Final Study report

Study title

A pilot open-label study to assess the efficacy and safety of tocilizumab in patients with active Schnitzler's syndrome

Short title: TOCISCH
Treatment with tocilizumab (RoActemra®)
Eudra-CT Number: 2016-003828-23
Phase II
19.07.2017 – 10.04.2019

Sponsor

Dermatological Allergology
Allergie-Centrum-Charité
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Version / Date - 3.0 / 27.05.2020

Abbreviations:

AE	Adverse event
AESI	Adverse event of special interest
CRP	C reactive Protein
DHAF	Daily Health Assessment Form
DLQI	Dermatology Quality of Life Index
ESR	Erythrocyte sedimentation rates
IL	Interleukin
IV	intravenous
mIL-6R	membrane-bound interleukin-6 receptor
PGA	physician global assessment
pJIA	polyarticular-course juvenile idiopathic arthritis
RA	rheumatoid arthritis
SAA	Serum Amyloid A
SC	subcutaneous
SchS	Schnitzler's syndrome
SchAS	Schnitzler acitivity scores
SD	Standard deviation
sIL-6R	soluble interleukin-6 receptor
sJIA	systemic juvenile idiopathic arthritis
TRAPS	tumor necrosis factor receptor-associated periodic syndrome

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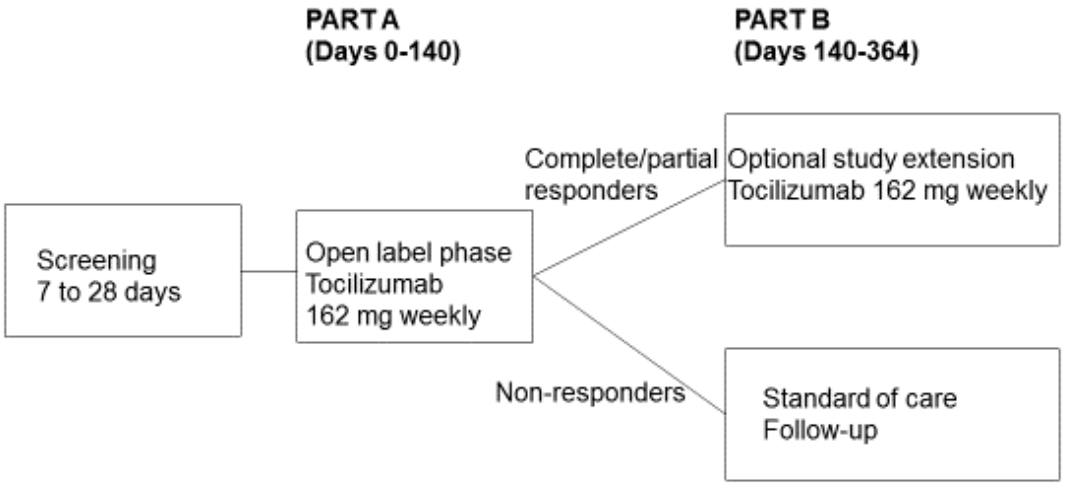
Name of Finished Product: Tocilizumab (RoActemra®) (ATC-Code: ATC L04AC07)

Name of Active Substance: RO4877533

Individual Study Table:



Title of Study:
A pilot open-label study to assess the efficacy and safety of tocilizumab in patients with active Schnitzler's syndrome (SchS) (TOCISCH)

Investigator and study center:
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Publication:
A publication reporting the results of the study is planned for Q3/2020 (target journal: JACI in practice).

first patient screened: 19.07.2017 **last patient out:** 11.03.2019	**Phase of development:** II

Objectives:

Primary objective:

- To assess the effect of tocilizumab on the clinical signs and symptoms of SchS

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Secondary objectives:

- To assess the effect of tocilizumab on inflammation markers (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], serum amyloid A [SAA], S100A8/9)
- To assess the effect of tocilizumab on the patient's quality of life
- To assess the safety and tolerability following administration of tocilizumab to patients with SchS

Introduction:

Tocilizumab ((RoActemra®, L04AC07,Roche/Chugai, CH-4070 Basel, Switzerland) is a recombinant humanized, anti-human monoclonal antibody of the IgG1 sub-class directed against the soluble (sIL-6R) and membrane-bound interleukin-6 receptor (mIL-6R). Interleukin-6 (IL-6) is a key mediator of local and systemic inflammatory reactions. The final tocilizumab drug has intravenous (IV) and subcutaneous (SC) formulations. Tocilizumab (IV and SC formulations) is indicated for adults for treatment of moderate to severe active rheumatoid arthritis (RA) in E.U. and U.S.. Moreover, tocilizumab (IV formulation) is approved for children 2 years of age and older for treatment of polyarticular-course juvenile idiopathic arthritis (pJIA) and systemic juvenile idiopathic arthritis (sJIA) in E.U. and U.S.. In India and Japan, tocilizumab is approved for treatment of Castleman's disease.

Clinical studies were conducted for Crohn's disease, multiple myeloma, systemic lupus erythematosus, ankylosing spondylitis and B-cell chronic lymphocytic leukemia, but tocilizumab is no longer being developed for these indications. Moreover, tocilizumab has been shown to be effective in severe uveitis associated with Behçet's disease. Effective treatment of single patients with autoinflammatory diseases tumor necrosis factor receptor-associated periodic syndrome (TRAPS) as well as Schnitzler's syndrome has been reported.

On the basis of the beneficial treatment response to tocilizumab in various chronic inflammatory diseases including RA, sJIA and single cases with TRAPS and SchS, it is supposed that tocilizumab may be highly effective in autoinflammatory diseases too. Therefore, this study will evaluate the efficacy and safety of tocilizumab in patients with active SchS.

Methodology:

N=9 patients entered the initial screening phase of the study. N=8 patients were eligible for the study and entered the treatment phase. N=4 patients discontinued the study. N=4 patients completed the study.

Patients received tocilizumab 162 mg subcutaneous injections every week within 52 weeks. Efficacy was monitored by changes in disease activity (physician global assessment [PGA; range 0-20]), inflammation markers (CRP, ESR, SAA, S100A8/9 and quality of life [DLQI, SF-36]). Safety assessment included adverse event reporting and routine clinical and laboratory assessments.

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Number of patients (planned and analyzed)

N (total) = 8 patients with SchS analyzed (max. n=12 patients were planned)

N=9 patients were screened, N = 8 patients entered the study

N = 4 patients completed whole study period (364 days)

Diagnosis and main criteria for inclusion:

Diagnosis: Patients with symptomatic SchS based on Strasbourg clinical criteria obligate: chronic urticarial rash, monoclonal paraprotein (IgM or IgG); minor: recurrent fever (must be >38 °C and otherwise unexplained), objective findings of abnormal bone remodeling with or without bone pain (as assessed by bone scintigraphy, MRI or elevation of bone alkaline phosphatase), a neutrophilic dermal infiltrate on skin biopsy, leukocytosis and/or elevated CRP. A patient can be diagnosed with Schnitzler's syndrome when there is a combination of both obligate criteria and at least 2 minor criteria if IgM and at least 3 minor criteria if IgG after exclusion of other causes.

