A Checklist to Aid in Identifying Patients with Atopic Dermatitis who are Candidates for Systemic Therapy

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BACKGROUND

- Systemic therapy is indicated for patients with moderate-to-severe atopic dermatitis (AD) who do not achieve adequate disease control with topical therapy or have frequent or severe flare-ups.[1]
- The decision to initiate systemic therapy in patients with AD is complex, with no consensus on criteria for initiation.
- To aid clinicians in this decision making, the "**When To Start Systemic Therapy Checklist**", comprising three sections, was developed. Systemic therapy is indicated when ≥1 criterion in each section is fulfilled.[2]

OBJECTIVE

To examine the validity of the "When To Start Systemic Therapy Checklist" by evaluating agreement between the decision to initiate systemic therapy using the Checklist, compared to the reference, patients in the CorEvitas AD Registry who were prescribed systemic therapy.

METHODS

Data source:

- Cross-sectional analysis using deidentified data from the CorEvitas AD Registry, a non-interventional, prospective, longitudinal registry for patients with AD under the care of a dermatologist or advanced practice practitioner.
- Patients enrolled in the CorEvitas AD registry between July 21, 2020 – July 31, 2023 **(N=3,331)**

Study population and analysis

Patients (≥18 years) diagnosed with AD included in this study **(N=1,696)**

→ Patients who initiated systemic therapy at enrollment or within 12 months prior to enrollment **(N=1,488)**

→ Patients with moderate-to-severe AD who did not initiate systemic therapy at enrollment (vIGA-AD™≥3 and EASI≥12[a]) **(N=208)**

[a]Only the patients with moderate-to-severe AD who enrolled before January 1, 2023, were required to have vIGA-AD≥3 and EASI≥12

Analysis

- The CorEvitas registry outcome measures were compared against the checklist criteria[b]; when a criterion did not match a measure, either a proxy measure was selected or that part of the questionnaire was excluded.
- Overall percent agreement with corresponding 95% confidence intervals (CIs) was calculated by comparing CorEvitas systemic therapy initiation status with Checklist criteria.
- All analyses were descriptive in nature.

[b]Data for 'AD flares" in Section A, "inadequate response to appropriate topical therapy" in Section B, and Section C addressing "lack of treatment response" of the "When To Start Systemic Therapy Checklist", could not be evaluated due to the absence of relevant data in the CorEvitas AD registry.

Checklist for the Treatment of Atopic Dermatitis (AD) With Systemic Medication

1. General conditions for systemic treatment

Age ≥6 months

Diagnosis Clinical diagnosis of atopic dermatitis; other conditions considered to explain lack of response (allergic contact dermatitis, scabies, mycosis fungoides, immunodeficiency, etc.)

2. Eligibility criteria for systemic treatment

A Clinical Severity (see scales)

At least one or more of the following criteria is fulfilled: ☐ Yes ☐ No

- vIGA-AD™ or IGA = 3 or 4
- Body Surface Area ≥10%
- Treatment-refractory atopic dermatitis in sensitive/visible areas (e.g. head/neck, hands, feet, genitalia)
- Despite appropriate maintenance topical therapy, persistent AD or multiple AD flares over a 3-month time period (episodes requiring an escalation of treatment, or seeking additional medical advice) (a)

B Subjective Burden (see scales)

At least one or more of the following criteria is fulfilled: ☐ Yes ☐ No

- Patient Global Assessment of Atopic Dermatitis = Moderate or severe
- Itch ≥6
- Sleep ≥6
- Bother = Moderate, very, or extreme
- Patient indicates that AD has a major impact on their quality of life
- Patient indicates that there is an inadequate response to appropriate prescription topical therapy

C Lack of Treatment Response

All other therapeutic approaches are insufficient because at least one or more of the following criteria is fulfilled: ☐ Yes ☐ No

- Inadequate response to appropriate prescription topical therapy for moderate-to-severe AD
- No provider expectation of success with prescription topical therapy alone
- Prescription topical therapy, as needed for control, is not safe or feasible

