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Original article

Efficacy and safety of belimumab given for 12 months in primary Sjögren's syndrome: the BELISS open-label phase II study

Salvatore De Vita[1], Luca Quartuccio[1], Raphaèle Seror[2,3], Sara Salvin[1], Philippe Ravaud[3], Martina Fabris[1,4], Gaétane Nocturne[2], Saviana Gandolfo[1], Miriam Isola[5] and Xavier Mariette[2]

Abstract

Objective. To report the efficacy and safety of long-term treatment of SS with belimumab, targeting the B-cell-activating factor.

Methods. Patients with primary SS were included in the BELISS open-label phase II study, a 1-year open-label trial, if they were positive for anti-SSA or anti-SSB antibodies and had systemic complications or persistent salivary gland enlargement or early disease or biomarkers of B-cell activation. They received belimumab, 10 mg/kg i.v., at weeks 0, 2 and 4 and then every 4 weeks; if response was observed at week 28, or if the clinician and the patient agreed to continue the study in the absence of side effects, treatment was continued for 1 year. Efficacy and safety were analysed during the 1-year period of treatment.

Results. Among the 30 patients recruited, 28 were evaluated at week 28 as already reported. Nineteen terminated the 52-week study, 15 of them being responders and 4 non-responders at week 28. Thirteen of the 15 responders at week 28 also responded at week 52 (86.7%). The improvement in the EULAR Sjögren's Syndrome Disease Activity Index and EULAR Sjögren's Syndrome Patient Reported Index scores observed at week 28 showed a trend to further improvement at week 52, and the amelioration of peculiar EULAR Sjögren's Syndrome Disease Activity Index domains (glandular, lymphadenopathy, articular) appeared of particular relevance. The decrease in biomarkers of B-cell activation observed at week 28 persisted unchanged until week 52, with RF decreasing further. Salivary flow, Schirmer's test and the focus score of salivary biopsy did not change. Safety of treatment was good.

Conclusion. Long-term treatment with belimumab may be beneficial in SS. Randomized, double-blind, controlled studies in larger populations are encouraged.

Key words: belimumab, primary Sjögren's syndrome, trial.

Rheumatology key messages

- Long-term belimumab treatment may be beneficial in SS.
- Long-term belimumab treatment improved glandular and lymphadenopathy EULAR Sjögren's Syndrome Disease Activity Index domains.
- Long-term belimumab treatment improved quality of life of SS patients.

[1]Clinic of Rheumatology, Department of Medical and Biological Sciences, Udine University, Udine, Italy, [2]Université Paris-Sud, Assistance Publique-Hôpitaux de Paris, Hôpitaux Universitaires Paris-Sud, INSERM U1012, Le Kremlin Bicêtre, [3]Assistance Publique-Hôpitaux de Paris, Hôtel Dieu Hospital, Centre of Clinical Epidemiology, INSERM, U738, University of Paris Descartes, Faculty of Medicine, Paris, France, [4]Institute of Clinical Pathology and [5]Institute of Statistics, Department of Medical and Biological Sciences, Udine University, Udine, Italy

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Correspondence to: Salvatore De Vita, Rheumatology Clinic, Department of Medical and Biological Sciences, Azienda Ospedaliero-Universitaria 'S. Maria della Misericordia' Piazzale Santa Maria Misericordia 1, 33100 Udine, Italy.
E-mail: devita.salvatore@aoud.sanita.fvg.it

CLINICAL SCIENCE

Introduction

SS is an autoimmune and lymphoproliferative disorder characterized by lymphocytic infiltration of the exocrine glands, typically the salivary and lacrimal glands, leading to sicca syndrome [1]. As it is a connective tissue disorder, systemic manifestations may occur. B-cell hyperexpansion and chronic inflammation of mucosa-associated lymphoid tissue (MALT) predisposes to B-cell malignant lymphoproliferation in SS, usually a B-cell non-Hodgkin's lymphoma [1, 2]. This complicates the course of about 5% of patients and represents the principal cause of increased mortality in this disease.

Effective treatments to modify the course of SS are lacking [3]. Targeting the B cells with drugs lacking oncogenic properties might be beneficial, however, in particular for patients with systemic complications [1, 3, 4].

B-cell-activating factor (BAFF) is increased in both the serum and the salivary pathological lesions of SS patients [4–7]. In addition, BAFF transgenic mice develop lymphoproliferation and autoimmune disease mimicking SS in part [8]. BAFF may be crucial in sustaining the overexpansion of autoreactive B-cell clones in the MALT microenvironment in SS, and it can also mediate the resistance to tissue MALT B-cell depletion with anti-CD20 therapy [9, 10].