Main inclusion criteria:

- Written informed consent
- Adults (18 years or older)
- SchS diagnosis based on Strasbourg clinical criteria
- Active SchS, refractory to treatment with antihistamines, NSAIDS or colchicine, hydroxychloroquine or dapsone
- Patients who have a symptom score (PGA) of at least 8 (0-20) at baseline
- If necessary, concurrent/ongoing treatment with a stable dose of systemic corticosteroids not greater than 10mg/d for 14 days prior to baseline
- If necessary, concurrent/ongoing treatment with a stable dose of antihistamines and NSAIDs for 7 days prior to baseline
- Able to read, understand and willing to sign the informed consent form and abide with study procedures
- Willing, committed and able to return for all clinic visits and complete all study-related procedures, including willingness to have SC injections administered by a qualified person
- In females of childbearing potential: Negative pregnancy test within 28 days of day 0; males and females willing to use highly effective contraception (Pearl-Index < 1) during study treatment and for a minimum of 3 months after last dose of tocilizumab. Pregnancies occurring up to 90 days after the completion of the study medication must be reported to the investigator. A woman will be considered not of childbearing potential if she is post-menopausal for greater

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than two years or surgically sterile (bilateral tubal ligation, bilateral oophorectomy or hysterectomy)

- Subjects are considered eligible, if they meet the following tuberculosis (TB) screening criteria: no history of active TB prior to screening, no signs or symptoms suggestive of active TB, no recent close contacts with a person with active TB, and negative QuantiFERON-TB test at screening (if QuantiFERON-TB test is positive, the patient can only be included, if active TB is ruled out with appropriate measurements according to standard of care, e.g. the patient is pre-treated with isoniazide for 4 weeks).
- No participation in other clinical trials 4 weeks before and after participation in this study

Main exclusion criteria:

•Concurrent/ongoing treatment with immunosuppressives, IL-1 blockers and other biologics

•History of severe allergic or anaphylactic reactions to human, humanized or murine monoclonal antibodies and/or to any constituent of the products of tocilizumab

•Significant concomitant illness such as, but not limited to, cardiac, renal, neurological, endocrinological, metabolic, or lymphatic disease that would adversely affect the subject's participation or evaluation in this study

•Evidence of of active, recurrent or latent systemic infection including tuberculosis, HIV, Hepatitis B, or Hepatitis C infection by clinical or serological history

•Active systemic inflammatory condition other than SchS including, but not limited to, rheumatoid arthritis

•History of malignancies within five years prior to screening

Test product, dose and mode of administration

• Tocilizumab (RoActemra ®)

•162 mg

•interval between tocilizumab doses is 1 week

• subcutaneous administration

Duration of treatment:
Treatment assignment to receive tocilizumab will occur at day 0 (Visit 2). Patients with symptomatic SchS (according to the physician's global assessment with a minimum score of 8 at visit 2 and elevated inflammation markers, i.e. CRP above ULN, who meet all inclusion and exclusion criteria, e.g. absence of current infections such as HIV, hepatitis B and C) will enter part A (days 1-140) of the study and receive a single tocilizumab (RoActemra®) 162 mg injection.

Day 0:
At day 0 (visit 2) treatment assignment to receive a single dose of tocilizumab. First study drug application will be performed in the clinic, after successful training, patients will self-administer study drug 1x/weekly at home.

Day 14 (visit 3) – Day 112, week 16 (visit 7)
At day 14 (visit 3) physical examination including vitals sign, laboratory analysis (hematology and chemistry panel, CRP, ESR, SAA, S100A8/9) and the physician's global assessment will be performed. Concomitant medications and adverse events as well as DLQI and SF36 will be documented. At visit 4 and 6 an ECG will be performed and at visit 3, 4 and 5 research blood samples will be taken. At visit 3 and 4, DHAF will be distributed and reviewed at visits 2-5.

Day 140 (visit 8):
At day 140 (visit 8), patients will be evaluated for efficacy and safety parameters as in all visits before. Treatment response will be determined.
tocilizumab -treated patients with complete or partial response: → will be eligible to enter part B and receive tocilizumab 162 mg.

- complete clinical response: no or minimal disease activity: total PGA score of 5 or less and no greater than 1 in any of the 5 constituent signs/symptoms
- A partial clinical response was defined as mild to moderate disease activity with a PGA score of more than 5 and PGA reduction of 30% or more as compared with baseline.
- No clinical response: high disease activity with PGA scores increased, stable, or showed less than 30% reduction.

tocilizumab -treated patients without clinical response: → will be considered a treatment failure and begin treatment with standard of care. These patients will be assessed 4 weeks later for an end of study (EOS) visit where all safety parameters and immunogenicity will be assessed. The patient will be contacted by phone 8 weeks after visit 8 to assess further AEs.

Patients will only be eligible to enter part B of the study, if they are evaluated as complete or partial responders to tocilizumab treatment at visit 8.

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Day 140 (visit 8) – Day 364 (visit 13) In part B (days 140-364) of the study, all patients will receive tocilizumab open-label treatment weekly at home, supervised by the study center. All patients will receive tocilizumab treatment over a time period of 32 weeks in part B. Tocilizumab treatment will occur weekly.
Reference therapy, dose and mode of administration Not applicable.

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Criteria for evaluation:
This study is a pilot study intended to provide efficacy, safety and tolerability data in a small patient population of SchS. With the small sample size and the unknown variability of the disease activity assessments in this population, statistical power considerations are unwarranted in principle. Due to the limited patient numbers with SchS, the sample size is not based on statistical methodology but reflects the number of patients that are currently treated at the Autoinflammation Reference Center Charité and thought to willing and suitable to participate in the study.

Primary objective:
- To assess the effects of TCZ on the clinical signs and symptoms of Schnitzler's syndrome (SchS)

Secondary objectives:
- To assess the effect of TCZ on inflammation markers (CRP, ESR, SAA, S100A8/9) in subjects with SchS
- To assess the effect of TCZ on the patient's quality of life
- To assess the safety and tolerability following administration of TCZ to patients with SchS

Primary endpoint:
- Change in the investigator's assessment of total disease activity (Physician global assessment [PGA], a composite score which includes the 5 key clinical symptoms of SchS) between baseline (week 0) and TCZ treatment (week 20)

Secondary endpoints:
- Proportion of patients with complete response (based on physician's global assessment [PGA] with no or minimal overall autoinflammatory disease activity and CRP </= 10 mg/l) at week 20
- Change in the patient based Schnitzler Activity Score (SchAS) during the treatment period (The SchAS combines the key symptoms of SchS)
- Change in inflammation markers (CRP, ESR, SAA, S100A8/9) during the treatment period
- Change in the patient's quality of life (assessed by the Dermatology Life Quality Index and SF 36)
- Safety and tolerability: This includes physical examination, electrocardiogram routine safety laboratory assessments, clinical observation, vital signs and adverse event reporting

Efficacy, Safety:

Efficacy Variables:
These include:

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PGA scores
Schnitzler acitivity scores (SchAS)
Patient-based DHAF scores
Inflammation markers (CRP, ESR, SAA, S100A8/9)
Quality of life assessment (DLQI, SF 36)

Safety Variables:

Safety assessment included adverse event reporting and routine clinical and laboratory assessments.

A TEAE is one that was not present prior to first dose of study medication or represents an exacerbation of a condition that was present prior to first dose. All adverse experiences, regardless of method of identification (e.g., patient reports, vital signs, physical examination, and laboratory tests), are expected to be reported as adverse events. All reported adverse events will be recorded using coded terms and safety data will be summarized using descriptive statistics.

Safety analysis will be performed on the safety population. Summary statistics for all safety variables will include the total number of subjects and the number experiencing the adverse event by body system using MedDRA terminology.

