

## CAR T-cell activity for autoimmune diseases across EBMT centers: an international survey on behalf of the Autoimmune Diseases Working Party and the Cellular Therapy and Immunobiology Working Party

by Giorgio Orofino, Raffaella Greco, Manuela Badoglio, Pascale Ambron, Marco Becilli, Stefania Bramanti, Thomas Pabst, Dominique Farge, Edouard Forcade, Laimonas Griškevičius, Joerg Henes, Inken Hilgendorf, Ben-Niklas Baermann, Mi Kwon, Franco Locatelli, Lucía López Corral, John Moore, Dimitrios Mougiakakos, Arnon Nagler, Antonio Perez-Martinez, Mathieu Puyade, Nuria Martinez-Cibrian, Bastian von Tresckow, Simona Sica, David Simon, Ludovic Gabellier, Pere Barba, Ibrahim Yakoub-Agha, Alberto Mussetti, Jurgen Kuball, Fabian Müller, Elisa Roldan Galvan, Florent Malard, Tobias Alexander and Annalisa Ruggeri

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**CAR T-cell activity for autoimmune diseases across EBMT centers: an international survey on behalf of the Autoimmune Diseases Working Party and the Cellular Therapy and Immunobiology Working Party**

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*Data availability statement:* All data of the study are deposited in the EBMT database, and are available on request from the corresponding author, Raffaella Greco (greco.raffaella@hsr.it).

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Chimeric antigen receptor (CAR) T-cell therapy has become an established treatment for patients with B-cell and plasma cell malignancies, with several products approved worldwide for a range of hematologic cancers <sup>1</sup>. More recently, the therapeutic potential of CAR T-cells has expanded into autoimmune diseases (ADs) <sup>2</sup>. A single administration of CAR T-cells targeting B and/or plasma cell antigens can induce remarkable clinical responses in patients with severe, refractory autoimmune conditions, including systemic lupus erythematosus (SLE), systemic sclerosis (SSc), and other difficult-to-treat immune-mediated disorders, in both adult <sup>2,3</sup> and pediatric populations <sup>4,5</sup>; these responses have been associated with sustained clinical remission across multiple severe ADs <sup>6</sup>.

Unlike B-cell targeting with monoclonal antibodies, CAR-T cell therapies induce a deeper remodeling of lymphoid tissues: depleting B cells not only in the blood, but also within lymph-nodes, bone marrow and inflamed tissues <sup>7,8</sup>.

Moreover, CAR T-cell therapy has also been explored as a treatment for autoimmune neurological diseases, including multiple sclerosis (MS) <sup>9,10</sup> and neuromyelitis optica spectrum disorders (NMOSD) <sup>11</sup>, as well as further hematological and pediatric applications <sup>2,4,12</sup>.

Notably, CAR T-cells show similar expansion in ADs and hematological malignancies, but causes less severe toxicity and faster immune recovery, likely reflecting distinct inflammation, products containing fewer terminally differentiated T-cells, and better baseline hematologic reserve <sup>13</sup>. As the number of treated patients increases, new specific toxicities such as LICATS (Local Immune Effector Cell-Associated Toxicity Syndrome) have been described, typically affecting organs previously involved by the underlying AD <sup>14</sup>.

While interest in CAR T for ADs continues to grow, and centers currently developing CAR T-cell therapies are progressively adapting their clinical infrastructures and care pathways to support the anticipated expansion of indications beyond hematologic malignancies, the real-world landscape of how centers are preparing for and implementing this approach remains incompletely characterized. Cellular therapies in ADs present unique clinical and organizational challenges compared to their use in hematologic malignancies, but these can be reduced by relying on the established expertise of specialized centers experienced in autologous and allogeneic hematopoietic cell transplantation (auto- and allo-HCT) in patients with ADs <sup>12</sup>. In particular, the management of these patients requires close collaboration among multiple specialties, including hematologists with experience in HCT and cellular therapies, immunologists, rheumatologists, neurologists and other disease specialists, supported by specialized nursing staff and advanced cell-processing and monitoring facilities <sup>15</sup>. Indeed, given that CAR T for autoimmune diseases remains an emerging and largely experimental field, assessing current institutional structures, clinical workflows, and real-world practice variation is essential to define the existing landscape across centers and countries, including differences in patients' access to active clinical trials or programs across different healthcare systems.

