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Treatment

Teclistamab for treatment-refractory autoimmune diseases: a multicentre case series

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ABSTRACT

Objectives: This study aimed to evaluate the safety and efficacy of teclistamab, a T cell–redirecting bispecific antibody targeting B-cell maturation antigen, in a case series of severe autoimmune diseases.
Methods: Data were retrospectively collected from patients with treatment-refractory systemic sclerosis (SSc), idiopathic inflammatory myopathies (IIMs), systemic lupus erythematosus (SLE), undifferentiated connective tissue disease (UCTD), or IgG4-related disease (IgG4-RD) who received 1 cycle of teclistamab at 5 European centres.
Results: Eighteen patients (72% women, median age 48.5 years, 10 SSc, 4 IIM, 2 SLE, 1 UCTD, and 1 IgG4-RD) with a median of 5 prior therapies and a median cumulative dose of 6.36 mg/kg teclistamab were included. The median follow-up was 5.1 months (range, 0.8-21.2 months). A total of 22 cytokine release syndrome episodes (16 grade 1 and 6 grade 2) occurred in 12 patients (67%). All patients developed severe hypogammaglobulinaemia, and 5 (28%) experienced severe infections. Two patients developed an inflammatory bowel disease–like colitis. Two patients with severe SSc-associated cardiac involvement died, 1 due to sudden cardiac death and the other following diffuse alveolar haemorrhage and heart failure. B-cell depletion was observed in all patients, accompanied by significant reductions in autoantibody levels. Teclistamab was associated with major clinical responses in 11 (61%) and minimal-to-moderate responses in 4 (22%) patients, despite discontinuation of immunosuppressive therapy.
Conclusions: Teclistamab demonstrated the potential to induce treatment-free responses in refractory autoimmune disease, but clinically relevant safety events, including infections and fatal outcomes in patients with advanced cardiac involvement, highlight the need for careful patient selection and monitoring.

WHAT IS ALREADY KNOWN ON THIS TOPIC

- Teclistamab, a B-cell maturation antigen–directed bispecific antibody that functions as a T cell engager, efficiently eliminates B and plasma cells.
- Early evidence for the use of teclistamab in autoimmune diseases (AIDs) suggests clinical efficacy, but is limited to case reports and 2 single-centre case series, 1 with 10 heterogeneous patients and 1 with 5 patients with systemic sclerosis (SSc).

WHAT THIS STUDY ADDS

- This case series includes 18 patients with various severe treatment-refractory AIDs such as systemic lupus erythematosus, SSc, idiopathic inflammatory myopathies, undifferentiated connective tissue disease, and IgG4-related disease, treated at 5 European centres.
- Two patients with SSc and advanced cardiac involvement died after treatment, with no clear evidence of a causal relationship to teclistamab. Other adverse events comprised hypogammaglobulinaemia requiring immunoglobulin replacement, severe infections, and colitis.
- Teclistamab treatment was associated with substantial clinical responses, even after discontinuation of background immunosuppressive therapies.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- Our data confirm plasma and B cells as crucial therapeutic targets in autoantibody-mediated AID and provide a rationale for evaluating teclistamab in prospective clinical trials, which should also explore comparative safety and long-term efficacy vs other advanced therapies such as chimeric antigen receptor T cells or haematopoietic stem cell transplantation.
- Severe hypogammaglobulinaemia after teclistamab treatment may predispose to infections and requires immunoglobulin replacement.
- Teclistamab should currently be reserved for selected patients in expert centres. Caution is warranted, especially in patients with advanced heart disease, underscoring the importance of comprehensive cardiopulmonary assessment and close monitoring.

INTRODUCTION

Antibody-based B-cell–targeting therapies, such as rituximab, have shaped the treatment landscape for autoantibody-mediated autoimmune diseases (AIDs) over the past few decades. Nevertheless, a subset of patients remains refractory to treatment, and repeated administrations are required in those who respond, presumably due to insufficient B-cell depletion in lymphoid and inflamed tissues [1], and the lack of targeting plasmablasts and plasma cells secreting autoantibodies [2] under antibody-mediated B-cell depletion. T cell–engaging bispecific antibodies have recently emerged as a strategy to redirect cytotoxic T cells against defined target cell populations. Teclistamab, a B-cell maturation antigen (BCMA)-directed bispecific antibody approved for relapsed multiple myeloma (MM) [3], targets plasmablasts, long-lived plasma cells, and their BCMA-expressing memory B-cell precursors, making BCMA an attractive target in refractory AID. Early clinical reports have demonstrated the therapeutic efficacy of teclistamab in severe cases of systemic lupus erythematosus (SLE), systemic sclerosis (SSc), and antisynthetase syndrome [4–8]. In particular, recent results from a single-centre case series of teclistamab in 10 patients with treatment-refractory AID reported beneficial clinical responses for up to 15 months of follow-up. Nine of 10 patients initially responded, and 4 patients subsequently developed disease progression or relapses [9]. Another recent case series reported sustained treatment responses for up to 8 months in 5 patients with SSc after sequential therapy with teclistamab and rituximab [10].

However, available data remain limited, and key questions regarding teclistamab dosing, long-term safety, and durability of responses remain unresolved. Although pharmacokinetic (PK) and dose–response analyses are available from haematologic indications [11], their applicability to AID is uncertain because of potential differences in target cell burden, immune status, and pharmacodynamics.

In this retrospective multicentre case series, we report the clinical outcomes with a focus on safety profiles of 18 patients

with severe, treatment-refractory AID who received teclistamab as an off-label therapy. Data were collected from 5 clinical centres specialised in the treatment of AID and included patients with SSc, undifferentiated connective tissue disease (UCTD), SLE, idiopathic inflammatory myopathies (IIM), and IgG4-related disease (IgG4-RD).

METHODS

Patients

Between March 2024 and October 2025, 18 patients with various AIDs received off-label teclistamab therapy at specialised centres. Teclistamab was considered on an individual basis in patients with severe, treatment-refractory AID, high unmet medical need, and no viable therapeutic alternatives, taking into account prior treatment failure, comorbidities, and individual risk–benefit considerations within a multidisciplinary shared decision-making process, informed by principles established for advanced immune therapies [12,13]. All patients provided written informed consent. Four patient cases have been reported previously [5–8] and are included in this report with a longer follow-up.

Treatment

Teclistamab was administered subcutaneously in a step-up regimen based on the approved schedule for MM [14], although dose intervals and the total number of doses varied among patients. Variability in treatment schedules was driven by centre-specific approaches, organisational constraints, and clinically indicated interruptions, including infectious complications. Premedication with dexamethasone (16 mg), diphenhydramine (50 mg or equivalent antihistamine), and acetaminophen (1000 mg) was administered before each step-up dose and at least the first target dose [14].

Safety assessment and management

Step-up doses and at least the first target dose were given under inpatient observation for at least 48 hours to monitor and manage potential treatment-related side effects. Further follow-up safety visits after completion of the teclistamab injections were usually scheduled every 2 to 4 weeks within the first 6 months, then usually every 4 to 8 weeks, taking into consideration the individual risk profiles and the course of serum immunoglobulins. Patients were closely followed for the development of cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS) [15]. CRS was managed according to established guidelines for cellular therapies [16,17], using acetaminophen, glucocorticoids, and tocilizumab as appropriate. Patients were examined for infections, cytopaenias, hypogammaglobulinaemia, and other adverse events throughout the follow-up period. Routine laboratory tests for blood cell counts, renal and hepatic function, coagulation, and inflammation were performed at most visits. All patients received prophylaxis with acyclovir (2 × 400 mg/d) and cotrimoxazole (sulfamethoxazole/trimethoprim 800/160 mg 3 × /wk, or low-dose atovaquone in case of cotrimoxazole intolerance) starting after the first teclistamab injection. Patients received prophylactic intravenous immunoglobulin (IVIG) replacement therapy when serum IgG levels dropped <4 g/L, following recommendations for teclistamab therapy in MM [18].

