**Regional differences in baseline disease activity and in remission rates following golimumab treatment for rheumatoid arthritis: results from the GO-MORE study**

Patrick Durez, Karel Pavelka, Maria Alicia Lazaro, Abraham Garcia-Kutzbach, Robert J. Moots, Howard Amital, Ruji Yao, Marinella Govoni, and Nathan Vastesaeger

***Objective***. Examine regional differences in baseline disease activity and remission rates following golimumab treatment for rheumatoid arthritis.

***Methods***. Descriptive, post-hoc analysis of data from the GO-MORE trial by geographical region.

***Results***. At baseline, disease activity was lowest in Europe, Canada, and the Middle East and highest in South Africa, Asia, and Latin America. Month-6 remission rates were highest in South Africa (29.1%), Europe (29.0%), Canada (23.0%), and the Middle East (21.9%) and lowest in Latin America (9.3%), South America (8.5%), and Asia (7.5%).

***Conclusion***. Remission rates in each geographical region generally corresponded with baseline disease activity.

**Key indexing terms:** rheumatoid arthritis; antirheumatic agents; golimumab; geographic locations

**From:** Pôle de Recherche en Rhumatologie, Institut de Recherche Expérimentale et Clinique, UCL Saint-Luc, Brussels, Belgium; Institute of Rheuamtology (Revmatologicky Ustav), Prague, Czech Republic; Instituto de Rehabilitacion Psicofisica de la Ciudad de Buenos Aires, Argentina; AGAR, UFM, Guatemala City, Guatemala; University Hospital Aintree, Liverpool, United Kingdom; Sheba Medical Center, Tel-Hashomer, Israel; Merck USA; MSD Italy; and MSD Belgium

**Financial support:** MSD

**Appointments and academic degrees:** P. Durez MD PhD, Chef de Clinique, Service de Rhumatologie, Cliniques Universitaires Saint-Luc; K. Pavelka MD PhD, Director, Institute of Rheumatology; M.A. Lazaro MD ; A. Garcia-Kutzbach MD,; R.J. Moots MD PhD, Professor of Rheumatology, University of Liverpool; H. Amital MD, Head of the Department of Medicine, Meir Medical Center and Senior Lecturer, Sackler Faculty of Medicine, Tel-Aviv University; R. Yao PhD, Statistician, Merck; M. Govoni PhD, Regional Director of Medical Affairs, Rheumatology, MSD Italy; N. Vastesaeger MD PhD, Medical Lead, Immuno-Oncology, MSD Belgium

**Correspondence and reprint requests to:** Prof Patrick Durez, Chef de Clinique, Service de Rhumatologie (RUMA 5390), Cliniques Universitaires Saint-Luc, Avenue Hippocrate 10, B-1200 Brussels, Belgium. Tel: +32 27646036. Fax: +32 27645394. Email: patrick.durez@uclouvain.be.

**Running footline**: GO-MORE regional analysis

# Introduction

Anti-tumor necrosis factor (TNF) biologics in are used in conjunction with conventional disease-modifying anti-rheumatic drugs (csDMARDs), usually methotrexate, for the second-line treatment of rheumatoid arthritis (RA) ([1](#_ENREF_1), [2](#_ENREF_2)). Golimumab, an anti-TNF monoclonal antibody, has been shown to be clinically effective in methotrexate-naïve patients ([3](#_ENREF_3)), in patients after methotrexate failure ([3](#_ENREF_3), [4](#_ENREF_4)), and in anti-TNF-experienced patients ([5](#_ENREF_5)).

GO-MORE was a large open-label, multinational, multicenter, prospective phase 3 trial evaluating add-on therapy with golimumab in biologic-naïve patients with active RA ([6](#_ENREF_6)). During the study, patients received subcutaneous golimumab 50 mg once monthly for 6 months in addition to the csDMARDs they were already receiving. At the end of 6 months, 82.1% of patients achieved a good or moderate response and 23.9% of patients achieved clinical remission according to European League Against Rheumatism (EULAR) criteria.

GO-MORE included 3336 patients recruited at 475 centers in 40 countries. This large, heterogeneous, and geographically disperse population was intended to obtain information relevant to daily clinical practice in each of the regions and countries. Therefore, in a planned post-hoc analysis, baseline characteristics and response at 6 months were determined for the different included geographical regions.

