Supplementary Table S1. Clinical parameters in patients with SSc and CREST-syndrome included in the study.

Clinical parameter	Patients with	
	SSc (n=151)	CREST-syndrome (n=88)
Sex distribution	1.8:1	17:1
Age at initial sample collection in years (range; median)	11-80	21-97
	47	55
Time between first diagnosis and serological analysis	0-434	0-194
in months (range; median)	21	19
Therapy: number (%)		
Without any therapy	42 (28)	70 (80)
Only steroids	14 (9)	6 (7)
Immunosuppressive therapy (cyclophosphamide, methotrexate, mycophenolate, azathioprine, leflunomide)	80 (53)	12 (14)
Autologous stem cell transplantation	15 (10)	0

Supplementary Table S2. Association of anti-CENP-A- and -B-antibodies of the IgG- and IgE-type in 73 patients with CREST-Syndrome.

IgG-type	IgE-type	anti-CENP-A	anti-CENP-B
		Number (%) positive	
+	+	48 (66)	56 (77)
+	-	20 (27)	13 (18)
-	+	1 (1)	1 (1)
-	-	4 (5)	3 (4)

Supplementary Table S3. Association of anti-topo-I antibodies of the IgG- and IgE-type in 116 patients with SSc.

anti-topo-I IgG	anti-topo-I IgE	Number (%) positive
+	+	62 (53)
+	-	44 (38)
-	+	3 (3)
-	-	7 (6)

Supplementary Table S4. Correlation of anti-CENP-A- and -B antibodies of the IgE-type with clinical manifestations in patients with CREST-syndrome.

Organ manifestations / clinical symptoms		Number patients	Anti-CENP-A-IgE	Anti-CENP-B-IgE
			Number (%) positive	
Number of organ manifestations	0-1	7	3 (43)	5 (71)
	2-4	37	19 (51)	25 (68)
	5-7	6	6 (100) *)	6 (100)
mRSS	0	6	1 (17)	5 (83)
	1-5	10	6 (60)	6 (60)
	6-10	2	2 (100)	2 (100)
cutaneous – general (*i.e.*, sclerodactyly, calcinosis, morphoea)	without	20	10 (50)	14 (70)
	with	30	18 (60)	22 (73)
cutaneous – ulceration	without	38	18 (47)**)	26 (68)
	with	12	10 (83)	10 (83)
musculoskeletal	without	43	24 (56)	31 (72)
	with	7	4 (57)	5 (71)
Lung fibrosis	without	41	23 (56)	30 (73)
	with	9	5 (56)	6 (67)
Pulmonary-arterial hypertension (PAH)	without	46	25 (54)	32 (70)
	with	4	3 (75)	4 (100)
cardiac	without	48	26 (54)	34 (71)
	with	2	2 (100)	2 (100)
renal	without	49	27 (55)	35 (71)
	with	1	1 (100)	1 (100)
gastrointestinal	without	33	17 (52)	23 (70)
	with	17	11 (65)	13 (76)
neuropsychiatric	without	47	26 (55)	34 (72)
	with	3	2 (67)	2 (67)
vasculopathy	without	3	2 (67)	2 (67)
	with	47	26 (55)	34 (72)
Sicca Syndrome	without	34	17 (50)	21 (62) *)
	with	16	11 (69)	15 (94)
lymphadenopathy	without	50	28 (56)	36 (72)
	with	0	0 (0)	0 (0)
Other parameters				
hepatic	without	47	26 (55)	34 (72)
	with	3	2 (67)	2 67)
haematological	without	45	27 (60)	33 (73)
	with	5	1 (20)	3 (60)
CRP	normal	31	19 (61)	20 (65)
	↑	8	3 (38)	5 (63)
C3 complement	normal	20	12 (60)	14 (70)
	↓	1	1 (100)	1 (100)
C4 complement	normal	20	12 (60)	14 (70)
	↓	1	1 (100)	1 (100)
eosinophil count	< 300/mm^3	41	39 (95)	40 (98)
	> 300/mm^3	8	6 (75)	6 (75)