Assessment of clinical, cellular, and serologic responses

Clinical disease activity assessment included the modified Rodnan skin score (mRSS) for patients with SSc, manual muscle-testing 8 (MMT-8) for IIM, and Systemic Lupus Erythematosus Activity Index 2000 (SLEDAI-2K) for SLE and UCTD. To enable cross-disease comparability, disease-specific response definitions were prespecified and mapped to a common 3-tier outcome (minimal, moderate, and major response) in accordance with established composite scores. The revised composite response index (rCRISS 3/5) was used for evaluating responses in SSc. After exclusion of major cardiopulmonary-renal progression, thresholds of 10%, 25%, and 50% (and 5% for forced vital capacity [FVC] in all categories) were used to categorise minimal, moderate, and major response [19]. In IIM, the established categories of the American College of Rheumatology/European Alliance of Associations for Rheumatology total improvement score [20] were used for response categorisation. In SLE and UCTD, SLEDAI-2K decrease ≥2 [21], SLE responder index 4 [22] and DORIS (Definition of Remission in SLE) remission [23] marked minimal, moderate, and major response. In IgG4-RD, improvements of 2, 4, and 6 points in the IgG4-RD responder index (IgG4-RD RI) [24] were used to categorise responses. The time to the first occurrence of a minimal, moderate, or major response to teclistamab treatment from baseline was depicted in a swimmer plot. Later transitions to 1 lesser category were not depicted because early fluctuations are expected and, in some cases, may be driven by incomplete available datasets (eg, because lung function tests were performed at larger intervals). Instead, disease worsening, flares, or relapses were evaluated from the maximum prior response value. This was defined as a confirmed decrease of ≥10% for FVC, ≥15% for DLCO (diffusing capacity of the lung for carbon monoxide), or ≥25% increase in mRSS, in accordance with relapse criteria after autologous haematopoietic stem cell transplantation in SSc [25]. A worsening of ≥2 in physician assessment of global disease activity or ≥20% in MMT-8 was used for relapse evaluation based on the IMACS (International Myositis Assessment and Clinical Studies Group) criteria for disease worsening in IIM [26,27]. The SELENA-SLEDAI (Safety of Estrogens in Lupus Erythematosus National Assessment - Systemic Lupus Erythematosus Disease Activity Index) flare index [21] was used for relapse assessment in SLE and UCTD, and an IgG4-RD RI increase ≥4 in IgG4-RD. Fatigue was assessed with the FACIT-Fatigue (Functional Assessment of Chronic Illness Therapy - Fatigue) scale questionnaire. Laboratory analyses were performed at the individual sites in accredited routine laboratories according to standard practice. Peripheral blood $CD19^+$ B cells and $CD3^+$ T cells were measured by fluorescence-activated cell sorting. Serum titres of antinuclear antibodies (ANAs) were assessed using an indirect immunofluorescence test on HEp-2 (Human Epithelial type 2) cells. Disease-specific autoantibodies were measured with enzyme-linked immunosorbent assays or blots. All safety and efficacy data were collected retrospectively from hospital records.

Simulation of PK, statistics, and graphical analysis

PK were simulated using a published population PK model from a phase I study in relapsed MM [11]. We applied this model to our patient cohort under the assumption that the structural model (2-compartment, first-order subcutaneous absorption) and linear clearance are transferable across both indications, as monoclonal antibody clearance is primarily driven by nonspecific IgG catabolism. In an additional analysis, the time-dependent clearance was removed to exclude the

influence of target-mediated drug disposition (TMDD), which may be higher in MM. The simulated exposure was evaluated in relation to the blood *ex vivo* 90% maximal effective cytotoxic concentration (EC90) of 6.04 µg/mL [28,29], which broadly correlates to the concentration above which the clinical response rate became increasingly dose-independent in patients with MM [11]. Graphical PK profiles and total drug exposure were calculated using R (version 4.5.1; R foundation for statistical computing, Vienna, Austria) with the RxODE2 and ggplot packages (see Supplementary Section 1.2 for further details). Associations between simulated exposure and continuous outcomes (eg, duration of B-cell depletion and IgM deficiency) were assessed using Spearman correlation, whereas comparisons between groups (eg, presence vs absence of CRS or infections) were performed using the Mann-Whitney U test. Statistical and graphical analyses other than the PK simulations were performed with GraphPad Prism (version 10.6.1; GraphPad Software, LLC, Boston, MA, USA).

RESULTS

Patient characteristics

Patients included in this case series had various AIDs (10 SSc, 4 IIM, 2 SLE, 1 UCTD, and 1 IgG4-RD, Table 1). Thirteen patients (72%) were female, and the median age was 48.5 years (range, 23-63 years). The median disease duration was 2.5 years (range, 0.5-22 years). Disease manifestations included involvement of the skin in 14 patients (78%), lung in 12 (67%), joints in 11 (61%), gastrointestinal tract, muscles and heart in 7 (39%). Patients had received a median of 5 (range, 2-11) previous therapies, including rituximab in 13 patients (72%) and cyclophosphamide in 12 patients (67%). The median follow-up after the first dose of teclistamab was 5.1 months (range, 0.6-21.2 months), corresponding to a total of 11.5 patient-years of follow-up.

Teclistamab treatment and simulated exposure

A median number of 4 (range 2-5) target doses of 1.5 mg/kg teclistamab were administered (Supplementary Fig S1 and Supplementary Table S1). Overall, patients received a median cumulative dose of 6.36 mg/kg (range, 3.36-8.66 mg/kg) over a median of 6 injections during a median period of 28 days (range, 11-70 days). Simulated teclistamab exposures based on the dosing regimens varied markedly between patients, with $AUC_{(0-\infty)}$ (area under the curve) values ranging from 197 to 814 µg·day/mL (Supplementary Fig S2 and Supplementary Table S2). Simulated time and AUC above the maximum EC90 ($t_{\geq EC90}$ and $AUC_{\geq EC90}$) ranged from 11 days to 50 days and from 87 to 682 µg·day/mL, respectively. After removing the time-dependent TMDD component, simulations showed expectedly higher exposures, with $AUC_{(0-\infty)}$ values showing a median relative difference of 33.5% (mean 32.8%) compared with the original model. All immunosuppressive therapies were discontinued before the first dose of teclistamab, except glucocorticoid treatment, which was continued for the first few weeks in patients 1, 2, 6, and 7, and continued throughout the follow-up period in patient 15 after teclistamab initiation.

Safety

During teclistamab treatment, a total of 22 CRS episodes (16 grade 1 and 6 grade 2) occurred in 12 (67%) patients (Table 2). The incidence gradually declined with repeated injections: 41%, 27%, 14%, 14%, and 5% of CRS episodes occurred after the first to fifth injection, respectively. In 91% of cases with CRS, the onset occurred within 2 days after the last teclistamab injection. Management of CRS included tocilizumab in 7 episodes (32%) in 4 patients and glucocorticoids in 5 episodes (23%) in 4 patients. No patient developed ICANS.

Infections occurred in 12 patients (67%), most commonly upper respiratory tract infections (URTIs), with 15 episodes reported in 10 patients. Five patients required hospitalisation for 7 events necessitating intravenous antibiotic treatment, predominantly due to early respiratory infections. Notably, 4 severe infections (2 pneumonia, 1 URTI, and 1 tonsillitis) occurred within the first 4 weeks after treatment initiation and were associated with treatment delays. Additional infections occurred later, including 1 severe URTI at 3 months after treatment and 2 events (acute undifferentiated fever, upper arm phlegmon) at least 1 year after treatment in patient 1. All severe episodes resolved without sequelae after antibiotic treatment. Tonsillitis was observed in 4 patients, predominantly early after treatment, with 2 cases being associated with prolonged fever. There was no clear association between simulated teclistamab exposure and the incidence of CRS or infections in this cohort.

Two patients developed severe, noninfectious colitis. One patient (SLE, patient 4) presented 6 months after treatment with Crohn's-like inflammatory bowel disease, including ulcerative lesions of the colon and terminal ileum, which resolved under mesalazine and vedolizumab treatment [6]. The second patient (SSc, patient 12) developed severe, nonbloody diarrhoea (up to 20-30 stools/d) 6 weeks after teclistamab initiation. Faecal calprotectin was markedly elevated (>800 µg/g), and MR enterography demonstrated proctitis. Endoscopic findings were consistent with ulcerative proctitis, and histology showed nonspecific mucosal inflammation, similar to that seen in microscopic colitis. Symptoms resolved under treatment with budesonide and mesalamine. Mucosal plasma cells and IgA were markedly reduced in immunohistochemistry.

