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LETTER

Response to the Letter to the Editor: Long-Term Psoriasis Control with Guselkumab, Adalimumab, Secukinumab, or Ixekizumab in the USA

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Dear Editor,

Blauvelt et al. [1] raise important questions about analysis of real-word drug performance data in response to our article "Long-Term Psoriasis Control with Guselkumab, Adalimumab, Secukinumab, or Ixekizumab in the USA" published in *Dermatology and Therapy* [2]. We appreciate this opportunity to address their questions and improve the understanding of methodologies and results of such analyses.

Determining persistence on a biologic with administrative claims data requires knowing when there is a gap in treatment, and the definition of a gap is complicated because the dosing regimens of different biologic products vary. Using a gap length proportional to the frequency of administration may favor biologics administered less frequently; using a fixed gap time may favor biologics administered more frequently. While our initial analysis was based on the former [2], analyses with fixed 90- and 60-day gaps to define discontinuation corroborate our findings; even when a fixed gap is used, median time to discontinuation and rates of discontinuation trend lower with guselkumab

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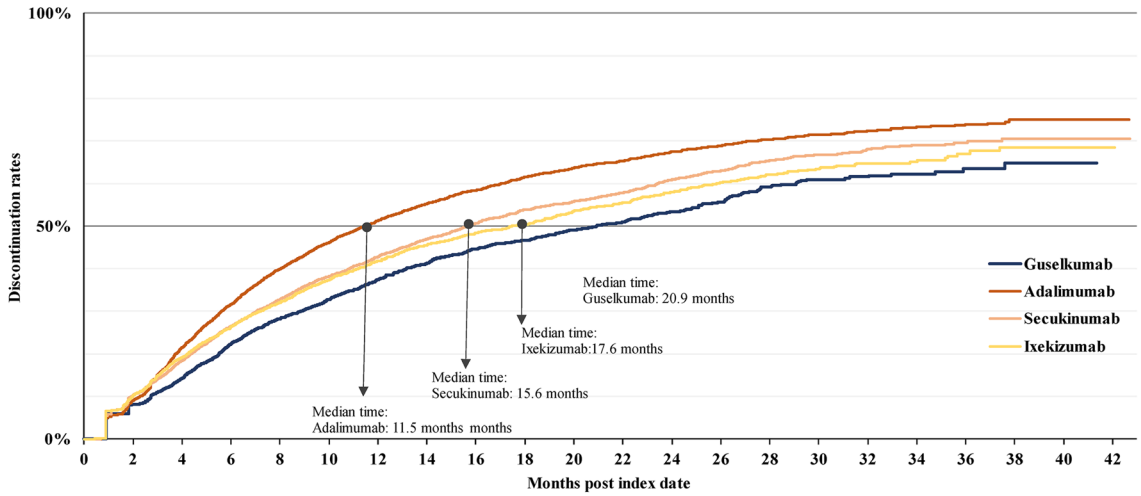

At risk[3], n (%)	3 months	6 months	12 months	18 months	24 months
Guselkumab	2,815 (82.6%)	2,242 (65.8%)	1,063 (31.2%)	634 (18.6%)	334 (9.8%)
Adalimumab	6,284 (78.4%)	4,573 (57.0%)	2,481 (30.9%)	1,457 (18.2%)	789 (9.8%)
Secukinumab	4,867 (79.5%)	3,805 (62.1%)	2,097 (34.2%)	1,179 (19.3%)	601 (9.8%)
Ixekizumab	2,913 (78.1%)	2,294 (61.5%)	1,241 (33.3%)	712 (19.1%)	326 (8.7%)
KM rates, % (95% CI)	**3 months**	**6 months**	**12 months**	**18 months**	**24 months**
Guselkumab	10.9% (9.9, 12.0)	22.2% (20.8, 23.7)	37.4% (35.6, 39.3)	46.3% (44.2, 48.5)	53.4% (51.0, 55.9)
Adalimumab	14.9% (14.1, 15.7)	31.3% (30.3, 32.4)	51.2% (50.0, 52.5)	61.0% (59.8, 62.3)	67.4% (66.1, 68.8)
Secukinumab	14.1% (13.2, 15.0)	26.2% (25.0, 27.3)	42.7% (41.4, 44.1)	53.5% (52.0, 55.0)	60.9% (59.2, 62.7)
Ixekizumab	14.7% (13.6, 15.9)	25.9% (24.5, 27.5)	41.8% (40.0, 43.6)	50.2% (48.2, 52.2)	57.9% (55.7, 60.2)

