Impact of Therapeutic Inertia on Patient-Reported Outcomes in Moderate-to-Severe Atopic Dermatitis: A 12-Month Longitudinal Study from the TARGET-DERM AD Registry

Brenda Simpson MD[1], Ayman Grada MD[2], Keith D. Knapp PhD[3], Breda Munoz PhD[3], Julie M. Crawford MD[3], Jonathan I. Silverberg MD PhD MPH[4] on behalf of the TARGET-DERM AD Investigators

[1]El Paso Dermatology, El Paso, Texas, USA; [2] AbbVie Inc. North Chicago, Illinois, USA; [3] Target RWE. Durham, North Carolina, USA; [4] George Washington University School of Medicine and Health Sciences, Washington D.C., USA

TARGET RWE
BETTER EVIDENCE • BETTER HEALTH

Introduction

- Therapeutic inertia is the delay or reluctance in modifying treatment despite treatment goals not being met
- According to the AHEAD treat-to-target recommendation[1], if the agreed treatment targets are not achieved within 3 to 6 months, the treatment response is considered inadequate, and a modification of therapy should be considered.
- Therapeutic inertia in AD leads to prolonged inadequate disease control, negatively affecting patient-reported outcomes such as quality of life and sleep, and maybe excessive reliance on concomitant topical treatment

Objective

- To evaluate the impact of therapeutic inertia on patient-reported outcomes (PROs) in individuals with moderate-to-severe AD undergoing systemic treatment over 3 to 12 months.

Methods

- We identified and compared the proportions of patients not achieving moderate or optimal patient-reported outcome targets on AD patients treated with their first systemic therapy advanced (abrocitinib, dupilumab, tralokinumab, or upadacitinib) or conventional (Methotrexate, cyclosporine, mycophenolate mofetil, azathioprine, systemic corticosteroids, and/or phototherapy).
- Inclusion Criteria
  - Enrolled in TARGET-DERM AD, an observational, longitudinal study of participants with AD across 39 academic and community centers in the United States and Canada.
  - All ages included.
  - Patient treated with their first advanced or conventional systemic therapy
  - Patient had a validated Investigators Global Assessment of AD (vIGA-AD) score of 3 or 4 within 45 days prior to systemic initiation or up to 14 days after
  - Patient had at least one vIGA-AD assessment 3-12 months after systemic therapy initiation
- Exclusion criteria
  - Patient had received advanced or conventional systemic AD therapy prior to the index date

Figure 1. Study Schematic

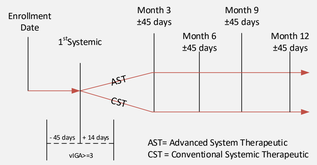

Table 1. Outcome Targets

Outcome	Moderate Target	Optimal Target
Skin	IGA ≤2 and 50% BSA improvement	IGA 0/1 and BSA ≤2%
Itch	WI-NRS ≥4-point improvement (reduction)	0/1
POEM	≥4-point reduction	≤2
PO-SCORAD	≤24	≤10
Sleep disturbance	Sleep-NRS ≥3 point reduction	≤1
Skin pain	Pain-NRS ≥3 point reduction	≤1

- Assessments
  - The Investigators Global Assessment of AD (IGA, range 0–4).
  - Patient-Reported Outcome Measurement Information System (PROMIS) Itch-Severity question evaluating Worst-Itch, (range 0–10).
  - Patient oriented eczema measure (POEM, range 0-28)
  - Patient-Oriented SCORing of Atopic Dermatitis (PO-SCORAD, range 0-103)
  - Numeric Rating Scale (NRS)-sleep and NRS-pain, (range 0-10)
- Analyses
  - Patient characteristics were summarized using descriptive statistics.
  - The frequency and proportion of patients not achieving moderate or optimal outcome targets at 3, 6, 9, and 12 months following systemic initiation.
  - The Kruskal-Wallis and Wilcoxon statistical tests compared the subgroups

Results

Table 2. Patient characteristics at enrollment

Patient Characteristic	N=445
Age (years) at enrollment	
Mean (SD)	30.8 (21.2)
Median (n)	24.0 (445)
Min – Max	0 - 86
Sex, n (%)	
Female	276 (62.0%)
Male	169 (38.0%)
Race-Ethnicity, n (%)	
Hispanic/Latino	88 (19.8%)
NH White	202 (45.4%)
NH Black	55 (12.4%)
NH Asian	63 (14.2%)
NH Other	19 (4.3%)
Missing	18 (4.0%)
IGA	
Mean (SD)	3.3 (0.5)
Median (n)	3.0 (445)
Worst-Itch	
Mean (SD)	7.6 (2.3)
Median (n)	8.0 (243)

