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BRIEF REPORT

Effects of Tirzepatide on Metabolic Parameters in Patients with Psoriasis and Obesity: 24-Week Real-World Study

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ABSTRACT

Introduction: Tirzepatide, a dual glucose-dependent insulinotropic polypeptide/glucagon-like peptide 1 (GIP/GLP-1) receptor agonist, has provided substantial efficacy in improving weight and cardiometabolic parameters in individuals with obesity. However, data on its metabolic effects in patients with psoriasis remain limited. The objective if the study was to investigate the effects of tirzepatide on selected metabolic parameters, in adults with psoriasis and obesity.

Methods: This prospective observational study included 64 adults with chronic plaque psoriasis and obesity (body mass index [BMI] ≥ 30 kg/m^2). All patients received tirzepatide 2.5 mg with titration to 5 mg weekly and were maintained on stable ixekizumab therapy. Anthropometric measures, fasting glucose, lipid profile, liver and renal function tests, and visceral adiposity indices were assessed at baseline and week 24.

Results: At week 24, significant reductions in body weight (– 10%), BMI (– 3.5 units) and waist-to-hip ratio (– 8%) ($p < 0.001$) were observed. Fasting glucose decreased by 11.9% ($p < 0.001$), while low-density lipoprotein (LDL)-cholesterol (– 6.7%, $p < 0.001$) and triglycerides (– 15.4%, $p = 0.003$) improved significantly. Aspartate aminotransferase (AST) and alanine transaminase (ALT) decreased by 12.4% and 11.6%, respectively. Renal function remained stable. Psoriasis Area and Severity Index (PASI) scores decreased from 4.2 ± 3.9 to 1.01 ± 0.9 (– 76%, $p < 0.001$).

Conclusions: In patients receiving low-dose tirzepatide, clinically relevant improvements in selected metabolic parameters were observed, indicating a possible contribution of this treatment within a comprehensive metabolic management strategy for psoriasis and obesity.

Keywords: Psoriasis; Tirzepatide; Obesity; Ixekizumab; Weight loss

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Key Summary Points

Why carry out this study?

The study was carried out to provide real-life data on the use of tirzepatide in patients with moderate to severe chronic plaque psoriasis and obesity.

The study investigated the effects of tirzepatide on selected metabolic parameters in patients with psoriasis on continuous treatment with ixekizumab.

What was learned from the study?

Serum glucose, lipids, body weight, and psoriasis severity reduced in patients with psoriasis treated with tirzepatide over 24 weeks.

Further controlled studies with larger sample size are needed to confirm these preliminary data.

INTRODUCTION

Tirzepatide is a novel dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP-1) receptor agonist that has recently emerged as an effective pharmacological approach for improving metabolic parameters in individuals with obesity and type 2 diabetes [1, 2]. Beyond its glucose-lowering properties, tirzepatide has demonstrated substantial benefits on body weight, insulin resistance and cardiometabolic risk factors, positioning it as a promising therapeutic tool in the management of metabolic dysfunction.

Psoriasis is a chronic immune-mediated inflammatory skin disease that is frequently associated with obesity, insulin resistance and metabolic syndrome [3]. As a result, individuals with psoriasis often present with a higher cardiometabolic burden and may benefit from therapeutic strategies targeting both cutaneous inflammation and metabolic dysregulation [4, 5]. Despite the growing interest in the metabolic management of patients with psoriasis, clinical evidence evaluating tirzepatide specifically in individuals with psoriasis and obesity remains scarce. Only a limited number of studies have explored whether the metabolic improvements induced by tirzepatide may translate into benefits for psoriatic disease activity or overall inflammatory status [6].

The objective of the present study is to investigate the effects of tirzepatide in patients with psoriasis and obesity, assessing its impact on metabolic parameters, anthropometric measures and potential implications for psoriatic disease control.

