

Comorbid obesity and history of diabetes are independently associated with poorer treatment response to biologics at 6 months: A prospective analysis in Corrona Psoriasis Registry

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Background: Psoriasis is associated with comorbid systemic metabolic disease.

Objective: To assess possible associations of comorbid obesity, history of diabetes, hypertension, and hyperlipidemia with response to biologic treatment at 6 months among patients in CorEvitas' Psoriasis Registry.

Methods: Participants included 2924 patients initiating biologic therapy (tumour necrosis factor inhibitors [TNFi], interleukin [IL]-17i, IL-12/23i, or IL-23i) with baseline and 6-month follow-up visits available. Logistic regressions resulted in adjusted odd ratios (OR) and 95% confidence intervals (CI) for achievement of response in select outcomes for those with obesity and history of diabetes, hypertension, and hyperlipidemia relative to those without each.

Results: Overall, obesity reduced by 25% to 30% odds of achieving PASI75 (OR, 0.75; 95% CI, 0.64-0.88) and PASI90 (OR, 0.70; 95% CI, 0.59-0.81). History of diabetes reduced odds of achieving PASI75 by 31% (OR, 0.69; 95% CI, 0.56-0.85) and PASI90 by 21% (OR, 0.79; 95% CI, 0.63-0.98). Obesity was associated with lower response to TNFi and IL-17i classes. Independent of obesity, diabetes was associated with poorer outcomes when on IL-17i therapy and hypertension, to a lesser extent, when on the TNFi class. No significant associations were found in the hyperlipidemia group.

Limitations: The study assessed only short-term effectiveness and small sample sizes limited the power to detect differences.

Conclusion: Assessment of comorbid disease burden is important for improved likelihoods of achieving treatment response with biologics. (J Am Acad Dermatol <https://doi.org/10.1016/j.jaad.2021.06.883>.)

Key words: biologics; biologic therapy; comorbid disease; metabolic disease; outcomes; psoriasis; psoriatic disease; treatment response.

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INTRODUCTION

Systemic inflammation and comorbidity are common complications of chronic disease.¹⁻³ Psoriasis, a chronic, immune-mediated disease of the skin and joints has been linked to increased comorbidity burden, dysmetabolism, and systemic inflammation.⁴⁻⁶ A dose response exists⁷ between psoriasis severity and comorbid disease and the impact of comorbidity in psoriasis lowers the quality of life and increases the risk of mortality overall.^{8,9} The management of moderate-to-severe psoriasis, especially with biologics, has been thoroughly reviewed¹⁰ and treatment targets to minimize disease activity have been proposed.¹¹ Despite the growing number of treatment choices, there is no universally accepted algorithm for choosing a drug, leaving providers challenged when choosing initial therapy.

Recommendations for choosing a biologic often depend on the presence of comorbid disease (eg, psoriatic arthritis), risk of worsening comorbid disease (eg, inflammatory bowel disease, multiple sclerosis, congestive heart failure, depression), chronic infectious disease, and special populations (eg, pregnancy).¹²⁻¹⁷

In the case of obesity, subanalyses of randomized controlled clinical trials revealed that fixed-dose tumor necrosis factor [TNF]- α -inhibitors have reduced efficacy in overweight and obese patients with psoriasis.¹⁸⁻²² The rationale for this may be related to increased clearance rates and lower serum trough concentrations at the time of redosing,¹⁸ a potential consequence of increased TNF- α expression and secretion from adipose tissue in obese patients.²³ These studies provide an insight into the contribution of comorbidity not only to systemic inflammation but also to poorer outcomes in the treatment of psoriasis. In contrast, randomized controlled clinical trials of interleukin (IL) 17 inhibitors (IL-17i), IL-23 inhibitors (IL-23i), and IL-12/23 inhibitors (IL-12/23i) have been equally effective in treating psoriasis patients irrespective of body weight.²⁴⁻²⁹ Yet, little is known of the effect of other metabolic comorbid conditions on biologic treatment efficacy despite frequently occurring at the same time.

