Symptom listed on MDHAQ/MEDI60	DMARD naïve N=149 (28%)	DMARD treated N=379 (72%)	Methotrexate N=153 (29%)
Headache	28%	36%	36%
Unusual fatigue	31%	33%	34%
Anxiety	23%	27%	
Cough	16%	18%	
Dizziness	14%	18%	20%
Hair loss	10%	17%	19%
Nausea	11%	13%	18%
Skin rash or hives	11%	14%	13%
Stomach pain/cramps	9%	16%	15%
Eye problems	9%	13%	14%
Anorexia/weight loss	10%	16%	17%
Diarrhea	5%	9%	8%
Fever	5%	8%	7%
Mouth sores	3%	7%	8%

stomach pain or cramps, eye problems, and/or weight loss; and 5-10% diarrhea, fever, and/or mouth sores (Table). Similar proportions were seen for MTx-treated patients, although anxiety and cough were not listed as specific adverse events.

Conclusion: The MDHAQ symptom checklist may prove valuable to detect adverse events of high-risk medications, including on an electronic MDHAQ, which could be completed at home for 12 weeks after initiation of a new medication as a cost-effective approach for early detection of adverse events.

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Dr. Pincus holds a copyright and trademark on MDHAQ and RAPID3 for which he receives royalties and license fees from profit-making organizations, all of which are used to support further development of quantitative clinical measures for patients and health professionals.

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FRI0518

BIOSIMILAR INFliximab THERAPY IN RHEUMATOID ARTHRITIS, SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS: A LONG-TERM FOLLOW-UP STUDY

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Background:

Objectives: REFLECT study has been carried out to assess in real life the use of CT-P13, the first monoclonal antibody biosimilar to infliximab (IFX) approved in France. Long-term real-life data on CT-P13 use are limited in patients (pts) suffering from rheumatic diseases and inflammatory bowel diseases.

Methods: REFLECT is a multicenter, prospective, observational study conducted in France which aims to describe characteristics of pts' receiving CT-P13 and to assess its safety and effectiveness in real-life conditions. Eligible pts for inclusion were pts (≥ 6 years old) with RA, axSpA, PsA, and inflammatory bowel disease treated with CT-P13. IFX naïve pts (IFX-N) or those having switched from IFX originator to CT-P13 were enrolled (IFX-S). An intermediate result in pts with rheumatic diseases using descriptive statistical analyses from inclusion after 18-month-follow-up period are described below.

Results: From 19 October 2016 to 31 January 2019, 1321 pts were included by 70 centres, and 616 pts with rheumatic diseases were analysed: 132 RA (25.0% males; mean age: 61.5 ± 10.5; median time since diagnosis: 12.9 years), 398 axSpA (59.0%; 48.0 ± 13.1 years; 10.7 years, respectively), and 86 PsA (41.9%; 53.0 ± 14.1 years; 10.3 years). Previous bDMARDs other than IFX were reported in 40.1%, 42.1% and 47.4% of RA, axSpA and PsA pts, respectively. More than 1/3 of pts switched from the IFX originator to CT-P13 (40.2% of RA, 42.7% of axSpA and 35.5% of PsA). At the first administration of CT-P13, the majority of IFX-N pts had active disease (92.0% of RA, 76.4% of axSpA and 55.0% of PsA) compared to IFX-S pts (39.5% of RA, 23.1% of axSpA and 26.3% of PsA). At the first infusion of CT-P13, the median DAS28 scores were 4.8 and 2.4 for RA pts in IFX-N and IFX-S pts, and 4 and 2.2 for PsA pts, respectively. In axSpA pts, the median BASDAI at baseline were 5.6 and 2.4 and the median BASFI was 5.3 and 2.8 in IFX-N and IFX-S pts, respectively. From the first administration of CT-P13 to 18 months follow-up the median DAS 28 decreased (-1 point) in both IFX-N pts and IFX-S for RA pts; for axSpA pts the BASFI and BASDAI scores decreased by -2 and -1, respectively in IFX-N and remained stable in IFX-S.

The analysis of pts suffering from PsA has not been reported due to the small number of patients with a follow-up at 18 months (4 IFX-N pts and 1 IFX-S pts).

