Early Remission Is a Realistic Target in a Majority of Patients with DMARD-naive Rheumatoid Arthritis

Tuomas Rannio, Juha Asikainen, Arto Kokko, Pekka Hannonen, and Tuulikki Sokka

ABSTRACT. ***Objective.*** We analyzed remission rates at 3 and 12 months in patients with rheumatoid arthritis (RA) who were naive for disease-modifying antirheumatic drugs (DMARD) and who were treated in a Finnish rheumatology clinic from 2008 to 2011. We compared remission rates and drug treatments between patients with RA and patients with undifferentiated arthritis (UA).

Methods. Data from all DMARD-naive RA and UA patients from the healthcare district were collected using software that includes demographic and clinical characteristics, disease activity, medications, and patient-reported outcomes. Our rheumatology clinic applies the treat-to-target principle, electronic monitoring of patients, and multidisciplinary care.

Results. Out of 409 patients, 406 had data for classification by the 2010 RA criteria of the American College of Rheumatology/European League Against Rheumatism. A total of 68% were female, and mean age (SD) was 58 (16) years. Respectively, 56%, 60%, and 68% were positive for anticyclic citrullinated peptide antibodies (anti-CCP), rheumatoid factor (RF), and RF/anti-CCP, and 19% had erosive disease. The median (interquartile range) duration of symptoms was 6 (4–12) months. A total of 310 were classified as RA and 96 as UA. The patients with UA were younger, had better functional status and lower disease activity, and were more often seronegative than the patients with RA. The 28-joint Disease Activity Score (3 variables) remission rates of RA and UA patients at 3 months were 67% and 58% ($p = 0.13$), and at 12 months, 71% and 79%, respectively ($p = 0.16$). Sustained remission was observed in 57%/56% of RA/UA patients. Patients with RA used more conventional synthetic DMARD combinations than did patients with UA. None used biological DMARD at 3 months, and only 2.7%/1.1% of the patients (RA/UA) used them at 12 months ($p = 0.36$).

Conclusion. Remarkably high remission rates are achievable in real-world DMARD-naive patients with RA or UA. (J Rheumatol First Release February 15 2016; doi:10.3899/jrheum.141480)

Key Indexing Terms:
RHEUMATOID ARTHRITIS OUTCOMES CLINICAL MONITORING DISEASE ACTIVITY

Treatment of rheumatoid arthritis (RA) has changed during the past 2 decades as awareness of the benefits of early targeted treatment[1,2,3] has increased. Early remission has been widely accepted to be the therapeutic target in RA. Effective biologic disease-modifying antirheumatic drugs (bDMARD) have become available and a treatment approach including tight control and quantitative monitoring of disease activity has been demonstrated to facilitate the attainment of the target. Several randomized controlled trials have demonstrated excellent and comparable[4,5] remission rates irrespective of whether conventional synthetic DMARD (csDMARD) in combinations[6,7] or bDMARD are used[8]. In general, the use of csDMARD combinations has not reached wide popularity in clinical practice worldwide; rheumatologists find it challenging to use csDMARD combinations[9,10,11].

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Historically, remission rates were low in patients who received usual care[12]. Reportedly, the average 28-joint Disease Activity Score (DAS28) remission rate in clinical observational studies from 1996 to 2008 was 29%[13]. In the Quantitative Standard Monitoring of patients with RA study (QUEST-RA), reflecting usual rheumatology care in 25 countries, the cross-sectional DAS28 remission rate varied between 7.7% and 41% across countries[14]. In the Canadian Early Arthritis Cohort (CATCH) study of 15 sites, remission rates defined with the Boolean and the DAS28 criteria were 9.6% and 30% at Month 3 and 20% and 45% at Month 12, respectively[15].

The objective of our study was to analyze the use of DMARD and the remission rates at 3 and 12 months in DMARD-naive patients treated in the Jyväskylä (Finland) outpatient rheumatology clinic from 2008 to 2011. Further, we examined whether the results differed in patients classified as having RA versus undifferentiated arthritis (UA) according to the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria[16].

