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A literature review on Janus kinase (JAK) inhibitors for the treatment of immunobullous disorders

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ABSTRACT

Janus kinases (JAKs) are a group of intracytoplasmic tyrosine kinase proteins that bind to the cytoplasmic part of the transmembrane cytokine receptors and regulate signaling. The pathophysiology of various autoimmune and autoinflammatory conditions relies on JAK/STAT signaling and therefore, the inhibition of JAK/STAT pathways can be a promising treatment for such diseases, especially inflammatory skin conditions. The current study aimed to evaluate the efficacy of JAK inhibitors in the treatment of immunobullous diseases, including pemphigus, pemphigoid, dermatitis herpetiformis, and epidermolysis bullosa. The databases used to identify the studies were Web of Science, Scopus, and PubMed/Medline for studies published until 2/3/2022. The current review suggests that JAK inhibitors may be revolutionary for the future treatments of dermatologic conditions, especially autoimmune bullous disease. Results also indicated the effectiveness of JAK inhibitors for the treatment of immunobullous diseases.

1. Introduction

Janus kinases (JAKs) are a group of intracytoplasmic tyrosine kinase proteins that bind to the cytoplasmic part of the transmembrane cytokine receptors and regulate signaling [1]. JAKs are activated following receptor-ligand interaction, leading to tyrosine phosphorylation of the receptor. This will result in the activation of molecules called signal transducers and activators of transcription (STATs) [1,2]. The JAK/STAT pathway conveys signals from the cell membrane toward the nucleus, enabling the transcription of target genes [1–4]. Moreover, the JAK/STAT pathway plays a significant role in the signal transmission of numerous cytokines, such as interferons (IFNs), interleukin (IL)-2, IL-4, IL-7, IL-9, IL-15, IL-21, IL-13, IL-23 [5]. In addition, the JAK/STAT pathway is essential for the T-helper 2 (Th_2) cell differentiation [5]. (SeeTable 1.).

The pathophysiology of various autoimmune and autoinflammatory conditions relies on JAK/STAT signaling. Therefore, inhibition of the JAK/STAT pathway can be a promising treatment for such diseases, especially inflammatory skin conditions [2]. Evaluation of JAK inhibitors in the treatment of some dermatologic diseases like psoriasis, alopecia areata (AA), and atopic dermatitis (AD) has shown positive outcomes [3]. Recently, the Food and Drug Administration (FDA) has approved topical ruxolitinib, oral upadacitinib, and oral abrocitinib for the treatment of moderate to severe refractory AD. On the other hand, JAK/STAT pathways are suggested to be involved in the pathogenesis of autoimmune blistering diseases such as pemphigus, pemphigoid, dermatitis herpetiformis, and epidermolysis bullosa [6–8] and therefore, inhibition of the JAK/STAT pathways might be effective in treating autoimmune bullous diseases.

2. Method and materials

A thorough search was conducted on PubMed (Medline), Scopus, and Web of Science databases to select relevant studies until March 2nd, 2022.

3. Results and discussion

Analyses of skin biopsies have revealed pathophysiological factors such as cytokines, receptors, and signaling molecules present at varying

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Table 1
Characteristics of the reviewed studies.