3. Summary

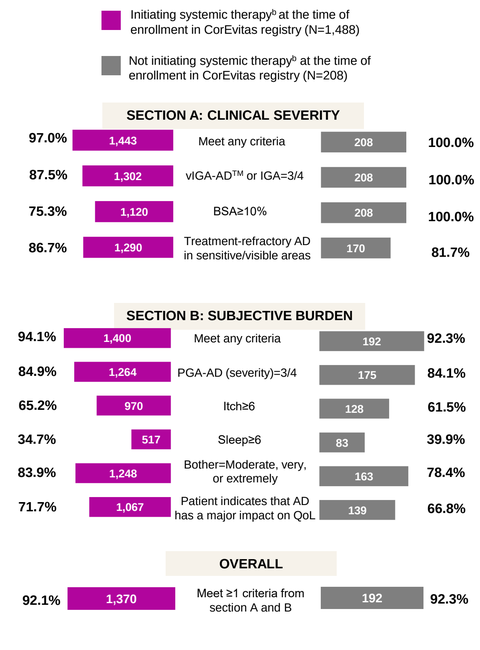
Systemic treatment is indicated because one or more criterion from each of the sections A, B, and C is fulfilled (b) ☐ Yes ☐ No

Treatment to be initiated with: ----------

a. Langan SM, Thomas KS, Williams HC. What is meant by a "flare" in atopic dermatitis? A systematic review and proposal. Arch Dermatol. 2006 Sep;142[9]:1190-6.
b. There may be patients who meet only criterion C that are medically appropriate for systemic therapy. For example, criteria A and B were met at baseline, but topical therapy is not safe or feasible.

KEY RESULTS

Frequency of CorEvitas AD registry data aligning with "When To Start Systemic Therapy Checklist" criteria[a]



Validity measure for the "When to Start Systemic Therapy Checklist" using the CorEvitas AD registry as the reference standard

OVERALL AGREEMENT → **81.7% [CI: 79.8%, 83.5%]**

Percentage of subjects with agreement between ≥1 criteria in the "**Clinical Severity**" or "**Subjective Burden**" sections of the checklist **AND** the CorEvitas systemic therapy initiation status among all subjects in the study

[a]Data for 'AD flares" in Section A, "inadequate response to appropriate topical therapy" in Section B, and Section C addressing "lack of treatment response" of the "When To Start Systemic Therapy Checklist", could not be evaluated due to the absence of relevant data in the CorEvitas AD registry.
[b]Systemic therapy includes eligible biologics (dupilumab, tralokinumab-ldrm, secukinumab, ustekinumab, rizankizumab-rzaa, ixekizumab, omalizumab); eligible small molecules (upadacitinib, abrocitinib); eligible small molecules prescribed off-label for AD (including baricitinib, apremilast, tofacitinib); and eligible non-biologic systemics prescribed off-label for AD (including azathioprine, cyclosporine, methotrexate, mycophenolate mofetil, mycophenolic acid, tacrolimus

CONCLUSIONS

- More than 90% patients taking systemic therapy at enrollment in the CorEvitas registry met at least one criterion from the "Clinical Severity" or "Subjective Burden" sections of the "When To Start Systemic Therapy Checklist", indicating strong alignment between the Checklist sections A and B and the registry.
- Most patients in the non-systemic therapy group met at least one criterion from the Severity and Burden sections of the checklist, potentially indicating therapeutic inertia.
- The decision to initiate systemic therapy is multifactorial. To ensure timely and appropriate access to care, future analyses should examine why some patients with high disease burden and severity remain untreated with systemics.

LIMITATIONS

- The CorEvitas Registry includes only a sample of adults with AD; therefore, may not be representative of all people with AD in the US or Canada.
- The statistical methods in this descriptive study did not correct for baseline differences between the groups.
- Checklist "Lack of Treatment Response" was not assessed given the limitations of this data set; subsequent research is needed to address this section.
- The study did not include a negative control due to registry limitations.

