A Review of the Safety of Interleukin-17A Inhibitor Secukinumab

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Abstract: Secukinumab is an anti-interleukin (IL)-17A IgG1-κ monoclonal antibody approved for psoriasis, psoriatic arthritis, and ankylosing spondylitis. Its efficacy is well documented, but the complete safety profile of secukinumab, especially on long-term use, needs to be studied. IL-17 inhibitors increase the risk of infections, especially respiratory tract infections and candidiasis, and inflammatory bowel disease; the causal relationships are well described. However, evidence regarding the other adverse events is scarce, and causal associations between the adverse events and the biologic remain unresolved. This review aims to present a narrative perspective on the safety of secukinumab and identify some key areas where the safety of secukinumab may potentially be useful in understanding the scope of secukinumab therapy and making informed clinical decisions.

Keywords: secukinumab; interleukin 17; adverse event; psoriasis; inflammatory bowel disease

1. Introduction

Secukinumab is a fully humanised immunoglobulin G1 (IgG1) κ monoclonal antibody that directly inhibits interleukin-17A (IL-17A). IL-17A is a proinflammatory cytokine; IL-17B to IL-17F are the other isoforms [1]. IL-17A and IL-17F are currently drug targets for the treatment of autoimmune diseases [2]. In normal conditions, IL-17 is involved in mucocutaneous defence [3] and immunity against extracellular pathogens [4]. However, elevated levels of IL-17 are associated with autoimmune diseases, immunopathological conditions, and cancer progression [5]. Figure 1 illustrates the physiological roles of IL-17A.

Figure 1. Physiological and immunological functions of IL-17A [6,7].

The emergence of biologics that inhibit IL-17 has provided new avenues in the maintenance therapy of many autoimmune diseases [8], in which secukinumab has proven...
efficacy in psoriasis, psoriatic arthritis, and ankylosing spondylitis. Though the treatment options for autoimmune diseases have increased recently, there is still little evidence in the form of efficacy studies comparing one biologic to another to make informed treatment decisions. As a result, the priority of choosing one cytokine inhibitor over another is still unclear. Secukinumab is indicated in moderate to severe plaque psoriasis and other psoriasis types. It can be started in patients who are naïve to biologics as well as in patients in whom other biologics have been ineffective or unsafe [9]. Other biologics used in psoriasis treatment are tumour necrosis factor (TNF)-α inhibitors, IL-12/23 inhibitors, and other IL-17 inhibitors. Secukinumab is also employed similarly in psoriatic arthritis, a heterogeneous inflammatory condition having musculoskeletal features associated with psoriasis [10]. In patients with ankylosing spondylitis, secukinumab is indicated when the symptoms remain unresolved with the use of nonsteroidal anti-inflammatory drugs. However, TNF-α inhibitors are preferred over IL-17 inhibitors in ankylosing spondylitis because of the availability of long-term efficacy and safety data to support the use of the former [11].

The involvement of IL-17 has also been described in certain nonpsoriatic dermatological conditions, such as hidradenitis suppurativa, pityriasis rubra pilaris, and Behçet’s disease, and secukinumab is used off-label in these conditions [12]. Secukinumab was shown to be efficacious, with a slow onset of action, in eight patients with refractory spontaneous chronic urticaria and reduced the severity and frequency of angioedema [13]. Secukinumab has also demonstrated significant improvement in papulopustular rosacea in an open-label study [14]. A child with ABCA12 deficiency-related ichthyosis showed improvement with secukinumab when given over 6 months [15]. As evidence regarding the role of IL-17 is beginning to unravel in various conditions, it becomes important to study the adverse events associated with the biologics that inhibit this cytokine. IL-17 inhibitors are novel drugs, with secukinumab being the oldest. There is little evidence of the long-term safety of this biologic.

Secukinumab has shown a favourable safety profile in clinical trials, with the most common adverse effects being upper respiratory tract infection, headache, nasopharyngitis, candida infection, hypersensitivity reaction, arthralgia, hypertension, diarrhoea, back pain, pruritus, and cough [16]. Other adverse events of interest associated with secukinumab use are neutropenia, malignant or unspecified tumours, inflammatory bowel disease (IBD), and major adverse cardiovascular events (MACE) [17]. Clinical trial data alone may be insufficient in describing the true adverse event profile of a drug used in chronic conditions. Hence, there is a need for robust pharmacovigilance measures in verifying the safety profile of the drug along with finding any new adverse event signals that are unknown yet [18].

We present here a narrative review of the safety of secukinumab, starting with the role of IL-17 in chronic immune disorders and general concerns associated with the use of IL-17 inhibitors, and then describing the literature for secukinumab and enumerating some of the important safety issues identified on the basis of available literature. The safety of secukinumab based on clinical trial data has been reviewed elsewhere [19]; we mainly focused on case reports and real-world studies in this review, with the key findings from clinical trials being mentioned briefly. The literature search methodology has been briefly described in Supplementary Material S1.

2. Role of IL-17 in Psoriasis and Related Disorders

Psoriasis is a chronic immune condition of the skin characterised by hyperproliferation and keratinocyte activation, manifesting as grey, scaly, erythematous plaques/lesions on the skin [20]. The role of many proinflammatory cytokines, such as TNF-α, IL-12, IL-17, IL-23, and interferon-γ (INF-γ), has been established [21]. The secretion of IL-17 is achieved through a number of immune cells, such as macrophages, dendritic cells, natural killer cells [22], and T-cells, driven with the help of T-helper cell 17 (Th17) [6]. IL-17 drives inflammation by increasing the levels of the psoriatic autoantigen, antimicrobial peptide LL37, which in turn increases the levels of another psoriatic autoantigen, ADAMTS-like
protein, which then increases the expression of IL-17 and INF-γ, forming a positive feedback loop [23]. In addition, IL-17 also promotes the production of proinflammatory cytokines such as IL-6, IL-8, granulocyte colony-stimulating factor, granulocyte-macrophage-colony-stimulating factor, and chemokine (C-C motif) ligand 20, further driving inflammation [24]. IL-17 also induces keratinocyte differentiation by forming a receptor complex through binding to the IL-17 receptor; the complex then binds to epidermal growth factor-α, which induces various signal transduction pathways, ultimately increasing keratinocyte levels [25]. The inflammatory phenomenon, coupled with the role of IL-17 role in influencing the proliferation of keratinocytes, is seen to be a key factor for the manifestation of psoriatic plaques. Psoriatic arthritis is a heterogenous immune condition having the features of both psoriasis and inflammatory arthritis [26]. IL-17 has similar effects in the synovial fluid, prolonging inflammation and inducing synovitis [27].

Ankylosing spondylitis is an autoimmune condition that affects the spine joints, causing severe long-term pain [28]. It is characterised by damage to the sacroiliac joints and spinal ankylosis due to new bone formation [29]. IL-17 promotes bone growth and regeneration by inducing the proliferation and differentiation of osteoclasts [30], along with inflammation which may worsen the radiographic progression of the disease [31].

3. Safety Concerns with IL-17 Inhibitors

Biologics are genetically engineered drugs [32] of biomolecular origin, i.e., proteins, nucleic acids, sugars, or a complex combination of these substances [33]. Monoclonal antibodies are generally well tolerated; however, serious, rare, and unpredictable adverse drug reactions are associated with their use [34]. Unlike chemically synthesised drugs, the adverse drug events that occur as a consequence of monoclonal antibody therapy are target-related and associated with the biological consequences of their action [35]. As far as IL-17 inhibitors are concerned, there are three different mechanisms by which the inflammatory signalling is inhibited: secukinumab and ixekizumab inhibit IL-17A [36,37]; bimekizumab inhibits IL-17A and -17F [38]; brodalumab inhibits IL-17RA and -17RC receptors [39].

Since there are considerable differences in the mechanism of IL-17 inhibition, there may be variations in the adverse events exhibited by individual monoclonal antibodies. A clinical trial comparing the safety and efficacy of bimekizumab versus secukinumab in patients with plaque psoriasis showed higher rates of oral candidiasis in those receiving the former drug, although the overall rates of adverse events, including serious adverse events, were similar in both groups [40]; this may be due to the dual-target inhibition of IL-17A and IL-17F. Inhibition of IL-17RA and IL-17RC hinders the actions of not just IL-17A but also its isoforms, which may also produce variations in the adverse event profiles of IL-17 inhibitors. Similarly, brodalumab is contraindicated in Crohn’s disease [41], whereas ixekizumab and secukinumab have warning labels in the prescribing information [42,43].

Hence, there is a need for more evidence to understand the safety profile of each monoclonal antibody in IL-17 inhibition. Pichler proposed a classification of adverse events on the basis of the use of monoclonal antibodies, which can aid in identifying and classifying newly discovered adverse events [44], such as reactions caused by high levels of cytokines, hypersensitivity reactions, those due to immune or cytokine imbalance, symptoms caused by cross-reactivity, and nonimmunological reactions. Table 1 lists the important adverse effects of secukinumab according to Pichler’s classification.

Many proinflammatory cytokines are associated with the progression of autoimmune diseases. Monoclonal antibodies selectively suppress these cytokines leading to alteration in immune homeostasis and physiological responses. This may directly affect the incidence of adverse events that are unique to each target cytokine. A meta-analysis of short-term efficacy and safety of biologicals for moderate to severe plaque psoriasis found secukinumab to have the second-highest risk of adverse events following ixekizumab [45]. Three cases of tooth abscess were reported in a pharmacovigilance study conducted in Italy assessing the safety of biologics in rheumatology [46]. Another pharmacovigilance study assessing the safety of biologics in psoriasis did not identify any adverse drug events...
with secukinumab [47]. In addition, a study aimed to understand the use of secukinumab in Asian and Middle-Eastern populations did not identify any new adverse signals [48]. In a real-world study involving Japanese patients, the most commonly reported adverse reaction was oral candidiasis (2.9%); the incidence of IBD was low, two patients developed tuberculosis, and the percentage of patients who developed cardiac adverse events was 2.3% out of 306 patients [49]. The important adverse effects of secukinumab are depicted in Figure 2 and described in detail below.