Reference number, First author, year of publication	Study type and Study population		Gender and age (years)	Past medical history	past drug history	Disease of interest	Treatment for disease of interest that were unsuccessful.	Treatment for disease of interest with JAK-inhibitor	Treatment duration of JAK-inhibitor	outcome	Adverse effects	recurrence
[9], James, 2021	Case report, 2	Case number 1	Female, 79	Hypertension and hyperlipidemia	N/A	Ocular MMP	Methotrexate, mycophenolate mofetil, and rituximab (1 g IV × 2 infusions separated by 14 days) was ineffective after 4-month courses each. Cyclophosphamide up to 1000 mg/m2 IV was trialed after this, but did not achieve resolution of conjunctival inflmmation after 5 monthly cycles of therapy. IVIg subsequently led to a partial, but incomplete, response after 2 months of therapy	Tofacitinib 11 mg extended-release daily by mouth every 3 weeks.	After 8 weeks, she had marked improvement in her ocular inflammation. She achieved essentially quiet disease, with trace superior tarsal injection, after 8 months of therapy that was sustained for 4 more months.	Durable control of conjunctival inflmmation	None	None
		Case number 2	Male, 70	Type 2 diabetes mellitus and myocardial infarction with subsequent stenting	N/A	Ocular, nasal, and oral MMP	Topical erythromycin and cyclosporine emulsion, methotrexate and mycophenolate mofetil, cyclophosphamide, Rituximab	Tofacitinib 11 mg extended-release daily by mouth with concurrent mycophenolate mofetil 1 g twice daily by mouth.	8 weeks	Durable control of inflmmation	None	Unfortunately, due to cost, he was off tofacitinib for over a month with return of conjunctival injection and active inflmmation. This resolved after restarting tofacitinib, with quiet disease again 4 months later on follow-up. His nasal and oral ulcers did not recur during this time period.
[12], Sarny, 2018	Case report,1		Male, 43	Psoriasis	N/A	Ocular MMP	Methotrexate cyclophosphamide mycophenolate mofetil methotrexate rituximab Intravenous immunoglobulin adalimumab, prednisolone. artificial tears	Baricitinib 4 mg daily	2 months	Significant improvement	None	None
[17], Kahn, 2021	Case report,1		Male, 76	Celiac, hypertension	N/A	Dermatitis herpetiformis	Dapsone, sulfasalazine. notably, daposne was discontinued because of the dapsone-hypersensitivity	Tofacitinib 5 mg twice daily	7 months	Significant improvement	None	None

(*continued on next page*)

Table 1 (*continued*)

Reference number, First author, year of publication	Study type and Study population	Gender and age (years)	Past medical history	past drug history	Disease of interest	Treatment for disease of interest that were unsuccessful.	Treatment for disease of interest with JAK-inhibitor	Treatment duration of JAK-inhibitor	outcome	Adverse effects	recurrence
						syndrome. Gluten free diet, topical corticosteroid, tetracycline and niacin combination, doxycycline and niacin combination, and apremilast.					
[18], Chen, 2021	Case report,1	Female, 26	N/A	N/A	Epidermolysis bullosa pruriginosa	N/A	Tofacitinib 5 mg twice daily	4 weeks	Significant improvement	None	N/A
[7], Jiang, 2021	Case report, 1	Male, 40	None	None	Epidermolysis bullosa pruriginosa	Moisturizers and topical corticosteroids did not improve the symptoms.	Baricitinib, 2 mg, daily	2 weeks	Substantial improvement	None	No recurrence was reported in the follow up. The patient was followed up every 2 weeks until 16 weeks and every 8 weeks thereafter

Xx Abbreviations used in the table: JAK: Janus kinase, MMP: mucous membrane pemphigoid, IV: intravenous, IVIG: Intravenous immune globulin.

levels in different skin disorders. Therefore, new treatments for dermatologic diseases can be developed by targeting these pathophysiological factors.

In general, the binding of cytokines to their receptors initiates an inflammatory inhibitory signal and this inhibitory action can be beneficial in various dermatologic conditions [3]. JAK inhibitors have a rapid clinical onset, 1–4 weeks, and they target all or some of the members of the JAKs family, *i.e.*, JAK1, JAK2, JAK3, and TYK2 [3,9–12]. Consequently, JAK inhibitors may potentially be a rational therapeutic option in treating several immune-mediated blistering diseases (Fig. 1).

3.1. Pemphigus

Both humoral and cellular immune responses are involved in the pathology of pemphigus vulgaris (PV). Studies discovered elevated levels of IL-1β, IL-4, IL-6, IL-8, IL-10, IL-12, IL-15, and tumor necrosis factor α (TNF-α) in patients with PV [8,13]. In the meanwhile, JAK1 and 3, STAT6, and IL-4 signaling pathways are necessary for the differentiation and upregulation of Th_2 cells. Further contribution of STAT6 to the pathogenesis of PV is also predictable [8]. Moreover, IL-4 and IL-21 play an important role in developing pemphigus by driving pathogenic T cells and developing autoreactive B cells. Some studies suggest that IL-7 and IL-9 promote B cell responses, and IL-15 is involved in CD8 + promotion and function in pemphigus [14] and the association of IL-2, IL-4, IL-7, IL-9, IL-15, and IL-21 with JAK1 and JAK 3 was also reported.