One patient developed histologically confirmed psoriasis guttata 15 weeks after treatment, which only partly responded to topical treatment and was ongoing at the end of the follow-up period.

Two patients with SSc and severe cardiac involvement, including myocardial fibrosis, myocarditis, chronic heart failure, and arrhythmias, died after treatment. They had the lowest simulated teclistamab exposures in the cohort because they did not complete the full treatment cycle (Supplementary Table S2). Both had suffered from SARS-CoV-2 infection 2 months before teclistamab initiation. One patient (patient 6) died on day 20 after teclistamab initiation. He had no evidence of CRS or infections following the first 4 teclistamab doses, which were preceded by tocilizumab treatment. The patient had worsened renal function, anaemia, and thrombocytopaenia during treatment. After the fifth total and second target dose of teclistamab, he developed arterial hypotension and dyspnoea without fever. His condition rapidly deteriorated and two days after the last dose he required resuscitation, which was unsuccessful. The autopsy report revealed diffuse alveolar haemorrhage and right-sided heart failure with extensive underlying heart fibrosis as causes of death. The second patient (SSc, patient 18) presumably died from sudden cardiac death 24 days after teclistamab initiation, and 12 days after the fourth total and second target dose of teclistamab without evidence of CRS or infections. She died at home, and no autopsy was performed. Both cases are described in detail in the supplementary material.

In addition to these clinical adverse events, laboratory analysis revealed transient cytopaenias (anaemia, thrombocytopaenia, and lymphopaenia) shortly after teclistamab

Table 1
Patient characteristics

Patient Nr.	Centre	Indication	Age (y)	Sex	Organ manifestations	Autoantibody profile	Disease duration (y)	Treatment history	Cumulative teclistamab dose (mg/kg)	Follow-up (mo)
1	BE	SLE	23	f	Kidneys (LN class II/V), skin (bullous lesions), cytopaenias, joints	ANA, dsDNA, SSA, U1-RNP, Sm	3	PRED, HCQ, MTX, DDS, AZA, MMF, BEL, ANI, VOC, IVIG	4.16	21.2
2	BE	UCTD	49	m	ILD, joints	ANA	3	RTX, CYC, DEX, DARA, PLEX	8.66	18.7
3	BE	SSc	48	f	Skin, ILD, heart, GI, joints	ANA, Scl70	7	HCQ, AZA, CYC, NIN, MMF, HSCT, CYC/ATG, RTX, PRED	5.66	17.0
4	HD	SLE	42	f	Kidneys (LN class II), joints, skin	ANA, dsDNA, Nucleosome	22	HCQ, AZA, MMF, BEL, MTX, CsA, GC, ANI, RTX	4.86	16.8
5	BE	IgG4-RD	49	f	Head (pachymeningitis, pseudotumor, sinusitis)	-	6	RTX, CYC, DEX, DARA, PLEX	4.16	14.3
6	BE	SSc	48	m	Skin (incl. DU), GI, heart	ANA, Scl-70	2	CYC, TOC, PRED	4.16	0.6
7	BE	IIM (ASyS)	57	m	Muscles, ILD, heart, joints	ANA, Jo-1, SSA	0.5	PRED, CYC, IVIG, TOF, RTX	6.36	8.5
8	HH	SSc	55	f	Skin (incl. DU), joints, muscles, GI	ANA, RNAP III	1	CYC, RTX, MMF	6.36	8.4
9	HH	SSc	49	f	Skin (incl. calcinosis), ILD, joints, muscles	ANA, PM-Scl75, PM-Scl100, SSA	4	CYC, RTX, MMF, TAC	6.36	5.6
10	BE	IIM	36	f	Muscles, joints, ILD, heart	ANA, Ku, SSA, RF, CENP-B	2	PRED, MTX, HCQ, RTX, IVIG, BAR, LEF	6.36	5.2
11	BE	SSc	35	f	Skin, joints, heart	ANA, Scl70	1	MMF, MTX	6.36	5.0
12	BE	SSc	55	m	Skin (incl. DU), ILD, GI	ANA, Scl-70	2	CYC, MTX, MMF	6.36	4.4
13	BE	IIM (DM)	47	f	Muscles, ILD, skin	MDA5, SSA	0.5	PRED, IVIG, RTX, HCQ, TOF, MMF, PLEX	6.36	4.0
14	BE	SSc	63	m	Skin, ILD, heart	ANA, RuvBL1/2	0.5	MMF, MTX, PRED	6.36	3.7
15	HH	IIM (ASyS)	37	f	Muscles, ILD, skin, joints	ANA, Jo-1, CENP-B	20	MTX, LEF, HCQ, ETN, ABT, CERT, RTX, CYC, MMF, BAR, DARA	6.36	2.8
16	AH	SSc	39	f	Skin (incl. DU), ILD, GI	ANA, Scl-70	18	PRED, CYC, ABT, MTX, MMF, RTX, TOC, ANI, NIN	6.36	1.9
17	AH	SSc	57	f	Skin, ILD, joints, GI	ANA, Scl-70	7	MMF, PRED, RTX, CYC, NIN	6.36	1.5
18	TU	SSc	53	f	Skin (incl. DU, calcinosis), ILD, heart, PAH, GI, muscles	ANA, U1-RNP, SSA	0.5	AZA, MMF, RTX, CYC	3.36	0.8

ABT, abatacept; AH, Aarhus; ANA, antinuclear antibody; ANI, anifrolumab; ASyS, antisynthetase syndrome; ATG, anti-thymocyte globulin; AZA, azathioprine; BAR, baricitinib; BE, Berlin; BEL, belimumab; CENP-N, anti-centromere protein N antibodies; CERT, certolizumab; CsA, cyclosporine A; CYC, cyclophosphamide; DARA, daratumumab; DDS, dapsone; DEX, dexamethasone; DM, dermatomyositis; DU, digital ulcers; ETN, etanercept; GC, glucocorticoids; GI, gastrointestinal tract involvement; HCQ, hydroxychloroquine; HD, Heidelberg; HH, Hamburg; HSCT, haematopoietic stem cell transplantation; IgG4-RD, IgG4-related disease; IIM, idiopathic inflammatory myositis; ILD, interstitial lung disease; IVIG, intravenous immunoglobulin; LEF, leflunomid; LN, lupus nephritis; MDA5, anti-melanoma differentiation-associated protein 5 antibodies; MMF, mycophenolate mofetil; MTX, methotrexate; NIN, nintedanib (anti-fibrotic); PAH, pulmonary arterial hypertension; PLEX, plasmapheresis; PM-Scl-75/100, anti-polymyositis-scleroderma 75/100 kDa antibodies; Pred, prednisolone; RF, rheumatoid factor; RTX, rituximab; RuvBL, anti-RuvBL1/2 antibodies; Scl-70, anti-scleroderma 70 kDa antibodies; SLE, systemic lupus erythematosus; SSA, anti-Sjögren's syndrome-related antigen A antibodies; SSc, systemic sclerosis; TAC, tacrolimus; TOF, tofacitinib; TU, Tuebingen; U1-RNP, anti-U1-ribonucleoprotein antibodies; UCTD, undifferentiated connective tissue disease; VOC, voclosporin.

