Effects of Blisibimod, an Inhibitor of B Cell Activating Factor, on Patient-Reported Outcomes and Disease Activity in Patients with Systemic Lupus Erythematosus

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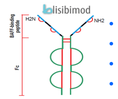
Introduction

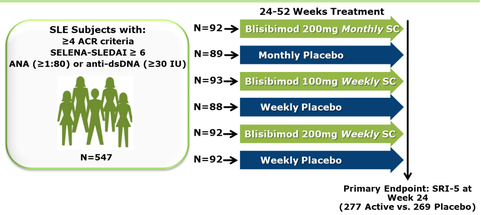
Fatigue is a common and burdensome symptom of SLE, for which therapeutic options are lacking. The randomized, double-blind, placebo-controlled PEARL-SC study evaluated the efficacy and safety of subcutaneously-administered blisibimod or placebo on top of standard-of-care medication in patients with moderate-to-severe, seropositive SLE. The effects of blisibimod on safety, efficacy and SLE biomarkers in these subjects compared with placebo were reported previously (Furie *et al.* 2014).

Here we report the observed effects of blisibimod on patient-reported outcomes using the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scale (Cella *et al.* 2005) amongst subjects enrolled in the PEARL-SC trial.



- Potent inhibitor of B-cell activating factor, BAFF: K_D=1pM
- A peptibody, composed of two identical polypeptides
- Binds soluble and membrane-bound BAFF (Hsu *et al*. 2012)
- 8-10-day human serum half-life (Stohl *et al.* 2008)

Methods



The 13-Item FACIT-Fatigue Questionnaire

	Not at all	A little bit	Somewhat	Quite a bit	Very much
I feel fatigued	0	1	2	3	4
I feel weak all over	0	1	2	3	4
I feel listless ("washed out")	0	1	2	3	4
I feel tired	0	1	2	3	4
I have trouble starting things because I am tired	0	1	2	3	4
I have trouble finishing things because I am tired	0	1	2	3	4
I have energy	0	1	2	3	4
I am able to do my usual activities	0	1	2	3	4
I need to sleep during the day	0	1	2	3	4
I am too tired to eat	0	1	2	3	4
I need help doing my usual activities	0	1	2	3	4
I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
I have to limit my social activity because I am tired	0	1	2	3	4

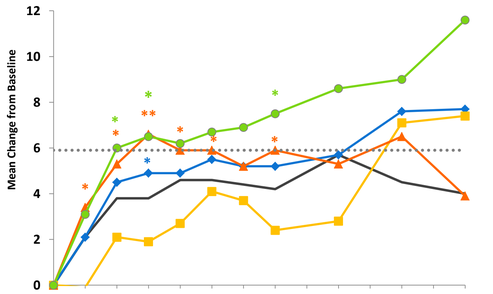
High score identifies worsening

High score identifies improvement

Cella *et al.*, 2005

Results

Change from Baseline Total FACIT-Fatigue Score in PEARL-SC



Study Week	4	8	12	16	20	24	28	36	44	52
Number of Subjects										
Placebo Pooled	258	245	240	236	232	229	189	142	73	37
Blisibimod Pooled	267	254	246	246	240	239	191	132	70	44
Blisibimod 200Q4W	90	85	85	86	83	82	65	42	24	17
Blisibimod 100QW	90	84	78	79	78	77	62	45	21	13
Blisibimod 200QW	87	85	83	81	79	80	64	45	25	14

placebo pooled
blisibimod pooled
blisibimod 200mg Q4W
blisibimod 100mg QW
blisibimod 200mg QW
min clinically-important difference =5.9 (Goligher *et al*. 2008)
*p<0.05, **p<0.01

