Review Article

Efficacy and safety of Belimumab in Treatment Of Systemic Lupus Erythematosus

Comment [R1]: If the work is systematic review and meta analysis (as author mentioned in the discussion) It should mentioned in the title

Abstract:

SLE is a fairly common and widespread condition. Currently, it is clinically relevant in most healthcare facilities and is discussed in both the medical and scientific literature. There is a wealth of data from both clinicians and researchers studying the problems and treatment options associated with SLE. Systemic lupus erythematosus is characterized by clinical variability, irregular course, and relapses (SLE). Although SLE is primarily a systemic autoimmune disease, it can sometimes be organ specific, creating diagnostic difficulties. B-cell activating factor (BAFF) is attacked by belimumab (a monoclonal antibody), which reduces the level of BLys (B-lymphocyte stimulating cell), which is a chief cytokine in the pathophysiology of SLE. In our review of the literature, we tried to determine efficacy and safety of drug belimumab in the context of patients with SLE and how it affects their recovery and management. We have reviewed the two studies which were conducted regarding the role of this drug which were found to be promising and beneficial for seeking a new treatment route for the clinicians. Also we have described different domains of the study and their mathematical results regarding the efficacy of the drug henceforth. We seek to describe the safest use and the best possible results that clinicians can achieve when treating patients with SLE, and we provide high levels of clinical care at the highest level. We urge physicians to monitor all areas of action of the drug and to make informed and informed decisions that are primarily reviewed in our article respectively.

Comment [R2]: Systemic Lupus Erythematosus abbreviation should not be added in abstract without explanation (please correct)

Comment [R3]: Please revise this part of the sentence

Keywords: SLE, Belimumab, Monoclonal Antibody, Flares, SFI index, SELENA SLEDAI score.

INTRODUCTION

SLE is a multifaceted chronic autoimmune disease represented by multiple B-cell abnormalities, high morbidity, and poor quality of life(1).It is a chronic disease with complicated underlying pathogenic processes and without treatment. It is caused by a series of immunological abnormalities and autoantibody production has been correlated to pathophysiology of the disease, which manifests in various organs. Ongoing treatments aim to control inflammation, avert relapses, and improve clinical symptoms, all with primary aim of averting irreversible organ damage. In the 1950s, the USFDA approved these drugs to treat SLE: which includes Aspirin, CS, and HCQ. This was prior to era of clinical trials with set endpoints and the establishment of statistical significance. All three drugs are still used as nonspecific drugs for some SLE symptoms. In recent efforts to reduce the toxicity of conventional drugs,

Comment [R4]: The United States Food and Drug Administration (USFDA)

Comment [R5]: Please clarify what do you mean by this abbreviation

Comment [R6]: hydroxychloroquine (HCQ)

Comment [R7]: please add reference

supplementation with adjunctive treatments has been used. Prasterone and vitamin D are two non-immunosuppressive immunomodulatory drugs that can be utilized as supplements to regulate disease activity or to minimize the use of Cs. Several clinical studies have included biologics in regimens for SLE patients who have responded poorly to conventional treatments or who have experienced significant side effects. A vital cytokine for B cells i.e. Lymphocyte stimulator is upregulated in sufferers with SLE & rest of autoimmune illnesses. BLyS concentrations are associated with variations in disease activity and anti-dsDNA antibody titers insufferers with SLE. The Drug Belimumab comes under the group of Monoclonal Antibody which acts by binding to the B lymphocyte stimulator cells and henceforthly reducing its activity. Other than this in SLE sufferers it suppresses the CD20+ B-lymphocyte count and also the temporary plasma cells & anti-dsDNA antibody titres respectively. Various disease activity scales are implicated in SLE due to its diversness hence none of the drugs particularly approved for SLE have been incredibly resistant in last 50yrs. The goal of this study was to compare the effectiveness, safety, and acceptability of belimumab to caliber of treatment in patients with SLE who were administered Belimumab as treatment drug.(2)

Comment [R8]: give references to theses studies

Comment [R9]: in sufferers

Comment [R10]: give references for all the illustrated data in this paragraph

Comment [R11]: how the aim of your work is referenced?

METHODS

DATA SOURCES

To find studies evaluating the efficacy and safety of belimumab in the treatment of SLE, we conducted a systematic literature search in PubMed, EMBASE, LILACS, and the Cochrane database. The keywords belimumab, SLE, safety and efficacy were used to find these articles. We have not limited our search to the English language and have translated the research into other languages if necessary. To eliminate selection bias, inclusion criteria were developed before this work was identified.