To address this knowledge gap, we conducted a cross-sectional survey on behalf of, and approved by, the Scientific Board of the Autoimmune Disease Working Party (ADWP) and the Cellular Therapy and Immunobiology Working Party (CTIWP) of the EBMT distributed from October 2025 to March 2026. The survey questionnaire was developed and reviewed by an interdisciplinary team with expertise in HCT, cellular therapies, ADs, and survey methodology, and included structured items grouped into predefined domains covering center characteristics, organizational models, clinical workflows, CAR T-cell activity, procedural aspects, and areas of consensus or heterogeneity. In particular, the survey was designed to capture inter-center variability and to identify areas of emerging convergence, as well as domains where consensus is still lacking. Data were collected according to EBMT rules. All patients or their legal guardians provided written informed consent for data collection and analysis in accordance with the Declaration of Helsinki, and with the centers' ethical research guidelines.

The survey was electronically distributed to 558 EBMT affiliated centers. Overall, we received 170 answers from the centers regarding the activity of CAR T cells for AD, resulting in a 30% overall response rate. Of these, 31 centers had already initiated CAR T-cell therapy for AD indications between 2021-2026 and provided data, while 42 others reported plans to start within 2026, with

reponses spanning most of the surveyed countries (Figure 1A). Among those 170 centers, 104 (61%) agreed to complete the survey online via the electronic system and were included in the main survey analyses.

Of the 104 centers responding to the full questionnaire, most already performed auto HCT in AD (63/104 centers, 61%), and 50 centers (48%) confirmed that they were performing or planning to start CAR T cell therapy for ADs and were included in the analysis; among those, 24 centers had already initiated CAR-T cell activity for ADs: rheumatological and neurological conditions were the most commonly targeted diseases. Specifically, 39% (9/24 centers) of the 24 centers responding to the questionnaire performing CAR T cell for ADs reported activity in both rheumatological and neurological ADs, while 35% (8/24 centers) reported treating rheumatological ADs only, 17% (4/24 centers) reported to treat rheumatological, neurological and hematological ADs and 9% (2/24 centers) reported to treat all indications including gastro-intestinal ADs (Figure 1B).

The majority of treatments in centers already active or planned to be active (50 centers) were conducted within clinical trials, reported by 69% of the centers. Additional 11% of the centers used CAR T cells under compassionate use/hospital exemption programs, while 10/50 centers (20%) reported utilizing both approaches (Figure 1C).

Regarding the product type, 30 of the 50 responding (60%) centers with CAR T activity for ADs used commercial products, 18% (9/50 centers) used academic products only, and 12% (6/50 centers) reported using both academic and commercial products. Autologous CAR T-cell products were most commonly available (74%, 37/50 centers), though some centers had or will have access to both autologous and allogeneic products (18%, 8/50 centers). Among the centers that have already started the activity of CAR T in ADs responding to the survey (24 centers), follow-up was organized through a multidisciplinary approach in 52% of centers (12/24 centers), whereas 43% (10/24 centers) reported parallel separate visits with hematologists and AD specialists, while 5% of centers did not define their policy yet. The follow-up schedule varied across centers: 39 % followed the same schedule as for hematologic diseases (9/24 centers), 43 % (10/24 centers) reported that the schedule depended on the type of AD and individual patient characteristics, and smaller proportions reported more frequent (8 %, 2/24 centers) or less frequent (4 %, 1/24 center) follow-up. Disease status re-evaluation during follow-up was managed by the AD specialist in most centers, (12/24 centers, 50%), while a joint discussion between the haematologist and the AD specialist on a per-patient basis was reported by 9/24 centers (37%); the remaining centers had not yet defined a policy. The duration of haematological follow-up varied considerably across centers: it was limited to the first 6 months after infusion in 9% (2/24 centers), to the first 2 years in 9% (2/24 centers) and to the first 5 years in 4.5% (1/24 center), after which patients were followed by the AD specialist alone, whereas 50% (12/24 centers) scheduled at least one yearly haematological visit indefinitely; 27% (6 centers) had not yet defined a policy. Moreover, multidisciplinary management<sup>15</sup>, was common, with 48% (11/24 centers) reporting periodic multidisciplinary meetings and 50 % (12/24 centers) discussing patients on a case-by-case basis. Among the 50 centers that started or planned to start their activity, CD19 was the predominant target antigen (87% of 50 centers), followed by BCMA, CD19/CD20, or CD19/CD22 (Figure 1D). The most frequently used co-stimulatory domains were 4-1BB and CD28 (61% and 23%, respectively of the 50 centers), while 16% of the 50 centers used either 4-1BB or CD28 (Figure 1E). Lymphodepletion regimens largely mirrored those used in hematologic settings, with the majority of centers, 36/50 centers combining fludarabine and cyclophosphamide, according to the institutional guidelines and clinical trial indications; only a small proportion of centers reported incorporating busulfan or bendamustine into their lymphodepleting regimens. Overall, responses revealed emerging common practice patterns together with relevant inter-center variability in several clinical, organizational, and procedural domains. A total of 161 patients with ADs were reported to