The Corrona Psoriasis Registry is a prospective, multicenter, noninterventional registry in North America.^{30,31} Previous work has identified metabolic disorders such as obesity, diabetes, hypertension, and dyslipidemia to be among the most commonly reported comorbidities in patients enrolled in the registry. Because evidence supports each having an independent association with psoriasis,^{5,32,33} we sought to investigate the impact of these metabolic comorbidities on treatment outcomes at 6 months following the initiation of a biologic. The results may inform treatment algorithms for psoriasis patients with concurrent metabolic disease.

Using a US-based registry, we assessed the associations between treatment response to biologic therapy at 6 months and history of metabolic comorbid disease among psoriasis patients,

while controlling for obesity. We hypothesized that patients with a history of comorbid diabetes, hypertension, or hyperlipidemia would respond less frequently to treatment than those without those comorbidities, independent of obesity.

METHODS

Study setting

The CorEvitas' Psoriasis Registry is a prospective, multicenter, noninterventional registry, launched in April 2015, for patients with psoriasis under the care of a dermatologist, as previously described.³¹ Patients starting a systemic therapy for psoriasis are enrolled in the registry and longitudinal follow-up data are collected from patients and their treating dermatologists through registry questionnaires completed during routine clinical visits approximately every 6 months. As of October 31, 2020, there were 12,738 patients enrolled from 251 private and academic clinical sites with 521 physicians throughout 46 states in the United States or provinces in Canada.

Study population

This analysis utilized data collected from April 2015 through June 2020 and included the 2924 patients with plaque psoriasis who initiated a biologic therapy (TNFi, IL-17i, IL-23i, or IL-12/23i) and

CAPSULE SUMMARY

- Psoriasis is associated with comorbid systemic metabolic disease.
- Obesity and diabetes, independently, decrease the likelihood of treatment response to biologics when treating psoriasis. Interleukin 12/23 and interleukin 23 inhibitors may be less affected by comorbid disease at 6-months. Assessment of comorbid disease is important to improve the likelihood of achieving treatment response with biologics.

Abbreviations used:

BSA:	body surface area
CI:	confidence intervals
DM:	diabetes mellitus
HTN:	hypertension
HLD:	hyperlipidemia
IGA:	Investigator's Global Assessment
IL:	interleukin
OR:	odds ratio
PASI:	Psoriasis Area and Severity Index
TNF:	tumor necrosis factor

who completed a baseline visit and a 6-month (5- to 9-month window) follow-up visit.

Outcomes

Disease severity measures included Psoriasis Area and Severity Index (PASI), percentage of affected body surface area (BSA), and Investigator's Global Assessment (IGA).³⁴ The following outcomes were calculated at the 6-month follow-up visit: achievement of 75% improvement in PASI (PASI75), 90% improvement in PASI (PASI90), BSA of 1% or lower ($BSA \leq 1$), and clear-to-minimal status for IGA (score of 0 or 1, IGA 0/1). The key independent variables included (obesity body mass index ≥ 30 kg/m² vs < 30 kg/m²), history of diabetes mellitus (DM), hypertension (HTN), and hyperlipidemia (HLD).

Covariates

Baseline characteristics included demographics (age, sex, race, ethnicity, health insurance type, education, work status), lifestyle (smoking status, alcohol use), biometrics (body weight, body mass index), weight status (normal, overweight, obese), history of comorbidities (HTN, HLD, and DM), duration of psoriasis, comorbid psoriatic arthritis, number of prior biologic therapies (0, 1, 2, 3+), and disease characteristics (BSA, IGA, PASI).

Statistical analysis

Baseline patient characteristics, including demographics, lifestyle, history of comorbidity, and disease characteristics, were described overall and by drug classes. Means and standard deviations (SD) were reported for continuous variables and counts and percentages were reported for categorical variables.