RESULTS

Demographic characteristics of AD patients who met ≥1 criterion of Checklist[a] vs. those who did not meet criteria[a], stratified by CorEvitas comparison groups

		CorEvitas systemic therapy group (N=1,488)		CorEvitas non-systemic therapy group (N=208)	
Characteristic	**Overall N=1,696**	**Did not meet checklist criteria[a] N=690**	**Met checklist criteria[a] N=798**	**Did not meet checklist criteria[a] N=105**	**Met checklist criteria[a] N=103**
Age (mean [SD], years)	50.3 (18.7)	51.7 (18.5)	49.8 (18.8)	48.3 (18.4)	46.9 (19.6)
Males, n (%)	709 (41.8)	292 (42.3)	317 (39.7)	54 (51.4)	46 (44.7)
White, n (%)	1,174 (69.3)	524 (75.9)	523 (65.8)	66 (62.9)	61 (59.2)
Geographic region, n (%)					
USA					
Northeast	219 (12.9)	87 (12.6)	122 (15.3)	*	*
Midwest	611 (36.0)	361 (52.3)	162 (20.3)	53 (50.5)	35 (34.0)
South	546 (32.2)	163 (23.6)	350 (43.9)	14 (13.3)	19 (18.4)
West	202 (11.9)	39 (5.7)	98 (12.3)	32 (30.5)	33 (32.0)
Canada	118 (7.0)	40 (5.8)	66 (8.3)	*	*

[a]Met at least one criterion from Clinical Severity and Subjective Burden sections of the checklist and had a Current Use of Topical Prescription Therapy at Enrollment in the CorEvitas registry
*Data not shown since there were some data points with less than 5 observations.

REFERENCES: [1]Siegels D, et al., Systemic treatments in the management of atopic dermatitis: A systematic review and meta-analysis. 2021 Apr;76(4):1053-1076. [2]Simpson EL, et al., When does atopic dermatitis warrant systemic therapy? Recommendations from an expert panel of the International Eczema Council. J Am Acad Dermatol. 2017 Oct;77(4):623-633.

