus now covers pediatric indications: patient selection, management, follow-up and immune monitoring [25].

Expert consensus covers pediatric use

Confidence: low

Who should benefit? Spot complex trajectories early

What CAR T costs a child

- Leukapheresis, weeks of manufacturing
- Fludarabine + cyclophosphamide 1,000 mg/m², gonadotoxic [2]
- Hospital stay, ICU access, qualified center
- B-cell aplasia ≈ 4 months (112 ± 47 days) [3]
- Years of follow-up [25]

benefit must outweigh burden

Signals of a complex trajectory

Clinical	**Pediatric SLE:** nephritis 40–60%, NPSLE 18–32% [29]; damage accrues without plateau, faster after life-threatening onset [37]
Serology	**JDM:** anti-MDA5 in 7.4%, a distinct phenotype with skin ulcers and ILD [38]
Molecular	**Blood transcriptome, 158 children:** plasmablast signature tracks activity, neutrophil signature tracks nephritis; 7 patient groups [39]
Genetic	**Monogenic lupus forms 3.5–7%:** response to CD19 depletion unknown [13–15]

The challenge: identify the child who will be refractory before damage accrues, not after the fifth line. Candidate markers still need prospective pediatric validation.

Early severe features predict damage accrual — Confidence: low

No validated predictor of refractoriness yet — Confidence: very low

· [2] Mackensen 2022 · [3] Müller 2024 · [25] Greco 2026 · [29] Wobma 2025 · [37] Lim 2017 · [38] Tansley 2014 · [39] Banchereau 2016 · [13–15]

Pediatric trials are multiplying, with uneven maturity

Lupus (cSLE, LN)

Largest portfolio

REACT-01 · NCT06465147
CD19 auto · P1 · 2–30 y* · Seattle
RECRUITING

CHOP · NCT06839976
CD19 auto · P1/2 · 10–29 y · Philadelphia
RECRUITING

Descartes-08 · NCT07089121
BCMA mRNA · P1/2 · ≥ 12 y · USA
RECRUITING

SNUH · NCT07855302
CD19 auto · P1 · ≤ 25 y · Seoul
NEW · OCT 2026

Juvenile dermatomyositis

Most advanced: phase 2/3

RESET-Myositis · NCT06154252
Rese-cel · P2/3 · ≥ 6 y · USA, Europe
RECRUITING

NCT06569472
CD19 auto · P1 · 5–17 y · Hangzhou
RECRUITING

NCT06686524
CD19 UCAR-T · P1 · ≥ 5 y · Hangzhou
RECRUITING

NCT07184450
BCMA/CD70 · P1 · ≥ 5 y · JDM, SSc, pJIA, pSS
RECRUITING

Juvenile systemic sclerosis

Least mature

NCT06792344
CD19 auto · P1 · 5–18 y · Hangzhou
SUSPENDED

NCT07184450
BCMA/CD70 · P1 · ≥ 5 y · includes SSc
RECRUITING

RD06-05 · NCT07674147
CD19/BCMA universal · early P1 · 5–20 y
NOT YET OPEN

CAR product in pink. auto = autologous; UCAR-T = allogeneic (donor cells); mRNA = transient expression; rese-cel, obe-cel, zola-cel = CD19 CAR T products.

One registered trial with children has published results (Shan 2026); most have not

Confidence: high

Most lupus trials open to children are in China



Registry corrections: NCT06839976 is in Philadelphia (USA), not UK or China; NCT07432334 is in Hanoi only.

First pediatric phase 3

NCT06904729: lupus nephritis, 6–18 y, open-label, two doses, Guangzhou (recruiting)

Europe

CARLYSLE (obe-cel): from 12 y, UK, not recruiting.
Zola-cel: from 16 y, incl. France, not recruiting since the BMS pause

China

Most trials accept children from age 3–6, including allogeneic and BCMA-based products

One pediatric phase 3 (open-label, lupus nephritis) is recruiting

Confidence: high

New products are coming, but none has pediatric results

Targets and formats in pediatric trials

CD19 autologous
Reference; most pediatric trials

CD19 allogeneic (UCAR-T)
Off-the-shelf donor cells

BCMA mRNA CAR T
Transient expression (Descartes-08)

CD19/BCMA, BCMA/CD70
Dual targets, deeper reset

Next platform: in vivo CAR T

1. **Targeted lipid nanoparticles** carry the CAR gene
2. **CAR T cells made inside the patient** no leukapheresis or ex vivo manufacturing
3. **First refractory SLE patients treated, 2025 [34]** data limited to a letter

No pediatric results for non-CD19 products Confidence: very low

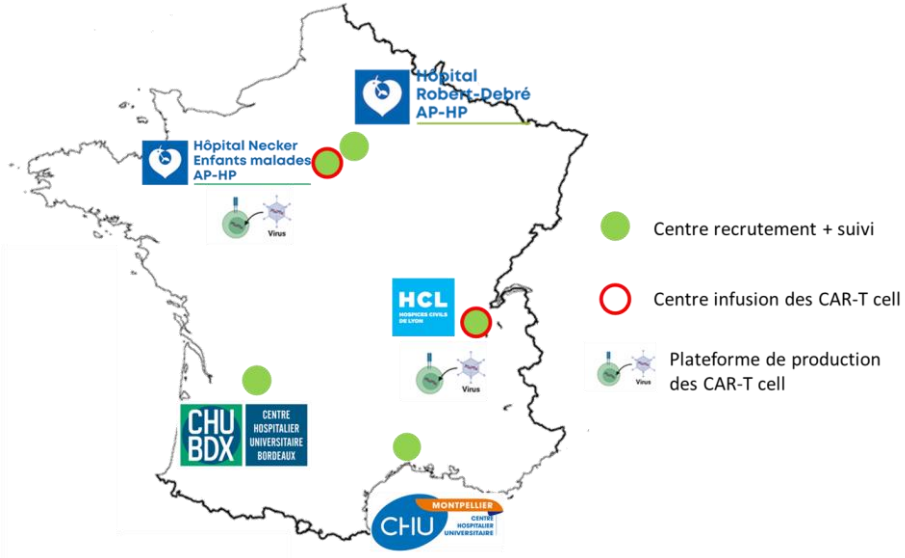
In vivo CAR T in lupus: first cases only Confidence: very low

