# Persistent Inadequate Disease Control and Therapeutic Inertia in Moderate-to-Severe Atopic Dermatitis: A 12-month Longitudinal Analysis of Real-world Outcomes from TARGET-DERM registry

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## Introduction

- Therapeutic inertia is the delay or failure to escalate treatment in patients who are not achieving adequate disease control
- Treatment response is considered inadequate if the agreed targets are not met within 3–6 months, treatment modification should then be considered
- Failure to adjust treatment delays achieving disease control in moderate-to-severe atopic dermatitis (AD)
- The extent of treatment success in real-world clinical practice remains underexplored

## Objective

- To evaluate the occurrence therapeutic inertia (assessed as non-escalation of therapy despite limited disease control) and the proportion of patients with moderate-to-severe AD who continue to show an inadequate response after receiving systemic therapies for a duration ranging from 3 to 12 months

## Methods

- We identified and compared the proportions of patients not achieving moderate or optimal clinician-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 first systemic therapy either advanced or conventional
  - 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**

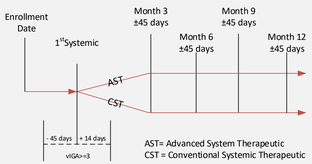



**Table 1. Outcome Targets**

| Outcome measure | Moderate target | Optimal target |
|---|---|---|
| IGA and BSA | IGA ≤2 and 50% BSA improvement | IGA 0/1 and BSA ≤2% |
| IGA | IGA ≤2 | IGA 0/1 |
| BSA | 50% BSA improvement | BSA ≤2% |
| Worst-Itch | ≥4-point improvement (reduction) | ≤1 |

- Assessments
  - The Investigators Global Assessment of AD (IGA, range 0–4)
  - Body surface area (BSA, range 0-100%) affected by AD
  - Patient-Reported Outcome Measurement Information System (PROMIS) Itch-Severity question evaluating Worst-Itch, (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 | 30.8 (21.2) | IGA | |
| Mean (SD) | 24.0 (445) | Mean (SD) | 3.3 (0.5) |
| Median (n) | 0 - 86 | Median (n) | 3.0 (445) |
| Min – Max | | BSA | |
| Sex, n (%) | | Mean (SD) | 26.1 (22.8) |
| Female | 276 (62.0%) | Median (n) | 18.0 (445) |
| Male | 169 (38.0%) | BSA Category, n (%) | |
| Race-Ethnicity, n (%) | | Mild, >0% to <16% | 212 (47.6%) |
| Hispanic/Latino | 88 (19.8%) | Moderate, 16% - 40% | 148 (33.3%) |
| NH White | 202 (45.4%) | Severe, >40% | 85 (19.1%) |
| NH Black | 55 (12.4%) | Worst-Itch | |
| NH Asian | 63 (14.2%) | Mean (SD) | 7.6 (2.3) |
| NH Other | 19 (4.3%) | Median (n) | 8.0 (243) |
| Missing | 18 (4.0%) | | |

SD=standard deviation; NH=Non-Hispanic; vIGA-AD validated Investigator's Global Assessment of Atopic Dermatitis; BSA=Body Surface Area

**Figure 2. Patient Disposition**

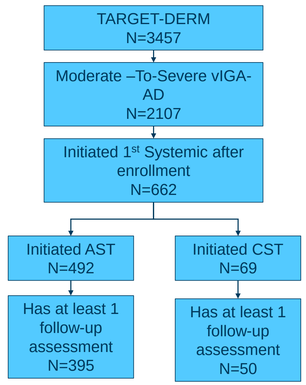
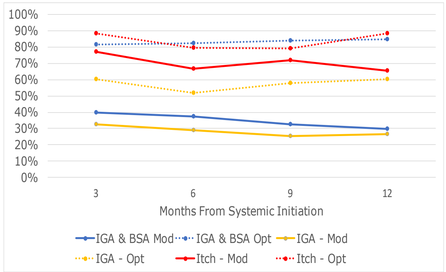



**Table 3. Medication Utilization at Initiation**

| Medications | 3 months (N=419) | 6 months (N=394) | 9 months (N=371) | 12 months (N=342) |
|---|---|---|---|---|
| Any Conventional Systemic, n (%) | 35 (8.4%) | 31 (7.9%) | 29 (7.8%) | 26 (7.6%) |
| Cyclosporine | 10 (2.4%) | 8 (2%) | 8 (2.2%) | 7 (2%) |
| Methotrexate | 13 (3.1%) | 12 (3%) | 11 (3%) | 10 (2.9%) |
| Mycophenolate mofetil | 2 (0.5%) | 2 (0.5%) | 1 (0.3%) | 1 (0.3%) |
| Prednisolone | 2 (0.5%) | 2 (0.5%) | 2 (0.5%) | 2 (0.6%) |
| Prednisone, unspecified | 8 (1.9%) | 7 (1.8%) | 7 (1.9%) | 6 (1.8%) |
| Any Advanced Systemic, n (%) | 384 (91.6%) | 363 (92.1%) | 342 (92.2%) | 316 (92.4%) |
| Abrocitinib | 3 (0.7%) | 3 (0.8%) | 3 (0.8%) | 3 (0.9%) |
| Dupilumab | 344 (82.1%) | 327 (83%) | 312 (84.1%) | 296 (86.5%) |
| Tralokinumab | 24 (5.7%) | 20 (5.1%) | 17 (4.6%) | 11 (3.2%) |
| Upadacitinib | 13 (3.1%) | 13 (3.3%) | 10 (2.7%) | 6 (1.8%) |