# Materials and methods

The objective of this planned post-hoc analysis was to compare, across geographic regions, baseline disease levels and remission rates among biologic-naïve RA patients during 6 months of add-on golimumab treatment in the GO-MORE trial ([6](#_ENREF_6)). GO-MORE was approved by the appropriate research ethics committees and was conducted in accordance with the Declaration of Helsinki and standards of good clinical research practice, and all included patients provided written informed consent.

The GO-MORE trial included adults with a diagnosis of RA according to the 1987 revised American College of Rheumatology (ACR) criteria who had active disease (28-joint disease activity score calculated using the erythrocyte sedimentation rate [DAS28-ESR] ≥ 3.2) despite csDMARD treatment. Patients had to have used at least one csDMARD at a stable dose for at least 1 month and had to have been able to maintain the dose during the trial. Patients received subcutaneous golimumab 50 mg administered by an autoinjector device once monthly for 6 months. The patients were allowed to continue the following csDMARDs: methotrexate, sulfasalazine, hydroxychloroquine, chloroquine, chloroquine phosphate, leflunomide, gold salts, azathioprine, and cyclosporine. The primary efficacy assessment was the proportion of patients who achieved a good or moderate EULAR response at the end of month 6 (DAS28-ESR improvement > 1.2 from any baseline score or improvement of 0.6–1.2 from a baseline score ≤ 5.1) ([7](#_ENREF_7)). No statistical tests were performed for this post-hoc analysis, and results are presented only using descriptive statistics as calculated using Microsoft Excel version 14.0.

# Results

This analysis included 3280 participants from the GO-MORE trial, including 1818 form Europe, 906 from Latin America, 218 from Canada, 133 from Asia, 117 from South Africa, and 88 from the Middle East.

## Baseline disease activity

All participants included in this analysis had high or moderate disease activity according to EULAR criteria ([7](#_ENREF_7)). High disease activity was most common in South Africa (91.5%), Asia (92.5%), and Latin America (90.7%) and least common in Europe (71.0%), Canada (77.0%), and the Middle East (78.2%) (**Table 1**). As expected, the main components of EULAR disease activity, namely, the 28-jount disease activity scores calculated using the erythrocyte sedimentation rate (DAS28-ESR) and the C-reactive protein concentration (DAS28-CRP) generally followed the same trend. In contrast, disease duration, 28-joint tender joint counts, and 28-joint swollen joint counts differed little between regions.

## Concomitant treatments

In all geographic regions, golimumab was used in combination with methotrexate alone or with a combination with methotrexate and other csDMARDs (**Table 2**). Concomitant corticosteroids were used by 44%–78% of patients.

## Efficacy

Rates of remission at 6 months, defined as a DAS28-ESR < 2.6, varied by region. Remission rates were highest in South Africa (29.1%), Europe (29.0%), Canada (23.0%), and the Middle East (21.9%) and lowest in Latin America (9.3%), South America (8.5%), and Asia (7.5%). Thus, rates of remission were generally highest in regions with the lowest baseline disease activity (**Figure 1**). An exception to this was South Africa, which had one of the highest remission rates but also one of the highest rates of severe disease activity.

# Discussion

The GO-MORE study examined the efficacy of add-on treatment with golimumab for 6 months in biologic-naïve patients with active RA. In a planned post-hoc analysis, we further examined efficacy and baseline activity by region in this GO-MORE study to help obtain information relevant to daily clinical practice. We found that remission rates at the end of 6 months were highest in South Africa, Europe, Canada, and the Middle East and lowest in Latin America, South America, and Asia. As in the combined population ([6](#_ENREF_6), [8](#_ENREF_8)), remission was more likely when disease activity was lower.

This finding probably cannot be explained by differences in concomitant treatments or baseline disease characteristics between regions because results from the full GO-MORE study ([6](#_ENREF_6)) and from a sub-analysis of GO-MORE data from Spain ([9](#_ENREF_9)) found that remission rates did not differ according to the type of concomitant csDMARDs or according to whether patients received concomitant corticosteroids. We suspect that the most important determinants were, instead, differences in access to care and implementation of the treat-to-target strategy ([10](#_ENREF_10)). Better quality of care might also lead to higher patient expectations and therefore better responses to treatment. These factors could underlie the relatively high response and remission rates in more wealthy regions such as Europe and Canada ([9](#_ENREF_9), [11-13](#_ENREF_11)).

In conclusion, this analysis found substantial differences between geographic regions in not only clinical response to golimumab 50 mg but also in baseline disease activity. Any connection between the two needs to be confirmed in a study that includes a statistical analysis of prognostic indicators.