In a study conducted by Tavakolpour *et al.* (2018), tofacitinib was suggested as a potential medication in the treatment of refractory pemphigus. Also, rituximab has been increasingly used in the treatment of refractory pemphigus; however, the results were not acceptable in some cases [15]. Alternatively, systemic and topical tofacitinib may be a beneficial therapeutic modality in the management of pemphigus (15); tofacitinib targets both T cell differentiation and B cells function, making it more effective than rituximab in pemphigus patients [15].

Juczynska *et al.* (2020) evaluated 15 cases of active PV who did not receive any treatments since the presence of their lesions. The expression of JAK3, STAT2, STAT4, and STAT6 were assessed using immunohistochemical methods in lesional and perilesional skin and the results were compared to healthy controls. The outcome pointed out that the expression of JAK3, STAT2, and STAT6 was significantly higher in individuals with PV compared to the control group.

3.2. Pemphigoid

The JAK/STAT pathways were also detected in the pathogenesis of pemphigoid. In a study performed by Juczynska *et al.* (2017), skin biopsies from 21 dermatitis herpetiformis (DH) patients, 20 bullous pemphigoid (BP) patients, and 10 healthy controls were obtained and assessed [6]. The evaluation of the localization and expression of STAT and JAK proteins by immunohistochemistry and immunoblotting methods revealed significantly higher JAK/STAT proteins expression among skin lesions resulting from BP and DH than in perilesional skin and the healthy subjects [6]. Moreover, IL-31 acts through the JAK/STAT signaling pathway and activates JAK-1, JAK-2, STAT-1, STAT-3, and STAT-5 in BP and DH lesions (10). JAK2 is more prominently expressed in BP lesions than in DH, which may contribute to the essential role of IL-5 in activating JAKs [16].

James *et al.* (2021) reported two cases of refractory ocular mucous membrane pemphigoid (MMP) that were successfully treated with tofacitinib [9]. MMP is a type 2 hypersensitivity reaction caused by autoantibodies against various conjunctival basement membrane zone antigens, such as the cytoplasmic domain of the β4 peptide of α6β4 integrin [9,11]. Therefore, JAK inhibitors may be effective options for individuals with severe ocular MMP, especially if they have already experienced significant fibrosis and need rapid control of the active disease [9,12]. The current review did not find any pemphigus and pemphigoid cases treated with JAK inhibitors. This might be due to the