MATERIALS AND METHODS

Patients. Data from all DMARD-naive patients with a new clinical diagnosis of RA or UA in Jyväskylä Central hospital rheumatology outpatient clinic from 2008 to 2011 were collected using GoTreatIt software. The data included demographic and clinical characteristics and measures reflecting disease activity, medications, and patient-reported outcomes (PRO). Diagnoses other than RA or UA were excluded. The rheumatology unit covers rheumatology care in the healthcare district with a population of 275,000.

Monitoring. The early treatment protocol includes clinical visits at 0, 3, 6, 12, and at 24 months with a multiprofessional team consisting of a rheumatologist, a nurse specialist, a physical therapist, an occupational therapist, and a social worker. Prior to each visit, the patient completes a self-report health questionnaire on a touch screen. The health questionnaire comprises Health Assessment Questionnaire (HAQ), duration of morning stiffness, and visual analog scales (VAS, 0-100 mm) for pain, fatigue, and patient's global assessment (PtGA). The physician records tender and swollen joint counts on an electronic homunculus (46 joints), and estimates the overall disease activity (physician's global assessment, PGA) on VAS (0-100). Data are available for health professionals as calculated scores such as HAQ and DAS28, and as raw data, and thus can be used as an aid for clinical decision making[17].

Treatment. Our treatment strategy follows the treat-to-target principles[9], electronic quantitative monitoring of disease activity, and multidisciplinary care. The goal is to reach a rapid and sustained remission.

The Finnish national treatment guidelines emphasize the use of csDMARD in combinations in early treatment strategy, implying excellent results of the national combination treatment trials[6,7]. In our cohort, the medication was individually decided by the treating rheumatologist in cooperation with the patient. Intraarticular glucocorticoid injections were used and encouraged when a swollen joint was detected.

The recorded variables are depicted and defined in Table 1.

Ethics approval. All data were obtained as part of routine clinical care in accordance with the national regulations regarding ethical issues[18].

Definitions of remission. Remission was defined as DAS28 < 2.6, and as ACR/EULAR Boolean-based definition, which required a tender joint count in 28 joints (TJC28) ≤ 1, swollen joint count in 28 joints (SJC28) ≤ 1, C-reactive protein (CRP) ≤ 1 mg/dl and PtGA (on 0 to 10 scale) ≤ 1[19]. Sustained remission was defined as remission at both the 3-month and 12-month visits.

Statistical analysis. Clinical and treatment variables were compared between patients with RA and patients with UA using the Mann-Whitney U test or Pearson chi-squared/Fisher's exact test when applicable. The level of significance was set at a p value < 0.05. Statistical analysis involved the use of IBM SPSS Statistics 21.0.

RESULTS

Patient and disease characteristics. Out of the 409 patients, 406 had data for classification according to the 2010 ACR/EULAR RA criteria and were included in the statistical analyses. At baseline, a total of 68% of the patients were female, and the patients' mean age (SD) at diagnosis was 58 (16) years. Respectively, 56%, 60%, and 68% were positive for anticyclic citrullinated peptide antibodies (anti-CCP), rheumatoid factor (RF), and RF/anti-CCP, and 19% had erosive disease. The median [interquartile range (IQR)] duration of symptoms was 6 (4–12) months. A total of 310 cases were classified as RA and 96 as UA.

Disease activity and PRO at baseline are described in Table 2. The patients with UA were younger, had better functional status, lower disease activity, and were more often seronegative than the patients with RA. Data were available from 73% to 100% of the patients except for PGA (39%–59%).

Disease activity at 3 months and 12 months is depicted in Table 3. In both patient groups, a majority of patients achieved DAS28 remission.

Remission rates at 3 months and 12 months. The DAS28(3),

Table 1. Description of variables.

Variable	Definition
PGA	Doctor global assessment of disease activity on 0-100 mm visual analog scale (VAS); higher scores imply more activity
DAS28	= 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.70*Ln(ESR) + 0.014 * PTglobal, range 0–9.4; cutpoints for remission, low, moderate, and high disease activity 2.6, 3.2, 5.1
DAS28(3 variables)	= [0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.70*Ln(ESR)]*1.08 + 0.16, range 0–9.4; cutpoints for disease activity: remission, DAS28 < 2.6; low, DAS28 2.6 to < 3.2; moderate, DAS28 3.2 to 5.1; high, DAS28 > 5.1
DAS28 remission	< 2.6
DAS28(3) remission	< 2.6
Boolean remission	(TJC28) ≤ 1, (SJC28) ≤ 1, CRP ≤ 1 mg/dl and (PtGA, on 0 to 10 scale) ≤ 1.
Boolean(3 variables) remission	(TJC28) ≤ 1, (SJC28) ≤ 1 and (PtGA, on 0 to 10 scale) ≤ 1.
Patient-reported outcomes	
HAQ	Range 0–3; higher scores imply more disability
Pain	Pain on 0–100 mm VAS
PtGA	Patient assessment of global health on 0–100 mm VAS
Fatigue	Fatigue on 0–100 VAS
Morning stiffness	Morning stiffness in 0–10 h