Statistical methods:
Due to the limited patient numbers with SchS, the sample size is not based on statistical methodology but reflects the number of patients that are currently treated at the Autoinflammation Reference Center Charité and thought to be willing and suitable to participate in the study. All patients who receive at least one treatment of study medication will be included in the safety analysis. All patients who continue until visit 8 will be included in the primary endpoint analysis.
Research question:
Tocilizumab treatment is effective in SchS (change from baseline in disease activity [PGA])
For comparisons between baseline and tocilizumab treatment, primarily descriptive statistics will be used. For continuous variables, the number of patients reflected in the calculation (n), mean, median, standard deviation, minimum, and maximum, including confidence intervals where applicable, will be assessed. For categorical data, frequencies and percentages will be displayed for each category.
If a sufficient number of subjects is recruited, appropriate statistical tests will be advanced; otherwise, only descriptive statistics will be provided.
For comparisons between baseline and open-label treatment period with continuous variables and expected normal distribution, a paired t-test will be used. If parametric assumptions are unwarranted, non-parametric analogies such as the Wilcoxon signed rank test will be advanced.

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All analyses will be performed with SPSS, GraphPad Prism or Excel.
Statistical analysis is supported by Stephanie Roll, PhD, Institute for Social Medicine, Epidemiology and Health Economics, Charité – Universitätsmedizin Berlin

RESULTS

Efficacy Results:

Open-label phase

A total of 9 patients were screened and 8 patients were included in the study. The primary endpoint showed a lower mean total PGA score at week 20 (3.3, SD 3.6; PGA change from baseline in disease activity: mean of differences -8.7, for further information see *Statistical Report*) compared to baseline (12.1, SD 2.5; p=0.0006) (**Fig. 1, Tab. 1**). Tocilizumab treatment resulted in reduction of mean total SchAS scores. (**Fig. 2**) Efficacy of tocilizumab was also shown by normalization of mean inflammation marker levels (CRP 0.6 mg/l, SD 1.0; SAA 4.1 mg/l, SD 3.5; ESR 12.6 mm/h, SD 13.1 at week 20) compared to baseline levels (CRP 31.67 mg/l, SD 54.1; SAA 176 mg/l, SD 260.2; ESR 37.6 mm/h, SD 29.3) (**Fig. 3-5**). Mean S100A8/9 levels showed lower levels at week 20 (2.4 µg/ml, SD 1.1) compared to baseline (6.6 µg/ml, SD 6.6) with a high intraindividual variability (**Fig. 6**). Quality of life scores DLQI and SF 36 did not show relevant changes over the course of the study. (**Fig. 7-9**) One patient discontinued the open-label treatment phase at week 16 because of occurrence of an adverse event and insufficient treatment response.

Optional study extension

6 patients with no or minimal overall autoinflammatory disease activity at week 20 participated in the optional study extension. 4 patients discontinued the study (1 after 16 weeks, 1 after 20 weeks, 2 after 36 weeks) due to insufficient treatment response/loss of efficacy and/or occurrence of adverse events. In cases of decreased efficacy, inflammation markers remained normal (**Fig. 2-6**), however total PGA scores increased in n=3/4 patients as shown by elevated scores for urticarial rash, fatigue, arthralgia and myalgia (**Fig.1**, **Tab. 1**). Testing for anti-drug antibodies was negative for all n=8 patients. (**Tab. 2**).

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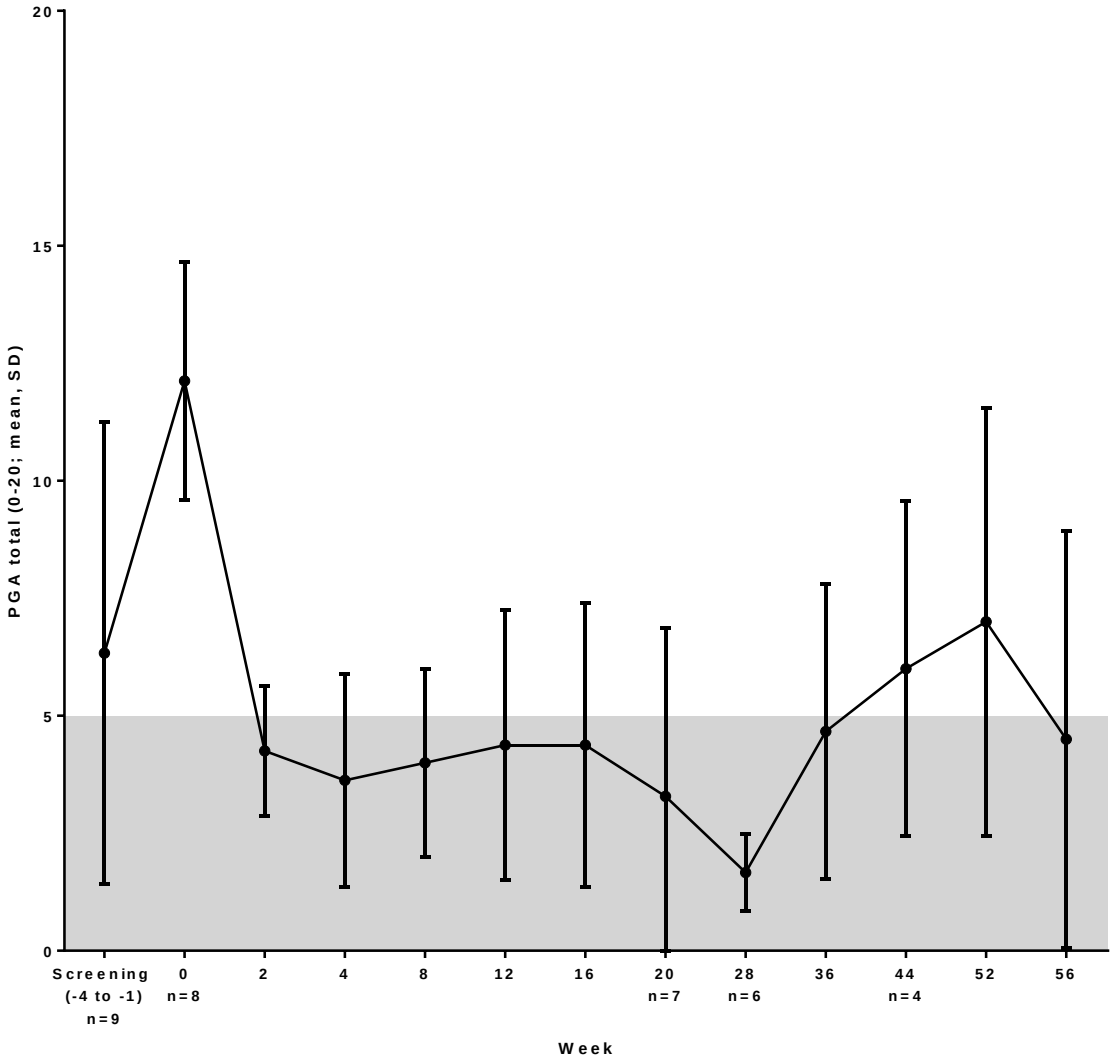

Figure 1: Physician global assessment (PGA, 0-20; mean, Standard deviation [SD]) values of tocilizumab-treated SchS patients over time shown for all visits. The light gray areas indicate minimal disease activity.

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PGA	**open label phase**		**optional study extension**
	Baseline (week 0) n=8 Mean (SD, range)	**Week 20 n=7 Mean (SD, range)**	**Week 52 n=4 Mean (SD, range)**
Total (0-20)	12.1 (2.5, 8-16)	3.3 (3.6, 1-11)	7 (4.5, 1-12)
Urticarial rash (0-4)	1.8 (1.5, 0-4)	1.0 (1.5, 0-4)	2 (1.4, 0-3)
Fatigue (0-4)	2.6 (0.7, 2-4)	0.6 (0.5, 0-1)	1.8 (1, 1-3)
Fever (0-4)	1.4 (1.3, 0-3)	0 (0, 0)	0 (0, 0)
Myalgia (0-4)	2.9 (0.8, 2-4)	0.9 (1.1, 0-3)	1.8 (1.3, 0-3)
Arthralgia /bone pain (0-4)	3.5 (0.5, 3-4)	0.9 (1.2, 0-3)	1.5 (1.3, 0-3)

Table 1: Overview on physician global assessement total score and subscores in tocilizumab treated patients.

