ONLINE SUPPLEMENTARY MATERIALS

SUPPLEMENTARY METHODS

Randomization and blinding

After eligibility had been confirmed, subjects were randomized by blinded study staff using IWRS (an automated web randomization system). The IWRS allocated the treatment group and assigned the study treatment. This system also managed drug supply management and visit dispensation. Blinded study staff requested study treatment assignment via IWRS for all subsequent treatment study visits. Cenduit Interactive Response Technology (C.I.R.T) system (Cenduit, LLC) was used in the study for this purpose. A top-down randomization was used in a 1:1:1 ratio for the three treatment groups: Olokizumab (OKZ) 64 mg (q4w), OKZ 64 mg (q2w), and Placebo. A block size of 6 was applied.

As this was a randomized, double-blind, placebo-controlled study, access to randomization codes was restricted. The treatment each subject received have not been disclosed to the blinded site staff, including the Investigator, study coordinator, subject, R-Pharm, or R-Pharm's designee. Since the study treatments were distinguishable, they have been prepared by the unblinded pharmacist (or their unblinded designee) out of sight of the subject and any blinded study team members and were provided to blinded site staff in blinded syringes that were identical in appearance. The study site staff have been trained in methods that must be followed and documented to prevent unblinding. Guidance on specific blinding procedures were provided in the Study Reference Manual. The treatment codes were held by the IWRS. Only the unblinded pharmacist (or their unblinded designee) or dedicated unblinded staff who were not directly involved in subject management were aware of the randomized drug assignment. The storage and preparation of study treatment were performed at a secured location that was not accessible to blinded investigational staff. Additional measures to ensure that both Investigators and subjects remained blinded to study treatment included the following:

· Joint assessments have been made by an independent assessor, blinded to both the dosing regimen and all other study assessments.

· Laboratory results for CRP and ESR samples collected during the Treatment Period were not available to blinded study site staff. As ESR was tested locally, the testing have been performed, reviewed, and registered by unblinded study site staff who were not responsible for managing subjects.

· Certain efficacy assessments (ACR20, ACR50, ACR70, DAS28 (CRP), DAS28 (ESR), SDAI, and CDAI) have not been calculated by the Investigator during the course of the study, but were instead computed in the statistical database for analysis purposes.
All blinded procedures have been respected.

Members of the independent DSMB reviewed separately safety data during the study. In the event that ongoing safety monitoring has uncovered an issue needed to be addressed by unblinding at the treatment group level, only members of the DSMB were permitted to conduct additional analysis of the safety data.

Patient inclusion criteria

Subjects could be enrolled in the study only if they had met all of the following criteria:

1. Male or female subjects ≥18 years of age
2. Subjects willing and able to sign informed consent
3. Subjects with a diagnosis of adult-onset RA classified by ACR/EULAR 2010 revised classification criteria for RA for at least 12 weeks prior to Screening
    - If the subject was diagnosed according to ACR 1987 criteria previously, the Investigator could classify the subject per ACR 2010 retrospectively, using available source data
4. Inadequate response to treatment with oral, SC, or intramuscular (IM) MTX (for definition of inadequate response to MTX treatment) for at least 12 weeks prior to Screening at a dose of 15 to 25 mg/week (or ≥10 mg/week if intolerant to higher doses)
    - The dose and means of administering MTX had to be stable for at least 6 weeks prior to Screening
5. Subjects had to be willing to take folic acid or equivalent throughout the study
6. Subjects with moderately to severely active RA disease as defined by all of the following:
    a. ≥6 tender joints (68-joint count) at Screening and baseline; and
    b. ≥6 swollen joints (66-joint count) at Screening and baseline; and
    c. CRP above ULN at Screening based on the central laboratory results

Patient exclusion criteria

Subjects who meet any of the following criteria were eligible for the study:

1. Diagnosis of any other inflammatory arthritis or systemic rheumatic disease (e.g., gout, psoriatic or reactive arthritis, Crohn's disease, Lyme disease, juvenile idiopathic arthritis, or systemic lupus erythematosus)
    - However, subjects could have secondary Sjogren's syndrome or hypothyroidism
2. Subjects who were Steinbrocker class IV functional capacity (incapacitated, largely or wholly bed-ridden or confined to a wheelchair, with little or no self-care)
3. Prior exposure to any licensed or investigational compound directly or indirectly targeting IL-6 or IL-6R (including tofacitinib or other Janus kinases and spleen tyrosine kinase [SYK] inhibitors)
4. Prior treatment with cell-depleting therapies, including anti-CD20 or investigational agents (e.g., CAMPATH, anti-CD4, anti-CD5, anti-CD3, and anti-CD19)
5. Prior use of bDMARDs, with the following exception:

- Subjects who discontinued TNFi therapy due to a reason other than lack of efficacy were allowed to enter the study (TNFi therapy should not have been discontinued to facilitate a subject's participation in the study, but should instead have been previously discontinued as part of a subject's medical management of RA). The use of TNFi therapy within the following windows prior to baseline was exclusionary:
    a. 4 weeks for etanercept
    b. 8 weeks for infliximab
    c. 10 weeks for adalimumab, certolizumab, and golimumab

6. Use of parenteral and/or intra-articular glucocorticoids within 4 weeks prior to baseline
7. Use of oral glucocorticoids greater than 10 mg/day prednisone (or equivalent), or change in dosage within 2 weeks prior to baseline
8. Prior documented history of no response to hydroxychloroquine and sulfasalazine
9. Prior use of cDMARDs (other than MTX) within the following windows prior to baseline (cDMARDs should not have been discontinued to facilitate a subject's participation in the study, but should instead have been previously discontinued as part of a subject's medical management of RA):
    a. 4 weeks for sulfasalazine, azathioprine, cyclosporine, hydroxychloroquine, chloroquine, gold, penicillamine, minocycline, or doxycycline
    b. 12 weeks for leflunomide unless the subject had completed the following elimination procedure at least 4 weeks prior to baseline: Cholestyramine at a dosage of 8 grams 3 times daily for at least 24 hours, or activated charcoal at a dosage of 50 grams 4 times daily for at least 24 hours
    c. 24 weeks for cyclophosphamide
10. Vaccination with live vaccines in the 6 weeks prior to baseline or planned vaccination with live vaccines during the study
11. Participation in any other investigational drug study within 30 days or 5 times the terminal half-life of the investigational drug, whichever was longer, prior to baseline
12. Other treatments for RA (e.g., Prosorba Device/Column) within 6 months prior to baseline
13. Use of intra-articular hyaluronic acid injections within 4 weeks prior to baseline
14. Use of non-steroidal anti-inflammatory drugs (NSAIDs) on unstable dose or switching of NSAIDs within 2 weeks prior to baseline
15. Previous participation in this study (randomized) or another study of OKZ
16. Abnormal laboratory values, as defined below:
    a. Creatinine level ≥1.5 mg/dL (132 µmol/L) for females or ≥2.0 mg/dL (177 µmol/L) for males

b. ALT or AST level ≥1.5× ULN

c. Platelets $<100\times10^9$/L ($<100{,}000/mm^3$)

d. White blood cell count $<3.5\times10^9$/L

e. Neutrophil count $<2000\times10^6$/L ($<2000/mm^3$)

f. Hemoglobin level ≤80 g/L

g. Glycosylated hemoglobin (HbA_{1c}) level ≥8%

17. Subjects with concurrent acute or chronic viral hepatitis B or C infection as detected by blood tests at Screening (e.g., positive for hepatitis B surface antigen [HBsAg], total hepatitis B core antibody [anti-HBc], or hepatitis C virus antibody [HCV Ab])

    a. Subjects who were positive for hepatitis B surface antibody (anti-HBs), but negative for HBsAg and anti-HBc, were eligible.

18. Subjects with HIV infection

19. Subjects with:

    a. Suspected or confirmed active TB disease or a history of active TB disease

    b. Close contact (i.e., sharing the same household or other enclosed environment, such as a social gathering place, workplace, or facility, for extended periods during the day) with an individual with active TB within 1.5 years prior to Screening

    c. History of untreated latent TB infection (LTBI), regardless of interferon-gamma release assay (IGRA) result at Screening

        i. Subjects with a history of untreated LTBI could be re-screened and enrolled if they fulfilled all 3 of the following criteria:

            1. Active TB was ruled out by a certified TB specialist or pulmonologist who was familiar with diagnosing and treating TB (as acceptable per local practice);

            2. The subject had completed at least 30 days of LTBI-appropriate prophylaxis prior to baseline with agents recommended as preventative therapy for LTBI according to country-specific/Centers for Disease Control and Prevention (CDC) guidelines (treatment with isoniazid for 6 months was not an appropriate prophylactic regime for this study and it should not have been used); and