Patient Characteristic	N=445
POEM:	
Mean (SD)	15.1 (7.0)
Median (n)	15.0 (264)
PO-SCORAD:	
Mean (SD)	38.5 (17.5)
Median (n)	38.5 (255)
NRS-Pain:	
Mean (SD)	3.3 (2.7)
Median (n)	3.0 (273)
NRS-Sleep:	
Mean (SD)	4.3 (2.8)
Median (n)	4.0 (272)
DLQI:	
Mean (SD)	9.6 (6.2)
Median (n)	9.0 (166)
CDLQI:	10.7 (5.6)
Mean (SD)	10.0 (69)
Median (n)	
PROMIS Itch-Mood and Sleep	
Mild	27 (14.9%)
Moderate	16 (8.8%)
Within normal limits	138 (76.2%)

Figure 2. Patient disposition

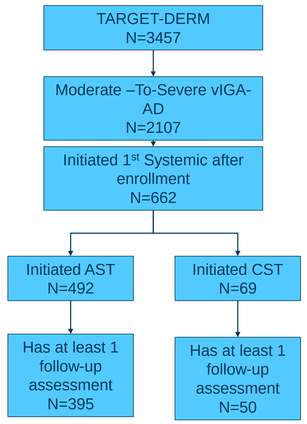

Table 3. The Distribution of Medication Duration

Medications	3 months (N=172)	6 months (N=164)	9 months (N=157)	12 months (N=144)
Any Conventional Systemic Therapy (CST), n (%)	11 (6.4%)	10 (6.1%)	9 (5.7%)	7 (4.9%)
Cyclosporine	2 (1.2%)	1 (0.6%)	1 (0.6%)	0 (0%)
Methotrexate	5 (2.9%)	5 (3%)	5 (3.2%)	4 (2.8%)
Mycophenolate mofetil	1 (0.6%)	1 (0.6%)	0 (0%)	0 (0%)
Prednisolone	1 (0.6%)	1 (0.6%)	1 (0.6%)	1 (0.7%)
Prednisone, unspecified	2 (1.2%)	2 (1.2%)	2 (1.3%)	2 (1.4%)
Any Advanced Systemic Therapy (AST), n (%)	161 (93.6%)	154 (93.9%)	148 (94.3%)	137 (95.1%)
Dupilumab	**145 (84.3%)**	**138 (84.1%)**	**134 (85.4%)**	**128 (88.9%)**
Tralokinumab	13 (7.6%)	13 (7.9%)	12 (7.6%)	8 (5.6%)
Upadacitinib	3 (1.7%)	3 (1.8%)	2 (1.3%)	1 (0.7%)

- Dupilumab was used by more than 84% of AST patients for the whole 12-month follow-up period

Figure 3. The percentage of patients on AST not achieving moderate or optimal targets for patient-reported Itch, POEM, PO-SCORAD, NRS-Sleep, or NRS-Pain targets.