Table 1. Reasons for treatment withdrawing

	RA		Ax Spa		PsA	
IFX pts (N)	IFXn (N=16)	IFXs (N=9)	IFXn (N=28)	IFXs (N=30)	IFXn (N=5)	IFXs (N=6)
Missing	0	0	1	0	0	0
Remission	0 (0.0%)	2 (22.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Therapeutic failure	9 (56.3%)	3 (33.3%)	18 (56.3%)	19 (63.3%)	3 (60.0%)	4 (66.7%)
Intolerance	2 (12.5%)	1 (11.1%)	3 (11.1%)	2 (6.7%)	0 (0.0%)	0 (0.0%)
Other	5 (31.3%)	3 (33.3%)	6 (22.2%)	9 (30.0%)	2 (40.0%)	2 (33.3%)

Table 2. Safety data

	RA (N=132)	ax Spa (N=398)	PsA (N=86)
Patients with at least one adverse event (AE)	49 (37.1%)	141 (35.4%)	25 (29.1%)
Patients with at least one serious AE	11 (8.3%)	19 (4.8%)	1 (1.2%)
Patients with at least one allergic infusion reaction†	3 (2.3%)	9 (2.3%)	-
Patients with at least one infection‡	3 (2.3%)	4 (1.0%)	1 (1.2%)

† Including acute and delayed hypersensitivity reactions

‡ Including severe infections, tuberculosis, opportunistic infections, hepatitis.

78.8%, 82.9% and 87.2% remain on treatment with CT-P13 in RA, AxSpA and PsA pts respectively. The reasons for treatment withdrawing are reported in table 1.

The safety data are presented in Table 2.

Conclusion: The results from this long-term follow-up period show that CT-P13 was effective in inducing and maintaining remission in both naïve and switched patients. This real-life study did not highlight any new safety concerns.

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FRI0519

IMPROVING RHEUMATOID ARTHRITIS COMPARATIVE EFFECTIVENESS RESEARCH USING THE TARGET TRIAL EMULATION FRAMEWORK: A SYSTEMATIC REVIEW

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Background: Methods used in observational comparative effectiveness research (CER) are highly variable. Target trial emulation is an intuitive design approach that encourages researchers to formulate their question as a hypothetical randomised controlled trial (RCT), or the "target trial". Using observational data to emulate the target trial helps avoid common biases and has been shown to better align results with actual RCTs.

Objectives: We systematically reviewed observational CER studies in rheumatoid arthritis to provide examples of design issues that might have been avoided by using target trial emulation.

Methods: We searched for head-to-head effectiveness comparisons of biologic DMARDs in RA. Study designs were reviewed for components of target trial emulation: 1) eligibility criteria, 2) treatment strategies, 3) assignment procedures, 4) follow-up period, 5) outcome, 6) causal contrasts of interest (i.e., intention-to-treat or per-protocol effect), and 7) analysis plan. Reported methods were taken as the "emulation" of a corresponding target trial, to assess design issues that might introduce bias.

Results: We found 31 CER studies, the majority of which had one design issue belonging to one of the 7 protocol components (Table 1). The most common issues were: 1) 17 out of 31 studies used post-baseline information to define baseline eligibility (e.g. requiring ≥1 follow-up), which can bias results; 2) 26 out of 31 studies did not declare their causal contrast of interest, which is often made difficult by issue 1 and impacts data analysis and interpretation; and 3) 9 out of 31 studies used statistical selection of confounders rather than pre-defining them, which can also introduce bias (e.g. through adjustment of collider or intermediate variables).

Table 1. Design issues identified in 31 studies and reasons why they do not correspond to well-defined “target trials”