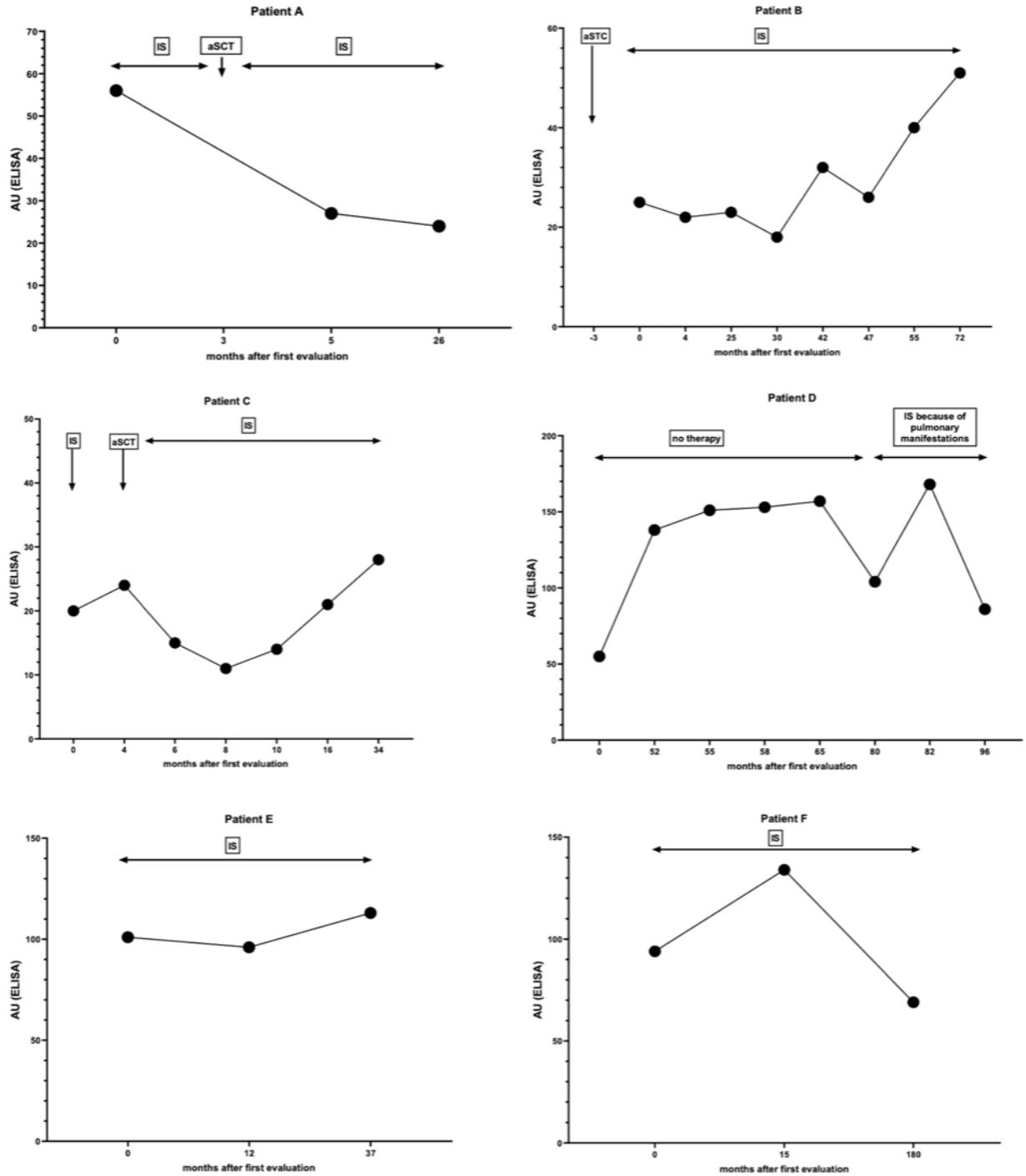
*) trend with p=0.07; **) p<0,05 as compared to patients with the respective clinical manifestation.

