Revista Médica del
Hospital General de México

PERMANYER

Check for updates

REVIEW ARTICLE

Biological therapy in the reduction of cardiovascular risk in patients with psoriasis

Andrés Tirado-Sánchez

Internal Medicine Service, Hospital General de Zona No.30, Instituto Mexicano del Seguro Social, Mexico City, Mexico

Abstract

Psoriasis is a chronic inflammatory disease that primarily affects the skin, and its complications include a predisposition to atherosclerosis and cardiovascular disease (CVD), with this risk related to the severity of psoriasis. The mechanisms by which psoriasis predisposes to CVD are not clear. They are attributed to persistent chronic inflammation, which is a common factor in both diseases. However, timely recognition of psoriasis and initiation of systemic therapy may improve the prognosis of the disease. The hypothesis that the inflammatory cascade activated in psoriasis contributes to the atherosclerotic process provides a basis for suggesting that anti-inflammatory therapy that ameliorates psoriasis activity would also reduce CVD risk. Biological therapy that inhibits certain proinflammatory cytokines, such as tumor necrosis factor-α, interleukin (IL)-12/23, and IL-17, has a direct effect on the development of psoriasis and, in addition to reducing the risk of developing psoriasis, may improve vascular damage. However, the available information is not entirely conclusive, and further studies are needed to define the true role of these drugs in the prevention and prognosis of CVD in patients with severe forms of psoriasis and with various comorbidities. This review analyzes recent studies that suggest a protective effect of biologic therapies in the risk of CVD in patients with psoriasis.

Keywords: *Psoriasis. Biological therapy. Cardiovascular diseases. Proinflammatory cytokines.*

Introduction

Psoriasis is a chronic inflammatory skin disease characterized by an increase in the speed of hematopoiesis that causes hyperplasia of the epidermis, clinically resulting in the formation of indurated erythematous squamous plaques[1]. Psoriasis vulgaris is far from being a disease with an exclusive impact on the skin, it is a systemic disease that seriously affects the general condition of the individual and can lead to serious complications, even leading to the death of the patient[2]. The causes of the disease are unknown, although its pathogenesis includes genetic and immunological aspects, and is also associated with different external factors that can exacerbate psoriasis, such as psychological stress, changes in environmental climate, infectious diseases, medications, physiological states such as pregnancy, among others[3]. The prevalence of the disease varies according to the geographical area, although it is accepted that the global prevalence is approximately 2%[4]; In Mexico, it is estimated that the prevalence is in line with that referred to worldwide.

Psoriasis predisposes to the development of cardiovascular disease (CVD) (25% increase in relative risk), with a relationship directly proportional to the severity of the disease[5]. The risk increases if the patient has other comorbidities associated with CVD such as obesity, dyslipidemia, hypertension, diabetes mellitus, and metabolic syndrome[4]. Chronic and persistent inflammation (PCI),

Correspondence:
Andrés Tirado-Sánchez
E-mail: atsdermahgm@gmail.com

Date of reception: 14-07-2023
Date of acceptance: 06-02-2024
DOI: 10.24875/HGMX.23000052

Available online: 05-02-2025
Rev Med Hosp Gen Mex. 2025;88(1)27-33
www.hospitalgeneral.mx

