**SUPPLEMENTARY FILE**

Figure 1: Initial combination with prednisone (arm 3) group BeSt-study flow chart treatment strategy

(uploaded as separate file)

CSA: ciclosporin A 2.5mg/kg/day; Depomedrol: 3 injections of 120mg in week 1, 4 and 8; Gold 50mg/week; IFX: infliximab, dosages once per 8 weeks; Leflunomide 20mg/day; MTX: methotrexate, dosage per week; Pred: prednisone 7.5mg/day unless indicated otherwise; SSA: sulfasalazine 2000mg/day.

Figure 2: IMPROVED-study flow chart

(uploaded as separate file)

MTX: methotrexate, 25mg/week; HCQ: hydroxychloroquine; SSZ: sulphasalazine. Colours: orange=prednisone, green=MTX, dark blue=treatment according to opinion rheumatologist (TAR), aqua=HCQ, yellow=SSZ, purple=adalimumab biweekly, double thickness purple=adalimumab weekly, grey=protocol not followed as required but remained in follow-up (outside of protocol, OOP).

All patients started with MTX and prednisone, tapered from 60mg/day to 7.5mg/day in 7 weeks. After 4 months if patients were in DAS-remission (DAS<1.6) prednisone was tapered to MTX monotherapy. If patients were not in DAS-remission they were randomized to arm 1 (MTX 25mg/week, HCQ 400mg/day, SSZ 2000mg/day and prednisone 7.5mg/day) or arm 2 (MTX 25mg/week plus adalimumab 40mg/2 weeks). Every four months if patients were in DAS-remission, the medication was tapered or stopped and if patients were not in DAS-remission, the medication was intensified or restarted.

**Supplementary table 1:** Univariable logistic regression analysis with DAS-remission at year 1, ACR/EULAR (Boolean) remission at year 1 and drug-free DAS-remission at year 5 as binomial outcome variables

|  |  |  |  |
| --- | --- | --- | --- |
| **Univariable logistic regression** | **DAS-remission at year 1** | **ACR/EULAR (Boolean) remission at year 1** | **Drug-free DAS-remission** **at year 5** |
|  | **OR** | **95% CI** | **p-value** | **OR** | **95% CI** | **p-value** | **OR** | **95% CI** | **p-value** |
| DAS<1.6 steered study | 2.47 | 1.51-4.02 | <0.001 | 2.31 | 1.30-4.14 |  0.005 | 3.13 | 1.45-6.77 |  0.004 |
| Age | 1.00 | 0.99-1.02 |  0.646 | 1.00 | 0.98-1.02 |  0.783 | 1.01 | 0.98-1.03 |  0.547 |
| Male gender | 2.25 | 1.35-3.76 |  0.002 | 1.85 | 1.05-3.26 |  0.034 | 1.34 | 0.66-2.73 |  0.416 |
| Symptom duration | 0.99 | 0.98-1.00 |  0.013 | 0.99 | 0.98-1.00 |  0.195 | 0.98 | 0.96-1.00 |  0.020 |
| Baseline DAS | 0.63 | 0.47-0.86 |  0.003 | 0.79 | 0.56-1.11 |  0.171 | 0.90 | 0.59-1.37 |  0.628 |
| Tender joint count | 0.92 | 0.88-0.97 | <0.001 | 0.94 | 0.89-0.99 |  0.028 | 0.94 | 0.88-1.01 |  0.091 |
| Swollen joint count | 0.97 | 0.94-1.01 |  0.138 | 1.00 | 0.96-1.05 |  0.858 | 1.01 | 0.96-1.07 |  0.758 |
| ESR | 0.99 | 0.99-1.00 |  0.268 | 1.00 | 0.99-1.01 |  0.623 | 1.00 | 0.99-1.02 |  0.521 |
| VAS general health | 1.00 | 0.99-1.01 |  0.894 | 1.00 | 0.99-1.01 |  0.614 | 1.01 | 0.99-1.02 |  0.530 |
| HAQ | 0.93 | 0.65-1.33 |  0.687 | 1.00 | 0.66-1.52 |  0.990 | 1.34 | 0.80-2.25 |  0.270 |
| RF positive | 1.20 | 0.73-1.97 |  0.470 | 1.59 | 0.86-2.92 |  0.138 | 0.50 | 0.25-1.01 |  0.053 |
| ACPA positive | 0.91 | 0.57-1.47 |  0.704 | 0.93 | 0.53-1.62 |  0.801 | 0.36 | 0.18-0.72 |  0.004 |
| Total SHS | 1.03 | 0.96-1.11 |  0.460 | 0.96 | 0.86-1.06 |  0.378 | 0.90 | 0.79-1.03 |  0.128 |
| Time on anti-TNF inhibitor | 0.96 | 0.93-0.98 | <0.001 | 0.95 | 0.91-0.98 |  0.004 | 0.94 | 0.90-0.99 |  0.012 |

DAS: disease activity score, ESR erythrocyte sedimentation rate, VAS: visual analogue scale, HAQ: health assessment questionnaire, RF: rheumatoid factor, ACPA: anti-citrullinated protein antibodies, SHS: Sharp/van der Heijde Score, anti-TNF: anti-tumour necrosis factor, OR: odds ratio, CI: confidence interval.