Mortality and Adverse Events of Special Interest in Adult Patients With Systemic Lupus Erythematosus Receiving Intravenous Belimumab: A Post Hoc Descriptive Summary of Serious Psychiatric Events

Introduction

- Systemic lupus erythematosus (SLE) is a chronic, autoimmune disease affecting multiple organ systems and reducing health-related quality of life.
- Intravenous (IV) belimumab, a B-lymphocyte stimulator (BLyS)-specific inhibitor, is approved for the treatment of patients 15 years of age and older, with active, subcutaneous-positive SLE who are receiving standard therapy.
- The BASE (GSK Study BIL11547; NCT01769577) was a Phase 4, international, multi-center, randomized, double-blind, placebo-controlled, 52-week safety study in adult patients with SLE treated with belimumab or placebo.
- BASE (GSK Study BIL11547; NCT01769577) was a Phase 4, international, multi-center, randomized, double-blind, placebo-controlled, 52-week safety study in adult patients with SLE treated with belimumab or placebo.

Methods

- BASE study population
- A total of 4003 patients with SLE were included in the BASE study (belimumab, n=2002; 7.5%) and placebo (6.6%)
- In patients who experienced a sponsor adjudicated event, approximately half of belimumab patients (8/15) and 60% of placebo patients (3/5) continued study treatment after experiencing the event.
- The median (interquartile range) time to onset of self-injury events per sponsor adjudication was 205 (83, 257) days for belimumab and 204 (173, 229) days for placebo.
- Worsening and development of suicidal ideation and/or behavior per C-SSRS
- The C-SSRS is a validated tool used to screen for the presence and severity of suicidal ideation and/or behavior.

Results

- Mortality and Adverse Events of Special Interest in Adult Patients With SLE
- The majority of these AESI resolved with treatment and study completion.
- The C-SSRS is a validated tool used to screen for the presence and severity of suicidal ideation and/or behavior.
- The median time to resolution of suicidal ideation and/or behavior was 100 (81, 139) days for belimumab and 70 (51, 90) days for placebo.

Post hoc analysis of psychiatric events

The following were summarized post hoc for on-treatment serious suicidal/self-injury events among patients who developed these events, and were thus also in the overall BASE patient population:

- The majority of these AESI resolved with treatment and study completion.
- No suicide-related deaths were observed as part of this study.

Conclusions

- In this largest SLE safety study to date, an imbalance with higher placebo onset of serious suicidal ideation/behavior and self-injury events was observed with belimumab compared to placebo (examined in a limited subpopulation of sponsor-reported serious suicidal/self-injury events).
- Mean SLE duration, mean baseline SELENA-SLEDAI score and the proportion of patients at baseline with prior/current history of psychiatric disorder were higher among belimumab-treated patients who reported sponsor-adjudicated serious suicidal/self-injury events than among placebo-treated patients who developed these events, and they were also higher than in the overall BASE patient population.
- However, conclusions based on these post hoc analyses are limited by the small number of patients reporting these events.

Disclosure

Figures 1, 4 and Table 1 are provided as an electronic supplement to this manuscript. Reprints may be obtained without permission from the authors and publisher.

References


Sara Sheikhtehrani,1,2,3,4,5 Rolf Klareskog,1,2,6,7,8,9 Jean Frölich,2,6,7,8,9 Anna-Rosemary Spence,2,6,7,8,9 Andrew B Imported,2,6,7,8,9 Andrew Liew,2,6,7,8,9 Kathleen Makowskie-Mckinnon,2,6,7,8,9,10,11,12 Holly Quaas,2,6,7,8,9 David Roth,2,6,7,8,9 Lilian Soto,2,6,7,8,9 Raj Prabhu,1,2,6,7,8,9

1University of North Carolina, School of Nursing, North Carolina, USA; 2University of North Carolina at Chapel Hill, USA; 3Center for the Advancement of Women’s Health, USA; 4Beth Israel Deaconess Medical Center, USA; 5Department of Dermatology, University of Massachusetts Medical School, USA; 6Center for Rheumatic Diseases, King’s College, London, UK; 7GlaxoSmithKline, Middlesex, UK; 8GlaxoSmithKline/Immunology, Molecular Life Sciences, USA; 9Department of Dermatology, King’s College, London, UK; 10Department of Dermatology, University of São Paulo, São Paulo, Brazil; 11Department of Dermatology, King’s College, London, UK; 12GlaxoSmithKline, College Park, USA; 13Imperial College London, London, UK; 14University of the Witwatersrand, Johannesburg, South Africa; 15GlaxoSmithKline, College Park, USA; 16University of the Witwatersrand, Johannesburg, South Africa

Acknowledgments

The authors acknowledge the contribution of all Study Investigators, the contribution of all Study Coordinators, local research assistants, data management, biostatistical analysis, copy editing and quality control teams of the BASE Study. The authors are responsible for the design and conduct of the study, for the collection, analysis, and interpretation of the data, and for the writing and approval of the final manuscript. The authors take full responsibility for the integrity of the data and accuracy of the data analysis. Financial disclosures for all Authors are listed in the Acknowledgments section. The study was sponsored by GlaxoSmithKline (GSK). Medical writing support was provided by Helen Taylor of Fishawack Indicia Ltd, UK, and was funded by GSK. Lilian Soto and their families, clinicians and study investigators.

Figure 1. BASE study design Figure 2. Overall BASE study findings related to the primary on-treatment endpoints incidence of suicidal ideation/behaviour and self-injury events per sponsor adjudication, 15 of whom received belimumab and 3 who received placebo. Two study periods (i.e. if the patient was followed after discontinuing study treatment) were used for the BASE study. When assessing suicidality AESI, an analysis approach was used that included baseline demographic and patient characteristics at baseline. When assessing suicidality AESI, an analysis approach was used that included baseline demographic and patient characteristics at baseline. The median recovery time (number of days from onset to ≥1 to 0 after event) was 205 (83, 257) days for belimumab and 204 (173, 229) days for placebo. The median recovery time (number of days from onset to ≥1 to 0 after event) was 205 (83, 257) days for belimumab and 204 (173, 229) days for placebo.

- Resolution occurred in 18/20 patients (90%). The median time to resolution of suicidal ideation and/or behavior was 100 (81, 139) days for belimumab and 70 (51, 90) days for placebo.

Post hoc population of patients reporting on-treatment suicidal ideation/behavior and self-injury events per sponsor adjudication (n=20)

- No suicide-related deaths were observed as part of this study.

Figure 4. Serious suicidal/self-injury event and resolution summary per sponsor adjudication (post hoc)

- In patients who experienced a sponsor adjudicated event, approximately half of belimumab patients (8/15) and 60% of placebo patients (3/5) continued study treatment after experiencing the event.
- The median time to onset of these AESI was 205 (83, 257) days for belimumab and 204 (173, 229) days for placebo.
- The majority of these AESI resolved with treatment and study completion.
- The C-SSRS is a validated tool used to screen for the presence and severity of suicidal ideation and/or behavior.
- The median time to resolution of suicidal ideation and/or behavior was 100 (81, 139) days for belimumab and 70 (51, 90) days for placebo.