**Table 1.** List of adverse drug reactions to secukinumab as per Pichler’s classification [44].

| Adverse Event Class | Adverse Events                                                                 |
|---------------------|-------------------------------------------------------------------------------|
| Type-α              | None reported to date                                                         |
| Type-β              | Hypersensitivity and injection site reactions                                 |
| Type-γ              | Inflammatory bowel disease, infections, allergic and atopic disorders, neutropenia, and paradoxical inflammatory adverse events. |
| Type-δ              | None reported to date                                                         |
| Type-ε              | Major adverse cardiovascular events, malignancy                               |

Type-α, due to high levels of cytokines and cytokine release syndrome; type-β, hypersensitivity reactions; type-γ, immune or cytokine imbalance syndromes; type-δ, symptoms due to cross reactivity; type-ε, nonimmunological reactions.

**Figure 2.** Potential adverse effects of secukinumab.

### 4. Important Adverse Effects of Secukinumab

#### 4.1. Infections

Cytokine inhibition leads to a diminished inflammatory response, especially adaptive immunity, against pathogens. IL-17 is involved in host immunity against extracellular bacteria and fungi, which may explain the higher incidence of infections and candidiasis [50]. Autoimmune diseases themselves are a risk factor for infection [51]. Upper respiratory tract infections are common with the use of monoclonal antibodies, including secukinumab use [17]. A register-linked cohort study of Swedish patients with psoriasis showed the occurrence of respiratory and urinary tract infections to be slightly higher with secukinumab than with ustekinumab with a hazard ratio of 1.22 (95% CI: 1.03–1.43) [52]. A
systematic review and meta-analysis suggested that the most occurring immune system adverse events in patients with ankylosing spondylitis treated with IL-17 inhibitors were mucosal and cutaneous infections [53].

Opportunistic infections, including tuberculosis, herpes zoster, pneumocystis jiroveci, legionella, and histoplasmosis, pose a safety concern with the use of monoclonal antibodies. Management of the opportunistic agents includes screening, immunisation, chemoprophylaxis, or treatment with antimicrobial agents [54,55]. A pooled cohort analysis of clinical trial data revealed no cases of active tuberculosis, and 0.1% of patients developed latent tuberculosis [56]. Herpes zoster infection occurred in 12/221 patients with an exposure-adjusted incidence rate (EAIR) of 2.9 per 100 patient-year [57]. A solitary case of viral pericarditis was seen in a 2-year observational study on 43 patients with palmoplantar psoriasis [58]. Two cases of cellulitis were observed in an observational study of 63 patients, where one patient had preseptal cellulitis and required hospitalisation, and the other discontinued treatment [59]. Another patient in the same study developed pneumonia requiring intensive care; secukinumab was discontinued in this patient [59].

Herpes simplex keratitis has also been described with the use of secukinumab [60]. A patient with psoriasis and psoriatic arthritis with hepatitis B was well-maintained on secukinumab with a follow-up of 2 years [61]. Similar results were also expressed in a case series of four patients with hepatitis B, although the authors have shared their concerns over the disparity of patient management at the individual level [62]. Long-term studies are required to establish the safety of secukinumab in patients with the hepatitis B virus. The occurrence of histoplasma capsulatum infection in a 45-year-old man with ankylosing spondylitis on secukinumab therapy has also been described [63]. Case reports of infections with secukinumab use are highlighted in Table 2.
| Author(s)          | Adverse Drug Event                      | Indication          | Age/Sex | Duration Since Initiation of Secukinumab | Previous History of Biologic Use | Concomitant Medication | Management                                                                                     | Discontinuation of Secukinumab |
|-------------------|----------------------------------------|---------------------|---------|-----------------------------------------|---------------------------------|------------------------|----------------------------------------------------------------------------------------------|-------------------------------|
| Sinha et al. [60] | Herpes keratitis                        | Psoriasis           | 35/M    | 4 weeks                                 | No                              | NA                     | 3% Acyclovir five times a day, topical moxifloxacin eye drops four times a day, along with topical lubricant eye drops, topical steroids, and emollients for psoriasis | NA                            |
| Wang [63]         | Scleritis due to *Histoplasma capsulatum* | Ankylosing spondylitis | 45/M    | NA                                      | NA                              | Intravitreal triamcinolone; topical prednisolone; oral prednisone | Left eye: oral itraconazole 200 mg twice daily and fortified topical amphotericin B 0.15% four times daily with a rapid taper of oral prednisone. Right eye: topical amphotericin for two months until the subconjunctival purulence resolved. Maintenance: 6-month course of itraconazole | NA                            |
| Martin et al. [64]| Staphylococcal toxic shock syndrome     | Psoriasis           | 6/F     | 2 weeks                                 | NA                              | NA                     | Levofoxacin and rifampin, followed by trimethoprim/sulfamethoxazole, and cefuroxime unt | Yes                           |
| Utiyama et al. [65]| Infective dermatitis                   | Psoriasis           | 71/F    | 2 months                                | No                              | NA                     | Sulfamethoxazole and trimethoprim followed by doxycycline.                                       | Yes                           |
| Fisher et al. [66]| Necrotising fasciitis                  | Psoriasis           | 18/M    | 4 weeks                                 | No                              | NA                     | Surgical debridement followed by intravenous antibiotics                                           | No                            |
| Anderson et al. [67]| Invasive *Haemophilus influenzae*       | Psoriatic arthritis | 42/F    | 18 months                               | Yes                             | NA                     | Empiric gentamicin and metronidazole, which was narrowed to ceftriaxone and metronidazole        | NA                            |

NA, data not available.
4.2. Candidiasis

Candida infection is the most common opportunistic fungal infection observed in immunocompromised patients. Candida species in the gut are hypothesised to worsen psoriasis by stimulating nonspecific T cells and superantigens contributing further to the inflammatory cascade observed in psoriasis [68]. IL-17 is involved in neutrophil recruitment, the release of antimicrobial peptides, and the protection of mucocutaneous barriers [69]. Impairment of this function by IL-17 inhibitors used in psoriasis is causal with a candida infection. Both oral and gastrointestinal candidiasis manifestations are observed with secukinumab use. A pooled analysis of clinical trial data revealed that all cases of candidiasis were mild to moderate in severity; no cases of systemic candidiasis were reported; the EAIR were 2.2, 1.5, and 0.7 per 100 patient-years in psoriasis, psoriatic arthritis, and ankylosing spondylitis groups, respectively [70]. A postmarketing study revealed that the incidence of candidiasis is 4–10 times higher in patients treated with IL-17 inhibitors compared with those treated with TNF-α inhibitors [71]. Such cases can be managed using clotrimazole troche, nystatin suspension, miconazole mucoadhesive buccal tablet, or oral fluconazole for 7–14 days [72]. Case reports of candidiasis are described in Table 3.
Table 3. Case reports of candidiasis associated with secukinumab use.

| Author(s)          | Adverse Drug Event                      | Indication       | Age/Sex | Duration Since Initiation of Secukinumab | Previous History of Biologic Use | Concomitant Medication | Management                                                                 | Discontinuation of Secukinumab |
|--------------------|-----------------------------------------|------------------|---------|------------------------------------------|---------------------------------|-------------------------|----------------------------------------------------------------------------|-------------------------------|
| Picciani et al. [73] | Oral candidiasis                        | Psoriasis        | 50/F    | 6 months                                 | Yes                             | NA                      | Miconazole gel                                                             | Resumed at a lower dose after management |
| Kang et al. [74]    | Oesophageal candidiasis                 | Psoriasis        | 61/M    | 3 weeks                                  | NA                              | NA                      | Fluconazole 200 mg/day for seven days; switched to guselkumab after infection resolved | Yes                           |
| Faccini et al. [75] | Candidemia                              | Psoriatic arthritis | 42/F    | 2 months                                 | Yes                             | NA                      | Amphotericin B switched to anidulafungin 100 mg OD.                          | Yes                           |
| Farah [76]          | Hyperplastic candidosis and oral lichenoid lesion | Psoriasis        | 52/F    | NA                                       | NA                              | Perindopril arginine, pantoprazole, mometasone furoate. | Oral                         | No                             |
| Capusan et al. [77] | Oral lichenoid reaction with candidiasis | Psoriasis        | 62/M    | 8 months                                 | Yes                             | NA                      | Intralesional corticosteroids and itraconazole; switched to apremilast for psoriasis | Yes                           |
| Komori et al. [78]  | Oral lichen planus with candidiasis     | Psoriasis        | 74/F    | 5 months                                 | Yes                             | NA                      | Amphotericin B syrup                                                        | Yes                           |

NA, data not available.
4.3. Injection Site Reactions

Monoclonal antibodies are proteins susceptible to gastrointestinal degradation. As a result, they are administered parenterally to attain clinically relevant plasma concentrations. The preferred route of administration of biologics is the subcutaneous route. Self-injector devices have made the administration of monoclonal antibodies easier. However, injection site reactions (ISR), such as swelling, erythema, pruritus, and pain around the site of injection [79], are seen with the use of monoclonal antibodies and biologics in general. ISR occurs either due to the excipients or the drug itself and can be irritative or allergic reactions [80]. A phase I study assessing the pharmacokinetics and tolerability of subcutaneous formulations of secukinumab injected using different devices showed the occurrence of erythema, induration, haemorrhage, pruritis, and leakage. However, apart from erythema, the overall incidence of the other ISR is low [81]. In contrast, a postmarketing study revealed pain, bruising, and haemorrhage to be common ISR with secukinumab use [82]; however, the incidence of erythema, pruritis, reaction (injection-site related), and swelling were higher with ixekizumab compared with secukinumab [82]. Some of the patient factors that indicate a higher risk of ISR are female gender, low body weight, and the presence of fibromyalgia, depression, or severe rheumatoid arthritis [83].