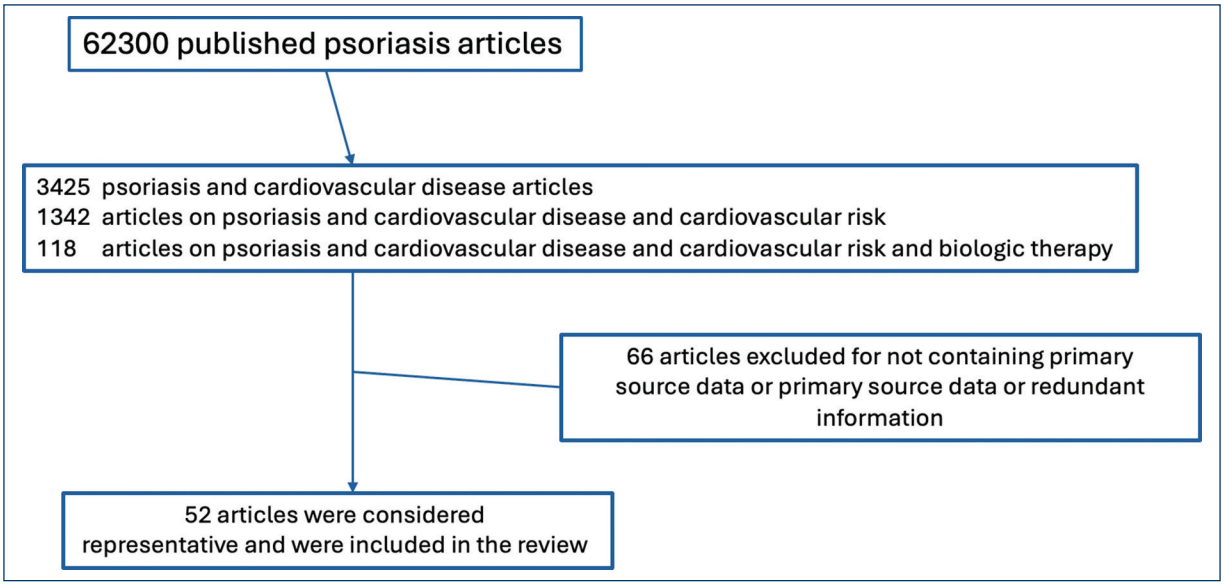

Figure 1. Search criteria and selection of the most representative articles.

which involves proinflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interferon γ (IFN-γ), interleukin (IL)-6, IL-8, IL-12, IL-17A, and IL-18, is a common factor in these diseases, including psoriasis[6]. This PCI directly contributes to the development of endothelial dysfunction, favoring atherosclerosis and CVD[7].

The CVDs that increase in prevalence in patients with psoriasis are mainly acute myocardial infarction and ischemic heart disease, in addition to thromboembolic disease and cerebrovascular events[8]. This makes it necessary to routinely review the cardiovascular health status of the patient with psoriasis and determine the strategy to be followed, which includes modifications in the patient's lifestyle, treatment of comorbidities, and control of PCI associated with psoriasis.

The development of biological therapy has considerably changed the evolution of psoriasis. Recently, it has been suggested that this therapy can effectively reduce cardiovascular risk[9]. This review will discuss the most recent studies suggesting a protective effect of biologic therapies on CVD risk in patients with psoriasis.

Material and methods

A narrative review, through searching PubMed, EMBASE, MEDLINE, and Web of Science up to January 2023, was conducted to identify all studies documenting the use of biologic therapy in patients with psoriasis and evaluating cardiovascular risk modification.

The following search terms were used alone or in combination with the Boolean operators "AND," "OR:" "Psoriasis," "Biological therapy," "cardiovascular risk," "therapy" and "proinflammatory cytokines." We did not apply any temporal (except for the date of closure of the search), study design, or language restrictions. We focused on full-text articles but considered abstracts if relevant (Fig. 1).

Results and discussion

The psoriasis-atherosclerosis-CVD (PAC) triad

The common factor that the components of the PAC triad have is PCI, a factor that also contributes to the development of other comorbidities such as metabolic syndrome, obesity, dyslipidemia, and diabetes mellitus[4]. This PCI is one of the triggers of psoriasis in genetically predisposed individuals; as part of the natural history of the disease, psoriasis can contribute to the development of endothelial dysfunction and atherosclerosis, directly influencing the appearance of CVD, which can manifest itself in less than a decade of development of psoriasis, a process that is part of the so-called "psoriatic march"[10] (Fig. 2).

Although endothelial dysfunction can be associated with different diseases such as hypertension, diabetes, insulin resistance, and dyslipidemia, in the case of patients with psoriasis, this dysfunction occurs even in

