**Supplementary Table 1:** Follow-up schedule and data to be collected.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Items** | **Induction treatment stage** | | **Randomized stage** | | | | | **Early exit** |
| Visit | S1 | S2–4 | V0 | V1–2 | V3 | V4–8 | V9 |  |
| Wk0 | Wk 4\8\12 | Wk0 | Wk4–8 | Wk12 | Wk20–52 | Wk60 |
| ICF | √ |  |  |  |  |  |  |  |
| Demographic data | √ |  |  |  |  |  |  |  |
| Past history and medication history collection | √ |  |  |  |  |  |  |  |
| Physical examination | √ | √ | √ | √ | √ | √ | √ | √ |
| Urine βHCG  (if applicable) | √ |  |  |  |  |  |  |  |
| BCC, renal and liver function, ESR, CRP, RF | √ | √ | √ | √ | √ | √ | √ | √ |
| Assessment committee examination | √ | √ | √ | √ | √ | √ | √ | √ |
| IC/EC judgement | √ |  |  |  |  |  |  |  |
| Randomization |  |  | √ |  |  |  |  |  |
| Hand X-ray | √ |  | √ |  |  |  | √ | √ |
| Ultrasound of double hands | √ |  | √ |  |  |  | √ | √ |
| Anti-CCP antibody | √ |  | √ |  |  |  | √ | √ |
| Cost record | √ |  | √ | √ | √ | √ | √ | √ |
| HAQ-DI/EQ-5D | √ |  | √ |  | √ |  | √ | √ |
| Study Medication record | √ | √ | √ | √ | √ | √ | √ | √ |
| Concomitant medication record | √ | √ | √ | √ | √ | √ | √ | √ |
| AE record | √ | √ | √ | √ | √ | √ | √ | √ |

Note: ICF: [Informed Consent Form;](http://www.baidu.com/link?url=-qoHJhsxlaBUznCd_ii5yrJ3kKdx9paV_i1HyYF7z_T_zpHGg7k-AePSpdWR89phJNHX5sUJyCbcvakS_c1xE2-wFaeVI9lDpxU1cvlFwtRmt5uLPO-7Q0fcLukdW_IL" \t "_blank)BCC: Blood cells count; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; RF: rheumatoid factor; IC/EC: inclusion criteria/exclusion criteria; Anti-CCP antibody: anti-cyclic citrullinated peptide antibody; HAQ-DI/EQ-5D: Health Assessment Questionnaire Disability Index/ Euro Qol five dimensions questionnaire; AE: Adverse event. WK: Week.

**Supplementary Table 2:** The multiple logistic regression analysis of predictive factors of

LDA/remission achievement in 12 weeks.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Items | Odds Ratio | Exp (B) 95%CI | *P* | B |
| Gender (Female) | 0.049 | 0.005–0.471 | **0.009** | **–3.022** |
| Disease duration | 0.997 | 0.993–1.002 | 0.217 | –0.003 |
| Baseline TJC | 0.834 | 0.719–0.968 | **0.017** | **–0.182** |
| Baseline DAS28-CRP | 1.011 | 0.107–9.543 | 0.992 | 0.011 |
| Baseline DAS28-ESR | 0.836 | 0.289–2.419 | 0.741 | –0.179 |
| Baseline SDAI | 0.881 | 0.667–1.165 | 0.375 | –0.126 |
| Baseline CDAI | 1.233 | 0.949–1.603 | 0.117 | 0.210 |
| Baseline HAQ | 0.984 | 0.941–1.029 | 0.483 | –0.016 |

Note: TJC: tender joint count; DAS: disease activity score; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; SDAI: simplified disease; activity index; CDAI: clinical disease activity index; HAQ-DI: Health Assessment Questionnaire-Disability Index.

**Supplementary Table 3:** Comparison of disease activity, HAQ-DI and EQ-5D in patients not relapsed at the end of 60 weeks among three groups.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Items | Group A (*n*=12) | Group B (*n*=13) | Group C (*n*=3) | *P* | F/χ2 |
| DAS28-CRP  (mean±SD) | 2.53±1.30 | 2.08±0.54 | 2.17±1.19 | 0.526 | 0.660 |
| DAS28-ESR  (mean±SD) | 2.78±1.55 | 2.26±0.84 | 1.26±2.19 | 0.213 | 1.645 |
| SDAI  (mean±SD) | 7.20±11.25 | 3.61±2.31 | 4.00±4.58 | 0.454 | 0.816 |
| CDAI  (mean±SD) | 7.72±11.85 | 3.04±2.37 | 4.51±5.10 | 0.409 | 0.928 |
| HAQ-DI  [median (min-max)] | 1 (0–1.95) | 0 (0–0.9) | 0 (0–0.1) | 0.658 | 0.837 |
| EQ-5D  [median (min-max)] | 0.961 (0.321–0.961) | 0.961 (0.530–0.961) | 0.862 (0.610–0.869) | 0.311 | 2.337 |

