Journal of IMIDs

PERMANYER

Check for updates

REVIEW ARTICLE

Neoplasms in IMIDs: a review of the literature

Jon Fulgencio-Barbarin, Mario Puerta Peña, Daniel Falkenhain-Lopez, Carmen Garcia-Donoso, and Raquel Rivera Diaz*

Department of Dermatology, Hospital Universitario 12 de Octubre, Madrid, Spain

Abstract

Immune-mediated inflammatory diseases (IMIDs) are chronic and disabling diseases that share common inflammatory and immunological dysregulation. The association between IMIDs and the risk of cancer remains debatable. Inflammation is a double-edged sword for cancer as it can help destroy malignant cells but it can also promote the development of some cancers. The following review aims to provide a summary of the associations of neoplasms and the most common IMIDs and the possible relationship of the indirect risk caused by their chronic therapy. The risk of developing neoplasm is higher globally in patients with IMID, with different risk profiles and tumor types depending on the inflammatory pathology. Overall, lymphoproliferative disorders are the most common cancer in IMID patients. Nowadays, data available on the safety of the drugs used in IMID patients showed no increased risk of neoplasms in general, although more studies are needed.

Keywords: *Immune-mediated inflammatory disease. Neoplasms. Cancer. Tumor. Inflammation.*

Introduction

Immune-mediated inflammatory disease (IMID) is an actual concept for describing a group of chronic and disabling diseases that share common immunological and inflammatory pathways. Most frequent belonging diseases include psoriasis, psoriatic arthritis (PsA), rheumatoid arthritis (RA), inflammatory bowel disease (IBD) – Crohn's disease (CD) and ulcerative colitis (UC) – and ankylosing spondylitis (AS).

Although each disease has its specific pathophysiology and epidemiology, the general prevalence of IMID is known to be about 5-7%[1]. Despite most IMIDs having a similar prevalence in both sexes, some of them have gender predominance like women in RA or men-predominance in SA. Furthermore, IMID patients had a higher risk of developing another IMID, with commonly known associations such as psoriasis and PsA or AR and IBD – with a relative risk (RR) of 7.63-8.62 in some studies[2].

Several studies in the last decades had associated IMID with a higher risk of other comorbidities in comparison to the general population with its consequent decrease in the health and quality of life (QoL), as well as the shorter life expectancy of these patients[3]. The positive association between these autoimmune diseases and increased risk of developing infections, cardiovascular and renal diseases had been recognized, as well as malignancies[4].

The risk of neoplasms in IMID patients might be increased direct and indirectly. First, the cytokine dysregulation and chronic inflammation of the disease itself it is thought to have a tumorigenic effect. Second, therapies for the control of IMIDs include mostly the decrease of the immune system using immunosuppressants, corticosteroids, and biological targeted therapy[5].

***Correspondence:**
Jon Fulgencio-Barbarin
E-mail: jonfulgencio@hotmail.com

Received: 31-01-2022
Accepted: 20-04-2022
DOI: 10.24875/JIMIDS.22000002

Disponible en internet: 08-05-2023
J IMIDs. 2022;2(4):106-111
www.JournalofIMIDs.com

Inflammation and malignancy

Although acute inflammation is beneficial and essential in normal circumstances, chronic inflammation is a well-known trigger for cancer and plays a main role in the molecular mechanisms of carcinogenesis. Indeed, inflammatory cells and mediators are present in most neoplasms, regardless of the location and causative agent[6]. In some neoplasms, inflammatory conditions are present before the malignant change increasing the cancer risk (as IBD and colonic cancer), while in other tumors, an oncogenic change will induce an inflammatory environment.

Inflammation in the tumor microenvironment is a feature of cancer and is known to be a key characteristic of carcinogens. Whereas the pathogenesis of carcinogenicity has been focused on external genotoxic activity, non-genotoxic mechanisms such as oxidative stress and inflammation promote mutation and DNA damage. In addition, carcinogens cause oxidative stress synergistically with inflammation, which fuels a vicious loop of cellular death, damage, and carcinogenesis[7].