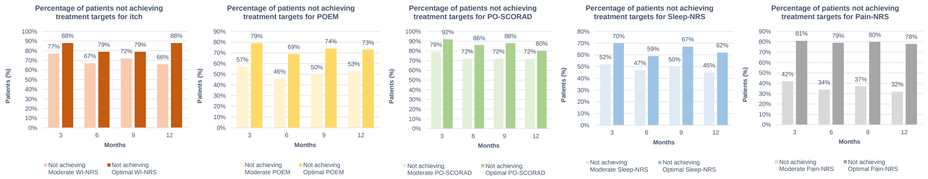

Table 4. Proportion of Patients Not Achieving Moderate Targets

Outcome Measure	3 Months from Initiating systemic Therapy			6 Months from Initiating systemic Therapy			9 Months from Initiating systemic Therapy			12 Months from Initiating systemic Therapy		
	AST	CST	Overall	AST	CST	Overall	AST	CST	Overall	AST	CST	Overall
WI-NRS, n/N	139/180	22 /24	161/204	133 /199	15/20	148/219	67/93	7/11	74/104	65/99	9/12	74/111
%	**77.2%**	**91.7%**	**78.9%**	**66.8%**	**75.0%**	**67.6%**	**72.0%**	**63.6%**	**71.2%**	**65.7%**	**75.0%**	**66.7%**
POEM: Patient-Oriented Eczema Measure, n/N	120/211	15/23	135/234	69/150	8/14	77/164	68/136	4/11	72/147	56/106	5/12	61/118
%	**56.9%**	**65.2%**	**57.7%**	**46.0%**	**57.1%**	**47.0%**	**50.0%**	**36.4%**	**49.0%**	**52.8%**	**41.7%**	**51.7%**
PO-SCORAD: Patient-Oriented Scoring Atopic Dermatitis, n/N	161/203	18/22	179/225	101/140	12/13	113/153	94/130	7/11	101/141	71/99	10/11	81/110
%	**79.3%**	**81.8%**	**79.6%**	**72.1%**	**92.3%**	**73.9%**	**72.3%**	**63.6%**	**71.6%**	**71.7%**	**90.9%**	**73.6%**
DLQI: Dermatology Life Quality Index, n/N	20/21	4/4	24/25	6/6	1/1	7/7	8/9	1/1	9/10	5/5	1/1	6/6
%	**95.2%**	**100.0%**	**96.0%**	**100.0%**	**100.0%**	**100.0%**	**88.9%**	**100.0%**	**90.0%**	**100.0%**	**100.0%**	**100.0%**
CDLQI: Children's Dermatology Life Quality Index, n/N	20/20	1/1	21/21	1/1	N/A	1/1	12/12	N/A	12/12	1/1	N/A	1/1
%	**100.0%**	**100.0%**	**100.0%**	**100.0%**	N/A	**100.0%**	**100.0%**	N/A	**100.0%**	**100.0%**	N/A	**100.0%**
Sleep-NRS, n/N	166/239	24/28	190/267	101/170	12/14	113/184	101/151	10/15	111/166	78/125	10/13	88/138
%	**69.5%**	**85.7%**	**71.2%**	**59.4%**	**85.7%**	**61.4%**	**66.9%**	**66.7%**	**66.9%**	**62.4%**	**76.9%**	**63.8%**
Pain-NRS, n/N	196/241	23/28	219/269	137/173	13/14	150/187	122/153	9/15	131/168	98/126	9/13	107/139
%	**81.3%**	**82.1%**	**81.4%**	**79.2%**	**92.9%**	**80.2%**	**79.7%**	**60.0%**	**78.0%**	**77.8%**	**69.2%**	**77.0%**
PROMIS Itch – Mood and Sleep, n/N	6/157	2/20	8/177	2/116	1/11	3/127	102/102	10/10	112/112	0/78	1/10	1/1
%	**3.8%**	**10.0%**	**4.5%**	**1.7%**	**9.1%**	**2.4%**	**100.0%**	**100.0%**	**100.0%**	**0.0%**	**10.%** **	**1.1%**
PROMIS-Depression, n/N	13/97	2/17	15/114	5/71	1/8	6/79	5/44	0/6	5/50	2/53	1/9	3/62
%	**13.4%**	**11.8%**	**13.2%**	**7.0%**	**12.5%**	**7.6%**	**11.4%**	**0.0%**	**10.0%**	**3.8%**	**11.1%**	**4.8%**
PROMIS-Pediatric Depressive, n/N	4/38	0/5	4/43	18/18	2/2	20/20	2/19	0/3	2/22	1/11	0/2	1/13
%	**10.5%**	**0.0%**	**9.3%**	**100.0%**	**100.0%**	**100.0%**	**10.5%**	**0.0%**	**9.1%**	**9.1%**	**0.0%**	**7.7%**