have received treatment in this survey, including five (3%) with concurrent hematologic malignancies (Figure 2). One center alone accounted for 63 treated patients (39%). The main indication was SLE, accounting for 36% of patients (58), followed by SSc for 21% of patients (34), and inflammatory myositis for 15% of patients (24). Other indications included multiple sclerosis (15 patients), rheumatoid arthritis (9 patients), and myasthenia gravis (5 patients). Less common conditions were NMOSD (3 patients), Stiff Person Syndrome (2 patients) and vasculitis (1 patient). Additionally, there were 10 patients (6%) with other unspecified autoimmune indications. This multinational EBMT survey provides the first broad overview of the rapidly evolving adoption of CAR T-cell therapy for ADs. The field is expanding rapidly, with a growing number of centers initiating programs and exploring CAR T-cell use across a range of indications, particularly in rheumatological, neurological and more recently hematological AD disorders. This trend reflects increasing clinical interest and the encouraging results emerging from early clinical experiences. As this therapeutic strategy develops, several key aspects will require careful definition, in particular standardization of indications and clear criteria for patient selection will be crucial to ensure that CAR T-cell therapy is used appropriately. This study has some limitations, including its survey-based design and a relatively low response rate of 30%. In line with similar studies, detailed information on patient selection, response assessment, supportive care, and lymphodepletion dosing was not systematically collected. Nevertheless, the survey captures the current EBMT landscape of CAR T-cell activity for ADs, including centers known to be active in this field within the network. Given the complexity of CAR T-cell therapy, its early implementation in ADs is likely to remain concentrated in high-volume centers with established cellular therapy programs, dedicated infrastructures, and expertise in patient monitoring and toxicity management—a factor that should be considered when interpreting the present findings. Moreover, this survey reflects that the majority of patients have access to this treatment mainly within clinical trials or compassionate use, predominantly in Western Europe. This currently restricts broader application to patients with ADs who may specifically benefit from cellular therapies<sup>6,12,15</sup>. Although the questionnaire was not designed to capture barriers to implementation, in our view access remains a major structural barrier, since treatment availability still depends largely on the availability of clinical trials or compassionate-use programmes and on protocol-defined eligibility criteria. Variability was particularly evident in the organization of follow-up, which was conducted either through multidisciplinary clinics or through parallel visits by AD specialists and hematologists. Differences were also observed in disease reassessment, which was managed primarily by AD specialists in approximately half of centers, while a shared approach was adopted on a case-by-case basis in a smaller proportion. The greatest heterogeneity concerned the duration of haematological follow-up, ranging from 6 months to continued annual assessments, with nearly one third of centers reporting no predefined policy. These findings highlight the need for greater harmonization of long-term follow-up strategies. In fact, given the complexity of ADs and the potential for immune-related complications, multidisciplinary management and structured long-term follow-up will be essential. Systematic data collection and bio-banking collection through large multinational registries will play a central role in evaluating outcomes, safety, and durability of responses, guiding responsible development of this approach and supporting its broader clinical implementation.