INCLUSION CRITERIA

All studies that described the unique efficacy and safety of belimumab in patients with SLE were eligible for inclusion. Patients (>18 yrs) who were eligible were the ones accomplishing the sle criteria given by rheumatology American college & who had functioning or ongoing disease (On screening having score >6 according to SELENASLEDAI)(3). Patients must have completed BLISS76 by week 72 and be able to start belimumab treatment in 4 weeks (a minimum of 2 weeks, a maximum of 8 weeks

Comment [R12]: The inclusion and exclusion criteria should be designed by authors nor referenced

Comment [R13]: SLE

Comment [R14]: SELENA-SLEDAI

Comment [R15]:

EXCLUSION CRITERIA

Those having serious active lupus nephritis ;or in pregnancy; and prior therapy rituximab (lymphocyte targeting drug) i.v cyclophosphamide in less than 6 months of study enrollment, or received i.v Ig or prednisone at a dose > 100 mg / day in < 3 months were important Exclusion criteria. .(4) Patients were excluded if they had clinical confirmation of an unconstrained, acute or chronic disorder unrelated to SLE, the investigator said. Other important exclusion criteria were the happening of an unfavourable event in the main study that set down the patient at inordinate risk, as well as laboratory abnormalities.

Comment [R16]: Please clarify what do you mean by this

Comment [R17]: unfavorable

RANDOMIZATION AND MASKING: Enrollment in the study was done of the patients who passed all the screening processes, and were randomized to therapy with help of central interactive voice response system and the List of Central Randomization of Human Genome Sciences). The patients were assigned to either of three groups: placebo, belimumab @ dose of 1 mg / kg, or @ dose of 10 mg / kg During Screening the parameters included the SELENA SLEDAI Score range of 6-9 vs 10 , protein concentration in urine 2g/24h vs 2g/24h and ethinic origin were used to stratify randomization. While the drug was given through iv route,patients were evaluated at every 4th week during 52-week study, sufferers, investigators, study coordinators, and all others were blinded to treatment allocation until the base was locked. of data.(5)

Comment [R18]: I could not understand what do authors mean by this section

STUDY DESIGNS

STUDY CARRIED OUT BY Navarra S et al

Comment [R19]: Navarra et al (1)(add the number of the reference
Authors discussed this study which is done in 2011 how they used references in 2020 as ref. (6) and 2018 in the same repeated paragraph reference (7)

The investigational drug was given to patients by i.v infusion over on 0, 14th, and 28th day over an hour respectively, and then every 28 days till 48 weeks. After 16 weeks of immunosuppressive drug therapy and 24 weeks of malaria drug treatment, changes in the quality of care were limited. The amount of prednisone wasn't restricted for the 1st 24 weeks, but was reduced to 25% or 5 mg of the starting dose without any rise for the duration of the study .according to the clinical opinion of the investigators dose of prednisone was reduced. It was proscribed to start any other immunosuppressive or biologic drug during the study at any random interval or any antimalarial medicine or an ACE inhibitor after 4 months, or Statins after 6 months of research. The sufferers who needed and took medications that violated the study guidelines were considered treatment errors and were excluded from the study. At each study visit, side effects, vital signs, concurrent medication, hematology, chemistry, Urinalysis were documented.(6)

Comment [R20]: Please specify the name of this drug

Response rate at 52nd week as calculated by SRI was the main efficacy endpoint. 19 One responder was defined as a decrease in SELENASLEDAI score by at least 4 points (interpreted as clinically relevant.

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Comment [R21]: This paragraph is repeated

STUDY, PERFORMED BY Richard A. et al

Comment [R22]: This reference is not included in the reference section of the manuscript.

For 76 weeks, patients received 1 mg / kg IV belimumab, 10 mg / kg IV belimumab, or placebo with standard therapy. In the extension study, patients who had previously taken placebo received 10 mg / kg of belimumab(.Patients randomized to belimumab received the same dose (1 or 10 mg / kg IV every 28 days) as in the original study plus conventional treatment. In patients who were given 1 mg / kg belimumab, the dose was raised to 10 mg / kg after a protocol change (March 9, 2011).The experiment must be terminated 5 calendar years after the Last patient is enrolled or with less than 100 patients remaining in the Study, whichever occurs first. The investigation lasted from 5th august, 2008 to 26th march, 2015, and data was collected for up to 8 calendar years (maximum exposure 2,908 days)(8).

Comment [R23]: This reference is published 2011 how the study last till 2015

The primary objective of this study was to investigate the long-term safety of belimumab using EA. Weeks 24 (middle of the academic year) and 48 (end of the academic year) were used to carry out the evaluations (end of the academic year, hereinafter referred to as the academic year).Organ damage was evaluated on every 48th week. The primary measure of efficacy was the response rate of the SRI , a certified composite endpoint that was expressed as a 4-point reduction in the version of the SLE Disease Activity Index.(SELENA-SLEDAI) Estrogen safety is defined in the National Lupus Erythematosus Assessment. Score from baseline, no deterioration in the PGA of disease activity on a scale 0f 0 to 10.

