**SUPPLEMENTAL MATERIAL**

**Table S1 OPTION, BREVACTA, and SUMMACTA study designs**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study** | **Description** | **Arms** | **Patient population** | **Time** | **Primary endpoint** |
| OPTION (NCT00106548) | Phase 3, randomized, double-blind, placebo-controlled, parallel-arm, multicenter trial | TCZ-IV 8 mg/kg q4w + MTX  (n = 205)  TCZ-IV 4 mg/kg q4w + MTX  (n = 214)  PBO + MTX  (n = 204) | Patients with moderately to severely active RA with an inadequate response to MTX | 24 weeks, double blind  5-year OLE: after 24 weeks, patients received TCZ-IV + MTX | ACR20 response at week 24 |
| BREVACTA (NCT01232569) | Phase 3, 2-arm, randomized, double-blind, parallel-arm, multicenter trial | PBO + csDMARDs  (n = 219)  TCZ-SC 162 mg q2w + csDMARDs  (n = 437) | Patients with moderately to severely active RA with an inadequate response to ≥ 1 DMARD(s) that may have included TNFis | 24 weeks, double blind  72-week OLE: at week 24, the PBO arm received TCZ-SC q2w and the TCZ-SC arm continued receiving TCZ-SC q2w; patients could receive open-label TCZ-SC qw as escape therapy at 12 weeks | ACR20 response at week 24 |
| SUMMACTA  (NCT01194414) | Phase 3, randomized, double-bind, active-controlled, parallel-group, multicenter trial | TCZ-IV 8 mg/kg q4w + PBO-SC qw  (n = 631)  TCZ-SC 162 mg qw + PBO-IV q4w  (n = 631) | Patients with active RA with an inadequate response to ≥ 1 DMARD(s) that may have included TNFis | 24 weeks, double blind  72-week OLE: at week 24, the TCZ-SC arm switched to TCZ-IV 8 mg/kg q4w and the TCZ-IV arm switched to TCZ-SC 162 mg qw | ACR20 response at week 24 |

ACR20, American College of Rheumatology criteria for 20% improvement; csDMARD, conventional synthetic disease-modifying antirheumatic drug; IV, intravenous; MTX, methotrexate; OLE, open-label extension; PBO, placebo; qw, once weekly; q2w, every 2 weeks; q4w, every 4 weeks; RA, rheumatoid arthritis; SC, subcutaneous; TCZ, tocilizumab; TNFi, tumor necrosis factor inhibitor.

**Table S2 Proportion of patients reporting improvements ≥ MCID† in PROs at 16 weeks in OPTION and 12 weeks in BREVACTA and NNT of TCZ-IV or TCZ-SC vs placebo**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **OPTION‡** | | | **BREVACTA‡** | | |
|  | **Improvement**  **≥ MCID, % of patients** | |  | **Improvement**  **≥ MCID, % of patients** | |  |
|  | **TCZ-IV** | **PBO** | **NNT** | **TCZ-SC** | **PBO** | **NNT** |
| PtGA | 75.8\*\*\* | 50.8 | 4.0 | 72.4\*\*\* | 53.1 | 5.2 |
| Patient pain | 69.1\*\*\* | 47.6 | 4.7 | 63.9\*\*\* | 46.0 | 5.6 |
| HAQ-DI | 62.5\*\* | 48.7 | 7.2 | 58.2\*\* | 46.7 | 8.7 |
| FACIT-Fatigue | 64.9\*\*\* | 46.0 | 5.3 | 57.7\* | 50.0 | 13.0 |
| SF-36 PCS | 76.6\*\*\* | 48.6 | 3.6 | 63.1\*\* | 51.7 | 8.8 |
| SF-36 MCS | 59.1 | 49.1 | 10.1 | 58.5\*\*\* | 44.1 | 6.9 |
| Physical functioning | 72.3\*\*\* | 50.0 | 4.5 | 59.2 | 50.2 | 11.1 |
| Role-physical | 56.8\*\*\* | 30.9 | 3.9 | 64.3\* | 55.0 | 10.8 |
| Bodily pain | 81.5\*\*\* | 54.5 | 3.7 | 72.7\*\*\* | 54.5 | 5.5 |
| General health | 64.0 | 57.1 | 13.1 | 60.9\* | 51.2 | 10.3 |
| Vitality | 73.8\*\*\* | 56.5 | 5.8 | 66.7\*\* | 54.5 | 8.2 |
| Social functioning | 60.5\*\*\* | 41.6 | 5.3 | 57.3\*\*\* | 41.7 | 6.4 |
| Role-emotional | 49.7\*\* | 32.8 | 5.9 | 53.5\* | 45.5 | 12.5 |
| Mental health | 50.6\*\* | 42.9 | 6.0 | 61.4\*\* | 47.9 | 7.4 |

FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire–Disability Index; IV, intravenous; MCID, minimum clinically important differences; MCS, mental component summary; MTX, methotrexate; NNT, number needed to treat; PBO, placebo; PCS, physical component summary; PRO, patient-reported outcome; PtGA, patient global assessment; SC, subcutaneous; SF-36, Short Form-36; TCZ, tocilizumab.

*\*P* < 0.05; \*\**P* < 0.01; \*\*\**P* < 0.001.

† The MCID for PROs were defined as follows: HAQ-DI, ≥ 0.22; PtGA, ≥ 10; patient pain, ≥ 10; FACIT-Fatigue, ≥ 4; SF-36 PCS/MCS, ≥ 2.5; and SF-36 domains, ≥ 5.0.

‡ Analyses were performed using the intention-to-treat population in OPTION (TCZ-IV, n = 205; PBO, n = 204), intention-to-treat population in BREVACTA (TCZ-SC, n = 437; PBO, n = 219), and per-protocol population in SUMMACTA (TCZ-SC, n = 558; TCZ-IV, n = 537).