Table 2
Adverse events after teclistamab treatment

Event	Number of patients (%)	Number of events	Events requiring hospitalisation
Immune mediated	12 (67)	27	22
CRS grade 1	10 (56)	16	16
CRS grade 2	4 (22)	6	6
CRS grade 3 or higher	0 (0)	0	0
ICANS	0 (0)	0	0
Injection site reaction	4 (22)	5	0
Haematological	17 (94)	n.a.	0
Hypogammaglobulinaemia (<4 g/L)	17 (100)[a]	n.a.[b]	0
Lymphopaenia (<0.5 /μL)	12 (67)	14	0
New anaemia (<10 g/dL)	4 (22)	4	0
New thrombocytopaenia (<100 /nL)	2 (11)	3	0
Neutropaenia (<1.5 /nL)	1 (6)	1	0
Infections	12 (67)	33	7
Upper respiratory tract infection	10 (56)	15	2
Sinusitis	4 (22)	4	0
Mild tonsillitis	2 (11)	2	0
Tonsillitis with fever over >2 wk	2 (11)	2	1
Pneumonia	2 (11)	2	2
Acute undifferentiated fever	1 (6)	1	1
COVID-19	1 (6)	1	0
Urinary tract infection	1 (6)	1	0
Gastroenteritis	1 (6)	1	0
Phlegmon	2 (11)	2	1
Superinfection of digital ulcer	1 (6)	1	0
Oral candidiasis	1 (6)	1	0
Cardiac	3 (17)	5	2
Sudden cardiac death	1 (6)	1	n.a.
Decompensated heart insufficiency	1 (6)	1	2
Death due to alveolar haemorrhage and heart failure	1 (6)	1	n.a.
Syncope	1 (6)	1	0
Atrial flutter	1 (6)	1	0
Renal	3 (17)	3	0
Creatinine increase (>1.5 mg/dL)	2 (11)	2	0
Oedema	1 (6)	1	0
Gastrointestinal	6 (33)	8	2
Mild/moderate diarrhoea	2 (11)	3	0
IBD-like colitis	2 (11)	2	2
Transaminase increase (>150 U/L)[c]	2 (11)	2	0
Cholecystolithiasis	1 (6)	1	0
Neurological	5 (28)	5	0
Headache	3 (17)	3	0
Worsened trigeminus neuralgia	1 (6)	1	0
Transient facial hypaesthesia	1 (6)	1	0
Dermatologic	6 (33)	7	0
Xerosis with scaling and pruritus	2 (11)	2	0
Exanthema	2 (11)	2	0
Eczema	2 (11)	2	0
Psoriasis guttata	1 (6)	1	0
Musculoskeletal	1 (6)	1	0
Tenosynovitis	1 (6)	1	0

CRS, cytokine release syndrome; IBD, inflammatory bowel disease; ICANS, immune effector cell–associated neurotoxicity syndrome; IVIG, intravenous immunoglobulin treatment; n.a., not applicable.
[a] Percent was calculated from 17 patients, as no IgG follow-up value was available for patient 18.
[b] The number of events was not calculated as it is confounded by IVIG treatment.
[c] Excluding increases due to myositis.

treatment initiation that resolved without treatment. Otherwise, white blood cell counts, liver, renal, and coagulation parameters demonstrated no significant adverse trends (Supplementary Figs S3-S5).

Teclistamab depleted peripheral B cells and was associated with hypogammaglobulinaemia

Teclistamab induced changes in B and T cell counts, and a decline of serum immunoglobulins, including autoantibodies and protective vaccine titres.

Consistent with data from treatments in MM [18], $CD19^+$ B-cell counts showed a rapid decrease to below the limit of detection in all patients, followed by an initial B-cell recovery (>0.01/nL) at a median of 20.0 weeks after teclistamab initiation (range, 17.1-36.4) in 10 patients. Normal levels (>0.1/nL) were reached by 4 patients after a median of 43.6 weeks (Fig 1A). Circulating $CD3^+$ T cell counts exhibited heterogeneous trajectories after treatment (Supplementary Fig S6).

As expected under BCMA targeting [18], serum immunoglobulins (IgG, IgA, and IgM) declined after treatment (Fig 1B) due to plasma cell depletion. All patients with available follow-up developed severe hypogammaglobulinaemia with IgG levels (<4 g/L) after a median of 8.9 weeks (range, 1.9-17.3 weeks). Of note, IgG values were still above 4g/L at the time point of the 4 severe infections occurring within the first 4 weeks after

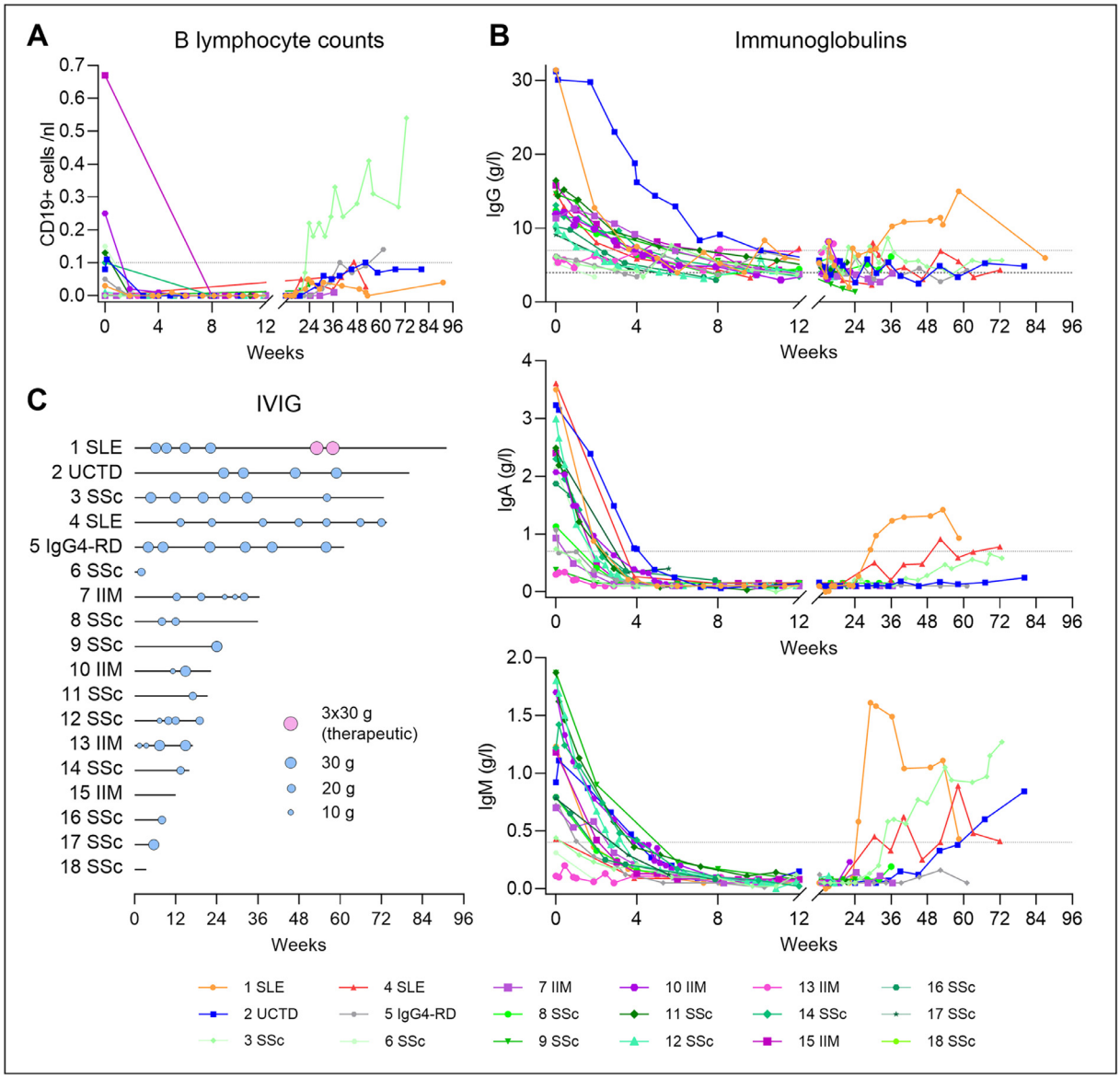

Figure 1. The cellular and serological responses to teclistamab treatment are depicted by (A) blood levels of B lymphocytes and (B) immunoglobulin levels (IgG, IgA, IgM). (C) Dosage and frequency of prophylactic IVIG treatments due to hypogammaglobulinaemia. IVIG treatment was associated with fluctuations in IgG levels. Dotted lines indicate lower limits of normal; the dashed line indicates 4 g/L for IgG. IgG4-RD, IgG4-related disease; IIM, idiopathic inflammatory myositis; IVIG, intravenous immunoglobulin replacement therapy; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; UCTD, undifferentiated connective tissue disease.

treatment. Immunoglobulin replacement therapy was administered to 16 patients (89%) and to all 13 patients with more than 3 months of follow-up (Fig 1C). Overall, patients received a mean monthly dose of 8.9 g of immunoglobulins during follow-up, and 4 of 5 patients with 1 year of follow-up remained on prophylactic IVIG. Protective vaccine titres against varicella zoster virus also declined (Supplementary Fig S6), with fluctuations coinciding with IVIG administrations. No cases of herpes zoster occurred during follow-up. Furthermore, serum levels of ANAs and disease-specific autoantibodies declined, with normalisation of ANAs in 5 patients (Fig 2). There was no clear association between simulated teclistamab exposure and the duration of B-cell depletion or immunoglobulin deficiency in this cohort.

