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Unmet needs in psoriatic arthritis patients receiving immunomodulatory therapy; results from a large multinational real-world study

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Abstract:	Objective There are limited data on therapy selection and switching in psoriatic arthritis (PsA). This 18 country, real-world study assessed use and switching of immunomodulatory therapy (biologic/apremilast), the extent of treatment failure and its association with reduced physical functioning, health related quality of life (HRQoL) and work productivity and activity impairment (WPAI). Methods PsA patients under routine care and their treating physicians provided demographics, current therapy, reasons for switching, duration of 1st therapy, HRQoL, HAQ-DI and WPAI. Current immunomodulatory therapy was determined as 'failing' if, after ≥3 months, physician-rated disease severity had worsened, remained severe, was 'unstable/deteriorating', or they were dissatisfied with disease control and/or did not consider treatment a 'success'. Results Included were 3,714 PsA patients; 1,455 (40.6%) had never received immunomodulatory therapy; 1796 (50.1%) had ever received 1 immunomodulatory therapy and 331 (9.2%) ≥1. Lack of efficacy with 1st immunomodulatory therapy was the most common reason for switching; patients whose physicians indicated 'primary lack of efficacy' as the reason, switched after a mean of 9.4 months. Patients currently failing immunomodulator therapies (n=246) had poorer HRQoL compared with treatment success (n=1,472) measured by EQ-5D-3L (0.60 vs 0.77%; P<0.0001); SF-36 PCS (40.8% vs 46.1%; P<0.0001) MCS (41.1% vs 45.3%; P<0.0001). Physical functioning, activity and work productivity were also more impaired (HAQ-DI: 0.88 vs 0.56; activity impairment: 46.7% vs 29.7%; overall work impairment: 35.4% vs 26.1%; all P<0.0001). Conclusions Poor treatment response in PsA is associated with substantial negative patient impact. In cases of primary treatment failure, timely switching is needed.
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Response to Reviewers:	We would like to thank the reviewer for the suggestion to add Reddy SM et al. Clin Rheumatol 2016; 35: 2955-2966, and agree that this addition provides further support for our conclusions. Please note that this addition can be found within the discussion section in page 10, reference #28. We have also used the Clinical Rheumatology Endnote output file to correct the reference style in our manuscript. We trust that these revisions meet the reviewers satisfaction.

Unmet needs in psoriatic arthritis patients receiving immunomodulatory therapy; results from a large multinational real-world study

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Running header: Treatment failure psoriatic arthritis

Abstract

Objective: There are limited data on therapy selection and switching in psoriatic arthritis (PsA). This 18 country, real-world study assessed use and switching of immunomodulatory therapy (biologic/apremilast), the extent of treatment failure and its association with reduced physical functioning, health related quality of life (HRQoL) and work productivity and activity impairment (WPAI).

Methods: PsA patients under routine care and their treating physicians provided demographics, current therapy, reasons for switching, duration of 1st therapy, HRQoL, HAQ-DI and WPAI. Current immunomodulatory therapy was determined as 'failing' if, after ≥3 months, physician-rated disease severity had worsened, remained severe, was 'unstable/deteriorating', or they were dissatisfied with disease control and/or did not consider treatment a 'success'.

Results: Included were 3,714 PsA patients; 1,455 (40.6%) had never received immunomodulatory therapy; 1796 (50.1%) had ever received 1 immunomodulatory therapy and 331 (9.2%) ≥1. Lack of efficacy with 1st immunomodulatory therapy was the most common reason for switching; patients whose physicians indicated 'primary lack of efficacy' as the reason, switched after a mean of 9.4 months. Patients currently failing immunomodulator therapies (n=246) had poorer HRQoL compared with treatment success (n=1,472) measured by EQ-5D-3L (0.60 vs 0.77%; *P*<0.0001); SF-36 PCS (40.8% vs 46.1%; *P*<0.0001) MCS (41.1% vs 45.3%; *P*<0.0001). Physical functioning, activity and work productivity were also more impaired (HAQ-DI: 0.88 vs 0.56; activity impairment: 46.7% vs 29.7%; overall work impairment: 35.4% vs 26.1%; all *P*<0.0001).

Conclusions: Poor treatment response in PsA is associated with substantial negative patient impact. In cases of primary treatment failure, timely switching is needed.

Keywords: Psoriatic arthritis, treatment, health-related quality of life, work, TNFi

Introduction

Psoriatic arthritis (PsA) is a multifaceted systemic chronic inflammatory disease with diverse features, varied outcomes and disease course, which affects skin and joints simultaneously [1-4]. The prevalence of psoriatic arthritis (PsA) varies by country, from 0.001% adults in Japan to 0.42% in Italy, and 0.16% in the USA, and is seen in up to 40% of psoriasis patients [1-4]. Patients with PsA experience pain, stiffness, enthesitis, swelling and tenderness of the joints, with 40-60% of patients developing erosive joint disease leading to impaired articular functioning and higher mortality [1,2]. These symptoms have a detrimental effect on social relationships, quality of life and mortality as well as burdening the patient and society with impaired ability to work and substantial healthcare costs [1,5].

Conventional Disease Modifying Anti-Rheumatic Drugs (cDMARDs) including sulfasalazine and methotrexate are widely used in the treatment of PsA [6]. However, advances in understanding PsA pathogenesis, especially the role of T cells and cytokines, have led to a range of immunomodulatory treatments for PsA. The therapeutic armamentarium now also includes biologic DMARDs (bDMARDs) such as tumor necrosis factor inhibitors (TNFis), anti-interleukin (IL)-12/23 ustekinumab, anti-IL-17A secukinumab and ixekizumab; and abatacept. Targeted synthetic DMARDs (tsDMARD) include phosphodiesterase-4 (PDE-4) inhibitor apremilast and janus kinase inhibitor (JAKi) tofacitinib [7-11].

The choice of first line therapy, and which treatment to switch to in the event of first-line treatment failure, is well described in several recent treatment guidelines. The American College of Rheumatology (ACR) and the National Psoriasis Foundation (NPF) most recent guideline for treating PsA recommends TNFi as 1st-line treatment for active PsA [12]. If a TNFi is not an option, conventional DMARDs (cDMARDs) are preferable to other biologics. Methotrexate is preferable to NSAID, and anti-IL17 is preferable to an IL-12/23 [12]. If PsA is still active after the change, switching to anti-IL-17 should be the next step rather than a cDMARD or other biologic. If PsA continues to be active, switching to an anti-IL12/23 rather than cDMARD, abatacept or tofacitinib is recommended [12]. The most recent GRAPPA and

EULAR recommendations also prefer switching to a bDMARD for patients with active PsA despite cDMARD treatment, usually TNFi, or anti-12/23 or anti-IL17 if TNFi is not appropriate, or apremilast if a bDMARD is inappropriate [13,14]. EULAR recommends switching TNFi if target is not achieved within 3-6 months [14].

The aim of this large multi-national study was to describe the use of immunomodulatory therapy in PsA patients using real-world data, and assess treatment switching and failure rates, as well as the association between treatment failure and reduced physical functioning, quality of life and work capability.

Materials and Methods

Data source

This was an analysis of data drawn from the Adelphi PsA Disease Specific Program (DSP) conducted between 2015 - 2016 in 18 countries: North America (USA, Canada), Latin America, (LatAm, covering Brazil, Mexico), EU5 (Europe, covering France, Germany, Italy, Spain, UK), Asia Pacific, (APAC, covering Japan, Malaysia, South Korea, Taiwan, Australia) and Turkey & Middle East, (T&ME, covering Egypt, Saudi Arabia, United Arab Emirates) regions [15]. DSPs are large, point-in-time surveys collecting evidence of real-world clinical practice, designed to identify current disease management and patient and physician reported disease impact.

Physicians included in the survey were instructed to complete a pre-specified questionnaire for the next 1 – 8 (variable by country) consecutive patients with active PsA who visited for routine care. Physician-reported questionnaires included detailed questions on patient demographics, clinical assessments, medication use and treatment history. Each patient with a physician-completed questionnaire was invited to fill out a patient-reported form after providing informed consent. Patients completed their forms independently from physicians, returning them in sealed envelopes to ensure confidentiality.

The Rheumatology DSPs were conducted in accordance with the relevant legislation at time of data collection, including US Health Insurance Portability and Accountability Act 1996 (HIPAA; www.hhs.gov/ocr/privacy/),[16] and Health Information Technology for Economic and Clinical Health Act legislation [17]. The DSP is a market research project and complies with all relevant market research guidelines and legal obligations. Data were collected according to European Pharmaceutical Marketing Research Association guidelines and thus did not require ethics committee approvals [18]. Namely the DSP is non-interventional and employs solely retrospective data collection, and no identifiable protected health information was extracted during the course of the study.

Participating physicians and patients

Rheumatologists (and orthopedists and internists in Japan) and dermatologists were eligible to participate if they had worked ≥3 years' as a physician, and had qualified between 1979-2012, and were responsible for treatment decisions. Rheumatologists were responsible for treatment decisions of axial SpA and PsA patients and Dermatologists were responsible for treatment decisions of PsA patients.

Patients were eligible for inclusion if aged ≥18 years, with a physician-confirmed diagnosis of PsA, not currently involved in a clinical trial. There were no restrictions according to treatments, clinical features such as disease activity/severity or demographics.

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Defining 'treatment switching'

'Treatment switching' was defined as progressing from a first immunomodulator therapy to a second therapy of the same or different class. Physicians reported reasons for switching from

a list of choices. Reasons for switch included factors associated with lack of initial or ongoing efficacy, failure to control (specific) symptoms, patient change (improvement, worsening), intolerability, issues associated with treatment administration, patient preference, administrative reasons including formulary requirements and physician preference for an alternative therapy. The full list is shown in **Supplementary Fig**. **1**.

Defining 'failing' and 'success' treatment groups

Patients were categorized as 'failing to respond" on current immunomodulatory treatment if, >3 months after initiating therapy with TNFi, apremilast or ustekinumab, ≥ 1 of the following criteria, assessed by the treating physician, were met: disease severity (reported as mild, moderate, severe PsA) had worsened or remained severe; disease activity (reported as improving, stable, unstable, deteriorating) was unstable or deteriorating; physicians reported dissatisfaction with current control of PsA; or reported they did not consider the patient's current treatment regimen a 'success'. Any patient not considered in the 'failing to respond' group was included as a 'treatment success'.

