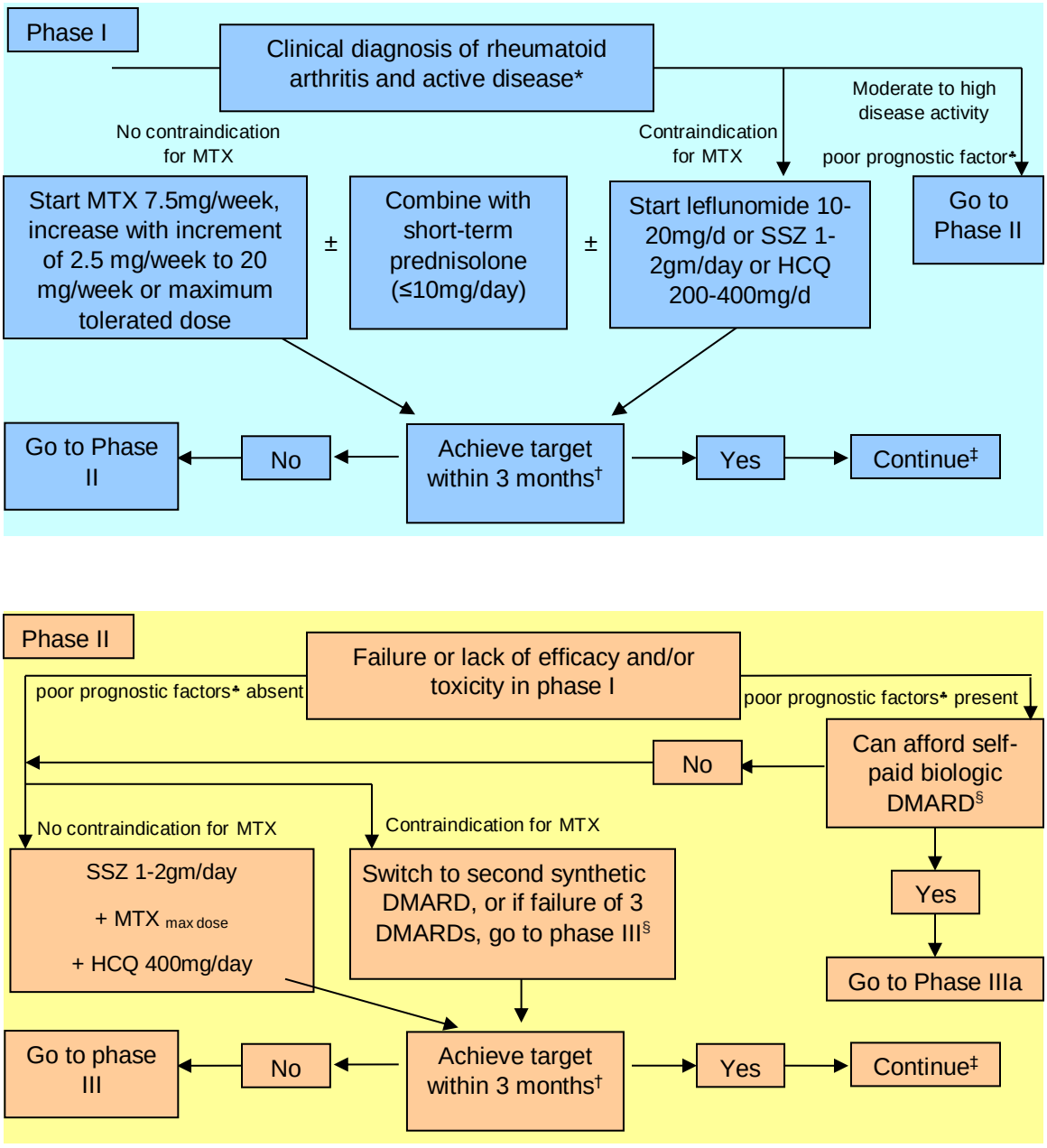
Online supplement to: Effect of Treat-to-target Strategies Aiming at Remission on Arterial Stiffness in Early Rheumatoid Arthritis: A Randomized Controlled Study. *The Journal of Rheumatology*. doi:10.3899/jrheum.171128

ONLINE SUPPLEMENTARY DATA.