Teclistamab induced marked clinical improvement

Overall, 11 of 18 patients (61%) achieved a major response, and 4 of 18 patients (22%) demonstrated a minimal or moderate response during the observation period (Fig 3). The median time to moderate and major response was 3.9 weeks (range, 1.9-12.3 weeks) and 8.1 weeks (range, 3.9-32.1 weeks), respectively. Major responses were observed in 8 of 14 (57%) patients with available follow-up by week 12 and 7 of 8 (88%) patients by week 24, whereas all 14 patients achieved at least a minimal response by week 12. Major responses were maintained in 4 of 5 patients (80%) by week 52, whereas 1 patient with SLE relapsed 31 weeks after treatment. Two patients died early and were not available for further response assessment. Definitions of response categories and supportive exploratory data on individual score components are provided in Supplementary Tables S3-S21. Key data with consistent results on organ manifestations are provided in Figure 4A. In patients with SSc, improvements in skin fibrosis were observed during the first 24 weeks. Lung function parameters showed stabilisation of FVC and improvement of DLCO (Supplementary Fig S7). In patients with IIM, muscle strength improved, reflected by an increase in MMT-8 scores and a marked decline in CK (creatine kinase) values. In patients with SLE, SLE-DAI, and C3 showed rapid improvements. In addition, patient-

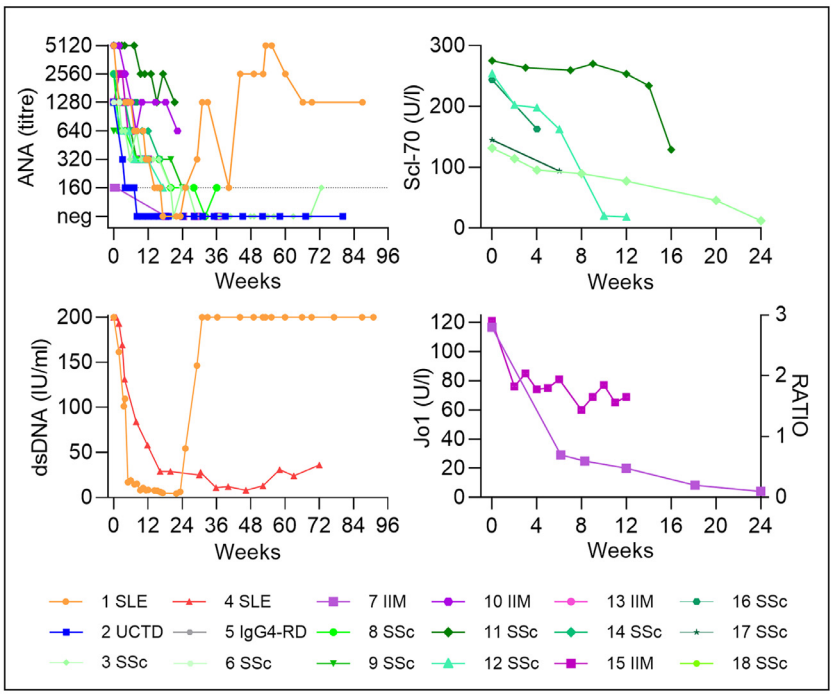

Figure 2. Time course of ANAs and the disease-specific autoantibodies Scl-70 in systemic sclerosis, dsDNA in systemic lupus erythematosus, and Jo-1 in idiopathic inflammatory myositis after treatment with teclistamab. ANA, antinuclear antibody; dsDNA, anti-dsDNA antibodies; IgG4-RD, IgG4-related disease; IIM, idiopathic inflammatory myositis; Jo-1, anti-Jo-1 antibodies; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; UCTD, undifferentiated connective tissue disease.

reported outcomes improved substantially. Patient global assessment of disease activity (0-10) decreased from a median of 8 before treatment (range, 4.2-10) to 1 (range, 0-7) at 24 ± 4 weeks after treatment, and patient-reported fatigue improved, with FACIT-F scores increasing from a median of 19 (range, 1-39) to 39 (range, 32-50) (Fig 4B).

DISCUSSION

In this multicentre case series, teclistamab treatment was associated with clinical responses across severe, treatment-refractory AID, accompanied by marked reductions in immunoglobulins and disease-associated autoantibodies, reflecting substantial plasma cell depletion. These findings extend emerging evidence that BCMA-positive B cells and plasma cells may contribute to chronic autoimmunity across distinct AID.

Safety represents a central consideration. CRS was frequent, but mild to moderate, and no ICANS was observed, in line with previous reports [9,10] and available evidence from haematologic indications suggesting less frequent neurotoxicity with T cell engagers compared with chimeric antigen receptor (CAR) T cells [30] and targeting BCMA compared with CD19 [31].

Notably, all patients developed hypogammaglobulinaemia, requiring repeated and prolonged IVIG replacement. No vaccinations were administered during follow-up in this cohort, but they should be considered according to interdisciplinary expert consensus.

Early infections were common, similar to a recent report [10], but appeared slightly more pronounced than in an earlier series [9] and more frequent than after blinatumomab [32,33], highlighting the importance of close monitoring and early antimicrobial intervention. Two patients developed noninfectious, inflammatory bowel disease–like colitis during follow-up, a complication previously described after rituximab and BCMA-directed CAR T cell therapy [34,35]. Given the high density of plasma cells in gut-associated lymphoid tissue and the role of BCMA in mucosal IgA responses [36,37], this finding may reflect immune dysregulation following depletion of mucosal B and plasma cells. Notably, BCMA is also expressed in tonsillar lymphoid tissue [38], consistent with the occurrences of severe tonsillitis in this cohort.

Importantly, 2 patients with severe SSc-related cardiac involvement died after receiving 2 target doses of teclistamab. One patient died from diffuse alveolar haemorrhage and heart failure, potentially secondary to a pulmonary-renal syndrome, a rare but reported severe complication of SSc [39], whereas the other patient presumably died from sudden cardiac death. Given the small number of events, absence of acute toxicity, and the patients' advanced cardiac involvement, causality cannot be inferred. Nevertheless, a treatment-related contribution cannot be excluded. In patients with MM, major cardiovascular events and arrhythmias have been reported in 7.3% of patients after teclistamab treatment, typically occurring within the first 2 weeks [40]. A recent case series also reported cardiac events after teclistamab in SSc [10]. The 2 fatal outcomes underline the importance of a stringent patient selection, including comprehensive cardiopulmonary assessment and close, longitudinal monitoring. This is of particular importance, as patients with SSc without previously known heart involvement may exhibit focal myocardial fibrosis [41], and the increased presence of activated T and B cells in cardiac tissue might predispose to local inflammation upon drug exposure.