Patient reported outcomes

Patient-reported forms included validated instruments including the Health Assessment Questionnaire – Disability Index (HAQ-DI)[19], 5-dimension EuroQoL (EQ-5D-3L),[20] Medical Outcomes Study Short-Form Health Survey version 2 (SF-36v2),[21] and the Work Productivity and Activity Impairment (WPAI-GH)[22] questionnaire.

Statistical analyses

Patient characteristics were descriptively analysed for the total study sample at global and regional levels (North America, LatAm, EU5, APAC, T&ME) by demographics and underlying patient condition (including age, gender, BMI, and BSA affected by psoriasis), number of immunomodulators received, reasons for switching from 1st to 2nd agent, duration patients

remained on 1st therapy and overall rates of patients failing to respond to immunomodulator therapy and according to line of therapy.

Categorical variables were described by counts and proportions of respondents and continuous numerical variables were described by their medians, means and standard deviations. Pearson's χ^2 test assessed differences in failure rates by lines of therapy.

Linear regression analyses were performed for EQ5D, SF-36 PCS and MCS, and WPAI. The independent variable was treatment response (failing to respond or success), and differences in age, gender, BMI, smoking status, time since symptom onset and region were controlled for. Predicted values for all outcomes were subsequently stratified by failure or success whilst all other variables were fixed at their means.

All analyses used Stata Statistical Software: Release 15 (StataCorp LP, College Station, TX).

Results

Patients and physicians

A total of 949 physicians from 18 countries (North America, n=155; LatAm, n=85; EU5, n=450; APAC, n=127; T&ME, n=132) and 3,714 PsA patients (North America, n=707; LatAm, n=281; EU5, n=1820; APAC, n=543; T&ME, n=363) from the DSP were eligible for inclusion in this analysis; in total 48.2% provided by Rheumatologists (including Orthopaedic Internal Medicine in Japan), 51.8% by Dermatologists.

Key patient demographic and disease characteristics are summarised in Table 1. Patient characteristics including mean age, BMI, time since diagnosis and HAQ-DI were comparable for most regions with some exceptions. In T&ME, median time since diagnosis and symptom onset was less than other regions at 0.5 year and 1 year compared to 2-3 years and 4-5 years respectively. HAQ-DI was higher for T&ME than for other regions. In addition, there were less patients with mild disease severity and more with moderate disease severity as reported by

the treating physician than for other regions. Among patients with psoriasis, those in APAC had the highest proportion of psoriasis affected BSA, with a mean of 13.6% compared to 8.5%-11.3% in other regions.

Of 3,714 patients with PsA, 1,856 patients completed the voluntary questionnaires, including EQ-5D (n=1,809), SF-36 (n=1,699), and WPAI (n=1,779). Patient reported outcomes were comparable across most regions, other than T&ME where they were notably poorer than other regions.

Use of immunomodulators

Of 3,582 patients with complete treatment data, 1,455 (40.6%) had never received immunomodulators, 1,796 (50.1%) were receiving the 1st immunomodulator, 243 (6.8%) the 2nd immunomodulator and 88 (2.5%) the 3rd or later immunomodulator (Table 2). Of 2221 globally treated patients (including 94 with incomplete data as to total number of immunomodulators used), the majority received TNFi (84.5%); true across all regions included in this study (Table 2).

Immunomodulator treatment switching

Supplementary Fig. 1 presents the data for reasons for switching from 1st to 2nd immunomodulatory therapy. Physicians selected reasons for switching from a pre-specified list for 304 PsA patients who had received >1 immunomodulator and reason for switch was known. Responses that explicitly indicated lack of efficacy were selected for more than two thirds of patients who switched therapy; “secondary lack of efficacy (loss of response over time)” was selected for 134 (44.1%) and “primary lack of efficacy (initial non-response)” for 69 (22.7%). Other selected reasons included “condition worsened” in 114 (37.5%), “lack of pain relief” in 58 (19.1%), “remission not maintained” in 57 (18.8%) and “remission was not induced” in 50 (16.4%).

For the 58 whose physicians reported that primary lack of efficacy was the reason for immunomodulator switch, mean duration of initial therapy was 9.4 months (standard deviation 11.9 months) before switching with a maximum time to switch of 84 months (Table 2).

Immunomodulator treatment response

Based on the definition provided, 246 (14.3%) of patients receiving immunomodulator were currently failing to respond. Rates of current treatment failure increased significantly with successive immunomodulators. Globally 12.7% of patients currently receiving 1st therapy were failing current treatment, this doubled to 26.6% for patients currently receiving their 3rd or later therapy (*P*=0.0022) (**Fig. 1**). In North America and LatAm, rates of failure followed this trend, 11.8% and 14.9% of patients currently failing 1st therapy increased to 16.7% and 50.0% at 3rd respectively (both *P*=NS). In Europe and APAC 12.8% and 12.1% of patients on 1st therapy were reportedly failing which increased to 33.3% (*P*=0.0030) and 20.0% (*P*=NS) failing 3rd respectively. In T&ME, 11.9% patients on 1st therapy were failing; data are only available for 2 patients who had switched to a 2nd therapy both of whom were failing (**Fig. 1**).

Patient demographics by therapy success and failure

Patient characteristics were similar between success and failing groups across all regions with some exceptions in the APAC region; mean BMI was significantly higher (26.1 vs 24.7, *P*=0.0309), and time since diagnosis significantly shorter (3.1 vs 5.1, *P*=0.0406) for those who were failing therapy (Table 3). Globally, BSA affected by psoriasis was significantly higher in patients failing therapy (14.5 vs 7.4, *P*<0.0001). This pattern was observed for every region apart from APAC (Table 3). Globally, ESR and CRP levels were significantly higher in patients failing treatment: ESR in North America, EU5, APAC and T&ME; CRP in North America, EU5 and T&ME and numerically higher in the APAC region. ESR and CRP data were too limited in LatAm to be meaningful (Table 3).

Association of failing treatment with HRQoL and WPAI

Linear regression analysis, controlling for age, gender, smoking status, BMI, time since onset of symptoms and region, confirmed that failing treatment was significantly associated across all regions with lower EQ-5D and HAQ-DI scores (**Fig. 2a and b**); and worse SF-36 PCS and MCS scores (**Fig. 2c**). We also observed that patients who were failing treatment reported significantly worse outcomes on all the individual SF-36 domains (**Fig. 3**).

Adjusted WPAI scores were higher in patients failing treatment indicating more work impairment, time missed at work, impairment while working and impairment in daily activities than in patients for whom therapy was not failing (**Fig. 2d**).

Discussion

This analysis of real-world data on immunomodulator use in patients with PsA from a large multi-national survey demonstrates that current therapies do not consistently deliver sustained efficacy, evidenced by high rates of primary and secondary lack of efficacy to the 1st treatment (predominantly TNFi), resulting in patients switching therapies, consistent with previous reports [23,24].

Time to switch therapy due to lack of efficacy may be longer than recommended by EULAR treatment guidelines [6]. In cases where physicians reported switching from 1st to 2nd immunomodulatory therapy was due to primary lack of efficacy, time to switch to an alternative therapy occurred at a mean of 9.4 months. An observational study based on the nationwide DANBIO registry of 1,422 patients with PsA initiating TNFis demonstrated that 39% switched to a 2nd TNFi over a median of 2.3 years follow-up and a US study conducted over 4 years reported 22.9% of patients switched biologic therapy [25]. However, in this global analysis of 3,582 patients, at the time of data collection 6.8% had received a 2nd and 2.5% a 3rd therapy, with 9.4% and 4.9% receiving a 2nd and 3rd therapy in the US respectively. These differing rates are a result of our analysis being based on a cross-section of patients with differing disease durations, rather than a longitudinal study of patients over time [26,27].

The likelihood of patients failing their current treatment was higher with each successive therapy. These data are consistent with other studies, including a metanalysis of observational studies published between 2007 and 2015 of patients with PsA who have failed at least one prior TNFi. Compared to patients with no TNFi treatment, TNFi in the second-line and subsequent lines demonstrated statistical improvement in PsA outcomes, however responses to first-line TNFi demonstrated statistically greater improvements than second- and third-line TNFi. No improvement was found at 24 weeks for fourth-line TNFi compared to second-line treatment [28]. In addition, studies reviewed by Merola et al indicate that treatment responses and length of treatment survival decrease in patients receiving a 2nd or 3rd TNFi [29-32].

Recently, large-scale randomized controlled trials of biologics and targeted small molecules demonstrated ACR20/50/70 and PASI-75 responses that were significantly improved versus placebo in patients who had failed one or more TNFi [32,11,33,34]. As a result, both updated GRAPPA and EULAR guidelines recommend switching to alternative biologics including those with different modes of action after TNFi failure [13,14]; ACR-NPF guidelines specify switching to an anti-IL17 if PsA remains active after failure of a TNFi, followed by an anti-IL12/23 if PsA continues to be active [12].

The current study was performed before the market authorization of recently approved immunomodulatory agents for PsA, however the real-world clinical impact of their availability would be expected to impact treatment switching.

Our analyses demonstrate that failure of immunomodulator therapy is associated with significantly poorer patient reported HRQoL by EQ-5D and SF-36, physical functioning by HAQ-DI and performance of daily activities and work by WPAI. We observed that the T&ME cohort had notably worse disease activity and patient reported outcomes compared with other regions. We hypothesize that this may be due to shorter disease duration and lower use of bDMARDs in this region which may have led to poorer disease control compared with other regions.

Although PsA has been reported to negatively impact HRQOL [35-40], and several studies report increased absenteeism and presenteeism in patients with PsA [41-43,36] to the best of our knowledge, this is the first real-world study to compare HRQoL and work productivity in PsA patients failing treatment , with those whose treatment is considered to working effectively (i.e. not failing).