## References

1. Zugasti I, Espinosa-Aroca, Lady, Fidyk K, et al. CAR-T cell therapy for cancer: current challenges and future directions. *Signal Transduct Target Ther*. 2025;10(1):210.
2. Müller F, Taubmann J, Bucci L, et al. CD19 CAR T-Cell Therapy in Autoimmune Disease - A Case Series with Follow-up. *N Engl J Med*. 2024;390(8):687-700.
3. Müller F, Hagen M, Wirsching A, et al. CD19 CAR-T cells for treatment-refractory autoimmune diseases: the phase 1/2 CASTLE basket trial. *Nat Med*. 2026;32(3):1142-1151.
4. Becilli M, Metzler M, Bracaglia C, et al. Anti-CD19 CAR T cells for pediatric patients with treatment-refractory autoimmune diseases. *Nat Med*. 2026;32(3):1105-1117.
5. París-Muñoz A, Alcobendas-Rueda RM, Verdú-Sánchez C, et al. CD19 CAR-T cell therapy in a pediatric patient with MDA5+ dermatomyositis and rapidly progressive interstitial lung disease. *Med*. 2025;6(8):100676.
6. Kayser S, Nagler A. CAR T cells and T cell engagers for autoimmunity-lessons from hematology. *Bone Marrow Transplant*. 2026;61(4):395-399.
7. Tur C, Eckstein M, Velden J, et al. CD19-CAR T-cell therapy induces deep tissue depletion of B cells. *Ann Rheum Dis*. 2025;84(1):106-114.
8. Minopoulou I, Wilhelm A, Albach F, et al. Anti-CD19 CAR T cell therapy induces antibody seroconversion and complete B cell depletion in the bone marrow of a therapy-refractory patient with ANCA-associated vasculitis. *Ann Rheum Dis*. 2025;84(3):e4-e7.
9. Qin C, Dong M-H, Zhou L-Q, et al. Anti-BCMA CAR-T therapy in patients with progressive multiple sclerosis. *Cell*. 2025;188(23):6414-6423.e11.
10. Fischbach F, Richter J, Pfeffer LK, et al. CD19-targeted chimeric antigen receptor T cell therapy in two patients with multiple sclerosis. *Med*. 2024;5(6):550-558.e2.
11. Qin C, Tian D-S, Zhou L-Q, et al. Anti-BCMA CAR T-cell therapy CT103A in relapsed or refractory AQP4-IgG seropositive neuromyelitis optica spectrum disorders: phase 1 trial interim results. *Signal Transduct Target Ther*. 2023;8(1):5.
12. Greco R, Ruggeri A, McLornan DP, et al. Indications for haematopoietic cell transplantation and CAR-T for haematological diseases, solid tumours and immune disorders: 2025 EBMT practice recommendations. *Bone Marrow Transplant*. 2025;60(11):1499-1525.
13. Müller F, Schwingen NR, Hagen M, et al. Comparison of the safety profiles of CD19-targeting CAR T-cell therapy in patients with SLE and B-cell lymphoma. *Blood*. 2025;146(9):1088-1095.
14. Hagen M, Müller F, Wirsching A, et al. Local immune effector cell-associated toxicity syndrome in CAR T-cell treated patients with autoimmune disease: an observational study. *Lancet Rheumatol*. 2025;7(6):e424-e433.
15. Greco R, Müller F, Haghighi A, et al. CAR T cells for autoimmune diseases: 2026 update of the EBMT–ISCT–JACIE practice harmonisation and consensus recommendations. *Lancet Rheumatol*. 2026 Oct 5. doi: 10.1016/S2665-9913(26)00249-3. [Epub ahead of print]

## Figure Legend

### **Figure 1 – Landscape of CAR T-Cell Therapy in Autoimmune Diseases across the centers that started or planned to start CAR T therapy for ADs**

A. Geographical distribution of the 73 centers, among the 170 respondents, reporting ongoing or planned CAR T-cell activity for ADs. Centers already delivering CAR T-cell therapy are shown in green (n=31) and centers planning to start are shown in yellow (n=42). B. Overview of CART-cell therapy indications for autoimmune diseases across participating centers that already started performing CAR T-cell therapies and responded to the survey (n=50). C. Overview of CART-cell programme types across participating centers that already started performing CAR T-cell therapies and responded to the survey (n=50). D. CAR T-cell antigen specificity: targeted antigens across participating centers that already started performing CAR T-cell therapies and responded to the survey (n=50). E. Co-stimulatory domains employed in CAR construct design across participating centers that already started performing CAR T-cell therapies and responded to the survey (n=50).

