Dermatol Ther (Heidelb) (2022) 12:5–8
https://doi.org/10.1007/s13555-021-00650-5

COMMENTARY

Arthritis Interception in Patients with Psoriasis Treated with Guselkumab

Alen Zabotti · Ivan Giovannini · Dennis McGonagle · Salvatore De Vita · Giuseppe Stinco · Enzo Errichetti

Received: November 1, 2021 / Published online: November 27, 2021

Keywords: Guselkumab; Interception; Psoriasis; Psoriatic arthritis

Psoriatic arthritis (PsA) is one of the main extracutaneous manifestations of psoriasis (PsO), with 20–30% of patients with PsO developing this condition over time [1–3]. Joint involvement typically follows PsO onset, although PsA may less commonly occur before or concomitantly with skin lesions [1–3]. Interestingly, growing evidence supports that patients with PsO go through three clinically silent and progressive stages before developing clinically evident PsA ("pre-PsA"), in a "multi-step PsO to PsA march" [1]. These preclinical stages are (I) immunological phase (typified by an aberrant immune system activation starting from skin, intestinal mucosa, or entheses), (II) subclinical phase (featuring soluble and/or imaging findings of joint inflammation with no clinical symptoms), and (III) prodromal phase (patients having arthralgia and fatigue without clinical evidence of arthritis, enthesitis, or spondylitis) [1]. Such a model of disease progression opens the way for an early intervention aiming to treat patients with PsO carrying a high risk of transition towards clinically full-blown synovio-entheseal inflammation ("PsA interception"), with consequent benefit on PsA-related morbidity [1–3]. Notably, two categories of predictors for PsA development have been identified in patients with PsO, including medium/long-term (PsA development greater than 2 years) and short-term (PsA development within 2 years) predictors [2]. The latter include arthralgia (defined as musculoskeletal symptoms not explained by other diagnosis without clinical evidence of PsA) and imaging evidence of synovio-entheseal inflammation, with PsA development risk ratio being 2.15 (95% CI 1.16–3.99) and 3.72 (95% CI 2.12–6.51), respectively [2, 3].

Herein, we report our experience of four patients with PsO carrying a short-term risk of PsA development treated with guselkumab for

A. Zabotti · I. Giovannini · S. De Vita
Rheumatology Institute, Department of Medicine, University of Udine, c/o Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy

D. McGonagle
Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), University of Leeds, Leeds, UK

G. Stinco · E. Errichetti
Institute of Dermatology, Department of Medicine, University of Udine, c/o Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy

E. Errichetti (✉)
Institute of Dermatology, "Santa Maria della Misericordia" University Hospital, Piazzale Santa Maria della Misericordia, 15, 33100 Udine, Italy
e-mail: enzoerri@yahoo.it

Table 1 Demographic and musculoskeletal features of the guselkumab-treated patients

	Patient 1	Patient 2	Patient 3	Patient 4
Demographic and PsO data				
Sex (M/F)	M	M	F	F
Age (years)	54	56	38	65
BMI	24.1	26.3	23.4	24.2
Smoke (yes/no)	No	Yes	Yes	No
Familiarity for PsA (yes/no)	Yes	No	No	No
PsO (yes/no)	Yes	Yes	Yes	Yes
PsO duration (years)	25	10	8	10
PsO previous treatment	MTX	CYS	CYS	MTX
PASI score	28.2	24.1	14.2	8*
NAPSI score	52	0	17	0
Preclinical PsA MSK features				
Arthralgia (yes/no)	Yes	Yes	Yes	Yes
Arthralgia duration (months)	24	12	12	36
VAS pain (0–10)	3	4	4.5	7
Fatigue (yes/no)	Yes	No	No	No
Tender joints count (0–68)	4	7	2	6
Swollen joints count (0–66)	0	0	0	0
Leeds Enthesitis Index (0–6)	0	1	1	2
HAQ	0.25	0.125	0.125	0.5
US-detected inflammatory signs (yes/no)	No	Yes	Yes	Yes

CYS cyclosporine, *MSK* musculoskeletal, *MTX* methotrexate, *PsA* psoriatic arthritis, *PsO* psoriasis, *US* ultrasonography
*Patient had the involvement of sensitive areas (face and hands)

skin disease. It included two women and two men, with a mean age of 53.3 years (38–65 years) and a mean PsO duration of 13.3 years (8–25 years). Baseline (guselkumab beginning) mean Psoriasis Area and Severity Index (PASI) score was 18.6 (SD 9.2), with figures ranging from 8 to 28.2, whereas nail involvement was present only in two cases (case 1 and 3, with NAPSI score of 52 and 17, respectively). All the patients reported arthralgia at baseline (mean duration of 21 months, range 12–36 months), with a mean tender joint count (TJC) of 4.74 (SD 2.2), without swollen joints and a mean VAS pain of 4.6 (SD 1.7). Sonographic evidence of subclinical active enthesitis/synovitis was present in one and three patients, respectively. More details are reported in Table 1. Guselkumab was the first-line biologic in all cases after the failure (primary/secondary) of at least one conventional treatment (i.e., methotrexate or cyclosporine). During a 1-year follow-up, no patient developed clinical arthritis and fulfilled ClASsification criteria for Psoriatic ARthritis (CASPAR). All

patients reported a significant reduction in VAS pain after 6 months of therapy, with three patients showing a complete regression of arthralgia (no tender joint and VAS pain of 0) and one patient (case 4) reporting a major regression of musculoskeletal pain and TJC (Fig. 1). No sonographic sign of active synovio-entheseal inflammation was observed in the present cohort from month 6; PASI 75 was reached in all cases (Fig. 1).