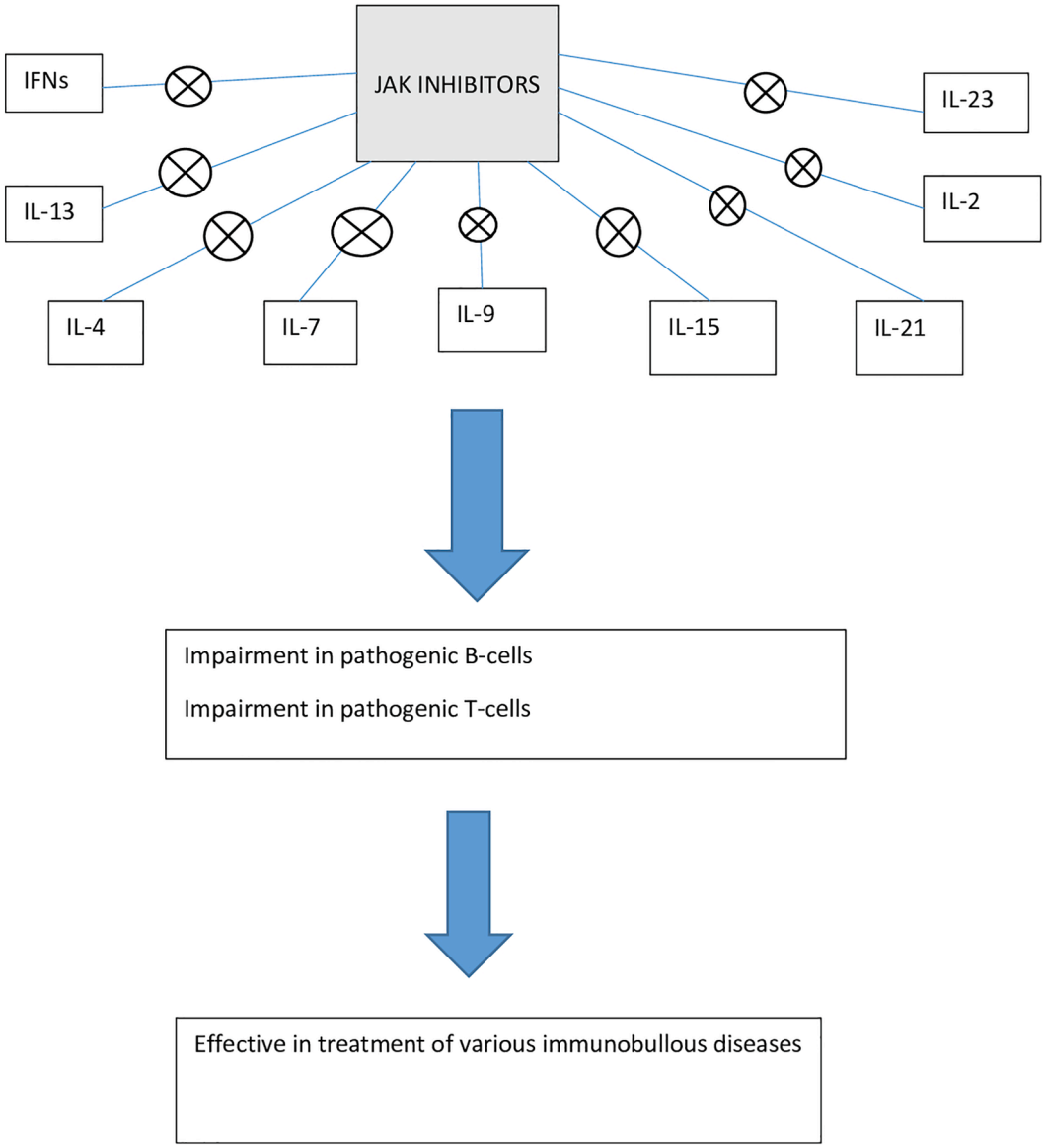

Fig. 1. JAK inhibitors' suggested mechanism of action in treating immunobullous diseases.

fact that these treatments are novel, and few studies have evaluated their efficacies in treating dermatological diseases. As discussed above, JAK inhibitors might be a promising treatment in pemphigus and pemphigoid patients, and we suggest further clinical studies assessing the efficacy of JAK inhibitors in these patients.

3.3. Dermatitis herpetiformis

Based on the study conducted by Juczynska *et al.* (2020), the expression of STAT3 and STAT4 is significantly higher in DH lesions, reflecting the crucial roles of IL-6, TNF-α, IL-8, IL-17, and IL-12 in DH [8]. The application of ruxolitinib in the treatment of BP and DH is under consideration since it inhibits JAK1 and JAK2 pathways and prevents differentiation of Th17 cells; these two pathways are essential in the pathogenesis of BP and DH [8].

Kahn *et al.* (2021) reported a case of DH who was unsuccessfully treated with topical corticosteroids, gluten-free diet, tetracycline-niacin combination, apremilast, and doxycycline-niacin combination. The patient also received a trial of oral dapsone, which was discontinued due to dapsone-hypersensitivity syndrome. Ultimately, the patient was successfully treated with oral tofacitinib 5 mg twice daily and no new lesions appeared afterward [17].