Belimumab, a mAb against BAFF registered for the treatment of SLE, was recently employed in primary SS in the Efficacy and Safety of Belimumab in Subjects With Primary Sjögren's Syndrome (BELISS) trial, with encouraging results reported after 6 months of treatment [11]. Here, we report the long-term efficacy and safety results in patients completing the BELISS trial at 12 months and highlight some disease manifestations where this treatment may be more useful.

Patients and methods

Patients

Patients with primary SS [12], positive for anti-SSA or anti-SSB antibodies, were included in two identical studies conducted in two European centres in Udine, Italy, and Paris, France [11]. Inclusion and exclusion criteria were described previously [11] and are reported in supplementary data, available at *Rheumatology* Online. Belimumab 10 mg/kg was administered at weeks (W) 0, 2 and 4 and then every 4 weeks for a minimum of 6 months (W24); it was planned to pursue the treatment every 4 weeks until W48 if response was observed at W28. Limited to the Italian BELISS protocol, to evaluate a possible delayed response, treatment with belimumab could also be continued up to W48 if both the clinician and the patient agreed to complete the study despite the lack of response at W28, but in the absence of clinical worsening or side effects. A final evaluation was scheduled at W52 (i.e. 4 weeks after the last dose of belimumab).

Institutional review boards or ethics committees of the individual study sites approved the protocols (clinicaltrials.gov, NCT01008982 and NCT01160666) of the BELISS open-label phase II study. The International Conference on Harmonization guidelines and the principles of the Declaration of Helsinki were followed. All patients provided written informed consent before participating in any protocol-specific procedures of the BELISS open-label phase II study. Ethical approval was given for all analysis of the BELISS open-label phase II study from the Comitato Etico dell'Azienda Ospedaliero Universitaria di Udine.

Purpose of the study

The purpose of the present study was to analyse efficacy and safety results of long-term belimumab therapy in SS in patients completing the 52-week BELISS study and to highlight the SS manifestations where belimumab therapy may be more useful.

Response to therapy at the midpoint of the BELISS study, that is, at W28, was the primary end point [11]. Response was defined as improvement in at least two of the following five items: $\geqslant$30% reduction in dryness score on a visual analogue scale (VAS), $\geqslant$30% reduction in fatigue score on a VAS, $\geqslant$30% reduction in musculoskeletal pain score on a VAS, $\geqslant$30% reduction in systemic activity score on a VAS assessed by the physician and/or $\geqslant$25% reduction in serum levels of any of the B-cell activation biomarkers (free light chains of immunoglobulin, β2-microglobulin, immunoglobulin monoclonal component, cryoglobulins, IgG) or $\geqslant$25% increase in C4 level.

Secondary end points of the BELISS study included the response (evaluated by using the same criteria) at W52, and changes from baseline to W28 and to W52 in the following items: EULAR SS Disease Activity Index (ESSDAI) [13] and related domains, EULAR SS Patient Reported Index (ESSPRI) [14] and SF36 quality-of-life index, each of the five items of the primary end point, Schirmer's *I* test and unstimulated salivary flow. The day before evaluation, the patients were asked not to take their saliva or tear substitutes. Levels of autoantibodies were monitored during the study, as was the focus score from biopsy of the labial salivary gland at baseline and at W28 in French patients and at W52 in Italian patients.

Statistical analysis

A sample size was not calculated because of the pilot nature of the study. Categorical variables are presented as frequency and percentage. Quantitative variables are presented as the mean (S.D.). Paired *t*-test was used to assess differences between baseline and W28 quantitative assessments, and mean differences were expressed with 95% CI. In the case of distributions with extreme outliers, a Wilcoxon's signed rank was used. Paired proportions were compared using McNemar mid-*p* test for paired data.

Results

Patient characteristics

Among the 30 patients starting the BELISS study, 28 were evaluated at W28 (time of the primary end point), and 19

terminated the 52-week study. The W28 results have been reported [11]. Briefly, the primary end point was reached at W28 in 18/30 patients (60%), with the ⩾30% decrease in the VAS dryness score decreased in 37% of the patients, in the VAS fatigue in 23%, in the VAS pain in 23% and in the physician VAS systemic activity score in 43%, while the biologic values improved in 73% of the patients [11]. The response rate in patients with systemic manifestations, early disease or biologic activity ranged between 50% and 60% [11].