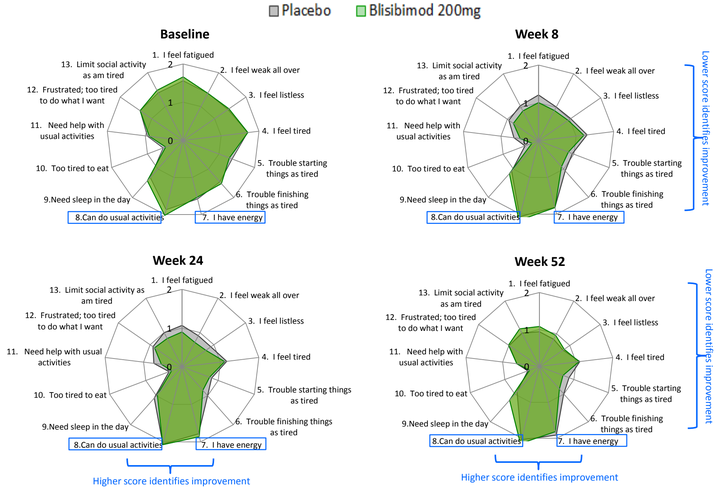
PEARL-SC Demographics and Baseline Disease Characteristics

Demographics	
Age	37.5
Weight (kg)	65.6
Gender, %	
Female	94.0
Male	6.0
Race, %	
White	25.0
Asian	19.7
Black or African	8.4
Other	46.8
Region, %	
Asia/Pacific	19.0
Latin America	71.1
North America	9.9
SLE Duration (years)	6.1

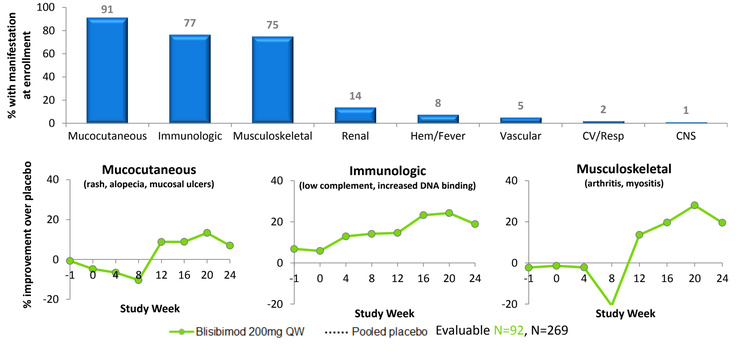
Baseline Disease Characteristics	
SELENA-SLEDAI (mean)	10.1
BILAG 1A or 2B, %	50.3
PGA (mean score)	1.4
ANA >1:80, %	78.8
Anti-dsDNA ≥30 IU, %	68.4
Low C3 (< 90 mg/dL), %	42.4
Low C4 (<16 mg/dL), %	50.2
Urinary Pr/Cr > 1.0, %	9.9
Prednisone dose (mg/day)	12.0
Prednisone >7.5 mg/day, %	60.1
Immunosuppressive use, %	45.0
Anti-malarial use, %	70.9

Results

Mean Scores Across All FACIT-Fatigue Questions



Percent Improvement in SELENA-SLEDAI Over Placebo For Most Common Organ Manifestations



Results

PEARL-SC Adverse Events Overview

Adverse Events	Placebo N=266	Blisibimod N=280
Overview (% incidence)		
All Adverse Events (AEs)	85.0	82.5
Serious AEs	15.8	11.1
AEs Related to Study Drug	37.2	40.0
AEs Leadieg to Withdrawal	7.9	5.7
AEs Leading to Death*	1.1	1.4
Severe Infection AEs	1.1	1.4
Severe Injection Site Reactions	0.0	0.0
Serious Adverse Events Occurring in >1 Subject, n(%)		
Herpes zoster	2 (0.8)	2 (0.7)
Pneumonia	7 (2.7)	3 (1.1)
Urinary tract infections	2 (0.8)	2 (0.7)
SLE	3 (1.1)	2 (0.7)
Deep vein thrombosis	2 (0.8)	3 (1.1)

Conclusions

- Patients randomized to blisibimod reported significantly better FACIT-fatigue scores compared with placebo at the 2 highest doses.
- As early as Week 8, 200mg QW blisibimod met the criteria for minimal clinically important difference in FACIT-fatigue score of 5.9-point change from baseline determined for SLE (Goligher et al., 2008). These improvements were sustained through the study.
- FACIT-Fatigue improvements were observed over a similar time course to observed effects of blisibimod on physician-evaluated disease activity, SLE biomarkers.
- Blisibimod effects were observed across the commonly-affected organ systems.
- These data support further evaluation of blisibimod in SLE. A Phase 3 trial in patients with SLE is currently enrolling.

References

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