Original Article

Disease Modifying Anti-Rheumatic Drugs [Dmards] Used and Treatment Outcome of Rheumatoid Arthritis in Rheumatology Clinic, Srinagarind Hospital

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Objective: To describe the pattern of DMARD used, treatment outcome, and factor affecting treatment outcome in RA patients treated at rheumatology clinic, Srinagarind Hospital, KhonKaen Universtiy.

Materials and Methods: Cross-sectional study was performed on data base of 359 RA patients who met 1987 ACR or 2010 Rheumatoid Arthritis Classification criteria for RA. We included patients older than 18 years-old who has been treated with ≥1 DMARDs for at least 1 year. Demographic data, co-morbidities, articular and extra-articular manifestations, current DMARDs used, DMARDs used during achieving treatment target, Disease activity score of 28 joints (DAS 28), laboratory and radiographic results was collected from RA database.

Results: Mean age of onset was 45 (SD±12.8) years with median disease duration of 12.4 (IQR 7.3 to 17.5) years. 338 (94.1%) of overall RA patients received conventional synthetic DMARDs [csDMARD], meanwhile based on reimbursement type, 9 out of 202 (4.45%) received biologic DMARDs [bDMARDs]. The most frequently use DMARD was methotrexate [MTX]. Currently 155 (43.2%) out of 359 were treated with 2 DMARDs, while 148 (41.2%) had DMARD monotherapy. Disease activity among patients received only csDMARD(s) was scored as low (≤3.2), moderate (>3.2 to 5.1), and high (>5.1) at the proportion of 44.4, 45.8, and 8.2% respectively. Number of patients who had received and recieved bDMARDs was small (21 cases). Among these, 76.2% were good responders of which 50% achieved treatment target, and (25%) had drug free remission. Only 4.5% needed long term bDMARDs of which 38.1% had low disease activity [LDA] and 61.9% had moderate DAS. Low dose corticosteroid [LDCS] was overall prescribed in 63.5%. In csDMARDs group, its use was related with higher DAS; 52.3, 69.7, and 82.1% among patients having low, moderate, and high DAS. In patients who achieved treatment target, 61.8% had sustained remission/LDA ≥1 year. Factors associated with achieving target were history of having remission, induction with MTX, and early remission after DMARDs initiation.

Conclusion: In this RA cohort, 94.1% received only csDMARD and 4.45% received long term bDMARD. 43.7% of csDMARD group and 38.1% of bDMARD group currently achieved treatment target. None of bDMARD group had high DAS. LDCS was overall prescribed in 63.5%. The factors associated with current LDA in RA patients were history of having remission, induction with MTX, and achieving remission within the first year after DMARDs initiation.

Keywords: DMARDs, Outcome, Rheumatoid arthritis

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Rheumatoid arthritis [RA] is a connective tissue disease, with the dominant feature of chronic inflammatory erosive polyarthritis. When the disease is untreated, it leads to severe joint deformities and disability[1,2]. The prevalence is 0.3 to 0.5% of adult worldwide[3,4]. During past 30 years, improved understanding of the pathophysiology of rheumatoid arthritis has led to several way change in the approach to therapy. First, early diagnosis and treatment is the most important. Second, disease-modifying anti rheumatic drug [DMARDs] used in combination with anti-inflammatory drug, both non-steroidal and/or steroidal drug is highly effective. This therapeutic

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strategies have resulted in markedly better clinical outcomes and delay long-term disability in both Early RA and Establish RA[5].

DMARDs, acted by altering the underlying disease rather than treating symptoms have been classified into two major types as synthetic DMARDs, which are divided into Conventional synthetic DMARDs [csDMARDs] and targeted synthetic DMARDs [tsDMARDs], and biologic DMARDs [bDMARDs][6]. The other Immunosuppressive agents used is also includes azathioprine [AZA] and cyclosporine A [CSA] as shown in Table 1.

