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REVIEW ARTICLE

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Unveiling the IL-17 axis: an immunometabolic bridge between psoriasis and metabolic syndrome

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ABSTRACT

Aim of the review: Psoriasis is increasingly recognized as a systemic inflammatory disease frequently associated with a cluster of cardiometabolic comorbidities, including obesity, type 2 diabetes, and cardiovascular disease. Central to this association is the interleukin-17 (IL-17) signaling axis, a key driver of both cutaneous inflammation and systemic metabolic dysfunction.

Materials and methods: This review examines the complex immunometabolic interactions mediated by IL-17 and synergistic cytokines such as TNF-α, IL-6, IL-1β, IL-23, and adipokines, which contribute to endothelial dysfunction, insulin resistance, and adipose-tissue inflammation.

Results: Beyond its established role in psoriasis pathogenesis, the IL-17 pathway is implicated in the 'psoriatic march,' linking chronic skin inflammation to accelerated atherosclerosis. The advent of IL-17 inhibitors has transformed the management of moderate-to-severe psoriasis, achieving unprecedented skin clearance (PASI 90/100). Emerging evidence suggests that these agents may also exert potential beneficial effects on selected inflammatory and cardiometabolic markers. However, their direct impact on metabolic parameters remains under investigation.

Conclusion: Understanding these shared molecular pathways is essential for adopting a holistic therapeutic approach that addresses both cutaneous disease and the systemic burden of psoriatic patients.

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KEYWORDS
Psoriasis; IL-17; IL-17 inhibitors; metabolic disorders

1. Introduction

Psoriasis is a chronic immune-mediated inflammatory disorder with systemic involvement and a pathogenesis driven by both innate and adaptive immune responses (1). Its immunologic signature is dominated by activation of the IL-23/IL-17 axis (2), which orchestrates keratinocyte hyperproliferation, neutrophil recruitment, and sustained cytokine release, thereby perpetuating cutaneous and entheseal inflammation (3). Over the past decade, psoriasis has been increasingly recognized as a systemic inflammatory condition closely linked to metabolic dysfunction (4).

Cytokines elevated in severe psoriasis, including IL-1β, IL-6, IL-17A/F, TNF-α, IFN-γ, and adipokines, exert pathogenic effects on the liver, adipose tissue, endothelium, and pancreatic β-cells, contributing to insulin resistance, hypertension, dyslipidemia, fatty liver disease, and accelerated atherosclerosis (5). Within this framework, IL-17A and IL-17F promote endothelial dysfunction, oxidative stress, adipose-tissue inflammation, and hepatic fibrogenesis, thereby linking cutaneous inflammation to cardiometabolic disease (6). Additional evidence showing IL-17-mediated modulation of keratinocyte metabolism, γδ T-cell activation, and cholesterol-synthesis pathways further supports its role as a central regulator at the interface between immunity and metabolism.

The introduction of IL-17 inhibitors has redefined therapeutic expectations in moderate-to-severe psoriasis, enabling high rates of complete skin clearance (7). Their potential impact on metabolic and cardiovascular comorbidities is now an area of active investigation. Early experimental data on IL-17-related metabolic reprogramming support the biologic plausibility of benefits beyond cutaneous disease control, although clinical cardiometabolic effects remain under investigation (8).

This narrative review synthesizes current knowledge on the IL-17 immunometabolic pathway in psoriasis and examines emerging evidence supporting the safety and potential metabolic benefits of IL-17 inhibitors in patients with concomitant cardiometabolic disorders. By integrating mechanistic insights with clinical data, we aim to clarify the role of IL-17 as a therapeutic target not only for skin inflammation but also for the systemic complications that contribute most to long-term morbidity in psoriatic disease.

2. Materials and methods

A comprehensive literature search was conducted using PubMed/MEDLINE to identify relevant publications up to January 2026. The search strategy combined the following keywords and Boolean operators: 'psoriasis', 'IL-17 pathway', 'metabolic disorders', 'IL-17 inhibitor drugs', 'IL-17 blockade', 'cardiovascular outcomes', and 'metabolic outcomes'. Additional terms related to specific IL-17 inhibitors (e.g., secukinumab, ixekizumab, brodalumab,

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bimekizumab) were included to ensure comprehensive coverage of therapeutic evidence. Eligible sources comprised original research articles, clinical trials, mechanistic studies, observational cohorts, meta-analyses, and high-quality reviews. Only English-language publications were considered. Reference lists of selected papers were manually screened to identify additional relevant studies. Given the narrative nature of this review, studies were selected based on scientific relevance, methodological quality, and contribution to current understanding of IL-17 biology and its metabolic and cardiovascular implications in psoriatic disease (Table 1).

3. Results

3.1. Pathogenesis of psoriasis and psoriatic arthritis

Psoriasis arises from a complex interplay between innate and adaptive immunity. Plasmacytoid dendritic cells (pDCs), activated by environmental triggers or autoantigens such as LL37-DNA complexes, stimulate IL-23 production by cutaneous and entheseal myeloid dendritic cells (mDCs) (9,10). IL-23 is considered the 'master regulator' of psoriatic T-cell responses because it promotes the expansion and survival of Th17 cells (3). These cells release key effector cytokines, including IL-17A/F, IL-22, IL-26, IFN-γ, and GM-CSF, which act synergistically to sustain inflammation.

In the skin, these cytokines drive keratinocyte hyperproliferation and induce the production of antimicrobial peptides, pro-inflammatory cytokines (TNF, IL-1β, IL-6), and chemokines (CXCL8-CXCL11, CCL20), establishing a self-amplifying inflammatory loop. In the joints, TNF and IL-17A/F activate synoviocytes, chondrocytes, and osteoclasts, promoting cytokine release, matrix degradation, and bone resorption (11).

Six IL-17 isoforms have been identified (IL-17A-F). Among these, IL-17A, IL-17C, IL-17E, and IL-17F signal through the IL-17RA receptor subunit and play key roles in cutaneous and joint inflammation (12). IL-17A is produced primarily by Th17 and Tc17 cells, but also by γδ T cells, ILC3s, and macrophages (5). Recent evidence shows that mast cells not only store but actively produce IL-17A and interact with tissue-resident memory T cells, potentially contributing to disease recurrence (13).

IL-17A forms homodimers (IL-17A/A) or heterodimers with IL-17F (IL-17A/F), with different affinities for the IL-17RA/RC receptor complex (IL-17A/A > IL-17A/F) (14). Receptor engagement activates Act1 and TRAF6, triggering NF-κB and MAPK signaling and amplifying inflammation (12).

IL-17C, produced mainly by keratinocytes, signals through IL-17RA/RE and acts in an autocrine and paracrine manner, promoting further IL-17A and IL-17C production and sustaining epidermal inflammation (15). IL-17E (IL-25), abundant in psoriatic skin, correlates with neutrophil infiltration and promotes keratinocyte proliferation and macrophage-mediated chemokine release (16,17).

IL-17F, structurally similar to IL-17A, is produced by Th17 cells and other innate lymphocytes. Although less potent than IL-17A, it acts synergistically to induce IL-6 and IL-8 production (18). IL-17F-producing T cells persist in resolved lesions, suggesting a role in disease memory (19).

Emerging evidence highlights additional regulatory influences on IL-17 biology. Testosterone suppresses Th17 differentiation and IL-17 production *via* RORγt inhibition (20). Obesity increases IL-17A-producing epidermal γδ T cells in murine models (21). Psoriatic γδ T cells shift toward glycolytic metabolism to sustain IL-17A production (8). Dysregulated cholesterol pathways in psoriatic keratinocytes provide a mechanistic rationale for the beneficial effects of statins (22,23).

3.2. IL-17 inhibitors in moderate-to-severe psoriasis

IL-17 inhibitors have redefined therapeutic goals in psoriasis, making complete skin clearance achievable for a substantial proportion of patients (Table 2). These agents target either IL-17A, IL-17A/F, or the IL-17RA receptor.

3.2.1. IL-17A inhibitors: secukinumab and ixekizumab

Secukinumab, the first IL-17A inhibitor approved by the FDA and EMA (2015), is indicated for adults and children ≥6 years with

Table 1. Pathogenic role of IL-17 in cardiovascular and metabolic diseases.