Note: DAS: disease activity score; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; SDAI: simplified disease; activity index; CDAI: clinical disease activity index; HAQ-DI: Health Assessment Questionnaire-Disability Index; EQ-5D: Euro Qol five dimensions questionnaire.

**Supplementary Table 4:** Comparison of proportion of patients with subclinical synovitis between randomization and week 60 in the three groups.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Items | Patients with PD ≥0 | | | | Patients with GS ≥1 | | | |
| Week 0 | Week 60 | *P* | χ2 | Week 0 | Week 60 | *P* | χ2 |
| Group A  (*n*=17) | 5/17 | 3/8 | 1.000 | 0.000 | 12/17 | 5/8 | 1.000 | 0.000 |
| Group B  (*n*=16) | **12/16** | **0/10 (0)** | **0.000** | **17.895** | 13/16 | 6/10 | 0.463 | 0.539 |
| Group C  (*n*=15) | 8/15 | 0/2 | 0.095 | 2.78 | 10/15 | 1/2 | 1.000 | 0.000 |

Note: PD: power Doppler; GS: gray scale

**Supplementary Table 5:** Comparison of ultrasound scores between randomization and week 60 in the three groups.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Items | Total PD score | | | | Total GS score | | | |
| Week 0 | Week 60 | *P* | Z | Week 0 | Week 60 | *P* | Z |
| Group A  (*n*=17) | 0 (0–4) | 0 (0–3) | 0.842 | –0.283 | **4 (0–15)** | **3 (0–4)** | **0.009** | **–2.587** |
| Group B  (*n*=16) | **1.5 (0–27)** | **0 (0–0)** | **0.001** | **–3.452** | **4 (0–40)** | **2 (0–6)** | **0.001** | **–3.275** |
| Group C  (*n*=15) | 1 (1–5) | 0 (0–0) | 0.294 | –1.294 | 2 (2–23) | 1 (0–2) | 0.235 | –1.291 |