ABBREVIATIONS: AD, Atopic Dermatitis; HRQoL, Health-related quality of life; vIGA-AD™, Validated Investigator Global Assessment for Atopic Dermatitis; IGA, Investigator Global Assessment; BSA, Body surface area; PGA-AD, Physician's Global Assessment for Atopic Dermatitis; EASI, Eczema Area Severity Index; CI, confidence intervals; US, United States. **DISCLOSURES: JS,** Consultant/advisory board member: AbbVie, AOBiome, Arcutis, Alamar, Amgen, Arena, Asana, Aslan, BioMX, Biosion, Bodewell, Boehringer-Ingelheim, Cara, Castle Biosciences, Celgene, Connect Biopharma, Dermavant, Dermira, Dermtech, Eli Lilly, Galderma, GlaxoSmithKline, Incyte, Kiniksa, Leo Pharma, Menlo, Novartis, Optum, Pfizer, RAPT, Regeneron, Sanofi-Genzyme, Shaperon, Union; speaker for AbbVie, Eli Lilly, Leo Pharma, Pfizer, Regeneron, Sanofi-Genzyme; institution received grants from Galderma, Pfizer. **ES,** personal fees: AbbVie, Advances in Cosmetic Medical Derm Hawaii LLC, Amgen, AOBiome LLC, Arcutis Biotherapeutics, Arena Pharmaceuticals, Aslan Pharma, Bristol Myers Squibb – BMS, CorEvitas, Dermira, Eli Lilly, Evelo Biosciences, ExcerptaMedica, FIDE, Forte Bio RX, Galderma, GlaxoSmithKline, Impetus Healthcare, Incyte, Innovaderm Reche, Janssen, Johnson & Johnson, Kyowa Kirin Pharmaceutical Development, Leo Pharm, Medscape LLC, Merck, MauiDerm, MLG Operating, MJH holding, Pfizer, Physicians World LLC, PRIME, Recludix Pharma, Regeneron, Revolutionizing Atopic Dermatitis Inc, Roivant, Sanofi-Genzyme, Trevi therapeutics, Valeant, Vindico Medical education, WebMD. Grants (or serves as Principal investigator role): AbbVie, Accelecch, Amgen, Arcutis, ASLAN, Castle, CorEvitas, Dermavant, Dermira, Incyte, Lilly, Kymab, Kyowa Kirin, National Jewish Health, Leo, Pfizer, Regeneron, Sanofi, Target, VeriSkin, **EGY,** Employee: Mount Sinai; research funds (grants paid to institution)/consultant for AbbVie, Almirall, Amgen, AnaplysBio, Asana BioSciences, ASLAN Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Connect Biopharma, Eli Lilly and Company, EMD Serono, Evidera, Galderma, Incyte Corporation, Innovaderm Research, Janssen, Kiniksa, Kyowa Kirin, LEO Pharma, Novartis, Pfizer, RAPT Therapeutics, Regeneron, Sanofi, Sato Pharmaceutical, TARGET PharmaSolutions, UCB Pharma, and Ventyx Biosciences. **MA,** Consultant/paid speaker: AbbVie, Almirall, Amgen, Beiersdorf, Biogen, Boehringer Ingelheim, Celgene, Centocor, Eli Lilly and Company, Galderma, GSK, Janssen-Cilag, Leo, Medac, Merck, MSD, Novartis, Pierre-Fabre, Pfizer, Sanofi, Trevi and UCB. **PL,** Research grants and/or funding from AbbVie, AOBiome, and Eczema Foundation; Speaker: AbbVie, Eli Lilly and Company, Galderma, Hyphens Pharma, Incyte Corporation, La Roche-Posay/L'Oréal, MyOR Diagnostics, ParentMD, Pfizer, Pierre Fabre, and Regeneron/Sanofi Genzyme; consultant/advisory boards member: AbbVie, Almirall, Amyris, Arbonne, Arcutis, ASLAN Pharmaceuticals, Bodewell, Boston Skin Science, Bristol Myers Squibb, Burt's Bees, Castle Biosciences, Codex Labs, Concerto Biosciences, Dermavant Sciences, Dermira, Dermveda, Eli Lilly and Company, Galderma, IntraDerm, Janssen, Johnson & Johnson, Kaleido Biosciences, Kimberly-Clark, L'Oréal, LEO Pharma, Lipidor, Menlo Therapeutics, Merck, Micreos, MyOR Diagnostics, Regeneron/Sanofi Genzyme, Sibel Health, SkinFix, Sonica, Theraplex, UCB Pharma, Unilever, Verrica Pharmaceuticals, and Yobee Care; Stocks: LearnSkin/Learn Health, Medable, Micreos, Modernizing Medicine, and Yobee Care; Patent: Theraplex product with royalties paid; board member and scientific advisory committee member: National Eczema Association. **LE,** consultant, speaker, advisory board member or investigator: AbbVie, Acrotech, Amgen, Arcutis, Aslan, Bausch Health, Bristol-Myers Squibb, Castle Biosciences, Dermavant, Eli Lilly, Forte, Galderma, Incyte, Janssen, Johnson & Johnson, LEO Pharma, Medscape, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi-Genzyme, Target RWE and UCB. **AL and YMM:** Employees of CorEvitas, LLC. **CorEvitas LLC,** contracted subscriptions: AbbVie, Amgen, Inc., Arena, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Chugai, Eli Lilly and Company, Genentech, Gilead Sciences, GlaxoSmithKline, Janssen Pharmaceuticals, Inc., LEO Pharma, Novartis, Ortho Dermatologics, Pfizer, Regeneron Pharmaceuticals, Sanofi, Sun Pharmaceutical Industries Ltd., and UCB S.A. **ARA, EP, MJR,** Employees and stockholders: Eli Lilly and Company

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