No increased risk of falls in patients treated with biologics compared to those under csDMARDs

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Conclusions

None of the inferential analyses could demonstrate an increased risk of falling for any of the bDMARDs compared to csDMARDs. Although descriptive analyses indicated an earlier fall event in RA patients treated with second-/third line biologics, these results could be explained by their particular characteristics that override the effects of those treatements.

Background

Adults with rheumatoid arthritis (RA) have an increased risk of falling. Previous studies on causes of falls have not sufficiently considered the effects of biologic disease-modifying antirheumatic drugs (bDMARDs), and a risk analysis of the individual substances has been lacking until now.

Objective

To analyze the fall risk under exposure with (b)DMARDs in comparison to conventional synthetic (cs)DMARDs taking co-medication and other risk factors such as disease activity and comorbidities into account.

Patients and Methods

Data of RA patients observed in RABBIT (***R***heumatoid ***A***rthritis: O***b***servation of ***bi****ologic* ***t***herapy) cohort from 01/2009 - 02/2018 with a follow-up of up to 5 years was used for the analysis. In accordance with consensus guidelines, a fall was defined as “an unexpected event in which participants come to rest on the ground, floor or other lower level” [1]. Effects of bDMARDs were examined using “inverse probability weighting“ with time-varying treatment on a monthly basis. Directed acyclic graphs were applied to support causal considerations.

[1] Lamb SE, et al. Journal of the American Geriatrics Society. 2005;53(9):1618-22.111
[2] Brenton-Rule A, et al.Seminars in Arthritis and Rheumatism. 2015;44(4):389-98.

Results

The percentage of patients with falls (2.7%) was significantly lower than the previously reported 10% and 50% [2]. This underreporting is explained by the fact that falls in RABBIT are reported by the physicians and are not recorded in patient diaries.
Falls occurred with older age, longer disease duration, poorer physical function and higher DAS28. Patients with a higher number of comorbidities had a significantly higher risk of falling. The number of patients treated with opiods was higher in the fall group and fallers had higher glucocorticoid doses. However, the values for pain and fatigue were comparable between the two groups.

Table 1: Baseline characteristics of fallers versus non-fallers	Faller n=263	Non - Faller n=9,405
Age [years]	62.9 ± 11.9	57.3 ± 12.6
BMI, kg/m²	27.4 ± 5.8	27.3± 5.5
Female patients, %	79.5	74.2
Disease duration [years]	10.8 ± 9.8	8.7 ± 8.5
Rheumatoid factor +, %	59.7	65.3
DAS28-ESR	5 ± 1.3	4.8 ± 1.3
Mean physical capacity [0-100], FFbH	61.2 ± 24.2	67.3± 22.7
Pain, 0 – 10 scale	5.8 ± 2.3	5.8 ± 2.3
Fatigue, 0 – 10 scale	5.1± 2.7	5.2 ± 2.7
No. of comorbidities	3.4 ± 3	2.2 ± 2.2
Arterial Hypertension, %	54	41.8
Chronic renal disease, %	9.9	4.7
Degenerative joints, %	25.9	19.9
Degenerative spinal disease, %	24.3	16.1
Diabetes, %	17.1	11.5
Heart failure, %	4.6	2
Osteoporosis, %	33.5	14.4
Opiod, yes %	8.4	3.2
Glucocorticoid dosage [mg/d]	6 ± 5.1	5.4 ± 6.3

The descriptive analysis showed that patients with second / third line biologics had a shorter duration from the inclusion into RABBIT to the fall event than patients treated with other DMARDs. However, this group comprised older patients more severely affected by RA.

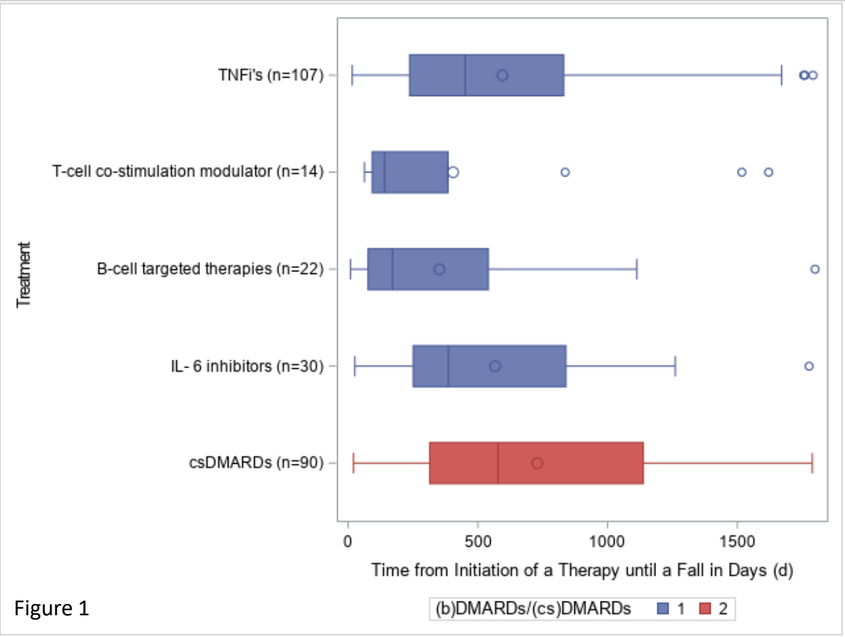

Figure 1

None of the regression models showed an increased risk for biologics compared to csDMARDs.

Table 2: Effects of bDMARDs vs. csDMARDs *(Reference)*	Univariate HR (95% CI)	Multivariate HR (95% CI)	Weighted HR** (95% CI)
TNFi‘s	1.12 (0.85; 1.48)	1.20 (0.90; 1.61)	1.16 (0.87; 1.55)
T-cell co-stimulation modulator	1.00 (0.57; 1.74)	0.87 (0.49; 1.54)	1.10 (0.63; 1.90)
B-cell targeted therapies	1.39 (0.88; 2.22)	1.28 (0.79; 2.08)	1.15 (0.68; 1.95)
IL- 6 inhibitors	0.88 (0.59; 1.33)	0.96 (0.63; 1.46)	0.78 (0.50; 1.21)

***IPW include: age, gender, disease duration, rheumatoid factor, joint surgery, pain, fatigue, FFbH, DAS28, count of csDMARDs, glucocorticoid dosage, opiods, analgesics, number of comorbidities, cardiovascular/ bone/ psychological/ lung/ renal/ liver diseases, osteoporosis, diabetes, malignancy*

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