For each 6-month outcome (PASI75, PASI90, $BSA \leq 1$, IGA 0/1), we reported the percentage achieving the outcome among patients with obesity or with a history of comorbidity (HTN, HLD, and DM) and those without, respectively. For each outcome and comorbidity, we reported 2 sets of ORs: the unadjusted OR and 95% CI, which was the

odds ratio of achieving the outcome for those with the comorbidity relative to those without; and adjusted OR, which was adjusted for age, sex, race, smoking, education, duration of psoriasis, psoriatic arthritis, obesity (only for the relationship with DM, HTN, and HLD, respectively), and the number of prior biologics.

The ORs were calculated using logistic regression to estimate the associations between a given outcome and current obesity, and history of each of DM, HTN and HLD, separately. The analysis (estimation of ORs) was conducted for all patients combined and then stratified by drug class.

RESULTS

Of the 2924 new biologic starts, 42.1% were initiated on an IL-17i, followed by IL-23i or IL-12/23i (39%) and TNFi (18.9%) (Table I). The cohort of all patients was predominantly White (76.1%), a college graduate or higher (39.1%), and had never smoked (48%). Over half of patients were obese (53.5%), while less than half of patients reported HTN (38.7%), HLD (28.5%), or DM (17.3%). Half of all patients (49.5%) reported no prior HTN, HLD, and DM, whereas 25.8% of patients reported history of 2 or more metabolic diseases. Depression was reported in 20.4% of patients.

Overall, the patient population had a mean BSA of 14.1% and 41.8% had comorbid psoriatic arthritis. Consistent with approval status at the time of data collection, comorbid psoriatic arthritis was more commonly reported in the TNFi and IL-17i cohorts. At initiation of therapy, 35.9% of patients were biologic naïve; 25.3% had been treated previously with 1 biologic and 22.4% reported a history of more than 3 biologics.

Association of individual comorbidities with treatment response

At 6 months, patients with obesity had a lower frequency of achieving PASI75 (54.1% vs 62.6%), PASI90 (37.8% vs 46.9%), IGA0/1 (47.0% vs 59.9%), and $BSA \leq 1$ (45.2% vs 56.5%) compared to those who were not obese (Table II) (Supplemental Table I; available via Mendeley at <https://data.mendeley.com/datasets/gnvm98my8c/1>). Likewise, patients reporting a history of another metabolic comorbidity reported lower proportions of achieving treatment outcomes. Those with DM less frequently achieved PASI75 (48.7% vs 59.9%), PASI90 (34.9% vs 43.4%), IGA0/1 (42.1% vs 55.2%), and $BSA \leq 1$ (39.2 vs 52.7%) compared to those without. Those with HTN less frequently achieved PASI75 (53.2% vs 60.9%), PASI90 (37.5% vs 44.7%), IGA0/1 (48.4% vs 55.7%), and $BSA \leq 1$ (46.0% vs 53.1%) compared to those without.

Table I. Baseline population and disease characteristics for patients with a corresponding 6-month follow up in CorEvitas' Psoriasis Registry, stratified by biologic class