System/district	Pathological effect of IL-17	Clinical consequence
Blood vessels	Production of pro-inflammatory cytokines (TNF-α, IL-1, IL-6) and adhesion molecules (ICAM-1, CCL20). Impairs eNOS phosphorylation, reducing nitric oxide production.	Endothelial dysfunction
Atherosclerotic plaque	Leukocyte recruitment, foam-cell formation, endothelial apoptosis. Shifts oxidative balance toward a pro-oxidant state *via* NADPH oxidase activation.	Plaque instability
Metabolic system	Synergizes with TNF-α to impair IRS-1 function and inhibits insulin receptor signaling. Activates the mTOR pathway, sustaining systemic inflammation.	Insulin resistance
Liver	Activates hepatic stellate cells and promotes collagen production.	MASLD
Adipose tissue	Drives 'adipoflammation' by dysregulating adipokines (↑ leptin, ↓ adiponectin).	Visceral obesity

Table 2. Efficacy of IL-17 inhibitors in chronic plaque psoriasis.

Biologic	Clinical trial/ timepoint	PASI75 (%)	PASI90 (%)	PASI100 (%)
Secukinumab	ERASURE—week 12	81.6	59.2	28
	FIXTURE—week 12	77.1	54.2	24.1
	ERASURE—week 52	80.5	60.0	39.2
	ERASURE/FIXTURE extension—year 5	81.1	62.8	35.1
Ixekizumab	UNCOVER1/2/3—week 12	88.7	69.9	37.6
	UNCOVER1/2/3—week 52	95.8	84.2	63.6
	UNCOVER1/2/3—year 5	97.4	90.2	66.5
Brodalumab	AMAGINE1—week 12	83.3	70.3	41.9
	AMAGINE1—week 52	83.1	78.3	67.5
Bimekizumab	BE READY/BE SURE/ BE RADIANT/BE VIVID—week 16	95–97	85–91	59–68
	BE READY/BE SURE/ BE RADIANT/BE VIVID—week 52	88–93	82–91	65–83
	Long-term extension—week 196	NR	88.0	72.6

moderate-to-severe plaque psoriasis and for psoriatic arthritis (PsA). It is administered as 300 mg subcutaneously at weeks 0, 1, 2, 3, 4, then every 4 weeks. In phase III trials, PASI75 was achieved by 81.6% (ERASURE) and 77.1% (FIXTURE) at week 12, and maintained by 80.5% and 84.3% at week 52 (24). In ERASURE, PASI90 and PASI100 at week 52 were 60.0% and 39.2%, respectively. Long-term extension data show sustained responses at year 5 (PASI75/90/100: 81.1%, 62.8%, 35.1%) (25).

Real-world studies confirm these findings, with PASI75/90/100 achieved by 73.6%, 38.5%, and 21.5% at week 12 and maintained by 67.6%, 48.5%, and 32.1% at week 52 (26). Long-term drug survival is high, with persistence rates of 86.8% at 24 months and 66.4% at 72 months (27).

Ixekizumab, a high-affinity IL-17A inhibitor, was approved in 2016 for psoriasis and later for PsA. It is administered as 160 mg at week 0, followed by 80 mg every 2 weeks until week 12, then every 4 weeks. In UNCOVER-1/2/3, PASI75/90/100 at week 12 were 88.7%, 69.9%, and 37.6%, increasing to 95.8%, 84.2%, and 63.6% at week 52 and maintained through 5 years (28,29). Real-world data show comparable effectiveness (7,30,31).

3.2.2. IL-17A/F inhibitor: bimekizumab

Bimekizumab, which neutralizes both IL-17A and IL-17F, was approved by the EMA (2021) and FDA (2023). In phase III trials (BE READY, BE SURE, BE RADIANT, and BE VIVID), PASI90 and PASI100 at week 16 ranged from 85% to 91% and 59%–68%, respectively, with sustained responses at 1 year (82.6%–91% and 65%–83%) and at 4 years (88.0% and 72.6%) (32–36). Real-world data confirm high effectiveness (37).

3.2.3. IL-17RA inhibitor: brodalumab

Brodalumab targets IL-17RA, blocking IL-17A, IL-17F, IL-17C, and IL-17E. In AMAGINE-1, PASI75/90/100 at week 12 were 83.3%, 70.3%, and 41.9%, increasing to 83.1%, 78.3%, and 67.5% at week 52 (38). Similar results were observed in AMAGINE-2/3 (39). Real-world data from the LIBERO study confirm high effectiveness and acceptable safety (40).

3.3. IL-17 pathway in cardiovascular disease

Adults with psoriasis exhibit a consistently increased risk of atherosclerosis and acute coronary syndrome (ACS) (41–44). Chronic systemic inflammation contributes to persistent endothelial injury, promoting endothelial dysfunction and the recruitment of neutrophils, particularly low-density granulocytes, platelets, and Th1-polarized lymphocytes. These processes collectively accelerate atherosclerotic progression and arterial wall thickening, as demonstrated by FDG PET/CT and vascular ultrasound studies (6,41, 45–49). Endothelial cells express IL-17 receptors, particularly IL-17RA. IL-17 stimulation induces TNF-α, IL-1, CCL20, and ICAM-1 production, enhancing leukocyte adhesion and transmigration. IL-17 also activates NADPH oxidase, shifting the redox balance toward oxidative stress and promoting vascular smooth muscle injury (50–54).

Within atherosclerotic plaques, IL-17 promotes lesion expansion by inducing chemokines that attract neutrophils and monocytes. Monocytes differentiate into macrophages that, under IL-17 stimulation, release TNF-α, IL-1, IL-6, and matrix metalloproteinases, contributing to foam-cell formation and plaque instability (50–54). IL-17A also induces endothelial apoptosis, facilitating platelet adhesion and aggregation.

Overall, IL-17 may exert context-dependent vascular effects, with pro-inflammatory activity depending on the local cytokine milieu and interactions with other immune pathways (50,51, 55,56). Mast-cell-associated IL-17A may further contribute to local inflammatory amplification and leukocyte recruitment, potentially reinforcing vascular inflammation (13,51).

Persistent elevation of IL-17 and other markers of endothelial dysfunction, platelet activation, and impaired fibrinolysis correlates with increased risk of major cardiovascular events (6,45, 52,53). Patients with acute myocardial infarction exhibit elevated circulating Th1 and Th17 cells and increased serum IL-17, IL-6, and hsCRP levels, all associated with worse prognosis. Conversely, Treg levels are reduced. Experimental models show that IL-17 inhibition attenuates plaque formation (6,50–56).

3.4. IL-17 pathway in hypertension

Hypertension arises from a complex interplay between immune activation, cytokine signaling, and renal inflammation. Both innate and adaptive immunity contribute, with IL-17A, IL-1β, IL-6, IL-18, IL-22, IL-23, TNF-α, and IFN-γ, alongside macrophages, γδ T cells, and CD4+/CD8+ T cells, playing central roles (6,57–61). Renal inflammation is particularly important in salt-sensitive hypertension. Activation of the NLRP3 inflammasome in renal tubular antigen-presenting cells triggers caspase-1-mediated maturation of IL-1β and IL-18 (62–65). Angiotensin II (ANG2)-dependent hypertension amplifies this pathway, promoting a pro-inflammatory and pro-fibrotic renal microenvironment.

IL-1β and IL-17 impair endothelial nitric oxide synthase (eNOS) phosphorylation, reducing nitric oxide bioavailability and impairing vasodilation. IL-17 appears to be a critical mediator of this effect (65,66). ANG2 also induces miR-214 expression in T cells, enhancing IL-17, TNF-α, IFN-γ, and chemokine production and promoting perivascular fibrosis. Mice lacking miR-214 are protected from oxidative stress and endothelial injury (67).

Hyperglycemia further exacerbates renal inflammation. In diabetic hypertensive mice, tubular epithelial cells exposed to glucose release IL-1β, which polarizes macrophages toward IL-17 and IL-6 production. Blocking IL-1 signaling reduces sodium channel expression and arterial pressure in experimental models, with parallel reductions in major cardiovascular events in clinical studies (68,69).

IL-18 and IL-22 also contribute to hypertension-associated renal inflammation and fibrosis. Mice deficient in IL-18 or IL-22 show protection from renal injury and elevated blood pressure (59–61). In psoriasis, adipose tissue contributes additional angiotensinogen, enhancing ANG2 production and linking metabolic dysfunction, hypertension, and IL-17-driven inflammation (57,70,71).

Although several studies report correlations between psoriasis severity, IL-17A levels, and hypertension, findings remain heterogeneous (72,73).