Eighteen patients were responders at W28, and 15 of them continued the study until W52. Three of the 18 responder patients interrupted treatment at W28 or before: two because improvement was felt to be too limited by the patient and the physician, and one owing to a previous serious adverse event at W16, namely a pneumococcal meningitis [11]. Four additional patients continued the study until W52: they were non-responders at W28, but they all felt better, improved in at least one item of the composite primary end point and were willing to undergo treatment until the end of the study.

The efficacy results were analysed in the subgroup of the 15 responders at W28 who completed the 52-week protocol. Efficacy is reported separately for the four cases treated for 1 year, but who were non-responders at W28. In contrast, safety data were analysed in all 19 patients treated until the end of the study. Characteristics at W28 of the 15 responder patients are reported in Table 1.

Efficacy

Thirteen of the 15 responders at W28 also responded at W52 (86.7%), consistent with a stable response to treatment in the long term. Two patients lost response from W28 to W52 due to an increase either in the pain VAS or in the fatigue VAS. Overall, however, fatigue, pain and disease activity appeared to improve with time from W28 to W52, although without any statistical significance, while dryness symptoms and B-cell activation biomarkers remained stable (Fig. 1). In detail, by comparing the results at W52 *vs* W28 in the single items contributing to the primary end point, improvement of ⩾30% in the VAS dryness score remained unchanged [improvement occurred in 8/15 (53.3%) patients at both W52 and W28; $P = 1.0$], while an increase in the rate of improved cases was observed in the VAS fatigue [9/15 (60%) improved ⩾30% at W52 *vs* 4/15 (26.7%) at W28; $P = 0.14$], in the VAS pain [9/15 (60%) *vs* 7/15 (46.7%); $P = 0.71$] and in the VAS score of disease systemic activity by the physician [13/15 (86.7%) *vs* 11/15 (73.3%); $P = 0.65$]; finally, biologic improvement was observed in 13/15 (86.7%) at W52 *vs* 14/15 (93.3%) at W28 ($P = 1.0$; Fig. 1).

When analysing the response at W52 *vs* W28 according to the three main characteristics of the SS patients leading to randomization (i.e. systemic disease, early disease or biological activity) response persisted in 10/10 of patients with systemic manifestations of SS, in 7/8 (87.5%) of the patients with biologic activity and in 3/4 (75%) of the patients with early disease.

The mean ESSDAI and ESSPRI scores improved significantly from baseline to W28 in the whole cohort of SS patients recruited in the study: from 8.8 (7.4) to 6.3 (6.6), and from 6.4 (1.1) to 5.6 (2.0), respectively [11]. In the 15 responders at W28, the ESSDAI was 7.5 (4.0) at baseline and 3.9 (3.1) at W28 ($P < 0.0001$ *vs* baseline), with a trend of further improvement at W52, that is, 3.1 (3.2) ($P < 0.0001$ *vs* baseline). In the same 15 responders, the ESSPRI was 6.0 (1.0) at baseline, 4.5 (1.8) at W28 ($P = 0.003$ *vs* baseline) and 4.3 (2.3) at W52 ($P = 0.01$ *vs* baseline; $P = 0.2$ and $P = 0.7$ between W28 and W52 for ESSDAI and ESSPRI scores, respectively; Fig. 2). Moderate disease activity (i.e. an ESSDAI score ⩾5) was observed in 5/15 (33.3%) patients at W52 *vs* 6/15 (40%) at W28 and *vs* 10/15 (66.7%) at baseline.

No significant improvement in the SF36 physical health and mental health component has been observed from baseline to W28 in the whole cohort of patients [11]. Likewise, in the 15 responder patients who continued the study after W28, the mean SF36 physical health component did not improve between baseline and W28 [from 44.3 (13.7) to 46.9 (13.4); not significant (NS)], but improved at W52 compared with baseline and with W28 [to 55.3 (20.3) at W52; $P = 0.03$ *vs* baseline; and $P = 0.04$ *vs* W28]. In contrast, the mean SF36 mental health component score remained stable [from 44.2 (15.2) at baseline

Table 1 Week 28 characteristics of patients who were responders at week 28 and who completed the 52-week study

