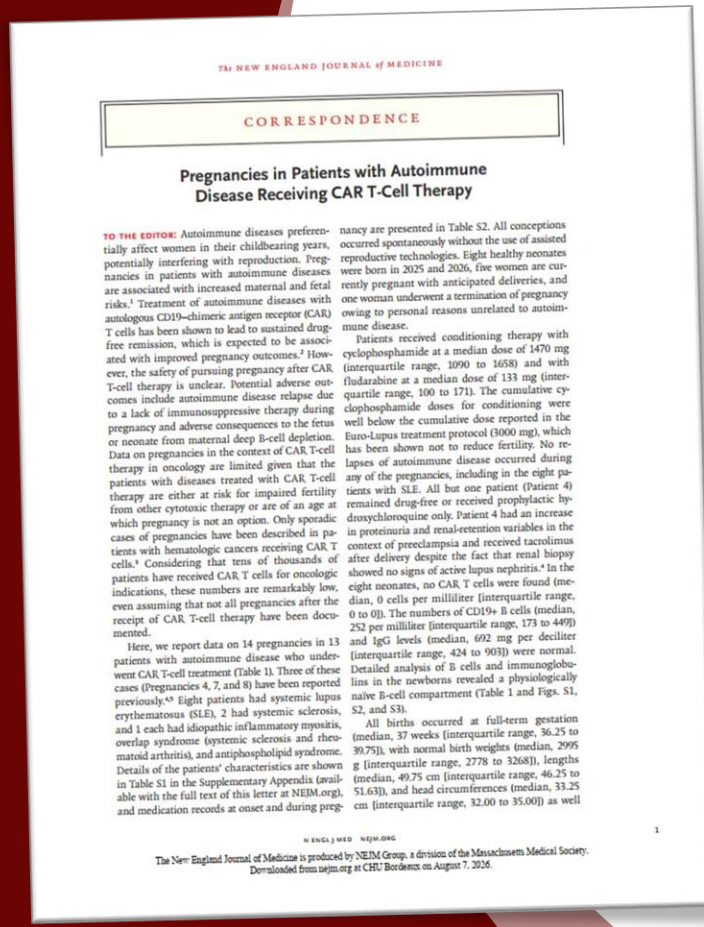

THE NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Pregnancies in Patients with Autoimmune Disease Receiving CAR T-Cell Therapy

TO THE EDITOR: Autoimmune diseases preferentially affect women in their childbearing years, potentially interfering with reproduction. Pregnancies in patients with autoimmune diseases are associated with increased maternal and fetal risks.[1] Treatment of autoimmune diseases with autologous CD19–chimeric antigen receptor (CAR) T cells has been shown to lead to sustained drug-free remission, which is expected to be associated with improved pregnancy outcomes.[2] However, the safety of pursuing pregnancy after CAR T-cell therapy is unclear. Potential adverse outcomes include autoimmune disease relapse due to a lack of immunosuppressive therapy during pregnancy and adverse consequences to the fetus or neonate from maternal deep B-cell depletion. Data on pregnancies in the context of CAR T-cell therapy in oncology are limited given that the patients with diseases treated with CAR T-cell therapy are either at risk for impaired fertility from other cytotoxic therapy or are of an age at which pregnancy is not an option. Only sporadic cases of pregnancies have been described in patients with hematologic cancers receiving CAR T cells.[3] Considering that tens of thousands of patients have received CAR T cells for oncologic indications, these numbers are remarkably low, even assuming that not all pregnancies after the receipt of CAR T-cell therapy have been documented.

Here, we report data on 14 pregnancies in 13 patients with autoimmune disease who underwent CAR T-cell treatment (Table 1). Three of these cases (Pregnancies 4, 7, and 8) have been reported previously.[4,5] Eight patients had systemic lupus erythematosus (SLE), 2 had systemic sclerosis, and 1 each had idiopathic inflammatory myositis, overlap syndrome (systemic sclerosis and rheumatoid arthritis), and antiphospholipid syndrome. Details of the patients' characteristics are shown in Table S1 in the Supplementary Appendix (available with the full text of this letter at NEJM.org), and medication records at onset and during pregnancy are presented in Table S2. All conceptions occurred spontaneously without the use of assisted reproductive technologies. Eight healthy neonates were born in 2025 and 2026, five women are currently pregnant with anticipated deliveries, and one woman underwent a termination of pregnancy owing to personal reasons unrelated to autoimmune disease.

Patients received conditioning therapy with cyclophosphamide at a median dose of 1470 mg (interquartile range, 1090 to 1658) and with fludarabine at a median dose of 133 mg (interquartile range, 100 to 171). The cumulative cyclophosphamide doses for conditioning were well below the cumulative dose reported in the Euro-Lupus treatment protocol (3000 mg), which has been shown not to reduce fertility. No relapses of autoimmune disease occurred during any of the pregnancies, including in the eight patients with SLE. All but one patient (Patient 4) remained drug-free or received prophylactic hydroxychloroquine only. Patient 4 had an increase in proteinuria and renal-retention variables in the context of preeclampsia and received tacrolimus after delivery despite the fact that renal biopsy showed no signs of active lupus nephritis.[4] In the eight neonates, no CAR T cells were found (median, 0 cells per milliliter [interquartile range, 0 to 0]). The numbers of CD19+ B cells (median, 252 per milliliter [interquartile range, 173 to 449]) and IgG levels (median, 692 mg per deciliter [interquartile range, 424 to 903]) were normal. Detailed analysis of B cells and immunoglobulins in the newborns revealed a physiologically naïve B-cell compartment (Table 1 and Figs. S1, S2, and S3).