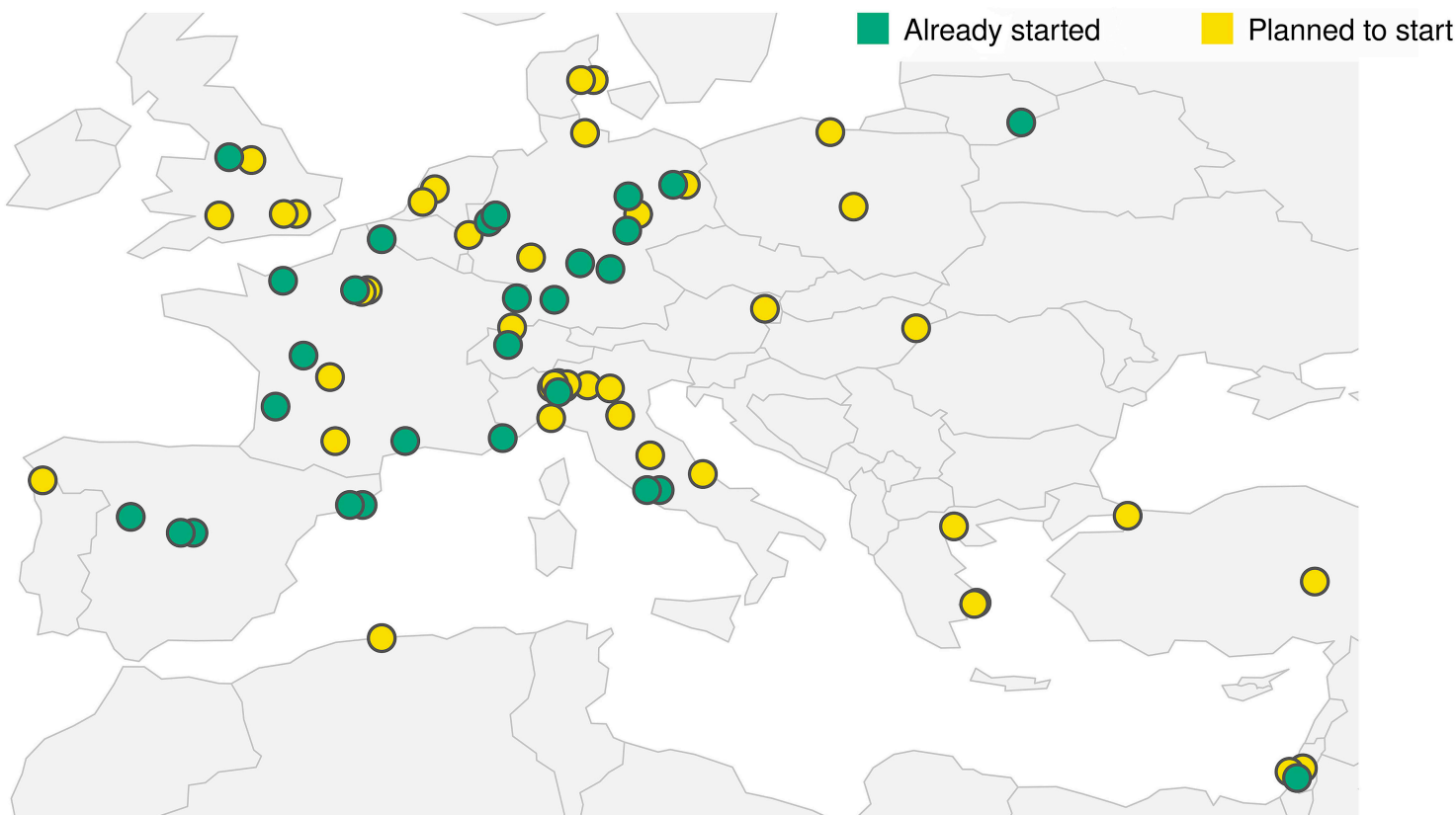
Abbreviations: AD – Autoimmune Diseases; Haemato – Haematological; RMD – Rheumatological; Neuro – Neurological; GI – Gastrointestinal; CT – Clinical trial; BCMA – B-Cell Maturation Antigen.

### **Figure 2 – Autoimmune Disease Patient Treated with CAR T-Cell Therapy**

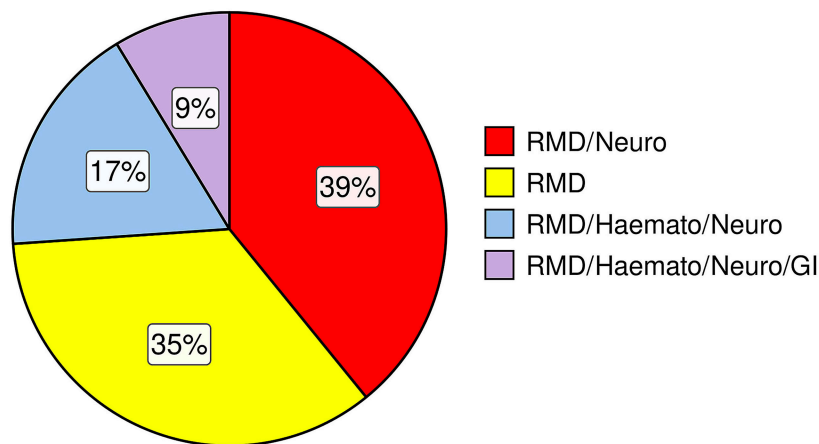
Number of patients treated with CAR T-cell therapy within this survey, stratified by diagnosis. Bars represent the total number of reported patients for each disease category.

Abbreviations: SLE – Systemic Lupus Erythematosus; SSc – Systemic Sclerosis; IIM – Inflammatory Myopathy; MS – Multiple Sclerosis; RA – Rheumatoid Arthritis; MG – Myasthenia Gravis; NMOSD – Neuromyelitis Optica Spectrum Disorder; SPS – Stiff Person Syndrome.