Our data support and extend previous reports on the clinical efficacy of teclistamab treatment [9,10]. A consistent finding across diseases and heterogeneous manifestations was evidence of clinical responses. Although individual patient and organ-level responses varied, composite response scores and clinical outcome measures such as mRSS for SSc or MMT-8 for IIM showed overall improvement, in parallel with trajectories of serological disease activity markers and autoantibodies. Responses were sustained in most patients despite partial recovery of circulating B cells, but longer follow-up will be needed to

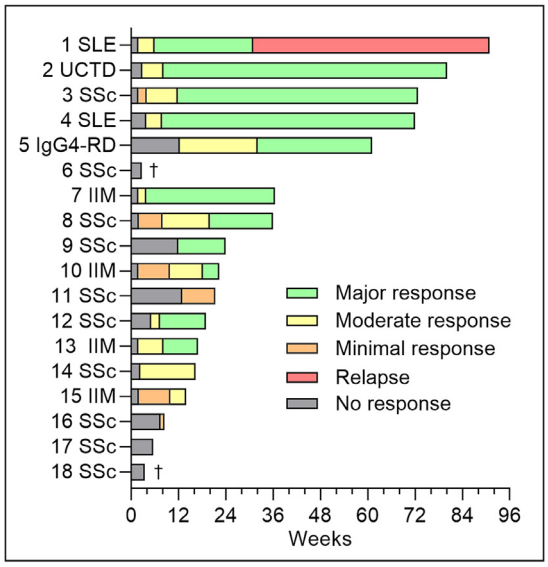

Figure 3. Time to the first occurrence of a minimal, moderate, or major response to teclistamab treatment from baseline and duration of follow-up with or without relapse. The 3-tier response categorisation was defined by rCRISS with an increase of 10%, 25%, and 50% (5% for forced vital capacity [FVC]) in 3/5 criteria in SSc [19]; minimal, moderate, and major TIS in IIM [20]; SLEDAI-2K decrease ≥2 [21], SRI-4 and DORIS remission in SLE and UCTD [22,23]; and IgG4-RD responder index (IgG4-RD RI) decrease ≥2, 4, and 6 in IgG4-RD [24]. Later transitions to 1 lesser category are not shown because early fluctuations are expected and may result from incomplete available datasets. Worsening/flare/relapse from the prior maximum response was defined by a confirmed worsening of ≥10% for FVC, 15% for DLCO, or ≥25% for mRSS in SSc [25]; worsening of physician global assessment ≥2 and/or MMT-8 ≥ 20% in IIM [27]; fulfilment of the SELENA-SLEDAI flare index [21] in SLE; an IgG4-RD RI increase ≥4 [24]. The individual score components are included in the Supplementary Tables S4-S21. †, patient died; DLCO, diffusing capacity of the lung for carbon monoxide; DORIS, Definition of Remission in SLE; IgG4-RD, IgG4-related disease; IIM, idiopathic inflammatory myositis; MMT-8, manual muscle-testing 8; mRSS, modified Rodnan skin score; rCRISS, revised composite response index; SELENA-SLEDAI, Safety of Estrogens in Lupus Erythematosus National Assessment–Systemic Lupus Erythematosus Disease Activity Index; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE disease activity index 2000; SRI-4, SLE responder index 4; SSc, systemic sclerosis; TIS, total improvement score; UCTD, undifferentiated connective tissue disease.

determine long-term responses following full B and plasma cell repopulation.

The optimal dose and schedule of teclistamab in AID remain undefined and will need to balance early toxicity against the durability of response. In our cohort, most patients received 4 target doses of 1.5 mg/kg, which was associated with fewer relapses/progressions than reported in a recent series using 2 target doses (1/7 [14%] vs 4/10 [40%] up to 8 months, Supplementary Table S1), despite similar initial response rates [9]. However, this comparison is limited by differences in diseases, follow-up duration, and small sample size. Notably, the only relapse in our cohort occurred in a patient who had received only 2 full target doses and consequently exhibited the lowest simulated teclistamab exposure and time above the *ex vivo* maximum blood EC90 among nonfatal cases. Conversely, adverse events were more frequent in our cohort, underscoring the need for prospective dose optimisation with integrated PK and pharmacodynamic analyses. Strategies for relapse management, including retreatment [9], remain to be defined. Whether adjunctive administration of rituximab, as recently reported [10], prolongs disease control following teclistamab therapy remains unclear.

Several limitations should be acknowledged. First, the analysis was retrospective and based on individual treatment attempts outside a prospective clinical trial protocol. Accordingly, the cohort was heterogeneous with variable disease duration, dosing regimens, and follow-up intervals. Clinical, serological, and B-cell assessments were not standardised across centres. Pulmonary outcomes were similarly assessed heterogeneously, limiting evaluation of interstitial lung disease-specific treatment effects. Second, the absence of a comparator group may have led to an overestimation of treatment effects, particularly for subjective outcomes. Third, variable follow-up duration and early deaths introduce potential bias, particularly survivorship bias. Response rates at defined time points were only calculated among patients with available follow-up at those time points. Response rates based on disease-specific composite outcomes such as rCRISS may be biased because of variable follow-up duration and may be overestimated among survivors, as 2 patients with the most advanced cardiac involvement died early after treatment and thus are not represented in longitudinal efficacy outcomes. In addition, the efficacy findings are potentially confounded by glucocorticoid premedication and additional treatments required for managing CRS, including glucocorticoids and tocilizumab, as well as immunoglobulins for hypogammaglobulinaemia. Finally, the heterogeneity of the included diseases, small cohort sizes, and diversity of outcome measures limit direct comparison of the risk–benefit profile across conditions, reflecting the exploratory, cross-disease design of this analysis. The PK analysis should similarly be considered as exploratory, given the limitations of applying a multiple myeloma–derived model in patients with AID, for example, antidrug antibodies were rare and low in patients with MM [11], but might be more prevalent in patients with AID. Analysis of associations between exposure and pharmacodynamic parameters or toxicity was limited because of the small number of observed outcomes.

In conclusion, this multicentre case series extends previous reports and indicates that BCMA-directed T cell engager may induce substantial clinical responses in highly selected patients with severe, treatment-refractory AID, even after withdrawal of concomitant immunosuppressive treatments. Together with the 2 previous case series [9,10], our findings support further evaluation of teclistamab as a potential treatment for highly selected patients with severe, treatment-refractory connective tissue diseases. Clinically significant adverse events, including infections related to hypogammaglobulinaemia and fatal events in patients with advanced cardiac involvement, underscore the need for careful patient selection and close monitoring and support the use of teclistamab only in experienced centres with established multidisciplinary teams that integrate expertise in AID with haematology-driven management of immune effector toxicities.

The study remains preliminary given the retrospective design, heterogeneous cohort, variable follow-up duration, and lack of a comparator group. Prospective controlled trials with standardised assessments, predefined safety boundaries, PK sampling, and systematic long-term follow-up are required to define the ideal patient population, optimal dosing regimens, durability of response after B and plasma cell recovery, long-term safety, and comparative effectiveness vs other advanced therapies such as CAR T cells or haematopoietic stem cell transplantation.

