**Supplemental Figure 1. ACT-RAY study design**

Oral MTX is blinded throughout the whole 3-year study. TCZ and the added csDMARD are open-label.

**Legend:**
- BL: Baseline
- MTX: Methotrexate
- PBO: Placebo
- TCZ: Tocilizumab

**Notes:**
1. BL, baseline; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAS28, Disease Activity Score in 28 joints; MTX, methotrexate; OL, open-label; PBO, placebo; TCZ, tocilizumab.
Supplemental Table 1. Number of patients adding first or second open-label csDMARDs—safety population

| Added csDMARD, n | Add-On (N=277) | | | Switch (N=276) | | |
|-----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 | Weeks 24-36    | Weeks 36-52    | Weeks 52-100   | Weeks 24-36    | Weeks 36-52    | Weeks 52-100   |
| Azathioprine    | 0              | 1              | 0              | 3              | 1              | 0              |
| Chloroquine     | 7              | 1              | 1              | 9              | 1              | 2              |
| Hydroxychloroquine | 34          | 9              | 21             | 31             | 9              | 20             |
| Leflunomide     | 6              | 4              | 7              | 15             | 2              | 7              |
| Sulfasalazine   | 27             | 8              | 8              | 32             | 7              | 8              |

csDMARD, conventional synthetic disease-modifying antirheumatic drug.
**Supplemental Table 2.** Adverse events leading to patient deaths—safety population

| Age/Sex | Study Day of Death | SAE Leading to Death [onset day] (other SAE [onset day]) |
|---------|------------------|----------------------------------------------------------|
| **Add-On** | | |
| 147738/0005 | 66/M | 168 | Sepsis [131] (Scrotal abscess [131]) (Acute renal failure [135]) (Skin necrosis [135]) (Congestive heart failure [138]) |
| 147645/0005 | 79/F | 205 | Sepsis [138] |
| 147697/0009 | 62/M | 783 | Gastrointestinal carcinoma [641] |
| 147714/0018 | 63/F | 831 | Haemorrhagic stroke [829] |
| **Switch** | | |
| 147642/0001 | 51/F | 107 | Meningitis [98] |
| 147739/0004 | 32/F | 104 | Myocardial infarction [104] |
| 147635/0005 | 63/M | 458 | Cardiac failure [445] |
| 147617/0004 | 56/F | 564 | Malignant hyperthermia [559] (Cerebral haemorrhage [460]) (Gastrointestinal disorder [514]) |
| 147616/0009 | 64/F | 550 | Sudden death [550] |
| 147622/0010 | 79/M | 613 | Death [613] (Gastric ulcer [521]) |

SAE, serious adverse event.