Characteristic	All patients ($n = 15$)
Age, mean (S.D.), years	40.2 (11.8)
Female, *n* (%)	15 (100.0)
Disease duration, mean (S.D.), years	5.9 (5.7)
Unstimulated whole salivary flow, <0.1 ml/min, *n* (%)	8 (53.3)
Schirmer's test ⩽5 mm, *n* (%)	10 (66.7)
Baseline focus score, mean (S.D.)	1.2 (0.7)
Anti-SSA antibodies, *n* (%)	14 (93.3)
Anti-SSB antibodies, *n* (%)	14 (93.3)
Presence of cryoglobulinaemia	0
Presence of lymphoma, *n* (%)	1 (6.7)
Current associated medication, *n* (%)	
CSs	3 (20)
HCQ	4 (26.7)
Reason for inclusion, *n* (%)	
Systemic complications	10 (66.7)
Recent-onset disease	4 (26.7)
Increase in B-cell biomarker values	7 (46.7)
ESSDAI (0–123), mean (S.D.)	3.8 (3.1)
ESSPRI (0–10), mean (S.D.)	4.5 (1.8)
Dryness VAS (0–10), mean (S.D.)	4.9 (2.8)
Pain VAS (0–10), mean (S.D.)	3.6 (2.1)
Fatigue VAS (0–10), mean (S.D.)	4.8 (2.1)

Values are *n* (%) unless otherwise indicated. ESSDAI: EULAR SS Disease Activity Index; ESSPRI: EULAR SS Patient Reported Index; VAS: visual analogue scale.

Fig. 1 The course of the single items contributing to the primary end point in the 15 patients responsive at week 28 and completing the study up to week 52

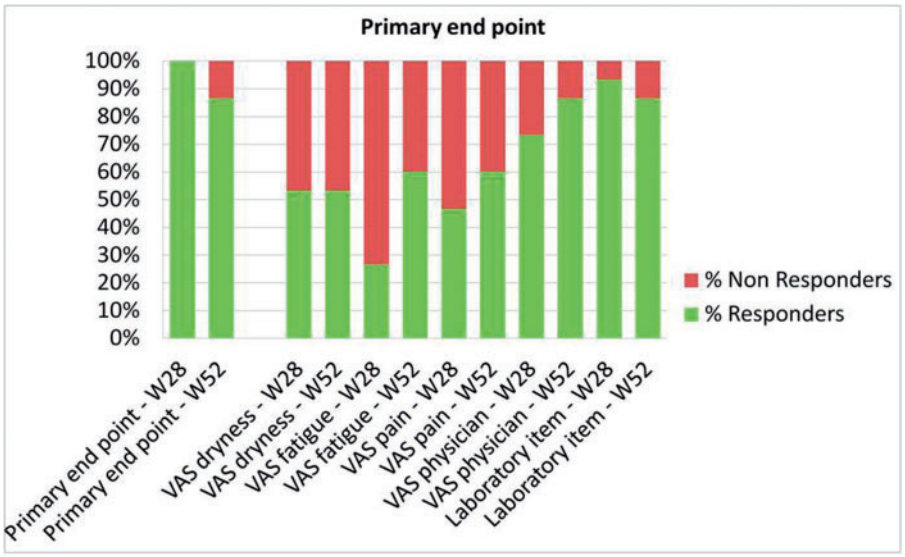
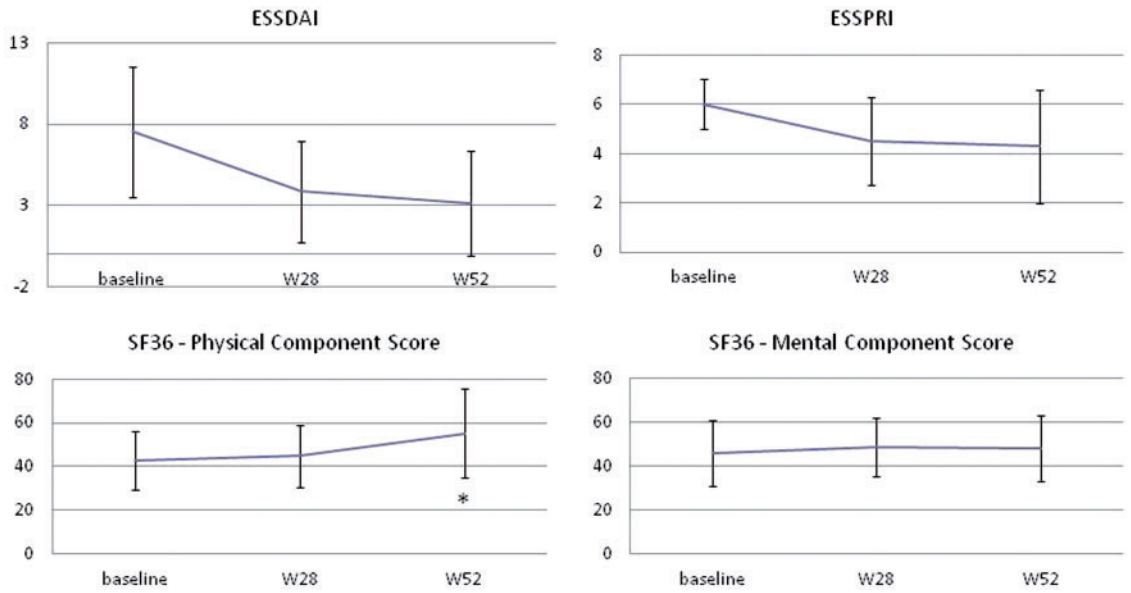