Supplementary Figure 1. Protocol for intensive treatment group for participants assigned to SDAI remission group



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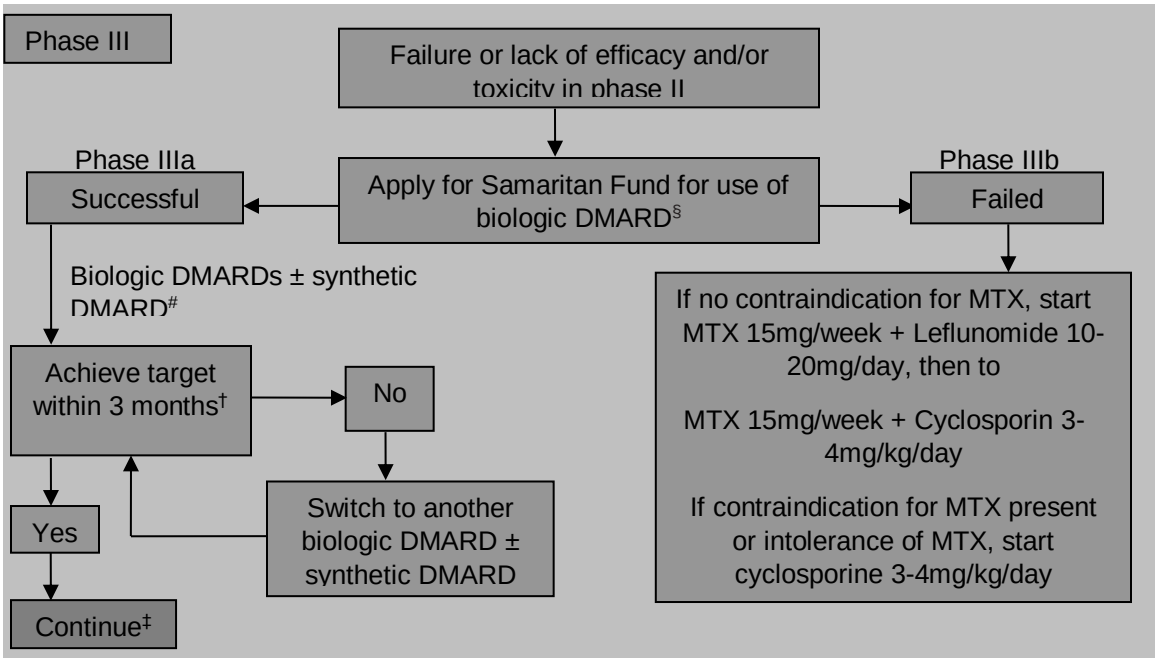

* Diagnosis of rheumatoid arthritis (RA) is according to the 2010 American College of Rheumatology /European League Against Rheumatism classification criteria. Disease activity is defined using the Disease Activity Score in 28 joints (DAS28). Active disease refers to DAS28 score ≥3.2.

† The treatment target is remission defined as SDAI≤3.3. The SDAI is the simple sum of the tender joint count (using 28 joints), swollen joint count (using 28 joints), patient global assessment (0-10 scale), physician global assessment (0-10 scale) and C-reactive protein level (mg/dl). It should be preferably achieved within 3 months of therapy, and definitely achieved by a maximum of 6 months.

‡ If treatment target is consistently achieved for at least 6 months, medication could be gradually tapered until 1 drug remained at a maintenance dose.

♣ ACR guideline for prognostically unfavorable factors include functional limitation (e.g. Health Assessment Questionnaire score or similar valid tools), extraarticular disease (e.g. presence of rheumatoid nodules, RA vasculitis, Felty syndrome), positive rheumatoid factor/anti-citrullinated peptide antibodies; very high disease activity (DAS28 score (ESR) >7.0 despite DMARDs); bone erosion on plain x-ray.

§ The biologic disease modifying anti-rheumatic drugs (DMARDs) are not reimbursed by the Hong Kong public healthcare system and are privately purchased by patients, which limit the use of these treatments. The Samaritan Fund provides financial assistance to these needy patients. The biologic DMARDs supported by Samaritan Fund

are infliximab, etanercept, adalimumab, rituximab, abatacept and tocilizumab. General principals in the use of Samaritan Fund for biologic DMARDs in RA include persistent high disease activity (DAS 28 ≥5.1) and failure of standard therapy of at least 4 standard synthetic DMARDs. Alternatively, patients who failed 2 DMARDs and fulfill one of the following HK guideline for prognostically unfavorable factors including high levels of rheumatoid factor/anti-citrullinated peptide antibodies; very high disease activity (DAS28 score (ESR) >7.0 despite DMARDs); bone erosion on plain x-ray at disease onset, family history of RA, swollen joint count > 20 are also eligible to apply.

Methotrexate is preferably used as combination therapy with biologic DMARDs, other synthetic DMARDs can be used if contraindication for methotrexate present. Prednisolone at a dose ≤10mg/day was allowed during the whole study period. For the management of acute disease flare, intra-articular glucocorticoids could be given, but this procedure was forbidden 4 weeks prior to the next efficacy assessment. Use of pulse methylprednisolone was forbidden during the whole study period for all participants.