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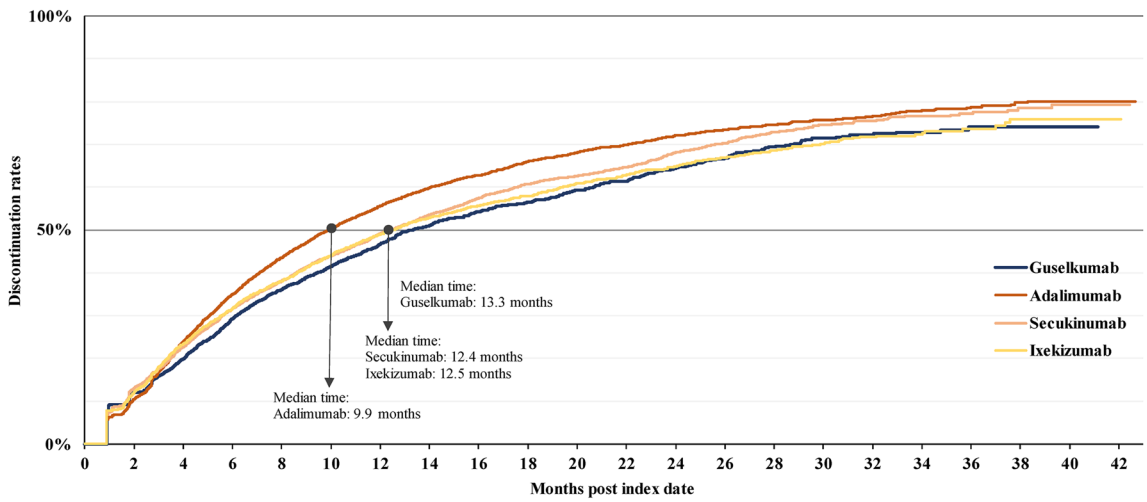


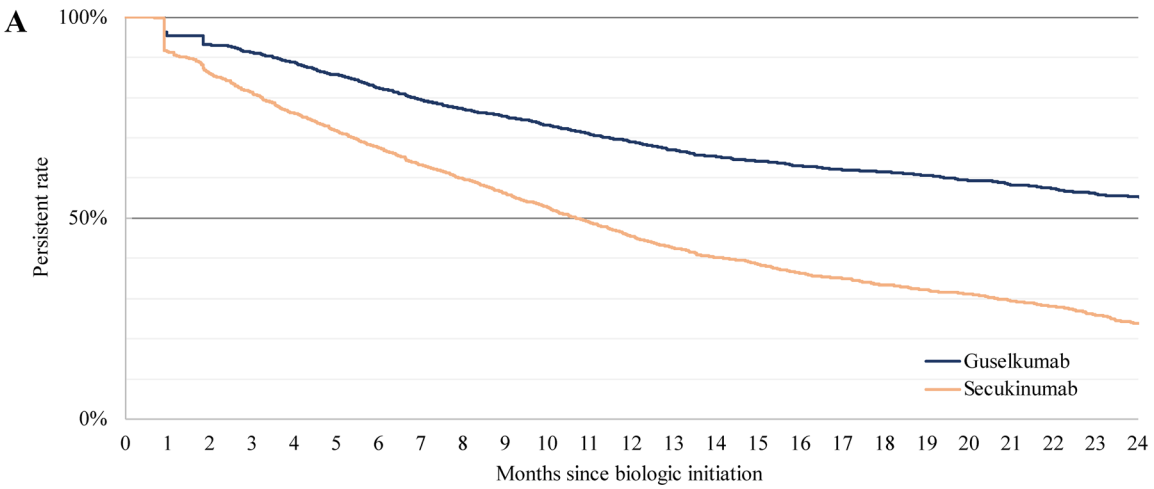
At risk[3], n (%)	3 months	6 months	12 months	18 months	24 months
Guselkumab	2,664 (78.2%)	2,054 (60.3%)	913 (26.8%)	528 (15.5%)	261 (7.7%)
Adalimumab	6,179 (77.1%)	4,421 (55.1%)	2,317 (28.9%)	1,331 (16.6%)	698 (8.7%)
Secukinumab	4,683 (76.5%)	3,571 (58.3%)	1,890 (30.9%)	1,022 (16.7%)	505 (8.2%)
Ixekizumab	2,818 (75.6%)	2,140 (57.4%)	1,115 (29.9%)	621 (16.7%)	286 (7.7%)
KM rates, % (95% CI)	**3 months**	**6 months**	**12 months**	**18 months**	**24 months**
Guselkumab	15.8% (14.6, 17.1)	29.1% (27.6, 30.8)	46.7% (44.8, 48.7)	56.2% (54.0, 58.3)	64.5% (62.1, 66.9)
Adalimumab	16.7% (15.9, 17.6)	34.5% (33.4, 35.6)	55.5% (54.3, 56.8)	65.6% (64.3, 66.8)	72.1% (70.8, 73.4)
Secukinumab	17.5% (16.6, 18.5)	31.2% (30.0, 32.5)	49.1% (47.7, 50.5)	60.6% (59.0, 62.1)	68.1% (66.5, 69.8)
Ixekizumab	17.8% (16.6, 19.1)	31.3% (29.8, 32.9)	48.9% (47.1, 50.7)	57.8% (55.9, 59.8)	64.8% (62.7, 67.0)