Chronic pro-inflammatory activity promotes genetic and epigenetic aberrations in various pathways due to oxidative and nitrative damage[8]. Inflammatory cells are present in most neoplasms, promoting a correct microenvironment for the migration, invasion, and metastasis of malignant cells, and it is currently associated with bad prognosis[6,7].

In the early neoplastic process, malignant cells are powerful inflammatory activators due to the multiple antigenic and mutational differences. As the tumor progress, less immunogenic tumoral cells will escape to the immune system and progressively proliferate in oncological patients.

Under physiological conditions, the immune system initially promotes inflammatory responses to eliminate potential malignant cells. Normal inflammation is self-limiting, as the production of anti-inflammatory factors follows closely the pro-inflammatory ones. Failure of these mechanisms made persistence of the inflammatory response and the subsequent damage.

Unfortunately, there is another side of that coin, in which inflammation itself contributes directly to tumorigenesis. Tumor cells produce various mediators (such as cytokines, chemokines, and prostaglandins) of the inflammatory environment. One of the significant components of the leukocyte infiltrate of neoplastic tissues is tumor-associated macrophages (TAMs). Even if TAMs participate in killing neoplastic cells, they also promote tumoral growth by releasing angiogenic and lymphangiogenic growth factors that may potentiate tumoral progression[7,9]. However, closer studies will be needed on the relationship between TAM and oncogenic clinical importance, as it remains unclear.

IMID and risk of neoplasms

As we mentioned, IMIDs are characterized by chronic inflammation. Given the fine line between inflammation and cancer, it is not surprising that these immune-mediated diseases had a higher potential risk of developing some neoplasms. The following table 1 summarizes the most common association of tumors in the most prevalent IMIDs that we will develop in the following review.

RA

RA is a polygenic inflammatory autoimmune condition characterized by chronic joint inflammation and damage with secondary deformity and extra-articular damage. Management of RA consists of disease-modifying antirheumatic drugs (DMARDs) which change the natural course of the immunologic pathways. Prolonged immune dysregulation and inflammatory responses associated with RA increased cancer development risk according to literature.

The expected survival of RA patients is likely to decrease by 3-10 years according to the severity of the disease and the age of disease onset. It has been demonstrated that the excess mortality in persons with RA is largely attributable to cardiovascular disease (CVD). After CVD, cancer is the second most common cause of mortality in RA patients. In the reported meta-analysis, the risk of developing lymphoma – either Hodgkin or non-Hodgkin types – is significantly increased in RA patients (overall risk 2.08 1.80-2.39)[10]. Furthermore, lung cancer risk is slightly increased than in the general population (1.63 1.43-1.87)[10] probably due to chronic lung inflammation, presents even at early stages of RA. It has been suggested that interstitial lung disease in RA patients could increase the risk of lung cancer because many patients present parenchymal damage imaging findings at the diagnosis of cancer[11]. Other tumors such as breast, colorectal, prostate, cervix, and melanoma showed no differences compared to the general population[10].

Furthermore, the indirect risk of developing malignancies because of other aspects as lifestyle factors, smoking, or treatments must be specified. It is important to see any differences between patients treated with

Table 1. Overview of most frequent IMID associated with a higher risk of neoplasm

IMID	Neoplasm association
Rheumatoid arthritis	Hodgkin and non-Hodgkin lymphoma and lung cancer, related to the disease[9] NMSC increased risk due to DMARD therapy, in debate[11-14]
Psoriasis	NMSC, lymphoproliferative disease, lung and bladder neoplasms[16,17] Secondary to comorbidities possible higher risk of bladder, kidney, oropharynx, stomach, liver, gallbladder, and pancreas[17] Similar incidence of malignancies in patients with psoriatic arthritis[18,24]
Ankylosing spondylitis	Digestive and lymphoid hematopoietic neoplasms (multiple myeloma and lymphoma) are still up for discussion[24,25]
UC	Higher risk of colorectal cancer in UC than CD[27] Liver-biliary cancer and leukemia[29]
CD	Higher incidence of extra-intestinal neoplasms in CD than UC[29]. Upper gastrointestinal system, lung, urinary, bladder, lymphoma, biliary-liver cancer, and NMSC[29]

