Supplementary Table S1. Previously published observational studies

Reference, study design, year	n, patient characteristics*	Variables	Main results
Gottenberg et al. 2005 **Retrospective cohort**	n = 13 Female: 10 (79.9%) Myocarditis/Evans: n=1; Pericarditis: n=1; AIHA: n=1; CNS: n=1; Skin: n=2; Articular: n=3 ; Vasculitis: n=2; Autoimmune thrombocytopenia: n=2; Kidney: n=2	Decrease of 50% (PR) or more of the initial DAS28 and SLEDAI values. CR defined as SLEDAI value between 0 and 12. PR defined as a decrease of ≥50% of the initial SLEDAI Index: SLEDAI	**CR**: 7/13 (53.8%) **CR and PR**: 9/13 (69.2%) **Remission of patients without renal disease:** 7/9 (77.7%) **Mean (±SD) SLEDAI:** 17±7 (range 3 - 28) to 5±6 (range 0 - 20) (p<0.002)
Smith et al. 2006 **Prospective cohort**	n = 11 Female: 10 (90.9%) Median age: 43 years Skin: n=11; Articular: n=11; Kidney: n=6; CNS: n=6; Lung: n=5; Ocular: n=2; Blood: n=1; Antiphospholipid syndrome: n=1; Gut: n=1; Heart: n=1	CR required the absence of BILAG A-, B- AND C-level disease activity. Index: BILAG	**CR:** 6/11 (54.5%) **CR and PR**: 11/11 (100%) **Median BILAG:** from 14 to 2 at 12 months (p<0.001) **Relapses:** 7/11 (63.6%) **Median duration of remission**: 12 months **B-cell depletion**: 11/11 (100%)
Tokunaga et al. 2007 **Prospective cohort**	n = 10 Female: 10 (100%) All patients had CNS involvement Acute confusional state: n=5; Psychosis: n=4; Seizure: n=2; Headache: n=1; Mood disorder: n=2; Demyelinating syndrome: n=1; Cognitive dysfunction: n=1; Myelopathy: n=1; Anxiety disorder: n=1	SLEDAI was determined before and after 1 – 6 months after treatment. Clinical symptoms and treatment-induced adverse reactions were assessed before and every week during treatment. Index: SLEDAI	**Improvement in neuropsychiatric manifestations:** 10/10 (100%) **Complete recovery:** 4 (40.00%) **Mean SLEDAI**: from 19.9 (range 2 - 49) to 6.2 (range 0 - 15) **Relapses**: 6/10 (60%) **Mean duration of remission**: 14 months (range 4 - 23) **B-cell depletion**: 8/8 (100%)
Jónsdóttir et al. 2008 **Prospective cohort**	n = 16 Female: 16 (100%) Mean age: 37 (range 19 – 56) Nephritis: n=9; Arthritis: n=4; General: n=4; Serositis: n=3; Skin: n=3; Blood: n=3; Neurological: n=2; Vasculitis: n=2	Global clinical response defined as a reduction of ≥50% in the SLEDAI score from baseline, or a reduction in the score of any organ system from BILAG A to B, or from B to C. Remission was defined as a SLEDAI score <3, or as the absence of any BILAG A or B. Relapse was defined as an occurrence of a new BILAG A or at least two new BILAG B in any organ system. Index: BILAG and SLEDAI	**Mean SLEDAI (±SD) at 6 months:** 12.1 ± 2.2-4.7 ± 1.1 (p<0.050). **BILAG at 6 months:** BILAG A organ domains = 20, 100% progressed to ≤BILAG B. BILAG B organ domains = 11. 8 (72.7%) organ domains progressed to ≤ BILAG C. **Global clinical response (6 months):** 13/16 (81.3%).