            3. The subject was willing to complete the entire course of recommended LTBI therapy.

    d. Positive interferon-gamma release assay (IGRA) result at Screening. If indeterminate, the IGRA could be repeated once during the Screening Period. If there was a second indeterminate result, the subject to be excluded.

        i. Subjects with a positive IGRA result at Screening could be re-screened and enrolled if they fulfilled all 3 of the following criteria:

            1. Active TB was ruled out by a certified TB specialist or pulmonologist who was familiar with diagnosing and treating TB (as acceptable per local practice);

2. The subject had completed at least 30 days of LTBI-appropriate prophylaxis prior to baseline with agents recommended as preventative therapy for LTBI according to country-specific/CDC guidelines (treatment with isoniazid for 6 months was not an appropriate prophylactic regime for this study and it should not be used); and

3. The subject was willing to complete the entire course of recommended LTBI therapy.

ii. If a subject with a positive IGRA result at Screening had documented evidence of completing treatment for LTBI with a treatment regime and treatment duration that was appropriate for this study, the subject could be enrolled without further prophylaxis if recommended by a certified TB specialist or pulmonologist who was familiar with diagnosing and treating TB (as acceptable per local practice) and no new exposure in close contact with an individual with active TB after completing the prophylactic treatment was suspected.

20. Concurrent malignancy or a history of malignancy within the last 5 years (with the exception of successfully treated carcinoma of the cervix in situ and successfully treated basal cell carcinoma and squamous cell carcinoma not less than 1 year prior to Screening [and no more than 3 excised skin cancers within the last 5 years prior to Screening])

21. Subjects with any of the following CV conditions:

    a. Uncompensated congestive heart failure, or class III or IV heart failure defined by the New York Heart Association classification (The Criteria Committee of the New York Heart Association, 1994)

    b. Untreated or resistant arterial hypertension Grade II-III (systolic blood pressure [BP] >160 mm Hg and/or diastolic BP >100 mm Hg)

    c. History or presence of concurrent severe and/or uncontrolled CV disorder (including but not limited to acute coronary syndrome or stroke/transient ischemic attack in the previous 3 months before Screening) that could, in the Investigator's judgment, contraindicate subject participation in the clinical study, or was clinically significant enough in the opinion of the Investigator to alter the disposition of the study treatment, or constituted a possible confounding factor for assessment of efficacy or safety of the study treatment

22. Subjects with a history or presence of any concurrent severe and/or uncontrolled medical condition (including but not limited to respiratory, hepatic, renal, GI, endocrinological, dermatological, neurological, psychiatric, hematological [including bleeding disorder], or immunologic/immunodeficiency disorder[s]) that could, in the Investigator's judgment, contraindicate subject participation in the clinical study, or was clinically significant enough in the opinion of the Investigator to alter the disposition of the study treatment, or constituted a possible confounding factor for assessment of efficacy or safety of the study treatment

23. Uncontrolled diabetes mellitus

24. Subjects with any infection requiring oral antibiotic or antiviral therapy in the 2 weeks prior to Screening or at baseline, injectable anti-infective therapy in the last 4 weeks prior to baseline, or serious or recurrent infection with history of hospitalization in the 6 months prior to baseline
25. Subjects with evidence of disseminated herpes zoster infection, zoster encephalitis, meningitis, or other non-self-limited herpes zoster infections in the 6 months prior to baseline
26. Subjects with planned surgery during the study or surgery ≤4 weeks prior to Screening and from which the subject had not fully recovered, as judged by the Investigator
27. Subjects with diverticulitis or other symptomatic GI conditions that could predispose the subject to perforations, including subjects with a history of such predisposing conditions (e.g., diverticulitis, GI perforation, or ulcerative colitis)
28. Pre-existing central nervous system demyelinating disorders (e.g., multiple sclerosis and optic neuritis)
29. History of chronic alcohol or drug abuse as judged by the Investigator
30. Female subjects who were pregnant, lactating, had lactated within the last 12 weeks, or who were planning to become pregnant during the study or within 6 months of last dose of study treatment
31. Female subjects of childbearing potential (unless permanent cessation of menstrual periods, determined retrospectively after a woman had experienced 12 months of natural amenorrhea as defined by the amenorrhea with underlying status [e.g., correlative age] or 6 months of natural amenorrhea with documented serum follicle-stimulating hormone levels >40 mIU/mL and estradiol <20 pg/mL) who were not willing to use a highly effective method of contraception during the study and for at least 6 months after the last administration of study treatment