A major strength of this study is that it presents real-world data from a large number of PsA patients around the world, providing insight into real rates of treatment failure and reasons for treatment switching. Several potential limitations of this Adelphi PsA DSP should be considered. A primary limitation of the analysis is that the source data is a point-in time survey

and does not capture the exact timepoint at which patients fail to respond to therapy, therefore it was necessary to rely on physician reported reasons for switching therapy to identify the sub-set who failed to respond. Other limitations relate to cross-sectional study design, and selection of patients based on those who agreed to participate. Physician reported disease activity/severity can reflect individual physician bias. Similarly, regional differences in patient characteristics, treatment practices and physician expertise may have influenced findings in this cross-sectional study. Recall bias is a common limitation of surveys, however as data was collected at the time of patients' appointments, the likelihood of recall bias is reduced. Finally, although the level of knowledge and management strategies for PsA treatment may differ between Rheumatologists and Dermatologists, thereby affecting treatment satisfaction and clinical outcomes, differences attributable to physician specialities were not evaluated.

In conclusion, this large multinational real-world survey in PsA patients demonstrated that lack of efficacy of immunomodulatory therapy was not uncommon and the predominant reason for treatment switching. Failure to respond was associated with significantly poorer patient reported HRQoL, physical functioning and work productivity. A significant proportion of patients who switched onto 2nd or 3rd therapy did not respond as expected, albeit the majority were TNFis. More regular monitoring and earlier use of appropriate therapies upon identification of lack of efficacy may lead to improvements in disease control and reduce progression leading to improved HRQoL, physical function and productivity benefits to society.

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Conflict of interest

RA has received grants or research support from Bristol-Myers Squibb, consulting fees from Bristol-Myers Squibb, Novartis, Pfizer Roche and Eli Lilly. PGC has received speakers' bureau or consulting fees from Bristol- Myers Squibb, Pfizer and Novartis. VS has received grants and/or consulting fees from AbbVie, Amgen, AstraZeneca, BMS, Boehringer Ingelheim, Celltrion, Corrona LLC, Crescendo Bioscience, EMD Serono, F. Hoffmann-La Roche Ltd/Genentech, Inc., GSK, Janssen, Eli Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi and UCB and has served on advisory boards for AbbVie, Amgen, AstraZeneca, BMS, Celltrion, Crescendo/Myriad Genetics, EMDSerono, Genentech/Roche, GSK, Janssen, Lilly, Novartis, Pfizer, Regeneron, Sandoz, Sanofi and UCB. AD has received grants or research support from AbbVie, Eli Lilly, GlaxoSmithKline, Janssen, Novartis, Pfizer and UCB Pharma, and consulting fees from Eli Lilly, Janssen, Novartis, Pfizer and UCB Pharma. ES & SB are employees of Adelphi Real World; HT and KG are shareholders and employees of Novartis; SJ is a shareholder and employee of Novartis Pharma AG

References

1. Liu JT, Yeh HM, Liu SY, Chen KT (2014) Psoriatic arthritis: Epidemiology, diagnosis, and treatment. World J Orthop 5 (4):537-543. doi:10.5312/wjo.v5.i4.537
2. Lloyd P, Ryan C, Menter A (2012) Psoriatic arthritis: an update. Arthritis 2012:176298. doi:10.1155/2012/176298
3. Reveille JD, Witter JP, Weisman MH (2012) Prevalence of axial spondylarthritis in the United States: estimates from a cross-sectional survey. Arthritis Care Res (Hoboken) 64 (6):905-910. doi:10.1002/acr.21621
4. Hukuda S, Minami M, Saito T, Mitsui H, Matsui N, Komatsubara Y, Makino H, Shibata T, Shingu M, Sakou T, Shichikawa K (2001) Spondyloarthropathies in Japan: nationwide questionnaire survey performed by the Japan Ankylosing Spondylitis Society. J Rheumatol 28 (3):554-559
5. Salaffi F, Carotti M, Gasparini S, Intorcia M, Grassi W (2009) The health-related quality of life in rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis: a comparison with a selected sample of healthy people. Health Qual Life Outcomes 7:25. doi:10.1186/1477-7525-7-25
6. Gossec L, Smolen JS, Gaujoux-Viala C, Ash Z, Marzo-Ortega H, van der Heijde D, FitzGerald O, Aletaha D, Balint P, Boumpas D, Braun J, Breedveld FC, Burmester G, Canete JD, de Wit M, Dagfinrud H, de Vlam K, Dougados M, Helliwell P, Kavanaugh A, Kvien TK, Landewe R, Luger T, Maccarone M, McGonagle D, McHugh N, McInnes IB, Ritchlin C, Sieper J, Tak PP, Valesini G, Vencovsky J, Winthrop KL, Zink A, Emery P, European League Against R (2012) European League Against Rheumatism recommendations for the management of psoriatic arthritis with pharmacological therapies. Ann Rheum Dis 71 (1):4-12. doi:10.1136/annrheumdis-2011-200350
7. Zerilli T, Ocheretyaner E (2015) Apremilast (Otezla): A New Oral Treatment for Adults With Psoriasis and Psoriatic Arthritis. P T 40 (8):495-500
8. Mease P, McInnes IB (2016) Secukinumab: A New Treatment Option for Psoriatic Arthritis. Rheumatol Ther 3 (1):5-29. doi:10.1007/s40744-016-0031-5
9. Nash P, Kirkham B, Okada M, Rahman P, Combe B, Burmester GR, Adams DH, Kerr L, Lee C, Shuler CL, Genovese M, Group S-PS (2017) Ixekizumab for the treatment of patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors: results from the 24-week randomised, double-blind, placebo-controlled period of the SPIRIT-P2 phase 3 trial. Lancet 389 (10086):2317-2327. doi:10.1016/S0140-6736(17)31429-0
10. Gladman D, Rigby W, Azevedo VF, Behrens F, Blanco R, Kaszuba A, Kudlacz E, Wang C, Menon S, Hendrikx T, Kanik KS (2017) Tofacitinib for Psoriatic Arthritis in Patients with an Inadequate Response to TNF Inhibitors. N Engl J Med 377 (16):1525-1536. doi:10.1056/NEJMoa1615977
11. Mease PJ, Gottlieb AB, van der Heijde D, FitzGerald O, Johnsen A, Nys M, Banerjee S, Gladman DD (2017) Efficacy and safety of abatacept, a T-cell modulator, in a randomised, double-blind, placebo-controlled, phase III study in psoriatic arthritis. Ann Rheum Dis 76 (9):1550-1558. doi:10.1136/annrheumdis-2016-210724
12. ACR and NPF Unveil New Clinical Guideline for Treating Psoriatic Arthritis. (2017) AMJC. http://www.ajmc.com/conferences/acr-2017/acr-and-npf-unveil-new-clinical-guideline-for-treating-psoriatic-arthritis. Accessed February 12 2018
13. Coates LC, Murphy R, Helliwell PS (2016) New GRAPPA recommendations for the management of psoriasis and psoriatic arthritis: process, challenges and implementation. Br J Dermatol 174 (6):1174-1178. doi:10.1111/bjd.14667
14. Gossec L, Smolen JS, Ramiro S, de Wit M, Cutolo M, Dougados M, Emery P, Landewe R, Oliver S, Aletaha D, Betteridge N, Braun J, Burmester G, Canete JD, Damjanov N, FitzGerald O, Haglund E, Helliwell P, Kvien TK, Lories R, Luger T, Maccarone M, Marzo-Ortega H, McGonagle D, McInnes IB, Olivieri I, Pavelka K, Schett G, Sieper J, van den Bosch F, Veale DJ, Wollenhaupt J, Zink A, van der Heijde D (2016) European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. Ann Rheum Dis 75 (3):499-510. doi:10.1136/annrheumdis-2015-208337