METHODS

Study Design and Population

This prospective real-world study was conducted between January 2025 and April 2026 at the Dermatology outpatient services of the University of Verona. The study enrolled 64 adult patients with chronic plaque psoriasis and obesity who were eligible for tirzepatide therapy. All participants provided written informed consent prior to inclusion. Participants were evaluated at baseline and after a 24-week follow-up period. All patients were receiving continuous and stable treatment with interleukin (IL)-17 inhibitor ixekizumab for psoriasis for at least 6 months prior to enrolment. The inclusion criteria were age ≥ 18 years; diagnosis of chronic plaque psoriasis confirmed by a dermatologist; obesity (body mass index [BMI] ≥ 30 kg/m^2); eligibility for tirzepatide therapy; ability and willingness to comply with scheduled visits and assessments. Exclusion criteria included prior treatment with GLP-1 receptor agonists, active malignancy, uncontrolled psychiatric disorders, use of medications known to affect appetite or metabolism, and any condition that could interfere with study participation.

Treatment

Tirzepatide was administered following standard clinical practice, beginning with 2.5 mg once weekly for the first 4 weeks, followed by titration to 5 mg weekly up to week 24. Dose escalation

beyond 5 mg was not undertaken in this study, reflecting the investigators' preference for maintaining a low-dose regimen expected to offer a more favourable safety and tolerability profile. Higher doses (>5 mg) were also avoided because they are associated with greater cost. All patients received general lifestyle counselling consistent with routine clinical care, but no structured dietary intervention was implemented. The study was conducted in accordance with the principles of the Declaration of Helsinki (1964) and its subsequent amendments. All patients provided consent for the anonymous and aggregated publication of baseline demographic and clinical characteristics, as well as study outcome measures. Formal ethics committee approval was not required because both ixekizumab and tirzepatide were prescribed within their approved indications in a routine real-world clinical setting.

Clinical and Biochemical Assessments

At baseline and at 24 weeks, participants underwent standardized clinical evaluations. Anthropometric measurements included body weight, height, BMI and waist circumference, obtained using calibrated instruments. Biochemical analyses included fasting glucose, fasting insulin, lipid profile (high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), triglycerides) and liver and renal function tests. Blood samples were processed in the central laboratory of the hospital. Waist-to-height ratio was calculated using established formulas. Psoriasis severity was assessed using the Psoriasis Area and Severity Index (PASI), recorded at each visit by trained dermatologists.

Sample Size and Statistical Analysis

Given the exploratory nature of the study, no formal a priori sample size calculation was performed. Continuous variables were expressed as mean ± standard deviation or median and interquartile range, depending on distribution. Normality was assessed using the Kolmogorov–Smirnov test. Paired *t* tests or Wilcoxon signed-rank tests were used to compare baseline and follow-up values. Categorical variables were analysed using Fisher's exact test. A two-tailed p value ≤ 0.05 was considered statistically significant. All analyses were performed using stata software.

Ethical Approval

The study was conducted in accordance with the Helsinki Declaration of 1964 and its later amendments. The patients gave consent to the anonymous and aggregated publication of baseline general and clinical characteristics, and the outcome measures of the study. The study was exempted from a formal approval from any IRB or ethics board because ixekizumab and tirzepatide have been used for approved label indication in a routine clinical practice and setting of a real-life study.

