Characterization of Non-Responders to IL-17 Inhibitors in Moderate-to-Severe Psoriasis Patients Enrolled in the Corrona Psoriasis Registry

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Background

- Psoriasis (PsO) is a chronic, immune-mediated disease with key clinical symptoms including skin itching and pain.[1] The impact of PsO is not limited to its cutaneous manifestations, but rather affects quality of life and is associated with several other comorbidities [2]
- IL-17 inhibitors approved by the FDA for PsO have been associated with rapid improvement in health-related quality of life and itch, work productivity, and both nail and scalp PsO [3-6]
- Studies of real-world use of IL-17 inhibitors in patients with PsO are emerging but there is a lack of understanding which patients may or may not respond to IL-17 inhibitors [7-9]

Objective

- To compare characteristics at drug initiation between those who did and did not respond to IL-17 inhibitor treatment at 6- and 12-months follow-up; and among the non-responders, and describe reasons for discontinuation

Methods

Data Source

- Data were derived from the Corrona Psoriasis Registry, launched in April 2015, an independent, prospective observational cohort of patients, aged ≥18 years, with PsO recruited from more than 212 practice sites across 44 states/provinces in the Unites States and Canada
- As of June 2019, data on 7,926 patients with PsO have been collected. Corrona's database includes information about 20,893 patient visits and 7,730 patient-years of follow-up observation time
- The mean duration of patient follow-up was 1.5 years (median, 1.2 years)
- A total of 448 prescribing dermatologists contributed to this data set

The Study Population

- Patients in the current analysis included those who:
  - Enrolled in the Corrona Psoriasis Registry from April 2015 to June 2019
  - Initiated (defined as first-ever use) IL-17 inhibitor treatment at or after enrollment
  - Have moderate-to-severe [Body Surface Area (BSA) ≥3%] PsO at IL-17 inhibitor initiation
  - Have a baseline, 6- and 12-month visit data available
- Based on information from 6- and 12-month visits, patients were defined as:
  - **Responders**: achieved mild disease severity BSA<3% or 75% improvement in BSA
  - **Non-responders**: failed to achieve BSA<3% or 75% improvement in BSA or discontinued/switched the index IL-17 inhibitor to another IL-17 inhibitor/other biologic

Methods

Variables of Interest at IL-17 Inhibitor Initiation

- Demographics/socioeconomic characteristics, lifestyle, and history of comorbidities
- Disease characteristics [PsO morphology, PsO duration, psoriatic arthritis (PsA), psoriatic arthritis duration, Psoriasis Epidemiology Screening Tool (PEST)]
- Treatment history: concomitant PsO therapy, biologic and non-biologic systemic experience including number of prior therapies (0, 1, 2, ≥3), and frequency of specific non-IL-17 inhibitor biologic usage prior to IL-17 inhibitor
- Disease activity measures [Body Surface Area (BSA), Psoriasis Area Severity Index (PASI) Investigator's Global Assessment (IGA)]
- Patient-reported outcomes [Dermatology Life Quality Index (DLQI), Work Productivity and Activity Impairment (WPAI), EuroQol EQ-5D-3L,itch, pain, fatigue, and patient global assessment (VAS 0-100 Scale)]
- Among non-responders, reasons for discontinuation of IL-17 inhibitor at follow-up (safety, efficacy, other) ***see footnote Figure 2

Statistical Analysis

- T-tests and chi-squared/Fisher's exact tests were used to compare means and frequencies, respectively, of baseline characteristics between responders and non-responders

Key Results

- Among the 533 patients who initiated IL-17 inhibitors and met study criteria, baseline mean age was 50 years, 47% were female, 77% were white, 53% were obese (BMI>30), 27% had hypertension, and 19% had hyperlipidemia
- The average PsO duration was 16.7 years, and 48% had PsA (Table 1)

Table 1. Patient demographics and clinical characteristics at index visit for patients who initiated an IL-17 inhibitor and had a 6-month follow-up visit.