	Overall	TNFi	IL-17i	IL-23i or IL-12/23i
Demographics				
Mean age in years (SD)	50.4 (14.4)	50.0 (14.4)	51.2 (13.8)	49.8 (15.0)
Female, n (%)	1378 (47.1)	268 (48.6)	576 (46.8)	534 (46.8)
Race, n (%)				
White	2226 (76.1)	421 (76.3)	929 (75.5)	876 (76.7)
African-American	82 (2.8)	19 (3.4)	34 (2.8)	29 (2.5)
Asian	276 (9.4)	39 (7.1)	136 (11.1)	101 (8.8)
Other	340 (11.6)	73 (13.2)	131 (10.7)	136 (11.9)
Hispanic ethnicity, n (%)	242 (8.4)	50 (9.2)	92 (7.6)	100 (8.9)
Education level, n (%)				
High school graduate or less	943 (32.3)	192 (34.8)	435 (35.4)	316 (27.7)
Some college	834 (28.6)	164 (29.7)	339 (27.6)	331 (29.1)
College graduate or higher	1143 (39.1)	196 (35.5)	455 (37.0)	492 (43.2)
Lifestyle				
Smoking status, n (%)				
Never	1389 (48.0)	279 (51.1)	581 (47.5)	529 (46.9)
Former smoker	982 (33.9)	166 (30.4)	421 (34.5)	395 (35.0)
Current smoker	524 (18.1)	101 (18.5)	220 (18.0)	203 (18.0)
Alcohol status, n (%)				
No alcohol use	1013 (37.1)	220 (42.6)	434 (38.0)	359 (33.5)
Casual	1297 (47.5)	225 (43.5)	538 (47.2)	534 (49.8)
Daily	420 (15.4)	72 (13.9)	169 (14.8)	179 (16.7)
Biometrics				
Body weight (kg), mean (SD)	93.1 (23.9)	92.2 (23.4)	93.9 (24.7)	92.7 (23.3)
BMI, mean (SD)	31.7 (7.4)	31.5 (7.4)	32.0 (7.5)	31.5 (7.2)
Normal (18.5-24.9)	516 (17.8)	97 (17.7)	207 (17.0)	212 (18.8)
Overweight (25.0-29.9)	829 (28.6)	171 (31.1)	339 (27.8)	319 (28.3)
Obese (≥ 30.0)	1550 (53.5)	281 (51.2)	673 (55.2)	596 (52.9)
History of comorbidities				
Cardiovascular disease	323 (11.1)	63 (11.4)	139 (11.3)	121 (10.6)
Hypertension	1132 (38.7)	206 (37.4)	508 (41.3)	418 (36.6)
Hyperlipidemia	832 (28.5)	156 (28.3)	372 (30.2)	304 (26.6)
Diabetes	507 (17.3)	96 (17.4)	219 (17.8)	192 (16.8)
Depression	595 (20.4)	119 (21.6)	256 (20.8)	220 (19.3)
Number of comorbidities (diabetes, hypertension, hyperlipidemia)				
0	1447 (49.5)	283 (51.4)	573 (46.6)	591 (51.8)
1	722 (24.7)	121 (22.0)	321 (26.1)	280 (24.5)
2+	754 (25.8)	147 (26.7)	336 (27.3)	271 (23.7)
Disease characteristics at baseline				
Psoriasis duration (years), mean (SD)	15.4 (13.4)	12.1 (12.5)	16.5 (13.5)	15.8 (13.5)
Comorbid psoriatic arthritis (PsA)	1203 (41.8)	262 (48.1)	601 (49.6)	340 (30.2)
IGA				
Clear	82 (2.8)	20 (3.6)	42 (3.4)	20 (1.8)
Almost clear	131 (4.5)	22 (4.0)	56 (4.6)	53 (4.6)
Mild	470 (16.1)	97 (17.6)	204 (16.6)	169 (14.8)
Moderate	1674 (57.3)	323 (58.5)	686 (55.8)	665 (58.3)
Severe	565 (19.3)	90 (16.3)	241 (19.6)	234 (20.5)
BSA, mean (SD)	14.1 (15.2)	14.1 (15.1)	13.9 (15.3)	14.3 (15.1)
PASI, mean (SD)	8.5 (7.5)	7.8 (6.9)	8.4 (7.7)	8.9 (7.5)
Biologic naïve	1050 (35.9)	361 (65.4)	291 (23.7)	398 (34.9)

Continued

Table I. Cont'd

	Overall	TNFi	IL-17i	IL-23i or IL-12/23i
Number of prior biologics, categorical				
0	1050 (35.9)	361 (65.4)	291 (23.7)	398 (34.9)
1	739 (25.3)	96 (17.4)	361 (29.3)	282 (24.7)
2	479 (16.4)	41 (7.4)	244 (19.8)	194 (17.0)
3+	656 (22.4)	54 (9.8)	334 (27.2)	268 (23.5)

BMI, Body mass index; *BSA*, body surface area; *IGA*, Investigator's Global Assessment; *IL*, interleukin; *PASI*, Psoriasis Area and Severity Index; *SD*, standard deviation; *TNFi*, tumor necrosis factor inhibitors.