◀**Fig. 1** Time to discontinuation among patients with psoriasis initiated on guselkumab, adalimumab, secukinumab, and ixekizumab using a gap of ≥ 90 days (A) or ≥ 60 days (B)[1,2]. **A** Time to discontinuation was longer with guselkumab despite the 90-day gap allowing patients on guselkumab to miss 1.5 prescription fills and patients on other study biologics 3 prescription fills before they were considered non-persistent. **B** Time to discontinuation was longer with guselkumab despite the 60-day gap allowing patients on guselkumab to miss 1 prescription fill and patients on other study biologics 2 prescription fills before they were considered non-persistent. *CI* confidence interval, *KM* Kaplan–Meier. [1]Discontinuation was defined based on a gap in consecutive days of index biologic supply or between the last day of supply and the end of the follow-up period. The discontinuation date was the last day of supply before the gap. [2]The probability of discontinuation of the index biologic was assessed using KM survival analysis. Patients for whom discontinuation was not observed during the follow-up time were censored on the last day of the index biologic supply before the end of follow-up. [3]Patients at risk of having the event are patients who have not had the event and have not been lost to follow-up at that point in time

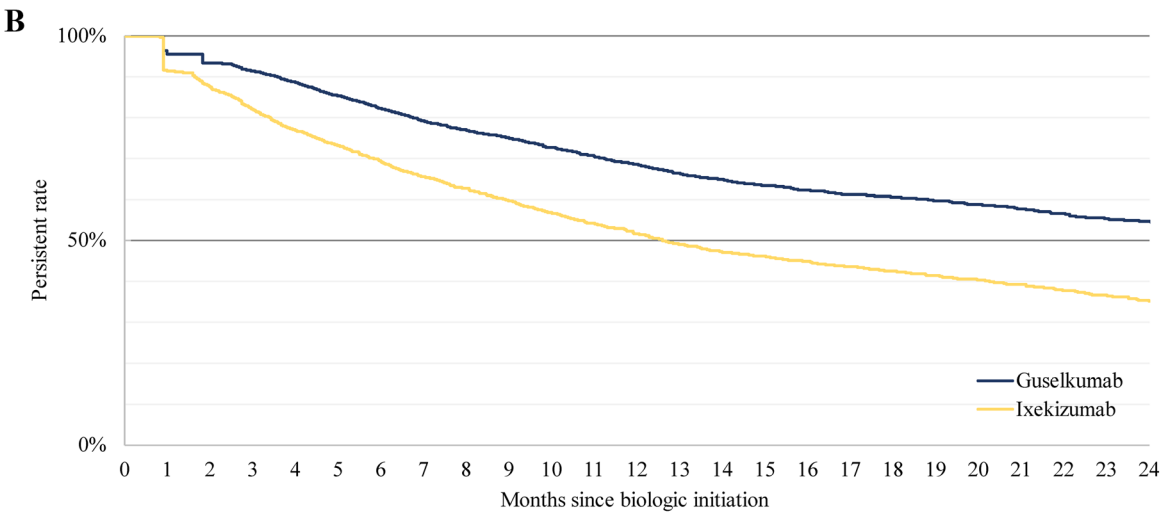
compared with other study biologics (Fig. 1A, B).