15. Anderson P, Benford M, Harris N, Karavali M, Piercy J (2008) Real-world physician and patient behaviour across countries: Disease-Specific Programmes - a means to understand. Curr Med Res Opin 24 (11):3063-3072. doi:10.1185/03007990802457040
16. Services UDoHaH (2003) Summary of the HIPAA Privacy Rule. http://www.hhs.gov/sites/default/files/privacysummary.pdf. Accessed May 11th 2017
17. Technology HI Health Information Technology Act. https://www.healthit.gov/sites/default/files/hitech_act_excerpt_from_arra_with_index.pdf. Accessed 11 May 2017
18. Association EPMR (2017) European Pharmaceutical Market Research Association (EphMRA) Code of Conduct http://www.ephmra.org/Code-of-Conduct-Support. Accessed 11 May 2017
19. Fries JF, Spitz PW, Young DY (1982) The dimensions of health outcomes: the health assessment questionnaire, disability and pain scales. J Rheumatol 9 (5):789-793
20. EuroQol G (1990) EuroQol--a new facility for the measurement of health-related quality of life. Health Policy 16 (3):199-208
21. Ware JE, Jr., Sherbourne CD (1992) The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 30 (6):473-483
22. Reilly MC, Zbrozek AS, Dukes EM (1993) The validity and reproducibility of a work productivity and activity impairment instrument. Pharmacoeconomics 4 (5):353-365
23. Lie E, van der Heijde D, Uhlig T, Mikkelsen K, Rodevand E, Koldingsnes W, Kaufmann C, Kvien TK (2011) Effectiveness of switching between TNF inhibitors in ankylosing spondylitis: data from the NOR-DMARD register. Ann Rheum Dis 70 (1):157-163. doi:10.1136/ard.2010.131797
24. Plasencia C, Pascual-Salcedo D, Garcia-Carazo S, Lojo L, Nuno L, Villalba A, Peiteado D, Arribas F, Diez J, Lopez-Casla MT, Martin-Mola E, Balsa A (2013) The immunogenicity to the first anti-TNF therapy determines the outcome of switching to a second anti-TNF therapy in spondyloarthritis patients. Arthritis Res Ther 15 (4):R79. doi:10.1186/ar4258
25. Walsh JA, Adejoro O, Chastek B, Palmer JB, Hur P (2018) Treatment Patterns Among Patients with Psoriatic Arthritis Treated with a Biologic in the United States: Descriptive Analyses from an Administrative Claims Database. J Manag Care Spec Pharm:1-11. doi:10.18553/jmcp.2018.17388
26. Davis K (2002) The Danish health system through an American lens. Health Policy 59 (2):119-132
27. StataCorp (2015) Stata Statistical Software: Release 14. . College Station, TX
28. Reddy SM, Crean S, Martin AL, Burns MD, Palmer JB (2016) Real-world effectiveness of anti-TNF switching in psoriatic arthritis: a systematic review of the literature. Clin Rheumatol 35 (12):2955-2966. doi:10.1007/s10067-016-3425-4
29. Glintborg B, Ostergaard M, Krogh NS, Andersen MD, Tarp U, Loft AG, Lindegaard HM, Holland-Fischer M, Nordin H, Jensen DV, Olsen CH, Hetland ML (2013) Clinical response, drug survival, and predictors thereof among 548 patients with psoriatic arthritis who switched tumor necrosis factor alpha inhibitor therapy: results from the Danish Nationwide DANBIO Registry. Arthritis Rheum 65 (5):1213-1223. doi:10.1002/art.37876
30. Fagerli KM, Lie E, van der Heijde D, Heiberg MS, Kalstad S, Rodevand E, Mikkelsen K, Lexberg AS, Kvien TK (2013) Switching between TNF inhibitors in psoriatic arthritis: data from the NOR-DMARD study. Ann Rheum Dis 72 (11):1840-1844. doi:10.1136/annrheumdis-2012-203018
31. Coates LC, Cawkwell LS, Ng NW, Bennett AN, Bryer DJ, Fraser AD, Emery P, Marzo-Ortega H (2008) Sustained response to long-term biologics and switching in psoriatic arthritis: results from real life experience. Ann Rheum Dis 67 (5):717-719. doi:10.1136/ard.2007.082925
32. Merola JF, Lockshin B, Mody EA (2017) Switching biologics in the treatment of psoriatic arthritis. Semin Arthritis Rheum. doi:10.1016/j.semarthrit.2017.02.001
33. Edwards CJ, Blanco FJ, Crowley J, Birbara CA, Jaworski J, Aelion J, Stevens RM, Vessey A, Zhan X, Bird P (2016) Apremilast, an oral phosphodiesterase 4 inhibitor, in patients with psoriatic arthritis and current skin involvement: a phase III, randomised, controlled trial (PALACE 3). Ann Rheum Dis 75 (6):1065-1073. doi:10.1136/annrheumdis-2015-207963

34. Kawalec P, Holko P, Mocko P, Pilc A (2018) Comparative effectiveness of abatacept, apremilast, secukinumab and ustekinumab treatment of psoriatic arthritis: a systematic review and network meta-analysis. Rheumatol Int 38 (2):189-201. doi:10.1007/s00296-017-3919-7
35. Husted JA, Gladman DD, Farewell VT, Cook RJ (2001) Health-related quality of life of patients with psoriatic arthritis: a comparison with patients with rheumatoid arthritis. Arthritis Rheum 45 (2):151-158. doi:10.1002/1529-0131(200104)45:2<151::AID-ANR168>3.0.CO;2-T
36. Armstrong AW, Schupp C, Wu J, Bebo B (2012) Quality of life and work productivity impairment among psoriasis patients: findings from the National Psoriasis Foundation survey data 2003-2011. PLoS One 7 (12):e52935. doi:10.1371/journal.pone.0052935
37. Helliwell P, Coates L, Chandran V, Gladman D, de Wit M, FitzGerald O, Kavanaugh A, Strand V, Mease PJ, Boehncke WH, Langley RG, Lubrano E, Maccarone M, Schulze-Koops H, Miceli-Richard C, Queiro R (2014) Qualifying unmet needs and improving standards of care in psoriatic arthritis. Arthritis Care Res (Hoboken) 66 (12):1759-1766. doi:10.1002/acr.22404
38. Strand V, Mease P, Gossec L, Elkayam O, van den Bosch F, Zuazo J, Pricop L, Mpofu S, group Fs (2017) Secukinumab improves patient-reported outcomes in subjects with active psoriatic arthritis: results from a randomised phase III trial (FUTURE 1). Ann Rheum Dis 76 (1):203-207. doi:10.1136/annrheumdis-2015-209055
39. Strand V, Schett G, Hu C, Stevens RM (2013) Patient-reported Health-related Quality of Life with apremilast for psoriatic arthritis: a phase II, randomized, controlled study. J Rheumatol 40 (7):1158-1165. doi:10.3899/jrheum.121200
40. Strand V, Sharp V, Koenig AS, Park G, Shi Y, Wang B, Zack DJ, Fiorentino D (2012) Comparison of health-related quality of life in rheumatoid arthritis, psoriatic arthritis and psoriasis and effects of etanercept treatment. Ann Rheum Dis 71 (7):1143-1150. doi:10.1136/annrheumdis-2011-200387
41. Kennedy M, Papneja A, Thavaneswaran A, Chandran V, Gladman DD (2014) Prevalence and predictors of reduced work productivity in patients with psoriatic arthritis. Clin Exp Rheumatol 32 (3):342-348
42. Tillett W, Shaddick G, Askari A, Cooper A, Creamer P, Clunie G, Helliwell PS, Kay L, Korendowych E, Lane S, Packham J, Shaban R, Williamson L, McHugh N (2015) Factors influencing work disability in psoriatic arthritis: first results from a large UK multicentre study. Rheumatology (Oxford) 54 (1):157-162. doi:10.1093/rheumatology/keu264
43. Walsh JA, McFadden ML, Morgan MD, Sawitzke AD, Duffin KC, Krueger GG, Clegg DO (2014) Work productivity loss and fatigue in psoriatic arthritis. J Rheumatol 41 (8):1670-1674. doi:10.3899/jrheum.140259

Figure Legends

Fig. 1 Patients currently 'failing' 1st, 2nd, 3rd or later immunomodulator therapy Rates of failure on successive lines of immunomodulator therapy. APAC, Asia Pacific region; EU5, European Union 5; LatAm, Latin America, T & ME, Turkey & Middle East

Fig. 2 EQ-5D scores (A), HAQ-DI scores (B), SF-36 scores (C) and WPAI (D) for patients failing immunomodulator therapy vs. immunomodulator therapy success Results are adjusted for age, gender, smoking status, BMI, time since onset of symptoms and region. ABS, absenteeism; ACT, activity impairment; APAC, Asia Pacific region; EU5, European Union 5; LatAm, Latin America; O, overall work impairment; PRES, presenteeism; SD, standard deviation; T & ME, Turkey & Middle East. SF-PCS, $P<0.0001$; SF-MCS, $P=0.0010$; overall work impairment, $P=0.0727$; presenteeism, $P=0.0212$; absenteeism, $P=0.3932$; activity impairment, $P<0.0001$

Fig. 3 Spydergram of adjusted SF-36 domain scores for patients failing immunomodulator therapy vs. immunomodulator therapy success Results are adjusted for age, gender, smoking status, BMI, time since onset of symptoms and region

Supplementary Fig. 1 Reasons for switching from 1st to 2nd TNFi (n=304) Physician reported reasons given for patient switching from 1st to 2nd line immunomodulator therapy. * Secondary lack of efficacy (loss of response over time); ‡ I wanted to use a bDMARD that can be used in combination; † I wanted to use bDMARD that can be used as a monotherapy. bDMARD: biologic Disease Modifying Anti-Rheumatic drugs; MOA, Mode of action

Table 1. Patient Characteristics

Characteristic	All (n=3714)	North America (n=707)	LatAm (n=281)	EU5 (n=1820)	APAC (n=543)	T & ME (n=363)
Age, years	**(n=3710)**	**(n=707)**	**(n=281)**	**(n=1820)**	**(n=539)**	**(n=363)**
Median	47.0	49.0	48.0	48.0	51.0	40.0
IQR	39.0, 57.0	39.0, 57.0	40.0, 58.0	40.0, 58.0	41.0, 61.0	35.0, 43.0
Mean (SD)	48.2 (12.5)	48.1 (12.6)	49.1 (12.1)	48.9 (12.4)	51.5 (13.5)	39.7 (7.3)
Male, n (%)	1916 (51.6)	345 (48.8)	141 (50.2)	956 (52.5)	320 (59.0)	154 (42.4)
BMI, kg/m^2	**(n=3708)**	**(n=707)**	**(n=281)**	**(n=1820)**	**(n=539)**	**(n=361)**
Median	25.7	26.7	26.0	25.4	23.9	26.1
IQR	23.3, 28.4	24.3, 30.4	23.9, 28.4	23.3, 28.0	21.7, 27.0	24.6, 28.4
Mean (SD)	26.4 (4.7)	28.0 (5.6)	26.4 (4.0)	26.1 (4.3)	25.0 (4.9)	26.8 (3.7)
Time since symptom onset (years)	**(n=2943)**	**(n=542)**	**(n=262)**	**(n=1405)**	**(n=390)**	**(n=344)**
Median	4.0	4.0	4.0	5.0	5.0	1.0
IQR	2.0, 8.0	2.0, 10.0	1.8, 8.0	2.0, 9.0	2.0, 10.0	1.0, 2.0
Mean (SD)	6.3 (7.4)	6.8 (7.1)	6.3 (6.7)	7.0 (7.9)	7.2 (7.7)	1.9 (2.0)
Time since diagnosis (years)	**(n=3210)**	**(n=583)**	**(n=267)**	**(n=1597)**	**(n=412)**	**(n=351)**
Median	3.0	3.0	2.0	3.0	3.0	0.5
IQR	1.0, 6.0	1.0, 6.0	0.8, 5.0	1.4, 7.0	1.0, 7.0	0.1, 1.0
Mean (SD)	4.7 (6.0)	4.9 (5.7)	4.4 (6.0)	5.5 (6.5)	5.1 (5.5)	1.0 (1.5)
Current severity (physician reported), n (%)						
Mild	2378 (64.1)	478 (67.6)	183 (65.1)	1159 (63.7)	379 (70.1)	179 (49.6)
Moderate	1162 (31.3)	208 (29.4)	80 (28.5)	568 (31.2)	149 (27.5)	157(43.5)
Severe	170 (4.6)	21 (3.0)	18 (6.4)	93 (5.1)	13 (2.4)	25 (6.9)
PsA with psoriasis, n %	**3512 (94.6)**	**677 (95.8)**	**261 (92.9)**	**1727 (94.9)**	**497 (91.9)**	**350 (96.4)**
% BSA currently affected by psoriasis	**(n=2731)**	**(n=562)**	**(n=259)**	**(n=1172)**	**(n=400)**	**(n=338)**
Median	5.0	5.0	1.8	7.0	8.0	6.0
IQR	2.0, 15.0	2.0, 15.0	0.0, 11.8	3.0, 15.0	2.0, 20.0	3.0, 12.0
Mean (SD)	11.1 (13.4)	11.3 (14.2)	8.5 (14.2)	11.2 (12.5)	13.6 (15.9)	9.5 (9.9)
EQ-5D utility score	**(n=1809)**	**(n=371)**	**(n=217)**	**(n=742)**	**(n=265)**	**(n=214)**
Median	0.8	0.83	0.77	0.84	0.85	0.08