Similarly, those with HLD less frequently achieved PASI75 (56.5% vs 58.5%), PASI90 (39.4% vs 42.9%), IGA0/1 (51.1% vs 53.6%), and $BSA \leq 1$ (50.0% vs 50.5%) (Table II, Table III, and Supplemental Table D).

After adjusting for covariates, among all patients, obesity was associated with a 25% to 30% reduced odds of achieving PASI75 (OR, 0.75; 95% CI, 0.64-0.88) and PASI90 (OR, 0.70; 95% CI, 0.59-0.81), 38% reduced odds of achieving IGA0/1 (OR, 0.62; 95% CI, 0.53-0.72), and 35% reduced odds for $BSA \leq 1$ (OR, 0.65; 95% CI, 0.56-0.76) (Tables II and III, and Supplemental Table II). In adjusted models that controlled for obesity, DM was associated with a 31% reduced odds of achieving PASI75 (OR, 0.69; 95% CI, 0.56-0.85); similarly, a reduced odds of 21%, 30%, and 34% were found for PASI90 (OR, 0.79; 95% CI, 0.63-0.98), IGA0/1 (OR, 0.70; 95% CI, 0.57-0.87), and $BSA \leq 1$ (OR 0.66; 95% CI, 0.53-0.81), respectively. HTN was associated with reduced odds of achieving PASI75 by 19% (OR, 0.81; 95% CI, 0.68-0.97) but no significant reduction was seen for PASI90, IGA0/1, and $BSA \leq 1$ in the adjusted model. The presence of hyperlipidemia was not associated with outcomes.

Among patients on TNFi, those with obesity had reduced odds of all outcome measures in the adjusted models (Tables II and III and Supplemental Table II): PASI75 by 33% (OR, 0.67; 95% CI, 0.46-0.97), PASI90 by 43% (OR, 0.57; 95% CI, 0.39-0.84), IGA0/1 by 47% (OR, 0.53; 95% CI, 0.37-0.77), and $BSA \leq 1$ by 52% (OR, 0.48; 95% CI, 0.33-0.71). DM was associated with reduced odds of achieving IGA 0/1 (OR, 0.63; 95% CI, 0.40-0.99) and $BSA \leq 1$ (OR, 0.60; 95% CI, 0.37-0.96) in unadjusted models; however, for the cohort on TNFi, DM did not meet the criteria for independent significance, when adjusted (Supplemental Table II). For patients on TNFi reporting HTN, odds of achieving PASI75 (OR, 0.61; 95% CI, 0.40-0.95) were reduced 39% in the adjusted model (Table II); however, the 95% CIs for all other outcome measures included the null in the adjusted model.

Hyperlipidemia was not associated with study outcomes for those on TNFi.

For patients started on IL-17i, the presence of obesity decreased odds of achieving all outcome measures in the adjusted model (Tables II and III): PASI75 by 34% (OR, 0.66; 95% CI, 0.52-0.84) and PASI90 by 37% (OR, 0.63; 95% CI, 0.50-0.81). Supplemental Table II provides the IGA0/1 and $BSA \leq 1$. Similarly, DM decreased odds of achieving all outcome measures in the adjusted model (Tables II and III): PASI75 by 39% (OR, 0.61; 95% CI, 0.45-0.85) and PASI90 by 31% (OR, 0.69; 95% CI, 0.49-0.96) Supplemental Table II provides the IGA0/1 and $BSA \leq 1$. While hypertension was negatively associated with outcomes in the unadjusted model for PASI75 (OR, 0.75; 95% CI, 0.59-0.94) and PASI90 (OR, 0.78; 95% CI, 0.62-0.98) (Tables II and III), these associations were not seen in the adjusted model for all outcomes. Hyperlipidemia was not associated with outcomes for those on IL-17i.