Supplementary Table S5. Correlation of anti-topo-I antibodies of the IgE-type and clinical manifestations in 63 patients with SSc.

Organ manifestations / clinical symptoms		Number patients	anti-topo-I IgE number (%) positive
Number of organ manifestations (max. 10)	0-1	1	0
	2-4	39	21 (54)
	5-8	23	11 (48)
dcSSc		40	20 (50)
lcSSc		21	11 (52)
mRSS	0-9	16	7 (44)
	10-19	16	7 (44)
	20-29	20	9 (45)
	>=30	5	4 (80)
cutaneous – general (*i.e.*, sclerodactyly, calcinosis, morphoea)	without	2	0
	with	61	32 (52)
cutaneous – ulcers	without	28	14 (50)
	with	35	18 (51)
musculoskeletal	without	37	17 (46)
	with	26	15 (58)
Lung fibrosis	without	14	9 (64)
	with	49	23 (47)
pulmonary-arterial hypertension (PAH)	without	58	31 (53)
	with	5	1 (20)
cardiac	without	45	25 (56)
	with	18	7 (39)
renal	without	59	31 (53)
	with	4	1 (25)
gastrointestinal	without	34	18 (53)
	with	29	14 (48)
neuropsychiatric	without	62	32 (52)
	with	1	0
vasculopathy	without	4	2 (50)
	with	59	30 (51)
Sicca syndrome	without	59	29 (49)
	with	4	3 (75)
lymphadenopathy	without	61	31 (51)
	with	2	1 (50)
Other parameters			
Hepatic	without	63	32 (51)
	with	0	0
haematological	without	48	26 (54)
	with	15	6 (40)
CRP	normal	17	8 (47)
	↑	43	22 (51)
C3 complement	normal	28	13 (46)
	↓	1	1 (100)
C4 complement	normal	28	13 (46)
	↓	1	1 (100)

Supplementary Table S6. Prevalence of anti-CENP-A/B and -topo-I antibodies of the IgE-type in relation to the time between first diagnosis of the disease and serological analysis.

Time between first diagnosis and time of serological analysis (months)	IgE-antibodies number positive/number tested (%)		
	anti-CENP-A	anti-CENP-B	anti-topo-I
0-12	12/22 (55)	16/22 (73)	13/19 (68)
13-24	2/5 (40)	2/5 (40)	7/17 (41)
25-48	2/5 (40)	3/5 (60)	5/12 (42)
>48	12/18 (67)	15/18 (83)	7/15 (47)



Supplementary Fig. S1. Course of anti-topo-I IgE-reactivity in six SSc patients for up to 180 months under different therapeutic conditions. aSCT: autologous stem cell transplantation; IS: immunosuppressive therapy.

Plain Language Summary

- Systemic sclerosis is an autoimmune disorder characterised by fibrosis of the skin but also visceral organs (lung, gastrointestinal tract, heart).
- Its aetiology and pathology are unknown but immune reactions to autoantigens may play an important role.
- Autoantibodies to nuclear antigens are important marker for the serological diagnosis and are mainly directed against topoisomerase-I and centromeric antigens.
- As in most autoimmune diseases the antibodies are of the IgG-type.
- In some autoimmune diseases also IgE-antibodies known to characterise a distinct immunological reaction resembling allergies has been described.
- In systemic sclerosis we now could detect also IgE antinuclear antibodies in a high prevalence.
- These IgE-autoantibodies to topoisomerase-I and centromeric proteins correlate with CREST-syndrome and systemic sclerosis, respectively.
- Especially IgE-anti-CENP-A antibodies correlate with clinical activity in CREST-syndrome.
- These data underline the concept that systemic sclerosis resembles from an immunological point of view allergic diseases.