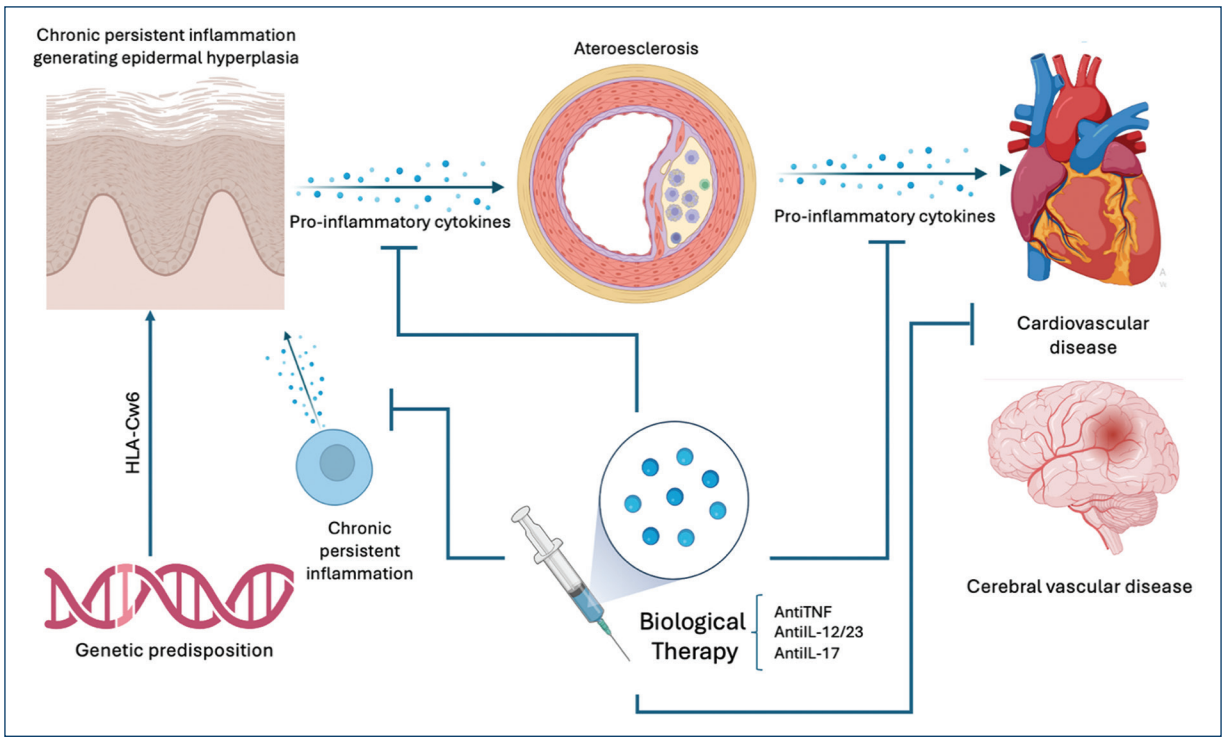

Figure 2. Sequence of pathophysiological events of the PAC triad that begins with genetic predisposition and the development of persistent chronic inflammation that favors the appearance of psoriasis and that, through the elevation of proinflammatory cytokines, contributes to the development of endothelial dysfunction, atherosclerosis, and increased cardio-cerebrovascular risk. It is suggested that the intervention of biologic therapy in the selective control of key cytokines such as tumor necrosis factor, IL-23, and IL-17, involved in the pathogenesis of the PAC triad, could decrease the risk of the aforementioned outcome.

IL: interleukin; PAC: psoriasis-atherosclerosis-cardiovascular disease.

the absence of such comorbidities, with psoriasis being an independent risk factor for CVD, 9 however, it is clear that the presence of these comorbidities substantially increases the risk of CVD, leading to a fatal outcome[11].

It has been observed that the life expectancy of patients with severe psoriasis is 6 years shorter than in healthy subjects; in addition, the risk of acute myocardial infarction and cerebral vascular disease is higher in patients with severe psoriasis than in those with mild-to-moderate form[12].

In an effort to reduce the risk of CVD in patients with psoriasis, Garshick and Berger[13], using an algorithm that determined the risk of CVD in patients with psoriasis, proposed that if the patient was at high risk of CVD, statins should be considered, but not for low-risk patients, where only CVD risk factors had to be identified and controlled.

Insulin resistance and elevated leptin levels in patients with psoriasis are associated with an increased risk of CVD due to endothelial dysfunction, and this risk increases in direct proportion to the severity of psoriasis. It is imperative to implement more rigorous control measures to address this issue. These factors have the potential to promote atherosclerosis by directly influencing immune responses in vascular tissue. Consequently, this can lead to PCI and a harmful cycle that may ultimately result in CVD and an increased risk of mortality[14]. Other factors involved in the outcome of the PAC triad are dyslipidemia (oxidized low-density lipoprotein that is highly atherogenic, alterations in the reverse transport of high-density lipoprotein cholesterol, and hypertriglyceridemia)[15] and the increase in the density of epicardial adipose tissue that promotes coronary heart disease,[16] representing risk factors for CVD and consequently increasing the risk of death if not identified and controlled in time.