IQR	0.59, 1.00	0.77, 1.00	0.59, 1.00	0.68, 1.00	0.73, 1.00	-0.02, 0.52
Mean (SD)	0.72 (0.32)	0.84 (0.17)	0.73 (0.29)	0.76 (0.28)	0.84 (0.19)	0.18 (0.32)
SF36 PCS	**(n=1657)**	**(n=382)**	**(n=69)**	**(n=728)**	**(n=263)**	**(n=215)**
Median	44.3	48.9	39.6	44.7	47.8	37.4
IQR	37.0, 52.0	40.2, 54.2	34.1, 44.1	36.9, 52.1	41.9, 52.8	33.6, 42.2
Mean (SD)	44.1 (9.2)	46.9 (9.2)	40.0 (7.3)	43.9 (9.6)	46.6 (8.2)	37.9 (6.0)
SF36 MCS	**(n=1657)**	**(n=382)**	**(n=69)**	**(n=728)**	**(n=263)**	**(n=215)**
Median	44.5	53.2	36.5	45.6	44.8	38.0
IQR	37.0, 53.0	42.9, 58.0	35.0, 41.6	37.0, 51.7	37.4, 52.2	34.2, 41.3
Mean (SD)	44.4 (10.4)	50.1 (9.9)	38.1 (8.0)	44 (10.7)	44.6 (9.4)	37.5 (5.7)
HAQ-DI	**(n=1668)**	**(n=383)**	**(n=69)**	**(n=735)**	**(n=266)**	**(n=215)**
Median	0.5	0.13	0.88	0.5	0.19	1.5
IQR	0.00, 1.13	0.00, 0.50	0.38, 1.13	0.00, 1.14	0.00, 0.63	1.13, 1.63
Mean (SD)	0.67 (0.70)	0.36 (0.48)	0.89 (0.64)	0.70 (0.76)	0.40 (0.52)	1.37 (0.45)
WPAI, overall work impairment	**(n=886)**	**(n=235)**	**(n=98)**	**(n=300)**	**(n=135)**	**(n=118)**
Median	20	10	20	20	20	67.6
IQR	10.0, 50.9	0.0, 30.0	0.0, 52.6	10.0, 40.0	10.0, 30.0	63.5, 78.3
Mean (SD)	29.2 (27.5)	17.1 (19.9)	30 (30.3)	25.2 (24.4)	24.2 (20.6)	68.7 (15.2)

APAC, Asia Pacific region; BMI, body mass index; BSA, body surface area; EQ-5D, EuroQol 5-dimensions questionnaire; EU5, European Union 5; HAQ-DI, health assessment questionnaire disability index ; MCS, mental component score; LatAm, Latin America; PsA, psoriatic arthritis; T & ME, Turkey & Middle East; PCS, physical component score; SD, standard deviation; SF-36, Medical Outcomes Study Short-Form (36-item) Health Survey; WPAI, work productivity and activity impairment questionnaire.

Table 2. Treatment with immunomodulating therapies

	All	North America	LatAm	EU5	APAC	T & ME
Number of immunomodulating therapy ever received, n (%)	**(n=3582)**	**(n=680)**	**(n=276)**	**(n=1780)**	**(n=491)**	**(n=355)**
0	1455 (40.6)	203 (29.9)	24 (8.7)	761 (42.8)	230 (46.8)	237 (66.8)
1	1796 (50.1)	380 (55.9)	229 (83.0)	848 (47.6)	229 (46.6)	110 (31.0)
2	243 (6.8)	64 (9.4)	19 (6.9)	130 (7.3)	23 (4.7)	7 (2.0)
3+	88 (2.5)	33 (4.9)	4 (1.4)	41 (2.3)	9 (1.8)	1 (0.3)
Current class of immunomodulator therapy, n (%)	**(n=2221)**	**(n=504)**	**(n=257)**	**(n=1059)**	**(n=276)**	**(n=125)**
TNFi	1877 (84.5)	355 (70.4)	254 (98.8)	924 (87.3)	238 (86.2)	106 (84.8)
Non-TNFi bDMARD	239 (10.8)	80 (15.9)	3 (1.2)	106 (10.0)	31 (11.2)	19 (15.2)
tsDMARD (oral)	105 (4.7)	69 (13.7)	0 (0.0)	29 (2.7)	7 (2.5)	0 (0.0)
Time on 1st immunomodulatory therapy when physician recorded 'primary lack of efficacy', months	**(n=58)**	**(n=20)**	**(n=2)**	**(n=29)**	**(n=4)**	**(n=3)**
Mean (SD)	9.4 (11.9)	12.8 (18.8)	3.5 (3.5)	7.7 (5.7)	7.0 (3.5)	10.7 (1.2)
Median	6.0	6.0	3.5	6.0	6.0	10.0
Min, max	1.0, 84.0	2.0, 84.0	1.0, 6.0	1.0, 24.0	4.0, 12.0	10.0, 12.0
IQR	4.0, 12.0	4.5, 11.0	1.0, 6.0	3.0, 12.0	5.0, 9.0	10.0, 12.0

Patient immunomodulator therapy exposure and switching. APAC, Asia Pacific region; BMI, body mass index; bDMARD: biologic Disease Modifying Anti-Rheumatic drug; EU5, European Union 5; LatAm, Latin America; SD, standard deviation; T & ME, Turkey & Middle East; TNFi, Tumor Necrosis Factor inhibitor; tsDMARD, targeted synthetic Disease Modifying Anti-Rheumatic drug.

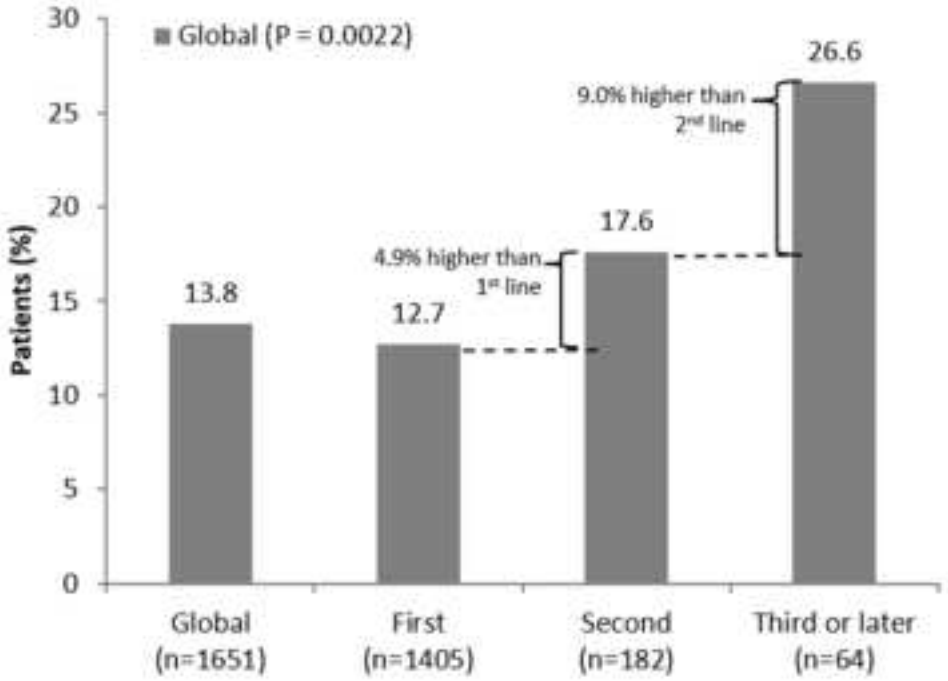
Table 3. Patient characteristics of 'immunomodulator therapy success' and 'immunomodulator therapy failing' cohorts

