Belimumab in Lupus Nephritis Patients with Impaired Renal Function: A Post-Hoc Analysis of the Bliss-LN Trial

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INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease with multiorgan involvement. Lupus Nephritis (LN) is a common severe manifestation of SLE which occurs in up to 60% of SLE[1]. Despite immunosuppressive therapies, long-term outcomes remain poor, with a significant proportion progressing to end-stage kidney disease. Belimumab, a monoclonal antibody targeting B-cell activating factor, has shown promise in SLE treatment. The BLISS-LN trial[2], a 104-week, phase 3, randomized, placebo-controlled study, demonstrated improved renal responses with belimumab added to standard therapy in patients with active LN. However, a key limitation of most trials, including BLISS-LN, is the underrepresentation of patients with impaired kidney function (eGFR <60 ml/min/1.73m^2). Considering the prognostic relevance of renal impairment at lupus nephritis onset, this study evaluates the effects of belimumab in the subgroup of patients with impaired kidney function from the BLISS-LN trial.

OBJECTIVES

To assess renal response and eGFR recovery in LN patients with impaired renal function treated with belimumab versus placebo at 52 and 104 weeks.

METHODS

Patients with baseline eGFR between 30–60 ml/min/1.73 m^2 (N=74) were included. Participants received belimumab or placebo in combination with corticosteroids and either mycophenolate mofetil or cyclophosphamide. Endpoints included were primary efficacy renal response (PERR), complete renal response (CRR), eGFR recovery ≥10%, ≥20%, ≥30%, and ≥50%, and time to renal-related events or death. Kaplan-Meier and log-rank tests were used for time-to-event analysis. All analysis was performed on the intention-to-treat population and stratified by three kidney-biopsy LN classes: Class III or IV, Class III+V or IV+V, and Class V.

RESULTS

In addition to corticosteroids, 41 patients received Belimumab (29 received mycophenolate and 12 cyclophosphamide) and 33 patients placebo (21 received mycophenolate and 12 cyclophosphamide). At time of kidney biopsy, 42 patients (26 on Belinumab; 16 on Placebo) had class III or IV, 9 (4 on Belinumab; 5 on Placebo) had class V, and 23 (11 on Belinumab; 12 on Placebo) had mixed forms. At 52 weeks, PERR was achieved in 19.5% (belimumab) versus 33.3% (placebo), while CRR was 12.2% vs 9.0%, respectively (Table). At 104 weeks, PERR was achieved in 29.3% (belimumab) versus 33.3% (placebo), while CRR was 14.6% vs 15.2%, respectively (Table). No significant differences emerged between the two groups. Notably, eGFR recovery at all thresholds was significantly higher in the Belimumab group compared to placebo one.

CONCLUSIONS

In LN patients with moderate renal impairment, belimumab showed no significant improvement in primary or complete renal response rates compared to placebo. However, it was associated with significantly better recovery of eGFR. These results suggest a potential renal benefit of belimumab in this high-risk population, particularly in preserving or improving kidney function.

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Table. Distribution (no., %) of achievement of Primary efficacy renal response rate (PERR), Complete renal response (CRR), and recovery eGFR at weeks 52 and 104 in patients treated with Belimumab or Placebo.

	52 week		104 week	
Overall sample	**Belimumab (N=41)**	**Placebo (N=33)**	**Belimumab (N=41)**	**Placebo (N=33)**
PEER	8 (19.5)	11 (33.3)	12 (29.3)	11 (33.3)
CRR	5 (12.2)	3 (9.0)	6 (14.6)	5 (15.2)
Recovery eGFR				
≥ 10%	24 (80.0)	21 (72.4)	23 (85.2)	13 (54.2)
≥ 20%	23 (76.7)	18 (62.1)	22 (81.5)	10 (41.7)
≥ 30%	23 (76.7)	14 (48.3)	22 (81.5)	8 (33.3)
≥ 50%	16 (53.3)	10 (34.5)	16 (59.3)	4 (16.7)
Class III and Class IV	**(N=26)**	**(N=16)**	**(N=26)**	**(N=16)**
PERR	7 (26.9)	7 (43.8)	8 (30.8)	7 (43.8)
CRR	4 (15.4)	1 (6.2)	4 (15.4)	2 (12.5)
Recovery eGFR				
≥ 10%	13 (81.2)	11 (78.6)	13 (86.7)	8 (66.7)
≥ 20%	13 (81.2)	10 (71.4)	13 (86.7)	7 (58.3)
≥ 30%	13 (81.2)	9 (64.3)	13 (86.7)	6 (50.0)
≥ 50%	11 (68.8)	7 (50.0)	9 (60.0)	3 (25.0)
Class III+V,IV+V	**(N=11)**	**(N=12)**	**(N=11)**	**(N=12)**
PERR	1 (9.1)	3 (25.0)	2 (18.2)	3 (25.0)
CRR	1 (9.1)	1 (8.3)	1 (9.1)	2 (16.7)
Recovery eGFR				
≥ 10%	10 (90.9)	8 (72.7)	9 (90.0)	4 (44.4)
≥ 20%	9 (81.8)	7 (63.6)	8 (80.0)	2 (22.2)
≥ 30%	9 (81.8)	5 (45.5)	8 (80.0)	2 (22.2)
≥ 50%	4 (36.4)	3 (27.3)	6 (60.0)	1 (11.1)
Class V	**(N=4)**	**(N=5)**	**(N=4)**	**(N=5)**
PERR	0	1 (20.0)	2 (50.0)	1 (20.0)
CRR	0	1 (20.0)	1 (25.0)	1 (20.0)
Recovery eGFR				
≥ 10%	1 (33.3)	2 (50.0)	1 (50.0)	1 (33.3)
≥ 20%	1 (33.3)	1 (25.0)	1 (50.0)	1 (33.3)
≥ 30%	1 (33.3)	0	1 (50.0)	0
≥ 50%	1 (33.3)	0	1 (50.0)	0

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