SUPPLEMENTARY APPENDIX

## Supplementary methods

### Randomisation

Randomisation was performed in blocks of six, without stratification factors, and generated by an online program (www.randomization.com). The randomisation list, an Excel document, was managed by an independent co-worker of Reade and a backup independent co-worker, who were not otherwise involved in this trial. Investigators and study staff had no access to the randomisation list.

### Statistical analysis

Unless otherwise indicated, analyses were by intention-to-treat. More specifically, where patients returned to standard dosing following (self-reported) unsuccessful interval prolongation, they stayed in prolongation group for the analysis. No imputations methods were used. All participants were included in this analysis, except those who withdrew from the study prior to the second visit without providing any follow-up information. For all analysis SPSS for Windows version 21.0 were used.

## Supplementary Results

### Patients

Fifty-five patients were randomised; 27 to interval prolongation and 28 to continuation of the standard-dose. One patient in the continuation group discontinued the study directly after inclusion because of disagreement with the allocation and one patient was lost to follow-up after week 12. In the continuation group, methotrexate dose was increased in one patient and decreased in one other. In the prolongation group, methotrexate was stopped in one patient and decreased in 3 others patients. Median dose at week 28 were comparable to baseline in both groups (Table 1). No changes in other DMARDs were reported. Patients were included between November 2011 and January 2016.

### CDAI and SDAI

Mean CDAI increased from 3.4 ± 3.3 to 3.9 ± 3.6 in the prolongation group and from 3.4 ± 2.7 to 4.9 ± 3.1 in de continuation group. Mean SDAI increased from 3.6 ± 3.3 to 4.0 ± 3.7 in the prolongation group and from 3.6 ± 2.7 to 5.2 ± 3.2 in the continuation group. T-test showed no significant difference in delta CDAI and SDAI between the groups (p=0.23 and p=0.36, respectively).

## Supplementary Tables and Figures

**Table S1.** DAS28 over time of patients in the prolongation group returned to standard-dose.

| | | DAS28 | | | |
|---|---|---|---|---|---|
| **Pt** | **Return (week)** | **Baseline** | **Week 12** | **Week 28** | **Sparkline†** |
| 1 | 8 | 1,46 | | 1,54 |  |
| 2 | 11 | 1,55 | 1,53 | 1,43 |  |
| 3 | 12 | 2,49 | 2,27 | 2,48 |  |
| 4 * | 14 | 2,48 | 3,89 | |  |
| 5 * | 16 | 1,64 | 3,25 | 1,77 |  |
| 6 | 16 | 3,06 | 1,89 | |  |

*† DAS28 sparklines have similar axes for all patients.*DAS28≥0.6*

**Table S2.** Number of adverse events in 28 weeks of follow-up

| Adverse event | Continuation | Interval prolongation |
|---|---|---|
| Respiratory tract infection | 3 | 2 |
| Urinary tract infection | 1 | 0 |
| Ocular infection | 2 | 0 |
| Injection side reaction | 2 | 0 |
| Bacterial infection | 1 | 0 |
| Gingivitis | 1 | 0 |
| Herpes labialis | 1 | 0 |
| Rhinitis | 1 | 0 |