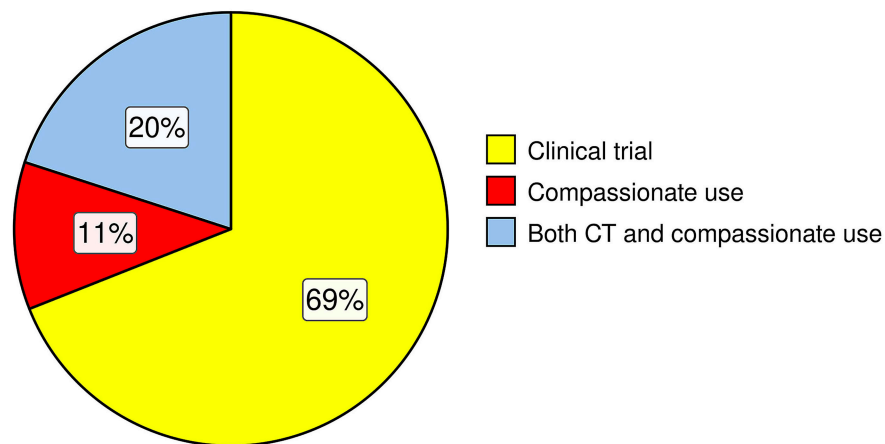
1A. Geographical distribution of centers performing CAR T-Cell for ADs



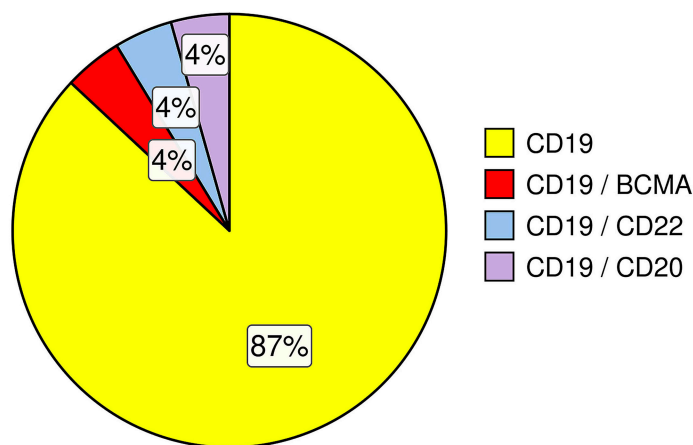
1B. Indications for CAR T-Cells in AD across centers



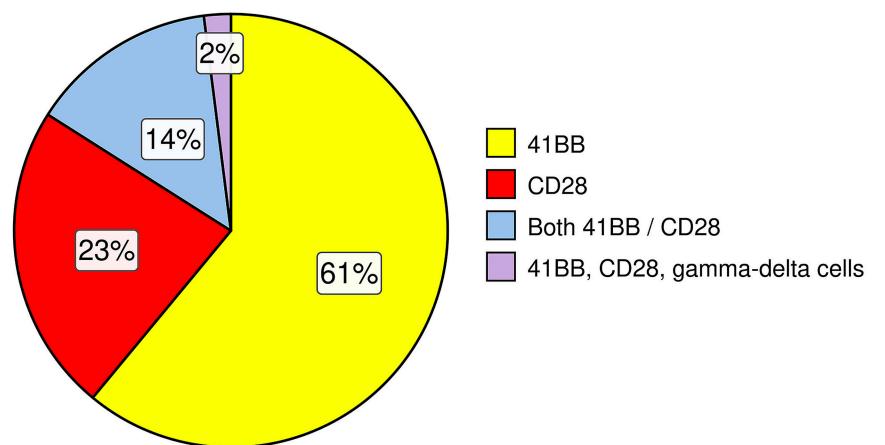
1C. Type of CAR T-Cells programs across centers