American College of Rheumatology [ACR] and The European League Against Rheumatism [EULAR] recommends early initiates DMARDs immediately after diagnosis and set a treatment target and to assess the disease on the way towards that target, employing a treat-to-target strategy[7-11] EULAR 2013 has recommended csDMARDs are the first choice with the reasonable cost-effectiveness, cost utility and easy access[12,13]. Patterns of DMARDs used are a variety as monotherapy and combination therapy. The efficacy referred to Best study[14], four treatment strategies: sequential monotherapy; step-up combination therapy; initial combination with prednisone; initial combination with infliximab indicate that clinical and radiological outcomes of all 4 groups can be achieved with the same remission rate in 5 years. Nevertheless, initial combination therapy resulted in earlier clinical improvement and less joint damage without more toxicity. Difference from EULAR 2013, ACR recommended bDMARDs are the first if patients have severe symptoms with the poor prognosis factor. In Thailand, bDMARDs has been limit used in under rheumatic disease prior authorization [RDPA] according to the bDMARDs indication for rheumatoid arthritis determine by Thai Rheumatism Association.

Table 1. DMARDs used to treat Rheumatoid arthritis[6,7]

sDMARDs	bDMARDs
- Methotrexate [MTX]	- Anti-TNFa: etanercept**, infliximab**, adalimumab, certolizumab pegol, golimumab**
- Sulfasalazine [SSZ]	- T cell costimulation inhibitor: abatacept**
- Leflunomide [LEF]	- B cell depleting agent: rituximab**
- Antimalarial agents (CQ, HCQ)	- Interleukin-6 receptor blocking agent: tocilizumab**
- Gold thiomalate	- Interleukin-1 receptor blocking agent: anakinra
- Tofacitinib*	

* Targeted synthetic DMARDs
** Biologic DMARDs available in Thailand

The concise criteria for bDMARDs and the restrictions on reimbursement people may widely affect to Thai RA patient. This may lead to the worse results of the treatment of rheumatoid arthritis in Thailand. Rheumatology outpatient clinic, Srinagarind hospital, Khonkaen university has been open since December, 1986. Data from the medical records based on ICD10 code found 728 patients in the last 10 years. However, there has never been a systematic study of the outcomes of patients. We are interested to study on the use of DMARDs and the results of the treatment during a period of 10 years, which will cover the types and patterns of DMARDs use, clinical history, co-morbidity diseases, disease time course, restriction of drug use, and outcome. The information will be used to develop conditioning guidelines for rheumatoid arthritis within the Institute and to be forwarded to develop public health policy of the country in the next opportunity. Objectives of our study was to describe the pattern of DMARD used, treatment outcome, and factor affecting treatment outcome in RA patients treated at Rheumatology Clinic, Srinagarind Hospital, Khon Kaen University.

Materials and Methods

Our Cross-sectional study was based on the descriptive and the research method and has included of 359 RA patients that were treated in the outpatient's clinic for rheumatology during 2005 to 2015 period. Diagnosis is based on the 1987 ACR[15] or 2010 ACR-EULAR[16] classification criteria for RA. Upon determining diagnose, each patient was assigned with the sheet record for RA, where the activity of illness has been assessed based on Disease activity score of 28 joints [DAS-28] calculation model[17-19]. We included patients older than 18 years-old that has been treated with ≥1 DMARDs for at least 1 year and excluded other diagnosed arthritis, overlapping syndrome and patients that loss follow-up before 1 year. Demographic data, co-morbidities, disease duration, articular and extra-articular manifestations, DAS 28 score, current DMARDs used, DMARDs used during achieving treatment target, steroid used, laboratory and radiographic results was collected from RA database.

Statistical processing has been carried out with program Epi 6 for DOS, SPSS 17.0 and Excel 2010.

Statistical analysis has helped us in descriptive analysis, whereas statistical parameters have helped us to determine the structure index, arithmetic median, standard deviation, confidence interval with accuracy 95% (95% CI), Pearson Chi-square, Mann-Whitney U test, t-test, odds ratio [OR], and Logistic regression.