For patients on IL-23i or IL-12/23i, obesity, DM, and HTN were associated with poorer outcomes in the unadjusted model (Tables II and III and Supplemental Table II). The presence of obesity and DM each decreased the odds of achieving IGA 0/1 by roughly 30% (OR, 0.68; 95% CI, 0.53-0.88 and OR, 0.70; 95% CI, 0.50-1.00, respectively) in the adjusted model (Supplemental Table II) for those on IL-23i or IL-12/23i. Hyperlipidemia was not associated with outcomes for those on IL-23i or IL-12/23i.

DISCUSSION

Using real-world data, we provide evidence for the association of specific metabolic comorbidities with reduced likelihood of achieving treatment responses among psoriasis patients initiating biologic therapy.

Previous data from multiple randomized controlled trials have assessed proportions of patients achieving outcomes in the presence or absence of obesity. Obese patients less frequently achieve treatment response when treated with

Table II. Odds of achieving PASI75 by drug class and metabolic comorbid disease.

Drug class	Comorbidity	n	% Achieving PASI75		Unadjusted OR (95% CI for yes vs no) of achieving PASI75 for comorbidity	Adjusted OR (95% CI for yes vs no) of achieving PASI75 for comorbidity*
			Yes	No		
Overall	Obesity	2895	54.1% (839/1550)	62.6% (842/1345)	0.70 (0.61, 0.82)	0.75 (0.64, 0.88)
	Diabetes	2923	48.7% (247/507)	59.9% (1446/2416)	0.64 (0.53, 0.77)	0.69 (0.56, 0.85)
	Hypertension	2923	53.2% (602/1132)	60.9% (1091/1791)	0.73 (0.63, 0.85)	0.81 (0.68, 0.97)
	Hyperlipidemia	2923	56.5% (470/832)	58.5% (1223/2091)	0.92 (0.78, 1.08)	1.02 (0.85, 1.22)
Patients on TNFi	Obesity	549	45.2% (127/281)	58.2% (156/268)	0.59 (0.42, 0.83)	0.67 (0.46, 0.97)
	Diabetes	551	43.8% (42/96)	53.0% (241/455)	0.69 (0.44, 1.08)	0.72 (0.44, 1.18)
	Hypertension	551	42.7% (88/206)	56.5% (195/345)	0.57 (0.40, 0.81)	0.61 (0.40, 0.95)
	Hyperlipidemia	551	54.5% (85/156)	50.1% (198/395)	1.19 (0.82, 1.73)	1.48 (0.97, 2.28)
Patients on IL-17i	Obesity	1219	53.8% (362/673)	64.3% (351/546)	0.65 (0.51, 0.82)	0.66 (0.52, 0.84)
	Diabetes	1230	47.5% (104/219)	60.6% (613/1011)	0.59 (0.44, 0.79)	0.61 (0.45, 0.85)
	Hypertension	1230	54.1% (275/508)	61.2% (442/722)	0.75 (0.59, 0.94)	0.79 (0.61, 1.03)
	Hyperlipidemia	1230	56.5% (210/372)	59.1% (507/858)	0.90 (0.70, 1.15)	0.91 (0.69, 1.20)
Patients on IL-23i or IL-23/12i	Obesity	1127	58.7% (350/596)	63.1% (335/531)	0.83 (0.65, 1.06)	0.93 (0.71, 1.20)
	Diabetes	1142	52.6% (101/192)	62.3% (592/950)	0.67 (0.49, 0.92)	0.77 (0.55, 1.09)
	Hypertension	1142	57.2% (239/418)	62.7% (454/724)	0.79 (0.62, 1.01)	1.00 (0.74, 1.35)
	Hyperlipidemia	1142	57.6% (175/304)	61.8% (518/838)	0.84 (0.64, 1.09)	1.02 (0.75, 1.38)

IL, Interleukin; OR, odds ratio; PASI75, Psoriasis Area and Severity Index 75; TNFi, tumor necrosis factor inhibitors.

*Adjusted for: age, sex, race, smoking, education, duration of psoriasis, psoriatic arthritis, number of prior biologics, and obesity (for nonobesity outcomes).

