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Table 1. Association between clinical and therapeutic factors with mortality in SLE patients.

Factors associated with mortality	Univariado	Multivariado
	β (95 % IC)	β (95 % IC) $\square$
Age	0.93 (0.96-1.02)	0.98 (0.96-1.02)
Use of mechanical ventilation	3.83 (1.07-13.4)*	3.07 (0.59-16.04)
Previous use of steroids	3.92 (1.51-10.15)*	2.04 (0.58-7.35)
Previous use of immunosuppression	4.04 (1.42-11.45)*	2.85 (0.71-11.48)
Infection	3.57 (1.41-9.01)*	3.25 (1.19-8.86)*

p <0.05 *

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AB0282

SAFETY, TOLERABILITY AND SELECTIVE EXPANSION OF REGULATORY T CELLS BY A SINGLE DOSE OF THE NOVEL IL-2 MUTEIN PT101 IN A PHASE 1 STUDY IN HEALTHY VOLUNTEERS

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Background: Activation and expansion of regulatory T cells (Tregs) has been proposed as a strategy to treat autoimmunity. When administered in low doses, IL-2 expands and activates Tregs leading to clinical response in several autoimmune diseases. However, the narrow therapeutic window of IL-2 results in loss of selectivity for Tregs and concurrent activation of conventional T cells (Tconv) and NK cells, limiting its clinical utility. This loss of selectivity may negate the clinical benefit of Treg activation and lead to dose-limiting side effects. PT101 is a novel engineered variant of IL-2 fused to an Fc protein backbone which in preclinical studies selectively activates Tregs without expanding Tconv or NK cells. PT101 is in clinical development for the treatment of patients with autoimmune diseases.

Objectives: To assess the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of PT101 after a single dose in healthy human volunteers.

Methods: We conducted a randomized, double-blind, single-ascending dose trial of PT101 or placebo (3:1 allocation). Five dose levels from 1 mg to 10 mg were administered by subcutaneous injection. Adverse events, physical examination findings, and clinical laboratory results were assessed for 29 days. Serum PT101 levels and antidrug antibody were assessed. Changes in mononuclear cell populations were measured in peripheral blood by flow cytometry.

Results: 56 subjects were administered PT101 or placebo. All subjects completed the study. There were no deaths, serious adverse events, dose limiting toxicities, or clinically significant changes in vital sign, ECG, or laboratory results. All adverse events were Grade 1 or 2 and self-limited. Injection site reactions were the most common adverse event. Transient increases in eosinophil counts were observed in some subjects, consistent with the known class effect of IL-2. Peak levels of PT101 occurred 11.0 to 14.6 hours after administration, and declined with a mean half-life of 20.4 to 28.3 hours, demonstrating linear exposure through the dose range. No anti-drug antibodies were induced. PT101 caused dose-related expansion of Tregs that plateaued at doses between 3.5 and 10 mg. Mean maximum expansion above baseline was 3.6-fold for total Tregs and 72.5-fold for the CD25bright subset of Tregs. Maximal expansion was observed by Day 8-10 with a return toward baseline by Day 29. Over 80% of subjects achieved a 2-fold or greater expansion of total Tregs (Table 1). No significant expansion of Tconv or NK cells was observed at any dose level.

Table 1. Percent Total Treg Responders

	Placebo (n=14)	1 mg (n=6)	3.5 mg (n=12)	5 mg (n=12)	7.5 mg (n=6)	10 mg (n=6)
Fold Change Total Tregs						
≥ 2X	7%	33%	83%	83%	100%	100%
≥ 3X	0%	0%	58%	75%	33%	50%
≥ 4X	0%	0%	24%	42%	33%	17%

Conclusion: PT101 was safe and well tolerated after a single dose in healthy volunteers. Marked expansion of both total Treg and CD25bright Treg cells was observed. High selectivity for Tregs was observed with no significant expansion of pro-inflammatory Tconv and NK cells even at the highest dose studied. These results support the therapeutic potential of PT101 in planned multiple dose studies in systemic lupus erythematosus, ulcerative colitis, and other autoimmune diseases.

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AB0283

CHOREOATHETOSIS AND LONGITUDINALLY EXTENSIVE TRANSVERSE MYELITIS AS RARE AND SEVERE MANIFESTATIONS OF NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS AND PRIMARY SJÖGREN'S SYNDROME – A TWO-CENTER EXPERIENCE

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Background: Systemic lupus erythematosus (SLE) can affect almost any organ system. Nevertheless, Lupus nephritis and neuropsychiatric manifestations (NPSLE) are associated with increased mortality (1). Therapeutic options include glucocorticoids, often pulse methylprednisolone (MP), and other immunosuppressive therapies. In refractory cases, therapeutic plasma exchange, rituximab, or intravenous immunoglobulins are often used (2). However, an optimal therapeutic strategy has not been established because NPSLE is an exclusion criterion in most clinical trials. In addition, NPSLE can present with a broad spectrum of manifestations ranging from cognitive dysfunction to severe and life-threatening disease with choreoathetosis or transverse myelitis (TM). In primary Sjögren's syndrome (pSS), neurological manifestations most often include peripheral neuropathies, but TM has also been reported.

Objectives: To analyze the clinical presentation and outcomes after treatment in severe, life-threatening NPSLE.

Methods: We retrospectively analyzed clinical, laboratory, and imaging features in severe NPSLE manifestations in SLE and pSS patients at two tertiary academic centers (University Medical Center Göttingen, Germany, and ASST Spedali Civili Brescia, Italy) with a high volume of SLE patients. Severe NPSLE was defined as either severe movement disorder or extensive tetra- or paraplegia secondary to (longitudinally extensive) transverse myelitis.

Results: Our retrospective chart review resulted in seven patients fulfilling the inclusion criteria (six with SLE and 1 with pSS). Of these, five were females (71.4%). Median age was 26 (16-55) years. Three were of Asian origin, four were of European descent. Median disease duration was 15 (2-228) months. Three patients presented with severe choreoathetosis, all had positive ANA, anti-dsDNA antibodies (abs), and complement consumption. Of note, all three had at least one positive antiphospholipid antibody (APLA). All patients received IV MP 1g x 3 and mycophenolate mofetil and achieved complete remission. Of the four patients with longitudinally extensive TM, all were ANA positive, only two had anti-dsDNA abs. None of them had APLA, and only one tested positive for anti-aquaporin-4 abs. Of all patients, only one had positive ribosomal P-abs. Patients with TM received IV MP 1g x 5 and either RTX (4 cycles with 375 mg/m² or IVIg 0.4 g/kg/d x 5). All four TM patients improved; two improved markedly, two moderately with residual deficits as assessed by EDMUS-grading scale and functional independence measure.

Conclusion: Severe NPSLE, defined as choreoathetosis or TM require intensive treatment. While the former patients achieved complete remission, two of four patients with TM only achieved partial remission. Our data support the use of early