	All		North America		LatAm		EU5		APAC		T & ME	
Group	Success (n=1472)	Failing (n=246)	Success (n=332)	Failing (n=49)	Success (n=159)	Failing (n=31)	Success (n=747)	Failing (n=130)	Success (n=172)	Failing (n=25)	Success (n=62)	Failing (n=11)
Age, years												
Median	49.0	49.0	50.5	51.0	49.0	45.0	49.0	49.0	51.0	49.0	40.0	39.0
IQR	41.0, 57.0	41.0, 57.0	42.0, 58.0	46.0, 59.0	41.0, 58.0	42.0, 57.0	41..0, 56.0	41.0, 58.0	41.0, 61.0	45.0, 56.0	35.0, 43.0	35.0, 44.0
Mean (SD)	48.8 (11.6)	49.3 (12.0)	49.1 (11.8)	51.4 (12.6)	49.2 (11.6)	48.5 (11.5)	48.7 (11.3)	49.3 (12.1)	51.1 (12.8)	50.6 (10.8)	39.5 (5.9)	38.6 (5.4)
P	0.6918		0.2225		0.7465		0.7560		0.7142		0.7452	
Male, n (%)	819 (55.6)	131 (53.3)	182 (54.8)	21 (42.9)	89 (56.0)	15 (48.4)	407 (54.5)	73 (56.2)	112 (65.1)	14 (56.0)	29 (46.8)	8 (72.7)
P	0.4894		0.1271		0.5546		0.7748		0.3813		0.1898	
BMI, kg/m²												
Median	25.8	26.4	27.2	27.3	26.4	25.0	25.5	26.3	23.5	25.7	26.0	26.5
IQR	23.4, 28.8	24.1, 29.4	24.8, 30.8	24.4, 34.6	24.2, 29.1	23.4, 28.1	23.3, 28.3	23.9, 29.4	21.6, 26.3	23.6, 29.1	24.9, 28.5	25.8, 27.7
Mean (SD)	26.6 (4.8)	27.2 (5.1)	28.4 (5.8)	29.2 (6.0)	27.0 (4.2)	25.9 (4.0)	26.2 (4.3)	27.1 (5.2)	24.7 (4.7)	26.1 (4.8)	26.9 (2.5)	26.6 (1.3)
P	0.0600		0.4942		0.1627		0.0578		0.0309		0.7402	
Time since symptom onset (years)												
n	1177	190	252	38	152	31	585	91	126	20	62	10
Median	5.0	5.0	5.0	7.0	5.0	4.0	6.0	7.0	5.0	3.0	2.0	3.0
IQR	3.0, 10.0	2.2, 10.0	3.0, 10.0	3.0, 12.0	3.0, 10.0	1.3, 7.0	3.0, 10.0	4.0, 15.0	2.0, 10.0	2.0, 7.5	2.0, 2.0	1.0, 4.0
Mean (SD)	7.6 (7.2)	8.6 (8.7)	8.0 (7.4)	8.7 (6.9)	7.4 (6.9)	6.3 (8.2)	8.3 (7.6)	10.3 (9.3)	6.5 (5.4)	7.0 (9.9)	2.4 (1.6)	2.6 (1.5)
P	0.7789		0.4084		0.1040		0.1140		0.4063		0.7294	
Time since diagnosis (years)												
n	1282	205	277	40	151	31	659	103	134	21	61	10
Median	4.0	4.0	4.0	5.0	3.0	2.0	5.0	6.0	3.0	2.0	1.0	1.5
IQR	2.0, 8.0	2.0, 8.0	2.0, 8.0	2.8, 10.0	2.0, 7.0	0.8, 5.0	2.5, 9.0	3.0, 10.0	2.0, 7.0	1.2, 3.0	0.8, 2.0	0.7, 3.0

Mean (SD)	6.0 (6.1)	6.3 (6.8)	6.0 (5.8)	6.8 (5.5)	5.5 (6.2)	4.9 (8.1)	6.8 (6.4)	7.6 (7.2)	5.1 (4.9)	3.1 (3.3)	1.6 (1.6)	1.7 (1.1)
P	0.6836		0.2577		0.1052		0.4101		0.0406		0.7275	
% BSA affected by psoriasis currently												
n	1143	179	280	38	155	30	509	80	138	20	61	11
Median	4.0	10.0	5.0	9.0	0.2	12.0	5.0	10.0	5.0	9.5	3.0	6.0
IQR	1.0, 10.0	5.0, 20.0	1.0, 10.0	5.0, 24.0	0.0, 7.3	1.8, 15.4	1.0, 10.0	5.0, 22.5	1.0, 10.0	5.0, 16.5	2.0, 5.0	5.0, 10.0
Mean (SD)	7.4 (10.4)	14.5 (14.4)	7.5 (10.1)	15.3 (16.9)	5.9 (11.7)	14.2 (16.3)	6.9 (8.5)	15.1 (13.0)	11.1 (15.4)	13.2 (13.9)	6.2 (7.6)	10.5 (10.9)
P	<0.0001		0.0004		<0.0001		<0.0001		0.0832		0.0072	
ESR, mm/hr (within 3 months)												
n	547	85	95	15	10	0	324	51	63	10	55	9
Median	12.0	23.0	16.0	23.0	11.5	-	11.0	22.0	10.0	22.0	15.0	25.0
IQR	7.0, 20.0	15.0, 34.0	10.0, 24.0	18.0, 43.0	10.0, 13.0	-	5.0, 19.0	15.0, 34.0	6.0, 16.0	8.0, 38.0	12.0, 19.0	19.0, 32.0
Mean (SD)	14.4 (10.4)	27.7 (20.9)	17.4 (9.7)	29.5 (20.3)	11.6 (4.5)	-	13.6 (10.4)	26.9 (20.6)	13.0 (13.0)	30.4 (31.0)	16.1 (6.6)	25.7 (9.9)
P	<0.0001		0.0276		-		<0.0001		0.0426		0.0050	
CRP, mg/l (within 3 months)												
n	506	82	74	12	11	0	307	52	62	10	52	8
Median	2.6	5.0	1.8	4.3	0.7	-	4.0	6.0	0.6	1.1	1.8	5.0
IQR	1.0, 5.4	2.4, 10.0	0.9, 3.4	2.7, 7.6	10.0, 13.0	-	2.0, 7.0	3.0, 10.5	0.2, 2.9	0.3, 3.0	1.3, 2.5	2.9, 6.5
Mean (SD)	4.5 (5.9)	8.9 (12.9)	4.7 (8.3)	5.5 (3.7)	0.8 (1.1)	-	5.4 (5.6)	9.9 (12.6)	2.5 (5.6)	5.0 (11.5)	2.3 (1.8)	12.4 (22.5)
P	<0.0001		0.0073		-		0.0004		0.8005		0.0003	

Patients were deemed to be failing immunomodulator therapy after at least 3 months if disease severity had worsened or remained severe, disease activity was unstable or deteroriating, disease was not considered by physician to be controlled, nor treatment a success. Patients not considered to be failing immunomodulator therapy were considered to be ‘immunomodulator therapy success’. APAC, Asia Pacific region; BMI, body mass index; BSA, body surface area; CRP, c-reactive protein; ESR, erthyrocyte sedimentation rate; EU5, European Union 5; LatAm, Latin America; T & ME, Turkey & Middle East; SD, standard deviation.

Figure 1



Global	(n=1718)	(n=1405)	(n=182)	(n=64)	
% Failing	14.3	12.7	17.6	26.6	*P* = 0.0022
North America	(n=381)	(n=288)	(n=50)	(n=24)	
% Failing	12.9	11.8	8.0	16.7	*P* = 0.5368
LatAm	(n=190)	(n=174)	(n=9)	(n=4)	
% Failing	16.3	14.9	33.3	50.0	*P* = 0.0674
EU5	(n=877)	(n=702)	(n=109)	(n=30)	
% Failing	14.8	12.8	18.3	33.3	*P* = 0.0030
APAC	(n=197)	(n=174)	(n=12)	(n=5)	
% Failing	12.7	12.1	25.0	20.0	*P* = 0.3934
T&ME	(n=73)	(n=67)	(n=2)	(n=1)	
% Failing	15.1	11.9	100.0	0.0	*P* = 0.002

Figure 2a

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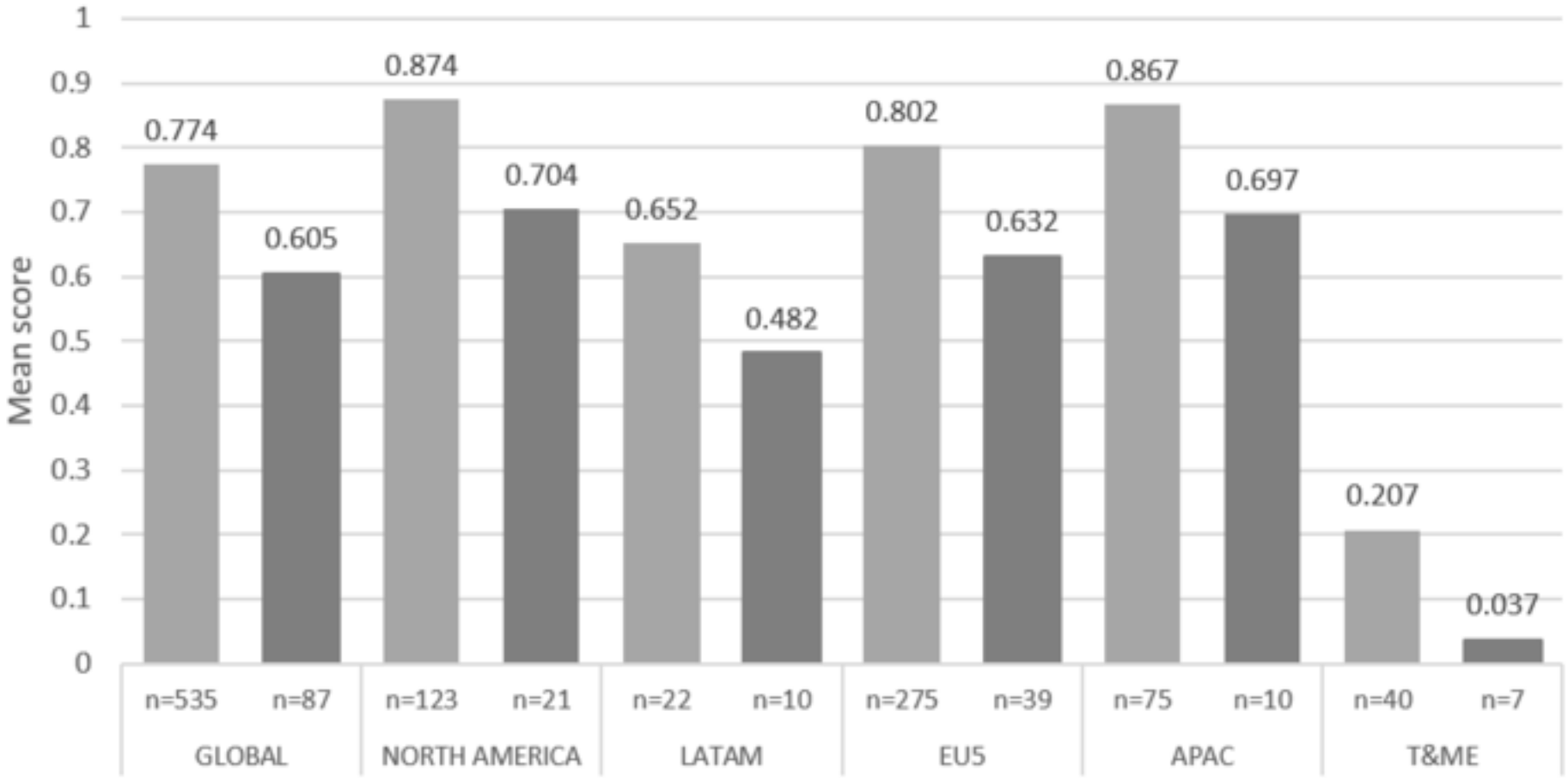