# Acknowledgments

Medical writing was provided by Dr. Phillip Leventhal (4Clinics, Paris, France) and paid for by MSD.

# References

1. Smolen JS, Aletaha D, Bijlsma JW, Breedveld FC, Boumpas D, Burmester G, et al. Treating rheumatoid arthritis to target: recommendations of an international task force. Ann Rheum Dis 2010;69:631-7.

2. Smolen JS, Landewe R, Breedveld FC, Buch M, Burmester G, Dougados M, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis 2014;73:492-509.

3. Emery P, Fleischmann R, van der Heijde D, Keystone EC, Genovese MC, Conaghan PG, et al. The effects of golimumab on radiographic progression in rheumatoid arthritis: results of randomized controlled studies of golimumab before methotrexate therapy and golimumab after methotrexate therapy. Arthritis Rheum 2011;63:1200-10.

4. Weinblatt ME, Bingham CO, 3rd, Mendelsohn AM, Kim L, Mack M, Lu J, et al. Intravenous golimumab is effective in patients with active rheumatoid arthritis despite methotrexate therapy with responses as early as week 2: results of the phase 3, randomised, multicentre, double-blind, placebo-controlled GO-FURTHER trial. Ann Rheum Dis 2013;72:381-9.

5. Smolen JS, Kay J, Doyle MK, Landewe R, Matteson EL, Wollenhaupt J, et al. Golimumab in patients with active rheumatoid arthritis after treatment with tumour necrosis factor alpha inhibitors (GO-AFTER study): a multicentre, randomised, double-blind, placebo-controlled, phase III trial. Lancet 2009;374:210-21.

6. Combe B, Dasgupta B, Louw I, Pal S, Wollenhaupt J, Zerbini CA, et al. Efficacy and safety of golimumab as add-on therapy to disease-modifying antirheumatic drugs: results of the GO-MORE study. Ann Rheum Dis 2014;73:1477-86.

7. Fransen J, van Riel PL. The Disease Activity Score and the EULAR response criteria. Rheum Dis Clin North Am 2009;35:745-57, vii-viii.

8. Vastesaeger N, Kutzbach AG, Amital H, Pavelka K, Lazaro MA, Moots RJ, et al. Prediction of remission and low disease activity in disease-modifying anti-rheumatic drug-refractory patients with rheumatoid arthritis treated with golimumab. Rheumatology (Oxford) 2016;55:1466-76.

9. Alonso A, Gonzalez CM, Ballina J, Garcia Vivar ML, Gomez-Reino JJ, Marenco JL, et al. Efficacy and safety of golimumab as add-on therapy to disease-modifying antirheumatic drugs in rheumatoid arthritis: results of the GO-MORE study in Spain. Reumatol Clin 2015;11:144-50.

10. Smolen JS, Breedveld FC, Burmester GR, Bykerk V, Dougados M, Emery P, et al. Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. Ann Rheum Dis 2016;75:3-15.

11. Putrik P, Ramiro S, Keszei AP, Hmamouchi I, Dougados M, Uhlig T, et al. Lower education and living in countries with lower wealth are associated with higher disease activity in rheumatoid arthritis: results from the multinational COMORA study. Ann Rheum Dis 2016;75:540-6.

12. Massardo L, Pons-Estel BA, Wojdyla D, Cardiel MH, Galarza-Maldonado CM, Sacnun MP, et al. Early rheumatoid arthritis in Latin America: low socioeconomic status related to high disease activity at baseline. Arthritis Care Res (Hoboken) 2012;64:1135-43.

13. Sokka T, Kautiainen H, Pincus T, Toloza S, da Rocha Castelar Pinheiro G, Lazovskis J, et al. Disparities in rheumatoid arthritis disease activity according to gross domestic product in 25 countries in the QUEST-RA database. Ann Rheum Dis 2009;68:1666-72.

