Real-World Assessment of Biologics Dose Elevation in a Canadian Psoriasis Population

Neil H. Shear, MD[1]; Wendy Dobson-Belaire, PhD, MBA[2]; Ginger Tey, MASc[2]; Richard Borrelli, MBA[2]; Fei Fei Liu, BSc(Pharm), MBA[3]; Zeba M. Khan, RPh, PhD[4]

[1]University of Toronto, Toronto, ON, Canada; [2]IMS Brogan, Mississauga, ON, Canada; [3]Celgene Inc., Mississauga, ON, Canada; [4]Celgene Corporation, Summit, NJ, USA

BACKGROUND

- The high efficacy of biologic therapies has had a positive impact on patients with moderate to severe forms of psoriasis. However, as protein-based therapeutics, they can illicit unwanted immune responses that diminish their effectiveness and prompt treatment intensification or dose elevation.[1]
- Treatment dose elevation can improve patient response to biologic treatment but can have negative downstream consequences, including increased adverse event risk and treatment cost, making it challenging to understand the true impact of biologics on patients and healthcare budgets.[2,3]
- Thus, an understanding of real-world psoriasis patient dose-elevation patterns can better inform biologic utilization.

OBJECTIVES

- The objective of this research was to quantify the real-world prevalence and extent of adalimumab, etanercept, infliximab, and ustekinumab dose elevation in a population of Canadian patients with psoriasis.

METHODS

Data

- The study was conducted using IMS Brogan's Canadian national private drug plan (PDP) and Ontario's (OPDP) and Quebec's (RAMQ) provincial public drug plan databases. All three are administrative claims-based databases with ~70% national market coverage for PDP and 100% and 75% market coverage for OPDP and RAMQ, respectively.

Study Period

- This retrospective study was conducted from October 1, 2006, to December 31, 2011.

Patient Selection

- Psoriasis patient diagnosis was inferred using a medication claim algorithm validated previously. Briefly, patients were required to have ≥2 claims for psoriasis medications with limited multi-indication use, defined as "Psoriasis-Defining Molecules," between October 2007 and September 2013. See **Table 1** for a summary of molecules used.
- Patients meeting the diagnosis criteria were then selected if they had ≥1 claim for adalimumab, etanercept, infliximab, or ustekinumab from October 2007 to September 2010, were naïve to biologic therapy, and were persistent on their respective therapy for a minimum of 1 year. Persistence was defined as having no more than a 60-day gap between index medication refills.

Table 1. Molecules Used to Define the Patient Population

Molecules Used to Define a Psoriasis Patient*	Molecules Used to Define the Study Population§
Acitretin	Adalimumab
Calcipotriol	Etanercept
Calcipotriol + betamethasone dipropionate	Infliximab
Calcitriol	Ustekinumab
Methoxsalen	
Trioxsalen	

*Patients with ≥2 claims for any of these molecules from October 2007 to September 2013 were classified as psoriasis patients.
§Patients naïve to biologic therapy and persistent on 1 of these biologic therapies for ≥1 year were included in the study.

Dose-Elevation Calculation

- A dose-elevation event was identified if ≥2 consecutive claims with a dose-elevation ratio of ≥1.2 were observed, signaling a ≥20% increase from the monograph-recommended dose.
- The dose-elevation ratio was defined as the days' supply for the studied claim divided by the duration to the next refill claim.
- Days' supply was standardized based on the claim cost vs. the expected cost associated with the treatment intervals specified in Canadian drug monographs.