Note: PD: power Doppler; GS: gray scale

**Supplementary Table 6:** Cost-effectiveness analysis of the three groups.

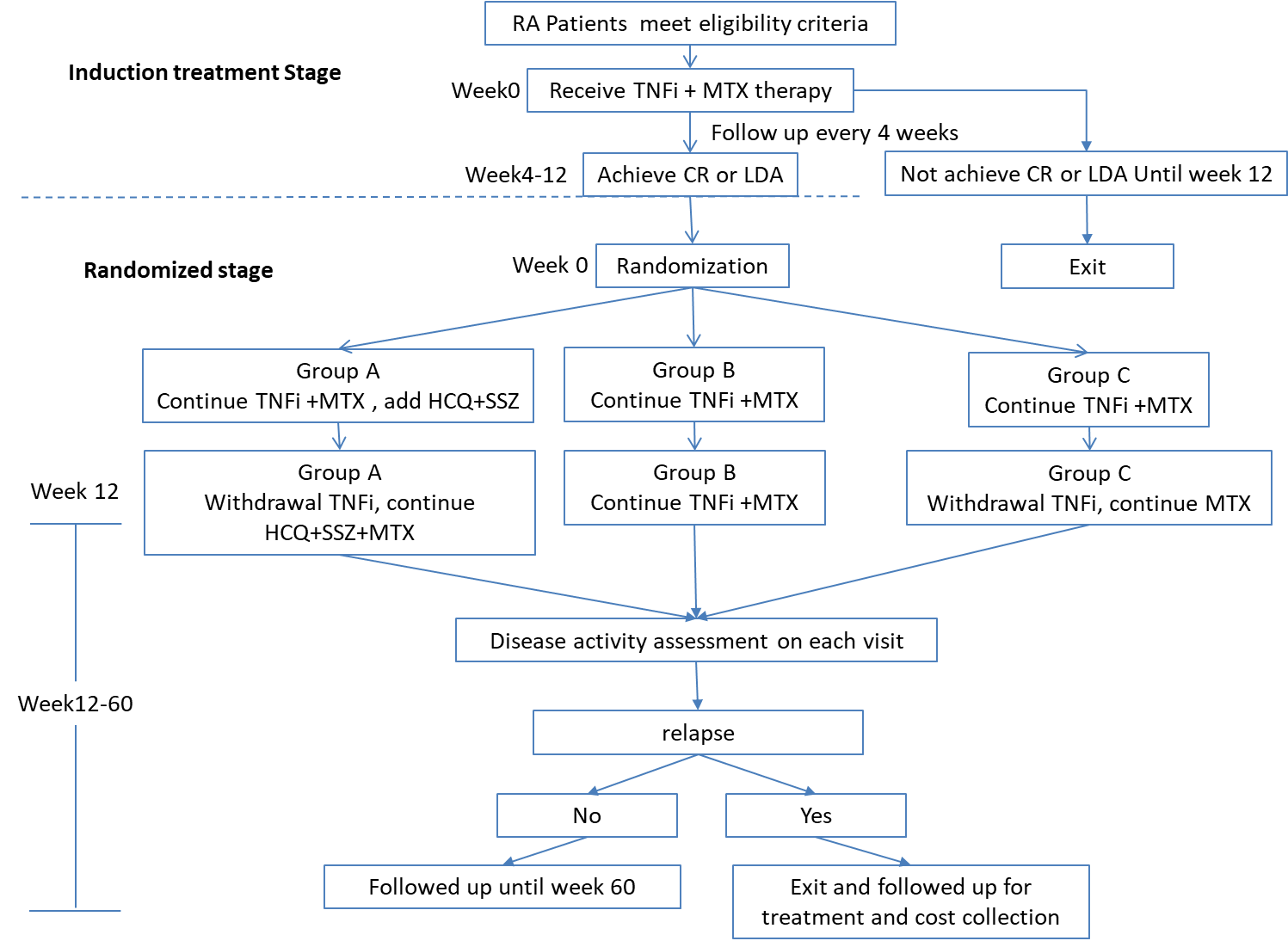
|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Items | Probability  of not relapse | Direct costs, ¥ | C/E, direct costs | ICER, direct costs, ¥/relapse rate | Total costs, ¥ | C/E, total costs | ICER, total costs, ¥/relapse rate |
| Group A  (*n*=24) | 0.55 | 20459 | 37198 | 7141 | 21146 | 38447 | 7626 |
| Group B  (*n*=21) | 0.65 | 61069 | 93952 | 406095\*/86934\*\* | 62567 | 96257 | 414205\*/88862\*\* |
| Group C  (*n*=22) | 0.15 | 17602 | 117347 | 0 | 18136 | 120907 | 0 |

Note: ICER:incremental cost-effectiveness ratio; C/E: cost effectiveness ratio.\*ICER against group A, \*\*ICER against group C.

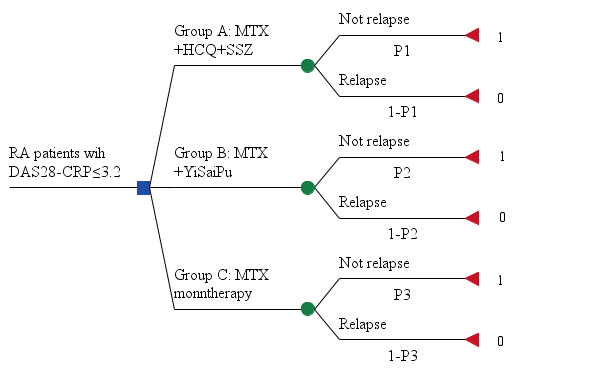
**Supplementary Table 7:** Cost-utility analysis of the three groups.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Items | QALYs  (60 weeks) | Direct costs, ¥ | C/U, direct costs | ICUR, direct costs, ¥/QALY | Total costs, ¥ | C/U, total costs | ICUR, total costs, ¥/QALY |
| Group A  (*n*=24) | 0.67775 | 20459 | 30187 | 10383.69 | 21146 | 31200 | 10944.41 |
| Group B  (*n*=21) | 0.69085 | 61069 | 88367 | 3097597.25\*  /150822.35\*\* | 62567 | 90565 | 3159454.61\*  /154167.25\*\* |
| Group C  (*n*=22) | 0.40265 | 17602 | 43715 | 0 | 18136 | 45041 | 0 |