PCI, the common denominator of the PAC triad, is directly mediated by proinflammatory cytokines such as TNF-α, IL-23, and IL-17A, the latter through the IL-17 receptor that stimulates the production of granulocyte colony-stimulating factor and IL-6, causing vascular damage that contributes to atherosclerosis and CVD. Therefore, it is suggested that treatment aimed at

Table 1. Main studies evaluating the effect of biologic therapy on the development of cardiovascular disease in patients with psoriasis

Author Reference	Country/year	Drug	Patients	Relative risk (95% CI)
Abaubara et al.[25]	U.S.A./2010	TNFi	12,224	0.68 (0.5-0.94)
Wu et al.[26]	U.S.A./2012	TNFi	1,673	0.56 (0.37-0.83)
Ahlehoff et al.[27]	Denmark/2013	TNFi	693	0.42 (0.13-1.31)
Wu et al.[28]	U.S.A./2013	TNFi	976	0.61 (0.41-0.91)
Ahlehoff et al.[29]	Denmark/2015	TNFi	959	0.46 (0.22-0.98)
Shaaban and Al-Mutairi[30]	Kuwait/2016	TNFi	1058	4.88 (2.5-7.2)*
Wu et al.[31]	U.S.A./2018	TNFi	11,410	0.77 (0.60-0.99)
Wu et al.[32]	U.S.A./2017	TNFi	9148	0.55 (0.45-0.67)
Rungapiromnan et al.[33]	U.K./2016	TNFi	5205	OR 0.67 (0.10-4.63)
Ryan et al.[34]	U.S.A./2011	TNFi	1078	–0.0005 (–0.01-0.009)**
Ahlehoff et al.[29]	Denmark/2015	IL-12/23i	178	1.52 (0.47-4.94)
Rungapiromnan et al.[33]	U.K./2016	IL-12/23i	2310	OR 4.48 (0.24-84.77)
Ryan [34]	U.S.A./2011	IL-12/23i	771	0.012 (–0.001-0.026)**
Reich et al.[42]	U.K./2011	IL-12/23i	1582	0.44 (0.27-0.67)
Tzellos et al.[43]	Germany/2012	IL-12/23i	3179	OR 4.23 (1.07-16.75)
Poizeau et al.[44]	France/2020	IL-12/23i	9290	OR 4.17 (1.19-14.59)
Papp et al.[45]	U.S.A./2013	IL-12/23i	3117	IR (45 mg) 0.56/100 SY IR (90 mg) 0.36/100 SY
Gordon et al.[46]	U.S.A./2012	IL-12/23i	981	Exposure-adjusted rate: 1.06/100SY, (0.43-2.18).
Rungapiromnan et al.[33]	U.K./2016	IL-17i	2549	OR 1.00 (0.09-11.09)
Gottlieb et al.[49]	U.S.A./2022	IL-17i	8819	IR 0.4/100 PY (no increase over time)
Van De Kerkhof et al.[50]	The Netherlands/2016	IL-17i	3430	IR: 0.42/100 SY (300 mg dose) IR: 0.35/100 SY (150 mg dose)

*Incidence rate of myocardial infarction per 1000 person-years (95% CI).
**Risk difference, events per person-year (95% CI).
OR: *odds ratio*; IR: incidence rate; SY: subject-year of exposure; PY: per year; CI: confidence interval; TNF: tumor necrosis factor; IL: interleukin.

blocking these cytokines could be beneficial not only for the control of psoriasis but also of atherosclerosis and the development of CVD[17].

Effect of biologic therapy on PCI/PAC

Table 1 summarizes the main studies evaluating the effect of biologic therapy on the development of CVD in patients with psoriasis.

It has been suggested that PCI in psoriasis contributes to the atherosclerotic process and that modification of the former may contribute to reducing atherosclerosis and consequently the risk of CVD. The different treatments available for the management of psoriasis in different degrees of severity such as topical therapy, phototherapy, and systemic immunosuppressants can largely control the disease, some of them can even increase the already high cardiovascular risk in patients with the disease. Some exceptions are obvious, such as the effect of methotrexate that can decrease cardiovascular risk[18].