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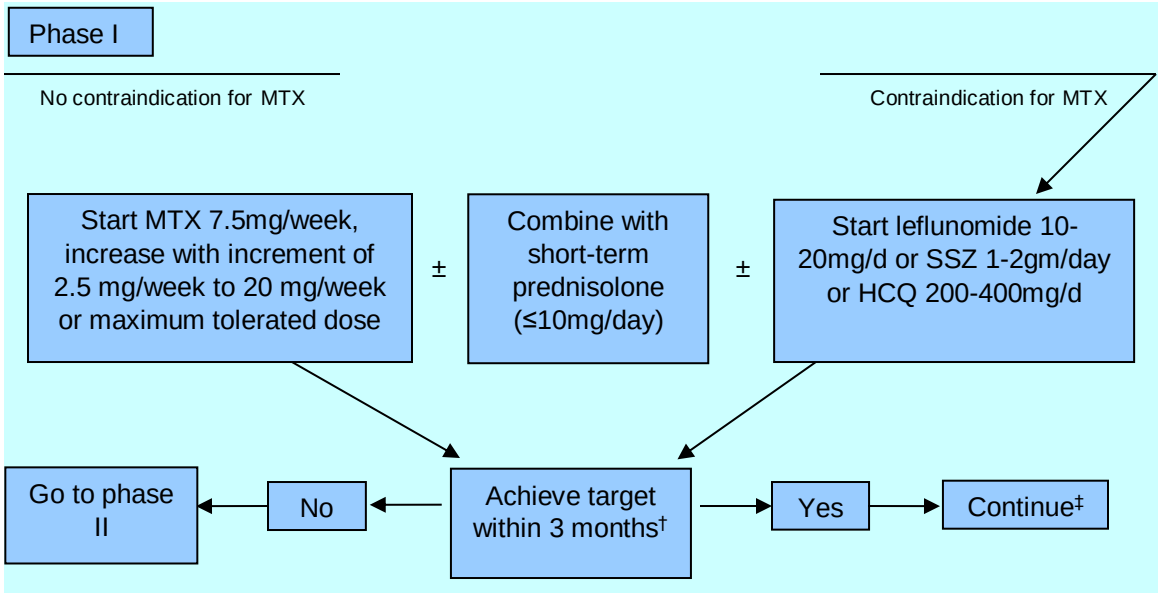
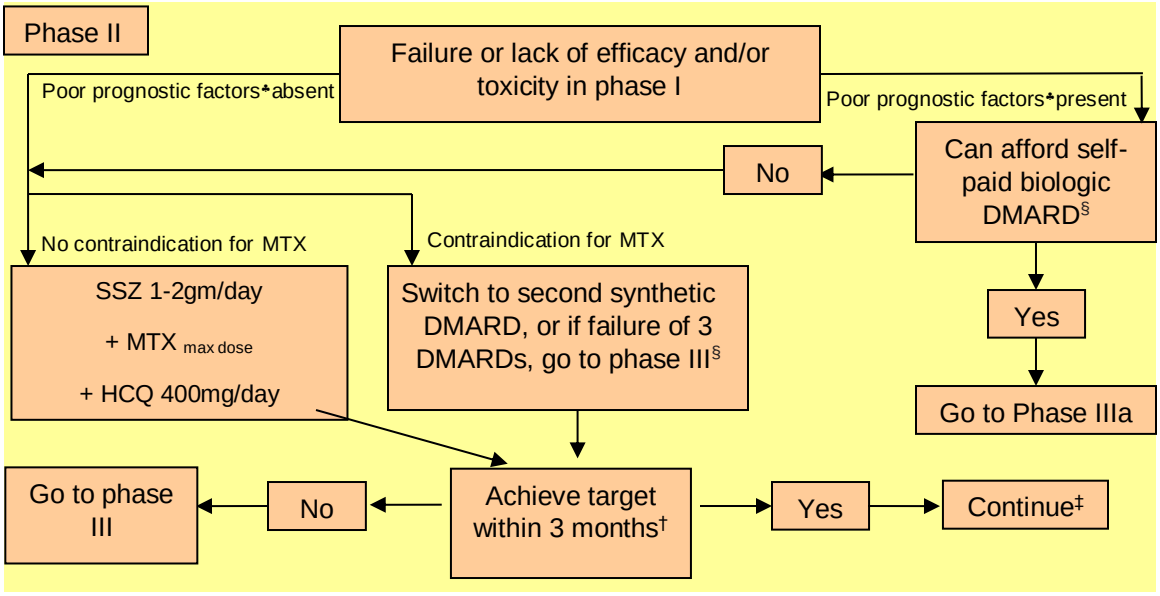
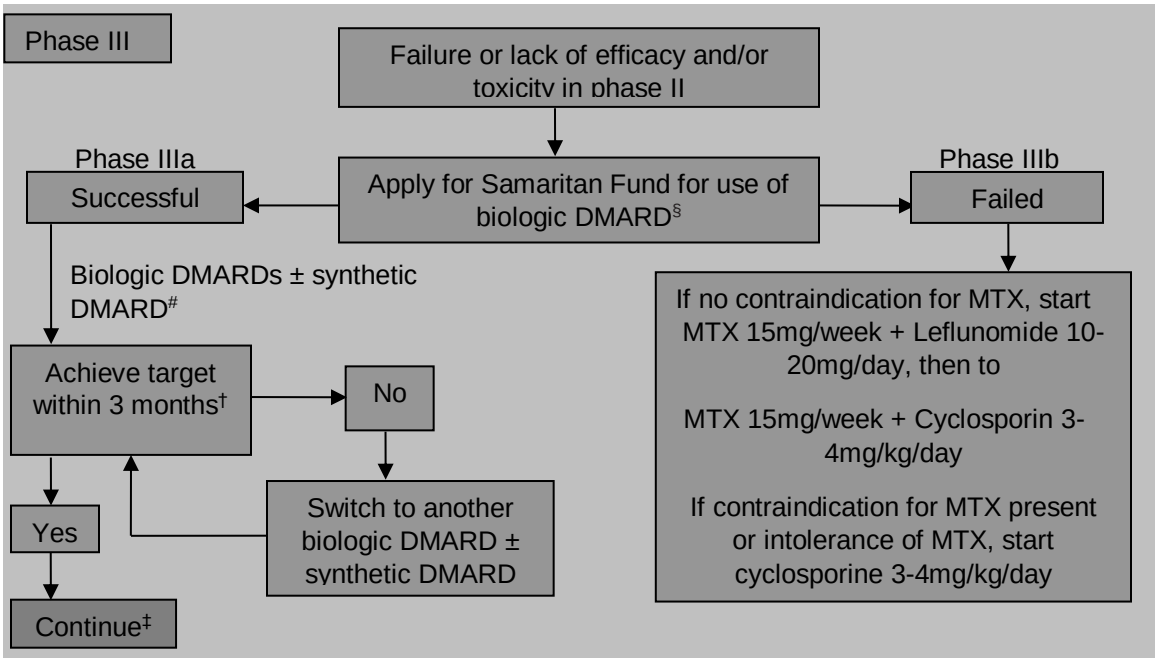
Supplementary Figure 2. Protocol for intensive treatment group for participants assigned to minimal disease activity group