4.4. Neutropenia

IL-17 has a role in neutrophil recruitment, function, and survival [84]. A proposed mechanism is by inducing chemokines CXCL1 and CXCL2 [85]. Neutropenia is a prevalent complication in immunocompromised patients with significant morbidity and mortality rate [86]. Grade-3 neutropenia (absolute neutrophil count ≥500 to 1000 cells/mm$^3$) and grade-4 neutropenia (absolute neutrophil count <500 cells/mm$^3$) have occurred in the clinical trial setting, with the latter being rare. However, the incidence of neutropenia with secukinumab is low, with an EAIR of 0.3, 0.2, and 0.5 per 100 patient-years in patients with psoriasis, psoriatic arthritis, and ankylosing spondylitis, respectively; uncomplicated viral upper respiratory tract infection was the most commonly observed adverse event co-reported with neutropenia [70]. A retrospective study that followed up 36 patients for 6 months on secukinumab revealed no significant difference in the haematologic parameters from baseline till the end of the study [87]. This may imply that IL-17 by itself does not have a major role in the recruitment of neutrophils [88].

4.5. Malignancy

The association between autoimmunity and cancer is a topic of great interest. Immune cells and cytokines dysregulated in autoimmune conditions may play a role in the development of cancer [89]. A meta-analysis showed that patients with psoriasis are 1.18 times at risk of developing cancer, with a 1.22-fold increase in cancer mortality compared with psoriasis-free patients [90]; however, none of the studies in the meta-analysis adequately adjusted for treatment exposure. Another study showed that the risk of developing high-grade cervical dysplasia and cervical cancer was 1.49 per 1000 patients [91]. In addition, the risk of keratinocyte cancer, lymphomas, lung cancer, bladder cancer, lymphoma, and non-Hodgkin’s lymphoma is increased in patients having psoriasis [92]. A higher risk of lymphohematologic malignancies and lymphoma was seen in a meta-analysis of observational cohort studies [93]. In a large-scale cohort study, males with ankylosing spondylitis had a higher risk of bone, prostate, and haematological malignancies, whereas females were at an increased risk of colon and haematological malignancies [94].

IL-17 has a controversial role in tumour immunity as it is hypothesised to play a role in both tumour suppression as well as proliferation [5]. Pooled data from clinical trials and postmarketing studies showed the low and infrequent incidence of malignancy in the secukinumab-treated patient population over a 5-year follow-up period [95]. As far as warnings in prescribing information are concerned, only ustekinumab and TNF-α have warnings against malignancy (especially lymphoma). This may be due to the availability
of long-term data for these monoclonal antibodies. There is a need for long-term studies to evaluate the safety of secukinumab and other IL-17 inhibitors.

4.6. IBD

IBD is a chronic autoimmune condition observed in the large intestine, manifesting as Crohn’s disease (CD) or ulcerative colitis (UC). IBD is well-documented comorbidity in psoriasis [96]. Patients with psoriasis are three times more likely to develop CD [97]. Earlier, it was postulated that high levels of IL-17 exacerbate IBD [85]. However, a phase II trial of secukinumab in IBD patients was terminated due to worsening disease and unsatisfactory efficacy. In this study, 4 out of 7 drug-related adverse events were worsening of Crohn’s disease, and two additional adverse events occurred: pilonidal cyst and ileostomy, which were related to the worsening of CD with secukinumab treatment [98]. The drug label of secukinumab contains warnings and precautions while administering the drug to patients suffering from IBD. A similar incident occurred in 1999 when a TNF-α inhibitor lenerecept was tried on patients with multiple sclerosis [99]. In a randomised phase II clinical trial of brodalumab, the worsening of CD represented 25% of the total adverse events, and brodalumab is contraindicated in CD [88]. Though the incidence of CD in the secukinumab trial was 15.4%, its incidence rate is similar to the placebo, whereas, with brodalumab, only 6% of the participants in the placebo group reported worsening of CD [98,100]. The increased severity found in brodalumab may be due to the inhibition of all the ligands of IL-17 through IL-17RA and IL-17 RC receptor inhibition. In contrast, secukinumab targets IL-17A with high specificity. In clinical trials, the EAIR of IBD was low; 0.01, 0.05, and 0.1 per 100 patient-year in those with psoriasis, psoriatic arthritis, and ankylosing spondylitis, respectively; this led to the discontinuation of secukinumab in all the affected cases [70].

The link between IBD and secukinumab has been identified in the postmarketing setting as well. A retrospective cohort study consisting of patients on secukinumab for ankylosing spondylitis and psoriatic arthritis found associations between secukinumab and low rates of absolute gastrointestinal-related adverse events. In addition, exacerbation of existing conditions is more likely and tends to occur within one year [101]. A retrospective analysis of Vigibase data showed anti-IL-17 use associated with an exacerbation or new onset of IBD and colitis [102]. A signal between secukinumab and IBD was also identified in the FAERS database [103]. There is no clear-cut guideline explaining the management of IBD with IL-17 inhibitor use. Based on the data from case reports, the following approaches have been used: discontinuation of the drug; treating IBD with conventional immunosuppressants [104] and/or glucocorticoids; switching biologic to either TNF-α inhibitors [105], ustekinumab [106] or tildrakizumab [107] and in one case subtotal ileectomy was performed [108]. The case reports of IBD are presented in Table 4.
**Table 4. Case reports of inflammatory bowel disease associated with secukinumab use.**

| Author(s)          | Adverse Drug Event | Indication                    | Age/Sex | Duration Since Initiation of Secukinumab | Previous History of Biologic Use | Concomitant Medication Management | Discontinuation of Secukinumab |
|--------------------|--------------------|-------------------------------|---------|------------------------------------------|---------------------------------|----------------------------------|-------------------------------|
| Achufusi et al. [105] | Ulcerative colitis | Psoriasis                     | 39/M    | 6 months                                 | NA                              | NA                               | Infliximab (symptomatic relief) and apremilast (for psoriasis) | Yes                           |
| Ehrlich et al. [109] | Ulcerative colitis | Ankylosing spondylitis       | 42/M    | 6 weeks                                  | Yes                             | Naproxen; Methotrexate            | Methylprednisolone for 1 month (unsatisfactory) followed by ixekizumab | Yes                           |
| Darch et al. [107]  | Inflammatory bowel disease | Psoriasis and psoriatic arthritis | 54/F   | 14 months                               | No                              | NSAIDs                          | Tildrakizumab                | Yes                           |
| Lozano et al. [106] | Ileocolic Crohn’s disease | Psoriasis                     | 19/F    | 2 months                                 | No                              | NA                               | Corticosteroid and switched to ustekinumab | Yes                           |
|                    | Ulcerative colitis | Ankylosing spondylitis       | 60/M    | 3 weeks                                  | No                              | Naproxen; sulphasalazine         | Full-dose intravenous steroid treatment, mesalazine enemas, and initiation of infliximab for corticosteroid refractoriness | Yes                           |
| Obeidat et al. [104] | Ulcerative colitis | Psoriatic arthritis          | 41/F    | 9 months                                 | NA                              | Venlafaxine, NSAIDs, and sulphasalazine | The patient was started on budesonide with significant improvement in her symptoms. Budesonide was eventually tapered, and the patient was started on azathioprine as a steroid-sparing agent and immunomodulator | Yes                           |
| Johnston et al. [110] | Ulcerative colitis | Ankylosing spondylitis       | 27/M    | 4 months                                 | Yes                             | NA                               | Intravenous cortisone and switch to infliximab | Yes                           |
| Shiga et al. [111]  | Crohn’s disease/Behcet’s disease–like lesions | Psoriasis                     | 56/M    | 8 weeks                                  | No                              | NA                               | Oral prednisolone 40 mg OD     | NA                           |
| Uchida et al. [112] | Ulcerative colitis | Psoriasis                     | 41/F    | 4 months                                 | Yes                             | NA                               | Mesalazine 2400 mg daily and switch to adalimumab 20 mg | Yes                           |
| Lee et al. [108]    | Ulcerative colitis | Psoriasis                     | 52/M    | 4 months                                 | Yes                             | NA                               | subtotal colectomy              | Yes                           |
| Uchida et al. [112] | Ulcerative colitis | Psoriasis                     | 38/M    | 3 weeks                                  | Yes                             | NA                               | IV infliximab 5 mg/kg           | Yes                           |
| Haidari et al. [113] | Asymptomatic Crohn’s disease | Psoriasis and psoriatic arthritis | 69/M   | 18 months                                | Yes                             | NA                               | Ustekinumab for CD and switch guselkumab for psoriasis and psoriatic arthritis | Yes                           |

NA, data not available.
4.7. MACE

Cardiovascular comorbidities have been linked to autoimmune diseases. Psoriasis is identified as an independent factor for myocardial infarction (MI), especially in the younger population [114]. The chance of being exposed to cardiovascular outcomes such as stroke, MI, and coronary artery disease (CAD) is higher in severe conditions [115]. Additionally, a meta-analysis assessing observational studies indicates that patients with ankylosing spondylitis are at a 1.41-fold risk of having CAD [116]. Psoriatic arthritis also increases the risk of clinical and subclinical cardiovascular disease, thus attributing to hastened atherosclerosis [117].

The role of biologics in directly precipitating cardiac adverse events is controversial. Infliximab at 10 mg/kg had significantly increased the risk of heart failure in a pilot study [118]; doses greater than 5 mg/kg of infliximab are contraindicated in moderate-to-severe heart failure. Etanercept did not show any significant cardiovascular harm [119]. A clinical trial on the effects of secukinumab in the aortic vascular inflammation in moderate-to-severe plaque psoriasis showed secukinumab to have a neutral effect on aortic vascular inflammation and biomarkers of cardiometabolic disease [120]. Case reports in the literature did show one case of IgA vasculitis associated with secukinumab [121] and one case of cutaneous vasculitis with gut involvement [122]. Pooled clinical trials and postmarketing studies showed a low incidence of MACE [70].

4.8. Other Adverse Events

A study evaluated the use of secukinumab in uveitis. Although it improved uveitis in that study [36], later on, it appeared as an adverse effect, which may be due to a paradoxical effect. In a pooled safety analysis, the incidence of uveitis was low (1.4/100 patient-years) [123], and two case reports of uveitis have been reported [124,125]. It should also be noted that uveitis itself has an increased chance of occurrence in patients with autoimmune diseases [126].