HAQ: Health Assessment Questionnaire; DAS28: 28-joint Disease Activity Score; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; PGA: physician's global assessment; TJC28: 28-joint tender joint count; SJC28: 28-joint swollen joint count; PtGA: patient's global assessment; VAS: visual analog scale.

Table 2. Description of baseline demographic and clinical characteristics of the 406 DMARD-naive patients.

Characteristics	Patients with RA		Patients with UA		p
No. patients	310	%*	96	%*	
Demographic variables					
Female, n (%)	215 (69)	100	59 (62)	100	0.15
Age, yrs, mean (SD)	60 (16)	100	52 (16)	100	< 0.001
Duration of symptoms, months, median (IQR)	6 (3–12)	98	6 (4–12)	99	0.88
Disease characteristics					
RF-positive, n (%)	219 (71)	100	23 (24)	100	< 0.001
Anti-CCP-positive, n (%)	207 (67)	100	21 (22)	99	< 0.001
RF/anti-CCP-positive, n (%)	249 (80)	100	28 (30)	99	< 0.001
Erosive disease at baseline, n (%)	74 (24.3)	98	0	100	< 0.001
PRO and disease activity at baseline					
HAQ (0–3), median (IQR)	1.0 (0.5–1.4)	76	0.6 (0.3–1.1)	77	0.002
Pain (0–100), median (IQR)	50 (28–64)	78	40 (24–61)	80	0.075
Fatigue (0–100), median (IQR)	42 (18–65)	75	37 (20–62)	76	0.44
Morning stiffness, 0–10 h, median (IQR)	1.0 (0.3–3)	78	1.0 (0.3–2)	77	0.24
DAS28, mean (SD)	4.3 (1.3)	73	3.2 (1.3)	74	< 0.001
DAS28(3 variables), mean (SD)	4.1 (1.3)	95	3.1 (1.2)	97	< 0.001
CRP, mg/l, mean (SD)	17 (24)	100	14 (21)	100	0.048
ESR, mm/h, mean (SD)	26 (21)	99	21 (22)	100	0.002
PtGA (0–100), median (IQR)	46 (27–57)	76	21 (14–30)	76	0.001
PGA (0–100), median (IQR)	35 (20–50)	45	21 (14–30)	44	< 0.001
TJC28, mean (SD)	5.1 (4.9)	95	2.3 (2.4)	97	< 0.001
SJC28, mean (SD)	5.3 (5.0)	95	1.8 (2.1)	98	< 0.001
TJC46, mean (SD)	8.9 (7.0)	95	4.3 (3.5)	97	< 0.001
SJC46, mean (SD)	8.6 (6.7)	95	2.9 (2.9)	98	< 0.001

* Percentages refer to the percentage of patients with data available. DMARD: disease-modifying antirheumatic drug; RA: rheumatoid arthritis; UA: undifferentiated arthritis; IQR: interquartile range; RF: rheumatoid factor; anti-CCP: anticyclic citrullinated peptide antibodies; PRO: patient-reported outcomes; HAQ: Health Assessment Questionnaire; DAS28: 28-joint Disease Activity Score; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; PtGA: patient's global assessment; PGA: physician's global assessment; TJC28: 28-joint tender joint count; SJC28: 28-joint swollen joint count; TJC46: 46-joint TJC; SJC46: 46-joint SJC.

referring to 3 variables, remission rates of RA and UA patients at 3 months were 67% and 58% (p = 0.13), and respectively at 12 months, 71% and 79% (p = 0.16), as depicted in Table 3 and Figure 1. Further, remission rates were similar regardless of RF/anti-CCP status and erosion status at baseline, except at 12 months: more RF/anti-CCP–positive versus negative patients were in Boolean remission (Table 4).