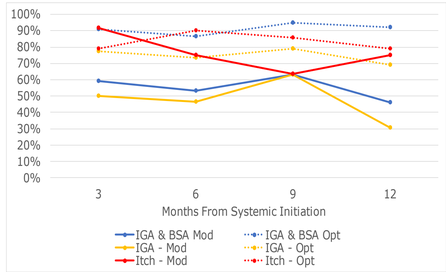
- Among systemic treatments Dupilumab was the most common AST, greater than 82% through the 12-month follow-up
- 145 of 395 (36.7%) AST patients had concomitant topical corticosteroids or calcineurin inhibitors

**Figure 3. Percentage of AST Patients Not Achieving With Moderate Targets**




Mod=Moderate; Opt=Optimal

**Figure 4. Percentage of CST Patients Not Achieving Optimal Targets**




Mod=Moderate; Opt=Optimal

**Table 4. Proportion of Patients Demonstrating Inadequate Response by Systemic Treatment Subgroup**

| Outcome Metric | 3 Months AST | 3 Months CST | 3 Months Overall | 6 Months AST | 6 Months CST | 6 Months Overall | 9 Months AST | 9 Months CST | 9 Months Overall | 12 Months AST | 12 Months CST | 12 Months Overall |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| IGA-AD and BSA n/N | 78/196 | 13/22 | 91/218 | 44/118 | 8/15 | 52/133 | 35/107 | 12/19 | 47/126 | 27/91 | 6/13 | 33/104 |
| % | **39.8%** | **59.1%** | **41.7%** | **37.3%** | **53.3%** | **39.1%** | **32.7%** | **63.2%*** | **37.3%** | **29.7%** | **46.2%** | **31.7%** |
| IGA-AD n/N | 64/196 | 11/22 | 75/218 | 34/118 | 7/15 | 41/133 | 27/107 | 12/19 | 39/126 | 24/91 | 4/13 | 28/104 |
| % | **32.7%** | **50.0%** | **34.4%** | **28.8%** | **46.7%** | **30.8%** | **25.2%** | **63.2%**** | **31.0%** | **26.4%** | **30.8%** | **26.9%** |
| Worst Itch n/N | 139/180 | 22/24 | 161/204 | 133/199 | 20/15 | 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%** |

*P<0.05; **P<0.01; n/N=numerator/denominator

- At 6 months, 37% and ~ 67% of AST-treated patients had inadequate responses in terms of skin clearance and itch outcomes, respectively.
- At 12 months, these figures were approximately 30% and 66%, respectively.
- CST-treated patients showed a similar trend.

**Table 5. Proportion of Patients Not Achieving Optimal Target by Systemic Treatment Subgroup**

| Outcome Metric | 3 Months AST | 3 Months CST | 3 Months Overall | 6 Months AST | 6 Months CST | 6 Months Overall | 9 Months AST | 9 Months CST | 9 Months Overall | 12 Months AST | 12 Months CST | 12 Months Overall |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| IGA-AD and BSA n/N | 160/196 | 20/22 | 180/218 | 97/118 | 13/15 | 110/133 | 90/107 | 18/19 | 108/126 | 77/91 | 12/13 | 89/104 |
| % | **81.6%** | **90.9%** | **82.6%** | **82.2%** | **86.7%** | **82.7%** | **84.1%** | **94.7%** | **85.7%** | **84.6%** | **92.3%** | **85.6%** |
| IGA-AD n/N | 118/196 | 17/22 | 135/218 | 61/118 | 11/15 | 72/133 | 62/107 | 15/19 | 77/126 | 55/91 | 9/13 | 64/104 |
| % | **60.2%** | **77.3%** | **61.9%** | **51.7%** | **73.3%** | **54.1%** | **57.9%** | **78.9%** | **61.1%** | **60.4%** | **69.2%** | **61.5%** |
| 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%** |

n/N=numerator/denominator

- At 6 months, 82% and 79% of AST-treated patients did not achieve optimal responses in terms of skin clearance and itch outcomes, respectively.
- At 12 months, these figures were approximately 85% and 88%, respectively.
- CST-treated patients showed a similar trend.

## Sensitivity Analyses

- For the subgroup of 198 patients starting an AST on or after September 1st 2021, when two additional AST options were available, similar percentages of patients achieved moderate clinician-reported outcome targets as for those in the overall cohort

## Conclusion

- The study reveals a significant portion of moderate-to-severe AD patients fail to achieve adequate disease control with systemic therapies over 12 months, indicating a substantial presence of therapeutic inertia.
- These findings suggest a need for alternative therapies and 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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