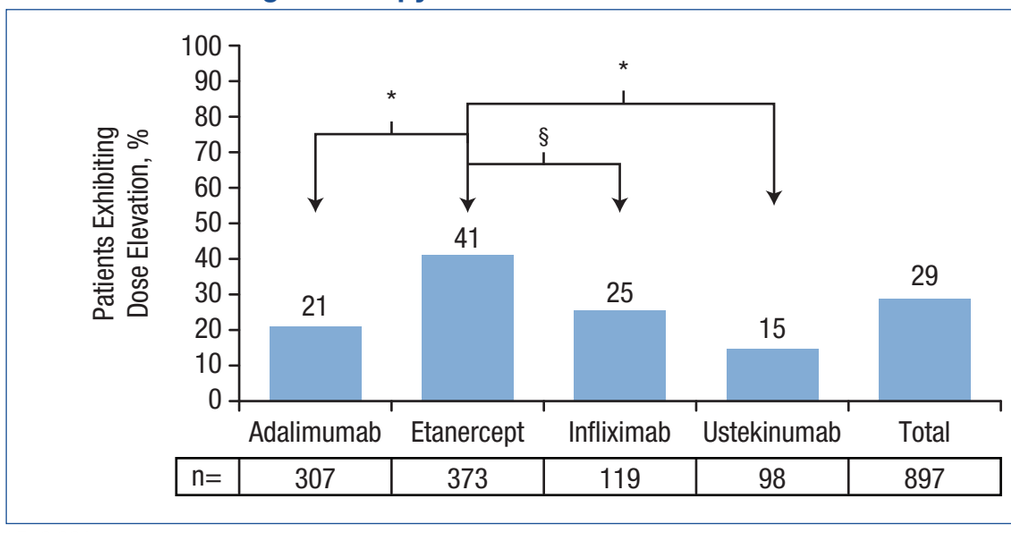
Statistical Testing

- Chi-square or 1-way analysis of variance (ANOVA) followed by pairwise comparisons was used to evaluate the dose-elevation prevalence, time to dose elevation, and dose-elevation ratio among the studied biologics.

RESULTS

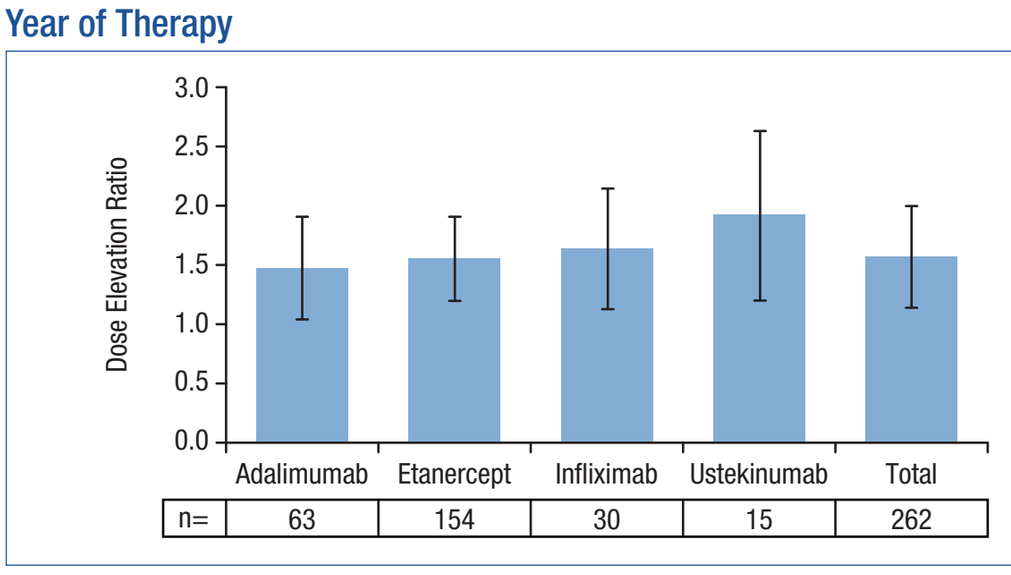
- A cohort of 897 patients met the criteria for inclusion in the dose-elevation study. As shown in **Figure 1**, 29% of the cohort (262 patients) exhibited dose elevation. The mean dose-elevation ratio among the biologics studied was 1.57 (**Figure 2**), and the mean time to dose elevation was 172 days from biologic initiation (**Figure 3**).
- As shown in **Figure 1**, the prevalence of dose elevation among etanercept patients (41%, n=154) was significantly higher than that among adalimumab (21%, n=65, $P<0.001$), infliximab (25%, n=30, $P=0.002$), and ustekinumab (15%, n=15, $P<0.001$) patients.
- The time to dose elevation for etanercept (153 days) was significantly shorter than that observed for adalimumab (202 days, $P<0.001$) (**Figure 3**).
- No other significant differences were observed in dose-elevation prevalence and time to dose elevation.