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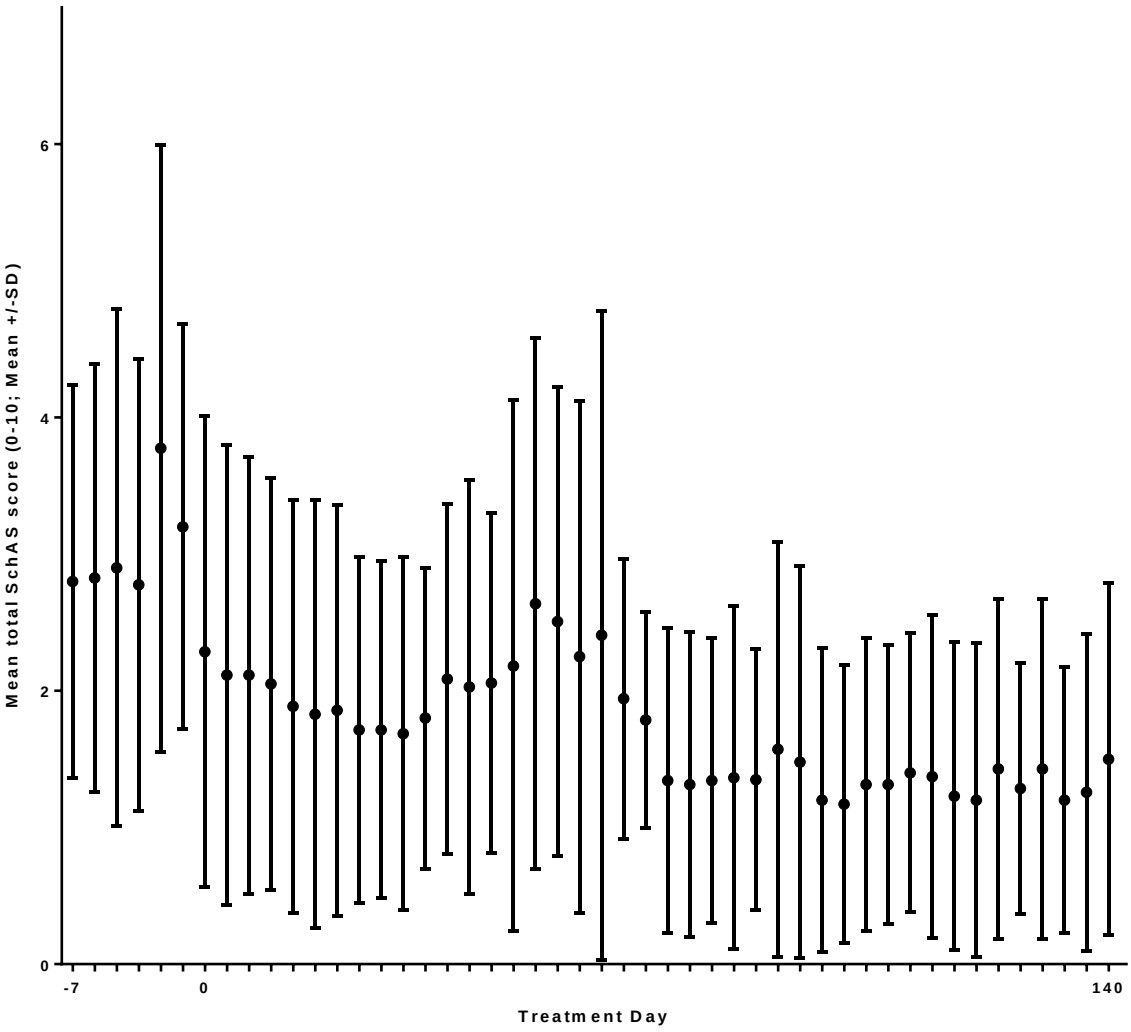

Figure 2: Mean total SchAS (Schnitzler's syndrome activity score, 0-10) as determined from the Daily Health Assessment Form (DHAF) during the screening phase (for 7 days) and open label treatment phase (140 days).

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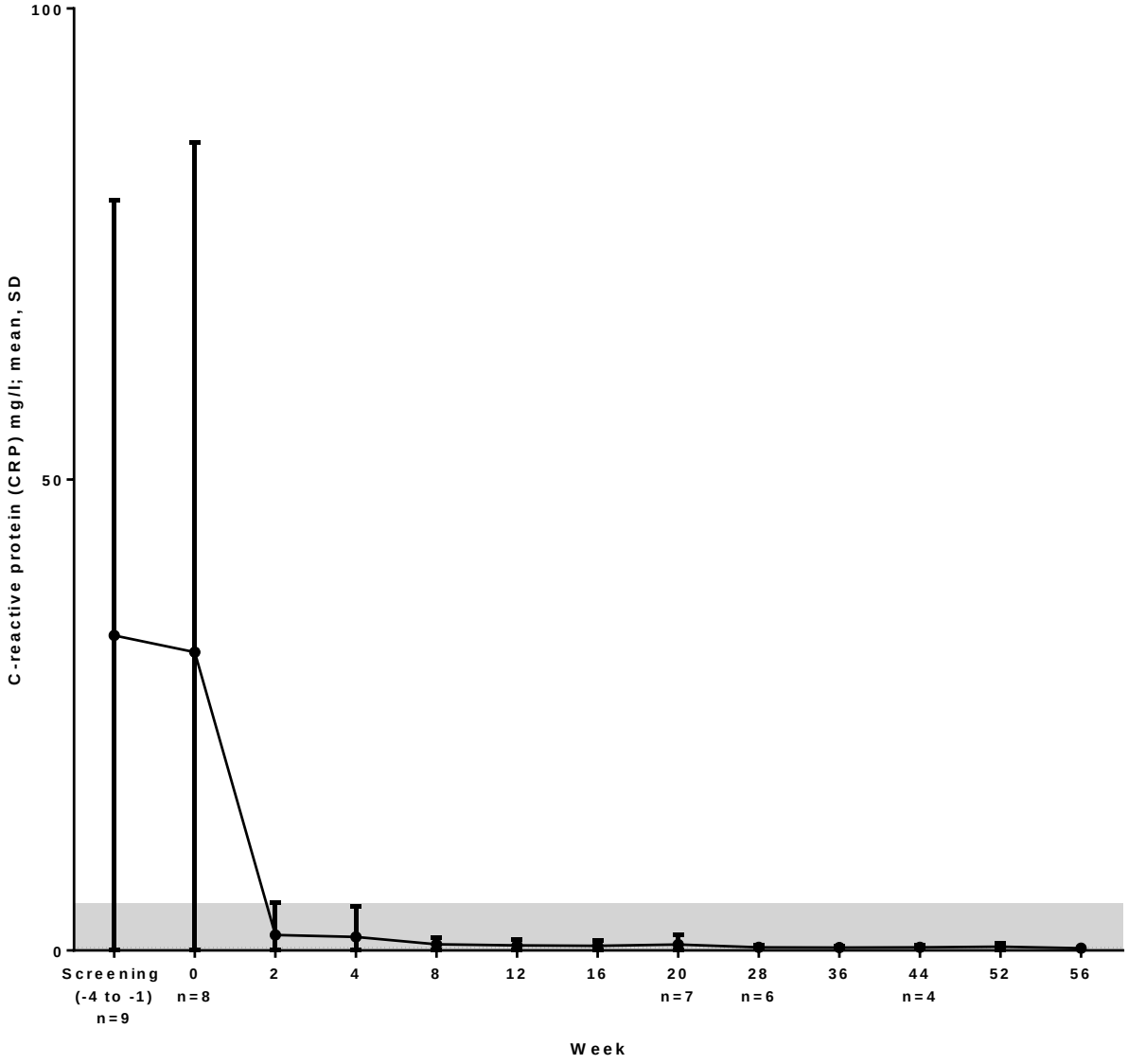

Figure 3: C-reactive protein (CRP, mg/l; mean, Standard deviation [SD]) levels of tocilizumab-treated SchS patients over time shown for all visits. The light grey area indicate normal values.

