Switching from synthetic to biologic DMARDs - is there an insufficient use of methotrexate?

Baganz L[1], Richter A[1], Meißner Y[1], Schneider M[2], Liebhaber A[3], Schwarze I[4], Strangfeld A[1], Zink A[1,5]

[1]German Rheumatism Research Center, Berlin, [2]Scientific Advisory Board, Düsseldorf, [3]Rheumatologist, Halle (Saale), [4]Rheumatologist, Leipzig, [5]Charité University Medicine, Berlin

DRFZ BERLIN
Deutsches Rheuma-Forschungszentrum
Ein Institut der Leibniz-Gemeinschaft

RABBIT

German Rheumatism Research Center, Epidemiology Unit — **ACR 2017 No. 1430**

Background & Objectives

An US american study suggested that patients with rheumatoid arthritis (RA) who do not respond adequately to methotrexate (MTX) are switched too quickly to a biologic DMARD (bDMARD)[1]. We were interested in whether this also applies to Germany and investigated MTX doses, treatment strategies and escalation as well as the influence of the route of administration on switching, using real-world data.

[1] Rohr et al. Arthritis Care & Res 2016; 69:794-800

Methods

- Data from the RABBIT register with database closing date on 30.4.2017
- Only biologic naïve patients with at least one DMARD failure,–enrolled with the start of a new MTX monotherapy (Mono) or MTX + one other csDMARD (Combi) and at least one follow-up
- Descriptive analysis of patients (n=1773) in the first year of observation
- Subanalysis: Descriptive investigation of patients with indication of the MTX route of administration (n=1091; oral (oMTX), subcutaneous (scMTX)).

Results

A total of 410 patients (23%) were enrolled with MTX monotherapy. Half of these received sulfasalazine before inclusion, one in four hydroxychloroquine and 14% leflunomide. In the 1363 patients with Combi therapy, leflunomide (57%), sulfasalazine (22%) and hydroxychloroquine (19%) were the most frequent partners to MTX. Combi patients were more likely to have positive rheumatoid factor and more frequently showed erosive changes (Table 1).

	Mono	*Combi*
N (%)	410 (23)	1363 (77)
Female patients (%)	79	71
Age in years	58	58
Disease duration in years	6,3	5,7
Rheumatoid factor positive (%)	46	58
Erosions (%)	22	30
DAS28	4,5	4,4
% of full physical function	71	72
No. csDMARD failures	1,2	1,3
GC in mg/d (mean over 6 months)	2,9	3,0

Table 1: Patient characteristics at baseline

Numbers are means unless otherwise specified.

Treatment strategies in the first year of observation

In the majority of patients receiving MTX monotherapy, treatment was not escalated in the first year. Of the patients who directly switched to a bDMARD, one in five received MTX doses >20 mg/week already at baseline (figure 1).

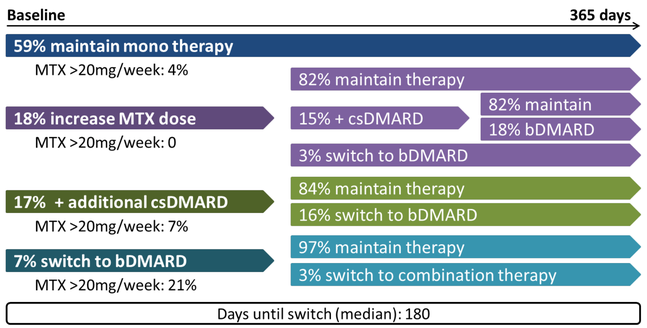

Figure 1: Treatment strategies in patients under MTX monotherapy

Compared to patients undergoing monotherapy, Combi therapy patients remained on their baseline therapy more often. However, if the response rate was not sufficient, dose escalation was less frequent and a switch to a biologic more frequent (figure 2).