Studies evaluating the protective effect of biological therapy on CVD are scarce in patients with psoriasis, although not in other diseases, and expectations for control of cardiovascular comorbidity have increased markedly, as they reduce the likelihood that patients with psoriasis will develop CVD, although their role in vascular damage processes remains controversial. Probably due

to the inconsistency of clinical data on its efficacy against increased cardiovascular risk[18]. At present, biologic drugs included in the therapeutic regimen for psoriasis target three main targets: TNF, IL-12/IL-23, and IL-17.

A recent study found that suppression of some proinflammatory cytokines could reduce the risk of CVD, as has been observed with inhibition of IL-1β and subsequent reduction of CVD recurrence[19]. In addition to this effect, biologic therapy may reduce coronary inflammation; therefore, biologic therapy predominantly targeting TNF-α, IL-23, and IL-17 may influence PCI and thus lessen the impact of the PAC triad in psoriasis patients[20]. In the case of IL-17 inhibitors such as secukinumab, ixekizumab, and brodalumab, the first two blocking IL-17A, while the third blocks the IL-17 receptor[21], could also impact the activation of neutrophils, crucial for psoriasis and PCI, in addition to the fact that these cells interact with the damaged endothelium and contribute to the development of atherosclerosis and CVD[22].

Recent studies, including two meta-analyses, suggest that treatment with anti-TNF-α reduces the risk of CVD and acute myocardial infarction[23-34]. The cardioprotective effect of some biological therapies, mainly anti-TNF, has been observed in patients with other auto-inflammatory diseases such as rheumatoid arthritis, where it improved endothelial function and reduced the risk of CVD by 70%[35]. Among the most commonly used TNF anti-TNFs in the management of psoriasis is adalimumab, which effectively reduces PCI, although with a variable impact on vascular inflammation and endothelial dysfunction[36].

Recent systematic reviews did not show a significant effect of TNF inhibitors on subclinical indicators of atherosclerosis in psoriasis or other chronic inflammatory diseases (including indicators of arterial stiffness, carotid intima-media thickness, endothelial dysfunction measured as forearm blood flow-mediated dilation, and aortic vascular inflammation)[37,38], however, this could occur by different routes such as remission of the primary disease or reduction of the prothrombotic tendency[37].

On the other hand, IL-23, a proinflammatory cytokine that induces the differentiation of Th17 and Th22 cells, is a key player in the pathogenesis of psoriasis, and its blockade is effective in the control of psoriasis and psoriatic arthritis[39]. We carry out this blockade in clinical practice with four drugs, including ustekinumab (the most commonly used), guselkumab, tildrakizumab, and risankizumab, the first inhibiting both IL-23 and IL-12, while the last three are selective toward IL-23[40]. IL-23 has been linked to the development of atherosclerosis, and its elevated serum levels are predictors of mortality in patients with CVD[41].

IL-23 also mediates the production of granulocyte-macrophage colony-stimulating factor which promotes the development of atherosclerosis and increases oxidative stress that contributes to the PAC triad[41]. There is still little evidence on the cardioprotective effect of anti-IL23[42-46], so more studies are needed in this regard.

IL-17 inhibitors have shown efficacy in the treatment of psoriasis, being comparable in their effect and even more effective than anti-TNF and anti-IL-23[47]. The cardioprotective effect of antiIL-17A has been documented in previous studies[6,48-50]. Considering the inhibition of the proatherogenic, proinflammatory, pro-oxidant, and prothrombotic effects of IL-17,48 however, more studies are needed to evaluate the impact of biological therapy on atherosclerosis, since previous studies have proposed that IL-17 could even have a protective effect against atherosclerosis and that its serum levels do not correlate with carotid intimal thickness[18].

Regarding the effect of antiIL-17A on vascular dysfunction, the results are contradictory; a previous study with secukinumab showed that the addition of the biologic did not modify endothelial function in the first 12 weeks of use in patients with psoriasis and vascular dysfunction, but later until 52 weeks[51]. While in another recent study, it was observed that the addition of anti-IL-17 therapy reduced the thickness of non-calcified plaque in patients with psoriasis, improving endothelial function[52].

Conclusion

Psoriasis is a systemic disease that increases the risk of CVD, and this increases in direct proportion to the severity of psoriasis. Therefore, biological therapies are an option to block proinflammatory signaling pathways common in these diseases. Biological therapies in their different modalities could reduce the risk of developing CVD, however, the available information is not entirely conclusive, so more studies are needed to define the real role of these drugs in CVD, mainly in patients with severe forms of psoriasis.