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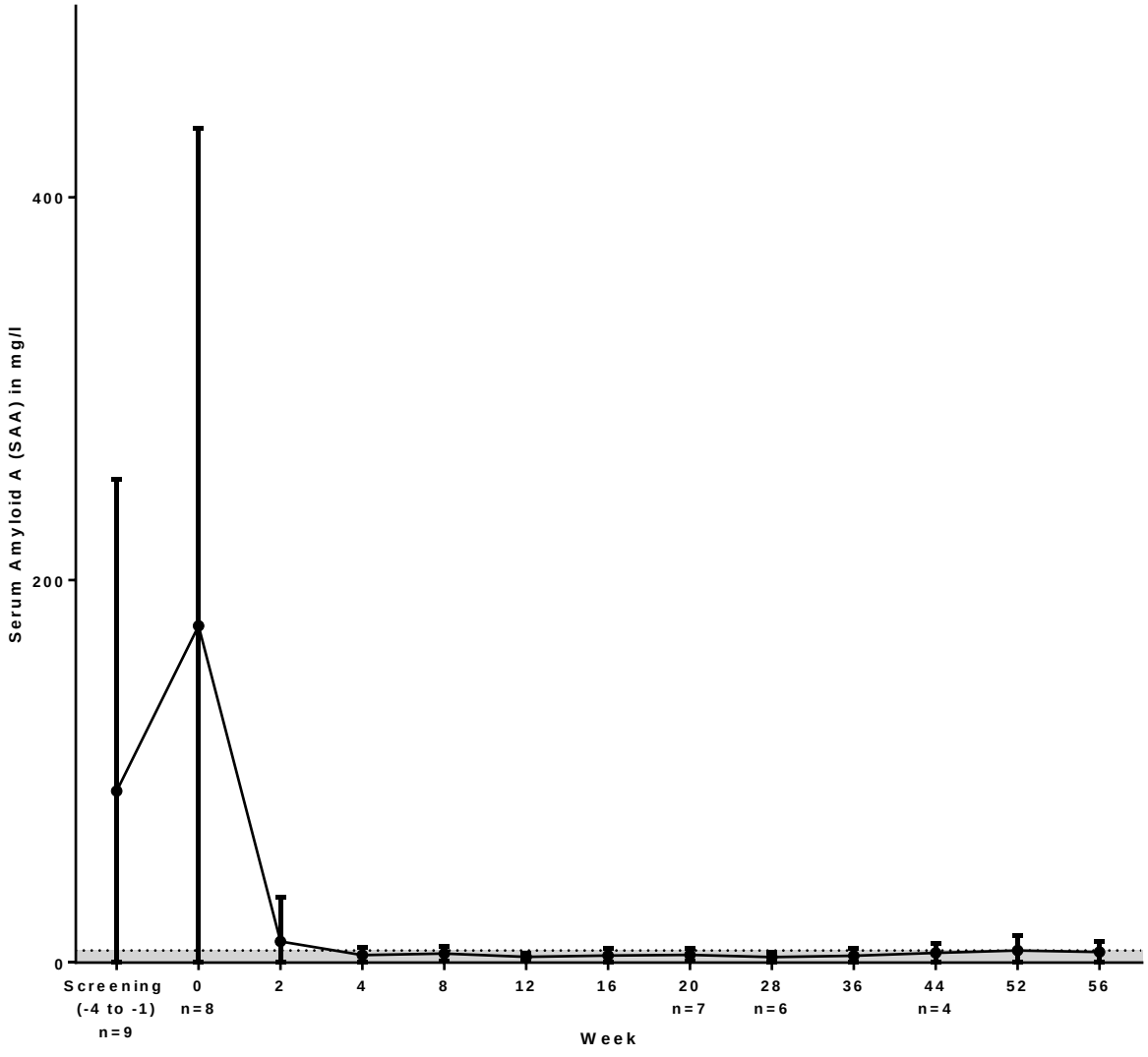

Figure 4: Serum Amyloid A (SAA, in mg/l; mean, Standard deviation [SD]) levels of tocilizumab-treated SchS patients over time shown for all visits. The light grey area indicate normal values.

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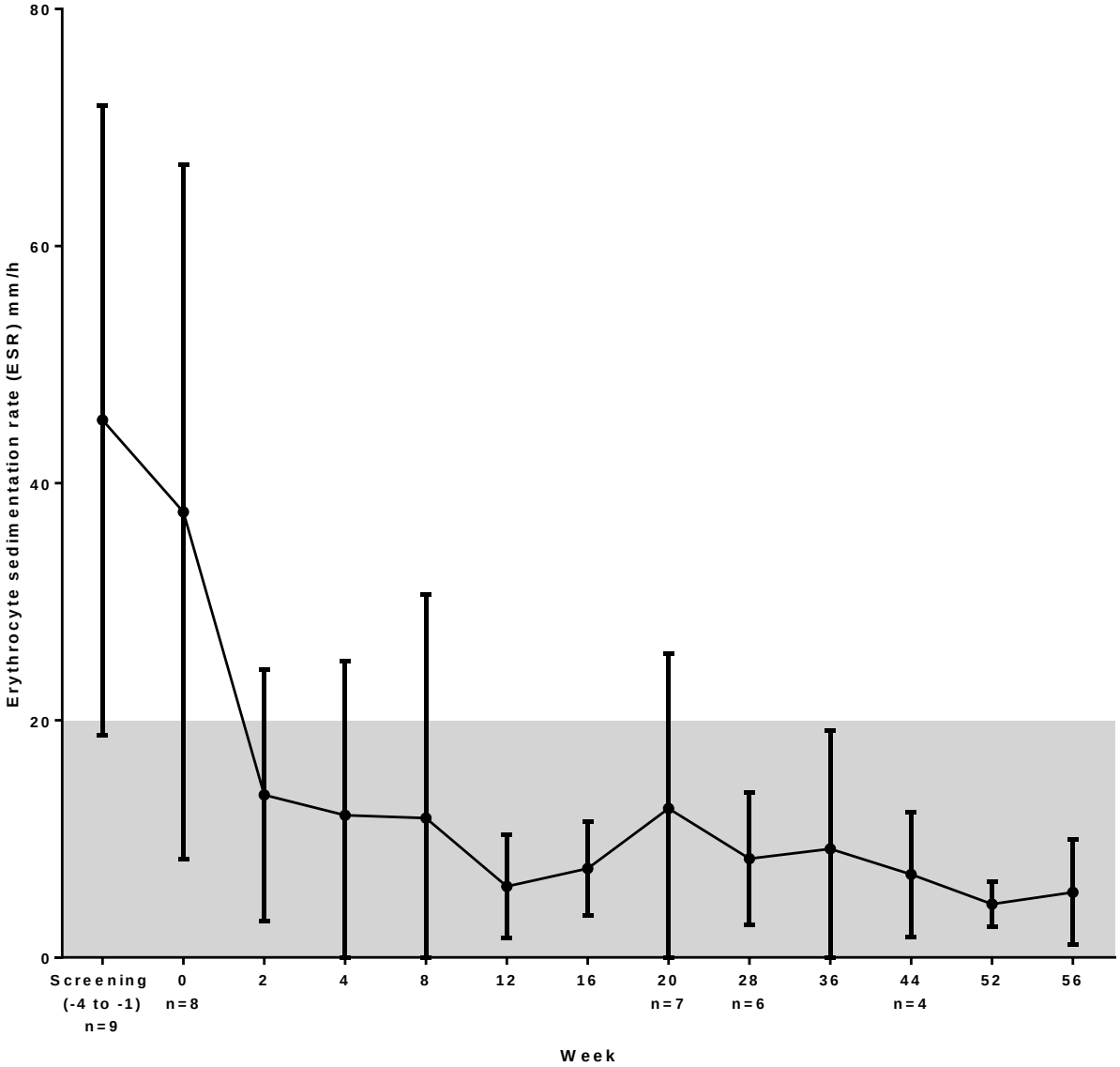

Figure 5: Erythrocyte sedimentation rates (ESR, mm/h; mean, Standard deviation [SD]) of tocilizumab-treated SchS patients over time shown for all visits. The light grey area indicate normal values.

