Drug survival of biologics in hidradenitis suppurativa: A systematic review and meta-analysis

To the Editor: Drug survival (DS) is a metric reflecting both efficacy and tolerability of treatments, defined as the proportion of patients remaining on treatment over time.[1] We conducted a systematic review and meta-analysis to benchmark DS of biologics in hidradenitis suppurativa (HS), PROSPERO registration CRD42023443159. Further details are provided in the Supplementary Methods (available via Mendeley at https://doi.org/10.17632/wm4gzhy7pd.1).

Seven studies were included (Supplementary Fig 1, available via Mendeley at https://doi.org/10.17632/wm4gzhy7pd.1), reporting on DS in 1170 patients—predominantly tumor necrosis factor-alfa (TNF-α) inhibitors (n = 1,060; 91%)—with mostly female (n = 739; 63%) and bionaive patients (n = 686; 58%) (Supplementary Table I, available via Mendeley at https://doi.org/10.17632/wm4gzhy7pd.1). One study at high risk of bias was excluded (Supplementary Table II, available via Mendeley at https://doi.org/10.17632/wm4gzhy7pd.1). More patients treated with anti−TNF-α biologics were bionaive than those treated with interleukin 17 (IL-17) or IL-23 inhibitors; 66% vs 13%, respectively ($P < .001$). Overall, median DS was 11.9 months (95% CI, 9.6-16.6), whereas 12-month DS was 48% (95% CI, 39%-60%; Fig 1, *A*).

Median DS was comparable between TNF-α and non−TNF-α inhibitors—11.9 (95% CI, 8.2-18.2) vs 10.7 (95% CI, 4.8-12.2) months, respectively ($P = .35$) (Fig 1, *B*), and longer in biologic-naive than biologic-experienced patients—14.4 (95% CI, 12.1-16.2) vs 9.1 (5.9−11.3) months, respectively ($P = .003$) (Supplementary Fig 2, available via Mendeley at https://doi.org/10.17632/wm4gzhy7pd.1). Cox-regression analysis, adjusting for biologic target and study country, affirmed this difference, with hazard ratio of 0.69 (95% CI, 0.60-0.79; $P < .001$).

Regarding reasons for cessation reported, these included lack of efficacy in 15% to 64% and 18% to 50% and side effects in 5% to 45% and 0% to 9% for TNF-α inhibitors and non−TNF-α inhibitors, respectively. Because the time points at which these were measured were not standardized, meta-analysis and significance testing were not undertaken because of risk of introducing immortal-time bias. Numerically lower rates of discontinuation because of side effects of non−TNF-α inhibitors may suggest greater tolerability in real-world settings, which require validation in future studies. However, given their similar DS outcomes, these may be appropriate first-line alternatives to TNF-α inhibitors in suitable patients.

Our analysis suggests that approximately half of patients with HS treated with biologics will cease treatment by 12 months. In contrast, 12-month DS rates for biologics range from 81% to 94% for psoriasis and 90% for atopic dermatitis.[2,3] In the open-label extension of the PIONEER trials of adalimumab in HS (n = 88), 51 patients (58%) had ceased treatment by 3 years.[4] A post-hoc analysis demonstrated that 80% of adalimumab responders experienced loss of response by 12 months, which may contribute to the high discontinuation rates observed.[4] Patients may also cease biologics in the absence of loss of response, warranting further evaluation, for example, before surgical interventions, which was not captured in our analysis.

Reasons for shorter DS of biologics in HS remain unclear; however, they may include the development of antidrug antibodies or upregulation of B-cell, monocyte, and complement pathways.[5] Our analyses suggest that prior biologic exposure may predict shorter DS; however, we were unable to adjust our Cox-regression model for age, biological sex, body mass index, or HS severity. In addition, increasing availability of treatment options for HS over time may bias our DS results in favor of TNF-α inhibitors, given their earlier availability.[5]

In summary, DS of biologics in HS appears shorter than that for other dermatologic indications. Future studies examining predictive factors for shorter DS will be essential in guiding optimal treatment selection and patient counseling in HS.