* Diagnosis of rheumatoid arthritis (RA) is according to the 2010 American College of Rheumatology /European League Against Rheumatism classification criteria. Disease activity is defined using the Disease Activity Score in 28 joints (DAS28). Variables used to calculate DAS28 score are tender joint count (using 28 joints), swollen joint count (using 28 joints), patient global assessment (0-100 scale), and CRP level (mg/L). Active disease refers to DAS28 score ≥3.2.

† The treatment target is minimal disease activity, defined as DAS28<2.6. It should be preferably achieved within 3 months of therapy, and definitely achieved by a maximum of 6 months.

‡ If treatment target is consistently achieved for at lease 6 months, medication could be gradually tapered until 1 drug remained at a maintenance dose.

♣ ACR guideline for prognostically unfavorable factors include functional limitation (e.g. Health Assessment Questionnaire score or similar valid tools), extraarticular disease (e.g. presence of rheumatoid nodules, RA vasculitis, Felty syndrome), positive rheumatoid factor/anti-citrullinated peptide antibodies; very high disease activity (DAS28 score (ESR) >7.0 despite DMARDs); bone erosion on plain x-ray.

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Methotrexate is preferably used as combination therapy with biologic DMARDs, other synthetic DMARDs can be used if contraindication for methotrexate present. Prednisolone at a dose ≤10mg/day was allowed during the whole study period. For the management of acute disease flare, intra-articular glucocorticoids could be given, but this procedure was forbidden 4 weeks prior to the next efficacy assessment. Use of pulse methylprednisolone was forbidden during the whole study period for all participants.

Supplementary Table 1. Serious adverse events between patients in group 1 and 2

	Group 1 (n=57)	Group 2 (n=60)
Serious adverse events (SAE)	3 (5%)	3 (5%)
Associated with DMARDs	3[1]	2[2]
Back injury due to fall	0	1

[1]Two due to MTX overdose, 1 due to marrow suppression; [2]One due to MTX overdose, one hip fracture developed after taking prednisolone for 5 months.