Blauvelt et al. noted that days of supply were imputed only for one study drug in our article [2]. No imputations were made for pharmacy claims of adalimumab, secukinumab, and ixekizumab because only 0.5% of adalimumab and 0.2% of both secukinumab and ixekizumab pharmacy claims in the maintenance phase had days of supply below 28 (the expected fill frequency for these biologics in maintenance phase). In all, 20.8% of guselkumab claims in the maintenance phase had 28–30 days of supply, while the labelled frequency is 56 days. Such discrepancy occurs for biologics with maintenance intervals greater than 4 weeks due to restrictions on the maximum of days of supply (typically, 30) imposed by some health plans [3]. Consistent with this hypothesis, the median time to next claim was 55 days among these claims; therefore, days of supply were imputed to 56.

Blauvelt et al. also noted limitations related to the unadjusted analysis in our article [2] as well as highlighted the need for supplementing persistence measures with adherence data. While we agree that a descriptive unadjusted analysis such as ours has limitations, it also affords an opportunity to consider multiple treatment options at the same time and evaluate a treatment landscape overall, which is not feasible with pairwise comparative studies. Nonetheless, to demonstrate that findings from our descriptive study remain robust in adjusted analyses, entropy balancing was used to adjust for differences in patient baseline characteristics, and guselkumab remained associated with about two times greater persistence compared with secukinumab and ixekizumab at



At risk[4], n (%)	3 months	6 months	12 months	18 months	24 months
Guselkumab	2,980 (84.8%)	2,430 (69.1%)	1,371 (39.0%)	823 (23.4%)	431 (12.3%)
Secukinumab	4,596 (75.8%)	3,414 (56.3%)	1,507 (24.8%)	849 (14.0%)	383 (6.3%)
Hazard ratio, guselkumab vs secukinumab (95% CI)	2.22 (1.95;2.52)	2.06 (1.87;2.26)	2.10 (1.94;2.26)	2.15 (2.01;2.31)	2.20 (2.05;2.35)
Chi-square P-value	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
KM rate, % (95% CI)	**3 months**	**6 months**	**12 months**	**18 months**	**24 months**
Guselkumab	91.2 (88.6;93.2)	82.7 (80.2;84.9)	69.1 (66.5;71.5)	61.5 (58.7;64.2)	55.4 (52.0;58.6)
Secukinumab	81.4 (79.1;83.4)	67.9 (65.2;70.3)	45.5 (42.2;48.8)	33.4 (29.5;37.4)	24.0 (19.3;28.9)
Log-rank test P-value	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*



At risk[4], n (%)	3 months	6 months	12 months	18 months	24 months
Guselkumab	3,236 (85.0%)	2,626 (69.0%)	1,454 (38.2%)	881 (23.2%)	471 (12.4%)
Ixekizumab	3,543 (75.8%)	2,734 (58.5%)	1,319 (28.2%)	768 (16.4%)	410 (8.8%)
Hazard ratio, guselkumab vs ixekizumab (95% CI)	2.17 (1.90;2.47)	1.90 (1.72;2.09)	1.80 (1.67;1.94)	1.77 (1.65;1.91)	1.77 (1.65;1.90)
Chi-square P-value	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
KM rate, % (95% CI)	**3 months**	**6 months**	**12 months**	**18 months**	**24 months**
Guselkumab	91.5 (89.0;93.4)	82.5 (80.1;84.6)	68.6 (66.1;70.9)	60.7 (58.0;63.3)	54.8 (51.5;57.9)
Ixekizumab	82.3 (79.9;84.3)	69.8 (67.4;72.2)	51.7 (48.6;54.6)	42.6 (39.0;46.1)	35.2 (30.7;39.8)
Log-rank test P-value	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*

◀**Fig. 2** Persistence in guselkumab cohort and weighted **A** secukinumab cohort and weighted **B** ixekizumab cohort. Pairwise comparisons using entropy balancing to account for differences in baseline characteristics (presented at the Fall Clinical Dermatology Annual Meeting 2022) confirmed the results of unadjusted analyses[1–3]. *CI* confidence interval, *KM* Kaplan–Meier. *statistical significance at 0.05 level. [1]Zhdanava M, Fitzgerald T, Pilon D, et al. Long term psoriasis control with guselkumab versus secukinumab and ixekizumab: analysis of drug persistence in large claims database. presented at: Fall Clinical Dermatology Annual Meeting; October 20–23, 2022 Las Vegas, NV. [2]Discontinuation was defined based on a gap (> 120 days for guselkumab or > 60 days for secukinumab/ixekizumab, representing twice the dosing frequency) in consecutive days of index biologic supply or between the last day of supply and the end of the follow-up period. The discontinuation date was the last day of supply before the gap. [3]The probability of persistence on the index biologic was assessed using KM survival analysis and Cox proportional-hazard models. Patients for whom discontinuation was not observed during the follow-up time were censored on the last day of the index biologic supply before the end of follow-up. [4]Patients at risk of having the event are patients who have not had the event and have not been lost to follow-up at that point in time