3.4. Epidermolysis bullosa

Successful treatment of epidermolysis bullosa pruriginosa has been reported following the use of tofacitinib in a 26-year-old female [18]. Another study reported the efficacy of Baricitinib in treating epidermolysis bullosa pruriginosa in a 40-year-old male [7]. JAK inhibitors have also demonstrated efficacy in other aspects in people with epidermolysis bullosa. Notably, squamous cell carcinoma (SCC) is the main cause of mortality in recessive dystrophic epidermolysis bullosa (RDEB) patients, with more than 80% death by age 55; targeting this altered and fibrotic microenvironment could be a beneficial therapeutic strategy. Ruxolitinib successfully prevented in vitro invasion of SCC tumors by targeting the cancer-associated fibroblasts [19,20].

3.5. Animal studies

Several preclinical studies demonstrated the inhibitory effects of JAK inhibitors on the production of autoantibodies [21]. Carrasco *et al.* (2021) reported a case of pemphigus foliaceus (PF) in a cat that was

successfully treated with oclacitinib [22]. Another case of autoimmune subepidermal blistering in a dog was successfully treated with oclacitinib 0.5 mg/kg, twice daily for one month, with no reported adverse effects [23]. Notably, oclacitinib modifies the production of cytokines such as IL-4 and IL-13, which are crucial for B-cell proliferation and maturation in the pathogenesis of PF [22].

Currently, corticosteroids and immunosuppressants are the main therapy for immune blistering diseases. The potential side effects of corticosteroids are local skin atrophy, telangiectasias, striae, acne, adrenal suppression, weight gain, glucose intolerance, and insomnia. [24,25]. Monoclonal antibodies are also one of the most effective therapies that directly block the cytokines or their receptors [24].

JAK inhibitors may cause unwanted adverse effects such as infections and, in some cases, cancer development; interferons and natural killer cells play a crucial role in tumor surveillance and their suppression by JAK inhibitors can increase the risk of malignant transformation [25]. Furthermore, serum creatinine elevation, thrombocytopenia, neutropenia, and hypercholesterolemia have been associated with tofacitinib. The effects of JAK proteins on pathways that affect intermediate metabolism can cause elevations in both low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol [26]. JAK inhibition may also lead to anemia in some patients since erythropoietin, one of the proteins that drive red blood cell production is also decreased by JAK inhibitors [26]. Some less severe side effects may include nausea, indigestion, diarrhea, or headaches. To prevent negative side effects, periodic blood tests such as complete blood count, lipid profile, and liver function tests are beneficial. JAK inhibitors are prescribed in both topical and systemic forms; the topical application may mitigate the side effects compared to systemic administration [25].

In vitro, JAK inhibitors interact with transporters in various ways, acting as inhibitors, substrates of transporters, or regulators of transporter expression. In theory, it may lead to drug-drug interactions (DDIs), with JAK inhibitors acting as perpetrators or victims, or in toxicity through impairment of thiamine transport [27,28]. JAK inhibitors are believed to interact with moderate cytochrome P450 (CYP) 3A4 inhibitors, strong organic anion transporter (OAT3) inhibitors, and strong CYP2C19 inhibitors [27].