	N = 533
Age in years, mean (SD)	50.3 (13.5)
Gender-female, n(%)	246 (46.6)
Race-White, n (%)	408 (77.3)
BMI > 30 (obese), n (%)	285 (53.8)
History of hypertension	145 (27.2)
History of hyperlipidemia	103 (19.3)
PsO morphology history, Plaque, n (%)	433 (81.2)
PsO duration (yrs), mean (SD)	16.7 (13.8)
Psoriatic arthritis (PsA)*, n (%)	253 (48.3)
BSA (% involvement), mean (SD)	16.9 (16.2)
PASI>10, n (%)	200 (37.5)

* Anyone reporting PsA, not rheumatologist confirmed PsA

Key Results

- Compared to responders (n=308), non-responders (n=225) were more likely to be current (19% vs 12%) or former smokers (40% vs 34%) and have a lower PASI score (8.9 vs 10.8) and PASI>10 (30% vs 43%), and less likely to have a history of diabetes mellitus (24% vs 14%)
- Non-responders were also more likely to have previously received two (25% vs 20%) or ≥3 (33% vs 18%) biologics (p<0.001)
- Baseline patient-reported outcome measures (DLQI, WPAI, EQ-5D VAS, itch, fatigue, pain, and problems sleeping) were not statistically significantly different between responders and non-responders (Table 2)

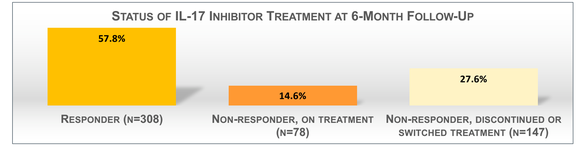
Table 2. Patient demographics and clinical characteristics at index visit for IL-17 inhibitor initiators who were responders and non-responders at 6-month follow-up visit.

	Responder	Non-responder	P-value[¤]
N	308	225	
Smoking history, n (%)			
Never smoked	125 (54.3)	56 (41.8)	**0.044**
Former smoker	78 (33.9)	53 (39.6)	
Current smoker	27 (11.7)	25 (18.7)	
BMI (kg/m^2), n (%)			
BMI < 25 (underweight/normal)	55 (17.9)	40 (17.9)	0.581
BMI 25-30 (overweight)	92 (30.0)	58 (26.0)	
BMI > 30 (obese)	160 (52.1)	125 (56.1)	
History of hypertension	118 (38.3)	98 (43.6)	0.259
History of hyperlipidemia	92 (29.9)	63 (28.0)	0.709
History of diabetes mellitus n (%)	43 (14.0)	53 (23.6)	**0.006**
History of anxiety	75 (24.4)	47 (20.9)	0.404
PsO morphology history, plaque, n (%)	302 (98.1)	223 (99.1)	0.477
PsO duration (yrs), mean (SD)	17.4 (14.1)	15.7 (13.3)	0.167
Psoriatic arthritis (PsA)*, n (%)	144 (47.4)	109 (49.5)	0.686
BSA (% involvement), mean (SD)	17.5 (16.6)	16.1 (15.6)	0.318
PASI (score: 0-72), mean (SD)	10.8 (8.8)	8.9 (7.3)	**0.007**
PASI>10, n (%)	132 (42.9)	68 (30.2)	**0.004**
Biologic-experienced, n (%)			**<0.001**
1 previous biologic agent received, n (%)	93 (30.2)	50 (22.2)	
2 previous biologic agents received, n (%)	60 (19.5)	56 (24.9)	
3+ previous biologic agents received, n (%)	55 (17.9)	74 (32.9)	
Reasons for starting IL-17 inhibitor, n (%)	N=302	N=222	0.057
Active disease, n (%)	257 (85.1)	182 (82.0)	
Patient preference, n (%)	24 (7.9)	12 (5.4)	
Other reasons, n (%)	21 (7.0)	28 (12.6)	
Patient overall itch/pruritis (VAS range 0-100), mean(SD)	55.0 (31.8)	56.7 (32.6)	0.540
Patient overall fatigue (VAS range 0-100), mean (SD)	39.6 (30.4)	41.2 (30.6)	0.533
Patient overall pain (VAS range 0-100), mean (SD)	38.2 (32.5)	38.7 (32.3)	0.869
Patient global assessment continuous, mean (SD)	53.0 (29.1)	50.7 (27.6)	0.355
DLQI (Score: 0-30), mean (SD)	8.6 (6.3)	8.8 (5.9)	0.692
Patient health state today (EQ-5D VAS range 0-100), mean (SD)	69.3 (22.2)	68.7 (21.8)	0.769
WAPI			
Percent** of work hours missed due to PsO, mean (SD)	4.4 (13.7)	4.9 (16.9)	0.802
Percent** impairment while working, mean (SD)	18.3 (25.8)	18.9 (24.6)	0.809
Overall percent** of work hours affected by PsO, mean (SD)	20.2 (27.4)	20.3 (25.6)	0.957
Percent of daily activities impaired by PsO, mean (SD)	25.7 (29.9)	26.4 (28.9)	0.779
Problems with sleeping, n (%)	58 (18.8)	46 (20.4)	0.724