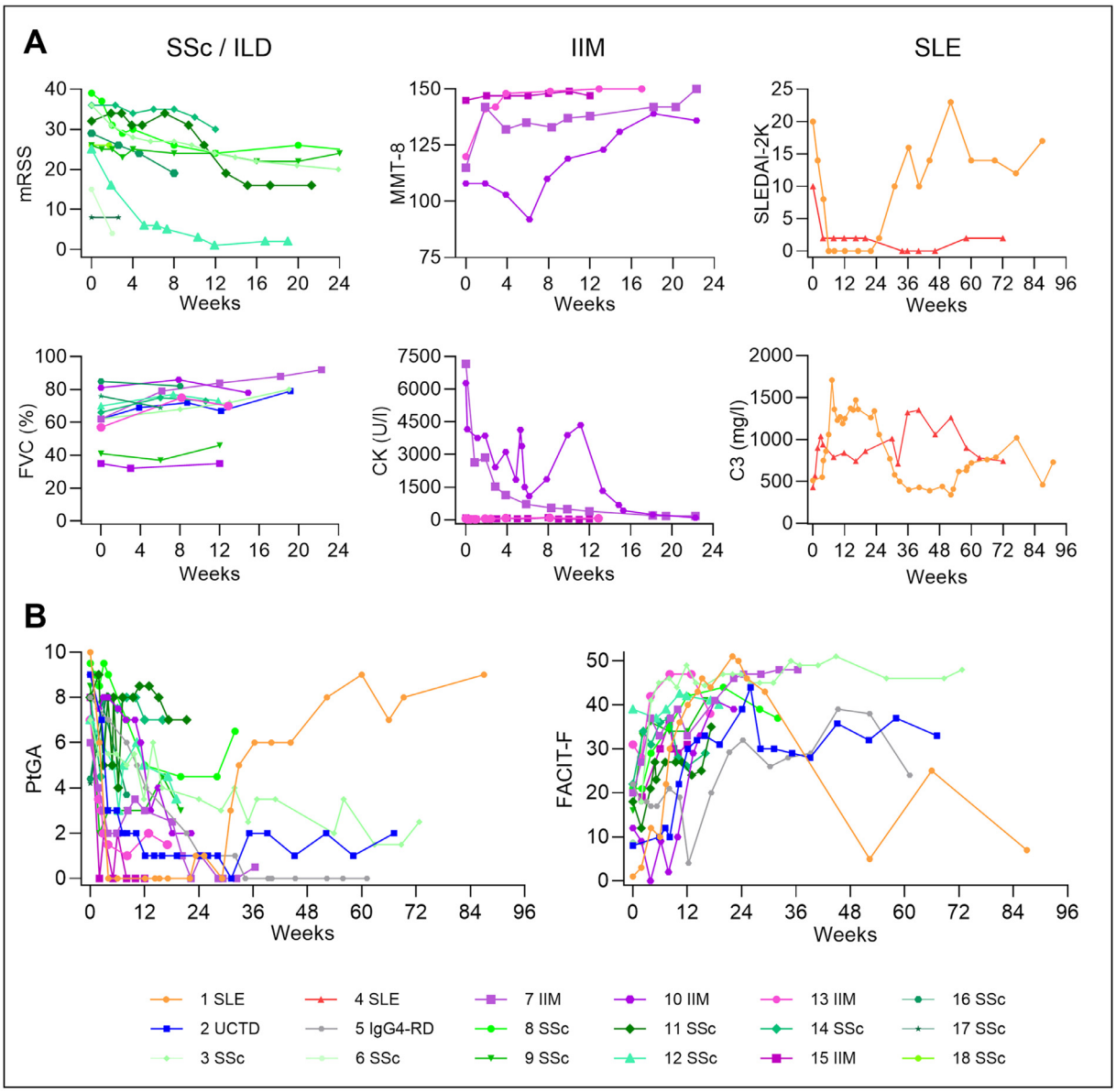

Figure 4. (A) Time course of disease-specific activity markers of the skin involvement (mRSS) in SSc, lung function (FVC) in AID-related ILD, and muscle parameters (MMT-8 and CK) in IIM within the first 24 wk after treatment with teclistamab, and overall and serological disease activity (SLEDAI and C3) in SLE until the end of follow-up. One patient with SLE relapsed after 7 mo. (B) Time course of the PtGA on a numeric rating scale from 0 to 10 and fatigue measured by the FACIT-Fatigue Scale. AID, autoimmune disease; CK, creatine kinase; FVC, forced vital capacity; IIM, idiopathic inflammatory myositis; ILD, interstitial lung disease; FACIT, Functional Assessment of Chronic Illness Therapy–Fatigue; MMT-8, manual muscle-testing 8; mRSS, modified Rodnan skin score; PtGA, patient-reported global assessment of disease activity; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE disease activity index 2000; SSc, systemic sclerosis; UCTD, undifferentiated connective tissue disease.

Competing interests

IM reports relationships with AbbVie Inc and Novartis that include speaking and lecture fees. DS reports relationships with AbbVie Inc, Bristol-Myers Squibb, Janssen-Cilag, Lilly, Novartis, and UCB that include board membership and speaking and lecture fees; Gilead Sciences that includes board membership; and Amgen and Alfasigma that include speaking and lecture fees. TA reports relationships with Abbvie, Amgen, AstraZeneca and GSK that include speaking and lecture fees; Johnson&Johnson that include research funding. AK reports relationships with AbbVie Inc, Bristol-Myers Squibb, Janssen-Cilag, Lilly, Novartis, and UCB that include board membership and speaking and lecture fees; Gilead Sciences that includes board membership; and Alfasigma that includes speaking and lecture fees. JH reports relationships with AbbVie, AstraZeneca, Boehringer Ingelheim, BMS, GSK, Johnson & Johnson, Lilly, Novartis, Pfizer, Roche, SOBI, and UCB that include board membership and speaking and lecture fees. MK reports relationships with AbbVie, Sobi, Novartis, AlfaSigma, UCB, Lilly, Medac, GSK, and Bristol-Myers Squibb that include speaking and lecture fees. IH reports relationships with AbbVie, Alfasigma, AstraZeneca, Boehringer Ingelheim, GSK, Johnson & Johnson, Lilly, Medac, Novartis, and UCB that include speaking and lecture fees. MLH-K reports relationships with Amgen, Jazz Pharmaceuticals, Novartis, Sanofi, and Sobi that include board membership and travel reimbursement. JK reports a relationship with Johnson & Johnson that includes board membership, speaking and lecture fees, and travel reimbursement. AT reports relationships with AstraZeneca and Roche that include board membership and speaking and lecture fees. KS reports a relationship with Boehringer Ingelheim that includes board membership. All authors declare they have no competing interests.

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Patient consent for publication

All patients provided informed consent for publication.

Ethics approval

The analysis was approved by the local ethics committee (EA1/002/24).

Provenance and peer review

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ard.2026.05.021.

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REFERENCES

[1] Tur C, Eckstein M, Bucci L, Auth J, Bergmann C, Rauber S, et al. Effects of different B-cell-depleting strategies on the lymphatic tissue. Ann Rheum Dis. 2025 Dec;84(12):2065–74.
[2] Hiepe F, Dörner T, Hauser AE, Hoyer BF, Mei H, Radbruch A. Long-lived autoreactive plasma cells drive persistent autoimmune inflammation. Nat Rev Rheumatol. 2011 Mar;7(3):170–8.
[3] Moreau P, Garfall AL, van de Donk NWCJ, Nahi H, San-Miguel JF, Oriol A, et al. Teclistamab in relapsed or refractory multiple myeloma. N Engl J Med. 2022 Aug;387(6):495–505.
[4] Hagen M, Bucci L, Böltz S, Nöthling DM, Rothe T, Anoshkin K, et al. BCMA-targeted T-cell-engager therapy for autoimmune disease. N Engl J Med. 2024 Sep;391(9):867–9.
[5] Alexander T, Krönke J, Cheng Q, Keller U, Krönke G. Teclistamab-induced remission in refractory systemic lupus erythematosus. N Engl J Med 2024 Sep;391(9):864–6.
[6] Lorenz HM, Merkt W, Brandt J, Giese T, Exner T, Blank N, et al. One-year remission of therapy-resistant SLE after a single course with the bispecific CD3: BCMA antibody teclistamab, but induction of a non-infectious Crohn's-like inflammatory bowel disease. Ann Rheum Dis. 2025 Jul;84(7):1277–9.
[7] Siegert E, Biesen R, Dzamukova M, Furth C, Probst M, Doellinger F, et al. Teclistamab in relapsed systemic sclerosis after autologous haematopoietic stem cell transplantation. Ann Rheum Dis. 2025 Apr;84(4):653–6.
[8] Phithak E, Albach FN, Minopoulou I, Biesen R, Kleyer A, Wiebe E, et al. Teclistamab-induced rapid remission in refractory Anti-Jo-1 Antisynthetase Syndrome. Ann Rheum Dis. 2026;85(1):212–5.
[9] Bucci L, Böltz S, Hagen M, Tur C, Noethling D, Rothe T, et al. BCMA T-Cell engager therapy in patients with refractory autoimmune disease. N Engl J Med. 2025 Oct;393(15):1544–7.
[10] Düsing C, Györfi AH, Stütz AN, Lahu LM, Deicher FS, Li YN, et al. Bispecific T cell engagers for treatment-refractory autoimmune connective tissue diseases. Nat Med. 2026;32(4):1530–42.
[11] Miao X, Wu LS, Lin SXW, Xu Y, Chen Y, Iwaki Y, et al. Population pharmacokinetics and exposure-response with teclistamab in patients with relapsed/refractory multiple myeloma: results from MajesTEC-1. Target Oncol. 2023 Sep;18(5):667–84.
[12] Alexander T, Roldan E, Del Papa N, Farge D, Henes J, Marjanovic Z, et al. Autologous haematopoietic stem cell transplantation for rheumatic diseases: best practice recommendations from the EBMT Practice Harmonization and Guidelines Committee. Bone Marrow Transplant. 2025 Nov;60(11):1451–64.
[13] Greco R, Alexander T, Del Papa N, Müller F, Saccardi R, Sanchez-Guijo F, et al. Innovative cellular therapies for autoimmune diseases: expert-based

