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

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Introduction

- Therapeutic inertia is the delay or reluctance in modifying treatment when goals are unmet
- Treatment response is considered inadequate if the agreed targets are not met within 3–6 months, treatment modification should then be considered
- Therapeutic inertia is a significant challenge in managing atopic dermatitis (AD) and can lead to suboptimal control of the disease, affecting patient outcomes.

Objective

- To evaluate the effect 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/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) of 3 or 4 less than 45 days prior to systemic initiation or up to 14 days after
  - Patient had at least one vIGA-AD assessment 3-12 months after initiation
- Exclusion criteria
  - Patient was treated with advanced or conventional systemic AD therapy prior to index date

Figure 1. Study Schematic

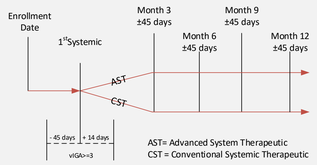


Table 1. Outcome Targets

Outcome measure	Moderate target (Mod)	Optimal target (Opt)
vIGA-AD	IGA ≤2	IGA 0/1
Worst-Itch	≥4-point improvement (reduction)	≤1
POEM	≥4-point reduction	≤2
PO-SCORAD	≤24	≤10
NRS-sleep	≥3 point reduction	≤1
NRS-pain	≥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)	Patient characteristic	(N=445)
Age (years) at enrollment		POEM:	
Mean (SD)	30.8 (21.2)	Mean (SD)	15.1 (7.0)
Median (n)	24.0 (445)	Median (n)	15.0 (264)
Min – Max	0 - 86	PO-SCORAD:	
Sex, n (%)		Mean (SD)	38.5 (17.5)
Female	276 (62.0%)	Median (n)	38.5 (255)
Male	169 (38.0%)	NRS-Pain:	
Race-Ethnicity, n (%)		Mean (SD)	3.3 (2.7)
Hispanic/Latino	88 (19.8%)	Median (n)	3.0 (273)
NH White	202 (45.4%)	NRS-Sleep:	
NH Black	55 (12.4%)	Mean (SD)	4.3 (2.8)
NH Asian	63 (14.2%)	Median (n)	4.0 (272)
NH Other	19 (4.3%)	DLQI:	
Missing	18 (4.0%)	Mean (SD)	9.6 (6.2)
IGA		Median (n)	9.0 (166)
Mean (SD)	3.3 (0.5)	CDLQI:	
Median (n)	3.0 (445)	Mean (SD)	10.7 (5.6)
Worst-Itch		Median (n)	10.0 (69)
Mean (SD)	7.6 (2.3)	PROMIS Itch-Mood and Sleep	
Median (n)	8.0 (243)	Mild	27 (14.9%)
		Moderate	16 (8.8%)
		Within normal limits	138 (76.2%)

Figure 2. Patient disposition

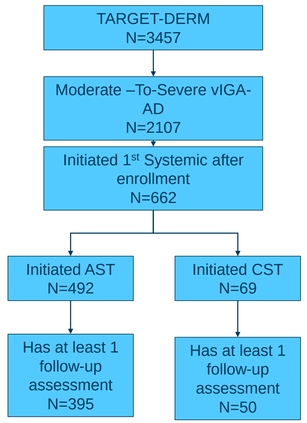
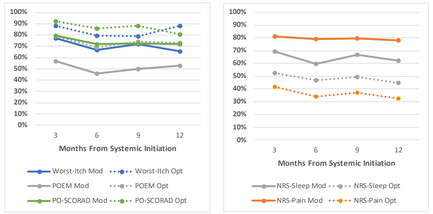


Table 3. The Distribution of Medication Duration

Medications	3 months (N=172)	6 months (N=164)	9 months (N=157)	12 months (N=144)
Any Conventional Systemic, 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, 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%)

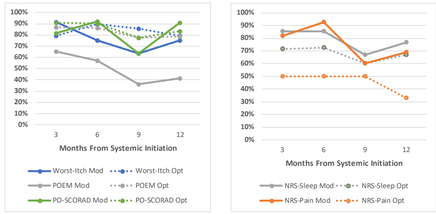
- Dupilumab was used by more than 84% of AST patients for the whole 12-month follow-up period

Figure 3. Percentage of patients on AST not achieving moderate or optimal targets for patient-reported outcomes



- Over half of AST patients did not achieve moderate target for Worst-Itch or disease severity (POEM/PO-SCORAD)

Figure 4. Percentage of patients on CST not achieving moderate or optimal targets for patient-reported outcomes



- Over 60% of CST patients did not even achieve moderate target for Worst-Itch

Table 4. Proportion of Patients Not Achieving Moderate Target

Outcome Metric	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
Worst Itch, n/N	139/180	22 /24	161/204	133 /199	15/20	148/219	67/93	7/11	74/104	65/99	12-Sep	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		1/1	12/12		12/12	1/1		1/1
%	100.0%	100.0%	100.0%	100.0%		100.0%	100.0%		100.0%	100.0%		100.0%
NRS-Sleep, 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%
NRS-Pain, 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

- The smallest proportion of AST patients with an inadequate response for both Worst-Itch was at 12 months on treatment (66%). The smallest proportion of CST patients was 64% at 9 months

Table 5. Proportion of Patients Not Achieving Optimal Target

Outcome Metric	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
Worst Itch, 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%

- The largest percentage of AST treated patients not achieving optimal PRO Itch targets was 88% at both 3 and 12 months of treatment.
- The largest proportion of AST treated patients not achieving optimal PRO Disease severity targets was 92% at 3 months.

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, J.I., et al., *327 Optimizing the management of atopic dermatitis with a new minimal disease activity concept and criteria and consensus-based recommendations for systemic therapy.* British Journal of Dermatology, 2023. **188**(Supplement_2).

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