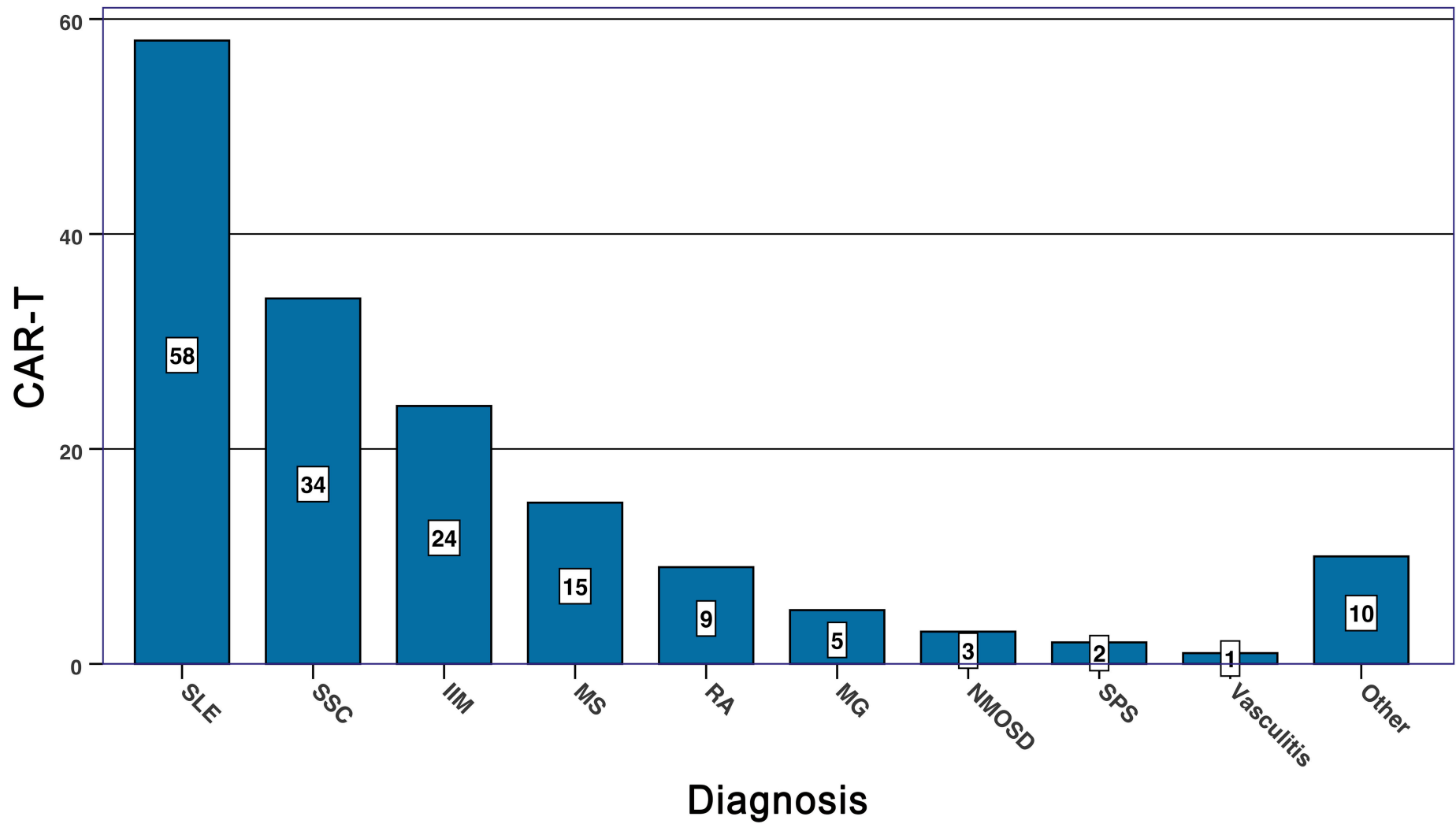


1D. CAR T-Cells antigen specificity



1E. Co-stimulatory domain used





# CAR-T Cell Therapy in Autoimmune Diseases as Concomitant or Main Indication

Page 1

## 1.1 CONTACT INFORMATION

1.2 CIC – Centre Identification Code

1.3 Hospital name - institution

1.4 City

1.5 Country

1.6 Contact person

1.7 Email address

1.8 JACIE or FACT accreditation

☐ YES

☐ NO

**2.1 Centre's characteristics**

2.2 When did your centre start performing CART cells in ADs? Please specify the year. If you centre has not yet started but is planning to start in 2025, please mention it clearly

2.3 Is your center performing autologous HCT in ADs?

☐ Yes

☐ No

☐ Not yet but my center will start in 2025

2.4 Is a multidisciplinary team (disease specialist and CART specialist) available in your center for ADs?

☐ Yes

☐ No

### 3.1 Managing Chimeric Antigen Receptors (CAR) T cells for autoimmune diseases (AD)

3.2 What are the AD indications for which you perform CART? (Please tick all that apply)

- ☐ Neurological [e.g. multiple sclerosis (MS), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), myasthenia gravis (MG), neuromyelitis optica spectrum disorder (NMOSP), Stiff person syndrome (SPS)]
- ☐ Rheumatological [e.g. systemic sclerosis (SSc), systemic lupus erythematosus (SLE), idiopathic inflammatory myopathies (IIM), juvenile dermatomyositis (JDM), rheumatoid arthritis (RA), vasculitis, anti-phospholipid syndrome. (APS)]
- ☐ Gastroenterological (e.g Crohn's disease)
- ☐ Haematological ADs [e.g. immune thrombocytopenia (ITP), autoimmune hemolytic anemia (AIHA)]
- ☐ My center will start in 2025
- ☐ Other (please specify)