Results

Population description

A total of 543 patients were recruited for study, of which 184 were excluded because they had others diagnosed arthritis, loss follow-up >1 year and not available data record. In the end, 359 patients (female 80.8%, male 19.2%) met all the criteria required to be evaluate in the study (Table 2). The mean age of onset was 45 (SD±12.8) years with total median disease duration of 12.4 (IQR 7.3 to 17.5) years. The patient's hometown was distributed in the northeast region, of which the most to the smallest proportions was Khon Kaen (37.9%), Mahasarakham (13.1%), Kalasin (8.4%), Chaiyaphum (7.5%), and Roi-Et (7%), respectively. The health insurances were Government or state enterprise officer [OFC] (56.3%), Universal coverage scheme [UCS] (38.7%), and Social security scheme [SS] (4.2%). The most patients had co-morbidity disease and osteoarthritis with little proportion of dependent status. At the time of current DMARDs, patients had a median of 2 swollen and 2 painful joints. The patients reported morning stiffness with a median duration of 5 minutes and the assessment of the disease by the patient using visual analogue scale [VAS] was score of 30. The mean ESR was 49 (32 to 75) mm/h and CRP was 4.4 (2.5 to 21.5) mg/dl. A total of 67.4%, and 88.5% of the patients were rheumatoid factor [RF] and anti-CCP positive respectively. RF and anti-CCP positivity was not correlated with DAS 28. 90.6% presented radiographic erosions. The mean DAS 28 at the time of current DMARDs was 3.53. Almost half of patients had moderate disease activity that classified by DAS 28 score [DAS]. Disease activity of all patients was scored as low (≤3.2), moderate (>3.2 to 5.1), and high (>5.1) with proportion of 43.7, 46.8, and 7.8% respectively (Figure 1). In subpopulation, the number of patients who received bDMARDs was small (21 cases) (Table 2). Among these, 76.2% (16 of 21) were good responders of which 50% (8 of 16) achieved treatment target, and (25%) had drug free remission. Disease activity of csDMARD and bDMARD group was scored as low DAS, moderate DAS, and high DAS with proportion 44.4%, 45.8, 8.2% and 38.1%, 61.9%, 0%. In subgroup analysis, the proportion of high DAS in patient with government or state enterprise officer insurance [OFC] was lower than one in non-OFC patient which classified by DAS as low, moderate, high with proportion 43%, 46%, 5.9% in OFC patient and 42%, 44%, 11% in non-OFC patients respectively.

Description of the therapy

338 (94.1%) of overall RA patients received csDMARD, meanwhile based on reimbursement type, 9 out of 202 (4.45%) received (Table 3). Currently 155 (43.2%) out of 359 were treated with 2 DMARDs, while 148(41.2%) had DMARD monotherapy. The most pattern used of DMARDs in all patients was step up combination (76%) followed by sequential monotherapy (15.3%) and the most frequently use DMARDs was methrotrexate (76.9%), followed by sulfasalazine (22.3%) and leflunomide (21.2%). However, in bDMARDs group, the patients had frequently used of leflunomide higher than in csDMARD (42.9% vs. 19.8%) (Figure 2). Rituximab was the higher proportion choice of bDMARDs treatment. Low dose corticosteroid [LDCS] was overall prescribed in 63.5% of all patients. In subgroup analysis, LDCS used in csDMARDs group was related with higher DAS; 54.8%, 68.9%, and 82.1% among patients having low, moderate, and high DAS. Highest LDCS used was noted among patients received long term bDMARDs with proportion of 71.4%. In patients who achieved treatment target, 61.8% had sustained remission/LDA ee1 year. Multivariate analysis showed that the patient who had history of disease remission (odds ratio [OR] = 15.4, 95% CI = 6.86 to 34.6, p<0.001), induction with MTX (OR = 2.97, 95% CI = 1.91 to 4.62, p<0.001), early remission (OR = 1.79, 95% CI = 1.05 to 3.2, p<0.032) and maintaining remission >1 year (OR = 2.06, 95% CI = 1.24 to 3.41, p<0.008) after DMARDs initiation was associated with current achieving target (Table 4).

During current DMARD used, 81 (22.5%) patients experienced at least one adverse event. In csDMARD group, 104 adverse events occurred in 79 (23.4%) patients, higher proportion than in bDMARDs group (Table 4). The majority of adverse events was mild to moderate and did not lead to treatment regimen adjustments. Hepatitis was the most common adverse event in csDMARD group (9.2%) and infection (9.5%) was one in bDMARD. During the current regime, the number of serious infection and malignancy were comparable across the groups. The majority of serious adverse events were in csDMARD group (18 patients). This is due to there was a small number of patient in bDMARD group.

