Incidence of infusion reactions to intravenous golimumab: results from a prospective, real-world community registry

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Golimumab (GLM) is a human IgG1κ anti-TNF-α monoclonal antibody. It inhibits TNF-α bioactivity by binding with high affinity and specificity to soluble and transmembrane TNF-α, available through either subcutaneous (SC) or intravenous (IV) routes of administration (1). The safety and efficacy of GLM-IV have been previously assessed in the GO-FURTHER (2) trial in patients with active RA receiving methotrexate (MTX). Through 24 weeks of therapy, 1.1% of GLM infusions were associated with an infusion reaction in 3.5% of patients in the GLM+MTX group. The results remained unchanged out to 112 weeks of therapy with a total of 3.9% (23/584) of patients experiencing ≥1 infusion reaction (3). Although the occurrence of infusion reactions in previous trials of GLM-IV was low, the real-world occurrence of infusion reactions has yet to be established. To establish the incidence in a real-World Canadian setting, we launched the GOlimumab IntraVenous infusion registry, GO-IV (NCT02390700) in 11 community-based infusion clinics. The primary objective of the GO-IV registry was to determine the incidence of infusion reactions (IR) and to investigate strategies to minimise future occurrences of these reactions. Unfortunately, due to lack of public drug coverage and associated low recruitment, the study was closed early. At the time of closure, a total of 79 patients were enrolled with 62 ongoing. 77 patients were included in our primary analysis of IRs. Most of the study participants were female (79.2%) with a mean age of 55.5 years. At baseline, the proportion of patients taking any concomitant DMARDs, corticosteroids or MTX were, 90.9%, 41.6% and 75.3%, respectively (Table I). Reasons for premature discontinuation included; AE (8.9%), lack of response (5.1%), geographic issues (3.8%), withdrawal of consent (1.3%), mis-randomised; wrong diagnosis (1.3%) and patient being switched to subcutaneous GLM (1.3%). Over 483 infusion visits, 4 patients (5.1%) documented an IR (0.8%). Three of the four IRs occurred at the first infusion and one at the third infusion.

Table I. Subjects' baseline characteristics and infusion outcomes. Values are n (%) unless otherwise specified.

	Primary analysis (n=77)
Age (years), mean (SD)	55.5 (11.58)
Female gender, n (%)	61 (79.2%)
Weight (kg), mean (SD)	77.2 (19.55)
Any co-morbidity, n (%)	19 (24.6%)
Concomitant medication	
Any DMARD, n (%)	70 (90.9%)
Corticosteroids, n (%)	32 (41.6%)
MTX, n (%)	58 (75.3%)
Number of infusions	
Mean per subject (SD)	6.1 (2.69)
Median per subject	6.0
Mean IV administration (minutes)	36.03
	Safety analysis (n=78)
No. subjects with at least 1 infusion reaction, n (%)	4 (5.1%)
Subject with ≥1 AE, n (%)	45 (57.7%)
Subject with ≥1 SAE, n (%)	2 (2.6%)

Infusion-related AEs included palpitations, nausea, fatigue, infusion site pain, dizziness and headache (one-each) all mild in nature. The impact of pre-medication could not be established due to insufficient infusion premedication in the registry, with only 4 infusions having pre-medication (3 with diphenhydramine, 1 with steroids), none of which resulted in an IR.

With respect to safety, a total of 164 adverse events (AEs) were reported in 45 patients (57.7%). Two patients (2.6%) reported a serious adverse event (one, an acute myocardial infarction; the other multiple fractures, pneumothorax, concussion, traumatic haematoma and pneumothorax resulting from a fall). There was one incidence of lipoma and no deaths. A total of 30 infectious AEs were reported in 24 patients, none serious.

With increasing biologic availability, the demand for real-world safety and efficacy data grows. Randomised clinical trials provide reliable clinical safety data, but are restrictive in design, representative patient population and duration of follow-up. GO-IV was established to provide local, Canadian safety data to determine the real-world incidence of IRs, severity, nature and management of those reactions and the impact of comorbidities, concomitant medication and premedication has on IRs. Unfortunately, the GO-IV registry was discontinued prematurely. Despite this, we found that IRs to GLM-IV were low with only 4 patients documenting an infusion AE over 483 infusion visits with the majority of reported AEs being mild in nature. Due to a low sample size and early termination, we were unable to fully assess the impact and frequency of premedication on IRs as we have done in the past with a similarly designed infliximab registry (4). Despite its limitations, the GO-IV registry shows that, in community-based infusion clinics, IRs to GLM-IV are infrequent, predominately mild in nature and consistent with findings from previous trials.

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Competing interests: none declared.

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