IMID: immune-mediated inflammatory disease, NMSC: non-melanoma skin cancer, DMARD: disease-modifying antirheumatic drugs, UC: ulcerative colitis, CD: Crohn's disease.

biological agents and DMARDs giving the chronic nature of the disease and the need for prolonged treatment. Some literature demonstrates that RA patients with prolonged doses of methotrexate and corticosteroids might also have an increased risk of non-melanoma skin cancer (NMSC)[12]. However, despite the immunomodulation of these therapies, the last studies showed no signal of increased risk for neoplasms in biologic and other therapeutic agents[13-15].

Treatment of RA in patients with cancer is complex. Given the lack of evidence for the use of specific therapies based on the risk of cancer, some published guidelines recommend that DMARDs should not be used in patients with active cancer and a recent diagnosis of RA, even if their use was considered safe[11,15]. For patients with a history of past cancer for at least 5 years, DMARDs can be used carefully. Some guidelines did not recommend the use of TNF inhibitors in patients with a history of cancer[11,13-15].

As for cancer treatments in patients with a known diagnosis of RA, it is common to discontinue the drugs for some time during the oncologic process. The consequences of the gaps in the RA treatment have not been clearly documented and there is no consensus for the management of the disease in patients with active cancer[11]. Conventional DMARDs should be used carefully in patients with active cancer if they are not receiving chemotherapy and if there are no interactions. These patients usually need specific and careful screening and monitoring as they are more susceptible to adverse reactions than patients without RA.

Psoriasis and psoriatic arthritis

Although we have pointed chronic inflammation as a major causal agent of carcinogenesis, this risk is more controversial in some inflammatory diseases as in psoriasis. Psoriasis is a chronic autoimmune inflammatory disease of the skin and joints. Some studies remark the importance of the macrophage phenotype, where M1 seems to have antitumoral activity – more active in psoriasis – meanwhile, M2 phenotype is more related to pro-tumoral environment – such as IBD and colorectal carcinoma[7]. The T helper 17, and to a lesser extent the T helper 1, mediated inflammatory response of psoriasis involves a huge number of neutrophils and monocytes in the skin that could destroy any emerging tumor cell[16].

The metabolic syndrome is an important driver of adverse cardiovascular outcomes and it has been proposed as an independent risk factor for developing myocardial infarction and neoplasia. Smoking, on the other hand, appears to have a role in the onset of psoriasis and increased risk of malignancies in this patient population[17]. The direct relation between neoplasm and psoriasis is still in debate. Baseline risk is difficult to assess due to usually chronic immunosuppressive treatments and higher rates of phototherapy and heliotherapy. Recent meta-analysis pointed out that patients with psoriasis appear to have a higher risk of keratinocyte cancer, lymphoproliferative diseases, lung, and bladder cancer[18]. Despite the data, cancer screening beyond the nationally recommended guidelines for age and sex is not required before initiating systemic therapy[17,18]. In subjects at increased risk for skin cancer, closer monitoring may be required. The highest association was keratinocyte

cancer, probably associated with the higher exposure to sunlight and more frequent follow-up of the patients with dermatologists than the general population.

When the association of developing tumors is compared between patients treated with biologic agents and conventional drugs, there is no association of higher risk[18-20]. Phototherapy with oral psoralen and ultraviolet A is directly and dose dependent related to increased risk of skin cancer but not for non-cutaneous malignancies[20,21]. No higher skin cancer was found with narrowband UVB and broadband phototherapies[22]. Treatment with methotrexate is related to a slightly increased risk of lymphoproliferative disorders according to some registers and also has been reported to be an independent risk factor for developing NMSC[20]. For cyclosporine A, there is an elevated risk of NMSC, especially when is associated with phototherapy[23].