Table 2. demographic data and clinical history of rheumatoid arthritis patient (n = 359)

Characteristic	Total n = 359 (%)	csDMARDs n = 338 (%)	bDMARDs n = 21 (%)
Sex			
Female	290 (80.8)	276 (81.7)	14 (66.7)
Male	69 (19.2)	62 (18.3)	7 (33.3)
Age, mean (SD), years	59.16 (11)	58.9 (11.2)	58.73 (9.55)
Age at onset, mean (SD), years	45 (12.7)	45 (12.8)	44.7 (12.7)
Irregular follow-up	67 (18.7)	66 (19.5)	1 (4.8)
Province			
Khon kaen	136 (37.9)	127 (37.6)	9 (42.9)
Mahasarakham	47(13.1)	43 (12.7)	4 (19)
Kalasin	30 (8.4)	28 (8.3)	2 (9.5)
Chaiyapum	27 (7.5)	27 (8)	2 (9.5)
Roi-Et	25 (7)	24 (7.1)	4 (19)
others	94 (26.1)	89 (26.3)	-
Health insurance			
OFC	202 (56.3)	183 (54.1)	19 (90.5)
UCS	139 (38.7)	137 (40.5)	2 (9.5)
SS	15 (4.2)	15 (4.4)	-
Self pay	3 (0.8)	3 (0.9)	-
Co-morbidity	284 (79.1)	263 (77.8)	21 (100)
Hypertension	147 (40.9)	133 (39.3)	14 (66.7)
Dyslipidemia	92 (25.6)	81 (24)	11 (52.4)
ACD	66 (18.4)	63 (18.6)	3 (14.3)
DM	65 (18.1)	62 (18.3)	3 (14.3)
Osteoporosis	57 (15.9)	50 (14.8)	7 (33.3)
CKD	16 (4.5)	16 (4.7)	1 (4.7)
Smoking	31 (8.6)	30 (8.9)	1 (4.8)
OA	254 (70.8)	237 (70.1)	17 (81)
Wrist	111 (30.9)	105 (31)	6 (28.5)
Knee	158 (44.0)	148 (43.7)	10 (47.6)
Dependent	24 (6.7)	22 (6.5)	2 (9.5)
Extra articular Manifestation	73 (20.3)	65 (19.2)	11 (33.3)
Sicca	49 (13.6)	43 (12.7)	6 (28.6)
Rheumatoid nodule	21 (5.8)	19 (5.6)	2 (9.5)
Splenomegaly	1 (0.3)	1 (0.3)	-
Tender joint count n = 120	2 (1 to 3)	2 (1 to 3)	1
Swollen joint count n = 130	2 (1 to 3)	2 (1 to 3)	1
Morning stiffness, mins n = 112	5 (3 to 10)	5 (3 to 10)	3.18
PGA (1-100) n = 355	30 (10 to 50)	30 (20 to 50)	21.5 (20 to 50)
Current ESR mm/hr, n = 344	49 (32 to 75)	52 (33 to 76)	38 (21 to 56)
Current CRP, mg/dl, n = 46	4.4 (2.5 to 21.5)	4.6 (2.7 to 28)	4.2 (0.3 to 9.6)
Rheumatoid factor positive	242 (67.4)	225 (66.6)	17 (81)
Anti-CCP positive, n = 52	46 (88.5)	43/49 (87.8)	3/3 (100)
Baseline radiographic change, n = 287	178 (62)	167/272 (61.4)	11/15 (73.3)
Current radiographic change, n = 257	233 (90.6)	221/243 (90.9)	12/14 (85.7)
Total disease duration, median (IQ), years	12.4 (7.3 to 17.8)	12.3 (7.2 to 17.6)	12.9 (9.8 to 23.5)
Disease duration before treatment* median (IQ),month	9 (3 to 9)	9 (3 to 24)	12 (4 to 24)
Time to first remission*, median (IQ), years	2.4 (12 to 60)	2.4 (1 to 5)	1.7 (0.7 to 6.2)
History of remission*	269 (74.9)	254 (75.1)	15 (71.4)

* At first remission after DMARDs

DAS = disease activity score 28; OFC = Government or state enterprise officer; UCS = universal coverage scheme; SS = social security scheme; ACD = anemia of chronic disease; DM = diabetes mellitus; CKD = chronic kidney disease; OA = osteoarthritis; PGA = patient global assessment; LDA = low disease activity; MDA = moderate disease activity; HDA = high disease activity

Table 2. Cont.