	Design issues identified in study methods	How these issues can be conceptualized in a RCT protocol
1. Eligibility criteria	Post-baseline data requirement (17 out of 31 studies). Differential eligibility for each arm (5 studies).	Impossible to use future data at enrolment. Breaks the notion of one group of people randomized to 2+ arms.
2. Treatment strategies	Mixing prevalent users and new users (1 study). Not defining treatment strategies beyond “initiate drug A at baseline” (31 studies).	Impossible to assign/randomize to “having used drug A for X months” Implied protocol leaves everything up to the treating physician and patient
3. Assignment procedures	Weak substantive justification for confounder selection (31 studies)	Broken randomization (due to insufficient emulation of randomization)
4. Follow-up	Unspecified follow-up duration in longitudinal analyses (5 studies)	Infeasible to conceive an RCT with unspecified duration. Analysis results may lack interpretability.
5. Outcome	Joint outcome of remaining on treatment and having a good response, to avoid missingness (3 studies)	Unusual outcome for RCT although technically possible.
6. Causal contrasts (i.e., ITT or per-protocol effect)	Failure to clarify the estimand (26 studies)	Problem also common in RCTs
7. Analysis plan	ITT-type analysis among those with follow-up Per-protocol analyses did not account for post-baseline selection bias	Deviates from the ITT principle (all randomized should be analysed) Problem also common in RCTs

Conclusion: The majority of observational CER studies in RA have one or more design issues that may introduce bias. Target trial emulation is a structured approach for designing observational CER studies that helps to avoid common biases.

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FRI0520

HOSPITALIZATIONS FOR HEMATOLOGICAL MALIGNANCIES WITH RHEUMATIC DISEASES: A NATIONAL INPATIENT SAMPLE ANALYSIS OF TEN YEARS (2005-2014)

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Background: Several rheumatic conditions have been associated with increased risk of malignancies, especially hematopoietic and lymphoproliferative malignancies. Rheumatoid arthritis has been associated with a relative risk of 1.5-4 for the development of hematological malignancies (HM).¹ A variety of immunosuppressive and immunomodulatory medications have also been linked to increased risk of HM.² Moreover, with advances in the field of biologic agents being used in the treatment of rheumatic diseases (RD), the landscape keeps changing. To our knowledge, data on general trends of HM as well as in RD is limited.

Objectives: Our study aimed to determine the trends of hospitalizations for HM in patients with RD.

Methods: We identified admissions with HM with underlying RD (including rheumatoid arthritis, systemic lupus erythematosus, inflammatory myositis, scleroderma, polymyalgia rheumatica, and connective tissue disease) from the NIS database using International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes from years 2005 to 2014. The primary outcome was the trends in hospitalizations for HM. We studied the yearly trends and the types of HM among hospitalizations with or without RD.

Results: 906,556 weighted hospitalizations were estimated for HM, and amongst those, 17,675 had underlying RD. The demographic analysis suggested that the average age of hospitalizations with HM and RD was higher, were more often females, and a higher number of comorbidities (Table 1). The average number of admissions remained stable for HM with and without HM, as described in Graph 1. There was a significant difference in the frequency of various subtypes in patients with and without RD (Graph 2). Non-Hodgkin's Lymphoma was the most common subtype in HM without and with RD (35.8% and 47.14%).

Table 1. Baseline Demographics of Hospitalizations for HM with and without RD

Characteristics	HM without RD	HM with RD	p value
Age (in years ± SD)	62.05 ± 0.23	67.41 ± 0.29	<0.05
Gender (%)			<0.05
Males	55.99	33.35	
Female	44.01	66.65	
Race (%)			<0.05
White	71.24	75.88	
Black	12.27	11.31	
Hispanic	10.21	7.62	
Asian or Pacific Islander	2.66	2.01	
Native American	0.43	0.62	
Other	3.18	2.55	
Charlson Category (%)			<0.05
2	55.07	3.76	
3	21.83	46.93	
4	11.55	23.71	
5	5.54	12.88	
≥6	6.01	12.73	
Type of Insurance (%)			<0.05
Medicare	49.49	66.35	
Medicaid	10.93	6.04	
Private	35.8	26.19	
Self-Pay	3.78	1.42

Graph 1. Hospitalizations per year for Hematologic Malignancies With Rheumatic Diseases 2005-2014 **Graph 2.** Types Of Hematological Malignancies In Hospitalizations With And Without Rheumatic Diseases (%)

Conclusion: To our knowledge, this is the first study to analyze trends in HM with RD. There has not been any significant change in the number of hospitalizations for HM from 2005-2014 with or without RD. The most common HM in admissions with RD were Non-Hodgkin's Lymphomas (NHL) and myeloid leukemias, followed by multiple myeloma. The trends suggest no significant change in subtypes of HM over the study period.