IL-17 is seen to play a pathophysiological role in the manifestation of nonpsoriatic dermatological diseases [127]; nonetheless, dermatological adverse events are observed with the use of IL-17 inhibitors. Adverse events such as eczema [128], hidradenitis suppurativa [129], psoriasiform eruptions [130], and pemphigus [131] are documented in case reports. The incidence of such adverse events can be explained as a paradoxical reaction attributed to the Th1/Th2 imbalance in the skin, where the latter is overexpressed in the Th1-suppressed state [132].

Brodalumab has a black box warning for suicidal tendencies, although studies did not identify a causal link between the two; however, depression has been identified as an adverse event [133,134]. There is also a concern about suicidal tendencies with autoimmune diseases per se. Patients with autoimmune diseases often lead a poor quality of life and face social stigma. It is seen that inflammation may be associated with depression [135], and cytokine levels in the blood may correlate with depression [136]. Additionally, high levels of IL-17 have been seen in anxious patients with rheumatoid arthritis [137]. However, in a pooled safety analysis, secukinumab posed no risk of suicidal tendency in 3430 patients followed for 52 weeks [138]. A case report of depression has been documented in the literature, which was managed well with the help of sertraline [139]. Other adverse events reported with secukinumab use are presented in Table 5.
### Table 5. Other adverse events reported with secukinumab use.

| Author(s) | Adverse Drug Event | Indication | Age/Sex | Duration since Initiation of Secukinumab | Previous History of Biologic Use | Concomitant Medication | Management | Discontinuation of Secukinumab |
|-----------|--------------------|------------|---------|------------------------------------------|---------------------------------|------------------------|------------|-------------------------------|
| Navarro-Triviño et al. [129] | Hidradenitis suppurativa | Psoriasis and psoriatic arthritis | 58/M | NA | Yes | Ustekinumab (45 mg) | 16 weeks | Yes |
| Blackcloud et al. [140] | Bullous acral eruption | Psoriasis | 44/F | ~1 month | Yes | Halobetasol ointment; fluocinonide gel; clobetasol propionate; tolbutamide | Yes |
| Gerhard Eichhoff [141] | Pemphigus | Psoriasis | 20/M | 3 months | Yes | NA | 0.05% clobetasol ointment cream | No |
| Blackcloud et al. [140] | Bullous acral eruption | Psoriasis | 44/F | ~1 month | Yes | Halobetasol ointment; fluocinonide gel; clobetasol propionate; tolbutamide | Yes |
| Clark et al. [142] | Granuloma annulare | Psoriasis | 60/M | 2 weeks | Yes | Methotrexate; levotiron; omeprazole; duloxetine | Yes |
| Zheutlin et al. [144] | Polychondritis | Ankylosing spondylitis | 56/M | 3–4 months | Yes | NA | 1% methylprednisolone cream | No |
| Hayashida et al. [131] | Pemphigus | Rheumatoid arthritis | 41/F | 3 months | Yes | Methotrexate; prednisone; paracetamol | Yes |
| Lalani et al. [118] | Pustulosis | Psoriasis | 61/M | 3 months | Yes | NA | 1% methylprednisolone cream | Yes |
| Dastoli et al. [145] | Erectile dysfunction | Psoriasis | 45/M | 2 months | Yes | NA | Infliximab | Yes |
| Peigout et al. [146] | Drug eruption | Psoriasis | 60/M | 45 days | No | NA | No treatment. Symptoms resolved on their own in 2 months | No |
| Shukla et al. [148] | Drug eruption | Psoriasis | 61/F | 3 months | Yes | NA | Topical betamethasone, clobetasol, and lidocaine | Yes |
| Thompson et al. [150] | Urticaria | Medication error | 62/M | 1 week | Yes | NA | 0.1% triamcinolone ointment paste | No |
| Ramos et al. [150] | Pityriasis amiantacea | Psoriasis | 48/M | 1 week | Yes | NA | 0.1% triamcinolone ointment paste | Yes |
| Nadvi et al. [128] | Anterior uveitis | Psoriasis | 47/M | 1 week | Yes | NA | 0.1% triamcinolone ointment paste | Yes |
| Xu et al. [157] | Urticaria | Psoriasis and psoriatic arthritis | 45/M | 3 weeks | Yes | NA | Infliximab 5 mg/kg | Yes |
| Liu et al. [191] | Cutaneous sarcoidosis | Psoriasis | 36/M | 45 days | No | NA | No treatment. Symptoms resolved on their own in 2 months | Yes |
| Carrado et al. [192] | Postoperative abscess | Psoriasis | 54/M | 11 months | Yes | NA | Calcipotriol, betamethasone cream and oral NSAIDs | Yes |
| Marchioli et al. [133] | Thrombophlebitis | Psoriasis | 46/M | 1 week | Yes | NA | Treatment with Infliximab | Yes |
| Pern et al. [134] | Palmoplantar pustulosis | Psoriasis | 63/F | 1 week | Yes | NA | Resolution of symptoms 4 weeks after secukinumab discontinuation | Yes |
| Palmoplantar pustulosis | Psoriasis | 64/F | 1 week | Yes | NA | Resolution of symptoms 1 month after secukinumab discontinuation and switch to ustekinumab | Yes |
| Wuermann et al. [139] | Drug-induced lupus | Psoriasis | 52/F | 5 months | Yes | NA | Infliximab | Yes |
| Bose et al. [128] | Eczema | Psoriasis | 52/F | 8 months | No | NA | Infliximab and guselkumab | Yes |
| Bose et al. [128] | Eczema | Psoriasis | 69/F | 7 months | Yes | NA | Infliximab and guselkumab | Yes |
| Author(s) | Adverse Drug Event | Indication | Age/Sex | Duration since Initiation of Secukinumab | Previous History of Biologic Use | Concomitant Medication | Management | Discontinuation of Secukinumab |
|-----------|-------------------|------------|---------|----------------------------------------|---------------------------------|------------------------|------------|-----------------------------|
| Roncada et al. [156] | Atopic dermatitis | Psoriasis | 59/F | 2 months | NA | NA | Cyclosporine, 5 mg/kg/dose intravenous antibiotic therapy, and skin barrier restorative creams and topical corticosteroids | Yes |
| Dinev et al. [157] | Behçet’s syndrome | Ankylosing spondylitis | 34/M | 3 weeks | Yes | NA | 10 mg/day of prednisolone and etanercept | Yes |
| Dinev et al. [157] | Behçet’s syndrome | Ankylosing spondylitis | 20/M | 2 weeks | Yes | NA | Three pulses of methylprednisolone and infliximab 5 mg/kg | Yes |
| Zhang et al. [158] | Multiple lentigines, porcelain | Psoriasis | 60/M | 3 months | NA | NA | NA | NA |
| De Grada et al. [159] | Paradoxical psoriatic psoriasis | Psoriasis | 52/M | 9 months | NA | NA | Complete remission was finally attained after intravenous administration of rituximab 300 mg | Yes |
| Kobayashi et al. [160] | Raynaud’s phenomenon | Ankylosing spondylitis | 35/F | 3 months | Yes | NA | Low-dose aspirin and calcium channel blockers | No |
| Feron et al. [161] | Aphthous stomatitis | Psoriatic arthritis | 32/M | 6 months | Yes | Chloroquine, bexarotene and oral potassium | High-dose of corticosteroids and then with adalimumab again | Yes |
| Gardiner et al. [162] | Vitiligo | Psoriatic arthritis | 42/F | 1 year | No | NA | NA | No |
| Poon et al. [163] | Crystalline corneal deposits | Ankylosing spondylitis | 18/M | 6 months | No | NA | Budesonide, formoteron/lutam, salbutamol, and montelukast | Observed for 12 months | No |
| Kirby et al. [164] | Multisystem sarcoidosis | Psoriatic arthritis | 52/F | 6 months | Yes | Long-acting beta-agonist and corticosteroid inhalers | Prednisolone 30 mg by mouth daily, tapered down to 5 mg monthly | Yes |
| Ellis et al. [165] | Scleroderma | Psoriatic arthritis | 40/F | 19 months | NA | Hydrochlorothiazide and levamisole | Secukinumab was discontinued, and symptoms resolved gradually | Yes |
| Petty et al. [166] | Pyoderma gangrenosum | Psoriasis | 50's/F | 2 weeks | No | NA | Ustekinumab 90 mg | Yes |
| Osra et al. [167] | Facial erythema with dryness and pruritus | Psoriasis | 69/M | 3 weeks | NA | NA | Petrolatum | NA |
| Haras et al. [168] | Localized interstitial pneumonia | Psoriasis | 66/M | 10 Months | NA | NA | Oral prednisolone and subsequent intravenous high-dose methylprednisolone were administered | Yes |
| Kasliwal et al. [169] | Interstitial pneumonia | Psoriasis | 36/M | 10 weeks | Yes | NA | Symptoms resolved 5 weeks after secukinumab discontinuation | Yes |
| Noll et al. [170] | Flared Psoriasis | Psoriasis | 53/F | Shortly after initiation | Yes | NA | Transition to infliximab after ustekinumab and corticosteroids. | Yes |
| Quach et al. [171] | Pterygium dermatitis | Psoriasis | 40's/F | 3 Months | NA | NA | Terbinafine 250 mg OD and budesonide cream BID for 1 month | NA |
| Perella et al. [172] | Pterygium dermatophytosis | Psoriasis | 60's/F | 5 weeks | NA | NA | Oral amphotericin B for 14 days and budesonide cream for 1 month | NA |
| Smerdack et al. [173] | Psorasis | Psoriasis | 56/M | 3 days | No | NA | Switch to topical therapy | Yes |
| Jin et al. [174] | Psoriasis | Psoriatic arthritis | 47/F | 4 months | Yes | NA | Oral cyclosporine 2.5 mg/kg per day | Yes |
| Botzas et al. [175] | Herpetiform aphthous ulcers | SAPHO syndrome | 35/F | 5 weeks | Yes | NA | 5 weeks with hemathene neutrotophils. Reduction of secukinumab dose to 150 mg | No |
| Herpetiform aphthous ulcers | Psoriasis | 37/F | 4 weeks | Yes | NA | Switch to ustekinumab, and lesions resolved within 4 weeks | Yes |
| Burlando et al. [176] | Atopic like dermatitis | Psoriasis | 70/F | 6 months | No | NA | Symptoms resolved after discontinuation and topical and phototherapy for psoriasis | Yes |
| Author(s) | Adverse Drug Event | Indication | Age/Sex | Duration since Initiation of Secukinumab | Previous History of Biologic Use | Concomitant Medication | Management | Discontinuation of Secukinumab |
|-----------|--------------------|------------|---------|------------------------------------------|----------------------------------|------------------------|------------|--------------------------------|
| Hoshina et al. [177] | Psoriatic eruptions | Psoriasis | 43/F | 4 weeks | Yes | NA | Cyclosporine 200 mg/day | Yes |
| Wollina et al. [178] | Pyoderma gangrenosum | Psoriasis | 33/F | 12 months | No | NA | Systemic prednisolone 100 mg/day, pantoprazole, topical corticosteroids | NA |
| Perkovic et al. [121] | IgA vasculitis | Ankylosing spondylitis | 39/F | 18 months | Yes | NA | Methotrexate reintroduced 15 mg/week | Yes |
| Chelli et al. [122] | Cutaneous vasculitis with gut involvement | Psoriatic arthritis | 54/F | 1 month | Yes | NA | Prednisone and colchicine for symptomatic management, Methotrexate 15 mg/kg was restarted | Yes |
| Stalsen et al. [179] | Terminal ileitis | Psoriatic arthritis | 39/M | 2 months | NA | NA | Ciprofloxacin and metronidazole later switched to piperacillin tazobactam and received total parenteral nutrition | Yes |
| Rahman et al. [180] | Autoimmune hemolytic anaemia | Psoriasis | 39/M | 8 weeks | NA | NA | No | No |