    OR

    Male subjects with partners of childbearing potential not willing to use a highly effective method of contraception during the study and for at least 3 months after the last administration of study treatment

    Highly effective contraception was defined as:

    - Female sterilization surgery: hysterectomy, surgical bilateral oophorectomy (with or without hysterectomy), or tubal ligation at least 6 weeks prior to the first dose of study treatment
        - In the case of oophorectomy alone, only when the reproductive status of the woman had been confirmed by documented follow-up hormone level assessment
    - Total abstinence if it was the preferred and constant lifestyle of the subject. Thus, periodic abstinence such as ovulation, symptothermal, postovulation, calendar methods, and withdrawal were not acceptable methods of contraception.

- Male sterilization surgery: at least 6 months prior to Screening (with the appropriate postvasectomy documentation of the absence of sperm in the ejaculate). For female subjects, the vasectomized male had to be the only partner.
- Placement of established intrauterine device (IUD): IUD copper or IUD with progesterone
- Barrier method (condom and intravaginal spermicide, cervical caps with spermicide, diaphragma with spermicide) in combination with the following: established oral, injected, or implanted hormone methods of contraception or contraceptive patch

32. Subjects with a known hypersensitivity to any component of the OKZ drug product or placebo
33. Subjects with a known hypersensitivity or contraindication to any component of the rescue medication
34. History of severe allergic or anaphylactic reactions to human, humanized, or murine monoclonal antibodies
35. Subject's unwillingness or inability to follow the procedures outlined in the protocol
36. Other medical or psychiatric conditions or laboratory abnormalities that could increase potential risk associated with study participation and administration of investigational products, or that could affect study results interpretation and, as per the Investigator's judgment, made the subject ineligible

Prior and Concomitant Treatments

Concomitant treatment with MTX was detailed in the protocol. Specifically, at the discretion of the Investigator, the dose of MTX could be reduced once during the study for safety reasons.

Concomitant treatment with folic acid ≥5 mg per week or equivalent was required for all subjects starting by Visit 2 (Week 0). Folic acid or equivalent should not have been taken on the same day as MTX.

Specific treatments prohibited prior to (as applicable) and during the course of the study were described in the Table below. Other medications and non-drug therapies not listed within the table that were considered necessary for the subject's safety and well-being could be given at the discretion of the Investigator and recorded in the appropriate sections of the eCRF. All medications/treatments received within 4 weeks prior to the Screening Visit were recorded in the eCRF. Prior MTX and all other treatments for RA for the 6 months prior to the Screening Visit were recorded in the eCRF. Doses, route of applications, duration of treatment, and reasons for prescription are also were recorded.

Table Prohibited Medications

Treatment	Restriction
cDMARDs other than MTX	• Treatment with cDMARDs other than MTX was prohibited during the entire study, with the exception of sulfasalazine and/or hydroxychloroquine, which were permitted as rescue medication for nonresponders starting at Week 14 • Prior use of cDMARDs other than MTX within the following windows prior to baseline was exclusionary (cDMARDs should not have been discontinued to facilitate a subject's participation in the study, but should instead have been previously discontinued as part of a subject's medical management of RA): o 4 weeks for sulfasalazine, azathioprine, cyclosporine, hydroxychloroquine, chloroquine, gold, penicillamine, minocycline, or doxycycline o 12 weeks for leflunomide unless the subject had completed the following elimination procedure at least 4 weeks prior to baseline: cholestyramine at a dosage of 8 grams 3 times daily for at least 24 hours, or activated charcoal at a dosage of 50 grams 4 times a day for at least 24 hours o 24 weeks for cyclophosphamide
bDMARDs/ kinase inhibitors	• Treatment with any licensed or investigational biologics directly or indirectly targeting IL-6 or IL-6R (including tofacitinib or other JAK or SYK inhibitors) was prohibited during the entire study and their use prior to Screening was exclusionary. • Treatment with cell-depleting therapies, including anti-CD20 agents or investigational agents (e.g., CAMPATH, anti-CD4, anti-CD5, anti-CD3, and anti-CD19), was prohibited during the entire study and their use prior to Screening was exclusionary. • Treatment with bDMARDs, including TNFi therapy, was prohibited during the entire study and their use prior to Screening was exclusionary.
Corticosteroids	• Treatment with an oral glucocorticoid greater than 10 mg/day prednisone or equivalent or a change in dosage within 2 weeks prior to baseline was exclusionary. • Use of parenteral glucocorticoids within 4 weeks prior to baseline was exclusionary. Use of parenteral glucocorticoids was strongly discouraged during the entire study, but limited use was allowed in the following circumstance: o No more than 2 joints could be injected at or after Week 14 after all study assessments for this time point are performed. The injection should not have to exceed 40 mg methylprednisolone or equivalent cumulative dose. Injected joints had to be rated as having their pre-injection status for the remainder of the study.
NSAIDs	• NSAIDs were prohibited during the entire study with the following exceptions: o Stable doses of NSAIDs were permitted during the study if the subject had received stable doses for ≥2 weeks prior to baseline. Doses of NSAIDs had to be kept constant throughout the entire study unless the Investigator changed the dose for safety reasons. Switching of NSAIDs was not allowed. However, if the subject had an AE that requires discontinuation of the NSAID, an alternative NSAID could be initiated per the local label (if not contraindicated).