Lu et al. 2009 **Prospective cohort**	n = 50 Female: 48 (96.0%) Mean age: 32.8 years (range 15 – 73) Arthritis: n=39; Skin: n=17; Serositis: n=16; Neuropsychiatric: n=6; Thrombocytopenia: n=4; AIHA: n=2; Antiphospholipid syndrome: n=2; Myositis: n=1; Gut vasculitis: n=1; Mouth ulcers: n=1	Clinical outcomes were assessed every 1 – 3 months. CR defined as a change from BILAG A or B score to BILAG C or D in every organ system. PR defined as a change from BILAG A or B to a C or D score in at least 1 system, but with persistence of 1 BILAG A or B in another system. NR defined as BILAG A or B that remains unchanged after treatment. Index: BILAG	**Median BILAG at 6 months**: from 12 (IQR 8- 15.5) to 5 (IQR 2.5 - 7); p < 0.001 **CR at 6 months:** 19/45 (42.2%) **PR at 6 months:** 21/45 (46.6%) Median anti-dsDNA at 6 months: from 106 (IQR 21 - 455) to 42 (IQR 13.5 - 181) IU/ml; p = 0.0001 Median C3 at 6 months: from 0.81 (IQR 0.52 - 1) to 0.95 (IQR 0.8 - 1.3) g/l; p < 0.02
Catapano et al. 2010 **Prospective cohort**	n = 31 Female: 28 (90.3%) Mean age: 40.2 ± 12.8 years Skin: n=30; Joint: n=30; Antiphospholipid syndrome: n=4; Ocular: n=12; Renal: n=13; Lung: n=13; CNS: n=13; Blood: n=5; Gut: n=2	Response was assessed at 3, 6, 12 and 24 months after treatment. CR defined as absence of BILAG A-, B-, and C-level disease activity. PR defined as the absence of BILAG A- and B-level disease activity. Relapse was defined as an increase in disease activity that required an increase in the prednisolone dose. Index: BILAG	**CR after the 1st RTX course:** 27/31 (87%) at median time of 4 months (IQR 1-9). **CR after the 2nd RTX course**: 15/16 (93.7%) at median time of 2 months (IQR 1-5). **BILAG median change** (2-year follow-up) (n=18): from 14.5 to 3 at 12 months and 3.5 at 24 months (p < 0.001). **Relapses:** 18/27 responders (67%) after a median of 11 months (IQR 4-24). Anti-dsDNA: from 147 to 54 IU/ml at 24 months. C3 and C4: before RTX C3 and C4 were low in 9 and 13 patients, respectively. C3 rose in 8/9 (88.8%) patients at 12 months from (mean ± SD) 0.52 ± 0.07 to 0.71 ± 0.09; p < 0.01) and in 7/9 (77.7%) patients at 24 months (from 0.52 ± 0.09 to 0.73 ± 0.1; p < 0.01). C4 rose in 11/13 (84.6%) patients at 12 months (from mean (± SD) 0.08 ± 0.01 to 0.14 ± 0.01; p < 0.01) and in 7/13 (53.8%) patients at 24 months (from 0.08 ± 0.01 to 0.15 ± 0.01; p < 0.01).
Terrier et al. 2010 **Prospective cohort**	n = 136 Female: 111 (81.6%) Mean (± SD) age: 39.1 ± 14.4 (range 9 - 87) Skin: n=72; Joint: n=58; Kidney: n=42; Blood: n=37; Serositis: n=18; CNS: n=10; Myocarditis: n=3; Peripheral neuropathy: n=3; Lung: n=2	Response was assessed at 6 ± 3 months (mean ± SD) after the last RTX infusion. Overall response defined as a reduction in the SELENA-SLEDAI score of ≥3. Cutaneous response: ≥50% improvement (PR) or disappearance (CR) of baseline manifestations. Articular response: ≥50% improvement in the number of painful and/or swollen joints (PR) or disappearance of pain and swelling from joints (CR). AIHA: PR defined as a haemoglobin level >10 g/dl. CR defined as a haemoglobin level >11 g/dl in women and 12 g/dl in men without haemolysis.	**Mean (± SD) SLEDAI:** from 10.8 ± 8.8 to 3.4 ± 5.2 at 6 ± 3 months; p < 0.0001. **Global clinical response**: 80/113 (71%). No differences in patients treated with and without immunosuppressive agents concomitantly. **Skin manifestations**: 48% CR and 23% PR **Joint involvement**: 52% CR and 20% PR **AIHA:** 69% CR and 15% PR. **Idiopathic thrombocytopenic purpura**: 77% CR and 15% PR. **Relapses**: 31/76 responders (41%) relapsed in 14.9 ± 7.6 months (mean ± SD).

		Autoimmune thrombocytopenic purpura: CR defined as a platelet count of ≥100,000/mm3, PR defined as 30,000 – 100,000/mm3 and at least a doubling of the baseline count. NR defined as a platelet count <30,000/mm3 or less than doubling of the baseline count. Index: SELENA-SLEDAI	**Mean (± SD) time-to-relapse**: 18.6 ± 13.5 months in patients with immunosuppressive agents vs. 13.5 ± 8.2 months in patients without concomitant immunosuppressive agents (p = 0.04).
