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Research Paper

Relationship Between Physician Global Assessment of Disease Severity and Objective Measures of Disease Severity in Rheumatoid Arthritis in the United States and Europe

Medical Science

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ABSTRACT

Evaluating the relationship between physician global assessment (PhGA) and objective measures for disease severity among patients with Rheumatoid Arthritis (RA) could reinforce the use of simple measures. A multi-center medical chart-review study of RA patients was conducted in 2011 among physicians in hospitals/private practices in Europe (EU5: UK/France/Germany/Italy/Spain) and United States (US) to collect data on RA diagnosis, treatment patterns/dynamics and patient symptomatology/disease status incl. physician-assessment of disease severity (per clinical judgment). In EU5 and US, 2208 and 851 patient charts were abstracted respectively. Per PhGA, 49%/41%/9% were mild/moderate/severe in EU and 59%/35%/6% were mild/moderate/severe in US. Recent disease severity scores (as measured by Tender Joint Count, Swollen Joint Count, 100mm VAS, HAQ, DAS28 and Total Sharp score) mostly increased with increasing PhGA score in both EU and US. The observed correlations strengthen the argument towards continued inclusion/use of simple physician-assessment scales in usual care practices around the world.

INTRODUCTION

Rheumatoid Arthritis (RA) is a chronic autoimmune disease that results in systemic inflammation and primarily attacks synovial joints. (Yao, 2012) Numerous disease activity measurement tools/indices are currently available for use, to manage RA patients, and they have varying levels of psychometric properties. The American College of Rheumatology (ACR) RA Clinical Disease Activity Measures Working Group performed a systematic review of available disease activity indices (DAIs) commonly used in RA; several of these tools are validated and include physician/provider global assessment (PrGA/PhGA), Tender Joint Counts, Swollen Joint Counts, 100mm Visual Analog Scale (VAS). (Anderson, 2011) Disease Activity Score with 28-Joint Counts (DAS-28) is generally considered as one of the viable composite measures of RA disease activity, and is hence often used in clinical practice settings around the world. Health Assessment Questionnaire (HAQ) is a patient-reported outcome (PRO) tool that clinicians often incorporate into their disease assessments during patient engagement. (Bruce & Fries, 2005) All the DAIs employ continuous indices or scores; as such scores (composite or stand-alone) have an advantage over the interpretation of individual components of disease activity due to their ability to provide clinically meaningful and reliable estimates of disease activity across the spectrum of score ranges (Verhoeven 2000; Felson 1993; Aletaha 2006). Health insurers and regulatory agencies have also started to request the use some of these DAIs to justify the initiation or escalation of RA therapy, thereby fueling the need to use these DAIs in routine clinical practice (Ledingham 2005; Smolen 2010).

As physicians determine the optimal ways to manage RA patients and monitor their disease activity/severity, the need for simplicity in patient management, and thus, the need for simpler DAIs for use in routine clinical practice assume importance. Assessing the use of PhGA and other DAIs in usual care and how they correlate to each other may assist the clinicians in their continued use of PhGA, the simplest form of DAI currently available.

MATERIAL AND METHODS

The study was a multi-country, multi-center retrospective medical chart review of RA patients, conducted among rheumatologists in the big-5 European countries (EU5), namely, the UK, France, Germany, Italy and Spain. Rheumatologists were sampled in each of the countries using online physician panels to attain a geographically representative sample in respective regions. Invitations to participate in our research were sent to a random set of rheumatologists in the existing online physician panels. The physicians representing both hospital-based and private practices in each geography, and treating a minimum of 2 RA biologic patients per week and having 3-30 years of clinical practice experience were screened for study participation. Each physician reported de-identified data on patients who were recently treated with a biologic as part of usual care. Up to 10 eligible patient charts were randomly selected by each physician from a sample of prospective patients visiting their respective center/practice during the study screening period in 2011.

The survey collected the following data elements: patient diagnosis, treatment patterns/dynamics, RA disease characteristics and outcomes (patient symptomatology/disease severity per both objective assessments and subjective assessments (per clinical judgment) made by their physician). The PhGA was assessed on a scale of 1-3, with 1: Mild, 2: Moderate and 3: Severe disease. Only de-identified anonymous data was collected from the patient charts by the treating physicians. This mode of data collection method met the criteria for IRB exemption per the physician/site requirements in the EU5 and the federal regulation 45 CFR 46.101(b)(4) in the U.S.

Descriptive statistics were utilized to analyze the data. Pearson R correlation coefficients were assessed comparing the PhGA of disease severity to mean standardized (objective) disease severity measures, quantified via joint counts, 100mm VAS, HAQ, DAS28 and Total Sharp Scores.