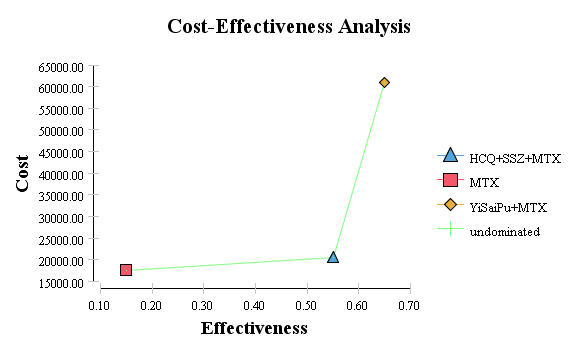
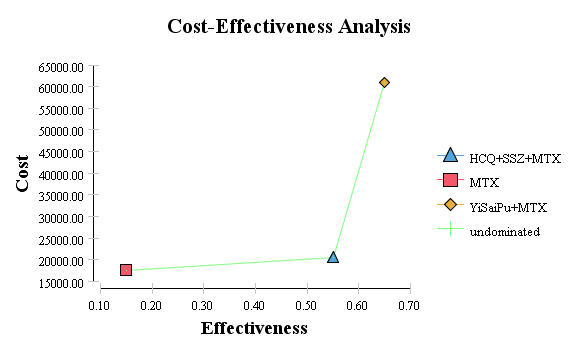
Note: ICUR: incremental cost-utility ratio; C/U: cost utility ratio; QALY: quality-adjusted life years. \*ICUR against group A, \*\*ICUR against group C.

**Supplementary Figure 1:** The flow-chart of the study.

Note: For patients who relapsed during follow up, the study treatment was stopped and patients were referred to appropriate alternative treatments and followed up for cost data collection. csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; MTX: methotrexate; CR: clinical remission; LDA: low disease activity; HCQ: hydroxychloroquine; SSZ: sulfasalazine.



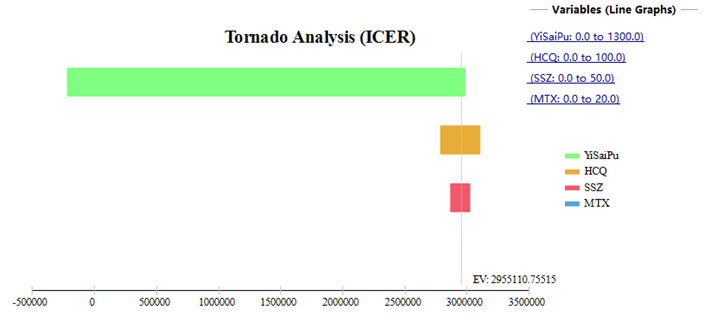
**Supplementary Figure 2:** The decision tree model of the study. RA: Rheumatoid Arthritis; MTX: methotrexate; HCQ: hydroxychloroquine; SSZ: sulfasalazine; YiSaiPu: Brand name of recombinant human tumor necrosis factor receptor II: IgG Fc fusion protein.



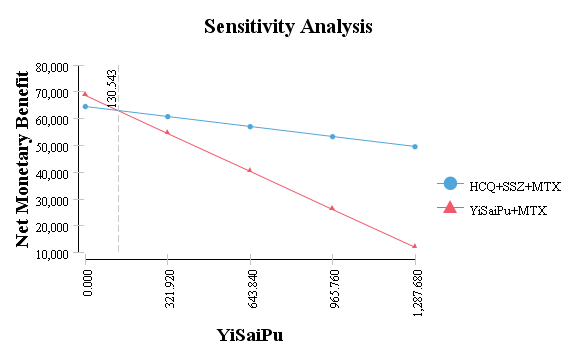
B

A

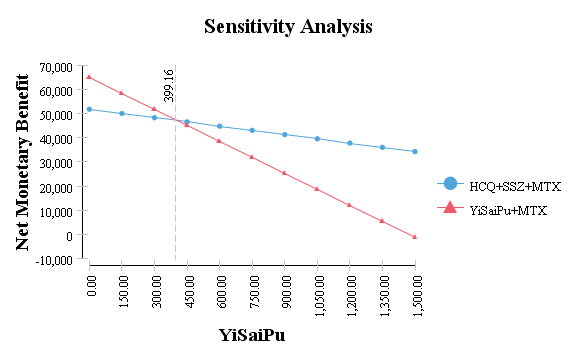
**Supplementary Figure 3:** Direct cost-effectiveness analysis (A) and total cost-effectiveness analysis (B). MTX: methotrexate; HCQ: hydroxychloroquine; SSZ: sulfasalazine; YiSaiPu: Brand name of recombinant human tumor necrosis factor receptor II: IgG Fc fusion protein.