Vital et al. 2011 **Prospective cohort**	n = 39 25/39 patients (64.1%) had BILAG grades of A in ≥1 domain 8/39 patients (20.5%) had BILAG grades of B in ≥2 domains. 5/39 patients (12.8%) had BILAG grade of B in only 1 domain but had disease that was resistant to alternative therapies and had more sever disease in the past.	Clinical response measured with the original BILAG index at baseline and every 3 months. CR defined as no domain rated BILAG A or B at week 26 and no A or B flare between weeks 0 and 26. PR defined as a maximum of 1 domain with a persistent B rating at 26 weeks with improvement in all other domains rated A or B at baseline, no new grade A flare between weeks 0 and 26, and no new grade B flare in more than 1 single domain between weeks 0 and 26. NR defined as patients not meeting the criteria for CR or PR. Relapse defined as a new BILAG grade A flare or 2 grade B flares following major clinical response or PR at 26 weeks. Index: BILAG	**Week 26: CR 20/39 (51%), PR 12/39 (31%), NR 7/39 (18%).** **Response in individual BILAG domains** (week 26): **General:** CR 9/10 (90%), PR 1/19 (5%), NR 0%, A or B flares 0%. **Mucocutaneous:** CR 12/19 (63%), PR 1/19 (5%), NR 6/19 (32%), A flares 1/19 (5%), B flares 2/19 (11%). **Neurologic:** CR 12/13 (92%), PR 0%, NR 1/13 (8%), A flares 0%, B flares 1/13 (8%). **Musculoskeletal**: CR 17/20 (85%), PR 2/20 (10%), NR 1/20 (5%), A flares 0%, B flares 3/20 (15%). **Cardiorespiratory:** CR 7/7 (100%), PR 0%, NR 0%, A or B flares 0%. **Vasculitis**: CR 6/6 (100%), PR 0%, NR 0%, A flares 0%, B flares 1/6 (17%). **Haematologic:** CR 8/12 (67%), PR 0%, NR 4/12 (33%), A or B flares 0%. **BILAG median change**: from 14 (IQR 9-23; n = 39) to 3 (IQR 2-5; n = 37) at 26 weeks and to 4 (IQR 2-8; n = 31) at 40 weeks (p < 0.0001). **Relapses:** 24/28 (85.7%) patients with major or partial clinical response at 26 weeks and total follow-up of at least 18 months. **Time-to-relapse:** earlier relapse at 12 months (n = 14) and later relapse at median 33 months (n = 10).
Turner-Stokes et al. 2011 **Prospective cohort**	n = 18 Female: 18 (100%) Mean age: 29.9 years (range 17 – 57) Joint: n=13; Kidney: n=12; Skin: n=10; Serositis: n=6; AIHA: n=2; Alopecia: n=2; Mouth ulcers: n=1; Neuropsychiatric: n=1; CNS vasculitis: n=1	Response was evaluated at 6 and 12 months following each cycle. CR defined as a change from a BILAG A or B score to a C or D score in every organ system. PR defined as a change from a BILAG A or B to a C or D score in at least one system, but with persistence of one BILAG A or B score in another system. NR defined as a BILAG A or B score that remained unchanged after treatment. Index: BILAG	**Median BILAG change after the 1st and 2nd cycle:** 6 months after the 1st cycle: from 12.5 to 8 (p < 0.01) 6 months after the 2nd cycle: from 13.5 to 8 (p < 0.01) 12 months after the 1st cycle: from 12.5 to 5 (p < 0.05) 12 months after the 2nd cycle: from 13.5 to 4 (p < 0.01) **Time-to-relapse:** 38% within 6 months and 82% within 12 months after the 1st cycle. 45% within 12 months after the 2nd cycle. Time-to-flare was significantly prolonged following the 2nd cycle vs. the 1st cycle ($X^2 = 32.39$; p < 0.01)

Pinto et al. 2011 **Prospective cohort**	n = 42 Female: 35 (83.3%) Mean (±SD) age: 29.7 ± 8.9 years Kidney: n=32; Neuropsychiatric: n=12; Blood: n=11; Musculoskeletal: n=10; Cardiopulmonary: n=9	Clinical and laboratory variables were measured before initiating therapy and every 3 months thereafter. Response to treatment was evaluated through the reduction of the SELENA-SLEDAI score, as well as the number of subjects with hypocomplementemia (C3 and C4). Neuropsychiatric SLE: response was evaluated through clinical neurologic exam. Autoimmune cytopaenias: CR defined as haemoglobin levels of ≥12 g/dl and a platelet count of >150,000/mm3 without requiring additional corticosteroids within 3 months. Index: SELENA-SLEDAI	**Significant reduction in SELENA-SLEDAI score**: reduction >60% at 3 months ($p < 0.005$). Improvement in 9/12 (75%) neuropsychiatric symptoms and cytopaenias at 3 months. The number of patients with hypocomplementemia (C3 and C4) decreased significantly after 3 months: from 26 to 5 patients and 25 to 5 patients, respectively).