RESULTS

In patients receiving low-dose tirzepatide, improvements in selected metabolic parameters were observed over the study period. Characteristics of patients and metabolic parameters at baseline and post tirzepatide treatment are reported in Table 1. Body weight decreased from 109.4 ± 19.5 kg to 98.5 ± 17.6 kg (– 10%, $p < 0.001$), accompanied by a reduction in BMI from 38.7 ± 5.1 to 35.2 ± 3.8 kg/m^2 (– 3.5 units, $p < 0.001$) and a decrease in waist-to-hip ratio from 0.76 ± 0.1 to 0.70 ± 0.1 (– 8%, $p < 0.001$), indicating a substantial reduction in central adiposity. Fasting glucose improved significantly, declining from 112.4 ± 46.4 mg/dL to 99.0 ± 44.9 mg/dL (– 11.9%, $p < 0.001$). Lipid parameters showed a favourable trend, with total cholesterol decreasing by 5.2% ($p = 0.055$) and HDL-cholesterol showing a non-significant reduction ($p = 0.06$), while LDL-cholesterol decreased significantly from 115.2 ± 16.8 to 107.5 ± 15.7 mg/dL (– 6.7%, $p < 0.001$) and triglycerides from 169.9 ± 71.9 to 142.9 ± 60.8 mg/dL (– 15.4%, $p = 0.003$). Liver enzymes also improved, with AST decreasing by 12.4% ($p = 0.017$) and ALT by 11.6% ($p = 0.044$). Renal function remained stable, with creatinine

Table 1 Characteristics of patients ($n = 64$) and metabolic parameters at baseline and post tirzepatide treatment

Parameter	Baseline	Week 24	Δ*	*P*
Male, *N* (%)	37 (57.8)	N/A		
Female, *N* (%)	27 (42.2)	N/A		
Age (years)	52 ± 11	N/A		
Weight (cm)	109.4 ± 19.5	98.5 ± 17.6	− 10%	< 0.001
Body mass index	38.7 ± 5.1	35.2 ± 3.8	− 3.5	< 0.001
Waist-to-hip ratio	0.76 ± 0.1	0.70 ± 0.1	− 8%	< 0.001
Glucose (mg/dL)	112.4 ± 46.4	99.0 ± 44.9	− 11.9%	< 0.001
Total cholesterol (mg/dL)	203.8 ± 43.8	193.2 ± 41.5	− 5.2%	0.055
HDL-c (mg/dL)	54.1 ± 9.3	51.9 ± 8.9	4.1%	0.06
LDL-c (mg/dL)	115.2 ± 16.8	107.5 ± 15.7	− 6.7%	< 0.001
Triglycerides (mg/dL)	169.9 ± 71.9	142.9 ± 60.8	− 15.4%	0.003
AST (U/L)	40.1 ± 16.3	35.1 ± 14.3	− 12.4%	0.017
ALT (U/L)	39.8 ± 17.9	35.2 ± 15.8	− 11.6%	0.044
Creatinine (mg/dL)	0.9 ± 0.3	0.8 ± 0.2	− 0.8%	0.8
PASI	4.2 ± 3.9	1.01 ± 0.9	− 76%	< 0.001

The mean and standard deviation of the numerical variables are reported. For sex variable, the absolute number and corresponding percentage are reported

HDL-c high-density lipoprotein cholesterol, *LDL-c* low-density lipoprotein cholesterol, *AST* aspartate aminotransferase, *ALT* alanine transaminase, *PASI* Psoriasis Area and Severity Index

*Indicates the difference between week 24 and baseline, expressed either as a percentage or as an absolute value

showing no clinically meaningful change (−0.8%, $p = 0.8$). Patients were uniformly maintained on ixekizumab administered at the approved label dose for a mean duration of 8.6 ± 1.4 months prior to initiating tirzepatide. Psoriasis severity improved markedly, with PASI scores decreasing from 4.2 ± 3.9 to 1.01 ± 0.9, corresponding to a 76% reduction ($p < 0.001$). The only reported adverse events likely related to tirzepatide but only at the dose of 5 mg were gastrointestinal events. The most frequently reported symptoms were constipation (25% of participants), nausea (12%) and diarrhoea (4%). No patients discontinued the study because of adverse events.