Funding

The authors declare that they have not received funding.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The author declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The author declare that no generative artificial intelligence was used in the writing of this manuscript.

References

1. Liu C, Chen H, Liu Y, Huang H, Yu W, Di T, et al. Immunity: psoriasis comorbid with atherosclerosis. Front Immunol. 2022;13:1070750.
2. Parab S, Doshi G. An update on emerging immunological targets and their inhibitors in the treatment of psoriasis. Int Immunopharmacol. 2022;113:109341.
3. Vičić M, Kaštelan M, Brajac I, Sotošek V, Massari LP. Current concepts of psoriasis immunopathogenesis. Int J Mol Sci. 2021;22:11574.
4. Bu J, Ding R, Zhou L, Chen X, Shen E. Epidemiology of psoriasis and comorbid diseases: a narrative review. Front Immunol. 2022; 13:880201.
5. Zhang L, Wang Y, Qiu L, Wu J. Psoriasis and cardiovascular disease risk in European and East Asian populations: evidence from meta-analysis and Mendelian randomization analysis. BMC Med. 2022;20:421.
6. 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;22:1443-8.
7. Anyfanti P, Margouta A, Goulas K, Gaveiilaki M, Lazaridou E, Patsatsi A, et al. Endothelial dysfunction in psoriasis: an updated review. Front Med (Lausanne). 2022;9:864185.
8. Orlando G, Molon B, Viola A, Alaibac M, Angioni R, Piaserico S. Psoriasis and cardiovascular diseases: an immune-mediated cross talk? Front Immunol. 2022;13:868277.
9. Doumas M, Katsiki N, Papademetriou V. Psoriasis and cardiovascular disease: two sides of the same coin? Angiology. 2018;69:5-9.
10. Furue M, Kadono T. "Inflammatory skin march" in atopic dermatitis and psoriasis. Inflamm Res. 2017;66:833-42.
11. Liu L, Cui S, Liu M, Huo X, Zhang G, Wang N. Psoriasis increased the risk of adverse cardiovascular outcomes: a new systematic review and meta-analysis of cohort study. Front Cardiovasc Med. 2022; 9:829709.
12. Correa TL, Quitete MA, De Azevedo LT, Fraga IA, Teixeira LC. Myocardial infarction, stroke, and psoriasis: a systematic review of observational studies. Ann Cardiol Angeiol (Paris). 2023;72(2):101574.
13. Garshick MS, Berger JS. Psoriasis and cardiovascular disease-an ounce of prevention is worth a pound of cure. JAMA Dermatol. 2022; 158:239-41.
14. Yan H, Yu B, Tian J, Xia D, Xu Y, Li C. Serum leptin and adiponectin: indicators of cardiovascular disease secondary to psoriasis. Indian J Dermatol. 2022;67:109-14.
15. Miao C, Li J, Li Y, Zhang X. Obesity and dyslipidemia in patients with psoriasis: a case-control study. Medicine (Baltimore). 2019; 98:e16323.
16. Ellis CN, Neville SJ, Sayyouh M, Elder JT, Nair RP, Gudjonsson JE, et al. Epicardial adipose tissue volume is greater in men with severe psoriasis, implying an increased cardiovascular disease risk: a cross-sectional study. J Am Acad Dermatol. 2022;86:535-43.
17. Michalak-Stoma A, Bartosińska J, Raczkiewicz D, Kowal M, Kosak J, Gujski M, et al. Multiple cytokine analysis of Th1/Th2/Th9/Th17/Th22/ Treg cytokine pathway for individual immune profile assessment in patients with psoriasis. Med Sci Monit. 2022;28:e938277.
18. Andújar I, Esplugues JV, García-Martínez P. Looking beyond the skin: pathophysiology of cardiovascular comorbidity in psoriasis and the protective role of biologics. Pharmaceuticals (Basel). 2022; 15:1101.
19. Baragetti A, Catapano AL, Magni P. Multifactorial activation of NLRP3 inflammasome: relevance for a precision approach to atherosclerotic cardiovascular risk and disease. Int J Mol Sci. 2020;21:4459.
20. Wang X, Kaiser H, Kvist-Hansen A, McCauley BD, Skov L, Hansen PR, et al. IL-17 pathway members as potential biomarkers of effective systemic treatment and cardiovascular disease in patients with moderate-to-severe psoriasis. Int J Mol Sci. 2022;23:555.
21. Lanna C, Lambiase S, Gaeta Shumak R, Borselli C, Cosio T, Dattola A, et al. Why targeted therapeutics have provided benefit in psoriasis: looking at IL-17 biology. Expert Rev Clin Pharmacol. 2022;15:1209-24.
22. Sileno S, Beji S, D'Agostino M, Carassiti A, Melillo G, Magenta A. microRNAs involved in psoriasis and cardiovascular diseases. Vasc Biol. 2021;3:R49-68.