Fernández-Nebro et al. 2012 **Retrospective cohort**	n = 128 Female: 115 (89.8%) Mean (±SD) age: 38.2 ± 12.1 years Musculoskeletal: n=42; Skin: n=25; Kidney: n=63; Blood: n=48; Neurological: n=27; Heart: n=18; Lung: n =22; Other: n=18	Rate of either CR or PR at 6 ± 3 months after the first course of RTX. CR defined as a SELENA-SLEDAI score of ≤2 points and a modified SELENA-SLEDAI Flare Index score of 0. PR defined by a reduction of at least 4 points in the SELENA-SLEDAI score with no new or worsening symptoms as measured by the SELENA-SLEDAI Flare Index. Index: SELENA-SLEDAI	**Response rate at 6 ± 3 months after the 1st course of RTX:** CR or PR: 73/116 (62.3%; 95% CI 49.3-79.1) CR: 22/116 (19.6%; 95% CI 12.3-29.7) PR: 51/116 (45.5%; 95% CI 36.1-55.2) **Clinical and serological response at 6 ± 3 months after 1st course of RTX**: Mean (±SD) SELENA-SLEDAI (n = 116): from 14.6 ± 10 to 4.8 ± 4.5, $p < 0.001$. **Joint involvement** (n = 45): from 54 (42.2%) to 4 (3.5%) patients, $p < 0.001$ **Skin manifestations** (n = 31): from 31 (24.2%) to 8 (7%) patients, $p < 0.001$ **Nasopharyngeal ulcers** (n =10): from 10 (7.8%) to 3 (2.6%)(patients, $p = 0.109$ **Thrombocytopaenia** (n = 21): from 21 (16.4%) to 3 (2.6%), $p < 0.001$ **Haemolytic anaemia** (n = 6): from 6 (4.7%) to 1 (1%), $p = 0.125$ **Systemic vasculitis** (n = 6): from 6 (4.7%) to 2 (1.7%), $p = 0.063$ **Pleuritis** (n = 8): from 8 (6.3%) to 1 (1%), $p = 0.031$ **Pericarditis** (n = 7): from 7 (5.5%) to 2 (1.7%), $p = 0.031$ **Fever** (n = 17): from 17 (13.3%) to 3 (2.6%), $p = 0.001$ **Response rate at the end of follow-up**: CR or PR: 97/125 (77.6%; 95% CI 62.9-94.7) PR: 47/125 (38.5%; 95% CI 29.8-47.8) **Median time to achieve best response** (n = 125): 6.5 months (IQR 5-8) **Relapse rate following the 1st course of RTX**: 37 patients (38.1%; 95% CI: 26.8-52.6) after a median of 10.8 months. **CR or PR at the end of follow-up:** Arthritis: 93% Skin: 87.5% Neuropsychiatric 73% Thrombocytopenia: 65% Severe generalised flare: 62%

Witt et al. 2013 **Retrospective cohort** **(GRAID registry)**	n = 85 Female: 69 (81.0%) Mean age: 36.6 years Fatigue: n=41; Erythema: n=36; Anemia: n=33; Myalgia: n=29; Arthritis: n=25; Kidney: n=31	Efficacy assessments were restricted to a categorization of CR, PR and NR as judged at the discretion of the treating physician. Response was further evaluated by comparison of mean SELENA-SLEDAI scores at baseline and after last infusion. Index. SELENA-SLEDAI	**CR**: n = 37 (46.8%) **PR**: n = 27 (34.2%) **NR:** n = 15 (19.0%) **Mean SELENA-SLEDAI** scores decreased significantly from 12.2 to 3.3 during rituximab treatment ($p<0.05$). **Presence of signs and symptoms**: Improvement in major manifestations ($p < 0.05$ each). Fever: 20.0% to 8.2%. Weight loss: 11.8% to 2.4%. Fatigue: 48.2% to 28.2%. Skin symptoms: 42.4% to 21.2%. Mucocutaneous involvement: 21.2% to 10.6%. Raynaud's syndrome: 35.3% to 18.8%. Pleuritic symptoms: 12.9% to 3.5%. Anemia: 38.3% to 23.5%. Leucopenia: 20.5% to 9.1%. Thrombocytopenia: 32.9% to 11.8%. Glomerulonephritis: 36.5% to 21.5%. Other manifestations such as musculoskeletal and neurologic manifestations also improved but did not reach statistical significance. The proportion of patients with leukopenia was reduced significantly from 20.5% to 9.1% ($p<0.05$). Mean complement C3 and C4 levels increased from 68.3 to 77.5 mg/dl and from 10.8 to 12.4 mg/dl, respectively (not significant). The proportion of patients with elevated dsDNA antibody levels decreased from 73.4% to 62.2% (not significant).