Characteristic	Total n = 359 (%)	csDMARDs n = 338 (%)	bDMARDs n = 21 (%)
Maintaining of remission*, median (IQ), month n = 267	17 (8 to 32)	17 (8 to 31)	23 (6 to 35)
<1 year	102 (38.2)	97/251 (38.5)	5/15 (33.3)
≥1 year	165 (61.8)	155/251 (61.5)	10/15 (66.7)
Current DAS28 mean (SD)	3.53 (1.07)	3.54 (1.08)	3.38 (0.92)
Achieving target (remission & LDA)	157 (43.7)	149 (44.9)	8 (38.1)
Remission, DAS 28 <2.6	62 (17.3)	56 (16.9)	6 (28.6)
LDA, DAS 28 = 2.6 to 3.2	95 (26.4)	93 (27.5)	2 (9.5)
MDA, DAS 28 >3.2-5.1	168 (46.8)	155 (45.8)	13 (61.9)
HAD, DAS 28 >5.1	28 (7.8)	28 (8.2)	-

* At first remission after DMARDs

DAS = disease activity score 28; OFC = Government or state enterprise officer; UCS = universal coverage scheme; SS = social security scheme; ACD = anemia of chronic disease; DM = diabetes mellitus; CKD = chronic kidney disease; OA = osteoarthritis; PGA = patient global assessment; LDA = low disease activity; MDA = moderate disease activity; HDA = high disease activity

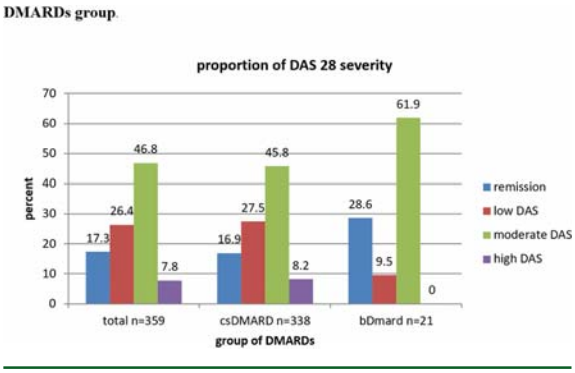
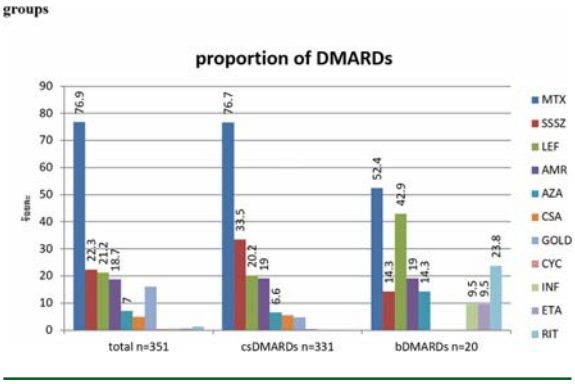


Figure 1. Proportion of DAS 28 level in all patients and in patients classified by DMARDs group.

Discussion

The descriptive study of RA included approximately 359 patients with RA in Srinagarind hospital, Khonkaen University. This sample represents a group of patients with typical and serological clinical features of RA: more common in women, with an average age of approximately 50 years, 67% of patients were RF positive, with acute phase reactants such as elevated ESR and CRP. The median disease duration of the patients who follow up in our clinic has been long which indicated that the result of this study is from the long term RA patient. It is noteworthy that more than half of RA patients have OFC health insurance to show that in who have more advantage to access to health service in university hospital than non OFC patients. We found that the patients in our rheumatology clinic had taken a long time to first remission up to 2.4 years. The possible reasons are in the beginning of our clinic, the treat-to-target strategy was not established in that time and the patient was sent to rheumatologist lately. Combination DMARDs therapy (≥2 DMARDs) was prescribed in more than half of all patients and the most frequently used pattern is step up combination. However, regardless of DMARDs patterns used: step up combination therapy, sequential monotherapy, initial combination with prednisone in the present study, the efficacy was similar defined by DAS 28 score as the result of BeSt study[14]. A popular DMARDs in combination regimen is methotrexate which is the highest proportion used in the time of first disease remission in this study as the previous several study and systematic review and meta-analysis, shown that methotrexate is the backbone DMARDs which has an efficacy to reduce swollen and tender joint, to prevent relapse, and to improve joint mobility[20,21]. Another interesting finding of the present study is that leflunomide is the second most DMARDs used in bDMARDs group with higher proportion used than csDMARDs group. This difference are definitely from inaccessibility to the drug outside of the national essential drug (non ED) list such as leflunomide, and all bDMARDs, regarding to limitation of non OFC patient's health insurance. Two third of patients currently use low dose corticosteroid [LDCS] but in csDMARDs group had proportion of LDCS used lower than in bDMARDs and both group its use was related to higher DAS 28. In this study from multivariate analysis, we found that LDCS used associated with lower DAS 28 (achieving target) which indicated to