A total of 28% of the patients (data for n = 340) achieved the strict ACR/EULAR 2011 Boolean remission criteria[19] at 12 months. Sustained DAS28(3; Table 1) and Boolean remissions were observed in 57% and 56% (p = 0.95), and 16% and 12% (p = 0.42) of patients with RA and UA, respectively. Data for sustained DAS28(3)/Boolean remissions were available from 80%/71% of RA, and 67%/63% of patients with UA, respectively.

PRO at 3 and 12 months are shown in Table 3. No statistically significant differences between the groups could be found in any of the PRO. PRO data were available from > 75% of the patients.

Patients with missing data. In our study, disease activity data were available in 361 patients at 3 months and 368 at 12 months, i.e., 38 patients missed the 12-month visit. Among these 38 patients, 27 (8.7% of patients with RA) were classified as RA, and 11 as UA (12% of patients with UA). At baseline, these 27 patients with RA were similar to the rest of the RA group (n = 283) in erythrocyte sedimentation rate (ESR), CRP, age, HAQ, erosion, RF/anti-CCP, symptom duration, and DAS28 status. There was 1 exception: sex (52% vs 71% female, respectively). Of the 27 with missing data at 12 months, 15 had later visits, 4 had died, 3 had many comorbidities and were too old for visits, 1 was too severely affected by dementia, 1 diagnosis was later changed to systemic lupus erythematosus and another to polymyalgia rheumatica, and 2 patients were lost to further followup. Also in the UA group, no differences in baseline characteristics were found between patients with and those lacking the 12-month visit data. Out of the 8 patients with missing data at 12 months, 6 had later visits, and in 2 patients diagnosis was changed to gout in 1 and erosive osteoarthritis in the other. At the subsequent visit, 17-60 months after diagnosis, 67% of 21 patients were in DAS28(3) remission, including 60% of 15 patients with RA versus 83% of the 6 patients with UA (p = 0.61).

Medications. Our patients with RA used more csDMARD combinations than did the patients with UA. Between 0 and 3 months, 53%, and at 12 months, 58% of patients with RA used combinations of csDMARD. Between 0 and 3 months, 20% of patients with RA used a methotrexate (MTX)-based

Table 3. Disease activity, patient-reported outcomes, and medications used during 12-month followup.

No. Patients	Patients with RA, 3 Months 310	%*	Patients with UA, 3 Months 96	%*	p	Patients with RA, 12 Months 310	%*	Patients with UA, 12 Months 96	%*	p
DAS28, mean (SD)	2.3 (1.1)	76	2.4 (1.0)	68	0.39	2.1 (1.0)	80	1.9 (0.9)	80	0.13
DAS28(3), mean (SD)	2.2 (1.1)	87	2.3 (0.9)	79	0.65	2.1 (0.9)	91	1.8 (0.9)	84	0.12
PtGA (0–100), median (IQR)	25 (5–46)	79	18 (5–37)	69	0.34	23 (6–47)	80	21 (9–39)	84	0.81
PGA (0–100), median (IQR)	5 (0–20)	53	10 (0.5–20)	39	0.20	5 (0–15)	65	5 (0–15)	59	0.75
SJC28, mean (SD)	0.9 (2.1)	89	0.6 (1.4)	80	0.75	0.5 (1.4)	91	0.5 (1.2)	88	0.57
TJC28, mean (SD)	1.1 (2.6)	89	1.1 (2.1)	80	0.20	0.7 (1.8)	91	0.7 (1.6)	88	0.76
SJC46, mean (SD)	1.7 (3.3)	89	1.1 (2.0)	80	0.54	0.9 (2.2)	90	0.6 (1.6)	88	0.16
TJC46, mean (SD)	2.3 (4.6)	88	2.1 (3.7)	80	0.38	1.5 (3.3)	90	1.1 (2.3)	88	0.75
CRP, mg/l, mean (SD)	6 (16)	90	5 (8)	80	0.40	6 (17)	91	6 (17)	85	0.76
ESR, mm/h, mean (SD)	13 (13)	89	12 (13)	80	0.60	11 (12)	91	9 (10)	84	0.016
Pain (0–100), mean (SD)	24 (23)	79	25 (23)	69	0.57	23 (22)	80	25 (23)	83	0.56
HAQ (0–3), median (IQR)	0.4 (0–0.9)	76	0.4 (0–0.8)	67	0.63	0.4 (0–0.9)	79	0.4 (0–0.8)	82	0.41
DAS28 remission, %	63.8	76	56.9	68	0.31	69	80	72.7	80	0.53
DAS28(3 variables) remission, %	67.2	87	57.9	80	0.13	71.2	91	79.0	84	0.16
Boolean remission, %	27.1	83	25.0	71	0.72	28.1	84	26.3	83	0.75
Boolean(3 variables) remission, %	28.6	82	26.5	71	0.73	30.3	82	29.6	84	0.91
Medications		100		100			97		98	
Triple therapy, %	20		6.3		0.002	19		5.3		0.001
Combination of MTX + HCQ/SSZ, %	33		28		0.41	36		36		0.90
MTX mono, %	36		43		0.25	30		29		0.75
Other mono, %	8.4		17		0.02	8.4		12		0.33
Other combo, %	0.3		3.1		0.015	2.7		7.4		0.035
No csDMARD, %	2.6		3.1		0.77	3.7		11		0.009
Prednisolone,%	83		78		0.29	66		61		0.39
bDMARD, %	0		0			2.7		1.1		0.36