All births occurred at full-term gestation (median, 37 weeks [interquartile range, 36.25 to 39.75]), with normal birth weights (median, 2995 g [interquartile range, 2778 to 3268]), lengths (median, 49.75 cm [interquartile range, 46.25 to 51.63]), and head circumferences (median, 33.25 cm [interquartile range, 32.00 to 35.00]) as well

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Veille bibliographique

Grossesses chez les patientes atteintes d'une maladie auto-immune recevant une thérapie par cellules CAR-T

Georg Schett, Andreas Wirsching, Tobias Rothe, Vanessa Visconti, Neil Kramer, Markus Metzler, Tobias Krickau, Gregory W. Kirschen, Daphne Landau, Caitlin Elgarten, Vikas Majithia, Ellen De Langhe, Peter Vandenberghe, Britta Maurer, Zahir Amoura, David Simon, Gerhard Krönke, Peter Gergely, Melissa Fernandes, Tamas Shisha, Brandon M. Law, Ashley Koegel, David J. Chang, Andreas Mackensen, Fabian Müller, and Melanie Hagen

Schett G. *et al.*; NEJM. 2026 Aug 8;395

CAR-T cells et grossesse : pourquoi la question se pose ?

Série de cas internationale — 14 grossesses chez 13 patientes traitées pour des maladies auto-immunes réfractaires

Contexte

- Maladies auto-immunes = femmes jeunes ; grossesse à risque maternel et fœtal accru
- Les CAR-T cells anti-CD19 induisent des rémissions prolongées sans traitement de fond, situation a priori favorable à une grossesse
- Mais 3 inconnues : rechute sans immunosuppression ? conséquences fœtales de la déplétion B maternelle ? fertilité après lymphodéplétion ?
- En oncologie, quasi aucune donnée (fertilité déjà altérée, âge)

Population

- 14 grossesses / 13 patientes : 8 lupus, 2 sclérodermies, 1 myosite, 1 chevauchement, 1 SAPL
- Maladie réfractaire avec atteinte d'organe sévère (0,8 à 17 ans d'évolution), après échec de multiples lignes dont rituximab et bélimumab
- Allemagne, États-Unis, Belgique, Chine, Suisse, France

Traitement

- CAR T autologues de 2e génération anti-CD19 (zorpo-, zola-, rap-, rese-, mivo-cabtagène) ou composé CD19/BCMA
- Lymphodéplétion : cyclophosphamide 1 470 mg (médiane) + fludarabine 133 mg, bien en deçà des 3 000 mg de l'Euro-Lupus

Schett G. et al.; NEJM. 2026 Aug 8;395

Caractéristiques de la population à l'inclusion

N°	Maladie	Âge	Produit CAR T	Délai → conception (mois)	LB CD19+ (/mL)	CAR T (/mL)	Terme (SA)	Issue
1	LES	17	Zorpo-cel	18	0	0	39	Naissance
2	LES	22	Zorpo-cel	42	334	0	37	Naissance
3	SAPL	29	Zorpo-cel	1	0	52	36	Naissance
4	LES	30	Zola-cel	2	0	0	37	Naissance *
5	LES	26	Rese-cel	3	> 0	0	37	Naissance *
6	LES	21	Zola-cel	2	0	0	40	Naissance
7	LES	24	CD19-BCMA	6	350	> 0	40	Naissance
8	LES	24	CD19-BCMA	21	312	0	32	Naissance
9	ScS	29	Zola-cel	3	312	0	36	En cours
10	LES	32	Rap-cel	22	296	0	28	En cours
11	LES	35	Rap-cel	19	27	0	25	En cours
12	Chev.	33	Miv-cel	21	260	0	15	En cours
13	Myosite	32	Miv-cel	18	200	0,7	14	En cours
14	ScS	29	Zorpo-cel	15	495	0	7	IVG †

*LES : lupus ; SAPL : syndrome des antiphospholipides ; ScS : sclérodermie ; Chev. : chevauchement. * prééclampsie (n° 4) ou HTA (n° 5). † interruption pour motif personnel.*

À retenir

- Conceptions toutes spontanées, sans AMP
- Délai médian CAR T → conception : 18 mois (1–42)
- Aucune rechute pendant les 14 grossesses
- Sans traitement de fond ou hydroxychloroquine seule
- Complications : 1 prééclampsie, 1 HTA, 1 nausées

Schett G. et al.; NEJM. 2026 Aug 8;395

Les nouveau-nés : profil rassurant

8 naissances (5 grossesses en cours)

- Terme médian 37 SA (IQR 36–40), une naissance à 32 SA
- Poids 2 995 g, taille 49,8 cm, PC 33,3 cm (médianes)
- Apgar ≥ 9 chez tous (10 chez 6 des 8 nouveau-nés)
- Aucune cellule CAR T détectable dans le sang de cordon
- Lymphocytes B CD19+ normaux (médiane 252/mL), compartiment naïf physiologique (90–97 %)
- IgG normales (médiane 692 mg/dL) ; IgA et IgM basses, comme chez tout nouveau-né
- Aucune infection néonatale ; développement normal (suivi 1–18 mois) ; allaitement chez toutes

Limites et perspectives

- Série de cas non consécutive, effectif limité, biais de déclaration possible
- Recul néonatal court (1 à 18 mois) ; 5 grossesses encore en cours
- Délai optimal perfusion → conception non défini
- Effet de la lymphodéplétion sur la réserve ovarienne non évalué

→ Registre prospectif des grossesses et études endocriniennes nécessaires

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