4. Conclusion

Numerous treatment options exist for immunobullous skin diseases [29–31]. JAK inhibitors may be revolutionary in treating dermatologic conditions, especially autoimmune bullous disease. Our study indicates the effectiveness of JAK inhibitors in the treatment of MMP, DH, and epidermolysis bullosa (EB); however, there has not been a clinical trial to test the efficacy and safety of JAK inhibitors in the treatment of immune blistering diseases. Larger scale studies with long-term follow-ups are essential to clarify the effectiveness and safety of JAK inhibitors in treating immunobullous disorders.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] V. Reddy, S. Cohen, Jak inhibitors: What is new? Curr. Rheumatol. Rep. 22 (9) (2020 Sep) 1.
[2] W. Damsky, B.A. King, JAK inhibitors in dermatology: the promise of a new drug class, J. Am. Acad. Dermatol. 76 (4) (2017 Apr 1) 736–744.
[3] F. Solimani, K. Meier, K. Ghoreschi, Emerging topical and systemic JAK inhibitors in dermatology, Front. Immunol. 2847 (2019).
[4] R. Shreberk-Hassidim, Y. Ramot, A. Zlotogorski, Janus kinase inhibitors in dermatology: a systematic review, J. Am. Acad. Dermatol. 76 (4) (2017 Apr 1) 745–753.
[5] P. Ciechanowicz, A. Rakowska, M. Sikora, L. Rudnicka, JAK-inhibitors in dermatology: current evidence and future applications, Journal of Dermatological Treatment. 30 (7) (2019 Oct 3) 648–658.
[6] K. Juczynska, A. Wozniacka, E. Waszczykowska, M. Danilewicz, M. Wagrowska-Danilewicz, J. Wieczfinska, R. Pawliczak, A. Zebrowska, Expression of the JAK/STAT signaling pathway in bullous pemphigoid and dermatitis herpetiformis, Mediators Inflamm. 2017 (2017) 1–12.
[7] X. Jiang, H. Wang, M. Lee, Z. Lin, Epidermolysis Bullosa Pruriginosa Treated With Baricitinib, JAMA dermatology. 157 (10) (2021 Oct 1) 1243–1244.
[8] K. Juczynska, A. Wozniacka, E. Waszczykowska, M. Danilewicz, M. Wągrowska-Danilewicz, A. Zebrowska, Expression of JAK3, STAT2, STAT4, and STAT6 in pemphigus vulgaris, Immunol. Res. 68 (2) (2020 Apr) 97–103.
[9] H. James, G.L. Paley, R. Brasington, P.L. Custer, T.P. Margolis, M.A. Paley, Tofacitinib for refractory ocular mucous membrane pemphigoid, American Journal of Ophthalmology Case Reports. 1 (22) (2021 Jun), 101104.
[10] L. Kulczycka-Siennicka, A. Cynkier, E. Waszczykowska, A. Woźniacka, A. Żebrowska, The role of intereukin-31 in pathogenesis of itch and its intensity in a course of bullous pemphigoid and dermatitis herpetiformis, BioMed Research International. 2017 (2017) 1–8.
[11] K.C. Bhol, M.J. Dans, R.K. Simmons, C.S. Foster, F.G. Giancotti, A.R. Ahmed, The autoantibodies to α6β4 integrin of patients affected by ocular cicatricial pemphigoid recognize predominantly epitopes within the large cytoplasmic domain of human β4, J. Immunol. 165 (5) (2000 Sep 1) 2824–2829.
[12] S. Sarny, M. Hucke, Y. El-Shabrawi, Treatment of mucous membrane pemphigoid with Janus kinase inhibitor baricitinib, JAMA ophthalmology. 136 (12) (2018 Dec 1) 1420–1422.
[13] Balighi K, Hatami P, Sheikh Aboli MJ, Daneshpazhooh M, Ghiasi M, Mahmoudi HR, Aryanian Z. Multiple cycles of rituximab therapy for pemphigus: A group of patients with difficult-to-treat disease or a consequence of late rituximab initiation?. Dermatologic Therapy. 2022 Feb;35(2):e15249.
[14] H.F. Pan, R.X. Leng, X.P. Li, S.G. Zheng, D.Q. Ye, Targeting T-helper 9 cells and interleukin-9 in autoimmune diseases, Cytokine Growth Factor Rev. 24 (6) (2013 Dec 1) 515–522.