3.3 If your center will start in 2025 (please specify **for which** disease indications)

3.4 In your centre, what CART are available for ADs? (Please tick all that apply)

- ☐ Commercial CART
- ☐ Academic CART

3.5 If commercial CART, please specify

3.6 If academic CART, please specify

3.7 In your centre, what types of CART are available for ADs? (Please tick all that apply)

- ☐ Autologous CART
- ☐ Allogeneic CART

3.8 If autologous CART, please specify

3.9 If allogeneic CART, please specify

3.10 In your centre, how CART is available for ADs? (Please tick all that apply)

- ☐ Clinical trial
- ☐ Compassionate use
- ☐ Other please specify

3.11 In your centre, what targets for CART are available in ADs? (Please tick all that apply)

- ☐ CD19
- ☐ BCMA
- ☐ Other targets (please specify)

3.12 In your centre, what co-stimulatory molecules for CART are available in ADs? (Please tick all that apply)

- ☐ 41BB
- ☐ CD28
- ☐ Other co-stimulatory molecules (please specify)

3.13 In your centre, is the lymphodepletion used for haematological indications the same as that adopted for AD?

- ☐ Yes
- ☐ No

3.14 What is the lymphodepletion used in your centre for ADs?

**4.1 Patients treated with CART for ADs**

4.2 How many patients with ADs have been treated overall in your centre? Please specify the number else complete "None"

4.3 How many patients with systemic lupus erythematosus (SLE) have been treated in your centre? Please specify the number else complete "None"

4.4 How many patients with systemic sclerosis (SSc) have been treated in your centre? Please specify the number else complete "None"

4.5 How many patients with idiopathic inflammatory myopathies (IIM) have been treated in your centre? Please specify the number else complete "None"

4.6 How many patients with rheumatoid arthritis (RA) have been treated in your centre? Please specify the number else complete "None"

4.7 How many patients with vasculitis have been treated in your centre? Please specify the number else complete "None"

4.8 How many patients with neuromyelitis optica spectrum disorder (NMOSP) have been treated in your centre? Please specify the number else complete "No"

4.9 How many patients with multiple sclerosis (MS) have been treated in your centre? Please specify the number else complete "None"

4.10 How many patients with myasthenia gravis (MG) have been treated in your centre? Please specify the number else complete "No"

4.11 How many patients with Stiff person syndrome (SPS) have been treated in your centre? Please specify the number else complete "None"

4.12 How many patients with other ADs have been treated in your centre? Please specify the number and the types of ADs treated else complete "None"

4.13 Do you have cases of concomitant AD in patients who have received CAR-T for hematological malignancies in your center?

☐ Yes

☐ No

4.14 If "Yes", please specify the number of patients and the types of ADs

## 5.1 Patient's Follow up

5.2 For AD patients treated with CART in your centre, do you perform Multidisciplinary follow up visits with ADs specialists?

- ☐ Yes
- ☐ We propose separate follow up visits with hematologists and ADs specialists
- ☐ My centre policy for follow up is not yet defined

5.3 For AD patients treated with CART in your centre, how often do you perform follow up visits?

- ☐ Same schedule as patients treated with CART for haematological diseases
- ☐ More frequently than patients treated with CART for haematological diseases
- ☐ Less frequently than patients treated with CART for haematological diseases
- ☐ The follow up schedule depends on the type of ADs disease and is discussed among hematologists and ADs specialist for each patient
- ☐ My centre policy for follow up is not yet defined for ADs patients treated with CART

5.4 For patients with ADs treated with cellular therapies in your centre, how often do you perform disease status re-evaluation?

- ☐ Disease status re-evaluation schedule is managed by ADs specialist
- ☐ Disease status re-evaluation schedule is discussed among hematology and ADs specialist for each patient
- ☐ My centre policies for follow up are not yet defined for ADs patients treated with cellular therapies

5.5 For AD patients treated with CART in your centre, for how long do you proceed with hematological follow up?

- ☐ For the first 6 months after cellular therapy and then the follow up is performed by ADs specialists
- ☐ For the first 12 months after cellular therapy and then the follow up is performed by ADs specialists
- ☐ For the first 2 years after cellular therapy and then the follow up is performed by ADs specialists
- ☐ For the first 5 years after cellular therapy and then the follow up is performed by ADs specialists
- ☐ Patients will continue to perform at least one hematological follow up visit every year
- ☐ My centre policy for follow up is not yet defined for ADs patients treated with CART

5.6 Do you have periodic Multidisciplinary meeting for patient discussion in your center?

- ☐ We do have a periodic Multidisciplinary meetings
- ☐ We have a Multidisciplinary patient discussion only when needed
- ☐ My centre policiy for follow up isnot yet defined for AD patients treated with CART