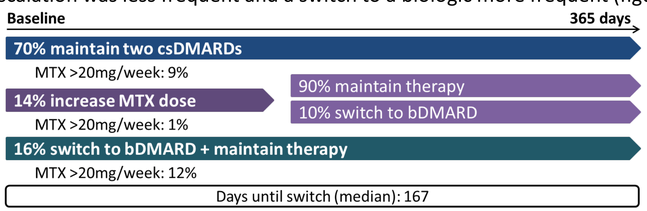

Figure 2: Treatment strategies in patients under MTX + one other csDMARD

Regardless of the baseline therapy, the glucocorticoid dose was frequently adjusted prior to the switch to a biologic: at inclusion and before switch to a biologic agent, the proportions of patients with doses >5 mg/d were 15% and 25%, respectively. In patients who did not switch to a biologic in the first year, this increase was not observed (13% with glucocorticoids >5 mg/d during follow-up vs. 14% at baseline).

Subanalysis: Route of MTX administration

Of the 1091 patients with information on the route of administration, 56% received oMTX and 44% scMTX. One in five scMTX patients switched to a biologic (oMTX: 10%). These patients received on average 17 mg MTX/week at baseline, 15% received doses of >20 mg/week. Thus higher doses were more frequent in scMTX than in oMTX patients who switched to a biologic (mean: 14.6 mg/week; 3% >20 mg/week). In addition, scMTX patients received more often glucocorticoid doses >5 mg/d (19 vs. 11% for oMTX).

Stop of MTX therapy

In the first year of observation, 428 patients (24%) discontinued MTX, in particular patients with doses ≤7.5 mg/week (Table 2). MTX was most frequently stopped due to adverse events, especially nausea and vomiting (17%), increased hepatic enzymes (12%), infections (7%), other gastrointestinal complaints (7%) and alopecia (4%).

	MTX-Dose (mg/week)			
	≤7,5	*<7,5 - ≤15*	*<15 - ≤20*	*>20*
Stop of MTX (%)	29	25	18	21
Days until stop, median	83	120	99	87
Reasons				
Adverse events (%)	64	66	75	70
Effectiveness failure (%)	20	20	23	33
Remission (%)	16	8	7	3
Non-Compliance (%)	12	8	5	6

Table 2: Stop of MTX-therapy with reasons for discontinuation (multiple answers possible).

Conclusion

If patients with rheumatoid arthritis respond insufficiently to MTX, German rheumatologists use differentiated strategies such as MTX dose increase, combination with additional csDMARDs or the increase of glucocorticoid dose. Too fast switching to a biologic was not found in the data of the RABBIT register. The observation from the USA could not be confirmed.

We thank all participating rheumatologists, especially those who have enrolled the highest number of patients: Kaufmann J, Klopsch T, Eisterhues C, Kaufmann J, Braun J, Liebhaber A, Rockwitz K, Schwarze I, Krause A, Tony H, Zinke S, Gräßler A, Berger S, Remstedt S, Wilden E, Ochs W, Haas F, Burmester G, Bruckner A, Richter C, Röser M, Kühne C, Bergerhausen H, Wassenberg S, Balzer S, Bohl-Bühler M, Harmuth W, Fricke-Wagner H, Wiesmüller G, Lebender S, Bussmann A, Ständer E, Kellner H, Edelmann E, Stille C, Tremel H, Körber H, Meier L, Hamann F, Müller L, Krummel-Lorenz B, Krüger K, Kapelle A, Thiele A, Möbius C, Pick D, Kekow J, Feuchtenberger M, Schmitt-Haendle M, Karberg K, Brandt H, Seifert A, Manger K, Weiß K, Prothmann U, Aringer M, Krause D, Müller-Ladner U, Richter C, Zänker M, Burmester G, Backhaus M, Reck A, Herzberg C, Schulze-Koops H, Grünke M, Baumann C, Eidner T, Dockhorn R, Herzer P, Heel N, Dahmen G, Wiesent F, Zeh G, Heel N, Roßbach A, Menne H, Sörensen H, Demary W, von Hinüber U, Winkler K, Schneider M, Bussmann A, Gause A, Euler H, Streibl H, Blank N, Häntsch J, Alliger K, Max R, Gause A, Moosig F, Bruns A, Iking-Konert C

Funding

RABBIT is funded by a joint, unconditional grant from AbbVie, Bristol-Myers Squibb, Celltrion, Hexal, Lilly, MSD Sharp & Dohme, Pfizer, Roche, Samsung und UCB.
www.biologika-register.de

baganz@ drfz.de