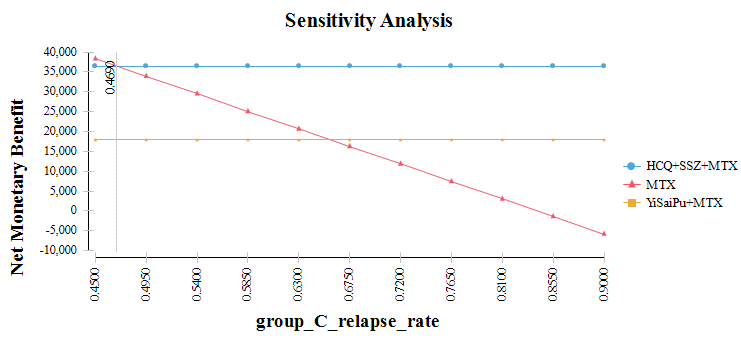
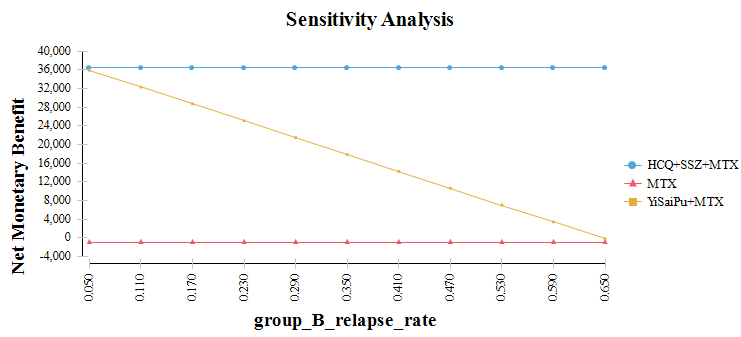
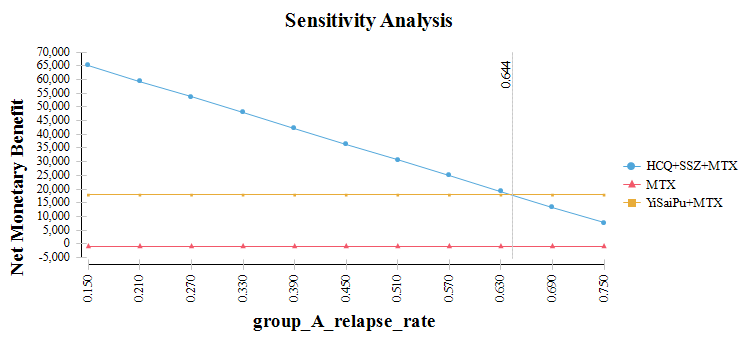
**Supplementary Figure 4:** Tornado chart of one-way sensitivity analysis of cost of each drug. MTX: methotrexate; HCQ: hydroxychloroquine; SSZ: sulfasalazine; YiSaiPu: Brand name of recombinant human tumor necrosis factor receptor II: IgG Fc fusion protein.



**Supplementary Figure 5:** One-way sensitivity analysis of cost of YiSaiPu of net monetary benefit of utility in group A (HCQ+SSZ+MTX) and group B (YiSaiPu+MTX). MTX: methotrexate; HCQ: hydroxychloroquine; SSZ: sulfasalazine; YiSaiPu: Brand name of recombinant human tumor necrosis factor receptor II: IgG Fc fusion protein.



**Supplementary Figure 6:** One-way sensitivity analysis of cost of YiSaiPu of net monetary benefit of effectiveness in group A (HCQ+SSZ+MTX) and group B (YiSaiPu+MTX). MTX: methotrexate; HCQ: hydroxychloroquine; SSZ: sulfasalazine; YiSaiPu: Brand name of recombinant human tumor necrosis factor receptor II: IgG Fc fusion protein.



C

B

A

**Supplementary Figur**e **7:** One-way sensitivity analysis by varying the relapse rate difference by 30% of the base case among three groups. MTX: methotrexate; HCQ: hydroxychloroquine; SSZ: sulfasalazine; YiSaiPu: Brand name of recombinant human tumor necrosis factor receptor II: IgG Fc fusion protein.