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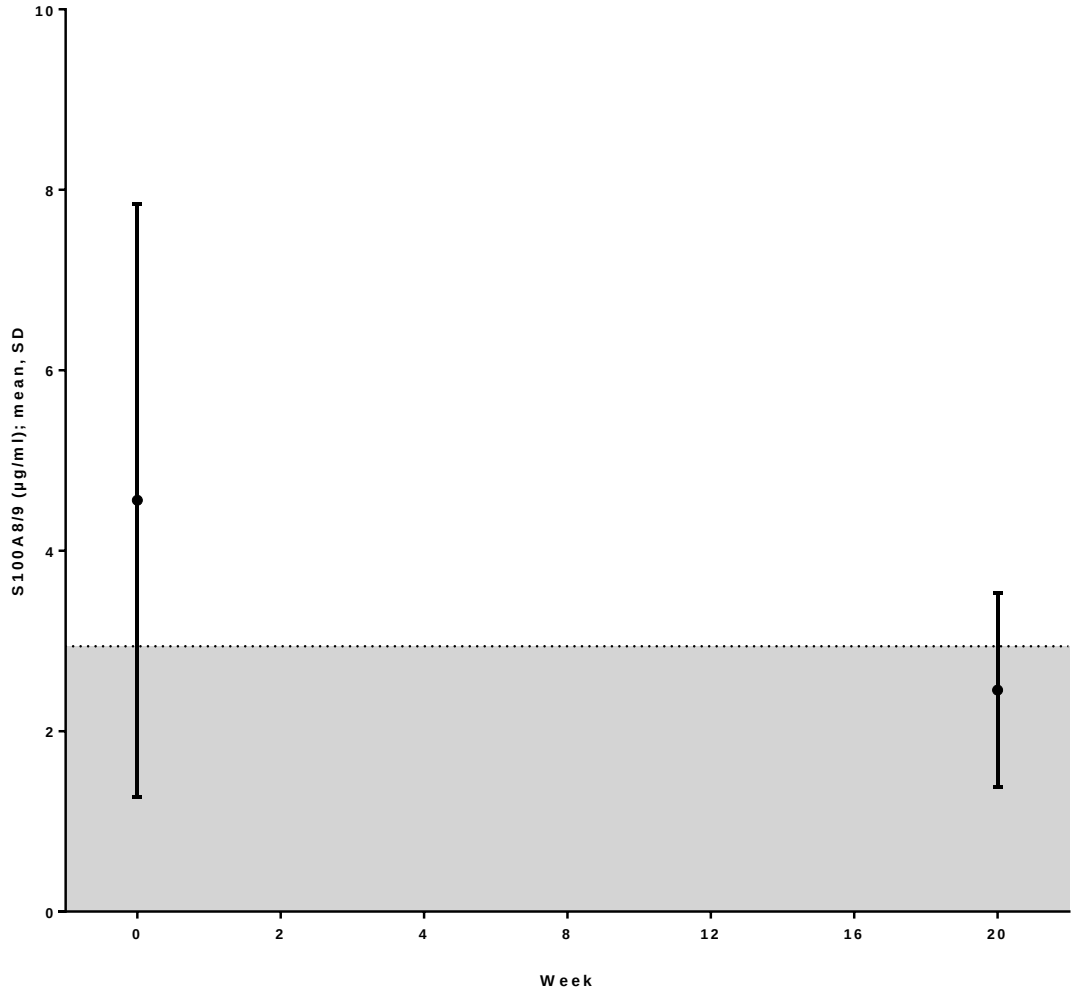

Figure 6: S100A8/9 (µg/ml; mean, Standard deviation [SD]) levels of tocilizumab-treated SchS patients at baseline and week 20. The light grey area indicate normal values.

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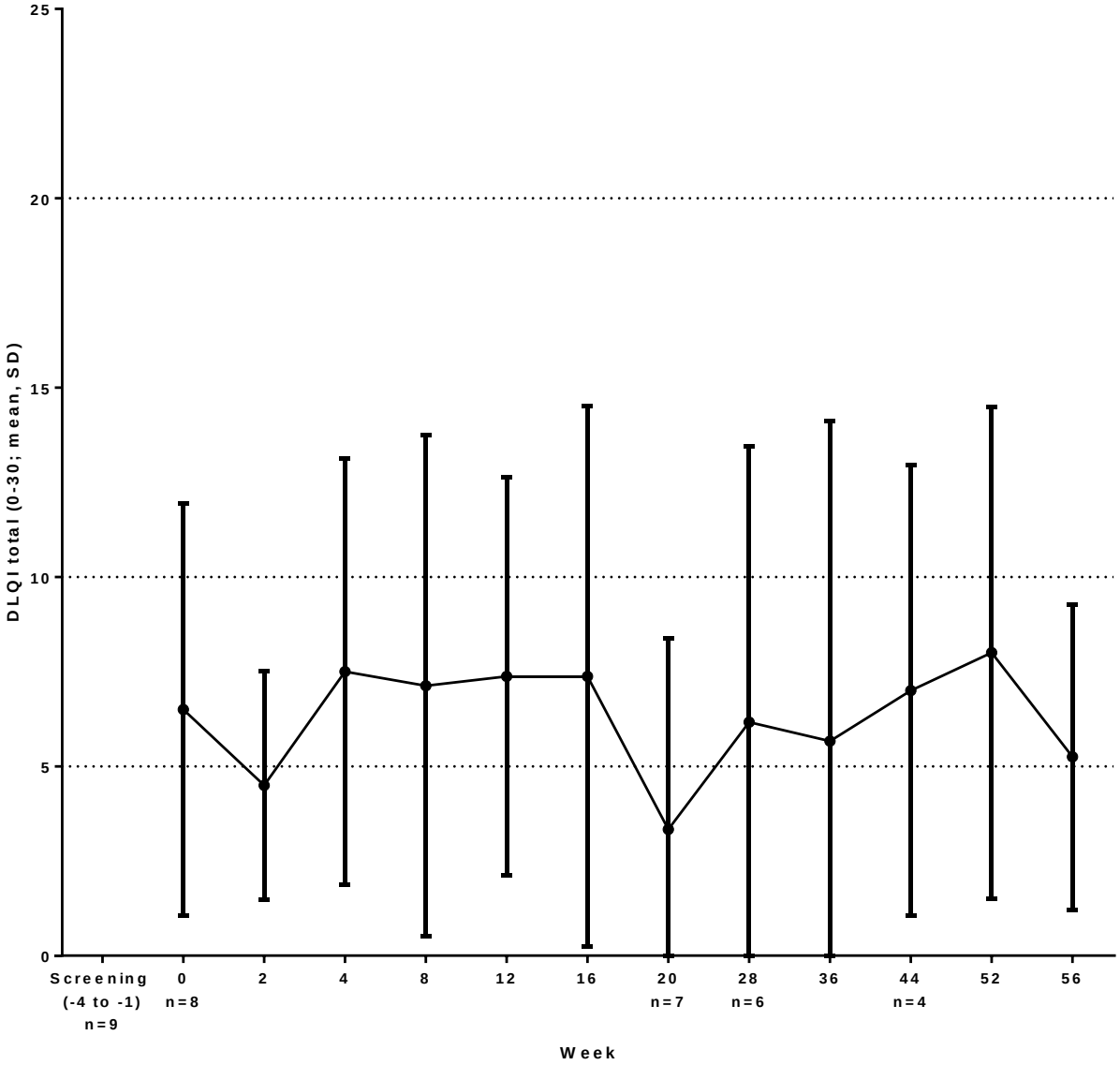