Figure 2b

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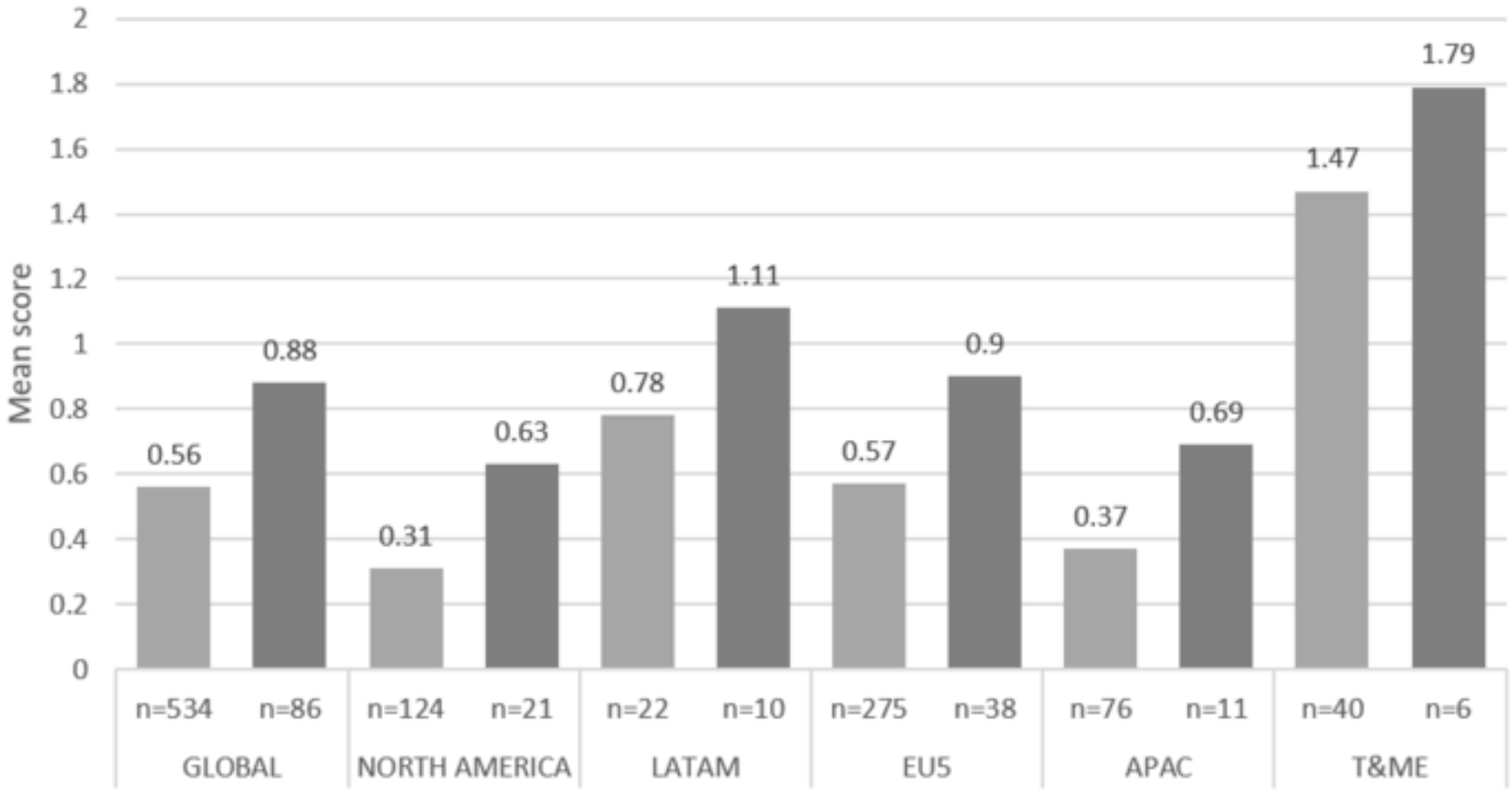

Figure 2c

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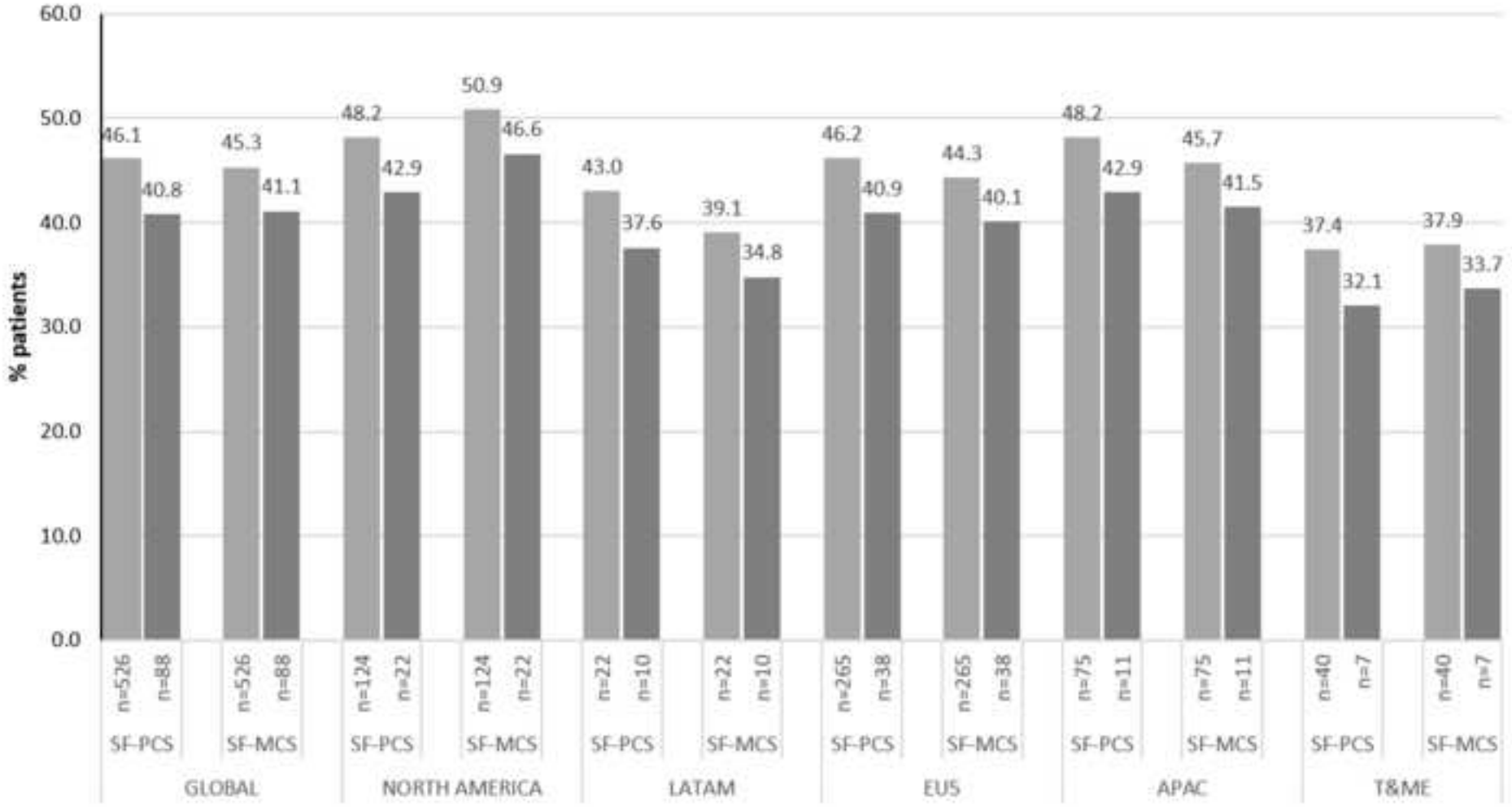