NA, data not available.
5. Conclusions and Future Perspectives

Autoimmune diseases are heterogeneous and can affect multiple organ systems. Target-based treatments through the introduction of monoclonal antibodies have revolutionised the treatment of autoimmune diseases with reliable efficacy. However, with any medication, there are potential adverse effects that need to be assessed and identified. It is important to correlate biologic therapy with the comorbidities associated with autoimmune diseases.

Secukinumab is an anti-IL-17 agent used in the treatment of psoriasis, psoriatic arthritis, and ankylosing spondylitis. Since IL-17 plays an important role in protecting the mucocutaneous barrier, induction of antimicrobial peptides, and driving innate inflammation in response to invading pathogens, secukinumab is prone to increase the risk of infections, dermatological and ISR, and IBD. Most cases of infections can be treated using appropriate antimicrobials and do not necessarily require drug discontinuation. The varying dermatological adverse effects that follow secukinumab use may require discontinuation of the drug and use of glucocorticoids and/or other immunosuppressants, as appropriate. Patients experiencing IBD will likely require drug discontinuation; alternatives used include other anti-IL-17 drugs, non-IL-17 biologics, glucocorticoids, and nonbiologic immunosuppressants. Other safety signals require long-term studies to establish definite causal associations. Additional studies on vulnerable populations are also essential. Existing literature has found no new safety signals for secukinumab in pregnant and pediatric populations [181,182]. A retrospective study on 29 geriatric patients also revealed no new safety signals [183]. The effect of biologics on comorbidities needs to be investigated. Interventional studies on patients with existing comorbidities or observational study data can also aid in understanding the true safety profile of secukinumab.

Unlike in the early 2000s, the use of biologics has expanded substantially. The long-term safety of biologics is vital in making informed clinical decisions. Though treatment guidelines have mentioned switching to biologics, there are insufficient head-on studies establishing their relative safety and efficacy [9]. As monoclonal antibodies face patent expiry, new opportunities to manufacture biosimilars are opening. It is impossible to completely replicate the composition of a biologic; as a result, further introduction of variations may be observed in their efficacy and adverse event profiles [184]. In this case, it would be important for the safety profile of the reference biologic to be well established.

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References
1. Park, H.; Li, Z.; Yang, X.O.; Chang, S.H.; Nurieva, R.; Wang, Y.H.; Wang, Y.; Hood, L.; Zhu, Z.; Tian, Q.; et al. A Distinct Lineage of CD4 T Cells Regulates Tissue Inflammation by Producing Interleukin 17. *Nat. Immunol.* 2005, 6, 1133. [CrossRef] [PubMed]
2. Adams, R.; Maroof, A.; Baker, T.; Lawson, A.D.G.; Oliver, R.; Paveley, R.; Rapecki, S.; Shaw, S.; Vajjah, P.; West, S.; et al. Bimekizumab, a Novel Humanized IgG1 Antibody That Neutralizes Both IL-17A and IL-17F. *Front. Immunol.* 2020, 11, 1894. [CrossRef] [PubMed]
58. Sinha, P.; Dash, M.; Bhatkoti, B.; Krishnan, L.P. Epithelial Herpes Simplex Keratitis in a Patient on Treatment with Secukinumab. *Acta Derm. Venereol.* 2022, 102, e423-e426. [CrossRef] [PubMed]

59. Galluzzo, M.; Talamonti, M.; Atzori, L.; Bardazzi, F.; Campanati, A.; Cesare, A.D.; Diotallevi, F.; Flori, M.L.; Mugheddu, C.; Offidani, A.; et al. Secukinumab for the Treatment of Palmoplantar Psoriasis: A 2-Year, Multicenter, Real-Life Observational Study. *Expert Opin. Biol. Ther.* 2022, 22, 547–554. [CrossRef] [PubMed]

60. Sinha, P.; Dash, M.; Bhatkoti, B.; Krishnan, L.P. Epithelial Herpes Simplex Keratitis in a Patient on Treatment with Secukinumab for Psoriasis: An Effect of Interleukin-17 Blockade? *Indian J. Dermatol. Venereol. Leprol.* 2022, 88, 225–227. [CrossRef]

61. Sanz-Bueno, J.; Vanaclocha, F.; Garcia-Doval, I.; Torrado, R.; Carretero, G.; Daudén, E.; Ruiz-Genao, D.P.; Alsina-Gibert, M.M.; Pérez-Zafrilla, B.; Pérez-Rial, G.; et al. Risk of Reactivation of Hepatitis B Virus Infection in Psoriasis Patients Treated with Biologicals: A Retrospective Analysis of 20 Cases from the BIOBADADERM Database. *Actas Dermosifiliogr.* 2015, 106, 477–482. [CrossRef]

62. Moneva-Leniz, L.M.; Sahuquillo-Torralba, A.; Vila-Payeras, A.; Mateu-Puchades, A. Risk of Hepatitis B Virus Reactivation in Patients on Secukinumab for Psoriasis: A Series of 4 Cases. *Actas Dermosifiliogr. Engl. Ed.* 2020, 111, 613–614. [CrossRef]

63. Wang, K.; Deane, J.D.; Knapp, A.; Baynes, K.; Srivastava, S.K. Bilateral Infectious Scleritis from Histoplasma Capsulatum in an Immunosuppressed Uveitis Patient. *Am. J. Ophthalmol. Case Rep.* 2021, 23, 101156. [CrossRef]

64. Sánchez Martín, M.; Amores Hernández, A.; Arguménez García, D.; Silva Hernández, M.; De Lucas Laguna, R.; Arcalís Santos, F.J.; López López, R.; de Ceano-Vivas La Calle, M. Staphylococcal Toxic Shock Syndrome in a Child with Interleukin-17 Inhibitor Treatment for Psoriasis. *Pediatr. Dermatol.* 2020, 37, 952-954. [CrossRef]

65. Utyayma, T.O.; Zerbini, C.; Guimarães, G. Infective Dermatitis after Treatment with Secukinumab. *Clin. Exp. Dermatol.* 2022, 47, 151–153. [CrossRef]

66. Fisher, S.; Ziv, M. Skin and Soft Tissue Infections in Biological Therapy for Psoriasis—A Case Report and Systematic Review of the Literature. *Int. J. Dermatol.* 2021, 60, 1429–1434. [CrossRef] [PubMed]

67. Howard-Anderson, J.; Satola, S.W.; Collins, M.H. Breech at the Border: An Atypical Case of Invasive Haemophilus Influenzae in a Patient on a Novel Immunotherapeutic. *Open Forum Infect. Dis.* 2018, 5, ofy146. [CrossRef] [PubMed]

68. Fry, L.; Baker, B.S. Triggering Psoriasis: The Role of Infections and Medications. *Clin. Dermatol.* 2007, 25, 606–615. [CrossRef] [PubMed]

69. Mengesha, B.G.; Conti, H.R. The Role of IL-17 in Protection against Mucosal Candida Infections. *J. Fungi* 2017, 3, 32. [CrossRef]

70. Deodhar, A.; Mease, P.J.; McInnes, I.B.; Baraliakos, X.; Reich, K.; Blauvelt, A.; Leonardi, C.; Porter, B.; Gupta, A.D.; Widmer, A.; et al. Long-Term Safety of Secukinumab in Patients with Moderate-to-Severe Plaque Psoriasis, Psoriatic Arthritis, and Ankylosing Spondylitis: Integrated Pooled Clinical and Post-Marketing Surveillance Data. *Arthritis Res. Ther.* 2019, 21, 111. [CrossRef]

71. Davidson, L.; van den Reek, J.M.P.A.; Bruno, M.; van Hunsel, F.; Herings, R.M.C.; Matzaraki, V.; Boahe, C.K.; Kumar, V.; Groenewoud, H.M.M.; van de Veerdonk, F.L.; et al. Risk of Candidiasis Associated with Interleukin-17 Inhibitors: A Real-World Observational Study of Multiple Independent Sources. *Lancet Reg. Health-Eur.* 2022, 13, 100266. [CrossRef]

72. Pappas, P.G.; Kauffmann, C.A.; Andes, D.R.; Clancy, C.J.; Porter, B.; Gupta, A.D.; Widmer, A.; et al. Risk of Candidiasis Associated with Interleukin-17 Inhibitors: A Real-World Observational Study of Multiple Independent Sources. *Lancet Reg. Health-Eur.* 2022, 13, 100266. [CrossRef]

73. Picciani, B.L.S.; Dziedzic, A.; Werneck, J.T.; Marinho, M.A.; Dick, T.N.A.; Quintanilha, N.R.; Dias, E.P. Atypical Oral Candidiasis in a Psoriatic Patient during Targeted Immunotherapy with an Interleukin 17 Inhibitor (Secukinumab). *BMJ Oral. Health* 2021, 21, 292. [CrossRef]