* Percentages refer to the percentage of patients with data available. RA: rheumatoid arthritis; UA: undifferentiated arthritis; csDMARD: conventional synthetic disease-modifying antirheumatic drug; bDMARD: biologic DMARD; IQR: interquartile range; HAQ: Health Assessment Questionnaire; DAS28: 28-joint Disease Activity Score; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; PtGA: patient's global assessment; PGA: physician's global assessment; TJC28: 28-joint tender joint count; SJC28: 28-joint swollen joint count; TJC46: 46-joint TJC; SJC46: 46-joint SJC; MTX: methotrexate; SSZ: sulfasalazine; HCQ: hydroxychloroquine.

triple csDMARD combination [MTX + sulfasalazine (SSZ) + hydroxychloroquine (HCQ)], and 6% of UA patients used it (p = 0.002). At 12 months, 19% of patients with RA and 5% of patients with UA used it (p = 0.001).

Between 0 and 3 months, the combination of MTX + SSZ/HCQ was used by 33% of patients with RA and 28% of patients with UA (p = 0.41). MTX monotherapy was used by 36% of patients with RA and 43% of patients with UA (p = 0.25). At 12 months, 36% of patients with RA and 36% of patients with UA used the MTX + SSZ/HCQ combination (p = n.s.). Also at 12 months, 30% of patients with RA and 29% of patients with UA received MTX monotherapy (p = 0.25).

Respectively, 83% and 66% of patients with RA received prednisolone between 0 and 3 months and at 12 months. The median (IQR) dose among patients treated with prednisolone was 5 (5–7.5) mg. The use of prednisolone did not differ statistically significantly between the RA and UA groups of patients. Other csDMARD monotherapy was used more frequently by the patients with UA than by those with RA at 3 months (17% vs 8.4%, p = 0.02). Not a single patient received bDMARD therapy at 3 months, and only 2.7% of the patients with RA and 1.1% of the patients with UA were treated with those drugs at 12 months (p = 0.36). Figure 2 represents csDMARD use at 3 and 12 months. Medication data were available for ≥ 97% of the patients (Table 3).

DISCUSSION

Our main observation was that the majority of DMARD-naive patients treated in a real-world rheumatology setting reached early and sustained remission, including the patients who can be classified as having RA. Our results are in line with a Canadian study determining best practices in early treatment. In 1 Canadian clinic among 8 studied, the 12-month remission rate was > 70%[20]. Regardless of the differences among clinics in their resources and patient populations, the remission rates we obtained are remarkable when considering that almost 70% of our patients were seropositive and a fifth had erosive disease at baseline. Contrary to high DAS28 remission rates, the Boolean remission rates were low. We used DAS28 remission rather than the Simplified Disease Activity or Clinical Disease Activity indices because of a high proportion of missing PGA data. We preferred to report DAS28 with ESR instead of DAS28 with CRP remissions because the latter has a

