A Pilot Phase 2a Study of the Safety and Efficacy of Bertilimumab, an Anti-Eotaxin-1 Antibody, in Bullous Pemphigoid

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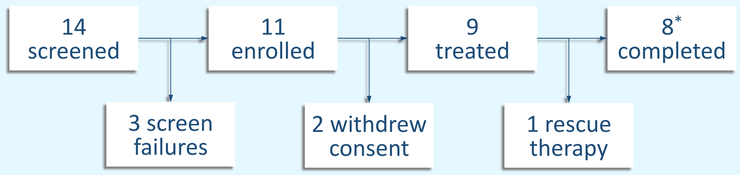
Introduction

Although patients with moderate-to-extensive BP can be managed with 0.5-1.0 mg/kg prednisone with a 6-12 month taper, this can cause immunosuppression, HPA axis suppression, and other serious side effects, and is poorly tolerated in an elderly population. Eotaxin-1, an eosinophil chemoattractant, is found in lesions and blister fluid in BP and is implicated in the eosinophil-mediated inflammatory cascade driven by IgE autoantibodies. Bertilimumab, a human monoclonal antibody that blocks eotaxin-1, may have a role as a steroid-sparing agent or steroid alternative in BP.

Methods

This was a single-arm, open-label phase 2a study (NCT02226146). Subjects with moderate-to-extensive BP received 3 biweekly doses of bertilimumab 10 mg/kg IV, and prednisone at a maximum initial dose of 30 mg, and were followed for 12 weeks. The primary endpoint was safety; key secondary endpoints include changes in BPDAI score, pruritus VAS, achievement of disease control, and tapering to a prednisone dose <10 mg/day.

Subject Disposition



**1 subject completed all study visits under the 60-day follow-up of the initial protocol*

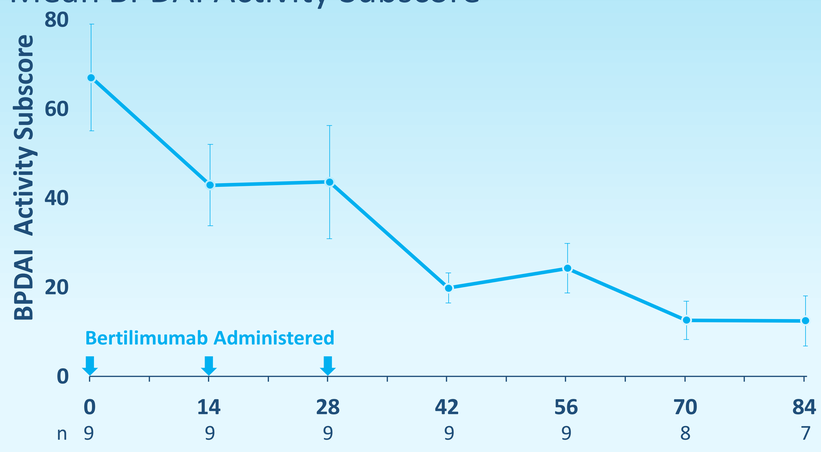
Baseline Characteristics

Age: 76 (range 62-87), 5 male / 4 female
Status: 6 newly diagnosed, 3 taper-resistant
Karnofsky performance status: 83 (70-100)
Eosinophils: blood: $0.34*10^9$/L
lesions: 32 per HPF
BPDAI Activity Subscore: 67 (range 26-136)
Pruritus VAS: 17.5
ABQOL score: 14.6

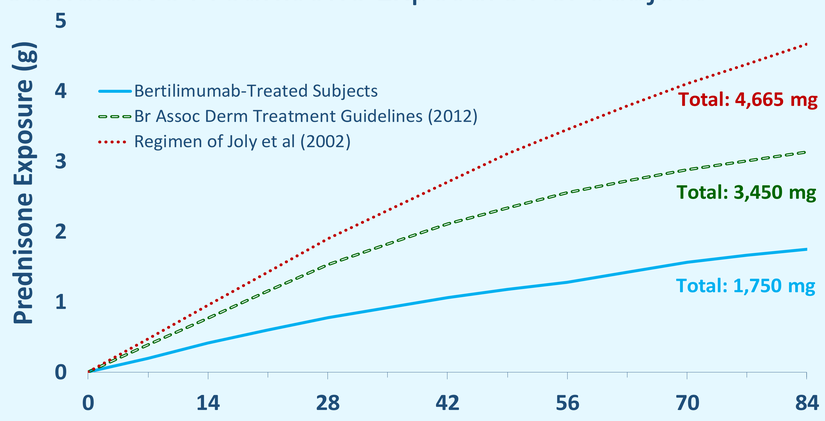
This trial is sponsored by Immune Pharmaceuticals. We gratefully acknowledge the support of our investigators and the participants in the study.