74. Kang, H.J.; Han, J.H.; Bang, C.H.; Kim, T.Y. Abrupt Development of Esophageal Candidiasis after Secukinumab Treatment in a Psoriatic Patient. *Ann. Dermatol.* 2021, 33, 584. [CrossRef]

75. Faccini, T.; Dhesi, Z.; Shah, S. Case Report: Death by Antibody. *BMJ Case Rep.* 2019, 12, e225519. [CrossRef]

76. Farah, C.S. Concurrent Chronic Hyperplastic Candidiasis and Oral Lichenoid Lesion as Adverse Events of Secukinumab Therapy. *Aust. Dent. J.* 2021, 66, 340–345. [CrossRef] [PubMed]

77. Capusan, T.M.; Herrero-Moyano, M.; Martinez-Mera, C.R.; Freih-Frah, A.W.; Dauden, E. Oral Lichenoid Reaction in a Psoriatic Patient Treated with Secukinumab: A Drug-Related Rather than a Class-Related Adverse Event? *JAAD Case Rep.* 2018, 4, 521. [CrossRef] [PubMed]

78. Komori, T.; Honda, T.; Endo, Y.; Kaku, Y.; Otsuka, A.; Kabashima, K. Oral Lichen Planus Associated with Candidiasis during Secukinumab Treatment. *J. Dermatol.* 2017, 44, e60–e61. [CrossRef] [PubMed]

79. Moreland, L.W.; Schiff, M.H.; Baumgartner, S.W.; Tindall, E.A.; Fleischmann, R.M.; Bulpitt, K.J.; Weaver, A.L.; Keystone, E.C.; Furst, D.E.; Mease, P.J.; et al. Etanercept Therapy in Rheumatoid Arthritis: A Randomized, Controlled Trial. *Ann. Intern. Med.* 1999, 130, 478–486. [CrossRef]

80. Thomaidou, E.; Ramot, Y. Injection Site Reactions with the Use of Biological Agents. *Dermatol. Ther.* 2019, 32, e12817. [CrossRef] [PubMed]

81. Bruin, G.; Hockey, H.U.P.; Stella, P.L.; Sigurgeirsson, B.; Fu, R.; Patekar, M.; Charel, P.; Woessner, R.; Boutouyrie-Dumont, B. Comparison of Pharmacokinetics, Safety and Tolerability of Secukinumab Administered Subcutaneously Using Different Delivery Systems in Healthy Volunteers and in Psoriasis Patients. *Br. J. Clin. Pharmacol.* 2020, 86, 338. [CrossRef]
82. Grace, E.; Goldblum, O.; Renda, L.; Agada, N.; See, K.; Leonardi, C.; Menter, A. Association Site Reactions in the Federal Adverse Event Reporting System (FAERS) Post-Marketing Database May Among Biologics Approved to Treat Moderate-To-Severe Psoriasis. *Dermatol. Ther.* 2020, 10, 99. [CrossRef]

83. St Clair-Jones, A.; Prignano, F.; Goncalves, J.; Paul, M.; Sewerin, P. Understanding and Minimising Injection-Site Pain Following Subcutaneous Administration of Biologics: A Narrative Review. *Rheumatol. Ther.* 2020, 7, 741–757. [CrossRef]

84. McCarthy, M.K.; Zhu, L.; Procario, M.C.; Weinberg, J.B. IL-17 Contributes to Neutrophil Recruitment but Not to Control of Viral Replication During Acute Mouse Adenovirus Type 1 Respiratory Infection. *Virology* 2014, 259, 259–267. [CrossRef]

85. Vaughan, G.; Elson, C.O.; Fouser, L.A.; Kolls, J.K. The Th17 Pathway and Inflammatory Diseases of the Intestines, Lungs, and Skin. *Annu. Rev. Pathol.* 2013, 8, 477–512. [CrossRef]

86. Antoniadou, A.; Giamarellou, H. Fever of Unknown Origin in Febrile Leukopenia. *Infect. Dis. Clin. N. Am.* 2007, 21, 1055–1090. [CrossRef]

87. Karatas, A.; Gercek, A.N.; Oez, B.; Guzel, N.; Sagir, R.P.; Gur, M.; Koca, S.S. The Effect of Secukinumab Treatment on Hematological Parameters in Ankylosing Spondylitis and Psoriatic Arthritis. *Eur. J. Rheumatol.* 2020, 7, 169. [CrossRef] [PubMed]

88. Griffin, G.K.; Newton, G.; Tarrio, M.L.; Bu, D.; Maganto-Garcia, E.; Azcutia, V.; Alcaide, P.; Grabie, N.; Luscinskas, F.W.; Croce, K.J.; et al. IL-17 and TNFα Sustain Neutrophil Recruitment During Inflammation Through Synergistic Effects on Endothelial Activation. *J. Immunol. Baltim. Md.* 2012, 188, 6287. [CrossRef]

89. Elkoshi, Z. Cancer and Autoimmune Diseases: A Tale of Two Immunological Opposites? *Front. Immunol.* 2022, 13, 71. [CrossRef] [PubMed]

90. Trafford, A.M.; Parisi, R.; Kontopantelis, E.; Griffiths, C.E.M.; Ashcroft, D.M. Association of Psoriasis With the Risk of Developing or Dying of Cancer: A Systematic Review and Meta-Analysis. *JAMA Dermatol.* 2019, 155, 1390–1403. [CrossRef]

91. Kim, S.C.; Glynn, R.J.; Giovannucci, E.; Hernández-Díaz, S.; Liu, J.; Feldman, S.; Karlson, E.W.; Schneeweiss, S.; Solomon, D.H. Risk of High-Grade Cervical Dysplasia and Cervical Cancer in Women with Systemic Inflammatory Diseases: A Population-Based Cohort Study. *Ann. Rheum. Dis.* 2015, 74, 1360. [CrossRef] [PubMed]

92. Vaengebjerg, S.; Skov, L.; Egeberg, A.; Loft, N.D. Prevalence, Incidence, and Risk of Cancer in Patients With Psoriasis and Psoriatic Arthritis: A Systematic Review and Meta-Analysis. *JAMA Dermatol.* 2020, 156, 421. [CrossRef] [PubMed]

93. Bellinato, F.; Gisondi, P.; Girolomoni, G. Risk of Lymphohematologic Malignancies in Patients with Chronic Plaque Psoriasis: A Systematic Review with Meta-Analysis. *J. Am. Acad. Dermatol.* 2022, 86, 86–96. [CrossRef]

94. Chang, C.C.; Chang, C.W.; Nguyen, P.A.A.; Chang, T.H.; Shih, Y.L.; Chang, W.Y.; Horng, J.T.; Lee, O.K.S.; Ho, J.H.C. Ankylosing Spondylitis and the Risk of Cancer. *Oncl. Lett.* 2017, 14, 1315. [CrossRef]

95. Lebwohl, M.; Deodhar, A.; Griffiths, C.E.M.; Menter, M.A.; Poddubnyy, D.; Bao, W.; Marfo, K.; Primavesta, P.; Shete, A.; 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, 935–944. [CrossRef]

96. Fu, Y.; Lee, C.H.; Chi, C.C. Association of Psoriasis With Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis. *JAMA Dermatol.* 2018, 154, 1417–1423. [CrossRef] [PubMed]

97. Oliveira, M.d.F.S.P.d.; Rocha, B.d.O.; Duarte, G.V. Psoriasis: Classical and Emerging Comorbidities. *An. Bras. Dermatol.* 2015, 90, 9. [CrossRef] [PubMed]

98. Hueber, W.; Sands, B.E.; Lewitzky, S.; Vandemeulebroecke, M.; Reinisch, W.; Higgins, P.D.R.; Wehkamp, J.; Feagan, B.G.; Yao, C.H.; Lee, C.H.; Chi, C.C. Association of Psoriasis With Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis. *J. Am. Acad. Dermatol.* 2021, 84, 16147. [CrossRef]

99. Espinoza-Paredes, R.; Haneef, P.; Rawlins, S.A. A Rare Case of New-Onset Ulcerative Colitis Following Initiation of Secukinumab. *Case Rep. Med.* 2019, 2019, 2975631. [CrossRef]

100. Fobelo Lozano, M.J.; Serrano Giménez, R.; Castro Fernández, M. Emergence of Inflammatory Bowel Disease During Treatment With Secukinumab. *J. Crohns Colitis* 2018, 12, 1131–1133. [CrossRef] [PubMed]
107. Darch, K.M.; Holland, T.L.; Spelman, L.J. Secukinumab-Induced Inflammatory Bowel Disease in a Patient Treated for Chronic Plaque Psoriasis and Psoriatic Arthritis: A Case Report and Review of the Role of Novel Biologic Agents Targeting the P19 Subunit of IL-23. Case Rep. Med. 2020, 2020, 9404505. [CrossRef] [PubMed]

108. Lee, A.S.W.; Levell, N.J.; Shah, S.N.; Gaffney, K.; Tremelling, M.A.W. Severe Colitis Complicating Secukinumab (Cosentyx®) Therapy. Clin. Exp. Dermatol. 2020, 45, 345–349. [CrossRef] [PubMed]

109. Ehrlich, D.; Jamaluddin, N.; Pisegna, J.; Padua, D. A Challenging Case of Severe Ulcerative Colitis Following the Initiation of Secukinumab for Ankylosing Spondylitis. Case Rep. Gastrointest. Med. 2018, 2018, 9679287. [CrossRef]

110. Johnston, D.N.; Veettil, R. A Case of New Onset Ulcerative Colitis Following Secukinumab Treatment. Br. J. Hosp. Med. 2019, 80, 544–545. [CrossRef]

111. Shiga, H.; Fukuda, S.; Iijima, K. Interleukin-17A Inhibitor–Induced Crohn’s Disease/Behçet’s Disease-like Lesions. Inflamm. Bowel Dis. 2017, 23, E38–E39. [CrossRef]

