RESULTS FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, EXPLORATORY, MULTICENTER STUDY OF GBR 830 IN ADULT PATIENTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS

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AUTHOR DISCLOSURES & FUNDING

Author Disclosures

- **E. Guttman-Yassky:** Advisory board participant, consultant, and/or investigator for: AbbVie Inc.; Allergan, Plc.; Asana BioSciences, LLC; Celgene; Concert Pharmaceuticals; DBV Technologies; Dermira, Inc.; DS Biopharma; Eli Lilly and Company; Galderma S.A.; Glenmark Pharmaceuticals; Innovaderm Research Inc.; Janssen Biotech, Inc.; Kyowa Hakko Kirin Co., Ltd.; LEO Pharma; Mitsubishi Tanabe Pharma; Novartis International AG; Pfizer Inc.; Regeneron Pharmaceuticals, Inc.; Sanofi S.A.; and Vitae Pharmaceuticals
- **H. Fang, Y. Salhi, F. Grossman, G. Wolff:** Employees of Glenmark Pharmaceuticals Inc., USA
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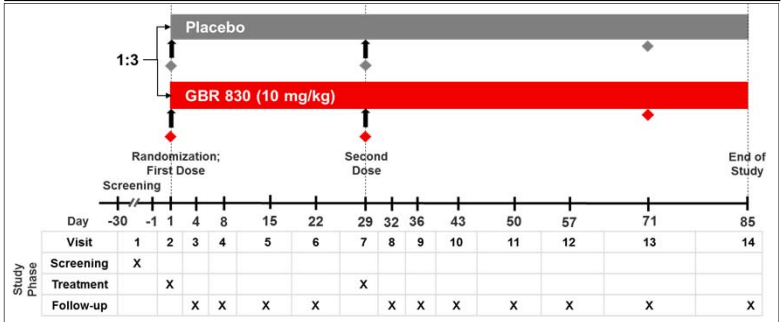
STUDY DESIGN & PATIENT CHARACTERISTICS

Study Design

- This 85 day study was conducted in the USA and Canada
- Patients were randomized in a ratio of 3:1 (GBR 830 and placebo)
- Patients received 2 repeated doses (each 10 mg/kg) administered intravenously on Days 1 and 29 with a follow-up phase of 56 days (**FIGURE 1**)

FIGURE 1. Study Design



Black arrows indicate intravenous dose administration; diamonds indicate skin punch biopsies

Study Population

- **Key Inclusion Criteria**: Male or female patients ≥18 years of age with chronic moderate-to-severe AD for >1 year; BSA affected ≥10%; EASI ≥12; SCORAD ≥20; IGA ≥3 (5-point scale); and history of inadequate response to topical therapies
- **Key Exclusion Criteria**: Live vaccination within 12 weeks; history of serious infection; prior treatment with systemic corticosteroids, topical steroids, phototherapy, and/or biologics

Study Endpoints

- **Co-primary**: TEAEs (frequency, severity); change from baseline in active AD mRNA expression signatures measured from skin biopsies
- **Key Secondary**: EASI 50 and 75 response; IGA score of 0 or 1; percent improvement from baseline in efficacy assessments (EASI, SCORAD, IGA, BSA, pruritus numerical rating scale, DLQI)

Patient Demographics & Baseline Disease Characteristics

- 62 patients were randomized and treated
- 34 patients completed study; the most common reason for early termination or withdrawal was withdrawal of consent (GBR 830, 23%; placebo, 13%)
- Patient demographics and most baseline disease characteristics were generally similar between treatment groups (**TABLE 1**)

TABLE 1. Demographics & Baseline Disease Characteristics

	Placebo (n=16)	GBR 830 (n=46)
Demographics		
Age, mean ± SD, years	40.4 ± 15.1	36.2 ± 13.4
Men, n (%)	11 (69.0)	21 (46.0)
White, n (%)	11 (69.0)	31 (67.0)
Body mass index, mean ± SD, kg/m^2	26.2 ± 3.7	26.1 ± 4.1
Baseline disease characteristics		
Body surface area affected, mean ± SD, m^2	1.9 ± 0.2	1.8 ± 0.2
Age at AD diagnosis, mean ± SD, years	15.3 ± 18.0	9.3 ± 14.8
Concomitant atopic illness, n (%)[a]	11 (69.0)	30 (65.0)
Prior treatment for AD or associated condition, n (%)	15 (94.0)	44 (96.0)
EASI, mean ± SD	23.3 ± 9.4	25.1 ± 12.3
Investigator's global assessment, n (%) Moderate Severe/very severe	 11 (69.0) 5 (31.0)	 26 (57.0) 20 (43.0)
SCORAD, mean ± SD	55.5 ± 10.4	61.8 ± 14.3
DLQI, mean ± SD	9.4 ± 5.7	14.5 ± 6.7
Pruritus numerical rating scale, mean ± SD	4.1 ± 2.6	6.4 ± 2.5

[a] Includes asthma, allergic rhinitis, skin conditions, and other atopic illnesses

AD, atopic dermatitis; BSA, body surface area; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, investigator's global assessment; SCORAD, Scoring of Atopic Dermatitis; TEAE, treatment-emergent adverse event

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PRIMARY & KEY SECONDARY ENDPOINTS