3.5. IL-17 pathway in diabetes

Psoriasis is strongly associated with type 2 diabetes mellitus (T2DM), with a prevalence of 11%–14% among psoriatic patients (74,75). The two conditions share genetic predispositions and overlapping inflammatory pathways. However, T2DM prevalence does not appear to increase with psoriasis severity or with the presence of psoriatic arthritis (74,76). Both psoriasis and T2DM are characterized by activation of the IL-23/Th17 axis and elevated levels of TNF-α, IL-1β, IL-6, IL-17, IL-22, and IL-23. This inflammatory milieu promotes insulin resistance, a key driver of T2DM. Patients with

severe psoriasis exhibit insulin resistance even in the absence of other metabolic syndrome features, and insulin resistance correlates with psoriasis severity and disease duration (77,78). Improvements in PASI scores following psoriasis treatment are accompanied by reductions in HOMA-IR (78).

TNF-α plays a central role by inhibiting tyrosine kinase activity essential for insulin receptor signaling. IL-17, IL-1β, IL-22, and IL-6 synergize with TNF-α to impair IRS-1 function (70). TNF-α also activates the mTOR pathway in keratinocytes, promoting IL-6, CXCL8, and VEGF production and sustaining inflammation. IL-1β, IL-17A, and IL-22 similarly activate mTOR, contributing to keratinocyte hyperproliferation and impaired differentiation (79,80).mTOR activation also promotes differentiation of effector T cells into Th1, Th2, and Th17 subsets and enhances IL-17 secretion by γδ T cells in response to IL-1β and IL-23 (79). Elevated IL-17 levels have been documented in patients with metabolic syndrome, cardiovascular disease, and type 1 diabetes (52,81).

IL-18 further links psoriasis, obesity, and diabetes. It is elevated in psoriatic lesions and in adipose tissue of obese individuals, correlating with insulin resistance, BMI, and triglyceride levels (52,82). Adipokine dysregulation, characterized by increased leptin, resistin, visfatin, IL-6, and TNF-α and reduced adiponectin, creates a pro-inflammatory environment that promotes insulin resistance and obesity (83,84).

4. Blocking IL-17 in patients with psoriasis and metabolic disorders

This section synthesizes clinical and translational evidence regarding the safety and potential cardiometabolic beneficial effects of IL-17 inhibitors (IL-17i), including secukinumab, ixekizumab, brodalumab, and bimekizumab—in patients with plaque psoriasis and concomitant metabolic dysfunction (Figure 1).

4.1. Cardiovascular safety and MACE

The cardiovascular safety of IL-17 inhibitors is supported by large integrated clinical trial datasets, pharmacovigilance analyses, and multiple systematic reviews/meta-analyses (85–92). In a pooled analysis of 10 phase II/III secukinumab trials (2,725 patient-years), the exposure-adjusted incidence of adjudicated MACE over 52 weeks was comparable across treatment groups: 0.42/100 patient-years (300 mg) and 0.35/100 patient-years (150 mg), similar to etanercept (0.34/100 patient-years) (85). These findings align with systematic reviews showing a neutral effect of IL-17 blockade on cardiovascular risk (88,90,92). Mechanistic data reinforce this safety profile. In the CARIMA trial, 52 weeks of secukinumab significantly improved flow-mediated dilation (FMD), indicating enhanced endothelial function without pro-atherogenic changes (93).

For ixekizumab, long-term pooled analyses similarly reported MACE rates comparable to etanercept (≈0.5/100 patient-years) (94). Some network meta-analyses have suggested higher odds ratios for cardiovascular events with certain IL-17 inhibitors, underscoring the need for individualized cardiovascular risk assessment (89,95).

Brodalumab, which blocks IL-17RA and inhibits multiple IL-17 isoforms, has shown no clear signal of increased MACE risk in available trial and meta-analytic data (38,39,88,92,94).

A recent network meta-analysis of randomized trials reported a reduced incidence of overall cardiovascular events with bimekizumab compared with placebo, supported by moderate-certainty

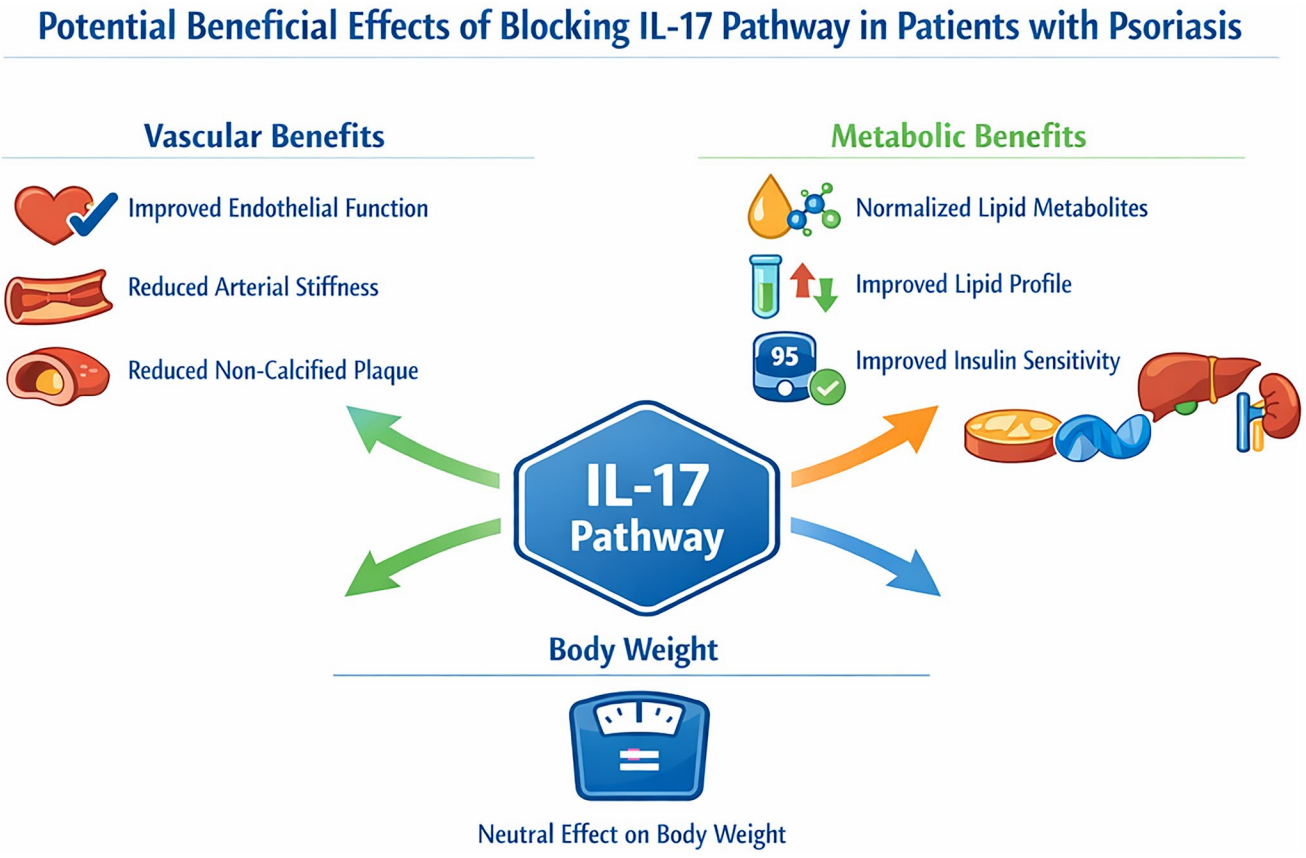

Figure 1. Potential beneficial effects of blocking IL-17 pathway in patients with psoriasis and metabolic comorbidities.

evidence (92). This may reflect the broader anti-inflammatory effect of dual IL-17A/IL-17F inhibition.

Overall, observational and pharmacovigilance data support the cardiovascular safety of IL-17 inhibitors, although heterogeneity across agents warrants continued long-term monitoring (91,92).

4.2. Impact on vascular health and atherosclerosis

Clinical studies targeting the IL-17 pathway suggest measurable effects on selected surrogate markers of subclinical atherosclerosis and vascular function. Psoriasis-associated systemic inflammation is closely linked to endothelial dysfunction, a key early event in atherogenesis. IL-17A, TNF-α, IL-6, IL-1β, IL-23, adipokines contribute to vascular inflammation, oxidative stress, and endothelial apoptosis, promoting plaque instability (96–98).