**Table 1. Baseline patient characteristics and disease activity by region**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Patient characteristic** | **Europe****N=1818** | **Canada****N=218** | **Middle East****N=88** | **Latin America****N=906** | **South Africa****N=117** | **Asia****N=133** |
| EULAR disease activity, n (%) |  |  |  |  |  |  |
| Moderatea | 525 (29.0) | 50 (23.0) | 19 (21.8) | 84 (9.3) | 10 (8.5) | 10 (7.5) |
| Highb | 1286 (71.0) | 167 (77.0) | 68 (78.2) | 821 (90.7) | 107 (91.5) | 123 (92.5) |
| DAS28-ESR, mean ± SD | 5.7 ± 1.0  | 5.9 ± 1.1 | 6.0 ± 1.0 | 6.4 ± 1.0 | 6.7 ± 1.1 | 6.2 ± 0.9 |
| DAS28-CRP, mean ± SD | 5.2 ± 1.0 | 5.5 ± 1.0 | 5.4 ± 0.9 | 5.8 ± 1.0 | 5.8 ± 1.0 | 5.4 ± 0.9 |
| Disease duration (y), mean ± SD | 7.5 ± 7.8 | 6.6 ± 8.4 | 6.9 ± 7.0 | 8.6 ± 8.2 | 7.6 ± 8.0 | 5.4 ± 4.8 |
| TJC28, mean ± SD | 11.6 ± 6.5 | 14.5 ± 7.5 | 12.6 ± 6.3 | 15.1 ± 6.1 | 15.3 ± 6.6 | 12.7 ± 6.1 |
| SJC28, mean ± SD | 8.3 ± 5.1 | 10.5 ± 4.7 | 7.5 ± 4.6 | 11.8 ± 5.7 | 14.1 ± 6.1 | 8.4 ± 4.4 |
| C-reactive protein (mg/L), median [IQR] | 6.4 [2.2–15.5] | 4.4 [1.8–9.4] | 9.9 [4.9–21.7] | 9.6 [3.9–23.4] | 6.7 [2.5–18.3] | 10.0 [4.2–20.7] |

Abbreviations: DAS28-CRP, disease activity score using the TJC28 and SJC28 based on C-reactive protein; DAS28-ESR, disease activity score using the TJC28 and SJC28 based on erythrocyte sedimentation rate; EULAR, European League Against Rheumatism; IQR, interquartile range; SD, standard deviation

aDAS28-ESR = 3.2–5.1

bDAS28-ESR > 5.1

**Table 2. Concomitant therapies**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Concomitant therapy** | **Europe****N=1818** | **Canada****N=218** | **Middle East****N=88** | **Latin America****N=906** | **South Africa****N=117** | **Asia****N=133** |
| MTX, n (%) |  |  |  |  |  |  |
| < 10 mg/week | 2 (2.3) | 4 (1.8) | 0 (0.0) | 53 (5.8) | 3 (2.3) | 81 (4.5) |
| ≥ 10 and < 15 mg/week | 25 (28.4) | 12 (5.5) | 11 (9.4) | 194 (21.4) | 12 (9.0) | 270 (14.9) |
| ≥ 15 mg/week | 45 (51.1) | 174 (79.8) | 93 (79.5) | 519 (57.3) | 117 (88.0) | 1050 (57.8) |
| Did not use MTX | 16 (18.2) | 28 (12.8) | 13 (11.1) | 140 (15.5) | 1 (0.8) | 417 (22.9) |
| Corticosteroids used, n (%) | 59 (67.0) | 95 (43.6) | 66 (56.4) | 681 (75.2) | 104 (78.2) | 1079 (59.4) |
| csDMARD combinationsa, n (%)MTX onlyMTX + chloroquine derivativesMTX + leflunomideMTX + sulfasalazineMTX + chloroquine derivatives + sulfasalazineLeflunomide only | 38 (43.2)14 (15.9)9 (10.2)1 (1.1)5 (5.7)5 (5.7) | 86 (39.4)69 (31.7)21 (9.6)4 (1.8)06 (2.8) | 51 (43.6)15 (12.8)11 (9.4)11 (9.4)11 (9.4)4 (3.4) | 462 (51.0)139 (15.4)72 (8.0)39 (4.3)19 (2.1)60 (6.6) | 29 (21.8)74 (55.6)4 (3.0)4 (3.0)14 (10.5)0 | 1014(56.1)123 (6.8)100 (5.5)92 (5.1)57 (3.2)227 (12.5) |

Abbreviations: csDMARD; conventional disease-modifying anti-rheumatic drugs; MTX, methotrexate

aListed are the six combinations most commonly used by the efficacy-evaluable population in all regions combined. All other concomitant csDMARD combinations were used by < 3% of the total efficacy-evaluable population.



**Figure 1. Rate of remission at month 6 for each region as a function of the rate of moderate disease activity at baseline**

Moderate disease activity at baseline was defined according to the European League Against Rheumatism (EULAR) as a 28-joint disease activity score based on erythrocyte sedimentation rate (DAS28-ESR) of 3.2 to 5.1. DAS28-ESR remission was defined as a DAS28-ESR > 2.6. The dotted line indicates the best-fit line for all data as determined by linear regression.