Fig. 2 The course of the EULAR SS Disease Activity Index, EULAR SS Patient Reported Index and SF36 in the 15 patients responsive at week 28 and completing the study



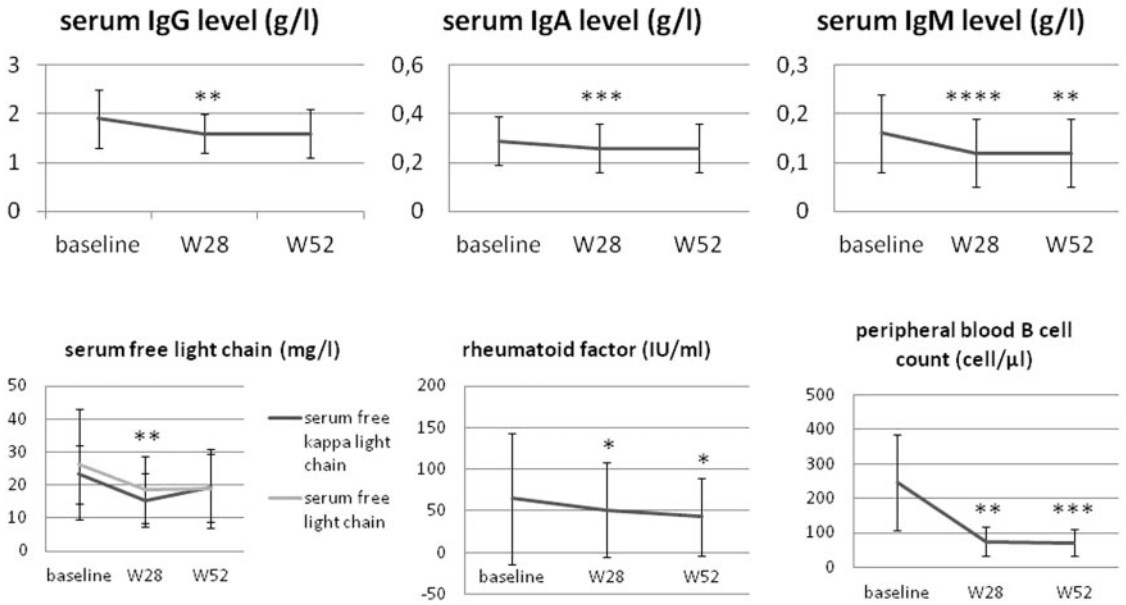
ESSDAI: EULAR SS Disease Activity Index; ESSPRI: EULAR SS Patient Reported Index; W: week.

to 49.4 (14.3) at W28 and 48.1 (15.0) at W52; P = NS in all the comparisons; Fig. 2].

No significant changes were observed from W28 to W52 in the mean values of VAS dryness [4.9 (2.8) at W28 *vs* 5.1 (2.5) at W52; $P = 0.7$], of VAS fatigue [4.9 (2.1) *vs* 4.5 (2.4); $P = 0.7$] and of VAS pain [3.6 (2.1) *vs* 3.3 (2.3); $P = 0.5$]. However, a significant improvement in the physician VAS systemic activity score was recorded [3.2 (1.2) at W28 *vs* 2.5 (1.1) at W52; $P = 0.04$], while this was not observed from baseline to W28 in the whole cohort [11].

No statistical differences were reported from W28 to W52 for the whole unstimulated salivary flow rate [0.6 (0.7) *vs* 0.5 (0.8); $P = 0.6$] and for the Schirmer's *I* test

FIG. 3 The course of B-cell biomarkers from baseline to week 28 and to week 52 in the 15 patients who were responders at week 28 and completed the study



*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ and ****$P < 0.0001$ when comparing W28 and W52 values to baseline. No significant differences were observed between W28 and W52 values in any comparison. W: week.