4.3. Endothelial function and arterial stiffness

Endothelial dysfunction, commonly assessed by FMD, is a strong predictor of cardiovascular outcomes; each 1% increase in FMD corresponds to an estimated 13% reduction in cardiovascular risk (99). In the CARIMA study, secukinumab did not differ from placebo at week 12, but at week 52 it significantly improved FMD in patients with psoriasis, supporting a beneficial effect on endothelial function (93). Additional surrogate markers reinforce these findings. In a non-randomized study comparing IL-17A inhibition with cyclosporine or methotrexate, IL-17 blockade resulted in a 14% improvement in global longitudinal strain and an 11% reduction in arterial stiffness (pulse wave velocity) after 12 months, whereas comparator groups showed minimal changes (100). Improvements in carotid intima-media thickness (IMT) have also been reported in severe psoriasis patients treated with IL-17 inhibitors, suggesting favorable effects on early atherosclerotic remodeling (90,101). Conversely, a small six-month pilot study targeting the IL-23/IL-17 axis showed neutral effects on IMT and PWV, highlighting variability across study designs and follow-up durations (102). In the randomized VIP-S trial, ^18F-FDG PET/CT revealed no significant change in aortic inflammation with secukinumab versus placebo at 12 weeks, suggesting no short-term pro- or anti-inflammatory effect at the level of large vessels (103).

4.4. Coronary plaque characteristics

One of the most compelling translational findings relates to improvements in high-risk coronary plaque features. A prospective observational study showed that biologic therapy improved coronary plaque characteristics in severe psoriasis. IL-17 inhibitors were associated with a 12% reduction in non-calcified coronary plaque burden, greater than the 5% reduction observed with TNF inhibitors (104,105). This is clinically relevant because non-calcified plaques represent the most vulnerable lesions associated with MACE (104,105).

4.5. Metabolic parameters and insulin sensitivity

Metabolomic profiling provides strong evidence that IL-17 inhibition restores lipid homeostasis. A non-targeted metabolomic analysis of ixekizumab demonstrated that dysregulated lipid metabolites, including lysophospholipids, diacylglycerols, and acylcarnitines, normalized to levels comparable to healthy controls, even in patients with coronary heart disease (106). Clinically, a randomized trial comparing IL-17/IL-23 biologics with cyclosporine found better improvements in glucose, lipid, and inflammatory parameters in biologic-treated patients after three months; an independent anti-IL-17 cohort also reported improvements in lipid and inflammatory parameters without changes in body composition (107,108). Additionally, ixekizumab significantly reduced the monocyte-to-HDL-cholesterol ratio (MHR), linking inflammation suppression to improved cardiometabolic risk (109).

4.6. Body mass index

Obesity is not only a comorbidity of psoriasis but also a driver of systemic inflammation through 'adipoflammation.' Visceral adipose tissue secretes pro-inflammatory adipokines (leptin, resistin) and cytokines (TNF-α, IL-6, IL-17), while adiponectin levels are reduced (110,111). Available data suggest that anti-IL-17 therapy is generally weight-neutral, with no meaningful change in body-composition parameters in a prospective anti-IL-17 cohort (108). Cross-sectional analyses show that young patients successfully treated with IL-17 inhibitors may still exhibit higher BMI and waist circumference compared with topical-therapy patients and healthy controls, indicating persistent metabolic burden despite immunologic control (112). Obesity and metabolic syndrome may also modestly reduce IL-17 inhibitor efficacy (107,113).

4.7. Glucose homeostasis and insulin resistance

Data on glucose regulation are promising but conflicting. Short-term randomized trials show that after three months, fasting plasma glucose and fasting insulin levels were significantly lower in IL-17 inhibitor-treated patients compared with cyclosporine (107). Observational studies in young patients on long-term biologics (including secukinumab) report HOMA-IR and TyG index values comparable to healthy controls, suggesting normalization of insulin sensitivity with effective inflammation control (112).

4.8. Hepatic function (MASLD/liver fibrosis)

Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly NAFLD, is highly prevalent in psoriasis (up to 65%) (114). The 'hepato-dermal axis' proposes that cutaneous inflammation promotes hepatic steatosis *via* circulating IL-17 and IL-6 (115). IL-17A activates hepatic stellate cells, promoting collagen deposition and progression toward NASH and fibrosis (115). A systematic review found that IL-17 inhibitors had either neutral (six studies) or beneficial (five studies) effects on liver tests or MASLD markers (114). Long-term secukinumab data show a neutral effect on AST/ALT over 52 weeks (116). Compared with methotrexate, secukinumab demonstrated a safer hepatic profile in patients with metabolic syndrome (117). Pilot studies using the FIB-4 index suggest potential improvement in liver fibrosis with secukinumab (114,118). Brodalumab pooled analyses also indicate possible improvements in early NAFLD markers (114).

4.9. Renal outcomes

Psoriasis is an independent risk factor for chronic kidney disease due to chronic inflammation-mediated glomerular and tubular injury (119). A network meta-analysis found no increased risk of renal adverse events with IL-17 inhibitors compared with placebo (92). Case reports describe improved renal function in severe psoriasis patients with renal impairment treated with ixekizumab, likely due to reduced systemic inflammation (120).

4.10. Mechanisms underlying metabolic benefits

The cardiometabolic improvements observed with IL-17 inhibition, often independent of weight loss, are attributed to targeted suppression of systemic inflammatory pathways linking skin, vasculature, and metabolic organs (89,93). IL-17, together with TNF-α, IL-6, IL-1β, IL-23, and adipokines, drives vascular inflammation and endothelial dysfunction. IL-17 blockade improves FMD and stabilizes high-risk plaques by reducing inflammatory mediators (93,98, 104,105, 121–123). IL-17 inhibition normalizes dysregulated lipid metabolites implicated in atherogenesis (106). By reducing IL-17-driven inflammation, IL-17 inhibitors help normalize glucose metabolism and insulin sensitivity (107,110,112).

5. Discussion

Psoriasis is increasingly recognized as a systemic immunometabolic disease in which inflammatory mediators, including IL-17, TNF-α, IL-6, IL-1β, IL-23, and adipokines, act as central drivers of both cutaneous inflammation and metabolic dysfunction. These inflammatory pathways promote endothelial dysfunction, oxidative stress, adipose-tissue inflammation, and hepatic injury, thereby linking the cutaneous phenotype to the broader spectrum of cardiometabolic comorbidities. The advent of IL-17 inhibitors has transformed psoriasis management, achieving unprecedented levels of skin clearance and demonstrating robust long-term safety. Recent real-life bimekizumab data mirror the efficacy and safety results observed in clinical trials (124,125). Emerging evidence suggests that IL-17 blockade may also modulate selected metabolic and vascular pathways. Although these systemic benefits require further confirmation in dedicated mechanistic and longitudinal studies, the current data support IL-17 as a therapeutic target with relevance extending beyond the skin. None of the IL-17 inhibitors has yet demonstrated reduction in hard cardiovascular outcomes in dedicated randomized controlled trials. Most favorable findings rely largely on surrogate markers of atherosclerosis, such as flow-mediated dilation, pulse wave velocity, and coronary plaque composition. Moreover, many influential studies, including metabolomic analyses and pivotal RCTs, are constrained by small sample sizes and short follow-up periods, limiting statistical power and the robustness of long-term metabolic assessments. In parallel, IL-17 inhibitors do not induce weight loss, so the cardiovascular risk associated with obesity and preexisting metabolic syndrome often persists (108,111,112). Moreover, we acknowledge that at least some observed improvements in cardiovascular or metabolic parameters may reflect reduction in systemic inflammatory burden with effective psoriasis treatment more broadly, rather than a uniquely IL-17-specific effect. Future research must therefore focus on well-designed, long-term prospective studies to determine whether improvements in surrogate endpoints translate into real reductions in clinical MACE rates; in this context, the METABOLyx trial (NCT03440736), which combines secukinumab with lifestyle intervention, represents a pragmatic step toward evaluating the additive value of simultaneously targeting immune-mediated inflammation and traditional metabolic risk factors (126). Dedicated long-term studies are also needed to more precisely define the impact of IL-17 inhibition on diabetes progression and on MASLD and liver fibrosis. Clinical and translational investigations confirm the favorable cardiovascular safety profile of IL-17 inhibitors (secukinumab, ixekizumab, brodalumab, and bimekizumab) in patients with moderate-to-severe psoriasis. The evidence demonstrates that IL-17 blockade confers systemic advantages beyond skin clearance, notably by improving endothelial function at 52 weeks, leading to stabilization of subclinical atherosclerosis through reduction of high-risk non-calcified coronary plaque burden, and effectively restoring dysregulated pro-atherogenic lipid metabolite profiles (93,104–106,109). Furthermore, IL-17 inhibition shows promise in normalizing insulin sensitivity markers in stable disease states and maintaining a neutral or beneficial effect on liver function in patients with MASLD (107,112,114).