n=numerator/N=Denominator;**P<0.05

Table 5. Proportion of Patients Not Achieving Optimal Targets

Outcome Measure	3 Months from Initiation Systemic Therapy			6 Months from Initiation Systemic Therapy			9 Months from Initiation Systemic Therapy			12 Months from Initiation Systemic Therapy		
	AST	CST	Overall	AST	CST	Overall	AST	CST	Overall	AST	CST	Overall
WI-NRS, n/N	159/180	19/24	178/204	158/199	18/20	176/219	91/115	12/14	103/129	159/180	19/24	178/204
%	**88.3%**	**79.2%**	**87.3%**	**79.4%**	**90.0%**	**80.4%**	**79.1%**	**85.7%**	**79.8%**	**88.3%**	**79.2%**	**87.3%**
POEM: Patient-Oriented Eczema Measure, n/N	167/211	20/23	187/234	138/199	19/22	157/221	126/170	14/18	140/188	105/144	15/19	120/163
%	**79.1%**	**87.0%**	**79.9%**	**69.3%**	**86.4%**	**71.0%**	**74.1%**	**77.8%**	**74.5%**	**72.9%**	**78.9%**	**73.6%**
PO-SCORAD: Patient-Oriented Scoring Atopic Dermatitis, n/N	187/203	20/22	207/225	161/188	19/21	180209	145/165	14/18	159/183	115/143	15/18	130/161
%	**92.1%**	**90.9%**	**92.0%**	**85.6%**	**90.5%**	**86.1%**	**87.9%**	**77.8%**	**86.9%**	**80.4%**	**83.3%**	**80.7%**
Dermatology Life Quality Index, n/N	12/21	2/4	14/25	77/124	12/15	89/139	8/13	1/1	9/14	59/92	9/14	68/106
%	**57.1%**	**50.0%**	**56.0%**	**62.1%**	**80.0%**	**64.0%**	**61.5%**	**100.0%**	**64.3%**	**64.1%**	**64.3%**	**64.2%**
Children's Dermatology Life Quality Index, n/N	14/20	1/1	15/21	25/40	4/4	29/44	13/15	0/1	13/16	26/35	1/3	27/38
%	**70.0%**	**100.0%**	**71.4%**	**62.5%**	**100.0%**	**65.9%**	**86.7%**	**0.0%**	**81.3%**	**74.3%**	**33.3%**	**71.1%**
NRS-Sleep, n/N	125/239	20/28	145/267	95/202	16/22	111/224	91/184	12/20	103/204	65/145	12/18	77/163
%	**52.3%**	**71.4%**	**54.3%**	**47.0%**	**72.7%***	**49.6%**	**49.5%**	**60.0%**	**50.5%**	**44.8%**	**66.7%**	**47.2%**
NRS-Pain, n/N	100/241	14/28	114/269	69/204	11/22	80/226	68/185	10/20	78/205	47/146	6/18	53/164
%	**41.5%**	**50.0%**	**42.4%**	**33.8%**	**50.0%**	**35.4%**	**36.8%**	**50.0%**	**38.0%**	**32.2%**	**33.3%**	**32.3%**
PROMIS Itch – Mood and Sleep, n/N	9/157	5/20	14/177	5/137	2/18	7/155	4/126	2/15	6/141	90/93	1/15	4/108
%	**5.7%**	**5 25.%**	**7.9%**	**3.6%**	**11.1%**	**4.5%**	**3.2%**	**13.3%**	**4.3%**	**3.2%**	**6.7%**	**3.7%**
PROMIS-Depression, n/N	22/97	7/17	29/114	27/129	5/15	32/144	11/60	2/9	13/69	14/92	5/13	19/105
%	**22.7%**	**41.2%**	**25.4%**	**20.9%**	**33.3%**	**22.2%**	**18.3%**	**22.2%**	**18.8%**	**15.2%**	**38.5%**	**18.1%**
PROMIS-Pediatric Depressive , n/N	6/38	0/5	6/43	9/45	1/4	10/49	4/25	0/3	4/28	6/35	0/3	6/38
%	15.8%	0.0%	14.0%	20.0%	25.0%	20.4%	16.0%	0.0%	14.3%	17.1%	0.0%	15.8%

- At 6 months, significant proportions of AST-treated patients failed to reach moderate and optimal targets for itch (67% and 79%, respectively), POEM (46% and 69%), and Sleep-NRS (59% and 47%).
- By 12 months, these figures were similar, with 66% and 88% failing to meet itch targets, 53% and 73% failing to meet POEM targets, and 62% and 45% failing to meet NRS-sleep targets, respectively.
- A similar pattern was observed for other PROs. CST-treated patients exhibited similar trends.

Conclusion

- The study reveals a significant portion of moderate-to-severe AD patients fail to achieve adequate itch and disease severity targets with systemic therapies over 12 months, indicating a substantial presence of therapeutic inertia
- As PROs are of increasing importance, these findings suggest a need for more proactive management strategies in AD treatment

References:

1. Silverberg JI, Gooderham M, Katoh N, Aoki V, Pink AE, Binamer Y, Rademaker M, Fomina D, Gutermuth J, Ahn J, Valenzuela F. Combining treat-to-target principles and shared decision-making: International expert consensus-based recommendations with a novel concept for minimal disease activity criteria in atopic dermatitis. Journal of the European Academy of Dermatology and Venereology. 2024 Jul 11.

Acknowledgements and Disclosures: Target RWE communities are collaborations among academic & community investigators, the pharmaceutical industry, and patient community advocates. Target RWE communities are sponsored by TARGET PharmaSolutions Inc (d.b.a., Target RWE). The authors would like to thank all the investigators, participants, and research staff associated with TARGET-DERM. ClinicalTrials.gov Identifier: NCT03661866.

BS has no financial disclosures. **AG** is an employee of AbbVie Inc. **KK** an employee of Target RWE and holds stock options; **BM** an employee of Target RWE may hold stock options; **JC** is an employee of Target RWE and may hold stock options; **JIS** received honoraria as a consultant and/or advisory board member for Abbvie, Alyx, Arbonne, Arena, Asana, BioMX, Bluefin, Bodewell, Boehringer-Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly, Galderma, GlaxoSmithKline, Incyte, Kiniksa, Leo Pharma, Luna, Menlo, Novartis, Pfizer, RAPT, Regeneron, Sanofi-Genzyme; speaker for Abbvie, Eli Lilly, Leo Pharma, Pfizer, Regeneron, Sanofi-Genzyme; institution received grants from Galderma, Pfizer.