[6.8 (10.1) *vs* 4.1 (4.7); $P = 0.3$], again in agreement with the lack of improvement in these objective tests from baseline to W28 in the whole cohort [11].

In general, when analysing the course of B-cell biomarker values from W28 to W52, the significant changes observed from baseline to W28 in the whole cohort were maintained until W52, while the level of serum RF seemed to improve further (Fig. 3). A significant decrease in serum IgG, IgA, IgM, κ and λ serum free light chains, serum RF and peripheral B-cell count from baseline to W28 has been observed in the whole cohort of SS patients [11]. In the 15 responder patients at W28, this decrease did not progress with ongoing belimumab therapy from W28 to W52 (Fig. 3), with the exception of the serum RF, which appeared to decrease further [64.8 (78.7) IU/ml at baseline, 51.1 (56.8) IU/ml at W28, $P = 0.028$ W28 *vs* baseline; and 42.6 (47.3) IU/ml at W52, $P = 0.048$ W52 *vs* baseline]. Finally, the focus score of labial salivary gland biopsy could be evaluated in 12 patients repeating this biopsy at W52 and compared with baseline; no significant change in the focus score was observed [from 1.3 (0.6) at baseline to 1.3 (0.9) at W52; $P = 0.9$].

Efficacy in the single ESSDAI domains

Importantly, a significant improvement in particular ESSDAI domains was observed in the whole cohort of patients at W28 if compared with study entry [11], that is, in the glandular domain ($P = 0.0078$), the articular domain ($P = 0.0313$) and the biologic domain ($P = 0.0078$). The improvement in the lymphadenopathy domain tended to be significant at W28 ($P = 0.0625$) [11]. In general, when evaluating the course of these four ESSDAI domains from W28 to W52 in the 15 responders at W28, further improvement or stabilization was noticed, and no loss of response was observed. No additional change was observed from W28 to W52 in the ESSDAI domains where no significant change had been previously observed in the whole cohort at W28 when compared with study entry, that is, the cutaneous, renal and peripheral nervous system domains (Figs 4 and 5).

Glandular domain

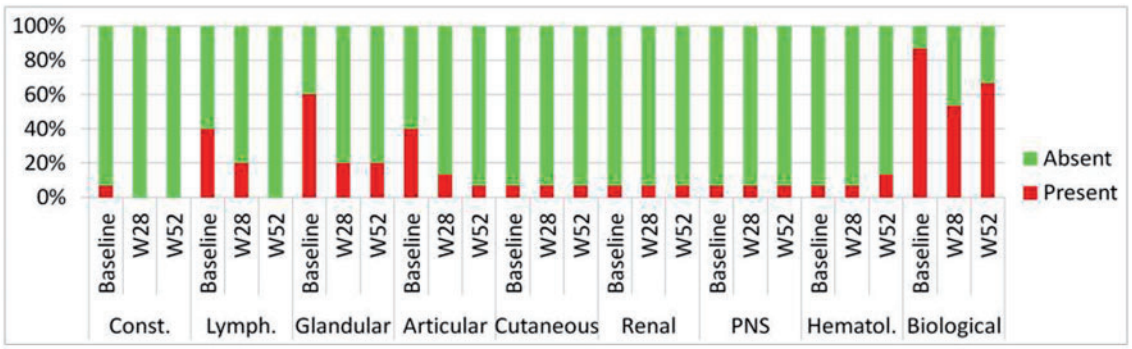
Among the 15 responder patients who continued the study, the glandular domain (parotid enlargement) had already improved at W28 in 8/9 patients with non-malignant persistent salivary gland enlargement at study entry. In detail, the glandular size normalized at W28 in 6/9, was reduced in 2/9 and was unchanged in 1/9, and no further improvement in the size was observed from W28 to W52 (Figs 4 and 5).

In contrast, the glandular domain did not improve in 2/2 patients with salivary gland enlargement due to salivary B-cell low-grade lymphoma. One of these two patients suspended the study at W12 and the further course is reported elsewhere [15], while the other one continued the study with a sustained response (but with no decrease in the parotid swelling due to indolent lymphoma). No new or increased salivary gland enlargement was observed throughout the study.

