Actas Dermo-Sifiliográficas xxx (xxxx) 104539

Contents lists available at ScienceDirect

Actas Dermo-Sifiliográficas

journal homepage: www.actasdermo.org

Resident's Forum

RF – Tildrakizumab 200 mg. Is Double Dosing Really a Window of Opportunity?

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ARTICLE INFO

Keywords:
Psoriasis
Intensive therapy
Tildrakizumab
Anti-interleukin 23

Tildrakizumab is a humanized IgG1/κ monoclonal antibody that binds specifically to the p19 subunit of the cytokine interleukin-23 (IL-23), thereby inhibiting its interaction with the receptor. According to its product information, the recommended dose is 100 mg by subcutaneous injection at weeks 0 and 4 and every 12 weeks thereafter; however, at the clinician's discretion, in patients with a high disease burden or in those weighing >90 kg, a 200 mg dose may be more effective.[1]

Tildrakizumab is the only IL-23p19 inhibitor that has approval for individualized, weight-adjusted dosing. Its introduction into our therapeutic arsenal was preceded by an evaluation of its tolerability and safety using a single 200 mg/2 mL subcutaneous injection.[2] In that study, safety outcomes were similar to those obtained with 2 100 mg/L injections, and most participants preferred the double dose because of easier administration.

In real-world clinical practice, only two studies have reported experience with the 200 mg dose of tildrakizumab. Gargiulo et al.[3] presented a 16-week retrospective multicenter study comparing both doses, including 134 patients treated with 200 mg and 364 treated with 100 mg. In the 200 mg group, the mean patient weight was 91.09 kg vs 79.95 kg in the 100 mg group. After 16 weeks, 57.5% of patients on 200 mg achieved PASI 90 vs 34.3% in the 100 mg group. Complete remission (PASI 100) was achieved by 39.6% of patients treated with 200 mg vs 24.2% of those treated with 100 mg. These results must be interpreted with caution due to the proximity to the weight threshold. We consider it necessary to re-evaluate the concept of disease burden in this context. Separately, Trovato[4] studied 30 patients over 28 weeks with both doses and found significantly greater improvements in outcomes (WHO-5 and DLQI) among patients on the 200 mg dose.

Table 1
Clinical characteristics and treatments received by patients in the unit.

Characteristics	Values
No. of patients	8
Sex, no. M/F	6/2
Age, years, mean (range)	48 (20–75)
BMI*, mean (range)	26.4 (19–37)
Weight, kg, mean (range)	80.4 (51–107)
Weight >90 kg	3
Time since diagnosis, years, mean (range)	17 (2–56)
No. of affected sites, mean (range)	2.4 (1–4)
No. of previous biologics, mean (range)	1 (0–2)
Adalimumab	6
Ustekinumab	1
Secukinumab	1
Super-nonresponder**	1
Dosing***	
Initiation (weeks 0 and 4)	
Standard dose	4
Weight >90 kg	2
Baseline PASI ≥8	3
Intensified dose	4
Weight >90 kg	1
Baseline PASI ≥8	2
Maintenance (from week 4 onward)	
Standard dose	4
Weight >90 kg	1
Baseline PASI ≥8	2
Intensified dose	4
Weight >90 kg	2
Baseline PASI ≥8	3

* Body mass index.
** Refractory to >3 previous biologics.
*** Standard dose = 100 mg subcutaneously at weeks 0 and 4, then every 12 weeks. Intensified dose = 200 mg following the same administration schedule.

In our Psoriasis Unit, we assessed the safety and efficacy outcomes of 8 patients – whose characteristics are summarized in Table 1 – who at some point received the 200 mg dose during six months of follow-

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https://doi.org/10.1016/j.ad.2025.104539

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Please cite this article as: C. Llamas-Segura, M. Cebolla-Verdugo and R. Ruiz-Villaverde, RF – Tildrakizumab 200 mg. Is Double Dosing Really a Window of Opportunity? ACTAS Dermo-Sifiliográficas, https://doi.org/10.1016/j.ad.2025.104539

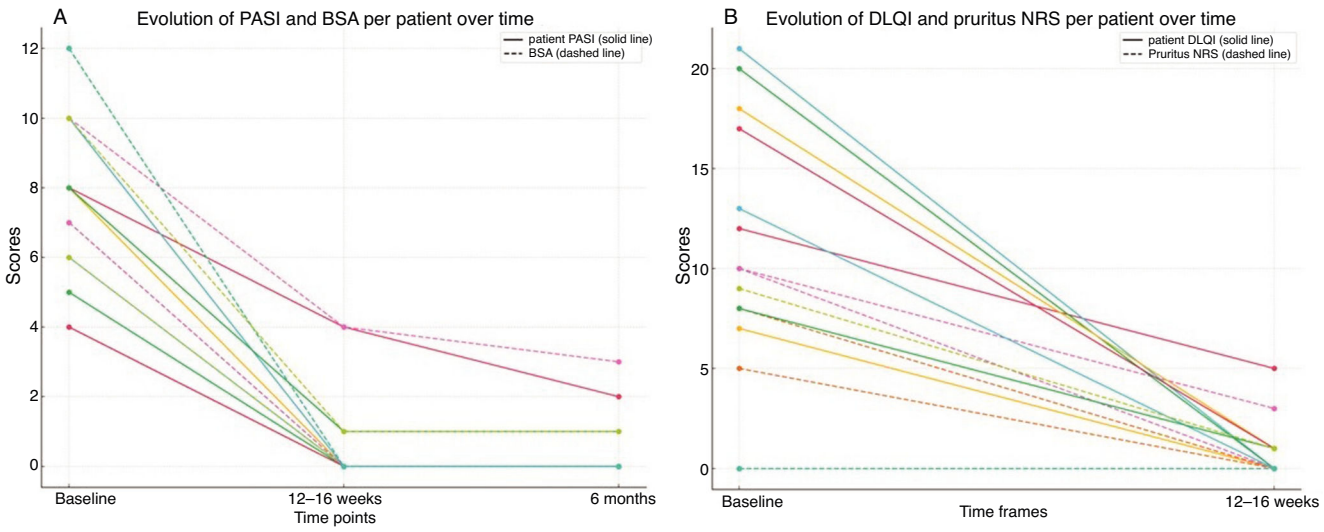

Fig. 1. (A) Progression of PASI and BSA from baseline to week 24 in our 8 patients. (B) Progression of pruritus NRS and DLQI from baseline to week 24 in our 8 patients.

up. These findings support the data published in the above-mentioned clinical trials and observational studies (Fig. 1). Four of the 8 patients began therapy at the standard dose and were subsequently escalated to the intensified dose due to either primary failure (failure to reach absolute PASI <3 at week 16) or secondary failure (loss of absolute PASI <3 after having achieved it). These 4 patients did not undergo dose escalation at the same follow-up visit.

In response to the initial question, we believe that a window of opportunity is opening not only for weight-based dose adjustment but also for patients with higher disease burden – understood as a greater number of comorbidities, involvement of difficult-to-treat areas, unsatisfactory response to several lines of biologic therapy, and high emotional impact – provided that accessibility maintains the same price for both doses. It would be desirable to evaluate direct costs and work productivity in daily practice, although systematic assessment of these aspects is currently far from being a reality.[5]

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