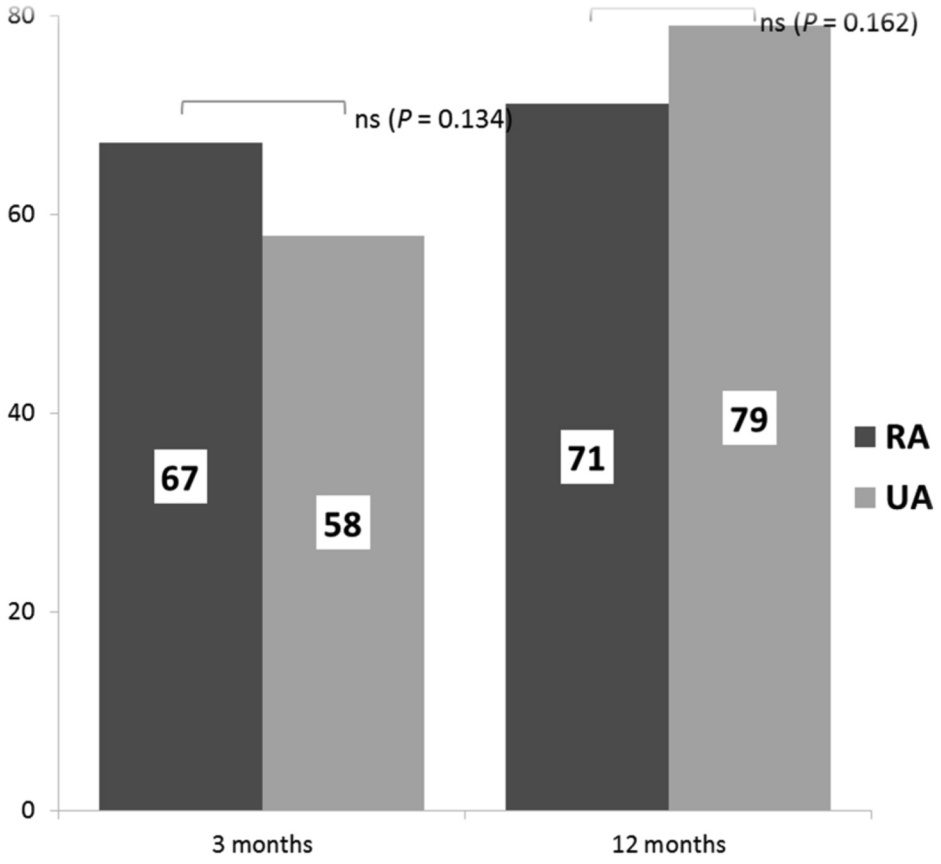

Figure 1. Proportion (%) of patients with RA versus UA in DAS28(ESR-3 variables) remission at 3 and 12 months. RA: rheumatoid arthritis; UA: undifferentiated arthritis; DAS28: 28-joint Disease Activity Score; ESR: erythrocyte sedimentation rate.

Table 4. Remission rates at 3 and 12 months concerning serology and erosive disease at baseline.

	RF/anti-CCP–positive Patients, 3 Months		RF/anti-CCP–negative Patients, 3 Months			RF/anti-CCP–positive Patients, 12 Months		RF/anti-CCP–negative Patients, 12 Months		
No. Patients	277	%*	128	%*	p	277	%*	128	%*	p
DAS28 remission, %	64.7	75	56.5	72	0.18	70.5	81	69	78	0.78
DAS28(3 variables) remission, %	66.4	86	62	84	0.43	72.3	91	75	84	0.60
Boolean remission, %	28.6	81	21.8	79	0.22	32.3	85	17.3	81	0.004
Boolean(3 variables) remission, %	32.1	75	24.5	73	0.18	35.1	81	21.6	80	0.014
	Patients with Erosive Disease at Baseline, 3 Months		Patients with Nonerosive Disease at Baseline, 3 Months			Patients with Erosive Disease at Baseline, 12 Months		Patients with Nonerosive Disease at Baseline, 12 Months		
No. Patients	113	%*	291	%*	p	113	%*	291	%*	p
DAS28 remission, %	56.2	79	65.1	72	0.33	63.5	75	72.7	82	0.024
DAS28(3) remission, %	59.6	88	67.5	85	0.33	71.3	89	74.1	89	0.071
Boolean remission, %	29.6	87	25.2	78	0.53	33.7	81	25.6	85	0.21
Boolean(3) remission, %	33.3	80	28.3	73	0.55	37.2	76	28.8	82	0.22

* Percentages refer to the percentage of patients with data available. RF: rheumatoid factor; anti-CCP: anticyclic citrullinated peptide antibodies; DAS28: 28-joint Disease Activity Score.

tendency to overestimate remission rates at a level of 2.6[21].

