How closely do German rheumatologists follow the EULAR recommendations for the management of rheumatoid arthritis when making therapeutic decisions?

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Background

EULAR developed recommendations for the management of rheumatoid arthritis (RA) suggesting treatment escalation and changes at different stages of the disease to reach at least low disease activity (table 1). The recommendation to add a bDMARD (or Janus kinase inhibitor [JAKi] since 2016) after the first csDMARD had failed and if at least one poor prognostic factors (PPF) is present, was strengthened in 2019.
The German recommendations of 2018 even go beyond the EULAR recommendations by suggesting treatment escalation also in the case of high disease activity.

Table 1: Overview of EULAR and German treatment recommendations.

Recommendation if treatment target was not achieved with first csDMARD in case of ...		
EULAR	... absent PPF	... present PPF
2013[1]	Change to another csDMARD strategy should be considered	Addition of a bDMARD *should be considered*
2016[2]	Another csDMARD should be considered	Addition of a bDMARD or a tsDMARD *should be considered*; current practice would be to start a bDMARD
2019[3]	Another csDMARD should be considered	A bDMARD or a tsDMARD *should be added*
DGRh	... absent PPF and moderate disease activity	... present PPF and/or high disease activity
2018[4]	Combination of several csDMARDs can be used	Combination of a csDMARD with a bDMARD or tsDMARD should be used

Objectives: How closely are EULAR recommendations followed in daily rheumatologic practice in Germany?

Patients & Methods

Data Source: German long-term observational cohort study RABBIT

Enrolment criteria:
- Rheumatologist confirmed diagnosis of RA
- Start of bDMARD/JAKi treatment, or csDMARD after at least one previous csDMARD

Patient selection:
- Treatment start with csDMARD, bDMARD or JAKi between 01/2014 and 04/2021
- At least moderate disease activity (DAS28 ≥3.2)

Analyses:
- Stratification of time periods (according to publication of EULAR recommendations) from [I] 01/2014 – 12/2016, [II] 01/2017 – 06/2020 and [III] 07/2020 – 04/2021
- Patient stratification by prior treatments and by the presence of PPF (≥4 swollen joints, positive rheumatoid factor or ACPA, erosions)

Results

Among the 15,150 eligible patients with RA, 2,922 treatments were initiated with csDMARD, bDMARD or JAKi in period [I], 4,580 in [II] and 415 in [III] (table 2).

The proportion of patients with one previous csDMARD and ≥1 PPF who – in agreement with the recommendations – switched to bDMARD or JAKi, increased from 30% (only bDMARDs) in period [I] to 68% (bDMARDs + JAKi) in period [III]. The proportions were even higher in patients with two previous csDMARDs (86% in [I], 93% in [III]).

Table 2: Number and percentages of treatment changes at different stages of the disease.

Patients with	1 previous csDMARD & no PPF	1 previous csDMARD & ≥1 PPF	2 previous csDMARDs	1 previous bDMARD/JAKi	≥2 previous bDMARDs/JAKi
EULAR recommends to	change/add csDMARD	add bDMARD/ JAKi	add bDMARD/ JAKi	change to another bDMARD/JAKi	
Total numbers of treatment changes	61	2073	2220	1700	1863
Period [I] 01/2014 – 12/2016* N=2,922	n=25	n=848	n=986	n=543	n=520
csDMARD	21 (84.0%)	594 (70.0%)	134 (13.6%)	199 (36.6%)	275 (52.9%)
bDMARD	4 (16.0%)	254 (30.0%)	852 (86.4%)	344 (63.4%)	245 (47.1%)
Period [II] 01/2017 – 06/2020 N=4,580	n=32	n=1,090	n=1,136	n=1,054	n=1,268
csDMARD	16 (50.0%)	469 (43.0%)	96 (8.5%)	261 (24.8%)	274 (21.6%)
bDMARD	13 (40.6%)	509 (46.7%)	822 (72.4%)	403 (38.2%)	288 (22.7%)
JAKi	3 (9.4%)	112 (10.3%)	218 (19.2%)	390 (37.0%)	706 (55.7%)
Period [III] 07/2020 – 04/2021 N=415	n=4	n=135	n=98	n=103	n=75
csDMARD	0	43 (31.9%)	7 (7.1%)	15 (14.6%)	9 (12.0%)
bDMARD	1 (25.0%)	64 (47.4%)	60 (61.2%)	36 (35.0%)	23 (30.7%)
JAKi	3 (75.0%)	28 (20.7%)	31 (31.6%)	52 (50.5%)	43 (57.3%)

*EULAR treatment recommendations are framed in pink. *JAKi were not available.*

Conclusion

- ✓ JAKi have become more established, especially in bionaive patients, but have not yet reached the significance of bDMARDs in certain patient groups.
- ✓ The early decision for a bDMARD or JAKi has been made more frequently in recent years. Still, one third of patients did not receive the recommended treatment escalation after the first csDMARD and at least one PPF.
- ✓ We cannot conclude from the data which considerations led to the decision not to escalate.
- ✓ Of note, German rheumatologists should rather follow the German treatment guidelines, which are, however, very similar to the EULAR recommendations.

References: [1]Smolen et al. Ann Rheum Dis 2014; 73: 492-509. [2] Smolen et al. Ann Rheum Dis 2017; 76: 960-977. [3] Smolen et al. Ann Rheum Dis 2020; 79: 685-699. [4]Fiehn et al. Z Rheumatol 2018; 77(Suppl 2):35-53.

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