Figure 7: Dermatology Quality of life index in total (DLQI; 0-1 no effect at all, 2-5 small effect, 6-10 moderate effect, 11-30 large effect on patient's life; mean, Standard deviation [SD]) in tocilizumab- treated SchS patients over time shown for all visits.

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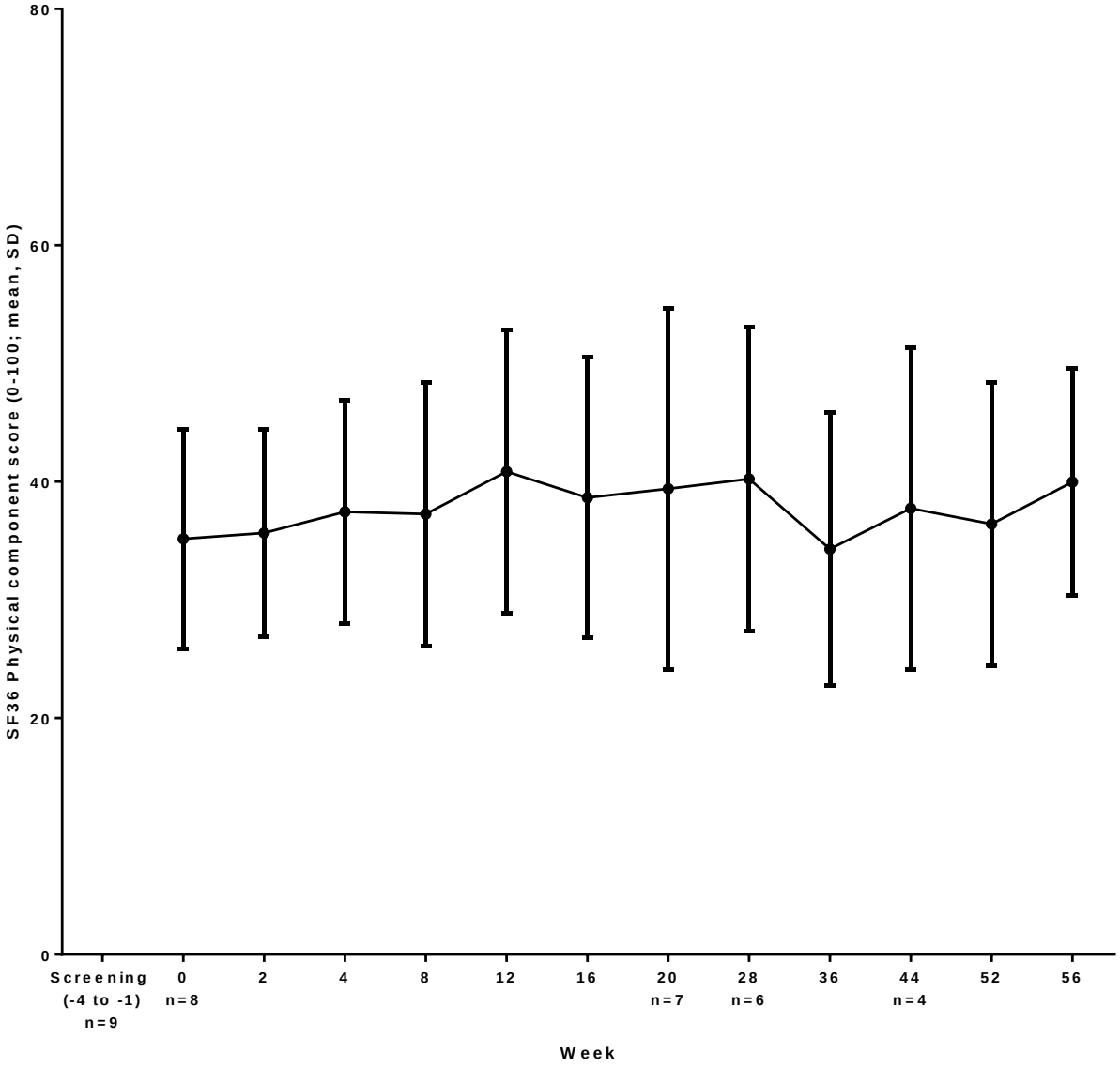

Figure 8: SF 36 physical component score (0-100; mean, Standard deviation [SD]) in SchS patients treated with tocilizumab over time shown for all visits. SF-36 levels (norm sample) of the age-matched healthy group: 44.81. (*Bullinger, Kirchberger SF-36 Fragebogen zum Gesundheitszustand Handweisung, Hogrefe-Verlag,1998*)

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Name of Finished Product: Tocilizumab (RoActemra®) (ATC-Code: ATC L04AC07)