23. Champs B, Degboé Y, Barnetche T, Cantagrel A, Ruyssen-Witrand A, Constantin A. Short-term risk of major adverse cardiovascular events or congestive heart failure in patients with psoriatic arthritis or psoriasis initiating a biological therapy: a meta-analysis of randomised controlled trials. RMD Open. 2019;5:e000763.
24. Ursini F, Leporini C, Bene F, D'Angelo S, Mauro D, Russo E, et al. Anti-TNF-alpha agents and endothelial function in rheumatoid arthritis: a systematic review and meta-analysis. Sci Rep. 2017;7:5346.
25. Abuabara K, Lee H, Kimball AB. The effect of systemic psoriasis therapies on the incidence of myocardial infarction: a cohort study. Br J Dermatol. 2011;165:1066-73.
26. Wu JJ, Poon KY, Channual JC, Shen AY. Association between tumor necrosis factor inhibitor therapy and myocardial infarction risk in patients with psoriasis. Arch Dermatol. 2012;148:1244-50.
27. Ahlehoff O, Skov L, Gislason G, Lindhardsen J, Kristensen SL, Iversen L, et al. Cardiovascular disease event rates in patients with severe psoriasis treated with systemic anti-inflammatory drugs: a Danish real-world cohort study. J Intern Med. 2013;273:197-204.
28. Wu JJ, Poon KY, Bebchuk JD. Association between the type and length of tumor necrosis factor inhibitor therapy and myocardial infarction risk in patients with psoriasis. J Drugs Dermatol. 2013;12:899-903.
29. Ahlehoff O, Skov L, Gislason G, Gniadecki R, Iversen L, Bryld LE, et al. Cardiovascular outcomes and systemic anti-inflammatory drugs in patients with severe psoriasis: 5-year follow-up of a Danish nationwide cohort. J Eur Acad Dermatol Venereol. 2015;29(6):1128-34.
30. Shaaban D, Al-Mutairi N. The effect of tumor necrosis factor inhibitor therapy on the incidence of myocardial infarction in patients with psoriasis: a retrospective study. J Dermatolog Treat. 2018;29(1):3-7.
31. Wu JJ, Sundaram M, Cloutier M, Gauthier-Loiselle M, Guérin A, Singh R, et al. The risk of cardiovascular events in psoriasis patients treated with tumor necrosis factor-α inhibitors versus phototherapy: an observational cohort study. J Am Acad Dermatol. 2018;79:60-8.
32. Wu JJ, Guérin A, Sundaram M, Dea K, Cloutier M, Mulani P. Cardiovascular event risk assessment in psoriasis patients treated with tumor necrosis factor-α inhibitors versus methotrexate. J Am Acad Dermatol. 2017;76:81-90.
33. Rungapiromnan W, Yiu ZZ, Warren RB, Griffiths CE, Ashcroft DM. Impact of biologic therapies on risk of major adverse cardiovascular events in patients with psoriasis: systematic review and meta-analysis of randomized controlled trials. Br J Dermatol. 2017;176:890-901.
34. Ryan C, Leonardi CL, Krueger JG, Kimball AB, Strober BE, Gordon KB, et al. Association between biologic therapies for chronic plaque psoriasis and cardiovascular events: a meta-analysis of randomized controlled trials. JAMA. 2011;306:864-71.
35. Deyab G, Hokstad I, Aaseth J, Smastuen MC, Whist JE, Agewall S, et al. Effect of anti-rheumatic treatment on selenium levels in inflammatory arthritis. J Trace Elem Med Biol. 2018;49:91-7.
36. Wegner J, Karbach S, Drosos I, Schnorbus B, Muxel S, Schmidt F, et al. TNF-α blockade may lead to improvement of vascular function in psoriasis patients. Exp Dermatol. 2022;31:237-41.
37. Knowles L, Nadeem N, Chowienczyk PJ. Do anti-tumour necrosis factor-α biologics affect subclinical measures of atherosclerosis and arteriosclerosis? A systematic review. Br J Clin Pharmacol. 2020;86: 837-51.
38. González-Cantero A, Ortega-Quijano D, Álvarez-Díaz N, Ballester MA, Jimenez-Gomez N, Jaen P, 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;141:2402-11.
39. Ruggiero A, Megna M, Fabbrocini G, Ocampo-Garza SS. Anti-IL23 biologic therapies in the treatment of psoriasis: real-world experience versus clinical trials data. Immunol Res. 2023;71:328-55.
40. Vu A, Ulschmid C, Gordon KB. Anti-IL 23 biologics for the treatment of plaque psoriasis. Expert Opin Biol Ther. 2022;22:1489-502.
41. Marovt M, Marko PB, Pirnat M, Ekart R. Effect of biologics targeting interleukin-23/-17 axis on subclinical atherosclerosis: results of a pilot study. Clin Exp Dermatol. 2020;45:560-4.
42. Reich K, Langley RG, Lebwohl M, Szapary P, Guzzo C, Yeilding N, et al. Cardiovascular safety of ustekinumab in patients with moderate to severe psoriasis: results of integrated analyses of data from phase II and III clinical studies. Br J Dermatol. 2011;164:862-72.