A deeper understanding of IL-17-driven immunometabolic interactions will be essential to optimize treatment strategies, refine risk stratification, and improve long-term outcomes for patients with psoriasis and metabolic comorbidities.

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Authors' contributions

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Data availability statement

All data generated or analyzed during this study are included in this article.

References

1. Armstrong AW, Read C. Pathophysiology, clinical presentation, and treatment of psoriasis. JAMA. 2020;323(19):1945–1960. doi: 10.1001/jama.2020.4006.
2. Sieminska I, Pieniawska M, Grzywa TM. The immunology of psoriasis—current concepts in pathogenesis. Clin Rev Allerg Immunol. 2024;66(2):164–191. doi: 10.1007/s12016-024-08991-7.

3. Girolomoni G, Strohal R, Puig L, et al. The role of IL-23 and the IL-23/TH17 immune axis in the pathogenesis and treatment of psoriasis. J Eur Acad Dermatol Venereol. 2017;31(10):1616–1626. doi: 10.1111/jdv.14433.
4. Jaswal A, Kumar A, Patel P, et al. Immunometabolic dysregulation in psoriasis: mechanisms driving inflammation and emerging therapeutic targets. Immunol Invest. 2026:1–27. doi: 10.1080/08820139.2026.2645963.
5. Mills KHG. IL-17 and IL-17-producing cells in protection versus pathology. Nat Rev Immunol. 2023;23(1):38–54. doi: 10.1038/s41577-022-00746-9.
6. Boehncke WH. Systemic inflammation and cardiovascular comorbidity in psoriasis patients: causes and consequences. Front Immunol. 2018;9:579. doi: 10.3389/fimmu.2018.00579.
7. Puig L, Sewerin P, Schuster C, et al. Real-world evidence for ixekizumab in the treatment of psoriasis, psoriatic arthritis, and axial spondyloarthritis: systematic literature review 2022–2023. Adv Ther. 2025;42(9):4224–4254. doi: 10.1007/s12325-025-03258-9.
8. Kao Y-S, Lauterbach M, Lopez Krol A, et al. Metabolic reprogramming of interleukin-17-producing γδ T cells promotes ACC1-mediated de novo lipogenesis under psoriatic conditions. Nat Metab. 2025;7(5):966–984. doi: 10.1038/s42255-025-01276-z.
9. Bridgewood C, Watad A, Russell T, et al. Identification of myeloid cells in the human enthesis as the main source of local IL-23 production. Ann Rheum Dis. 2019;78(7):929–933. doi: 10.1136/annrheumdis-2018-214944.
10. Whitley SK, Li M, Kashem SW, et al. Local IL-23 is required for proliferation and retention of skin-resident memory TH17 cells. Sci Immunol. 2022;7(77):eabq3254. doi: 10.1126/sciimmunol.abq3254.
11. Veale DJ, Fearon U. The pathogenesis of psoriatic arthritis. Lancet. 2018;391(10136):2273–2284. doi: 10.1016/S0140-6736(18)30830-4.
12. Huangfu L, Li R, Huang Y, et al. The IL-17 family in diseases: from bench to bedside. Signal Transduct Target Ther. 2023;8(1):402. doi: 10.1038/s41392-023-01620-3.
13. Benezeder T, Bordag N, Woltsche J, et al. Mast cells express IL17A, IL17F and RORC in lesional psoriatic skin, are activated before therapy and persist in high numbers in a resting state with IL-17A positivity after treatment. J Dermatol Sci. 2025;119(2):53–63. doi: 10.1016/j.jdermsci.2025.05.006.
14. Wright JF, Guo Y, Quazi A, et al. Identification of an interleukin 17F/17A heterodimer in activated human CD4+ T cells. J Biol Chem. 2007;282(18):13447–13455. doi: 10.1074/jbc.M700499200.
15. Han G, Armstrong A, Krueger JG, et al. IL-17C as a driver of inflammation in psoriasis. Adv Ther. 2025;42(11):5451–5467. doi: 10.1007/s12325-025-03363-9.
16. Senra L, Stalder R, Alvarez Martinez D, et al. Keratinocyte-derived IL-17E contributes to inflammation in psoriasis. J Invest Dermatol. 2016;136(10):1970–1980. doi: 10.1016/j.jid.2016.06.009.
17. Borowczyk J, Buerger C, Tadjrischi N, et al. IL-17E (IL-25) and IL-17A differentially affect the functions of human keratinocytes. J Invest Dermatol. 2020;140(7):1379–1389.e2. doi: 10.1016/j.jid.2019.12.013.
18. Burns LA, Maroof A, Marshall D, et al. Presence, function, and regulation of IL-17F-expressing human CD4 + T cells. Eur J Immunol. 2020;50(4):568–580. doi: 10.1002/eji.201948138.
19. Peng L, Liu W, Cheng Y, et al. IL-17A/F double producing T cells, unstable Tregs and quiescent TRMs in clinically healed lesions are potential cellular candidates for recurrence of psoriasis. Clin Immunol. 2024;266:110328. doi: 10.1016/j.clim.2024.110328.
20. Binayke A, Dalal R, Suri C, et al. Testosterone suppresses IL-17 expression by targeting RORγt functions. Eur J Immunol. 2025;55(8):e70016. doi: 10.1002/eji.70016.
21. Lawler W, Castellanos T, Engel E, et al. Impact of obesity on the CCR6-CCL20 axis in epidermal γδ T cells and IL-17A production in murine wound healing and psoriasis. J Immunol. 2025;214(1):153–166. doi: 10.1093/jimmun/vkae011.
22. Møller LBP, Kromann B, Kabatnik S, et al. Spatial proteomic profiling reveals increased levels of cholesterol synthesis proteins in psoriasis vulgaris. J Invest Dermatol. 2025;145(12):3051–3063.e2. doi: 10.1016/j.jid.2025.05.002.
23. Socha M, Pietrzak A, Grywalska E, et al. The effect of statins on psoriasis severity: a meta-analysis of randomized clinical trials. Arch Med Sci. 2020;16(1):1–7. doi: 10.5114/aoms.2019.90343.
24. Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in plaque psoriasis—results of two phase 3 trials. N Engl J Med. 2014;371(4):326–338. doi: 10.1056/NEJMoa1314258.
25. Langley RG, Sofen H, Dei-Cas I, et al. Secukinumab long-term efficacy and safety in psoriasis through to year 5 of treatment: results of a randomized extension of the phase III ERASURE and FIXTURE trials. Br J Dermatol. 2023;188(2):198–207. doi: 10.1093/bjd/ljac040.
26. Chiricozzi A, Balato A, Conrad C, et al. Secukinumab demonstrates improvements in absolute and relative psoriasis area severity indices in moderate-to-severe plaque psoriasis: results from a European, multicentric, retrospective, real-world study. J Dermatolog Treat. 2020;31(5):476–483. doi: 10.1080/09546634.2019.1671577.
27. Galluzzo M, Trovato E, Talamonti M, et al. Long-term persistence rate of secukinumab in psoriatic patients: a six-year multicenter, real-world experience, retrospective study. J Clin Med. 2024;13(13):3864. doi: 10.3390/jcm13133864.
28. Papp KA, Leonardi CL, Blauvelt A, et al. Ixekizumab treatment for psoriasis: integrated efficacy analysis of three double-blinded, controlled studies (UNCOVER-1, UNCOVER-2, UNCOVER-3). Br J Dermatol. 2018;178(3):674–681. doi: 10.1111/bjd.16050.
29. Blauvelt A, Lebwohl MG, Mabuchi T, et al. Long-term efficacy and safety of ixekizumab: a 5-year analysis of the UNCOVER-3 randomized controlled trial. J Am Acad Dermatol. 2021;85(2):360–368. doi: 10.1016/j.jaad.2020.11.022.
30. Kojanova M, Hugo J, Velackova B, et al. Efficacy, safety, and drug survival of patients with psoriasis treated with IL-17 inhibitors—brodalumab, ixekizumab, and secukinumab: real-world data from the Czech Republic BIOREP registry. J Dermatolog Treat. 2022;33(6):2827–2837. doi: 10.1080/09546634.2022.2082354.
31. Herrera-Acosta E, Garriga-Martina GG, Suárez-Pérez JA, et al. Comparative study of the efficacy and safety of secukinumab vs ixekizumab in moderate-to-severe psoriasis after 1 year of treatment: real-world practice. Dermatol Ther. 2020;33(3). doi: 10.1111/dth.13313.
32. Gordon KB, Foley P, Krueger JG, et al. Bimekizumab efficacy and safety in moderate to severe plaque psoriasis (BE READY): a multicentre, double-blind, placebo-controlled, randomised withdrawal phase 3 trial. Lancet. 2021;397(10273):475–486. doi: 10.1016/S0140-6736(21)00126-4.
33. Warren RB, Blauvelt A, Bagel J, et al. Bimekizumab versus adalimumab in plaque psoriasis. N Engl J Med. 2021;385(2):130–141. doi: 10.1056/NEJMoa2102388.

