

Induction and Maintenance Trough Levels of Golimumab Predict Drug Retention Rate in Ulcerative Colitis Treated with Golimumab

Sebastian Stefanović¹, David Drobne¹, Iris Detrez², Anouck Thienpont², Borut Štabuc¹, Ivo Ferkolj¹, Nataša Smrekar¹, Gregor Novak¹, Matic Koželj¹, Marc Ferrante³ and Ann Gils²

¹Department of Gastroenterology, University Medical Center Ljubljana, Ljubljana, Slovenia

²Department of Pharmaceutical and Pharmacological Sciences, Laboratory for Therapeutic and Diagnostic Antibodies, KU Leuven, Leuven, Belgium

³Department of Gastroenterology and Hepatology, University Hospitals Leuven, KU Leuven, Leuven, Belgium
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Background: Golimumab is a recently approved TNF inhibitor for moderate to severe ulcerative colitis. Real life data on clinical efficacy and pharmacokinetics are scarce.

Aims: We aimed to study clinical outcome and pharmacokinetics of golimumab in real life settings and to identify biochemical and clinical predictors of response.

Methods: We prospectively studied 19 patients who started golimumab for treatment of ulcerative colitis in a tertiary university referral medical IBD center. We collected clinical data and serum for golimumab trough level determination at prespecified time points after start of golimumab: day 3, week 1, 2, 3, 4, 6, 10, 14, 26, 38, 40, 44, 50. The main outcomes were short-term response (defined by absence of blood and diarrhea at week 14) and drug retention rate at the end of follow-up. Golimumab trough levels were measured after the completion of the study (ELISA, Leuven in-house assay). Statistical analysis included correlation of clinical predictors (disease duration, corticosteroid therapy at start of golimumab, disease extent, age, body weight) and golimumab trough levels with short-term response and drug retention rate. Predictors for drug retention rate were analyzed with Kaplan-Meier analysis.

Differences in median induction (defined as median of day 3, week 2, 3, 4, 6 golimumab trough level) and median maintenance trough levels (defined as median of 10, 14, 26, 38, 40, 44, 50 golimumab trough levels) in responders compared to non-responders were analyzed with Mann-Whitney - U test. P value < 0.05 was considered significant.

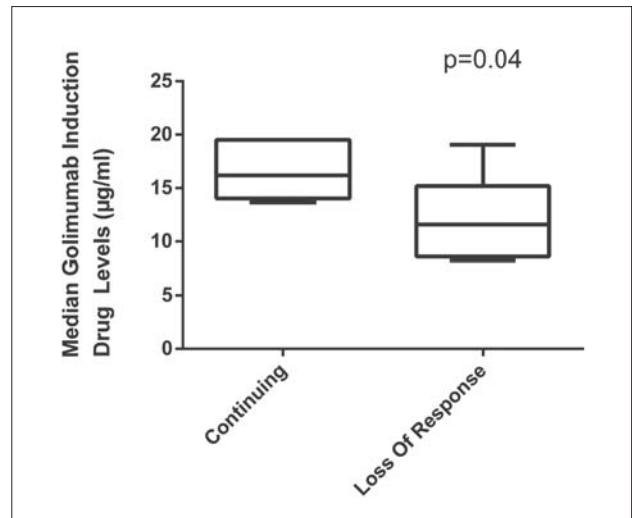
Results: 19 patients have started golimumab since 2014. Patients' demographics are given in Table 1. Short-term response was observed in 11/19 (57.9%) patients. None of the studied parameters were predictive for short-term response. Drug retention rate after the median follow-up period of 11 months (Interquartile Range (IQR): 7.3 months to 20.8 months) was 12/19 (63.2%). The Kaplan-Meier analysis did not reveal disease duration prior to golimumab (Hazard Ratio (HR); 0.9–1.2, p=0.7), use of concomitant systemic steroids (HR: 0.1–6.3, p=0.4), age at start of golimumab (HR: 0.9–1.1, p=0.8), body weight at start of golimumab (HR: 0.9–1.1, p=0.9), disease extent (HR: 0.1–4.7, p=0.6) as predictive for drug retention rate at the end of follow-up. However, golimumab trough levels during induction and maintenance were predictive for continuous response to golimumab at the end of follow-up as golimumab trough levels were higher in end-of-follow-up responders (median induction