The majority of observed DAS28 remissions were sustained (57% of patients with RA and 56% of patients with UA). However, only 16% of RA and 12% of patients with UA reached sustained remission by the Boolean criteria.

In observational settings, sustained remissions have seldom been reported, and there is a lack of consensus on the definition of sustained remissions. In the Dutch Rheumatoid

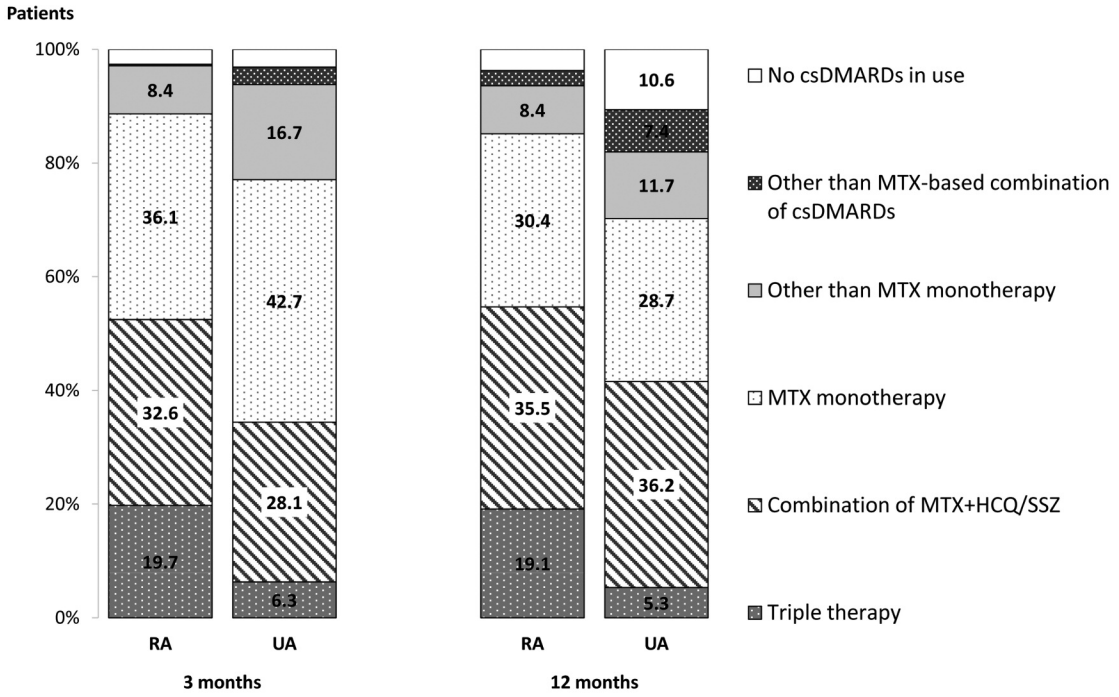

Figure 2. Use of csDMARD at 3 and 12 months. RA: rheumatoid arthritis; UA: undifferentiated arthritis; csDMARD: conventional synthetic disease-modifying antirheumatic drug; MTX: methotrexate; HCQ: hydroxychloroquine; SSZ: sulfasalazine.