34. Reich K, Warren RB, Lebwohl M, et al. Bimekizumab versus secukinumab in plaque psoriasis. N Engl J Med. 2021;385(2):142–152. doi: 10.1056/NEJMoa2102383.
35. Reich K, Papp KA, Blauvelt A, et al. Bimekizumab versus ustekinumab for the treatment of moderate to severe plaque psoriasis (BE VIVID): efficacy and safety from a 52-week, multicentre, double-blind, active comparator and placebo controlled phase 3 trial. Lancet. 2021;397(10273):487–498. doi: 10.1016/S0140-6736(21)00125-2.
36. Blauvelt A, Langley RG, Lebwohl M, et al. Bimekizumab durability of efficacy through 196 weeks and safety through 4 years in patients with moderate to severe plaque psoriasis: results from the BE BRIGHT open-label extension trial. J Am Acad Dermatol. 2025;93(3):644–653. doi: 10.1016/j.jaad.2025.04.038.
37. Fratton Z, Bighetti S, Bettolini L, et al. Real-world experience of bimekizumab in a cohort of 109 patients over 48 weeks and identification of predictive factors for an early super response and risk of adverse events. Psoriasis (Auckl). 2025;15:145–158. doi: 10.2147/PTT.S514249.
38. Papp KA, Reich K, Paul C, et al. A prospective phase III, randomized, double-blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis. Br J Dermatol. 2016;175(2):273–286. doi: 10.1111/bjd.14493.
39. Lebwohl M, Strober B, Menter A, et al. Phase 3 studies comparing brodalumab with ustekinumab in psoriasis. N Engl J Med. 2015;373(14):1318–1328. doi: 10.1056/NEJMoa1503824.
40. von Kiedrowski R, Hinz T, Mauer G, et al. Management of moderate to severe psoriasis with brodalumab—Real-world evidence from the LIBERO study. J Eur Acad Dermatol Venereol. 2024;38(11):2156–2166. doi: 10.1111/jdv.19974.
41. Korman NJ. Management of psoriasis as a systemic disease: What is the evidence? Br J Dermatol. 2020;182(4):840–848. doi: 10.1111/bjd.18245.
42. Gelfand JM, Neimann AL, Shin DB, et al. Risk of myocardial infarction in patients with psoriasis. JAMA. 2006;296(14):1735–1741. doi: 10.1001/jama.296.14.1735.
43. Visseren FLJ, Mach F, Smulders YM, et al. 2021 esc guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2021;42(34):3227–3337. doi: 10.1093/eurheartj/ehab484.
44. Bu J, Ding R, Zhou L, et al. Epidemiology of psoriasis and comorbid diseases: a narrative review. Front Immunol. 2022;13:880201. doi: 10.3389/fimmu.2022.880201.
45. Egeberg A, Skov L, Joshi AA, et al. The relationship between duration of psoriasis, vascular inflammation, and cardiovascular events. J Am Acad Dermatol. 2017;77(4):650–656.e3. doi: 10.1016/j.jaad.2017.06.028.
46. Naik HB, Natarajan B, Stansky E, et al. Severity of psoriasis associates with aortic vascular inflammation detected by FDG PET/CT and neutrophil activation in a prospective observational study. Arterioscler Thromb Vasc Biol. 2015;35(12):2667–2676. doi: 10.1161/ATVBAHA.115.306460.
47. Youn SW, Kang SY, Kim SA, et al. Subclinical systemic and vascular inflammation detected by 18 F-fluorodeoxyglucose positron emission tomography/computed tomography in patients with mild psoriasis. J Dermatol. 2015;42(6):559–566. doi: 10.1111/1346-8138.12859.
48. Hjuler KF, Gormsen LC, Vendelbo MH, et al. Increased global arterial and subcutaneous adipose tissue inflammation in patients with moderate-to-severe psoriasis. Br J Dermatol. 2017;176(3):732–740. doi: 10.1111/bjd.15149.
49. Gonzalez-Cantero A, Gonzalez-Cantero J, Sanchez-Moya AI, et al. Subclinical atherosclerosis in psoriasis. Usefulness of femoral artery ultrasound for the diagnosis, and analysis of its relationship with insulin resistance. PLoS One. 2019;14(2):e0211808. doi: 10.1371/journal.pone.0211808.
50. Man AM, Orăsan MS, Hoteiuc OA, et al. Inflammation and psoriasis: a comprehensive review. Int J Mol Sci. 2023;24(22):16095. doi: 10.3390/ijms242216095.
51. Sajja AP, Joshi AA, Teague HL, et al. Potential immunological links between psoriasis and cardiovascular disease. Front Immunol. 2018;9:1234. doi: 10.3389/fimmu.2018.01234.
52. DE Luca DA, Papara C, Hawro T, et al. Psoriasis and diabetes: a review of the pathophysiological and therapeutic interconnections. Minerva Med. 2025;116(3):195–222. doi: 10.23736/S0026-4806.24.09570-3.
53. Nielsen HJ, Christensen IJ, Svendsen MN, et al. Elevated plasma levels of vascular endothelial growth factor and plasminogen activator inhibitor-1 decrease during improvement of psoriasis. Inflamm Res. 2002;51(11):563–567. doi: 10.1007/PL00012428.
54. Zhou Q, Mrowietz U, Rostami-Yazdi M. Oxidative stress in the pathogenesis of psoriasis. Free Radic Biol Med. 2009;47(7):891–905. doi: 10.1016/j.freeradbiomed.2009.06.033.
55. Cheng X, Yu X, Ding Y-J, et al. The Th17/Treg imbalance in patients with acute coronary syndrome. Clin Immunol. 2008;127(1):89–97. doi: 10.1016/j.clim.2008.01.009.
56. Erbel C, Chen L, Bea F, et al. Inhibition of IL-17A attenuates atherosclerotic lesion development in ApoE-deficient mice. J Immunol. 2009;183(12):8167–8175. doi: 10.4049/jimmunol.0901126.
57. Deussen A, Kopaliani I. Targeting inflammation in hypertension. Curr Opin Nephrol Hyperten. 2023;32(2):111–117. doi: 10.1097/MNH.0000000000000862.
58. Cai T, Zhang Y, Ho Y-L, et al. Association of interleukin 6 receptor variant with cardiovascular disease effects of interleukin 6 receptor blocking therapy. JAMA Cardiol. 2018;3(9):849–857. doi: 10.1001/jamacardio.2018.2287.
59. Thomas JM, Ling YH, Huuskes B, et al. IL-18 (Interleukin-18) produced by renal tubular epithelial cells promotes renal inflammation and injury during deoxycorticosterone/salt-induced hypertension in mice. Hypertension. 2021;78(5):1296–1309. doi: 10.1161/HYPERTENSIONAHA.120.16437.
60. Lu Y, Peng L, Li X, et al. Changes in serum IL-22 level in patients with hypertensive renal damage and its clinical significance. Zhong Nan Da Xue Xue Bao Yi Xue Ban. 2019;44(8):871–877. doi: 10.11817/j.issn.1672-7347.2019.180680.
61. Wang W, Lu Y, Hu X, et al. Interleukin-22 exacerbates angiotensin II-induced hypertensive renal injury. Int Immunopharmacol. 2022;109:108840. doi: 10.1016/j.intimp.2022.108840.
62. Pitzer A, Elijovich F, Laffer CL, et al. DC ENaC-dependent inflammasome activation contributes to salt-sensitive hypertension. Circ Res. 2022;131(4):328–344. doi: 10.1161/CIRCRESAHA.122.320818.
63. Barbaro NR, Foss JD, Kryshtal DO, et al. Dendritic cell amiloride-sensitive channels mediate sodium-induced inflammation and hypertension. Cell Rep. 2017;21(4):1009–1020. doi: 10.1016/j.celrep.2017.10.002.
64. Hou Y, Wang Q, Han B, et al. CD36 promotes NLRP3 inflammasome activation via the mtROS pathway in renal tubular epithelial cells of diabetic kidneys. Cell Death Dis. 2021;12(6):523. doi: 10.1038/s41419-021-03813-6.
65. Li X, Zhang Z, Luo M, et al. NLRP3 inflammasome contributes to endothelial dysfunction in angiotensin II-induced hypertension in mice. Microvasc Res. 2022;143:104384. doi: 10.1016/j.mvr.2022.104384.