Results

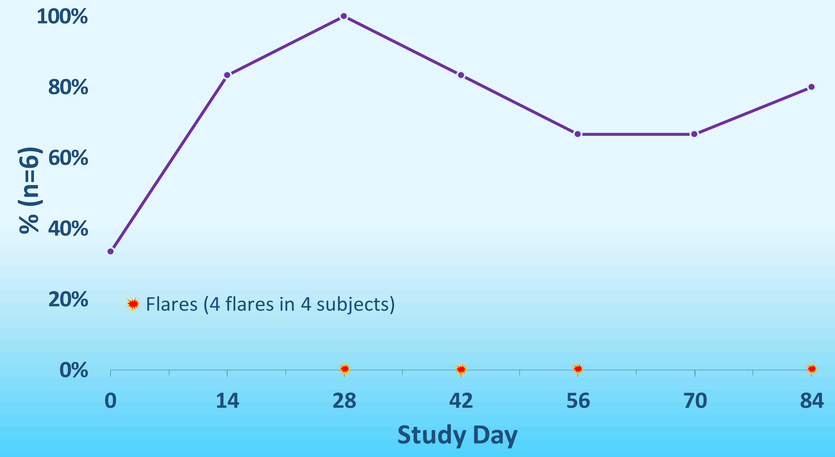
Mean BPDAI Activity Subscore



Cumulative Prednisone Exposure Per Subject



Re-Epithelialization of Prior Lesions



Measure	Baseline (mean)	% Improvement		
		Day 0-84	Day 0-42	Day 42-84
BPDAI Activity Subscore	**67.1**	**81%**	**70%**	**37%**
BPDAI Total Score	69.4	75%	67%	25%
Erosions/Blisters	38.3	83%	81%	11%
Urticaria	26.6	78%	54%	52%
Mucosa	2.1	93%	89%	36%
Pigmentation/Damage	2.3	-108%	-33%	-56%
Pruritus VAS (prior 24h)	5.2	56%	62%	-14%
Pruritus VAS (total)	17.5	51%	66%	-43%
ABQOL	14.6	26%	31%	-16%
Prednisone dose (mg)	**27.8**	**55%**	**43%**	**20%**
Prednisone dose (mg/kg)	0.33	58%	40%	29%
Responder Analysis		**Day 84**	**Day 42**	
>50% improvement in BPDAI		86%	89%	
>70% improvement in BPDAI		71%	44%	
>90% improvement in BPDAI		57%	11%	
Prednisone dose ≤10 mg		58%	40%	

Subject	Adverse Event Description	Intensity	SAE	Relationship to Drug
S01-02	Blurred vision	Mild	No	Unrelated
S02-02	Traumatic laceration right big toe	Mild	No	Unrelated
	Angiography of femoral and lower extremity arteries due to PVD	Mild	Yes	Unrelated
S02-03	Upper respiratory tract infection	Mild	No	Possibly
S04-01	Night sweating	Mild	No	Unlikely
	Edema (bilateral)	Mild	No	Unrelated
S01-06	Muscle cramps	Moderate	No	Probably
	Fall	Mild	No	Possibly

Conclusions

- Bertilimumab appears safe in moderate-to-extensive BP.
- Subjects had rapid and durable improvement in disease activity despite receiving low doses of prednisone and a rapid taper.
- Compared to standard of care, these subjects received 1,700-2,900 mg less prednisone over 12 weeks.
- After the conclusion of bertilimumab dosing, subjects were more likely to flare, BPDAI improvements and prednisone tapering slowed while pruritus and ABQOL worsened, suggesting additional bertilimumab exposure could have had additional benefit.
- Bertilimumab merits further study in a controlled trial of longer duration.