43. Tzellos T, Kyrgidis A, Zouboulis CC. Re-evaluation of the risk for major adverse cardiovascular events in patients treated with anti-IL-12/23 biological agents for chronic plaque psoriasis: a meta-analysis of randomized controlled trials. J Eur Acad Dermatol Venereol. 2013; 27:622-7.
44. Poizeau F, Nowak E, Kerbrat S, Nautout BL, Droitcourt C, Drici MD, et al. Association between early severe cardiovascular events and the initiation of treatment with the anti-interleukin 12/23p40 antibody ustekinumab. JAMA Dermatol. 2020;156:1208-15.
45. Papp KA, Griffiths CE, Gordon K, Lebwohl M, Szapary PO, Wasfi Y, et al. Long-term safety of ustekinumab in patients with moderate-to-severe psoriasis: final results from 5 years of follow-up. Br J Dermatol. 2013;168:844-54.
46. Gordon KB, Langley RG, Gottlieb AB, Papp KA, Krueger GG, Strober BE, et al. A phase III, randomized, controlled trial of the fully human IL-12/23 mAb briakinumab in moderate-to-severe psoriasis. J Invest Dermatol. 2012;132:304-14.
47. Reich K, Pinter A, Lacour JP, Ferrandiz C, Micali G, French LE, et al. Comparison of ixekizumab with ustekinumab in moderate-to-severe psoriasis: 24-week results from IXORA-S, a phase III study. Br J Dermatol. 2017;177:1014-23.
48. Piros ÉA, Szabó Á, Rencz F, Brodszky V, Szalai K, Galajda N, et al. Impact of interleukin-17 inhibitor therapy on arterial intima-media thickness among severe psoriatic patients. Life (Basel). 2021;11:919.
49. Gottlieb AB, Deodhar A, Mcinnes IB, Baraliakos X, Reich K, Schreiber S, et al. Long-term safety of secukinumab over five years in patients with moderate-to-severe plaque psoriasis, psoriatic arthritis and ankylosing spondylitis: update on integrated pooled clinical trial and post-marketing surveillance data. Acta Derm Venereol. 2022;102:adv00698.
50. Van de Kerkhof PC, Griffiths CE, Reich K, Leonardi CL, Blauvelt A, Tsai TF, 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;75:83-98.e4.
51. Von Stebut E, Reich K, Thaçi D, Koenig W, Pinter A, Köber A, et al. Impact of secukinumab on endothelial dysfunction and other cardiovascular disease parameters in psoriasis patients over 52 weeks. J Invest Dermatol. 2019;139:1054-62.
52. Elnabawi YA, Dey AK, Goyal A, Groenendyk JW, Chung JH, Belur AD, et al. Coronary artery plaque characteristics and treatment with biologic therapy in severe psoriasis: results from a prospective observational study. Cardiovasc Res. 2019;115:721-8.