IGA x BSA: An Alternative to EASI in Assessing Disease Severity and Responsiveness in Pediatric Patients With Moderate-to-Severe Atopic Dermatitis

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BACKGROUND

- The Eczema Area and Severity Index (EASI) is a validated, widely used, multi-item outcome instrument that measures the extent and severity of atopic dermatitis (AD); however, it can be complicated and time consuming to complete, making it impractical in clinical practice[1,2]
- The Investigator's Global Assessment (IGA) is a validated, global physician assessment tool that measures overall disease severity, providing a faster assessment that is easier to understand by both patients and physicians[3]
- IGA is used as a standard by which other scales are validated and is required by the US Food and Drug Administration as a measure in AD clinical studies[4]
- IGA, however, does not account for the extent of AD involvement (measured by body surface area [BSA] affected) that is captured in EASI[5]
- A previous study has shown that the product of validated IGA (vIGA) and BSA has correlated well with EASI and other severity measures in pediatric patients with AD[6]; however, the study was limited to a small US pediatric cohort
- As differences have been reported in the visual presentation of AD based on skin type[7], it is important to assess the validity of outcome measurements across different races

OBJECTIVES

- **To evaluate the IGA × BSA composite as a simple and alternative tool to EASI for assessing disease severity and extent, and responsiveness in pediatric patients with moderate-to-severe AD**
- **To assess the validity of IGA x BSA in patients with diverse ethnicity**

METHODS

Study design

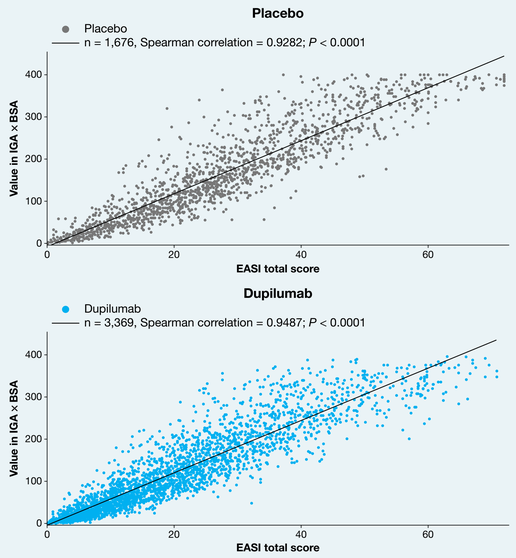
- We report pooled data from phase 3 trials in pediatric patients with moderate-to-severe AD: randomized, placebo-controlled trials LIBERTY AD PEDS (NCT03345914)[8] and LIBERTY AD ADOL (NCT03054428)[9], and LIBERTY AD PED-OLE (NCT02612454), an ongoing open-label extension (OLE) trial
- Patients received subcutaneous dupilumab (every 2 weeks [100/200/300 mg, depending on weight] or every 4 weeks [300 mg]; doses were pooled in this analysis) or placebo; all patients in LIBERTY AD PEDS received concomitant topical corticosteroids

Analysis

- Validation of IGA × BSA
  - Spearman correlations with EASI in the overall population and stratified by race (White, Asian, Black/African American)
  - Spearman correlations with other severity measures: IGA, BSA, EASI, SCORing AD (SCORAD), Peak Pruritus Numerical Rating Scale (PP-NRS), Patient-Oriented Eczema Measure (POEM), and Children's Dermatology Life Quality Index (CDLQI)
- Disease responsiveness (IGA × BSA vs EASI)
  - Overall change from baseline to Week 16

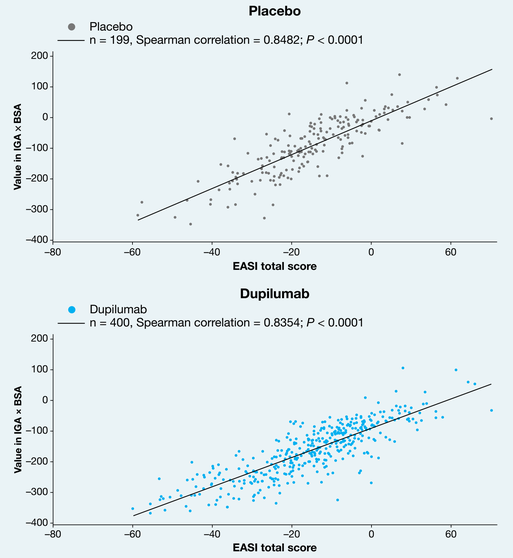
RESULTS

Figure 1. Strong correlation of IGA × BSA with EASI in the placebo and dupilumab treatment groups (overall population).