66. Nguyen H, Chiasson VL, Chatterjee P, et al. Interleukin-17 causes Rho-kinase-mediated endothelial dysfunction and hypertension. Cardiovasc Res. 2013;97(4):696–704. doi: 10.1093/cvr/cvs422.
67. Nosalski R, Siedlinski M, Denby L, et al. T-cell–derived miRNA-214 mediates perivascular fibrosis in hypertension. Circ Res. 2020;126(8):988–1003. doi: 10.1161/CIRCRESAHA.119.315428.
68. Rothman AM, MacFadyen J, Thuren T, et al. Effects of interleukin-1β inhibition on blood pressure, incident hypertension, and residual inflammatory risk. Hypertension. 2020;75(2):477–482. doi: 10.1161/HYPERTENSIONAHA.119.13642.
69. Veiras LC, Bernstein EA, Cao D, et al. Tubular IL-1β induces salt sensitivity in diabetes by activating renal macrophages. Circ Res. 2022;131(1):59–73. doi: 10.1161/CIRCRESAHA.121.320239.
70. Benigni A, Cassis P, Remuzzi G. Angiotensin II revisited: new roles in inflammation, immunology and aging. EMBO Mol Med. 2010;2(7):247–257. doi: 10.1002/emmm.201000080.
71. Trovato E, Rubegni P, Prignano F. Place in therapy of anti-IL-17 and 23 in psoriasis according to the severity of comorbidities: a focus on cardiovascular disease and metabolic syndrome. Expert Opin Biol Ther. 2022;22(12):1443–1448. doi: 10.1080/14712598.2022.2093106.
72. Takeshita J, Wang S, Shin DB, et al. Effect of psoriasis severity on hypertension control. JAMA Dermatol. 2015;151(2):161–169. doi: 10.1001/jamadermatol.2014.2094.
73. Madhur MS, Lob HE, McCann LA, et al. Interleukin 17 promotes angiotensin II–induced hypertension and vascular dysfunction. Hypertension. 2010;55(2):500–507. doi: 10.1161/HYPERTENSIONAHA.109.145094.
74. Wan MT, Shin DB, Hubbard RA, et al. Psoriasis and the risk of diabetes: a prospective population-based cohort study. J Am Acad Dermatol. 2018;78(2):315–322.e1. doi: 10.1016/j.jaad.2017.10.050.
75. Holm JG, Thomsen SF. Type 2 diabetes and psoriasis: links and risks. Psoriasis (Auckl). 2019;9:1–6. doi: 10.2147/PTT.S159163.
76. Brazzelli V, Maffioli P, Bolcato V, et al. Psoriasis and diabetes, a dangerous association: evaluation of insulin resistance, lipid abnormalities, and cardiovascular risk biomarkers. Front Med (Lausanne). 2021;8:605691. doi: 10.3389/fmed.2021.605691.
77. Abdel-Moneim A, Bakery HH, Allam G. The potential pathogenic role of IL-17/Th17 cells in both type 1 and type 2 diabetes mellitus. Biomed Pharmacother. 2018;101:287–292. doi: 10.1016/j.biopha.2018.02.103.
78. Wen S, Liu C, Li Y, et al. Psoriasis exacerbates the state of insulin resistance in patients with type 2 diabetes. Diabetes Metab Syndr Obes. 2021;14:2389–2397. doi: 10.2147/DMSO.S312420.
79. Karagianni F, Pavlidis A, Malakou LS, et al. Predominant role of mTOR signaling in skin diseases with therapeutic potential. Int J Mol Sci. 2022;23(3):1693. doi: 10.3390/ijms23031693.
80. Patel AB, Tsilioni I, Weng Z, et al. TNF stimulates IL -6, CXCL 8 and VEGF secretion from human keratinocytes via activation of mTOR, inhibited by tetramethoxyluteolin. Exp Dermatol. 2018;27(2):135–143. doi: 10.1111/exd.13461.
81. Sarandi E, Krueger-Krasagakis S, Tsoukalas D, et al. Psoriasis immunometabolism: progress on metabolic biomarkers and targeted therapy. Front Mol Biosci. 2023;10:1201912. doi: 10.3389/fmolb.2023.1201912.
82. Companjen A, van der Wel L, van der Fits L, et al. Elevated interleukin-18 protein expression in early active and progressive plaque-type psoriatic lesions. Eur Cytokine Netw. 2004;15(3):210–216.
83. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. J Clin Endocrinol Metab. 2004;89(6):2548–2556. doi: 10.1210/jc.2004-0395.
84. Abramczyk R, Queller JN, Rachfal AW, et al. Diabetes and psoriasis: different sides of the same prism. Diabetes Metab Syndr Obes. 2020;13:3571–3577. doi: 10.2147/DMSO.S273147.
85. van de Kerkhof PCM, Griffiths CEM, Reich K, et al. Secukinumab long-term safety experience: a pooled analysis of 10 phase II and III clinical studies in patients with moderate to severe plaque psoriasis. J Am Acad Dermatol. 2016;75(1):83–98.e4. doi: 10.1016/j.jaad.2016.03.024.
86. Balato A, Burlando M, Campanati A, et al. Strategies for optimal use of biological therapies in managing psoriasis: focus on secukinumab. Dermatol Ther (Heidelb). 2025;15(11):3089–3108. doi: 10.1007/s13555-025-01515-x.
87. Raby M, Balusson F, Oger E, et al. Interleukin-17 inhibitors and early major adverse cardiovascular events. JAMA Dermatol. 2025;161(11):1107–1115. doi: 10.1001/jamadermatol.2025.2972.
88. Ni R, Zheng J, Varghese J, et al. The Impact of interleukin-17 inhibitors on major adverse cardiovascular events in psoriasis or psoriatic arthritis patients naive to biologic agents: a systematic review and meta-analysis of randomized controlled trials. Cureus. 2024;16(5):e60980. doi: 10.7759/cureus.60980.
89. Terui H, Asano Y. Biologics for reducing cardiovascular risk in psoriasis patients. J Clin Med. 2023;12(3):1162. doi: 10.3390/jcm12031162.
90. González-Cantero A, Ortega-Quijano D, Álvarez-Díaz N, et al. Impact of biological agents on imaging and biomarkers of cardiovascular disease in patients with psoriasis: a systematic review and meta-analysis of randomized placebo-controlled trials. J Invest Dermatol. 2021;141(10):2402–2411. doi: 10.1016/j.jid.2021.03.024.
91. Al-Yafeai Z, Sondhi M, Vadlamudi K, et al. Novel anti-psoriasis agent-associated cardiotoxicity, analysis of the FDA adverse event reporting system (FAERS). Int J Cardiol. 2024;402:131819. doi: 10.1016/j.ijcard.2024.131819.
92. Shi A, Shu Y, Haddad JE, et al. Cardiovascular and kidney outcomes after systemic treatment for plaque psoriasis: a systematic review and network meta-analysis. Dermatol Ther (Heidelb). 2025;15(9):2455–2482. doi: 10.1007/s13555-025-01472-5.
93. von Stebut E, Reich K, Thaçi D, et al. Impact of secukinumab on endothelial dysfunction and other cardiovascular disease parameters in psoriasis patients over 52 weeks. J Invest Dermatol. 2019;139(5):1054–1062. doi: 10.1016/j.jid.2018.10.042.
94. Lockshin B, Balagula Y, Merola JF. Interleukin 17, inflammation, and cardiovascular risk in patients with psoriasis. J Am Acad Dermatol. 2018;79(2):345–352. doi: 10.1016/j.jaad.2018.02.040.
95. Garshick MS, Ward NL, Krueger JG, et al. Cardiovascular risk in patients with psoriasis. J Am Coll Cardiol. 2021;77(13):1670–1680. doi: 10.1016/j.jacc.2021.02.009.
96. Gisondi P, Bellinato F, Girolomoni G, et al. Pathogenesis of chronic plaque psoriasis and its intersection with cardio-metabolic comorbidities. Front Pharmacol. 2020;11:117. doi: 10.3389/fphar.2020.00117.
97. Piaserico S, Orlando G, Messina F. Psoriasis and cardiometabolic diseases: shared genetic and molecular pathways. Int J Mol Sci. 2022;23(16):9063. doi: 10.3390/ijms23169063.