As for psoriatic arthritis, 25% of patients with psoriasis will develop joint inflammation during the disease course and it is considered to be more severely affected. Malignancy rates in patients with PsA remain understudied. Even if the association of arthritis and cancer is still in debate, nowadays, investigations found similar prevalence and incidence rates of neoplasms compared with the general population[18,24].

AS

AS is an autoimmune disease that mainly affects the axial skeleton with male preponderance. Until now, the risk of neoplasms related to AS had not been fully clarified. Literature review and meta-analysis associated 14% increased risk of overall malignancy, with a specific higher risk of digestive and lymphoid hematopoietic neoplasms – principally multiple myeloma and lymphomas[25]. However, in recent studies, this increased specific risk was not significantly different from the general population when is adjusted for smoking and common comorbidities but AS patients had a 37% increased risk of mortality in the 5 years following cancer compared with patients without AS[26]. In summary, available data are still inconclusive but some clinical guides recommend tumor screening during the first 3 years of the diagnosis as the risk of neoplasia appears to be more frequent in the initial stages of the disease[27].

IBD

IBD is a chronic idiopathic inflammatory disorder of the gastrointestinal tract with possible systemic extension to joints, skin, and hepatobiliary system. The two main disorders include CD and UC. In patients with IBD, chronic inflammation is a major risk factor for the development of malignancies. It has been well demonstrated that patients with UC have an increased incidence of colitis-associated cancer (CAC) that correlates with the disease duration, activity, and location, as CD remains similar to the general population[28]. Bacterial invasion and chronic inflammatory response dysregulation are the main contributors of CAC with the subsequent inflammatory progression of hyperplasia, dysplasia, and carcinoma[29].

The risk of extra-intestinal cancer in patients with IBD remains uncertain, despite knowledge of a relatively high frequency of extra-intestinal manifestations among these patients. Some meta-analysis revealed that patients with CD were at an increased risk of extraintestinal cancer than UC, more specifically with higher rates of lung and urinary bladder (probably due to higher smoking rates), upper gastrointestinal system and NMSC, as well as potentially biliary liver cancer and lymphoma. On the other hand, UC patients were at an increased risk for liver-biliary cancer and leukemia, which was offset by a lower risk for lung cancer[30].

Patients with IBD have an increased risk of cancer from long-term intestinal inflammation and immunosuppressive treatments, especially classic immunosuppressive such as thiopurines or methotrexate. These medications promote direct DNA alterations and oncogene activation, and several studies have demonstrated an overall increased risk of cancer (RR 1.3-1.7)[31] with apparently no differences using TNF inhibitors[32].

Targeted therapies and cancer

Biologic agents have revolutionized the treatment of autoimmune diseases. The potential increased risk of malignancies due to the partial immune incompetence of these therapies is still controversial. Nowadays, experience with anti-TNF, anti-interleukin-1, or CD20 blockers like rituximab seems to be safe, with no clear risk of higher lymphomas or solid neoplasm[1,13].

Tumor necrosis factor inhibitors are commonly used in patients with IMID acting in the dysregulated immune system. TNF has been demonstrated to play a key role in the inflammation pathways and the ability to lyse tumors. The initial concern is that inhibition of TNF may also induce or increase the risk of malignancies, particularly lymphoma and skin cancers, including melanoma. However, despite anti-TNF therapy being often avoided in patients with a history of cancer, little is known about the risk of recurrence but, based on clinical trial data

and literature of observational studies or meta-analyses, showed no increased risk of recurrent or new primary cancer[15,33].

Rituximab is a monoclonal antibody against the protein CD20 approved for refractory RA. The latest researches on this drug seem to point rituximab as a safe and effective medication, and the most common concerning side effects include reactivation or development of infections, failure of immunization, and paradoxical reactions[34]. For the moment, the use of rituximab in the treatment of IMIDs has not been associated with a long-term increased risk of malignancies[35].