Comment [R24]: The patient global assessment (PGA)

STATISTICAL ANALYSIS

FROM THE STUDY OF Navarra S et al

stated that the main objective was to measure the response rate of each belimumab group with SRI and to collate with control group by implicating Logistic Regression model.Eighty-one percent of the 810 patients (270 per group) found an Complete improvement of 14 percent (According to response rate calculated by SRI) after 52nd week with belimumab 10 mg / kg compared to placebo. a standard deviation of 50% was chosen in account for worst case unevenness.When comparing belimumab 10 mg / kg with placebo, a reduction technique was handed down to control for type 1 error (two-tailed = 005); if 10 mg / kg was superior to placebo, belimumab 1 mg / kg was contrasted with placebo, and so on.Treatment failures were found to be those patients who stopped using background medications for Sle or required modifications that were not approved by the protocol (9).

Comment [R25]: These results belong to ref. 1 not ref 9

Statistical Analysis Of Another Study Performed By Richard A. et al. stated that belimumab was administered to people who were registered in the extension study and who had received not less than one dose. In the main study, belimumab was administered at a dose.

Comment [R26]: Incomplete Data

RESULTS

The Study Of Navarra S et al : 2 of the 867 sufferers who were randomized and treated during study were withdrawn;865 sufferers in the study who were randomized , monitored were the intention to treat crowd. At week 52, significantly more participants in the 1 mg / kg and 10 mg / kg groups of belimumab drug showed a response than in the control group as assessed by SRI.From 16th week and 28th week significantly improved responses were recorded on sequential visits by belimumab 10mg/kg and 1mg/kg respectively. At week 52, significantly more patients who were in the group receiving the drug improved their SELENASLEDAI score by at least 4 points compared to those in the placebo group .At week 52, no disease worsening was recorded of the patients on corresponding belimumab doses respectively which those with placebo-treated patients. At week 52, patients who received belimumab were more likely than those who received placebo to have disease stability (ie, no deterioration in PGA score .Compared with placebo,the likelihood of developing the IFS symptoms of varying intwnsity was reduced by 24% and 25% when the sufferers were on belimumab doses.The sufferers who were given both doses of the drug resulted in increment or normalizing the complement concentrations at 4th week & also diminution of anti-ds Dna antibody titres at 8th week as compared to control group also resolving the increased gamma globulins in the dose dependent sequence respectively. The responses to the infusion were recorded indistinguishable in all groups .As compared to the control group those receiving the Drug shown a high rate of hypersensitivity reactions respectively .Administration of 1st dose of the drug resulted in 3 anaphylactic reactions , 2 severe cases presented with angioedema, total 9 deaths were observed during the study .3 sufferers in the group which was administered drug died due to infections while the one who was in the placebo group had episode of sepsis which terminated into cardiac arrest. no reports of cancerous diseases were noted (10).

Another Study Conducted By Richard A related to drugs Adverse effects commonly seen included Joint pain, Nausea, Infections including The URTI and UTI, headache respectively . 112 of 268 patients (41.8%) had a significant adverse event (Grade 3 or 4 events classified as potentially fatal), while 100 of 268 patients had at least one severe AE (37.3 percent) .Two deaths occurred (0.7 percent); none could be attributed to study drugs (hypertension, politoxicity [later assessed as suicide]). Effectiveness. SRI response.[1] 96 of 229 patients (41.9 percent) and 90 of 119 patients (41.9 percent) had an SRI response (75.6 percent).The baseline SELENA-SLEDAI score showed an increment from 44.4% to 78.2% respectively. At the middle of the study, 125 of 127 patients (98.4%) met this criterion.(11).

DISCUSSION

The current systematic review and meta-analyzes provide data on the safety and efficacy of belimumab in the treatment of SLE. As can be seen in our review, there were two primary lines of research (Navarra S et al. And Richard A. et al.) That were part of the existing literature:

* the results of this phase 3 study, which focused on The safety of belimumab indicates the profile and efficacy in the management of Sle in wide range of sufferers and * the abiding benefits of the drug in patients with active SLE when added to conventional treatment(12-15). Few studies on SLE were reviewed(16-17).

According to these studies, which were evaluated with the help of SRI at 52nd week onwards showed that the group who ere receiving the drug belimumab significantly had a higher response rate as compared with the control group respectively. A dose-response pattern showed that there

Comment [R27]: Authors previously mentioned that the patient were 810 in the statistical analysis section

Comment [R28]: Irrelevant reference

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Comment [R30]: The current manuscript needs to follow The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA)

Comment [R31]: SLE

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was a significantly great improved response in the sufferers who were on the drug as compared to the placebo group in all 3 components of the SRI and 2 components of SELENA SELDAI indices respectively. There was overall reduction in relapse in the group receiving belimumab as compared to the control group accordingly. Belimumab improved serologic activity rapidly, selectively, and in the long term. Both the groups who were on the drug had a similar safety profile as compared to the ones receiving the placebo and did not have any adverse events respectively. Long term therapy with the drug belimumab resulted into a constant or decreased incidence of the adverse events and also the long term efficacy which was over a 7yr study span resulted in an overall decrease in the severity of SLE(15).

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