Gómez et al. 2018 **Retrospective cohort**	n = 20 Female: 16 (80.0%) Mean (±SD) age: 43.9 ± 15.8 years Arthritis: n=10; Kidney: n=8; Hematologic: n=6; Cutaneous: n=5; Pericarditis: n=3; Neurologic: n=1	Results were evaluated before and 3 months after each cycle of RTX. Clinical and laboratory variables were collected, as well as SLEDAI before and after treatment. Index: SLEDAI	**Median SLEDAI** Before: 10 (IQR 8-12); After: 4 (IQR 2-8) ($p<0.001$). Median ESR Before: 33.5 (IQR 15.2-54.7); After: 18.5 (IQR 5.7 – 27.7) ($p = 0.017$) Significant improvement of C4 levels after treatment ($p = 0.014$) No significant reduction of anti-dsDNA ($p = 0.125$)
Cassia et al. 2019 **Retrospective cohort**	n = 147 Female: 134 (91.2%) Mean age: 44 (range 41 – 46) Musculoskeletal: n=87; Skin: n=80; Hematologic: n=63; Lung: n=24; Kidney: n=52; Neurologic: n = 22	Results were assessed 6 months after the first RTX course. CR was defined as a physician assessment of disease activity score of 0 or 1, a reduction in the ECLAM score of ≥50%, and a decrease in the dose of immunomodulating agents of ≥25% from baseline. PR was defined as a physician assessment of disease activity score of >0, a reduction in the ECLAM score of 25 – 50%, and a decrease in the dose of immunomodulating agents of 0 – 25%.	**CR:** 67 patients (45%) **PR:** 41 patients (28%) **NR:** 39 patients (27%) **Mean ECLAM score**: from 4 (95% CI 3.65 – 4.34) to 1.9 (95% CI 1.66 – 2.14) at 6 months; $p < 0.0001$. Of the 67 patients who received a single course of RTX, 54 (80%) achieved a CR or PR, and 18 (33%) experienced a disease flare (51.5 flares per 100 patient-years). Of the 80 patients that received RTX as a maintenance treatment, 28 (35%) did not experience any flares during the maintenance period and were classified as sustained

		Any other response was defined as a NR. Disease flares were defined as an increase in at least 2 of the 3 parameters (physician assessment of disease activity, ECLAM score, and number or dose of immunosuppressive agents or glucocorticoids).	responders. Follow-up data were available for 21 of the 28 sustained responders. Ten (48%) of the 21 patients experienced a flare (27 flares per 100 patient-years).

*Patients could have more than one clinical manifestation of SLE.

AIHA: autoimmune haemolytic anaemia; anti-dsDNA: anti-double stranded DNA antibodies; BILAG: British Isles Lupus Assessment Group; CNS: central nervous system; CR: complete response; C3: complement component 3; C4: complement component 4; ECLAM: European Consensus Lupus Activity Measurement; ESR: erythrocyte sedimentation rate; IQR: interquartile range; NR: no response; PR: partial response; RTX: rituximab; SD: standard deviation; SLE: systemic lupus erythematosus; SELENA-SLEDAI: Safety of Estrogens in Lupus Erythematosus National Assessment- Systemic Lupus Erythematosus Disease Activity Index; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index.