Table 1. Patient characteristics

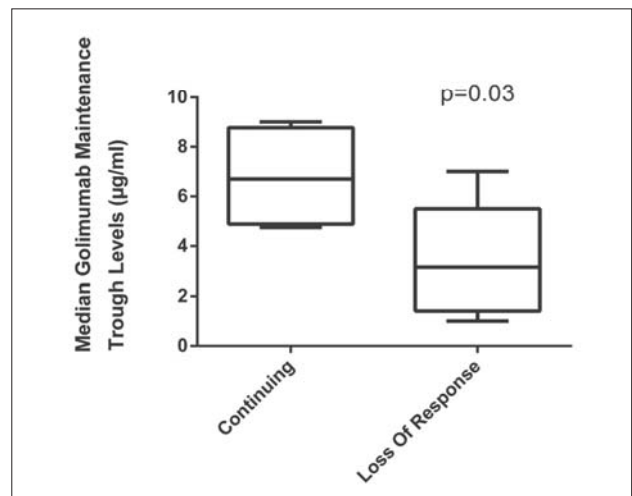
Male (%)	6/21 (31.6%)
Median (IQR) age at diagnosis (years)	36.7 (22.7–43.7)
Median age at start of golimumab (years, IQR)	46.0 (36.0–51.0)
Median weight at start of golimumab (kg's, IQR)	66.0 (59.0–81.5)
Median disease duration before golimumab (years, IQR)	9.6 (6.1–13.4)
Median follow - up (months, IQR)	11 (7.3–20.8)
Disease extent (n = 19) (%)	
E1 - proctitis	4 (21.1%)
E2 - left sided	5 (26.3%)
E3 - extensive	10 (52.6%)
Smoking status % (n = 11)	
Smokers	0 (0%)
Non - smokers	9 (81.8%)
Previous smokers	2 (18.2)
Concomitant medication at start of golimumab (%)	
Aminosalicylates	8 (73.7%)
Systemic steroids	8 (42.1%)
6-MP/AZA	8 (42.1%)
Topical steroids	5 (26.3%)
Anti - TNF-alpha naive before golimumab	17 (89.5%)
Number of patients with induction	19 (100%)

drug levels 17.9 µg/ml [IQR:14.2–20.6], median maintenance levels 6.7 µg/ml [IQR:4.9–8.8]) compared to patients who stopped golimumab due to loss of response (median drug induction levels 11.6 [IQR 8.6–15.2] median maintenance trough levels 3.15 (1.4–5.5); P-value for drug induction levels 0.04 (Graph 1), p-value for trough maintenance levels 0.03 (Graph 2). Similarly, last available maintenance trough levels were higher in patients with continuous response at the end of follow-up (12,1 [IQR: 5,4–14,4] compared to patients who lost response at the end of follow-up (3.9 [IQR: 1.3–5.9]) (p=0.055). Interestingly, none of the four patients with golimumab maintenance trough levels above six µg/ml lost response at the end of follow-up.

Conclusions: Drug retention rate of this real life, predominantly bio naïve cohort of ulcerative colitis patients, is comparable to registration trial of golimumab. Golimumab drug levels during induction and golimumab maintenance trough levels were highly correlated to drug retention rate at the end of follow-up. Clinical outcome was especially favorable for patients with maintenance golimumab trough levels > six µg/ml.



Graph 1. Prediction of Drug Retention Rate by Median Induction Drug Levels in Patients with Ulcerative Colitis Treated with Golimumab.



Graph 2. Prediction of Drug Retention Rate by Median Maintenance Trough Levels in Patients with Ulcerative Colitis Treated with Golimumab