18 months after therapy initiation (Fig. 2A, B) [4, 5]. Approaches to calculating medication adherence such as the medication possession ratio (MPR) and the proportion of days covered (PDC) vary and must be tailored to the objectives of a specific study [6]. The Pharmacy Quality Alliance recommends using the PDC for chronic therapies [7], which is calculated as the number of days of supply over a fixed period (e.g., 18 months); using this approach, the mean PDC and the proportion of patients with PDC ≥ 80% trend higher for guselkumab compared with other study biologics (Table 1).

Lastly, claims data indeed do not provide exact information on "disease control," but lack of change in treatment may be a reasonable proxy. Defining remission with claims data also has limitations, but identifying patients off all psoriasis treatment (while remaining insured) may be a reasonable proxy for full remission. Being off systemic treatment may be a reasonable proxy for remission of moderate-to-severe psoriasis (allowing that topicals may be used for residual mild disease). These proxy definitions of remission are an exploratory approach; other reasons for remaining off biologic therapy include pregnancy, upcoming surgery, cancer diagnosis, or other patient factors [2]. While recognizing the limitations of this approach, the possibility of long-term treatment-free disease control we observed would likely be welcomed enthusiastically by patients and their physicians.

Table 1 Adherence to index biologic based on proportion of days covered[1,2]

	Guselkumab cohort *N* = 3408	Adalimumab cohort *N* = 8017	Secukinumab cohort *N* = 6123	Ixekizumab cohort *N* = 3728
At 12 months of follow-up				
Number of patients with available follow-up, *n* (%)	1887 (55.4)	5463 (68.1)	3930 (64.2)	2309 (61.9)
PDC, mean ± SD [median]	0.68 ± 0.26 [0.76]	0.62 ± 0.29 [0.69]	0.65 ± 0.28 [0.74]	0.63 ± 0.28 [0.73]
PDC ≥ 80%, *n* (%)	847 (44.9)	2199 (40.3)	1663 (42.3)	930 (40.3)
At 18 months of follow-up				
Number of patients with available follow-up, *n* (%)	1368 (40.1)	4137 (51.6)	2818 (46.0)	1589 (42.6)
PDC, mean ± SD [median]	0.62 ± 0.28 [0.71]	0.54 ± 0.31 [0.54]	0.59 ± 0.29 [0.67]	0.58 ± 0.30 [0.65]
PDC ≥ 80%, *n* (%)	525 (38.4)	1321 (31.9)	982 (34.8)	544 (34.2)
At 24 months of follow-up				
Number of patients with available follow-up, *n* (%)	843 (24.7)	2806 (35.0)	1775 (29.0)	904 (24.2)
PDC, mean ± SD [median]	0.59 ± 0.29 [0.67]	0.49 ± 0.31 [0.43]	0.55 ± 0.30 [0.58]	0.53 ± 0.31 [0.57]
PDC ≥ 80%, *n* (%)	288 (34.2)	729 (26.0)	539 (30.4)	263 (29.1)

[1]PDC was defined as the sum of non-overlapping days of supply of the index biologic divided by days in a fixed period (i.e., 12, 18, and 24 months) among patients followed for at least the same fixed period

[2]Evaluated during the follow-up period defined as the time between the index biologic initiation date and the earliest between the end of data or the end of continuous health plan eligibility

PDC proportion of days covered, *SD* standard deviation

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Declarations

Conflict of Interest. Timothy Fitzgerald is an employee of Janssen Scientific Affairs, LLC, and holds stock in Johnson & Johnson. Maryia Zhdanava, Dominic Pilon, Aditi Shah, and Patrick Lefebvre are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to Janssen Scientific Affairs, LLC. Steven R. Feldman received research, speaking and/or consulting support from Janssen Scientific Affairs, LLC and is the founder and majority owner of www.DrScore.com [drscore.com] and founder and part owner of Causa Research.

Ethical Approval. This letter is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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