JAK inhibitors such as tofacitinib and baricitinib have also revealed a safe profile in long-term security in controlled trials with slightly more risk of some infections such as opportunistic infections and viral infections as herpes zoster, but no greater number of neoplasms[36,37]. Despite the available data, long-term follow-up and further studies are needed.

As for IL-17 inhibitors, recently, it has been suggested the role of IL-17 in cancer surveillance with pro- and/or anti-tumorigenic function depending on the context[38]. Nowadays, according to prospective studies from clinical trials about observed versus expected number of malignancies, no higher significant risk in patients treated with anti IL17 has been demostrated[39-41]. Despite the given information, long-term safety data from patient registries are still needed to provide a complete overview of cancer risk.

However, the interpretation of the data should have some considerations. First, the selection of patients therapy usually is correlated with its severity, as patients initiating biologic therapy usually had more active disease than those treated with other immunosuppressive agents. Second, therapy switching is common in real practice which makes it difficult to differentiate de exposure of the different drugs. In addition, many patients treated with biologic therapy had been previously treated with other drugs.

Conclusion

It seems that the diversity and plasticity of chronic inflammation and the dual potential of cancer-related inflammation (pro-tumoral vs. antitumoral activity) are the two faces of the same coin, with different inflammatory cell phenotypes. The exact mechanism of "good" immune responses is not clear yet but promoting cancer-inhibiting inflammatory responses with low cancer-promoting inflammatory response might be the clue for useful approaches in the prevention, diagnosis, and treatment of cancer. It has been well demonstrated that some IMIDs had an increased risk of cancer when compared with the general population. RA has a strong relation with higher rates of lymphoma and lung cancer. Psoriasis patients are more likely to have NMSC and an indirect higher risk of neoplasms due to comorbidities such as alcohol and smoking. In subjects at increased risk for skin cancer, closer monitoring may be required. As for IBD patients, a higher risk of colorectal cancer is more associated with CD than in UC.

The therapeutic aims for IMIDs include the control of chronic inflammation, prevention of tissue damage and comorbidities, and improvement of QoL and long-term remission. The risk of new recurrent systemic malignancies is similar between biologics and non-biologic treatments and they are generally considered safe. Conventional therapy with MTX and CsA had a higher risk of NMSC, especially when they are used associated with phototherapy or other treatments.

Given the complexities in the clinical management of patients with IMID and cancer, a multidisciplinary approach is always preferable to enhance patient welfare. Therapeutic choices should be consensual with the patient assuring a balance between QoL and survival.

Funding

None.

Conflicts of interest

None.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

References

1. Kuek A, Hazleman BL, Ostör AJ. Immune-mediated inflammatory diseases (IMIDs) and biologic therapy: a medical revolution. Postgrad Med J. 2007;83:251-60.
2. Brophy S, Pavy S, Lewis P, Taylor G, Bradbury L, Robertson D, et al. Inflammatory eye, skin, and bowel disease in spondyloarthritis: genetic, phenotypic and environmental factors. J Rheumatol. 2001;28:2667-73.
3. El-Gabalawy H, Guenther LC, Bernstein CN. Epidemiology of immune-mediated inflammatory diseases: incidence, prevalence, natural history, and comorbidities. J Rheumatol Suppl. 2010;85:2-10.