Table III. Odds of achieving PASI90 by drug class and metabolic comorbid disease

Drug class	Comorbidity	n	% Achieving PASI90		Unadjusted OR (95% CI for yes vs no) of achieving PASI90 for comorbidity	Adjusted OR (95% CI for yes vs no) of achieving PASI90 for comorbidity*
			Metabolic comorbidity			
			Yes	No		
Overall	Obesity	2895	37.8% (586/1550)	46.9% (631/1345)	0.69 (0.59, 0.80)	0.70 (0.59, 0.81)
	Diabetes	2923	34.9% (177/507)	43.4% (1048/2416)	0.70 (0.57, 0.85)	0.79 (0.63, 0.98)
	Hypertension	2923	37.5% (424/1132)	44.7% (801/1791)	0.74 (0.64, 0.86)	0.84 (0.71, 1.01)
	Hyperlipidemia	2923	39.4% (328/832)	42.9% (897/2091)	0.87 (0.74, 1.02)	0.98 (0.82, 1.18)
Patients on TNFi	Obesity	549	29.2% (82/281)	41.8% (112/268)	0.57 (0.40, 0.82)	0.57 (0.39, 0.84)
	Diabetes	551	29.2% (28/96)	36.5% (166/455)	0.72 (0.44, 1.16)	0.81 (0.47, 1.38)
	Hypertension	551	29.6% (61/206)	38.6% (133/345)	0.67 (0.46, 0.97)	0.86 (0.54, 1.36)
	Hyperlipidemia	551	37.8% (59/156)	34.2% (135/395)	1.17 (0.80, 1.72)	1.58 (1.01, 2.48)
Patients on IL-17i	Obesity	1219	38.3% (258/673)	48.2% (263/546)	0.67 (0.53, 0.84)	0.63 (0.50, 0.81)
	Diabetes	1230	33.8% (74/219)	44.4% (449/1011)	0.64 (0.47, 0.87)	0.69 (0.49, 0.96)
	Hypertension	1230	39.0% (198/508)	45.0% (325/722)	0.78 (0.62, 0.98)	0.81 (0.62, 1.06)
	Hyperlipidemia	1230	39.2% (146/372)	43.9% (377/858)	0.82 (0.64, 1.06)	0.81 (0.62, 1.07)
Patients on IL-23i or IL-23/12i	Obesity	1127	41.3% (246/596)	48.2% (256/531)	0.76 (0.60, 0.96)	0.82 (0.64, 1.06)
	Diabetes	1142	39.1% (75/192)	45.6% (433/950)	0.77 (0.56, 1.05)	0.92 (0.65, 1.30)
	Hypertension	1142	39.5% (165/418)	47.4% (343/724)	0.72 (0.57, 0.93)	0.93 (0.69, 1.24)
	Hyperlipidemia	1142	40.5% (123/304)	45.9% (385/838)	0.80 (0.61, 1.04)	1.03 (0.76, 1.40)

CI, Confidence interval; IL, interleukin; OR, odds ratio; PASI90, Psoriasis Area and Severity Index 90; TNF, tumor necrosis factor.

*Adjusted for: age, sex, race, smoking, education, duration of psoriasis, psoriatic arthritis, number of prior biologics, and obesity (for non-obesity outcomes).

fixed-dose TNFi¹⁸⁻²² and expert opinions have recommended the use of infliximab and ustekinumab specifically for their weight-based dosing.³⁵ More recent data from clinical trials have shown comparable proportions of obese and nonobese patients achieving treatment response at 12 months when on an IL-17i or IL-12/23i and IL-23i.^{25,26,28} In our study, when considering proportions achieving treatment response, obese patients less frequently achieved response in all biologic class cohorts compared to nonobese patients. Further, not previously assessed in randomized controlled trials, the presence of diabetes or hypertension also correlated with a lower frequency of successful treatment response.