Figure 2d

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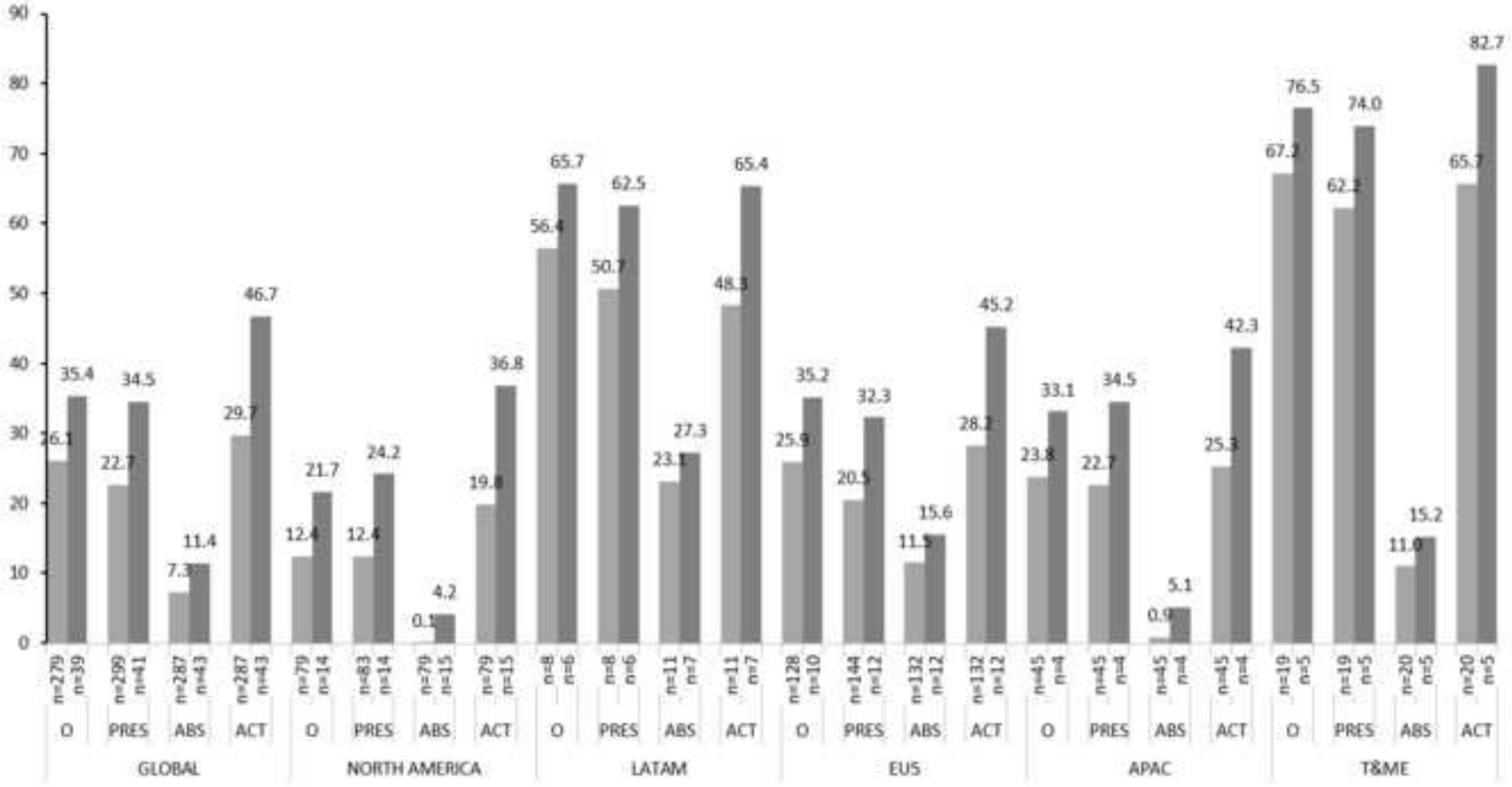
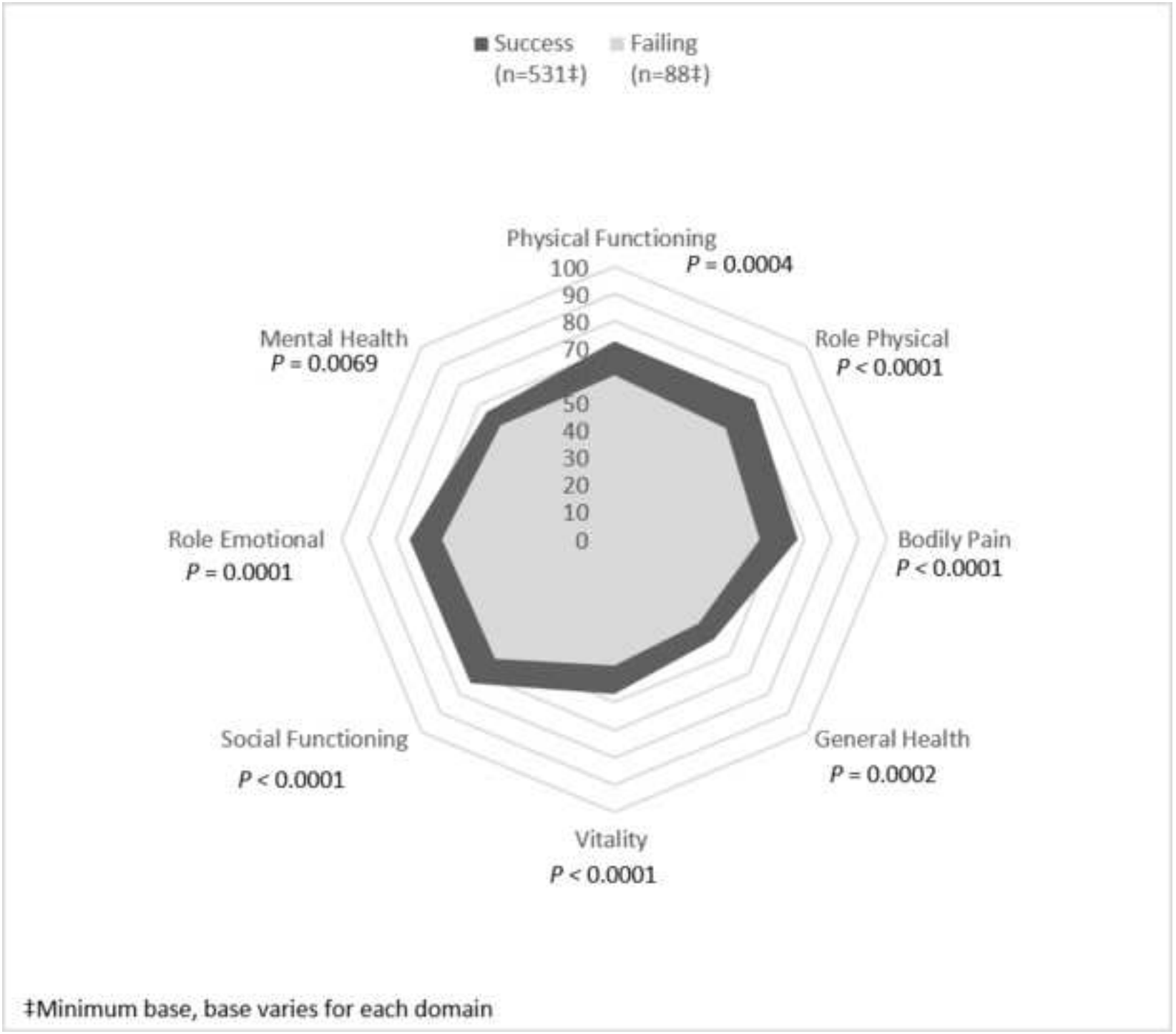
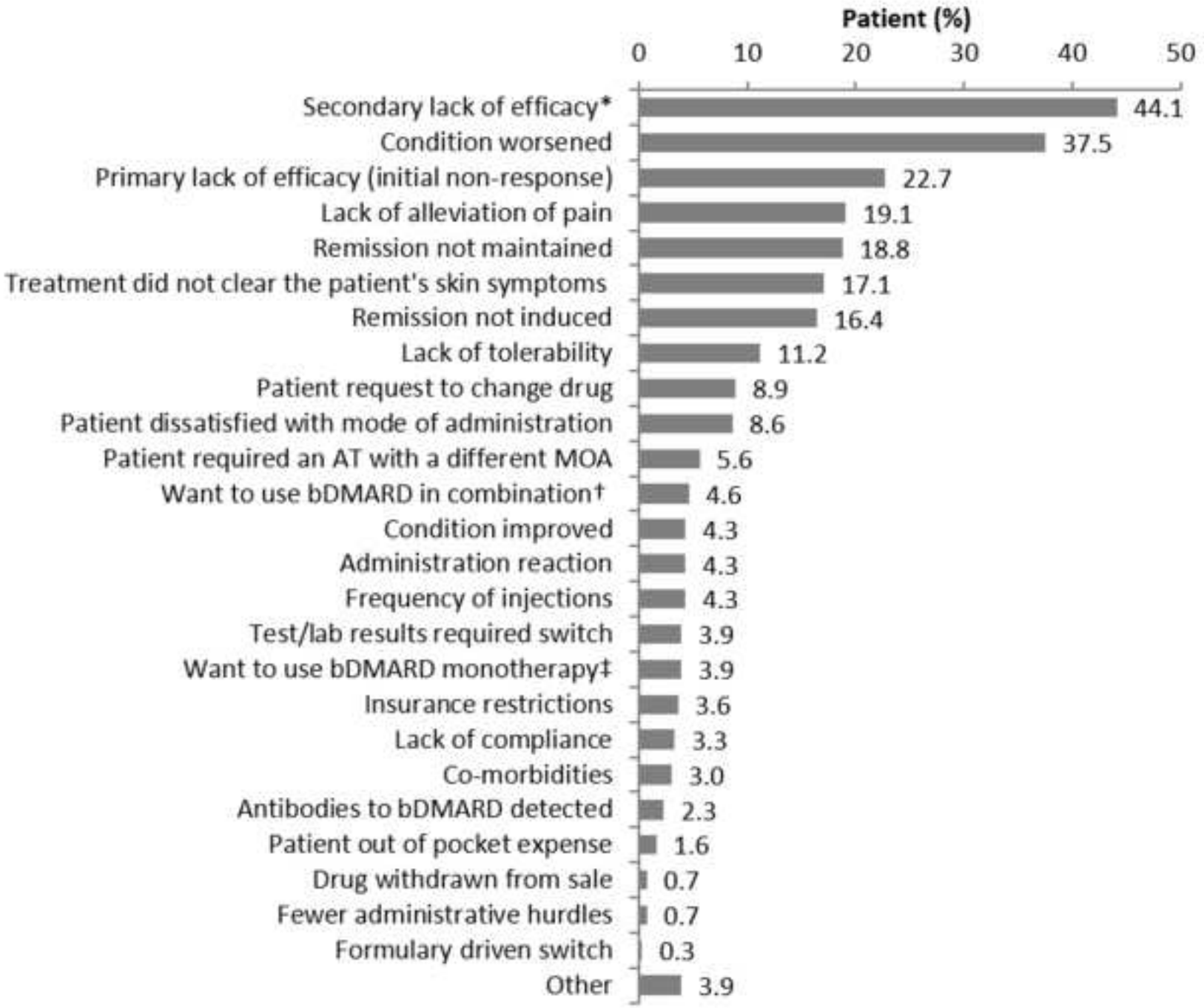


Figure 3



Supplementary Figure 1

Click here to access/download;Supplementary Material;Suppl Figure 1.tif



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