Journal of Dermatological Treatment

ISSN: (Print) (Online) Journal homepage: informahealthcare.com/journals/ijdt20

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To cite this article: Diem-Phuong D. Dao, Jessica N. Pixley & Steven R. Feldman (2023) When should systemic biologic therapy for psoriasis be discontinued?, Journal of Dermatological Treatment, 34:1, 2173516, DOI: 10.1080/09546634.2023.2173516

To link to this article: https://doi.org/10.1080/09546634.2023.2173516

Published online: 07 Feb 2023.

JOURNAL OF DERMATOLOGICAL TREATMENT
2023, VOL. 34, NO. 1, 2173516
https://doi.org/10.1080/09546634.2023.2173516

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EDITORIAL

When should systemic biologic therapy for psoriasis be discontinued?

Systemic biologics have revolutionized the treatment of psoriasis, offering patients substantial lesion clearance—and for some, complete disease resolution (1,2). When psoriasis lesions fully resolve, patients may ask to discontinue their biologic therapies. There are currently unclear guidelines regarding the duration of biologic therapy for psoriasis (1). Clinical recommendations for whether to continue or stop systemic biologics after resolution of visible psoriasis lesions may be helpful.

The risks and adverse effects of systemic biologics are frequently central to the discussion of continuing or ceasing treatment after visible lesion resolution (1,3,4). Biologic treatments for psoriasis have an established safety profile with minimal adverse events. After one year of biologic treatment use, drug survival (which serves as a measure for effectiveness and safety) ranged from 91% to 96% for five different biologic therapies (3). After year two of biologic treatment, drug survival ranged from 87% to 93% for the same five therapies (3). During the Psoriasis Longitudinal Assessment and Registry (PSOLAR) trials, there was a cumulative serious infection rate of 1.45 per 100 patient-years across all treatments (5). The rates of serious infections ranged from 0.83 to 2.49 per 100 patient-years in the ustekinumab and infliximab groups, respectively, while the nonmethotrexate/nonbiologics cohort had a risk of 1.05 and the methotrexate/nonbiologics cohort risk was 1.28. Factors associated with an increased risk of serious infection included: increasing age, diabetes mellitus, smoking, history of significant infection, and exposure to infliximab or adalimumab. Compared to nonbiologic therapies, there was no increased risk of infection associated with ustekinumab or etanercept (5). Patients with moderate to severe psoriasis who were receiving biologic therapy additionally had a lower risk of death compared to their matched controls, and undergoing biologic treatment was a protective factor against mortality (6). There were no safety concerns regarding mortality, malignancy, or major adverse cardiovascular events among patients receiving biologic therapy (7). Because continued treatment with biologic therapies is safe for most patients, there is little clinical benefit, aside from cost reduction, for discontinuing treatment.

On the risk side of the balance, discontinuation of biologics may result in recurrence of psoriasis or reduced efficacy of the biologic treatment (8). After discontinuation of treatment, time to relapse of psoriasis varies among patients, typically ranging from 12 to 34 weeks (9). Although biologic therapies are associated with a longer time to relapse than nonbiologic oral systemic agents, intermittent therapy may result in decreased efficacy of the drug due to development of anti-drug antibodies or from idiopathic causes (9–11). Therefore, for those who develop antibodies as a result of intermittent usage or who have tried and failed multiple different biologics, clinicians may advise against discontinuation of a successful biologic treatment. Alternatively, since there are multiple systemic biologics on the market, patients who develop these antibodies have several other options for treatment, a luxury that was not available years ago when there were few available biologics.

Although many treatments can clear visible psoriasis lesions, plaques tend to recur at sites previously affected after treatment discontinuation. The concept of local immunological memory has been investigated through evaluation of immunological markers including interleukin (IL)-23, IL-17, T helper 17 cells, and CCR4+, a dermotropic phenotype, as well as through general markers of proliferation and inflammation such as Ki67, IL-12 and interferon gamma (IFN-γ), among others (12). IL-23 and IL-17 likely have a large role in local memory, because there was a sustained response from IL-17 and IL-23 inhibitors in phase III data, ranging from 16 to 23 weeks, which is greater than what would be expected from their elimination half-lives of 18 and 13 days for guselkumab and ixekizumab, respectively (12). As a result, in the future, it is possible that following these biomarkers to examine the impact of biologics on the immune system after the medication is discontinued may inform treatment decisions based on immunological memory. Discontinuation may be appropriate after eliminating immunological memory.

Ultimately, patient and clinician preferences play the largest role in the decision to continue or to stop a biologic treatment. Biologic treatment success varies among patients and therefore, each treatment plan, including choice of biologic and duration of treatment, should be tailored to each unique clinical situation (13). For instance, guttate psoriasis has a favorable prognosis with rapid involution and long remission (14). Patients with this type of psoriasis may be able to have a shorter treatment duration and to discontinue the biologic therapy once lesions have cleared. For individuals who prefer to discontinue their biologic treatment, alternative strategies to prevent disease relapse may include discontinuation of the biologic with the use of a topical corticosteroid or a topical calcineurin inhibitor to treat a limited flare, or phototherapy to help maintain a remission. Intermittent biologic treatment for recurrent psoriasis remains an option; however, decreased efficacy and increased adverse reactions may occur due to development of anti-drug antibodies (11). Although there are no formal guidelines on when to continue or discontinue biologic treatment, analyzing factors such as disease clearance, risks vs. benefits, immunological memory, and patient preference can inform clinical decisions on duration of treatment.

Disclosure statement

Feldman has received research, speaking and/or consulting support from Eli Lilly and Company, GlaxoSmithKline/Stiefel, AbbVie, Janssen, Alovtech, vTv Therapeutics, Bristol-Myers Squibb, Samsung, Pfizer, Boehringer Ingelheim, Amgen, Dermavant, Arcutis, Novartis, Novan, UCB, Helsinn, Sun Pharma, Almirall, Galderma, Leo Pharma, Mylan, Celgene, Ortho Dermatology, Menlo, Merck & Co, Qurient, Forte, Arena, Biocon, Accordant, Argenx, Sanofi, Regeneron, the National Biological Corporation, Caremark, Teladoc, BMS, Ono, Micreos, Eurofins, Informa, UpToDate and the National Psoriasis Foundation. He is founder and part owner of Causa Research and holds stock in

Sensal Health. Ms. Dao and Ms. Pixley have no conflicts to disclose.

Funding

The author(s) reported there is no funding associated with the work featured in this article.

Data availability statement

The data that support the findings of this study are available in the PubMed database at https://pubmed.ncbi.nlm.nih.gov/. These data were derived from the following resources available in the public domain: https://pubmed.ncbi.nlm.nih.gov/.

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Received 20 January 2023; Accepted 23 January 2023