Lymphadenopathy domain

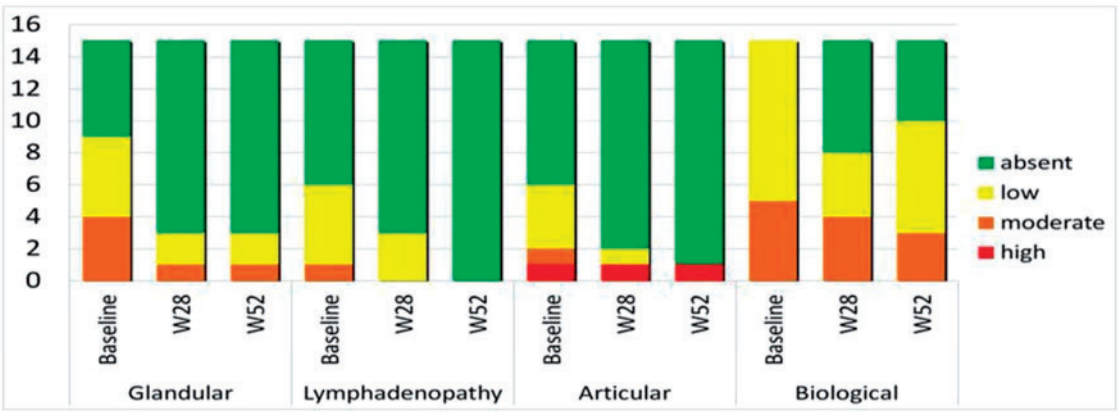
Among the 15 responder patients who continued the study, the lymphadenopathy domain had already improved at W28 in four of the six patients showing lymphadenopathy at study entry (disappearing in 3/6, being reduced in 1/6 and unchanged in 2/6). Of note, all three

Fig. 4 Positivity in the single EULAR SS Disease Activity Index domains during the whole study course the 15 responders at week 28 who completed the study up to week 52



Const.: constitutional domain; ESSDAI: EULAR SS Disease Activity Index; Haematol.: haematological domain; Lymph.: lymphadenopathy domain.

Fig. 5 The EULAR SS Disease Activity Index score of the single clinical domains that mainly contributed to the disease activity in the 15 responders at week 28 who completed the study



ESSDAI: EULAR SS Disease Activity Index.

patients with lymphadenopathy still detectable at W28 and who continued the study improved further after W28, with no detectable lymphadenopathy at W52 (Figs 4 and 5). Thus, these patients showed a later improvement, from W28 (at this time: 2/3 unchanged and 1/3 reduced *vs* study entry) to W52. No patient treated with belimumab developed lymphadenopathy *ex novo*.

Articular domain

Among the 15 responder patients who continued the study, the articular domain had already improved at W28 in 5/6 patients with arthralgias or arthritis at study entry (disappearing in 4/6, being reduced in 1/6 and unchanged in 1/6). Of the two patients with the articular involvement still active at W28 and who continued the study, one improved further with no articular disease at W52, and the other remained active (Figs 4 and 5). No patient treated with belimumab developed arthritis or arthralgias *ex novo*.

Biologic domain

Among the 15 responder patients who continued the study, the biologic domain became negative from baseline to W28 in 5 of the 13 patients with a positive domain at study entry. Two of these five patients worsened at W52 (both showing an increase in serum IgG levels to >1.6 g/l), presenting again the same biologic ESSDAI domain score as at the study entry (Figs 4 and 5). Of the eight patients with the biologic domain still positive at W28, 1/8 improved at W52, while no improvement was observed in 7/8.

Patients not responding at W28 but continuing the study

Interestingly, in the subgroup of four patients who continued the study despite not being responders at W28, a response (defined as for the study primary end point) was achieved in 3/4 patients at W52. Interestingly, 2/4 patients showed a further improvement in the ESSDAI score from W28 to W52, one patient improving further in

the constitutional, lymphadenopathy and glandular domains, and the other patient further improving in the cutaneous domain.

Tolerance

Safety of belimumab treatment in SS was evaluated in all 19 patients who completed the W52 protocol. From baseline to W28, headache at the end of the infusion (duration <24 h), mild transient neutropenia (1000–1500 neutrophils/mm^3; two episodes in the same patient), rhinopharyngitis (two cases), one gastroenteritis, one urinary tract infection and one pneumonia requiring antibiotic therapy were observed in these 19 patients.

Other adverse events recorded from W28 to W52 in these 19 patients were as follows: one vaginal fungal infection, one non-complicated cutaneous infection and two more episodes of transient, mild neutropenia (1000–1500 neutrophils/mm^3) in the same patient suffering from this side effect in the first half of the study. Of note, no serious adverse events were noticed from W28 to W52. No infusion reaction occurred throughout the study.