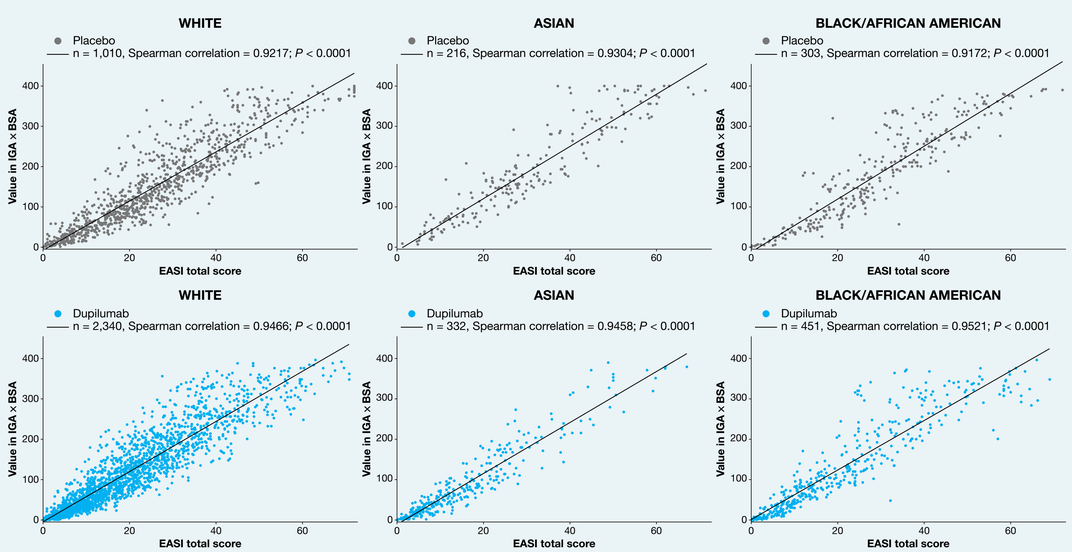
This analysis includes data from RCTs and OLE studies. n, number of assessment points.

Figure 2. Strong correlation of change in IGA × BSA vs change in EASI from baseline to Week 16 (responsiveness) (overall population).



This analysis includes only data from RCTs (PEDS, ADOL). n, number of patients at baseline.

Figure 3. Strong correlation of IGA × BSA with EASI in placebo and dupilumab treatment groups, stratified by race.



This analysis includes data from RCTs and OLE studies. n, number of assessment points.

Figure 4. Correlation of IGA × BSA with other AD disease measures at baseline (overall population).

Treatment		IGA × BSA	IGA	BSA	EASI	SCORAD	POEM	CDLQI	PP-NRS
Placebo (n = 205)	IGA × BSA	1	0.7817	0.9715	0.9282	0.8142	0.3488	0.3982	0.3752
	IGA	0.7817	1	0.6267	0.7614	0.7558	0.3948	0.3526	0.3484
	BSA	0.9715	0.6267	1	0.8906	0.7508	0.3004	0.3738	0.3488
	EASI	0.9282	0.7614	0.8906	1	0.8749	0.3874	0.4016	0.3972
	SCORAD	0.8142	0.7558	0.7508	0.8749	1	0.5305	0.5297	0.5344
	POEM	0.3488	0.3948	0.3004	0.3874	0.5305	1	0.6398	0.5229
	CDLQI	0.3982	0.3526	0.3738	0.4016	0.5297	0.6398	1	0.5248
	PP-NRS	0.3752	0.3484	0.3488	0.3972	0.5344	0.5229	0.5248	1
Dupilumab (n = 775)	IGA × BSA	1	0.8619	0.9779	0.9487	0.8627	0.5424	0.5013	0.4652
	IGA	0.8619	1	0.7446	0.8572	0.8554	0.5858	0.5292	0.4865
	BSA	0.9779	0.7446	1	0.9119	0.8016	0.4876	0.4547	0.4189
	EASI	0.9487	0.8572	0.9119	1	0.9143	0.5682	0.5194	0.4885
	SCORAD	0.8627	0.8554	0.8016	0.9143	1	0.6818	0.64	0.6164
	POEM	0.5424	0.5858	0.4876	0.5682	0.6818	1	0.7211	0.6183
	CDLQI	0.5013	0.5292	0.4547	0.5194	0.64	0.7211	1	0.6239
	PP-NRS	0.4652	0.4865	0.4189	0.4885	0.6164	0.6183	0.6239	1

Key	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1

This analysis includes data from RCTs and OLE studies. Numbers in the heatmap represent Spearman's rank correlation coefficient; all values are significant ($P < 0.0001$). n, number of patients at baseline.

Table. Baseline demographics and disease characteristics.