98. Karbach S, Croxford AL, Oelze M, et al. Interleukin 17 drives vascular inflammation, endothelial dysfunction, and arterial hypertension in psoriasis-like skin disease. Arterioscler Thromb Vasc Biol. 2014;34(12):2658–2668. doi: 10.1161/ATVBAHA.114.304108.
99. Inaba Y, Chen JA, Bergmann SR. Prediction of future cardiovascular outcomes by flow-mediated vasodilatation of brachial artery: a meta-analysis. Int J Cardiovasc Imaging. 2010;26(6):631–640. doi: 10.1007/s10554-010-9616-1.
100. Makavos G, Ikonomidis I, Andreadou I, et al. Effects of Interleukin 17A inhibition on myocardial deformation and vascular function in psoriasis. Can J Cardiol. 2020;36(1):100–111. doi: 10.1016/j.cjca.2019.06.021.
101. Piros ÉA, Szabó Á, Rencz F, et al. Impact of interleukin-17 inhibitor therapy on arterial intima-media thickness among severe psoriatic patients. Life (Basel). 2021;11(9):919. doi: 10.3390/life11090919.
102. Marovt M, Marko PB, Pirnat M, et al. Effect of biologics targeting interleukin-23/-17 axis on subclinical atherosclerosis: results of a pilot study. Clin Exp Dermatol. 2020;45(5):560–564. doi: 10.1111/ced.14180.
103. Gelfand JM, Shin DB, Duffin KC, et al. A Randomized placebo-controlled trial of secukinumab on aortic vascular inflammation in moderate-to-severe plaque psoriasis (VIP-S). J Invest Dermatol. 2020;140(9):1784–1793.e2. doi: 10.1016/j.jid.2020.01.025.
104. Elnabawi YA, Dey AK, Goyal A, et al. Coronary artery plaque characteristics and treatment with biologic therapy in severe psoriasis: results from a prospective observational study. Cardiovasc Res. 2019;115(4):721–728. doi: 10.1093/cvr/cvz009.
105. Ji L, Ravi S, Wright L, et al. Psoriasis treatments in the stabilization of atherosclerosis: a systematic review. Arch Dermatol Res. 2024;317(1):159. doi: 10.1007/s00403-024-03625-6.
106. Cao H, Su S, Yang Q, et al. Metabolic profiling reveals interleukin-17A monoclonal antibody treatment ameliorate lipids metabolism with the potentiality to reduce cardiovascular risk in psoriasis patients. Lipids Health Dis. 2021;20(1):16. doi: 10.1186/s12944-021-01441-9.
107. Jiang W, Li Q, Zheng W. The impact of biologics targeting the IL-17 and IL-23 pathways on metabolic indicators in plaque psoriasis. Arch Dermatol Res. 2025;317(1):643. doi: 10.1007/s00403-025-04174-2.
108. Piros ÉA, Szabó Á, Rencz F, et al. Anti-interleukin-17 therapy of severe psoriatic patients results in an improvement of serum lipid and inflammatory parameters' levels, but has no effect on body composition parameters. Life (Basel). 2021;11(6):535. doi: 10.3390/life11060535.
109. Tamer F, Kucukhemek F, Gulekon A. Monocyte to high-density lipoprotein cholesterol ratio decreased in patients with psoriasis treated with ixekizumab. Rev Invest Clin. 2023;75(4):187–192. doi: 10.24875/RIC.23000085.
110. von Stebut E, Boehncke W-H, Ghoreschi K, et al. IL-17A in psoriasis and beyond: cardiovascular and metabolic implications. Front Immunol. 2019;10:3096. doi: 10.3389/fimmu.2019.03096.
111. Zafiriou E, Daponte AI, Siokas V, et al. Depression and obesity in patients with psoriasis and psoriatic arthritis: Is IL-17-mediated immune dysregulation the connecting Link? Front Immunol. 2021;12:699848. doi: 10.3389/fimmu.2021.699848.
112. Merzel Šabović EK, Kraner Šumenjak T, Janić M. Residual metabolic burden in young psoriasis patients successfully treated with biologics. Arch Dermatol Res. 2024;316(9):647. doi: 10.1007/s00403-024-03403-4.
113. Xia Y, Lan J, Yang J, et al. Saturated fatty acid-induced neutrophil extracellular traps contribute to exacerbation and biologic therapy resistance in obesity-related psoriasis. Cell Mol Immunol. 2025;22(6):597–611. doi: 10.1038/s41423-025-01278-7.
114. González Fernández J, Prieto-Torres L, Ara Martín M, et al. MASLD and liver fibrosis in patients with psoriasis receiving IL-17 or IL-23 inhibitors: a systematic review. Ther Adv Gastroenterol. 2025;18:17562848251335824. doi: 10.1177/17562848251335824.
115. Olveira A, Augustin S, Benlloch S, et al. The essential role of IL-17 as the pathogenetic link between psoriasis and metabolic-associated fatty liver disease. Life (Basel). 2023;13(2):419. doi: 10.3390/life13020419.
116. Gerdes S, Pinter A, Papavassilis C, et al. Effects of secukinumab on metabolic and liver parameters in plaque psoriasis patients. J Eur Acad Dermatol Venereol. 2020;34(3):533–541. doi: 10.1111/jdv.16004.
117. Gisondi P, Bellinato F, Bruni M, et al. Methotrexate vs secukinumab safety in psoriasis patients with metabolic syndrome. Dermatol Ther. 2020;33(6):e14281. doi: 10.1111/dth.14281.
118. Magdaleno-Tapial J, López-Martí C, Ortiz-Salvador JM, et al. Can secukinumab improve liver fibrosis? A pilot prospective study of 10 psoriatic patients. Dermatol Ther. 2021;34(5). doi: 10.1111/dth.15065.
119. Wan J, Wang S, Haynes K, et al. Risk of moderate to advanced kidney disease in patients with psoriasis: population based cohort study. BMJ. 2013;347(Oct15 7):f5961–f5961. doi: 10.1136/bmj.f5961.
120. Amoruso GF, Nisticò SP, Iannone L, et al. Ixekizumab may improve renal function in psoriasis. Healthcare (Basel). 2021;9(5):543. doi: 10.3390/healthcare9050543.
121. Elnabawi YA, Oikonomou EK, Dey AK, et al. Association of biologic therapy with coronary inflammation in patients with psoriasis as assessed by perivascular fat attenuation index. JAMA Cardiol. 2019;4(9):885–891. doi: 10.1001/jamacardio.2019.2589.
122. Berg AR, Hong CG, Svirydava M, et al. Association of S100A8/A9 with lipid-rich necrotic core and treatment with biologic therapy in patients with psoriasis: results from an observational cohort study. J Invest Dermatol. 2022;142(11):2909–2919. doi: 10.1016/j.jid.2022.05.1085.
123. Schüler R, Brand A, Klebow S, et al. Antagonization of IL-17A attenuates skin inflammation and vascular dysfunction in mouse models of psoriasis. J Invest Dermatol. 2019;139(3):638–647. doi: 10.1016/j.jid.2018.09.021.
124. Hagino T, Onda M, Saeki H, et al. Effectiveness of bimekizumab for genital, nail, and scalp lesions with psoriasis: a 24-week real-world study. J Dermatol. 2024;51(12):1658–1664. doi: 10.1111/1346-8138.17427.
125. Hagino T, Saeki H, Fujimoto E, et al. Effectiveness of long-term bimekizumab treatment and predictive factors for responders in moderate-to-severe psoriasis: a 52-week real-world study. J Dermatol. 2025;52(2):317–328. doi: 10.1111/1346-8138.17532.
126. Pinter A, Schwarz P, Gerdes S, et al. Biologic treatment in combination with lifestyle intervention in moderate to severe plaque psoriasis and concomitant metabolic syndrome: rationale and methodology of the METABOLyx randomized controlled clinical trial. Nutrients. 2021;13(9):3015. doi: 10.3390/nu13093015.