RESULTS AND DISCUSSIONS

Physicians abstracted 2208 eligible RA patient charts in the EU5 (UK: 410), France: 499, Germany: 404, Italy: 415, Spain: 480) and 851 eligible RA patient charts in the US. Approximately 74% and 20% of patients in EU5 were on 1st and 2nd biologic line of therapy respectively, while 70% and 23% of patients in the US were on 1st and 2nd biologic line of therapy respectively; 5% and 2% were on 3rd line and 4+ line of treatment respectively in both the regions.

Per PhGA, approximately half of the patients had moderate/severe disease in EU5, whereas, 41% in the US had moderate/severe disease. (Table 1)

Table 1. Patient biosimilar-infliximab suitability by country

PhGA	EU5 (n=2208)	US (n=851)
Patients with Mild Disease, %	49	59
Patients with Moderate Disease, %	41	35
Patients with Severe Disease, %	9	6

Among those with available data, recent objective disease severity scores, as measured by mean SJC, TJC, 100mm VAS, HAQ, SAS-28 and Total Sharp Scores, indicated comparable disease severity among the EU5 and US cohorts. These objective disease severity scores increased with increasing levels of disease severity based on PhGA (per clinical judgment), in both EU5 and US and exhibited high correlations. (Tables 2A, 2B)

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Table 2A. Latest Measures of Disease Severity in EU5 Cohort

DAIs	Overall DAI Score N=2208	PhGA			Pearson R Correlation
		Mild N=1088	Moderate N=915	Severe N=197	
Tender joint count: mean (n)	4.1 (2069)	2.5 (1017)	5.3 (860)	7.4 (185)	0.996
Swollen joint count: mean (n)	2.6 (2068)	1.3 (1015)	3.6 (861)	5.3 (185)	0.996
100mm VAS Score: mean (n)	30.1 (1630)	19.8 (831)	38.9 (664)	51.4 (130)	0.993
HAQ Score: mean (n)	1.1 (537)	0.8 (261)	1.4 (237)	1.5 (39)	0.921
DAS28 Score: mean (n)	3.4 (1477)	2.6 (750)	4.1 (584)	5.1 (138)	0.994
Total Sharp Score: mean (n)	2.3 (54)	2.4 (30)	2.1 (23)	4.0 (1)	0.794

Table 2B. Latest Measures of Disease Severity in the US Cohort

DAIs	Overall DAI Score N=851	PhGA			Pearson R Correlation
		Mild N=502	Moderate N=294	Severe N=49	
Tender joint count: mean (n)	4.1 (808)	2.3 (483)	6.6 (275)	8.9 (49)	0.985
Swollen joint count: mean (n)	3.0 (807)	1.5 (482)	5.0 (275)	6.7 (49)	0.979
100mm VAS Score: mean (n)	29.2 (390)	17.2 (234)	47.0 (136)	48.6 (19)	0.888
HAQ Score: mean (n)	1.1 (156)	0.7 (86)	1.4 (57)	1.9 (13)	0.989
DAS28 Score: mean (n)	3.2 (172)	2.5 (102)	4.0 (64)	5.3 (6)	1.000
Total Sharp Score: mean (n)	3.0 (31)	3.1 (14)	2.3 (15)	7.0 (2)	0.773

The American College of Rheumatology (ACR) Core Data Set includes 7 measures--swollen joint count, tender joint count, patient assessment of global status, an acute phase reactant [erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)], health professional/physician global assessment (PhGA), physical function, and pain; the first four of these measures are included on the DAS28. These DAIs contributed to composite measures that are used to define the level of improvement (such as ACR 20, ACR 50 and ACR 70) that could discriminate therapeutic efficacy/effectiveness of products. (van der Heijde, 1993; Felson, 1995; Felson, 1998; Pincus, 2005) These DAIs have been tested for validity and reliability. (Anderson, 2011)

The PhGA tend to be used in different formats within auto-immune disease cluster, encompassing the format recommended by ACR - the classically anchored unnumbered 10-cm horizontal lines as well as a numerical/discrete scale to classify the patients into mild, moderate and severe disease severity. The traditional PhGA with a continuous scale has been shown to correlate very well with other DAIs in RA arena (Anderson, 2011), while there is inadequate information regarding the utility of numerical/discrete scale version of PhGA. This study has depicted how well the PhGA with numerical/discrete scale correlated with other standard DAIs. A recent research report portraying the properties of PhGA in predicting remission at 12 months in early RA further lends credibility to the exploration of PhGA in clinical practice settings, in relevant easy formats. (Choy, 2014)

Although physicians were randomly recruited for this study, the findings represent only the participating physicians, and may vary from those of non-participating physicians. Additional studies are warranted to further test the psychometric properties of PhGA with discrete scale and its ability to discriminate therapeutic outcomes.

In conclusion, across the geographies, physician global assessment of disease severity (on a discrete scale) strongly correlated with the objective measures of disease severity among RA patients. These findings further strengthen the argument towards continued inclusion/use of simple physician-assessment scales in usual care practices around the world.

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