Appendix S1

SUPPLEMENTARY MATERIALS AND METHODS

Data collection

In this observational, multicentre study, prospective data from the BioCAPTURE database (www.biocapture.nl) was combined with retrospective data collected from 4 other centres in the Netherlands. Patients provided written informed consent for inclusion in the BioCAPTURE registry, or written informed consent for retrospective data collection for this specific study (CMO Radboudumc, dossier 2020-6187). In 1 academic centre (University Medical Centre Groningen; UMCG), an opt-out approach was used: written informed consent was not required, as only retrospective pseudonymized data from regular care were collected, and the study was granted exemption from reviewing by the institutional review board from the UMCG.

All adult patients with plaque psoriasis who were treated with guselkumab in a daily practice setting were eligible for inclusion. Patients were actively recruited between November 2020 and July 2021. Inclusion was allowed during the entire study period, leading to various lengths in follow-up duration. Patients were eligible for inclusion if they started guselkumab for psoriasis in a daily practice setting, and had at least 1 follow-up visit after guselkumab initiation before 1 July 2021. If patients also had psoriatic arthritis (PsA), plaque psoriasis had to be the main reason for prescribing biological therapy. All PsA diagnoses were confirmed by a rheumatologist.

Patient and treatment characteristics

Pseudonymized data on baseline patient characteristics, medication history, guselkumab start- and stop dates, disease parameters during guselkumab treatment (Psoriasis Area and Severity Index (PASI), Dermatology Life Quality Index (DLQI)) and reasons for guselkumab discontinuation were collected. Data were stored in Castor, a cloud-based electronic data management platform in compliance with Good Clinical Practice (GCP) standards (www.castoredc.com). Reasons for discontinuation of treatment were classified as: ineffectiveness, side-effects, pregnancy wish, other reasons, a combination of the aforementioned reasons, or for unknown reasons. Increase in musculoskeletal complaints in patients with PsA was classified as a possible side-effect. Treatment deviations from per-label guselkumab dosing (100 mg guselkumab at week 0, 4, and every 8 weeks thereafter) were recorded in case of treatment interruptions and/or application of an altered dosing regimen. Treatment interruptions <2 weeks were not recorded.

Outcome definitions for statistical analysis

A treatment episode (TE) was defined as the period in which the patient actively used guselkumab. When guselkumab was interrupted for ≥90 days, the TE ended. Two special circumstances were applicable to this cohort, for which this rule was adapted. Firstly, in case of treatment interruptions due to fear of COVID-19, TEs were viewed as continuous as long as: (*i*) both patient and doctor had the intention to continue guselkumab, (*ii*) no new systemic anti-psoriasis treatment was started, and (*iii*) guselkumab was re-initiated within 1 year from interruption. Furthermore, a second group showed very good response, for which time between doses was prolonged beyond the 90-day window. The first 2 criteria mentioned above were also applied to this group. In patients with multiple guselkumab TEs, only the first TE was used for analysis. Active guselkumab users were censored at the moment of the last contact with their treating physician (either clinic visit or by phone), or after 2 years of follow-up. The use of accompanying conventional systemic antipsoriatic therapies (methotrexate, acitretin, ciclosporin or dimethyl fumarates) was classified into bridging therapy or combination therapy. To be classified as bridging therapy, the conventional systemic had to be initiated prior to the start of guselkumab and continued for ≥28 but ≤90 days. To be classified as combination therapy, the conventional systemic was added at the start of or during guselkumab treatment and used for ≥28 days. Patients who initiated their systemic medication prior to guselkumab initiation, but continued to use it for ≥90 days, were assigned to a "bridging and combination therapy" group.

Statistical analyses

Descriptive statistics were used to display patient and treatment characteristics (mean ± standard deviation (SD), median and interquartile range (IQR), *n* (%)). To generate survival curves, survival analysis was performed using Kaplan–Meier estimates. In the primary analysis, 3 separate survival curves were created with an event for discontinuation (*i*) in general, (*ii*) due to ineffectiveness, or (*iii*) due to side-effects. Overall survival (*i*), covered discontinuation due to any reason, including pregnancy, "unknown" and "other reasons". If a patient discontinued guselkumab due to a combination of both ineffectiveness and side-effects, discontinuation was taken into account in all 3 analyses. In univariable Cox-regression analyses, the following clinically relevant baseline characteristics were tested for a possible association with drug survival related to ineffectiveness- or side-effects: age, age at guselkumab initiation, age at psoriasis diagnosis, sex, history of biologic use, baseline PASI, weight, body mass index (BMI), family history of psoriasis, psoriatic arthritis (PsA), diabetes mellitus (DM) type 2, hypertension, depression and liver steatosis/fibrosis. These variables were only analysed for ineffectiveness- or side-effect-related survival, as some reasons for discontinuation in the overall survival curve are not (e.g. pregnancy) or may not be (e.g. "unknown reasons") related to the effects of guselkumab. Potential predictor variables that had a p-value ≤0.2 in univariable analysis were entered in a multivariable Cox regression model with backward selection to identify factors affecting drug survival prognosis. Multivariable Cox regression models were repeated with imputed data (multiple imputation, $n=10$) of baseline variables in case of large numbers of missing values. Analyses were performed in SPSS version 25.0 (IBM, Armonk, NY, USA). A p-value <0.05 was considered statistically significant.