SHORT COMMUNICATION

Real-world Data Reveal Long Drug Survival for Guselkumab in Patients with Plaque Psoriasis

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Guselkumab has been registered as the first interleukin-23 (IL-23) inhibitor for treatment of psoriasis. Randomized controlled trials (RCTs) have shown a favourable efficacy and safety profile for guselkumab (1, 2). However, RCTs may not adequately reflect the real-world situation (3). The primary objective of this real-world observational multicentre study was to evaluate 1- and 2-year drug survival (DS) of guselkumab, split for discontinuation due to ineffectiveness or side-effects. A further aim was to elucidate predictors for a shorter guselkumab DS.

METHODS AND RESULTS

A detailed description of the methods is given in Appendix S1. Data from patients with plaque psoriasis treated with guselkumab were collected from the prospective BioCAPTURE registry (www.biocapture.nl) and retrospective data from 4 other centres in the Netherlands (time-frame 2020 to 2021). Temporary treatment interruptions for any reason were allowed if <90 days. This 90-day gap was prolonged up to 1 year if patients discontinued due to fear of COVID-19 or due to remission. In the Kaplan–Meier analyses, 3 separate DS curves were created with an event for discontinuation in general (all reasons), due to ineffectiveness or to side-effects. Discontinuation due to an increase in musculoskeletal complaints in patients with psoriatic arthritis (PsA) was considered as an event in side-effect analyses. Univariable and multivariable Cox regression models were used to identify factors affecting DS.

Participating centres and patient and treatment characteristics are shown in Tables SI and SII, respectively. A total of 195 patients (288.4 actively-treated patient years) were included; 110 (56.4%) were male, and 58 (29.7%) were biologic naive at guselkumab initiation. Forty (20.5%) patients had a rheumatologist-confirmed diagnosis of PsA. Six (3.1%) patients shortened the dosing interval, and 27 (13.8%) lengthened the interval.

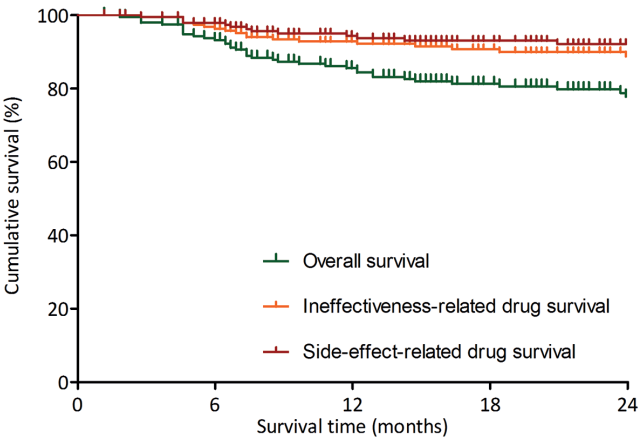

Fig. 1. Kaplan–Meier drug survival analysis of guselkumab during 2 years, split for reason of discontinuation.

Overall guselkumab DS rates after 1 and 2 years were 85.5% and 77.8%, respectively. One- and 2-year DS rates for discontinuation related to ineffectiveness were 92.8% and 88.7%, and for discontinuation related to side-effects were 94.3% and 92.1%, respectively (**Fig. 1**). The outputs of the Cox regression analyses are shown in Table SIII.

The multivariable model showed a significant association between diabetes mellitus type 2 (DMt2) and a shorter DS (hazard ratio (HR) 3.69 (95% confidence interval (95% CI) 1.14–11.98) ($p=0.030$) due to ineffectiveness. Multivariable analyses for predictors of side-effect-related DS showed a significant association for a shorter DS in patients with PsA (HR 7.51 (95% CI 2.26–24.95) ($p=0.001$)).

DISCUSSION

This study shows that 1- and 2-year DS for guselkumab was high, both for discontinuation due to side-effects and ineffectiveness. The latter finding is notable, as in previous literature higher discontinuation rates due to ineffectiveness have been described for other types of biologics (4). Previous studies on guselkumab DS in real-world settings have also reported high first-year DS (ranging from 68.0% (5) to 95.0% (6)), although sample size was often small, and the event definition and duration of follow-up varied (5–11).

A substantial number of patients in this study ($n=27$, 13.8%) used a lengthened dosing interval, which suggests that, for guselkumab, high therapeutic effectiveness can be maintained even on a lower dose. In ongoing studies on guselkumab for psoriasis, the use of a prolonged dosing interval is currently being evaluated (12, 13).

Having PsA was associated with a shorter DS due to side-effects. It should be noted that the association between side-effect-related discontinuation and PsA was largely explained by patients with pre-existent PsA who experienced an increase in musculoskeletal complaints. In contrast, a systematic review on predictors of persistence for other biologics, described having PsA as predictive for longer survival (14). Furthermore, we found an association between DMt2 and a higher risk of discontinuation due to ineffectiveness. In support of our

findings, the Corrona psoriasis registry has previously reported that diabetes reduced the risk of achieving various biologic treatment goals (15).

A strength of this study is the large study population, and high external validity due to the multicentre design. Due to the COVID-19 pandemic, there were fewer clinical visits during the study period and more treatment interruptions due to fear of COVID-19. These interruptions were handled differently (see Appendix S1), leading to a more realistic reflection of DS in non-COVID-19 time-frames.

In conclusion, this study found a high 1- and 2-year DS for guselkumab. Reassuringly, discontinuation due to ineffectiveness or side-effects was very uncommon. Having DMt2 was associated with a shorter DS due to ineffectiveness, whereas having PsA was associated with a shorter DS due to side-effects. A substantial proportion of patients (14%) was able to prolong their dosing interval.

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