112. Uchida, S.; Oiso, N.; Komeda, Y.; Kudo, M.; Kawada, A. Paradoxical Ulcerative Colitis during Treatment with Secukinumab for Psoriasis. Eur. J. Dermatol. 2019, 29, 444–445. [CrossRef]

113. Haidari, W.; Al-Naqshabandi, S.; Ahn, C.S.; Bloomfeld, R.S.; Feldman, S.R. Asymptomatic Crohn’s Disease Identified in a Patient Being treated with Secukinumab: A Case Report. SAGE Open Med. Case Rep. 2019, 7, 2050313X1989358. [CrossRef]

114. Gelfand, J.M.; Neumann, A.L.; Shin, D.B.; Wang, X.; Margolis, D.J.; Troxel, A.B. Risk of Myocardial Infarction in Patients With Psoriasis. JAMA 2006, 296, 1735–1741. [CrossRef]

115. Samarasekera, E.J.; Neilson, J.M.; Warren, R.B.; Parnham, J.; Smith, C.H. Incidence of Cardiovascular Disease in Individuals with Psoriasis: A Systematic Review and Meta-Analysis. J. Invest. Dermatol. 2013, 133, 2340–2346. [CrossRef]

116. Ungprasert, P.; Srivall, N.; Kitanamongkolchai, W. Risk of Coronary Artery Disease in Patients with Ankylosing Spondylitis: A Systematic Review and Meta-Analysis. Ann. Transl. Med. 2015, 3, 51. [PubMed] [CrossRef]

117. Zhu, T.Y.; Li, E.K.; Tam, L.S. Cardiovascular Risk in Patients with Psoriatic Arthritis. Int. J. Rheumatol. 2012, 2012, 11. [CrossRef] [PubMed]

118. Chung, E.S.; Packer, M.; Lo, K.H.; Fasanmade, A.A.; Willerson, J.T. Randomized, Double-Blind, Placebo-Controlled, Pilot Trial of Infliximab, a Chimeric Monoclonal Antibody to Tumor Necrosis Factor-α, in Patients with Moderate-to-Severe Heart Failure: Results of the Anti-TNF Therapy against Congestive Heart Failure (ATTACH) Trial. Circulation 2003, 107, 3133–3140. [CrossRef] [PubMed]

119. Coletta, A.P.; Clark, A.L.; Banarjee, P.; Cleland, J.G.F. Clinical Trials Update: RENEWAL (RENAISSANCE and RECOVER) and ATTACH. Eur. J. Heart Fail. 2002, 4, 559–561. [CrossRef]

120. Gelfand, J.M.; Shin, D.B.; Duffin, K.C.; Armstrong, A.W.; Blauvelt, A.; Tynter, S.; Gottlieb, S.; Lockshin, B.N.; 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, 1784. [CrossRef]

121. Perkovic, D.; Simac, P.; Katic, J. IgA Vasculitis during Secukinumab Therapy. Clin. Rheumatol. 2020 405–407, 2020, 2020, 20–2071. [PubMed]

122. Chelli, C.; Loget, J.; Vanhaecke, C.; Durlach, A.; Gagneux-Lemoussu, L.; Soriano, C.; Viguier, M. Cutaneous Vasculitis with Gut Associated with Systemic Diseases and Infections—A Systematic Review of 2619 Patients. Acta Derm. Venereol. 2018, 544–545. [CrossRef] [PubMed]

123. Deodhar, A.A.; Miceli-Richard, C.; Baraliakos, X.; Marzo-Ortega, H.; Gladman, D.D.; Blanco, R.; Gupta, A.D.; Martin, R.; Safi, J.; et al. Incidence of Ulcerative Colitis in Patients with Ankylosing Spondylitis: Pooled Data Analysis From Three Phase 3 Studies. ACR Open Rheum. 2020, 2, 294. [CrossRef]

124. Nadwi, H.; Janaini, M.; Zammo, M.; Cheikh, M.; Almoallim, H. New-Onset Uveitis Possibly Caused by Secukinumab in a 47-Year-Old Male Patient with Long-Standing Ankylosing Spondylitis. Int. Med. Case Rep. J. 2020, 3, 331. [CrossRef] [PubMed]

125. Su, P.; Pan, J.Y. Paradoxical Flare of Psoriasis, Psoriatic Spondyloarthritis, and Psoriatic Uveitis after Switching from Infliximab to Secukinumab. Dermatol. Sin. 2017, 35, 112–113. [CrossRef]

126. Barisani-Asenbauer, T.; Maca, S.M.; Mejdboubi, L.; Emminger, W.; MacHold, K.; Auer, H. Uveitis—A Rare Disease Often Associated with Systemic Diseases and Infections—A Systematic Review of 2619 Patients. Orphanet J. Rare Dis. 2012, 7, 57. [CrossRef]

127. Liu, T.; Li, S.; Ying, S.; Tang, S.; Ding, Y.; Li, Y.; Qiao, J.; Fang, H. The IL-23/IL-17 Pathway in Inflammatory Skin Diseases: From Bench to Bedside. Front. Immunol. 2020, 11, 594735. [CrossRef] [PubMed]

128. Bose, R.; Beecker, J. Dyshidrotic Eczema in Two Patients on Secukinumab for Plaque: A Case Report. SAGE Open Med. Case Rep. 2020, 8, 2050313X2090456. [CrossRef] [PubMed]

129. Navarro-Triviso, F.; Sanchez-Parera, R.; Ruiz-Villaverde, R. Secukinumab-Induced Paradoxical Hidradenitis Suppurativa. Dermatol. Ther. 2020, 33, e13510. [CrossRef] [PubMed]

130. Sladden, M.J.; Sladden, C.S.; Gulliver, W.P.F. Secukinumab-Induced Psoriasisform Eruption. JAMA Dermatol. 2017, 153, 1194–1195. [CrossRef]

131. Hayashida, M.Z.; Pinheiro, J.R.S.; Enokihara, M.M.S.e.S.; Vasconcellos, M.R.d.A. Biologic Therapy-Induced Pemphigus. An. Bras. Dermatol. 2017, 92, 591–593. [CrossRef]

132. Herman, S.; Zurgil, N.; Machlav, S.; Shinberg, A.; Langevitz, P.; Ehrenfeld, M.; Deutsch, M. Distinct Effects of Anti-Tumor Necrosis Factor Combined Therapy on TH1/TH2 Balance in Rheumatoid Arthritis Patients. Clin. Vaccine Immunol. CVI 2011, 18, 1077–1082. [CrossRef]
133. Lebwohl, M.G.; Papp, K.A.; Marangell, L.B.; Koo, J.; Blauvelt, A.; Gooderham, M.; Wu, J.J.; Rastogi, S.; Harris, S.; Pillai, R.; et al. Psychiatric Adverse Events during Treatment with Brodalumab: Analysis of Psoriasis Clinical Trials. *J. Am. Acad. Dermatol.* 2018, 78, 81–89.e5. [CrossRef]

134. Lebwohl, M.; Leonardi, C.; Wu, J.J.; Armstrong, A.; Rawnsley, N.; Merchant, M.; Alexander, B.; Jacobson, A. Two-Year US Pharmacovigilance Report on Brodalumab. *Dermatol. Ther.* 2021, 11, 173–180. [CrossRef]

135. Lee, C.H.; Giuliani, F. The Role of Inflammation in Depression and Fatigue. *Front. Immunol.* 2019, 10, 1696. [CrossRef]

136. Janelidze, S.; Mattei, D.; Westrin, A.; Träskman-Bendz, L.; Brundin, L. Cytokine Levels in the Blood May Distinguish Suicide Attempters from Depressed Patients. *Brain. Behav. Immun.* 2011, 25, 335–339. [CrossRef] [PubMed]

137. Liu, Y.; Ho, R.C.M.; Mak, A. The Role of Interleukin (IL)-17 in Anxiety and Depression of Patients with Rheumatoid Arthritis. *Int. J. Rheum. Dis.* 2012, 15, 183–187. [CrossRef]

138. Strober, B.E.; Langley, R.G.B.; Menter, A.; Magid, M.; Porter, B.; Fox, T.; Safi, J.; Papavassilis, C. No Elevated Risk for Depression, Anxiety or Suicidality with Secukinumab in a Pooled Analysis of Data from 10 Clinical Studies in Moderate-to-Severe Plaque Psoriasis. *Br. J. Dermatol.* 2018, 178, e105–e107. [CrossRef] [PubMed]

139. Komori, T.; Otsuka, A.; Honda, Y.; Kanameishi, S.; Honda, T.; Kabashima, K. Exacerbation of Depression in a Psoriatic Arthritis Patient Possibly Induced by Secukinumab. *Eur. J. Dermatol.* 2016, 26, 506–507. [CrossRef] [PubMed]

140. Blackcloud, P.; Dupuy, E.; Kang, Y.; Smart, C.; Hsiao, J. Bullous Acral Eruption Related to Secukinumab. *Dermatol. Online J.* 2019, 25, 9. [CrossRef]

141. Eichhoff, G. Secukinumab-Induced Pompholyx in a Psoriasis Patient. *Dermatol. Online J.* 2020, 26, 16–17. [CrossRef]

142. Clark, M.L.; Tobin, C.A.; Sutton, A.; Missall, T.A. Granuloma Annulare in the Setting of Secukinumab. *Case Rep. Dermatol. Med.* 2018, 2018, 1–3. [CrossRef]

143. Bonomo, L.; Ghoneim, S.; Levitt, J. A Case of Granuloma Annulare Associated with Secukinumab Use. *Case Rep. Dermatol. Med.* 2017, 2017, 1–4. [CrossRef]

144. Zheutlin, A.; Schiopu, E. Relapsing Polychondritis Following Treatment with Secukinumab for Ankylosing Spondylitis: Case Report and Review of the Literature. *Case Rep. Rheumatol.* 2018, 2018, 6706806. [CrossRef]

145. Dastoli, S.; Iannone, L.F.; Bennardo, L.; Silvestri, M.; Palleria, C.; Nisticò, S.P.; De Sarro, G.; Russo, E. A Rare Case of Drug-Induced Erectile Dysfunction with Secukinumab Solved After Switch to Ixekizumab in A Psoriatic Patient: A Case Report. *Curr. Drug Saf.* 2020, 15, 69–72. [CrossRef]