4. Robinson D Jr., Hackett M, Wong J, Kimball AB, Cohen R, Bala M, et al. Co-occurrence and comorbidities in patients with immune-mediated inflammatory disorders: an exploration using US healthcare claims data, 2001-2002. Curr Med Res Opin. 2006;22:989-1000.
5. Grivennikov SI, Karin M. Inflammation and oncogenesis: a vicious connection. Curr Opin Genet Dev. 2010;20:65-71.
6. Mantovani A, Allavena P, Sica A, Balkwill F. Cancer-related inflammation. Nature. 2008;454:436-44.
7. Fishbein A, Hammock BD, Serhan CN, Panigrahy D. Carcinogenesis: failure of resolution of inflammation? Pharmacol Ther. 2021;218:107670.
8. Murata M. Inflammation and cancer. Environ Health Prev Med. 2018;23:50.
9. Coussens LM, Werb Z. Inflammation and cancer. Nature. 2002;420:860-7.
10. Simon TA, Thompson A, Gandhi KK, Hochberg MC, Suissa S. Incidence of malignancy in adult patients with rheumatoid arthritis: a meta-analysis. Arthritis Res Ther. 2015;17:212.
11. Pundole X, Suarez-Almazor ME. Cancer and rheumatoid arthritis. Rheum Dis Clin North Am. 2020;46:445-62.
12. Tseng HW, Lu LY, Lam HC, Tsai KW, Huang WC, Shiue YL. The influence of disease-modifying anti-rheumatic drugs and corticosteroids on the association between rheumatoid arthritis and skin cancer: a nationwide retrospective case-control study in Taiwan. Clin Exp Rheumatol. 2018;36:471-8.
13. Simon TA, Boers M, Hochberg M, Baker N, Skovron ML, Ray N, et al. Comparative risk of malignancies and infections in patients with rheumatoid arthritis initiating abatacept versus other biologics: a multi-database real-world study. Arthritis Res Ther. 2019;21:228.
14. Xie W, Yang X, Huang H, Gao D, Ji L, Zhang Z. Risk of malignancy with non-TNFi biologic or tofacitinib therapy in rheumatoid arthritis: a meta-analysis of observational studies. Semin Arthritis Rheum. 2020;50:930-7.
15. De Cock D, Hyrich K. Malignancy and rheumatoid arthritis: epidemiology, risk factors and management. Best Pract Res Clin Rheumatol. 2018;32:869-86.
16. Chang SH. T helper 17 (Th17) cells and interleukin-17 (IL-17) in cancer. Arch Pharm Res. 2019;42:549-59.
17. Ji J, Shu X, Sundquist K, Sundquist J, Hemminki K. Cancer risk in hospitalized psoriasis patients: a follow-up study in Sweden. Br J Cancer. 2009;100:1499-502.
18. Vaengebjerg S, Skov L, Egeberg A, Loft ND. Prevalence, incidence, and risk of cancer in patients with psoriasis and psoriatic arthritis: a systematic review and meta-analysis. JAMA Dermatol. 2020;156:421-9.
19. Fiorentino D, Ho V, Lebwohl MG, Leite L, Hopkins L, Galindo C, et al. Risk of malignancy with systemic psoriasis treatment in the psoriasis longitudinal assessment registry. J Am Acad Dermatol. 2017;77:845-54.e5.
20. Geller S, Xu H, Lebwohl M, Nardone B, Lacouture ME, Kheterpal M. Malignancy risk and recurrence with psoriasis and its treatments: a concise update. Am J Clin Dermatol. 2018;19:363-75.
21. Stern RS. The risk of squamous cell and basal cell cancer associated with psoralen and ultraviolet a therapy: a 30-year prospective study. J Am Acad Dermatol. 2012;66:553-62.
22. Weischer M, Blum A, Eberhard F, Rocken M, Berneburg M. No evidence for increased skin cancer risk in psoriasis patients treated with broadband or narrowband UVB phototherapy: a first retrospective study. Acta Derm Venereol. 2004;84:370-4.
23. Paul CF, Ho VC, McGeown C, Christophers E, Schmidtmann B, Guillaume JC, et al. Risk of malignancies in psoriasis patients treated with cyclosporine: a 5 y cohort study. J Invest Dermatol. 2003;120:211-6.
24. Perez-Chada LM, Merola JF. Comorbidities associated with psoriatic arthritis: review and update. Clin Immunol. 2020;214:108397.