position statement and clinical practice recommendations from the EBMT practice harmonization and guidelines committee. EClinicalMedicine 2024 Mar;69:102476.
[14] Teclistamab: summary of product characteristics. First published: 13/10/2022. Last updated: 08/10/2025 [cited 05 Jan 2026]. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/tecvayli
[15] Lee DW, Santomasso BD, Locke FL, Ghobadi A, Turtle CJ, Brudno JN, et al. ASTCT consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. Biol Blood Marrow Transplant. 2019 Apr;25(4):625–38.
[16] Santomasso BD, Nastoupil LJ, Adkins S, Lacchetti C, Schneider BJ, Anadkat M, et al. Management of immune-related adverse events in patients treated with chimeric antigen receptor T-Cell therapy: ASCO guideline. J Clin Oncol. 2021 Dec;39(35):3978–92.
[17] Crombie JL, Graff T, Falchi L, Karimi YH, Bannerji R, Nastoupil L, et al. Consensus recommendations on the management of toxicity associated with CD3×CD20 bispecific antibody therapy. Blood. 2024 Apr;143(16):1565–75.
[18] Frerichs KA, Verkleij CPM, Mateos MV, Martin TG, Rodriguez C, Nooka A, et al. Teclistamab impairs humoral immunity in patients with heavily pretreated myeloma: importance of immunoglobulin supplementation. Blood Adv. 2024 Jan;8(1):194–206.
[19] Khanna D, Huang S, Lin CJF, Spino C. New composite endpoint in early diffuse cutaneous systemic sclerosis: revisiting the provisional American College of Rheumatology Composite Response Index in Systemic Sclerosis. Ann Rheum Dis. 2021 May;80(5):641–50.
[20] Aggarwal R, Rider LG, Ruperto N, Bayat N, Erman B, Feldman BM, et al. 2016 American College of Rheumatology/European League Against Rheumatism criteria for minimal, moderate, and major clinical response in adult dermatomyositis and polymyositis: an International Myositis Assessment and Clinical Studies Group/Paediatric Rheumatology International Trials Organisation Collaborative Initiative. Ann Rheum Dis. 2017 May;76(5):792–801.
[21] Thanou A, Jupe E, Purushothaman M, Niewold TB, Munroe ME. Clinical disease activity and flare in SLE: Current concepts and novel biomarkers. J Autoimmun. 2021 May;119:102615.
[22] Luijten KM, Tekstra J, Bijlsma JW, Bijl M. The Systemic Lupus Erythematosus Responder Index (SRI); a new SLE disease activity assessment. Autoimmun Rev. 2012 Mar;11(5):326–9.
[23] van Vollenhoven RF, Bertsias G, Doria A, Isenberg D, Morand E, Petri MA, et al. 2021 DORIS definition of remission in SLE: final recommendations from an international task force. Lupus Sci Med. 2021 Nov;8(1):e000538.
[24] Wallace ZS, Khosroshahi A, Carruthers MD, Perugino CA, Choi H, Campochiaro C, et al. An International Multispecialty Validation Study of the IgG4-Related Disease Responder Index. Arthritis Care Res (Hoboken). 2018 Nov;70(11):1671–8.
[25] Del Papa N, Labopin M, Badoglio M, Farge D, Henes J, Snowden JA, et al. Definition of relapse criteria in patients with rapidly progressive systemic sclerosis treated with autologous haemopoietic stem cell transplantation. Bone Marrow Transplant. 2025 Nov;60(11):1537–40.
[26] Oddis CV, Rider LG, Reed AM, Ruperto N, Brunner HI, Koneru B, et al. International consensus guidelines for trials of therapies in the idiopathic inflammatory myopathies. Arthritis Rheum. 2005 Sep;52(9):2607–15.
[27] Rider LG, Aggarwal R, Machado PM, Hogrel JY, Reed AM, Christopher-Stine L, et al. Update on outcome assessment in myositis. Nat Rev Rheumatol. 2018 May;14(5):303–18.
[28] European Medicines Agency. Tecvayli (teclistamab): EPAR—Public Assessment Report. EMA/789141/2022. 2022 Jul 21 [cited 05 Jan 2026]. Available from: https://www.ema.europa.eu/en/documents/assessment-report/tecvayli-epar-public-assessment-report_en.pdf
[29] Girgis S, Lin SXW, Pillarisetti K, Banerjee A, Stephenson T, Ma X, et al. Translational modeling predicts efficacious therapeutic dosing range of Teclistamab for multiple myeloma. Target Oncol. 2022 Jul;17(4):433–9.
[30] Markouli M, Ullah F, Unlu S, Omar N, Lopetegui-Lia N, Duco M, et al. Toxicity profile of chimeric antigen receptor T-cell and bispecific antibody therapies in multiple myeloma: pathogenesis, prevention and management. Curr Oncol. 2023 Jul;30(7):6330–52.
[31] Han MW, Jeong SY, Suh CH, Park H, Guenette JP, Huang RY, et al. Incidence of immune effector cell-associated neurotoxicity among patients treated with CAR T-cell therapy for hematologic malignancies: systematic review and meta-analysis. Front Neurol. 2024;15:1392831.
[32] Scherlinger M, Dieudonné Y, Hilliquin S, Chatelus E, d'Alessandro R, Gies V, et al. Safety and efficacy of blinatumomab in the treatment of refractory systemic sclerosis: a case series. Ann Rheum Dis. 2026 Mar S0003-4967(26)00077-4.
[33] Bucci L, Hagen M, Rothe T, Raimondo MG, Fagni F, Tur C, et al. Bispecific T cell engager therapy for refractory rheumatoid arthritis. Nat Med. 2024 Jun;30(6):1593–601.
[34] Fortuna GG, Banerjee R, Savid-Frontera C, Song J, Morán-Segura CM, Nguyen JV, et al. Immune effector cell-associated enterocolitis following chimeric antigen receptor T-cell therapy in multiple myeloma. Blood Cancer J. 2024 Oct;14(1):180.
[35] Cavalcanti E, Armentano R, Lolli I. Crohn's disease following Rituximab treatment for follicular lymphoma in a patient with synchronous gastric signet ring cells carcinoma: a case report and literature review. Cancer Res Treat. 2020 Oct;52(4):1291–5.
[36] Mesin L, Di Niro R, Thompson KM, Lundin KE, Sollid LM. Long-lived plasma cells from human small intestine biopsies secrete immunoglobulins for many weeks in vitro. J Immunol. 2011 Sep;187(6):2867–74.
[37] Spencer J, Sollid LM. The human intestinal B-cell response. Mucosal Immunol. 2016 Sep;9(5):1113–24.
[38] Barone F, Patel P, Sanderson JD, Spencer J. Gut-associated lymphoid tissue contains the molecular machinery to support T-cell-dependent and T-cell-independent class switch recombination. Mucosal Immunol. 2009 Nov;2(6):495–503.
[39] Bar J, Ehrenfeld M, Rozenman J, Perelman M, Sidi Y, Gur H. Pulmonary-renal syndrome in systemic sclerosis. Semin Arthritis Rheum. 2001 Jun;30(6):403–10.
[40] Dae HL, Saurabh Z, Danai D, Utkarsh G, Austin C, Kyle L, et al. Major adverse cardiovascular events after teclistamab in relapsed refractory multiple myeloma: a multicenter study from the U.S. multiple myeloma immunotherapy consortium. The 67th ASH Annual Meeting Abstract. Blood. 2025;146(Supplement 1):4066.
[41] Ross L, Costello B, Brown Z, Hansen D, Lindqvist A, Stevens W, et al. Myocardial fibrosis and arrhythmic burden in systemic sclerosis. Rheumatology (Oxford). 2022 Nov;61(11):4497–502.