France: no pediatric trial open yet, CARES in preparation

CARES · IN PREPARATION

Anti-CD19 CAR T in adolescents with severe, refractory SLE

- PI: A. Belot (Hospices Civils de Lyon)
- 5 centers (CRMR and CCMR RAISE, incl. Montpellier); 2 infusion centers
- 2 academic production sites (HCL, Necker), MB-CART19.1 platform
- IMP dossier in preparation; not yet registered



Regulation and pathway

Arrêté of 28 June 2024: autologous CAR T restricted to qualified centers, written before rheumatology indications; infusion through hematology, multi-site pathway [35]

No pediatric access open today

FT819: French arm ended 21 Jul 2026 [28] · SCLEROCAR: 18–64 y · zola-cel: ≥ 16 y, not recruiting

No pediatric CAR T trial open in France

Confidence: moderate

[36] A. Belot, CARES (personal communication; map courtesy of the author) · [35] Arrêté 28 June 2024 · [27] ClinicalTrials.gov · [28] CTIS

KEY MESSAGES

Eight messages to take home

1. Adults: disease-specific efficacy in 22/24; all 24 off immunosuppressants at week 24
2. Children: consistent but uncontrolled signal in 26 unique pediatric patients
3. CRS is mostly grade 1 in autoimmune disease
4. Fatal IEC-HS in 2026 adult trials (trade press)
5. Children differ: genetics, growth, fertility, vaccination
6. Toxicity management extrapolated from oncology
7. Pediatric trials multiplying; CARES in preparation in France
8. Treat only in trials or hospital exemption, expert centers, long follow-up

C3i: a club to advance innovative immunotherapies in IMIDs

C3i CLUB DES IMMUNOTHÉRAPIES INNOVANTES DANS LES IMIDS

OUR MISSION

Physicians, researchers, pharmacists and other experts pooling their skills to advance innovative immunotherapies in immune-mediated inflammatory diseases

110
members

16
multidisciplinary working groups

Understand 1
Immunological mechanisms, linking biological questions to clinical stakes

Evaluate 2
Scientific data: methodological quality and open questions

Exchange 3
Clinical perspectives, compared across specialties

www.club-c3i.fr
Contact: maurine.jouret@chu-lyon.fr (secretary)

Scan to visit and join the club

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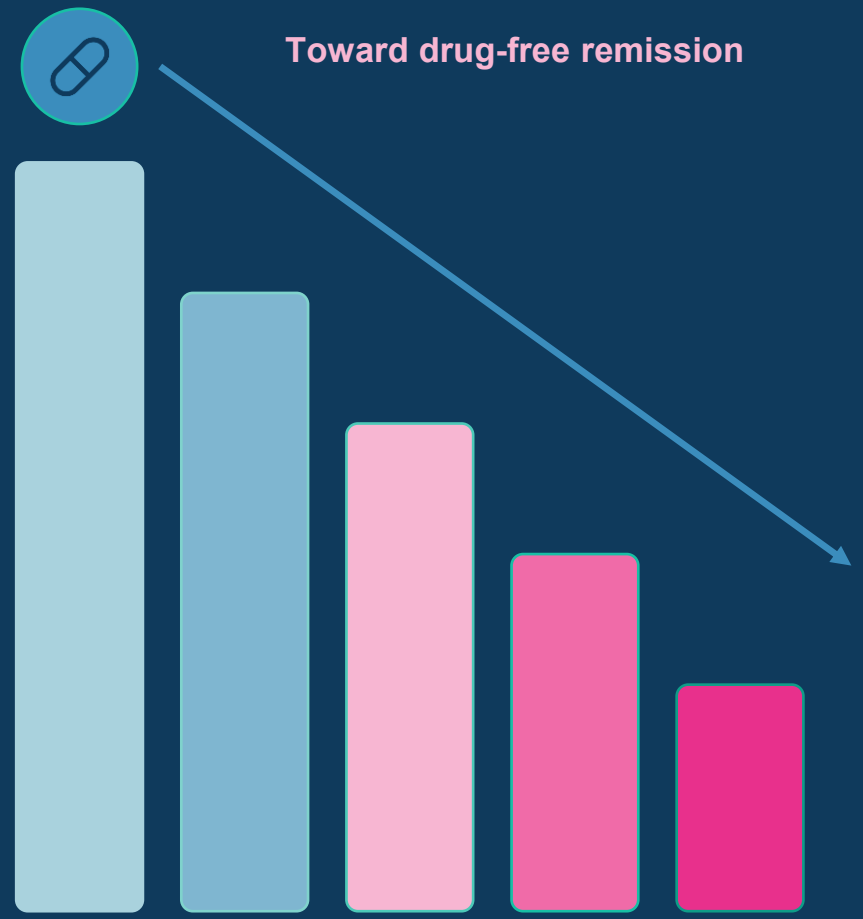
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THANK YOU · QUESTIONS

CAR T may spare children decades of immunosuppression, if we stay cautious



Prospective pediatric trials, harmonized definitions, patient-level safety reporting, long-term growth and fertility follow-up.

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