25. Deng C, Li W, Fei Y, Li Y, Zhang F. Risk of malignancy in ankylosing spondylitis: a systematic review and meta-analysis. Sci Rep. 2016;6:32063.
26. Kelty E, Raymond W, Inderjeeth C, Keen H, Nossent J, Preen DB. Cancer diagnosis and mortality in patients with ankylosing spondylitis: a Western Australian retrospective cohort study. Int J Rheum Dis. 2021;24:216-22.
27. Chang CC, Chang CW, Nguyen PA, Chang TH, Shih YL, Chang WY, et al. Ankylosing spondylitis and the risk of cancer. Oncol Lett. 2017;14:1315-22.
28. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut. 2001;48:526-35.
29. Yao D, Dong M, Dai C, Wu S. Inflammation and inflammatory cytokine contribute to the initiation and development of ulcerative colitis and its associated cancer. Inflamm Bowel Dis. 2019;25:1595-602.
30. Pedersen N, Duricova D, Elkjaer M, Gamborg M, Munkholm P, Jess T. Risk of extra-intestinal cancer in inflammatory bowel disease: meta-analysis of population-based cohort studies. Am J Gastroenterol. 2010; 105:1480-7.
31. Beaugerie L, Carrat F, Colombel JF, Bouvier AM, Sokol H, Babouri A, et al. Risk of new or recurrent cancer under immunosuppressive therapy in patients with IBD and previous cancer. Gut. 2014;63:1416-23.
32. Andersen NN, Pasternak B, Basit S, Andersson M, Svanström H, Caspersen S, et al. Association between tumor necrosis factor-α antagonists and risk of cancer in patients with inflammatory bowel disease. JAMA. 2014;311:2406-13.
33. Waljee AK, Higgins PD, Jensen CB, Villumsen M, Cohen-Mekelburg SA, Wallace BI, et al. Anti-tumour necrosis factor-α therapy and recurrent or new primary cancers in patients with inflammatory bowel disease, rheumatoid arthritis, or psoriasis and previous cancer in Denmark: a nationwide, population-based cohort study. Lancet Gastroenterol Hepatol. 2020;5:276-84.
34. Tavakolpour S, Alesaeidi S, Darvishi M, GhasemiAdl M, Darabi-Monadi S, Akhlaghdoust M, et al. A comprehensive review of rituximab therapy in rheumatoid arthritis patients. Clin Rheumatol. 2019;38:2977-94.
35. Silva-Fernández L, Lunt M, Kearsley-Fleet L, Watson KD, Dixon WG, Symmons DP, et al. The incidence of cancer in patients with rheumatoid arthritis and a prior malignancy who receive TNF inhibitors or rituximab: results from the British society for rheumatology biologics register-rheumatoid arthritis. Rheumatology (Oxford). 2016;55:2033-9.
36. Winthrop KL. The emerging safety profile of JAK inhibitors in rheumatic disease. Nat Rev Rheumatol. 2017;13:234-43.
37. Harigai M. Growing evidence of the safety of JAK inhibitors in patients with rheumatoid arthritis. Rheumatology (Oxford). 2019;58 Suppl 1:i34-42.
38. Kuen DS, Kim BS, Chung Y. IL-17-producing cells in tumor immunity: friends or foes? Immune Netw 2020;20:e6.
39. Lebwohl M, Deodhar A, Griffiths CE, Menter MA, Poddubnyy D, Bao W, et al. The risk of malignancy in patients with secukinumab-treated psoriasis, psoriatic arthritis and ankylosing spondylitis: analysis of clinical trial and postmarketing surveillance data with up to five years of follow-up. Br J Dermatol. 2021;185:935-44.
40. Armstrong A, Paul C, Puig L, Boehncke WH, Freeman M, Torii H, et al. Safety of ixekizumab treatment for up to 5 years in adult patients with moderate-to-severe psoriasis: results from greater than 17,000 patient-years of exposure. Dermatol Ther (Heidelb). 2020;10:133-50.
41. Genovese MC, Mysler E, Tomita T, Papp KA, Salvarani C, Schwartzman S, et al. Safety of ixekizumab in adult patients with plaque psoriasis, psoriatic arthritis and axial spondyloarthritis: data from 21 clinical trials. Rheumatology (Oxford). 2020;59:3834-44.