DISCUSSION

The findings of this study show that low-dose tirzepatide could provide substantial metabolic benefits in adults with chronic plaque psoriasis and obesity, a population characterized by elevated cardiometabolic risk. The significant reductions in body weight, BMI and waist-to-hip ratio observed in our cohort are consistent with the known pharmacological profile of tirzepatide and closely mirror the magnitude of weight loss reported in clinical trials involving individuals with obesity without psoriasis [7]. The improvement in central adiposity is particularly relevant, as visceral fat is strongly associated with insulin resistance and systemic inflammation [8]. The reduction in fasting glucose further supports the glucose-lowering efficacy of

tirzepatide in a population in which insulin resistance is highly prevalent, even in the absence of overt diabetes [9]. Improvements in lipid parameters, particularly the significant reductions in LDL-c and triglycerides, highlight the drug's capacity to modulate cardiometabolic risk factors that contribute to the elevated cardiovascular morbidity observed in patients with psoriasis. The reductions in AST and ALT suggest a beneficial effect on hepatic steatosis, a common comorbidity in psoriasis that contributes to metabolic dysfunction [10]. All patients were maintained on stable ixekizumab for at least 6 months prior to enrolment, to minimize the possibility that changes in metabolic parameters were attributable to modifications in biologic therapy. Beyond metabolic outcomes, we observed a marked improvement in psoriasis severity, with PASI scores decreasing by 76%. This observation aligns with emerging evidence linking visceral adiposity, adipokine dysregulation and insulin resistance to psoriasis severity [11, 12]. In addition, this finding is consistent with the TOGETHER-PsA trial showing greater disease control in adults with psoriatic arthritis and overweight or obesity [13]. Moreover, the TOGETHER-PsO trial found that combining ixekizumab with tirzepatide leads to significantly greater skin clearance and weight loss than ixekizumab alone, with major implications for treating psoriasis in patients with obesity. In particular, the trial shows that weight reduction enhances biologic efficacy, supporting a dual-target approach for patients with psoriasis and obesity. According to the authors of the trial, the combination of an IL-17A inhibitor with a dual incretin agonist suggests that treating metabolic dysfunction may boost skin clearance [14].

This study has several limitations that should be acknowledged. First, its observational, single-centre design without a control group limits causal inference and prevents definitive attribution of the observed improvements to tirzepatide alone. The sample size, although adequate for exploratory analysis, remains relatively small and may not capture the full heterogeneity of patients with psoriasis and obesity. Additionally, lifestyle factors such as diet and physical activity were not captured. Finally, the follow-up period of 24 weeks provides valuable short-term insights, but longer-term data are needed to determine the durability of metabolic improvements and their potential impact on long-term psoriatic disease control and cardiometabolic risk.

Taken together, these findings indicate that tirzepatide could represent a valuable therapeutic option for comprehensive metabolic management in patients with psoriasis and obesity, complementing biologic therapy and addressing systemic comorbidities. Future controlled studies are warranted to elucidate the mechanistic links between metabolic improvement and psoriasis outcomes and to determine whether tirzepatide may play a role in integrated management strategies for psoriatic disease.

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Author Contributions. Paolo Gisondi conceived the study, collected the data, performed the statistical analysis and drafted the manuscript. Giampiero Girolomoni revised and corrected the draft of the manuscript.

Both authors have read and approved of the final version of this manuscript.

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Data Availability. The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of Interest. Paolo Gisondi has received honoraria as consultant and/or speaker for AbbVie, Almirall, Amgen, Bristol-Myers

Squibb, Eli Lilly, Leo Pharma, Janssen, Novartis, Pfizer, Takeda and UCB. Paolo Gisondi is an Editorial Board member of *Dermatology and Therapy*. Paolo Gisondi was not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions. Giampiero Girolomoni has received honoraria as consultant and/or speaker for AbbVie, Almira l, Bristol Myers Squibb, Eli Lily, Leo Pharma, Janssen, Novartis, Pfizer, Samsung and UCB.

Ethical Approval. The study was conducted in accordance with the Helsinki Declaration of 1964 and its later amendments. The patients gave consent to the anonymous and aggregated publication of baseline general and clinical characteristics, and the outcome measures of the study. The study was exempted from a formal approval from any IRB or ethics board because ixekizumab and tirzepatide have been used for approved label indication in a routine clinical practice and setting of a real-life study.

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