Name of Active Substance: RO4877533

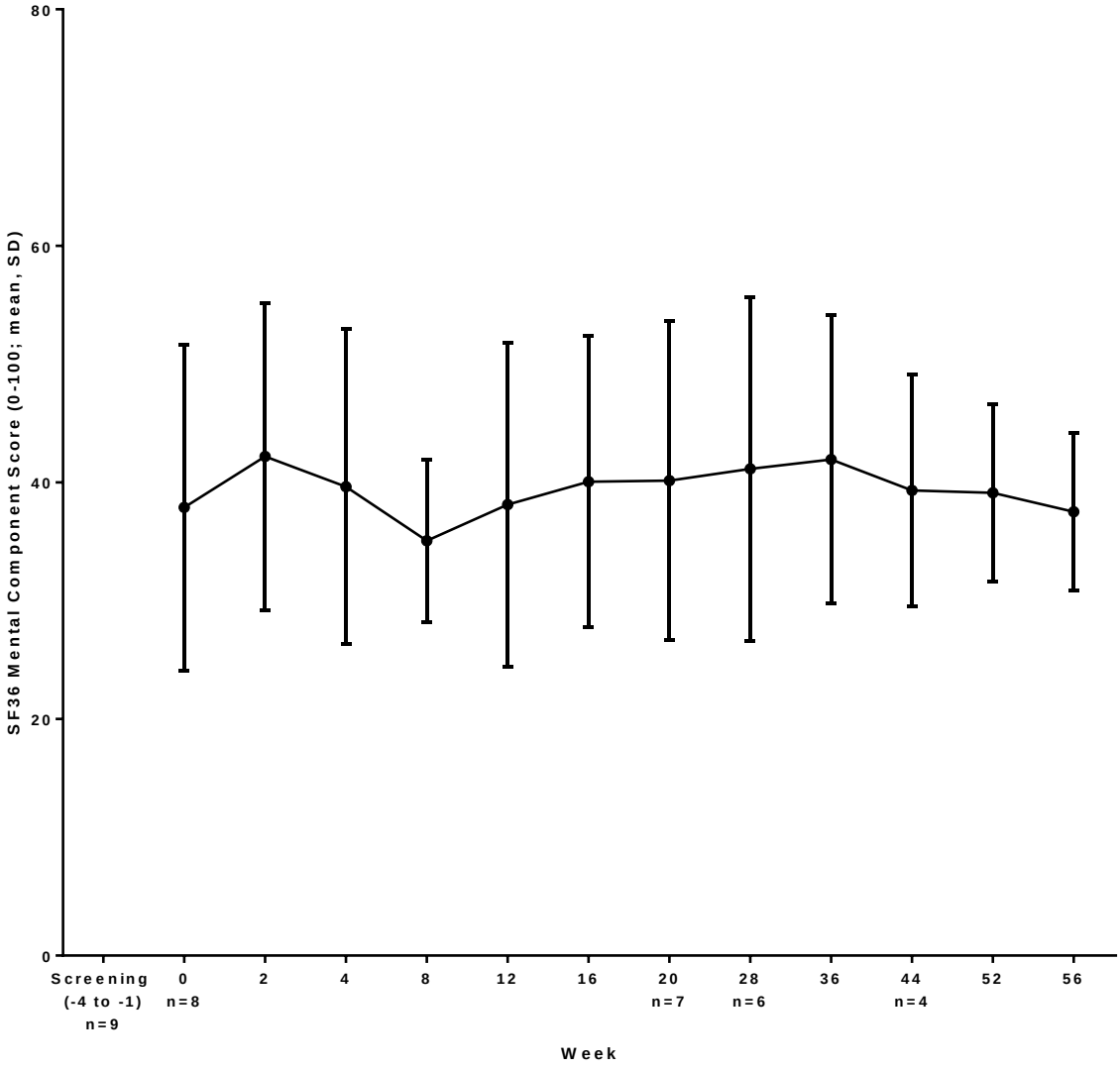

Figure 9: SF 36 mental component score (0-100; mean, Standard deviation [SD]) in SchS patients treated with tocilizumab over time shown for all visits. SF-36 levels (norm sample) of the age-matched healthy group 53.18. (*Bullinger, Kirchberger SF-36 Fragebogen zum Gesundheitszustand Handweisung, Hogrefe-Verlag,1998*)

visit	Patient_No	draw_date_dd-mm-yyyy	results_screening
V1	SN01	19-07-2017	NEGATIVE
V4	SN01	25-08-2017	NEGATIVE
V5	SN01	22-09-2017	NEGATIVE
V1	SN02	19-09-2017	NEGATIVE
V7	SN02	09-02-2018	NEGATIVE

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V10	SN02	26-06-2018	NEGATIVE
V1	SN04	05-10-2017	NEGATIVE
V5	SN04	11-12-2017	NEGATIVE
V7	SN04	05-02-2018	NEGATIVE
V1	SN05	08-11-2017	NEGATIVE
V6	SN05	01-03-2018	NEGATIVE
V10	SN05	15-08-2018	NEGATIVE
V1	SN06	14-11-2017	NEGATIVE
V6	SN06	13-02-2018	NEGATIVE
V12	SN06	20-11-2018	NEGATIVE
V1	SN07	22-11-2017	NEGATIVE
V5	SN07	01-02-2018	NEGATIVE
V12	SN07	07-12-2018	NEGATIVE
V1	SN08	15-12-2017	NEGATIVE
V6	SN08	12-04-2018	NEGATIVE
V12	SN08	17-01-2019	NEGATIVE
V1	SN09	18-01-2018	NEGATIVE
V6	SN09	09-05-2018	NEGATIVE
V12	SN09	13-02-2019	NEGATIVE

Table 2: Overview on patients and timepoints of screening for anti-drug antibodies.

Safety Results:
In brief, there were 57 adverse events in 8 patients, three during the screening period, 31 during the open-label phase and 23 during the optional study extension. There were no serious AEs reported during the study. The 54 adverse events during tocilizumab open-label treatment and optional study extension were mild or moderate and included infections (n=15) (e.g. skin [n=5], respiratory tract [n=5] and urinary tract [n=3] infections) musculoskeletal/connective tissue symptoms (n=10), endocrinological (n=6) and gastrointestinal (n=5) complaints as well as skin symptoms (n=6) (**Supp. Tab. 1**).

Adverse Events leading to study discontinuation
One patient discontinued the open-label treatment phase because of adverse event erysipelas and SchS exacerbation due to infection after 16 weeks. 2 patients discontinued the optional study extension after 36 weeks because of n=1 loss of efficacy of treatment and n=1 loss of efficacy of treatment and adverse event lymphopenia (listed as reason for termination in the study protocol).

No further significant changes of safety laboratory parameters were observed, and tocilizumab injections were generally well tolerated, injection site reactions were reported twice during the study. No serious adverse events were observed and no pregnancies

(neither father nor mother exposed) or deaths occurred. Disease-specific Adverse events of special interests (AESIs) were not defined for this study.

Safety Summary:
The safety profile of tocilizumab in this pilot open-label study showed a similar overall safety profile to previous tocilizumab trials in patients with RA and sJIA with the most common events being infections. No novel safety signals were observed.

Discussion:
This is the first open-label study of tocilizumab in SchS. We could confirm that tocilizumab reduces clinical symptoms and inflammation markers in SchS patients as reported earlier from single case studies. (*Krause K J Allergy and Clin Immunol 2012*) However, we observed a loss of efficacy of tocilizumab treatment and an increase in clinical symptoms in the majority of patients over time. Interestingly, a mixed response to tocilizumab in n=4 SchS patients was recently reported. (*Claus J J. Clin. Immunol. 2019*) Here, two of the four patients responded well but needed glucocorticoids in addition. The remaining two patients did not or only partially respond to tocilizumab. Similar to the results of our study, the partial responder experienced a loss in clinical efficacy after 4 months of treatment.
In our study, tocilizumab showed a long-term effect in reducing inflammatory markers CRP and SAA, thereby affirming the inhibition of IL-6-signaling in SchS patients. In line with this, fever was absent in all patients. In regard to the other clinical symptoms, the urticarial rash was not efficiently suppressed as demonstrated by elevated PGA subscores urticarial rash and mirrored by elevated DLQI scores in most patients. Furthermore, myalgia and arthralgia reoccurred over time or persisted and fatigue was increasingly present in all patients over time. In comparison to former studies with IL-1 blockers anakinra, rilonacept and canakinumab (*Neel A Autoimmun Rev 2014; Krause K Allergy 2012; de Koning H Ann Rheum Dis 2012; Krause K J Allergy and Clin Immunol 2017 and 2020*) which showed a good clinical and laboratory response in SchS over long-term use, tocilizumab in our study was less effective on long-term application. The reason for the observed loss of efficacy over time remains unknown. No anti-drug antibodies were detected in our patients and clinical characteristics did not differ between the good responders and those who lost efficacy over time.
In line with the data on anti-IL-1 treatment in SchS and tocilizumab in RA, most commonly observed adverse events were mild to moderate infections. (*Krause K J Allergy and Clin Immunol 2020, Biggioggero M Drug Des Devel Ther. 2018*) We did not observe any new safety concerns. Given the elderly population affected by SchS, close monitoring for infections in SchS patients treated with tocilizumab should be implemented.

Conclusion:
In this pilot exploratory open-label study, tocilizumab treatment initially decreased clinical symptoms and inflammatory markers in patients with SchS. However, most of the patients

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showed loss of efficacy as mirrored by an increase in clinical symptoms over long-term use. Tocilizumab may be considered a therapeutic option of second choice in single patients with SchS. In particular, patients with insufficient responses or side-effects following anti-IL-1 treatment may benefit from IL-6 blockade.
Date of report: 27.05.2020

Karoline Krause

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