Yet, when the association of these comorbid disease states and outcomes were tested in the adjusted logistic regression model, we showed decreased odds of achieving response to biologic therapy consistently among patients with obesity or DM when compared to those without. When considering each biologic class as its own cohort, obese patients were less likely to achieve treatment response when on a TNFi or IL-17i. The odds ratio of PASI90 was decreased by approximately 40% for both these drug classes. Independent of obesity, history of diabetes reduced the likelihoods of achieving PASI75 and PASI90 by roughly 40% and 30%, respectively, among those treated with IL-17i. Of note, these associations were not consistently found among those on IL-12/23i or IL-23i. Associations between HTN and treatment outcomes were more attenuated than obesity and DM; HLD was not found to be correlated with treatment response.

The impact of comorbid disease on psoriasis treatment may be explained by shared pathogenic mechanisms.³⁶ Obesity-related adipose tissue is biologically active and contributes to systemic inflammation through the secretion of proinflammatory and T helper 17 polarizing cytokines.^{23,37-39} Likewise, patients with diabetes have elevated levels of T helper 17 cytokines circulating in the peripheral blood.⁴⁰ These systemic processes may contribute to the inflammatory milieu of psoriasis, possibly leading to less satisfactory results. The moderate effect observed in those with hypertension here may be supported by the fact that increased levels of circulating TNF-alpha and IL-17 have been found in patients with hypertension.^{41,42}

Given the shared immunologic pathways between obesity, diabetes, hypertension and psoriasis, considerations should be made for a patient's burden of comorbid disease when choosing a treatment. Further, the question arises as to whether dosing regimens should be adjusted for psoriasis patients with comorbid disease on TNFi and IL-17i.

Additional consideration should be made for the IL-12/23i and IL-23i class and that these agents may show less susceptibility to the effect of comorbid disease at 6 months. Choosing a biologic that targets an upstream/maintenance signal of T helper 17-mediated disease may improve the likelihood of response when treating a patient with comorbidity, given the shared immunology.⁴³ Future research is needed to understand the impact of this shared immunopathology and its impact on treatment response with biologics.

Although in this study the associations of hypertension and hyperlipidemia with treatment outcome were not as strong as obesity and diabetes, the presence of these comorbid diseases are essential to consider in the overall management of psoriasis given their contributions to cardiovascular disease and major adverse cardiac events.⁴⁴

The strength of this study is the use of real-world data with which we were able to show associations of poorer outcomes in the presence of concurrent metabolic disease stratified across multiple biologic classes. This study did, however, have several limitations. Multimorbidity is common in chronic disease,⁴⁵ and while obesity and psoriatic arthritis were controlled for, the presence of multiple other comorbid diseases were not. Histories of comorbid conditions were assessed at baseline; however, improvement in the status of comorbid conditions at follow up is not captured in the registry. Recruitment of study participants was voluntary and may not reflect the general population of psoriasis patients. Further, only short-term effectiveness (6 months after initiation) was examined. Finally, we combined the IL-12/23i and IL-23i classes because the numbers of patients with some comorbidities (eg, diabetes, hyperlipidemia) were small, precluding calculation of robust effect estimates. Thus, we were neither able to analyze these classes individually nor account for weight-based dosing, when available.

CONCLUSION

Our real-world findings suggest that for those on TNF and IL-17 inhibitors, obesity or a history of diabetes was associated with reduced odds of achieving treatment outcomes. Our study highlights the potential importance of screening for comorbidities and developing a personalized treatment plan for psoriasis patients. Additional research is needed to better understand the underlying mechanisms of these associations and to determine if higher dosing or dose escalation is necessary to achieve an optimal response in these patients.

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Conflicts of interest

Dr Enos has served as a consultant on an advisory board for UCB. Drs McLean and Lin and authors Foster and Dube are employees of CorEvitas LLC. Dr Van Voorhees has received grant/research support from Celgene, Lilly, and AbbVie, and is a consultant for Amgen, Boehringer Ingelheim, Bristol Myers Squibb, UCB. Author Ramos has no conflict of interest to disclose.

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