Arthritis Monitoring remission induction cohort, newly diagnosed patients with RA from 2006 to 2009 were treated according to treat-to-target strategy with protocolized DMARD adjustment. After 3 years, 61.7% of patients were in DAS28 remission, and 25.3% met the remission by the Boolean criteria. Sustained remission was defined as a DAS28 < 2.6 during ≥ 6 consecutive months, and was experienced by 70.5% in a 3-year followup period, which in the majority was achieved with csDMARD only[22]. In the Swedish BARFOT registry, only 14% of patients with RA during 1995-1999 were in sustained DAS28 and 3% in Boolean remission. However, radiographic damage and disability were similar regardless of the sustained remission criteria used[23]. A recently published paper from the CATCH study reported that 8.5% of patients with early RA (ERA) were in sustained Boolean remission in < 2 years of followup. Sustained Boolean remission was defined as patients satisfying corresponding Boolean remission definition for ≥ 6 months or ≥ 2 consecutive visits[24]. Taking into account a more stringent definition of sustained Boolean remission, our remission rates were substantial.

Our RA patient group was more extensively treated with csDMARD versus the UA group. Patients with UA received less csDMARD combination therapy than did the patients with RA. Eleven percent of the patients with UA used no csDMARD at 12 months compared to only 3.7% of the patients with RA. Most probably this reflects less severe disease courses in UA cases. The 2010 ACR/EULAR classification criteria were developed especially for early detection of RA. However, our results indicate that patients with UA also should receive adequate csDMARD treatment. A study concerning 3 UA cohorts shows that a total of 12% to 26% of these patients progress to RA during the first year[25].

Compared to reports from the Early Rheumatoid Arthritis Network[26], our patients had a shorter median time from onset of symptoms to the start of first DMARD (8 vs 6 months). Therefore, our patients may have had a better chance to reach the "window of opportunity" of DMARD treatment. Nevertheless, a 6-month delay cannot be considered optimal. The referring physicians in our healthcare district are aware of the benefits of rapid rheumatology assessment because of previously conducted national clinical DMARD trials. The structured "treatment path," a formal protocol of multidisciplinary visits, strengthens the patients' adherence to DMARD treatment. Computer-assisted monitoring of disease activity with tight control facilitates reaching the target.

In an observational setting, we cannot estimate the efficacy of various medications. However, most of our patients were treated with csDMARD combinations and with low-dose glucocorticoids, as well as intraarticular glucocorticoid injections to swollen joints. Our treatment approach implements the results from clinical trials showing that conventional DMARD in combination are more effective than csDMARD monotherapy[4,5,6,7]. A recent subanalysis of the FIN-RACo trial showed equal and additive importance of tight control and the use of csDMARD combinations[27]. The high remission rates in our cohort were achieved with negligible use of bDMARD. Our results confer hope to

real-world rheumatology clinics where expensive bDMARD are less affordable.

Two-thirds of our patients with early RA received oral glucocorticoids at 12 months. A relatively high proportion is typical for usual care[28] and indicates that low-dose glucocorticoid therapy is used as a disease-modifying drug rather than a bridging therapy. However, recent EULAR recommendations for the treatment of ERA limit glucocorticoid use to 6 months[29]. Less glucocorticoid use has been advocated because of concerns about steroid-related adverse events, on which our data unfortunately offer no insight. According to the Finnish recommendations, all swollen joints need to be treated with local glucocorticoid injections at any time of the disease course, and especially in early disease, and therefore > 90% of patients received several joint injections at baseline — and at followup if needed.

A limitation of our study is the lack of data for 32% and 29% of patients for DAS28 and Boolean remissions, respectively. However, data for DAS28(3) remission were available in 80-91% of the patients. Missing data for DAS28 was mainly due to missing PtGA (24%). Only 5% of TJC28/SJC28 data were missing, and only 2 patients were lacking ESR levels at baseline. Generally in Finland, patients with RA are rarely lost to followup and can be tracked through an up-to-date population register. Missing data were evenly dispersed in RA/UA groups at 12 months, and the majority of patients missing the 12-month visit were in DAS28(3) remission at a later visit. Among patients missing the 12-month visit, 4 had died for reasons other than RA comorbidities. Therefore, missing data do not have a major influence on the results. Missing data are common in a real-world setting and in our case data were missing because of a pilot period of data collection with GoTreatIt software, when both patients and rheumatologists were learning to use it. The software was introduced to usual care in 2008.

In contrast to former more pessimistic views, substantially high remission rates can be achieved in real-world rheumatology clinics when treating DMARD-naive patients with new diagnoses of RA and UA. We encourage a multiprofessional, targeted-to-remission approach preferring csDMARD combination therapy and the use of quantitative monitoring for better outcomes of patients with RA.

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