Discussion

The results of this preliminary study highlight that belimumab might represent a novel useful treatment for primary SS in the long term. Clinical and biologic efficacy of belimumab in SS was observed throughout 1 year of therapy, and improvement in some disease manifestations, including parotid swelling and lymphadenopathy, was particularly relevant. Of note, treatment was safe over 12 months.

Overall, the beneficial results observed in ~60% of SS patients at 6 months after the beginning of belimumab treatment [11] persisted at 1 year, with the lack of any new relevant side effect. Consistent with the prolonged follow-up data available on belimumab treatment in SLE [16], it then appears that, if a patient responds to belimumab, this treatment can be maintained safely for a more prolonged time also in SS.

Improvement of parotid swelling was rapid and persisted at W52 in SS patients with non-malignant parotid swelling, while belimumab was ineffective in both patients with parotid indolent lymphoma (one interrupting the study before W28, and the other being treated until W48 for other active domains) [11, 15]. Improvement in the lymphadenopathy domain, active at study entry in about one-third of patients, was more consistent at W52 than at W28. The improvement in the articular domain and the decrease in peripheral blood markers of B-cell hyperactivation observed at W28 [11] were maintained until W52 when continuing belimumab treatment. Of note, the RF appeared to decrease further from W28 to W52, while a further decrease in peripheral blood B-cells and serum immunoglobulin levels was not observed (Fig. 3). An ongoing functional effect of belimumab therapy on RF-positive B cells in SS, in the lack of B-cell depletion, might be then hypothesized. A limitation of this study is represented by the rather low number of patients analysed, with further limitation when considering the very low number of patients active in some rare ESSDAI domains (such as the cutaneous, renal and peripheral nervous system involvement; Figs 4 and 5).

Overall, when considering the previous results at 6 months [11], without new safety concerns, and given the current absence of effective treatments to modify the course of SS, the present data encourage further exploration of the therapeutic potential of belimumab in SS.

Whether a more prolonged treatment with belimumab may be more effective remains to be elucidated in SS. A very prolonged suppression of BAFF, lasting even longer than 1 year, might be needed to allow a gradual clinical and biologic improvement. This was suggested in some SLE subsets, for example, patients with anti-dsDNA antibodies or low complement levels [16]. Interestingly, of the four patients continuing the study despite the lack of response (according to the criteria employed) at W28, three responded at W52 and two showed a further decrease in ESSDAI score.

Significant changes in lacrimal and salivary function in SS during belimumab therapy did not occur, but this should be evaluated better in larger populations. Other SS manifestations showed a major benefit from belimumab treatment. The evidence that parotid swelling and lymphadenopathy improved significantly with treatment may have important implications for the issue of lymphoproliferation in SS. SS is characterized by an increased risk of malignant lymphoma [1, 2], leading to decreased patient survival. Non-malignant parotid swelling and mixed cryoglobulinaemia are the major risk factors for lymphoma in SS [1, 2, 17]. Besides the persistent improvement of non-neoplastic parotid swelling in almost all the patients recruited in this study, the disappearance of cryoglobulinaemia in 3/3 patients where it was present at baseline is highlighted [11]. Anti-CD20 treatment is usually effective for cryoglobulinaemic vasculitis [18], while the efficacy of rituximab appears more conflicting as monotherapy in SS-related MALT lymphoproliferation [1]. Importantly, BAFF can mediate the resistance to anti-CD20 tissue B-cell depletion in the MALT microenvironment [9], and recently, it was reported that anti-CD20 therapy showed effectiveness on SS-associated parotid lymphoma and cryoglobulinaemia only when given soon after belimumab [15]. In addition, as the BAFF level is increased by rituximab therapy [19], BAFF could play a role in the repopulation of autoimmune B cells also after rituximab therapy. Thus, treatments with either an initial treatment with belimumab, facilitating the effect of anti-CD20 therapy given subsequently [15], and/or the reverse sequence deserve consideration in SS.

Finally, it is important to stress that the SS sicca manifestations and patient-reported outcomes, such as fatigue and pain, were modestly affected by belimumab treatment. While this could again imply that belimumab might finally prove more useful for some SS manifestations, more extensive data are needed. It is important to note that the SF36 physical health component score improved significantly from W28 to W52, whereas in the same patients it was not improved at W28. Very prolonged

treatment with belimumab might be needed for improving the quality of life of patients, as in SLE [20].

Overall, based on the results of the BELISS study at 1 year, belimumab may be beneficial in SS, especially on glandular and lymphadenopathy domains. Randomized, double-blind, controlled studies in larger populations are encouraged.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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