Guselkumab is a human immunoglobulin G1λ monoclonal antibody blocking the interleukin-23 (IL-23)-mediated signaling pathway [4]. It is approved for moderate to severe plaque-type PsO and administered subcutaneously at the dose of 100 mg at week 0, week 4, and every 8 weeks thereafter [4]. Our data support the possible usefulness of this biologic therapy to revert preclinical manifestations of PsA (i.e., arthralgia/sonographic enthesitis/synovitis) carrying a high risk of short-term development of clinically full-blown synovio-entheseal inflammation, thereby potentially modifying the natural course of PsA. Interestingly, in all our patients, conventional treatments failed to control such PsA preclinical stages, thus backing a higher efficacy of anti-IL-23 agents for this purpose. In this regard, IL-23R blockade has been shown to completely prevent spondylitis and arthritis development in HLA-B27tg rats [5]. The same study showed that IL-23 would be more involved in the initiation rather than persistence of SpA as downstream effector cytokines (IL-17A/IL-22) were down-regulated only after prophylactic and not therapeutic IL-23R blockade [5].

In conclusion, guselkumab might intercept PsA during a potential "window of opportunity" in individuals with moderate-severe PsO having short-term predictors of PsA development. Randomized controlled trials are needed to confirm our preliminary findings.

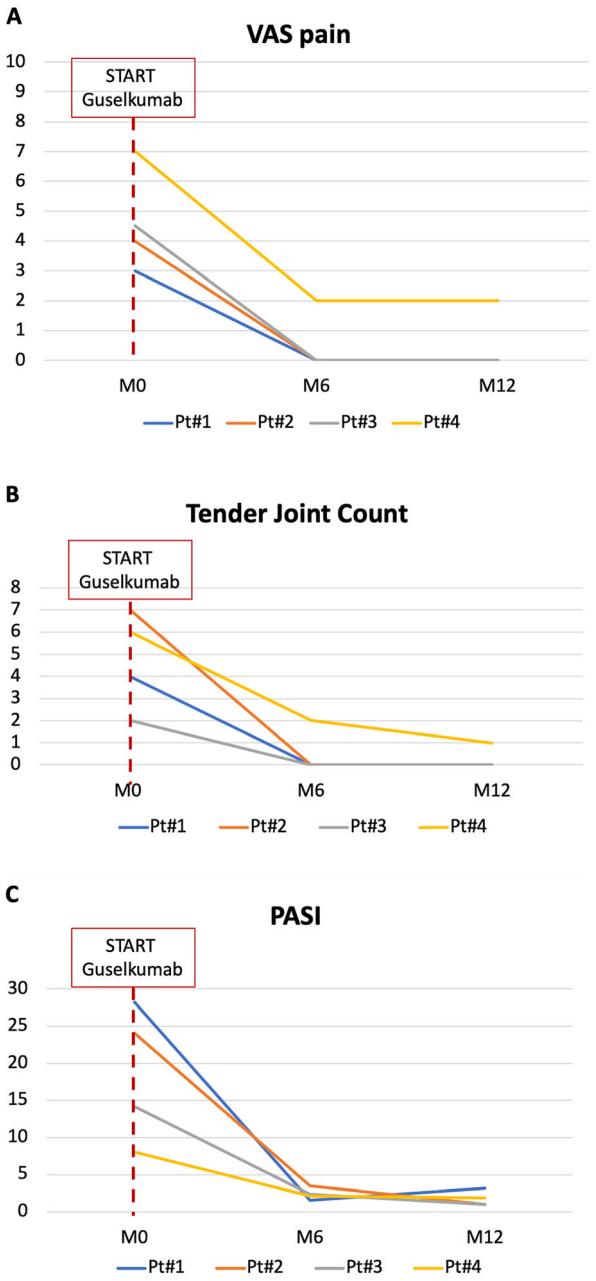

Fig. 1 Variation of VAS pain (**a**), tender joint count (TJC) (**b**), and PASI score (**c**) over 1 year

ACKNOWLEDGEMENTS

Funding. No funding or sponsorship was received for this study or publication of this article.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Author Contributions. Alen Zabotti and Enzo Errichetti (concept and design + manuscript writing); Ivan Giovannini (drafting the manuscript); Dennis McGonagle, Salvatore De Vita, and Giuseppe Stinco (review of the paper).

Disclosures. Alen Zabotti has received research funding or honoraria from Novartis, Lilly, Janssen, Abbvie, Amgen, UCB. Ivan Giovannini has received research funding or honoraria from Lilly. Dennis McGonagle has received research funding or honoraria from Novartis, Lilly, Janssen, Pfizer, Abbvie, Celgene, Amgen, Gilead, UCB. Enzo Errichetti has received research funding or honoraria from Janssen and Abbvie.

Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

REFERENCES

1. Scher JU, Ogdie A, Merola JF, Ritchlin C. Preventing psoriatic arthritis: focusing on patients with psoriasis at increased risk of transition. Nat Rev Rheumatol. 2019;15:153–66.

2. Zabotti A, De Lucia O, Sakellariou G, et al. Predictors, risk factors, and incidence rates of psoriatic arthritis development in psoriasis patients: a systematic literature review and meta-analysis. Rheumatol Ther. 2021. https://doi.org/10.1007/s40744-021-00378-w.

3. Zabotti A, McGonagle DG, Giovannini I, et al. Transition phase towards psoriatic arthritis: clinical and ultrasonographic characterisation of psoriatic arthralgia. RMD Open. 2019;5:e001067.

4. Al-Salama ZT, Scott LJ. Guselkumab: a review in moderate to severe plaque psoriasis. Am J Clin Dermatol. 2018;19:907–18.

5. van Tok MN, Na S, Lao CR, et al. The initiation, but not the persistence, of experimental spondyloarthritis is dependent on interleukin-23 signaling. Front Immunol. 2018;9:1550.