*Anyone reporting PsA, not rheumatologist confirmed PsA; **Only among those who are currently employed, responders (n=104) and non-responders (n=116); ¤ T-tests and chi-squared/Fisher's exact tests

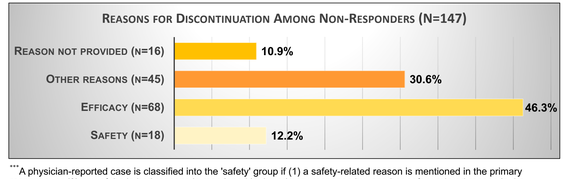
Key Results

Figure 1. Status of IL-17 inhibitor treatment at 6-month follow-up among responders and non-responders.



- Among the 147 non-responders who discontinued or switched, 18 (12%), 68 (46%), and 45 (31%) did so due to safety, efficacy, and other reasons, respectively; 16 (11%) did not provide a reason (Figure 2)

Figure 2. Reasons for discontinuation among non-responders who discontinued or switched IL-17 inhibitor treatment at 6-month follow-up.



***A physician-reported case is classified into the 'safety' group if (1) a safety-related reason is mentioned in the primary response, or (2) any of the 'other' reasons is mentioned in the primary response but another safety-related reason in the secondary response. The same definition applies to the efficacy group. A case is classified as "Reason not Provided" if no reason is provided for the first and second responses. Safety-related reasons can be minor or serious. Efficacy-related reasons include inadequate/failure to maintain initial response. Other reasons include temporary interruption, patient preference, copay/patient cost, denied by insurance, patient doing well, frequency of administration, active disease, alternative mechanism, and other.

- IL-17 inhibitor treatment and reasons for discontinuation findings were similar at the 12-month follow-up visit

Conclusion

- In these unadjusted analyses of real-world patients with PsO initiating IL-17 inhibitors, baseline characteristics were largely similar between responders and non-responders, though non-responders were more likely to be current or former smokers, have a history of diabetes mellitus, and to have previously received two or three biologics.

References

1. *Nat Rev Dis Primers.* 2016 Nov 24;2; *Cutis.* 2017 Feb;99(2):123-127; 3. *J Eur Acad Dermatol Venereol.* 2017;31:1483-1490; 4. *JAMA Dermatol.* 2016 Jun 1;152(6):661-9; 5. *J Eur Acad Dermatol Venereol.* 2017 Mar;31(3):447-482; 6. *J Dermatolog Treat.* 2017 Jun;28(4):282-287; 7.*Br J Dermatol* 2018;178:509-19; 8. *J Eur Acad Dermatol Venereol* 2018;32:411-9; 9. *Dermatolog Treat* 2018 May 24 [Epub ahead of print].

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