Primary Endpoint: Safety & Tolerability

- Of 62 treated patients, 39 (63.0%) experienced at least 1 TEAE (**TABLE 2**)
  - Equal proportions of patients experienced ≥1 TEAE
- There were few discontinuations due to TEAEs in either treatment group
- Most TEAEs were mild or moderate in intensity

TABLE 2. Summary of TEAEs

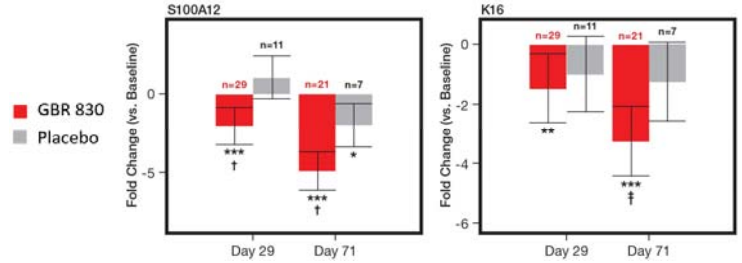
TEAE summary, n (%)	Placebo (n=16)	GBR 830 (n=46)
Any TEAE	10 (62.5)	29 (63.0)
Severe	1 (6.3)[a]	1 (2.2)[b]
Serious	0	1 (2.2)[b]
Leading to discontinuation	1 (6.3)	2 (4.3)
Leading to withdrawal	1 (6.3)	2 (4.3)
Deaths	0	0
TEAEs by MedDRA preferred term, n (%)[c]	**Placebo (n=16)**	**GBR 830 (n=46)**
Headache	4 (25.0)	6 (13.0)
Dermatitis atopic	2 (12.5)	6 (13.0)
Nasopharyngitis	2 (12.5)	4 (8.7)
Upper respiratory tract infection	2 (12.5)	4 (8.7)
Post-procedural infection	0	4 (8.7)
Myalgia	0	3 (6.5)

[a] Supraventricular tachycardia; not related to study treatment
[b] Coronary artery occlusion; not related to study treatment
[c] Reported in ≥5% of patients in the GBR 830 group

Primary Endpoint: Change in mRNA Expression Signatures

- GBR 830-treated patients evidenced significant reductions in mRNA biomarkers of disease activity (quantified via qRT-PCR[1]) compared with baseline and placebo (**FIGURE 2**)

FIGURE 2. Change in S100A12 and K16 mRNA Expression



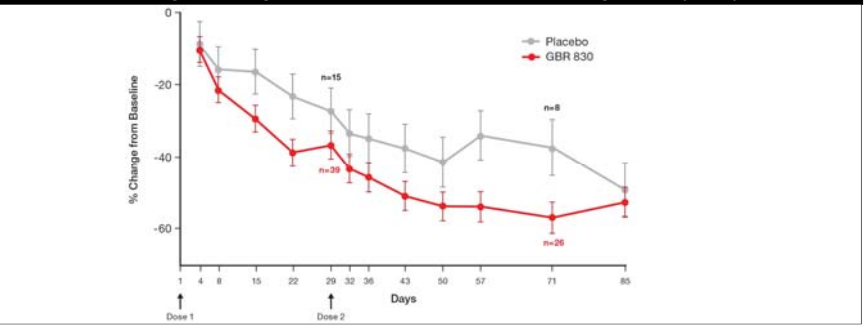
*p<0.05; **p<0.01; ***p<0.001 versus baseline; †p<0.05; ‡p<0.01 versus placebo

Undetected qRT-PCR values (equal to 0) are estimated for each gene as the 20% of the minimum across all samples; data were log-transformed prior to statistical analysis; p-values are from a linear mixed effect model with time, tissue, and treatment as fixed effects and a random intercept for each patient

Key Secondary Endpoint: Change in EASI Score

- Change in EASI score in GBR 830-treated patients separated from placebo as early as Day 15 and was maintained during the course of the study up to Day 71 (**FIGURE 3**)

FIGURE 3. Percentage Change in EASI from Baseline Through Study Day 85



1. Hamilton et al. *J Allergy Clin Immunol.* 2014;134(6):1293-1300

EASI, Eczema Area and Severity Index; MedDRA, Medical Dictionary for Regulatory Activities; qRT-PCR, quantitative real-time polymerase chain reaction; TEAE, treatment-emergent adverse event

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SUMMARY & CONCLUSIONS

Primary Endpoints

- Safety & Tolerability
  - GBR 830 was generally safe and well tolerated
    - Similar incidence of TEAEs between treatment groups
    - Most TEAEs were mild or moderate in intensity
    - The most common TEAE was headache, with no clinically meaningful differences between GBR 830 and placebo (n=6 and n=4, respectively)
- Biomarker Response
  - Clinical improvement was associated with a reduction in mRNA biomarkers for disease activity, including S100A12 and K16, indicating an effect on both the acute and chronic stages of AD

Key Secondary Endpoints

- Although the study was not powered for statistical differences between GBR 830 and placebo, results suggest clinically meaningful improvement of symptoms that was continuous and sustained, with consistency observed between biological and clinical response[1]

1. http://www.glenmarkpharma.com/sites/default/files/Glenmark-Pharmaceuticals-Reports-Positive-Data-in-a-Phase-2a-Study-of-GBR-830-for-the-Treatment-of-Patients-with-Atopic-Dermatitis.pdf

AD, atopic dermatitis; TEAE, treatment-emergent adverse event

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