MTX = Methotrexate; SSZ = Sulfasalazine; LEF = Leflunomide, AMR = Antimalarial; AZA = Azathioprine; CSA = Ciclosporin A; CYC = Cyclophosphamide; INF = infliximab; ETA = Etanacept; RIT = Rituximab

Figure 2. Proportion of current DMARDs type based on csDMARDs and bDMARD groups.

two direct way conclusion. The first is that the remission of disease is not result from higher corticosteroid use, and the second is that the high DAS28 patients have higher corticosteroid use to reduce inflammation. However, it is important to mention that the design of this study is cross sectional study which not suitable to determine cause and effect.

The outcome of RA treatment in our DAS 28 driven clinic was found that almost half of all patients had achieving target and remission of disease is higher in bDMARDs. However, 10% of csDMARDs had high DAS 28 but none of bDMARDs. This signifies from inaccessibility to drug of non ED list due to limitation of non OFC health insurance. The solution of accessibility to drug of non ED list should be consider to help non OFC patients improved disease activity, and feel better up to 76.2% regarding to this study, which would make the quality of life of vast majority of Thai RA patients.

Table 3. Current DMARDs and Steroid used

	Total n = 359 (%)	csDMARDs n = 338 (%)	bDMARDs n = 21 (%)
No. of current DMARDs			
0	8 (2.2)	7 (2.1)	1 (4.8)
1	148 (41.2)	142 (42)	6 (28.6)
2	155 (43.2)	144 (42.6)	11 (52.4)
3	43 (12)	43 (12.7)	-
4	4 (1.1)	2 (0.6)	2 (4.8)
5	1 (0.3)	1 (0.3)	-
Pattern of DMARDs			
Step up combination	273 (76)	254 (75.1)	19 (90.5)
Sequential monotherapy	55 (15.3)	54 (16)	1 (4.8)
Initial combination	18 (5.0)	12 (3.6)	1 (4.8)
Current DMARDs			
Methotrexate	276 (76.9)	265 (78.4)	11 (52.4)
Sulfasalazine	80 (22.3)	111 (32.8)	3 (14.3)
Leflunomide	76 (21.2)	67 (19.8)	9 (42.9)
Antimalarial	67 (18.7)	63 (18.6)	4 (19)
Azathioprine	25 (7)	22 (6.5)	3 (14.3)
Ciclosporin	18 (5)	18 (5.3)	-
Gold	16 (4.5)	16 (4.7)	-
Cyclophosphamide	1 (0.3)	1 (0.3)	-
Infliximab	2 (0.6)	-	2 (9.5)
Etamacept	2 (0.6)	-	2 (9.5)
Rituximab	5 (1.4)	-	5 (23.8)
Current prednisolone, n = 353	224 (63.5)	209 (63)	15 (71.4)
≤5 mg	157 (44.5)	147 (44.2)	10 (47.6)
>5 mg	67 (19)	62 (18.6)	5 (23.8)
Prednisolone dose, mean (SD), mg	5.5 (5)	5.5 (3.1)	5.4 (2.3)
Median duration of prednisolone, months	12 (12 to 24)	12 (5 to 22)	20 (3 to 34)

Table 4. Adverse events and serious adverse event during current DMARD use

	Total n = 359 (%)	csDMARDs n = 338 (%)	bDMARDs n = 21 (%)
Any adverse event during current DMARD	81 (22.5)	79 (23.4)	2 (9.5)
Infection	25 (6.9)	23 (6.8)	2 (9.5)
Dermal/mucosal	10 (2.8)	10 (2.9)	1 (4.7)
Urinary tract	6 (1.7)	6 (1.8)	0
Respiratory tract	4 (1.1)	4 (1.2)	0
others	5 (1.4)	3 (0.9)	1 (4.7)
Gastrointestinal	33 (9.2)	32 (9.5)	1 (4.8)
Hematologic	18 (5)	17 (5)	1 (4.8)
Renal	1 (0.3)	1 (0.3)	
Neurological	3 (0.8)	3 (0.9)	
Other	3 (0.8)	3 (0.9)	
Any SAE during current DMARD	19 (5.3)	18 (5.3)	1
Serious infection (n)	9	8	0
Tuberculosis (any sites)	3	3	0
Pheochromomycosis	3	3	0
others	3	2	1
Malignancy (n)	10	10	0
Breast cancer	3	3	0
Lung cancer	2	2	0
Others	5	5	0