[15] Tavakolpour S. Tofacitinib as the potent treatment for refractory pemphigus: a possible alternative treatment for pemphigus. Dermatologic Therapy. 2018 Sep;31 (5):e12696.
[16] K. Takatsu, H. Nakajima, IL-5 and eosinophilia, Curr. Opin. Immunol. 20 (3) (2008 Jun 1) 288–294.
[17] J.S. Kahn, K. Moody, D. Rosmarin, Significant improvement of dermatitis herpetiformis with tofacitinib, Dermatol. Online J. 27 (7) (2021).
[18] K.J. Chen, S. Fang, Q. Ye, M. Jia, Successful use of tofacitinib in epidermolysis bullosa pruriginosa, Clin. Exp. Dermatol. 47 (3) (2022 Mar) 598–600.
[19] A.G. Condorelli, E. Dellambra, E. Logli, G. Zambruno, D. Castiglia, Epidermolysis bullosa-associated squamous cell carcinoma: from pathogenesis to therapeutic perspectives, Int. J. Mol. Sci. 20 (22) (2019 Jan) 5707.
[20] J. Uitto, Toward treatment and cure of epidermolysis bullosa, Proc. Natl. Acad. Sci. 116 (52) (2019 Dec 26) 26147–26149.
[21] M. Onda, K. Ghoreschi, S. Steward-Tharp, C. Thomas, J.J. O'Shea, I.H. Pastan, D. J. FitzGerald, Tofacitinib suppresses antibody responses to protein therapeutics in murine hosts, J. Immunol. 193 (1) (2014 Jul 1) 48–55.
[22] I. Carrasco, M. Martínez, G. Albinyana, Beneficial effect of oclacitinib in a case of feline pemphigus foliaceus, Vet. Dermatol. 32 (3) (2021 Jun) 299–301.
[23] E. Aymeric, E. Bensignor, A case of presumed autoimmune subepidermal blistering dermatosis treated with oclacitinib, Vet. Dermatol. 28 (5) (2017 Oct) 512–e123.
[24] Y. Jamilloux, T. El Jammal, L. Vuitton, M. Gerfaud-Valentin, S. Kerever, P. Sève, JAK inhibitors for the treatment of autoimmune and inflammatory diseases, Autoimmun. Rev. 18 (11) (2019).
[25] E.H. Wang, B.N. Sallee, C.I. Tejeda, A.M. Christiano, JAK inhibitors for treatment of alopecia areata, J, Invest. Dermatol. 138 (9) (2018 Sep 1) 1911–1916.
[26] B. Feagan, Update on tofacitinib for inflammatory bowel disease, Gastroenterology & hepatology. 12 (9) (2016 Sep) 572.
[27] A. Walton, J. Paik, A. Quebe, C.L. Kannowski, C. Choong, S. Anderson, J. K. Owensby, Frequency of Prescription Claims for Drugs that May Interact with Janus Kinase Inhibitors Among Patients with Rheumatoid Arthritis in the US, Rheumatology and Therapy. 8 (1) (2021 Mar) 599–607.
[28] K. Alim, A. Bruyère, A. Lescoat, E. Jouan, V. Lecureur, M. Le Vée, O. Fardel, Interactions of janus kinase inhibitors with drug transporters and consequences for pharmacokinetics and toxicity, Expert Opin. Drug Metab. Toxicol. 17 (3) (2021 Mar 4) 259–271.
[29] Z. Aryanian, K. Balighi, M. Daneshpazhooh, E. Karamshahi, P. Hatami, A. Goodarzi, M. Tajalli, T.M. Vance, Rituximab exhibits a better safety profile when

used as a first line of treatment for pemphigus vulgaris: A retrospective study, International Immunopharmacology. 1 (96) (2021 Jul), 107755.

[30] A. Goodarzi, A comprehensive review on vitamin D receptor (VDR) gene polymorphism in immune-related diseases with emphasis on dermatologic disorders, Iranian Journal of Dermatology. 22 (4) (2020 Jan 1) 151–160.

[31] S. Tavakolpour, Z. Aryanian, F. Seirafianpour, M. Dodangeh, I. Etesami, M. Daneshpazhooh, K. Balighi, H. Mahmoudi, A. Goodarzi, A systematic review on efficacy, safety, and treatment-durability of low-dose rituximab for the treatment of Pemphigus: special focus on COVID-19 pandemic concerns, Immunopharmacology and Immunotoxicology. 43 (5) (2021 Sep 3) 507–518.