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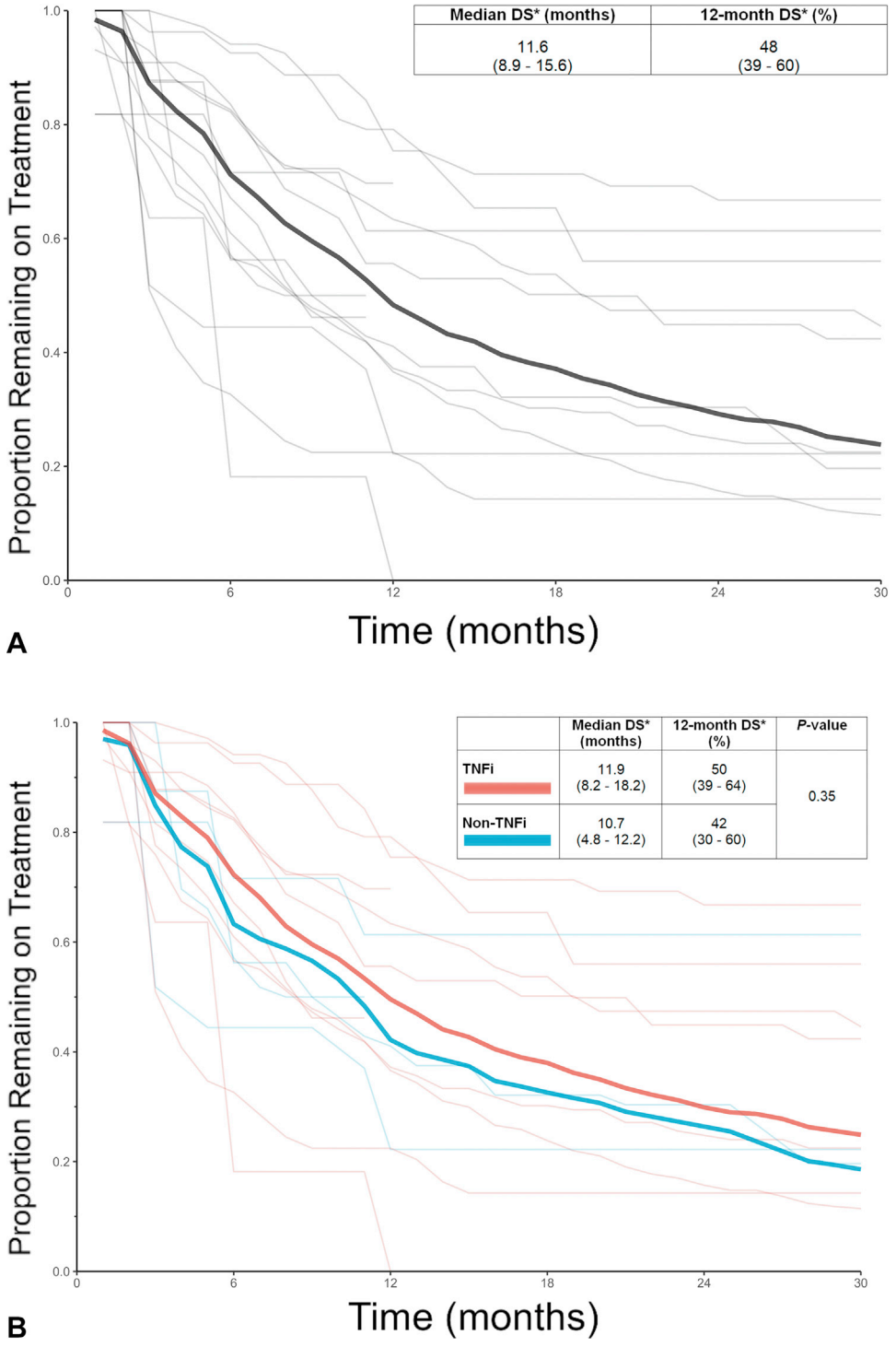

Fig 1. Pooled Kaplan-Meier curves for drug survival of biologics in hidradenitis suppurativa (**A**) overall and (**B**) stratified by inflammatory cytokine target (tumor necrosis factor-alfa [TNF-α] vs non−TNF-α inhibitors).

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Conflicts of interest

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Dermatologic toxicity associated with targeted and immunotherapies in stage-IV non-small cell lung cancer patients: A 14-year cohort

To the Editor: Dermatologic toxicities occur in non-small cell lung cancer (NSCLC) patients treated with targeted therapies and immune checkpoint inhibitors (ICIs) and most frequently in epidermal growth factor receptor inhibitors (EGFRIs), presenting an therapeutic challenge.[1] EGFRIs-related rashes were associated with prolonged survival in clinical trials with small datasets.[2] However, information is limited on dermatologic toxicities of newer-generation targeted drugs and ICIs in advanced-stage NSCLC, especially under real-world conditions. We report a 14-year clinical cohort study of 3767 stage-IV NSCLC.

Patients were enrolled from 2006 to 2019[3] and followed through 2022 (Supplementary Fig 1, available via Mendeley at https://data.mendeley.com/datasets/ynnstgsbnj/1). Treatment-related toxicities were identified and evaluated by healthcare providers within 3 months of drug initiation using Common Terminology Criteria for Adverse Events (CTCAE) v5.0. We analyzed 596 patients with targeted therapies or ICIs and divided them into those with dermatologic, nondermatologic, or no toxicities. Survival analyses employed Cox Proportional Hazard models (measured as hazard ratio, HR [95% CI]).

Dermatologic with or without nondermatologic toxicity occurred in 361/596 (61%) patients, only nondermatologic toxicity 184 (31%), and no toxicity 51 (8.6%). Patients receiving EGFRIs (329/442, 74%), especially erlotinib (260/333, 78%), had higher dermatologic toxicity rates than those receiving *anaplastic lymphoma kinase* (*ALK*)/*c-ros oncogene 1* (*ROS1*) inhibitors (10/63, 16%), other targeted therapies (7/41, 17%) or ICIs (10/91, 11%) (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/ynnstgsbnj/1). Included, shown in Table I, were 340 never-smokers, 256 smokers, 322 *EGFR*-mutated and 159