SAE = Serious adverse event

Conclusion

In this RA cohort, 94.1% received only csDMARD and 4.45% received long term bDMARD. 43.7% of our patients currently achieved treatment target, of whose 52.3% having low dose corticosteroid in their treatment regimen. The factors associated with current LDA in RA patients were history of having remission, induction with MTX, and achieving remission within the first year after DMARDs initiation.

What is already known on this topic?

The recent guidelines for RA treatment by EULAR and ACR recommended initially started with csDMARDs and favored the use of bDMARDs first over the combination of csDMARDs following the failure of methotrexate in patient with such poor prognostic factor. Whereas long-term follow-up of landmark trials such as BeSt study (10 years) and NEO-RACo study (5 years) as well as other trials supports similar efficacy of both strategies (csDMARDs and bDMARDs) in terms of clinical and functional outcome. Nevertheless, initial bDMARDs combination therapy resulted in earlier clinical improvement and less joint damage without more toxicity. In Thailand, csDMARDs has been widely used in all Thai RA patients, conversely bDMARDs has been limit used with concise criteria and the restriction on reimbursement people. In fact that bDMARDs was lower cost-effectiveness than csDMARDs. However, there has never been a systematic study of the outcomes of Thai RA patients in comparing of both strategies.

What this study adds?

The outcome of Thai RA treatment, following the present conditioning guidelines under public health policy seem to be similar efficacy with other developed countries in both csDMARDs and bDMARDs group. Nevertheless, therapy was limit used on reimbursement people. This may lead to widely affect to Thai non reimbursement RA patient whom indicated with criteria for bDMARDs (HDA patients 8.2%). The result will be used as part of the development of new revised flexible criteria for bDMARDs reimbursement base on cost utility and cost effectiveness in the next opportunity.

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Table 5. Factors associated with achieving target (DAS 28 ≤3.2) (multivariate analysis)

Factor (multivariate analysis)	OR (DAS ≤3.2)	95% CI	*p*-value
Anemia of chronic disease	0.25*	0.13 to 0.49	0.046
Chronic kidney disease	0.40	0.12 to 1.26	0.110
Smoking	0.89	0.42 to 1.89	0.770
OA	0.59	0.32 to 1.11	0.100
Dependent	0.42	0.16 to 1.08	0.121
Extraarticular manifestation (Y/N)	0.41*	0.23 to 0.73	0.004
Sicca	0.32*	0.16 to 0.66	0.030
Rheumatoid factor (Y/N)	0.70	0.41 to 1.20	0.123
Anti-CCP	0.18	0.02 to 1.69	0.113
History of Achieving target	15.4*	6.86 to 34.6	<0.001
Time to remission <1 year	1.79*	1.05 to 3.2	0.032
Maintaining remission >1 year (Y/N)	2.06*	1.24 to 3.41	0.008
Monotherapy/combination	1.78*	1.15 to 2.74	0.004
Baseline erosion	0.68	0.42 to 1.11	0.089
Current erosion	0.70	0.34 to 1.99	0.450
Current prednisolone (Y/N)	0.45*	0.29 to 0.70	<0.001
Current DMARDs			
Sulfasalazine	0.61	0.36 to 1.03	0.056
Leflunomide	0.78	0.46 to 1.31	0.163
Azathioprine	0.22*	0.07 to 0.65	0.002
DMARDs during achieving target			
Methotrexate	2.97*	1.91 to 4.62	<0.001
Sulfasalazine	1.52	0.94 to 2.45	0.084
Leflunomide	1.90	0.98 to 3.67	0.054
Antimalarial	1.52	0.91 to 2.54	0.110

*$p<0.05$

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Author contribution

All of the authors have read and prepared the manuscript.

Potential conflicts of interest

The authors declare no conflict of interest.

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