146. Peigottu, M.F.; Montesu, M.A. Adverse Skin Reaction to Secukinumab. *J. Eur. Acad. Dermatol. Venereol.* 2017, 31, e432–e433. [CrossRef] [PubMed]

147. Hitaka, T.; Sawada, Y.; Okada, E.; Nakamura, M. Recurrent Angular Cheilitis after Secukinumab Injections. *Australas. J. Dermatol.* 2018, 59, e79–e80. [CrossRef] [PubMed]

148. Shibata, M.; Sawada, Y.; Yamaguchi, T.; Ohmori, S.; Omoto, D.; Haruyama, T.; Yoshioka, M.; Okada, E.; Nakamura, M. Drug Eruption Caused by Secukinumab. *Eur. J. Dermatol.* 2017, 27, 67–68. [CrossRef] [PubMed]

149. Thompson, J.M.; Cohen, L.M.; Yang, C.S.; Kroumpouzos, G. Severe, Ulcerative, Lichenoid Mucositis Associated with Secukinumab. *J.AAD Case Rep.* 2016, 2, 384–386. [CrossRef] [PubMed]

150. Ramalho, D.; Araújo, A.; Rocha, G.; Duarte-Ribeiro, F. Secukinumab, Pituitary Enlargement and Panhypopituitarism: Are They Related? *Eur. J. Case Rep. Intern. Med.* 2021, 8, 003099. [CrossRef]

151. Lu, J.W.; Zhang, M.H.; Gopée, S.; Lu, Y. Cutaneous Sarcoidosis after Application of Secukinumab in a Patient with Plaque Psoriasis. *J. Dermatol.* 2021, 48, E494–E495. [CrossRef] [PubMed]

152. Currado, D.; Margiotta, D.P.E.; Conforti, C.; Coppola, R.; Panasiti, V.; Afeletra, A.; Navarin, L. New Onset of Psoriasis Induced by Secukinumab in a Patient with Ankylosing Spondylitis: A Case Report. *Scand. J. Rheumatol.* 2019, 49, 75–76. [CrossRef]

153. Mammadli, K.; Ceken, K.; Unal, B.; Karakas, A.; Yilmaz, E.; Alpsoy, E. Superficial Thrombophlebitis during Secukinumab Therapy in a Patient with Psoriasis. *Indian J. Dermatol. Venereol. Leprol.* 2020, 86, 699–701. [CrossRef]

154. Peera, M.; Smith, A. Palmoplantar Pompholyx Secondary to Interleukin 17A Inhibitor Therapy for Psoriasis: A Case Series. *J.AAD Case Rep.* 2021, 13, 46. [CrossRef]

155. Wehrmann, C.; Sondermann, W.; Körber, A. Secukinumab-Induzierter Subakut-Kutaner Lupus Erythematoses. *Hautarzt* 2017, 68, 64–66. [CrossRef]

156. Mendes Roncada, E.V.; Brambilla, V.R.; Freitas Filìtto, B.; Genta, M.P.; Morgado De Abreu, M.A.M. Atopic Dermatitis as a Paradoxical Effect of Secukinumab for the Treatment of Psoriasis. *Case Rep. Dermatol.* 2021, 13, 336. [CrossRef] [PubMed]

157. Dincses, E.; Yurttas, B.; Esatoglu, S.N.; Melikoglu, M.; Hamuryudan, V.; Seyahi, E. Secukinumab Induced Behçet’s Syndrome: A Report of Two Cases. *Oxf. Med. Case Rep.* 2019, 2019, 239–241. [CrossRef]

158. Zhang, S.; Liang, J.; Tian, X.; Zhou, X.; Liu, W.; Chen, X.; Zhang, X. Secukinumab-Induced Multiple Lentigines in Areas of Resolved Psoriatic Plaques: A Case Report and Literature Review. *Dermatol. Ther.* 2021, 34, e15048. [CrossRef] [PubMed]

159. Dogra, S.; Khullar, G. Tumor Necrosis Factor-α Antagonists: Side Effects and Their Management. *Indian J. Dermatol. Venereol. Leprol.* 2013, 79 (Suppl. 7), 35. [CrossRef] [PubMed]

160. Kobby, G.; Gerfaud-Valentin, M.; Durupt, F.; Seve, P. Aphthous Stomatitis in a Man with Psoriatic Arthritis. *Am. J. Med.* 2021, 134, 749–750. [CrossRef]
162. Giordano, D.; Magri, F.; Persechino, F.; Lepore, A.; Verde, R.; Capalbo, A.; Persechino, S. Vitiligo with Progressive Repigmentation during Secukinumab Treatment in a Patient with Psoriatic Arthritis: A Case Report. *Case Rep. Dermatol.* 2021, 13, 209. [CrossRef] [PubMed]

163. Power, B.; Pilson, Q.; Fulcher, T. Secukinumab-Associated Crystalline Corneal Deposition. *Cornea* 2019, 38, 249. [CrossRef] [PubMed]

164. Petty, A.J.; Whitley, M.J.; Balaban, A.; Ellington, K.; Marano, A.L. Pyoderma Gangrenosum Induced by Secukinumab in a Patient with Psoriasis Successfully Treated with Ustekinumab. *JAAD Case Rep.* 2020, 6, 731. [CrossRef]

165. Elias, N.; Sami, N.; Shulman, K.; Bög, S. Secukinumab-Induced Scleroderma: A Case Report. *Rheumatology* 2021, 60, e99–e100. [CrossRef]

166. Noell, C.; McQuade, B.; Gottlieb, A.; Rosmarin, D. Anti IL-17 Flared Psoriasis in a Patient on Secukinumab. *Dermatol. Ther.* 2021, 6, 12505. [CrossRef]

167. Oiwa, T.; Honda, T.; Otsuka, A.; Kabashima, K. Three Cases of Facial Erythema with Dryness and Pruritus in Psoriasis Patients during Treatment with IL-17 Inhibitors. *J. Eur. Acad. Dermatol. Venereol.* 2018, 32, e122–e123. [CrossRef]

168. Hayashi, M.; Igarashi, A.; Nakamura, K.; Suzuki, T. Paradoxical Exacerbation of Latent Interstitial Pneumonia by Secukinumab in a Patient with Psoriasis Vulgaris. *Br. J. Dermatol.* 2019, 180, 684–685. [CrossRef]

169. Kajihara, I.; Yamada-Kanazawa, S.; Maeda-Otsuka, S.; Jinnin, M.; Akaike, K.; Ihn, H. Secukinumab-Induced Interstitial Pneumonia with Psoriasis Vulgaris. *J. Dermatol.* 2017, 44, e322–e323. [CrossRef]

170. Quach, O.L.; Hsu, S. Perianal Dermatophytosis During Secukinumab Therapy for Plaque Psoriasis. *JAMA Dermatol.* 2016, 152, 486–487. [CrossRef]

171. Benzaquen, M.; Yawalkar, N.; Feldmeyer, L.; Borradori, L.; Schlabach, C. Herpetiform Aphthous Ulcerations Induced by Secukinumab: Report of 2 Cases. *JAAD Case Rep.* 2020, 6, 1107. [CrossRef]

172. Hoshina, D.; Haga, N.; Furuya, K.; Nakano, H.; Sawamura, D. Pyoderma Gangrenosum Triggered by Switching from Adalimumab to Secukinumab. *J. Dermatol.* 2019, 46, e108–e109. [CrossRef]

173. Burlando, M.; Cozzani, E.; Russo, R.; Parodi, A. Atopic-like Dermatitis after Secukinumab Injection: A Case Report. *Dermatol. Ther.* 2019, 32, e12751. [CrossRef]

174. Giordano, D.; Magri, F.; Persechino, F.; Lepore, A.; Verde, R.; Capalbo, A.; Persechino, S. Vitiligo with Progressive Repigmentation during Secukinumab Treatment in a Patient with Psoriatic Arthritis: A Case Report. *Case Rep. Dermatol.* 2021, 13, 209. [CrossRef] [PubMed]

175. Warren, R.B.; Reich, K.; Langley, R.G.; Strober, B.; Gladman, D.; Deodhar, A.; Bachhuber, T.; Bao, W.; Altemeyer, E.; Hussain, S.; et al. Secukinumab in Pregnancy: Outcomes in Psoriasis, Psoriatic Arthritis and Ankylosing Spondylitis from the Global Safety Database. *Br. J. Dermatol.* 2018, 179, 1205–1207. [CrossRef]

176. Blair, H.A. Secukinumab: A Review in Moderate to Severe Pediatric Plaque Psoriasis. *Pediatr. Drugs* 2021, 23, 601. [CrossRef]

177. Wollina, U.; Schönlebe, J.; Fürl, C. Pyoderma Gangrenosum Induced by Secukinumab—A Late Paradoxical Drug Reaction. *Dermatol. Ther.* 2020, 33, e13161. [CrossRef]

178. Shaheen, A.A.; Hader, I.; Aqel, Z. Novel Presentation of Terminal Ileitis Associated with Secukinumab Therapy. *Case Rep. Gastrointest Med.* 2021, 2021, 5213876. [CrossRef]

179. Rahman, P.A.; Kalim, H.; Pravitasari, S.; Raharjo, F.M. Possible Autoimmune Hemolytic Anemia Induced by Secukinumab: A Case Report. *Fan Afr. Med. J.* 2022, 41, 41. [CrossRef]

180. Megna, M.; Camela, E.; Cinelli, E.; Fabbrocini, G. Real-Life Efficacy and Safety of Secukinumab in Elderly Patients with Psoriasis over a 2-Year Period. *Clin. Exp. Dermatol.* 2020, 45, 848–852. [CrossRef]

181. Megna, M.; Camela, E.; Cinelli, E.; Fabbrocini, G. Real-Life Efficacy and Safety of Secukinumab in Elderly Patients with Psoriasis over a 2-Year Period. *Clin. Exp. Dermatol.* 2020, 45, 848–852. [CrossRef]

182. Burlando, M.; Cozzani, E.; Russo, R.; Parodi, A. Atopic-like Dermatitis after Secukinumab Injection: A Case Report. *Dermatol. Ther.* 2019, 32, e12751. [CrossRef]