Figure 1. Prevalence of Dose Elevation Among Psoriasis Patients in Their First Year of Biologic Therapy



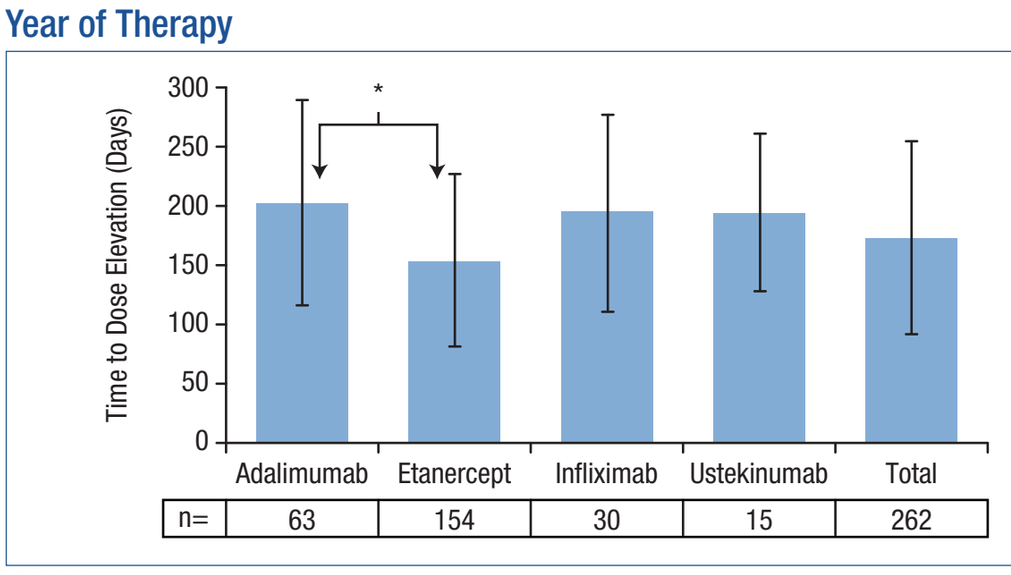
*$P<0.001$
§$P=0.002$
Note: Chi-square tests were used to evaluate the dose-elevation prevalence.

Figure 2. Average Dose-Elevation Ratio Among Psoriasis Patients Who Exhibited Dose Elevation on Their First Biologic Therapy Within the First Year of Therapy



Note: The average dose-elevation ratio was calculated by summing the biologics days' supply from the first dose-elevation defining event over the remaining days within the year. 1-way ANOVA followed by pairwise comparisons was used to evaluate the differences between dose-elevation ratios among the studied biologics. Error bars represent ± 1 standard deviation.

Figure 3. Average Time to Dose Elevation Among Psoriasis Patients Who Exhibited Dose Elevation on Their First Biologic Therapy Within the First Year of Therapy



*$P<0.001$
Note: One-way ANOVA followed by pairwise comparisons was used to evaluate the differences between dose-elevation ratios among the studied biologics. Error bars represent ± 1 standard deviation.

LIMITATIONS

- Psoriasis diagnosis was inferred based on a validated medication claims algorithm; therefore, the studied biologics' use for the treatment of psoriasis cannot be completely assured.
- Because the amount of biologic therapy used was standardized to claim cost, dose increases in drugs with flat pricing, such as ustekinumab, could be underestimated.
- Dose elevation beyond the first year of biologic treatment was not evaluated.
- Dose elevation among individuals who were not persistent on their respective biologic therapy was not evaluated.

CONCLUSIONS

- Dose elevation is prevalent in all major biologics used to treat psoriasis for at least 1 year and leads to increased costs.
- Etanercept had the highest prevalence and shortest time to dose elevation.
- These results suggest that further investigation into the impact of dose elevation on clinical outcomes, including drug efficacy and patient safety, is warranted.

REFERENCES

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