Race:[b]	Pooled pediatric studies (ages 6–17 years) (N = 980[a])							
	Overall population		White		Asian		Black/African American	
Treatment (n):	Placebo RCT (n = 205)	Dupilumab RCT (n = 407)	Placebo RCT (n = 123)	Dupilumab RCT (n = 283)	Placebo RCT (n = 26)	Dupilumab RCT (n = 40)	Placebo RCT (n = 37)	Dupilumab RCT (n = 55)
Age, mean (SD), years	10.9 (3.5)	10.9 (3.4)	10.6 (3.5)	10.8 (3.3)	11.5 (3.4)	12.5 (3.1)	11.2 (3.5)	9.8 (3.4)
Male, %	55.1	52.8	52.0	51.9	61.5	47.5	56.8	54.5
Duration of AD, mean (SD), years	9.3 (3.7)	9.3 (3.6)	9.0 (3.7)	9.2 (3.5)	9.5 (4.2)	10.7 (4.1)	10.0 (3.5)	8.1 (3.2)
EASI, mean (SD)	37.5 (12.9)	36.6 (12.8)	36.1 (12.5)	36.6 (12.5)	40.7 (13.7)	33.8 (13.3)	39.6 (13.3)	38.3 (14.3)
% BSA affected, mean (SD)	58.6 (22.6)	56.3 (21.5)	55.7 (21.9)	56.3 (21.1)	66.7 (21.8)	50.9 (22.0)	60.4 (24.5)	60.1 (22.7)
IGA score 3, %	19.0	19.2	22.0	18.0	15.4	32.5	10.8	10.9
IGA score 4, %	81.0	80.8	78.0	82.0	84.6	67.5	89.2	89.1
PP-NRS, mean (SD)	7.7 (1.6)	7.7 (1.6)	7.6 (1.6)	7.8 (1.5)	7.7 (1.6)	7.2 (1.6)	7.9 (1.4)	7.6 (1.8)
SCORAD, mean (SD)	72.1 (12.6)	72.4 (12.6)	72.3 (11.8)	73 (12.3)	73.8 (14.3)	68.3 (14.9)	71.3 (13.0)	73.1 (12.2)
POEM, mean (SD)	20.9 (5.5)	21.0 (5.4)	21.2 (5.3)	21.4 (5.2)	20.7 (4.8)	20.2 (5.2)	19.3 (6.0)	19.8 (6.1)
CDLQI, mean (SD)	14.1 (7.1)	14.7 (7.2)	14.5 (6.9)	15.0 (7.1)	14.1 (7.7)	14.5 (7.0)	12.0 (6.9)	13.8 (7.8)

[a]OLE patients were included in a RCT before starting OLE and are therefore not reported separately in this table, but are included in the total N. [b]Not all racial subgroups are included.
RCT, randomized controlled trial; SD, standard deviation.

Safety

- Dupilumab was generally well tolerated, and safety in pediatric patients was consistent with the safety profile observed in adults[8–11]

CONCLUSION

- **This analysis, comprising 980 pediatric patients aged 6–17 years and > 5,000 data points, demonstrates that IGA x BSA is a comparable alternative to EASI in assessing AD disease activity and treatment response in pediatric patients, regardless of race**

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Acknowledgments: Data first presented at the World Congress of Pediatric Dermatology (WCPD), September 22–25, 2021, Edinburgh, UK. Research sponsored by Sanofi and Regeneron Pharmaceuticals, Inc. ClinicalTrials.gov Identifiers: NCT03054428, NCT03345914, NCT02612454. Medical writing/editorial assistance was provided by Anne Slomp, PhD, of Excerpta Medica, and was funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc., according to the Good Publication Practice guideline.

Disclosures: Tan JKL: Regeneron Pharmaceuticals, Inc., Sanofi – investigator/consultant. **Bagel J:** AbbVie, Amgen, Arcutis Biotherapeutics, Boehringer Ingelheim, BMS, Corrona, Dermavant, Dermira, Eli Lilly, Glenmark, Janssen Biotech, Kadmon, LEO Pharma, Lycera, Menlo Therapeutics, Novartis, Ortho Dermatologics, Pfizer, Regeneron Pharmaceuticals, Inc., Sun Pharma, Taro Pharmaceutical Industries, UCB – research funding; AbbVie, Amgen, BMS, Eli Lilly, Janssen Biotech, Novartis, Sun Pharma, UCB – consultant; AbbVie, BMS, Eli Lilly, Janssen Biotech, Novartis – speaker. **Zhang H:** Regeneron Pharmaceuticals, Inc. – employees and shareholders. **Rodríguez Marco A:** Sanofi Genzyme – employee, may hold stock and/or stock options.

Presented at the Skin of Color Update Virtual Learning Experience (SOCU 2021); Virtual meeting; September 10–12, 2021.