Treatment	Restriction
	• Aspirin use at daily doses up to 325 mg was permitted if indicated for CV protection. At this dose, aspirin will not be considered an NSAID.
Analgesics	• Analgesics, including opioids, were prohibited during the entire study with the following exception: • Paracetamol/acetaminophen: Maximum 2000 mg per day (maximum 1000 mg per dose). Paracetamol/acetaminophen was not to be taken within 24 hours prior to joint assessment, including baseline assessment.
Hyaluronic acid	• Intra-articular hyaluronic acid was prohibited during the entire study and its use within 4 weeks prior to baseline was exclusionary.
Vaccination	• Live vaccinations were prohibited during the entire study and their use within 12 weeks prior to baseline was exclusionary.

Abbreviations: AE = adverse event; bDMARD = biologic disease-modifying anti-rheumatic drug; cDMARD = conventional disease-modifying anti-rheumatic drug; CV = cardiovascular; DMARD = disease-modifying anti-rheumatic drug; IL-6 = interleukin-6; IL-6R = IL-6 receptor; JAK = Janus kinase; MTX = methotrexate; NSAID = non-steroidal anti-inflammatory drug; SC = subcutaneous(ly); SYK = spleen tyrosine kinase; TNFi = tumor necrosis factor-α inhibitor.

Allowed Medications

The following medications were allowed (non-exhaustive list), including clarifications of the above prohibited medications:

- Inhaled corticosteroids
- Topical corticosteroids
- Oral corticosteroids
  - Doses of ≤10 mg/day of prednisone or equivalent were permitted as long as the dose had not been changed within the 2 weeks prior to baseline; dose adjustments were not permitted during the study unless the Investigator changed the dose for safety reasons.
- Intra-articular corticosteroids
  - No more than 2 joints could be injected during the study at or after Week 14, after all study assessments for this time point had been performed. The cumulative dose for both injections should not have to exceed 40 mg methylprednisolone or equivalent. Joints treated with IA corticosteroids had to be rated with their pre-injection status for the remainder of the study and had to be omitted from all subsequent joint assessments.
- NSAIDs
  - The subject must have received a stable dose for ≥2 weeks prior to baseline, and the dose must be kept constant throughout the entire study unless the Investigator changes the dose for safety reasons.
- Analgesic treatment with paracetamol/acetaminophen was permitted up to a maximum dose of 2000 mg per day (maximum 1000 mg per dose) or up to the maximum dose in the local label, whichever was lower. Paracetamol/acetaminophen could not to be taken within 24 hours prior to joint assessment, including baseline assessment.

Rescue Medication Starting at Week 14

Subjects were classified in terms of their response to study treatment at Week 14, with nonresponders defined as all subjects who did not improve by at least 20% in both SJC and TJC (66-68 joint assessment). Nonresponders in all groups were prescribed sulfasalazine and/or hydroxychloroquine according to the local label of the prescribed drug(s) as rescue medication starting at or as close as possible to Week 14, in addition to the assigned study treatment.

The maximum allowed doses of sulfasalazine and hydroxychloroquine were:

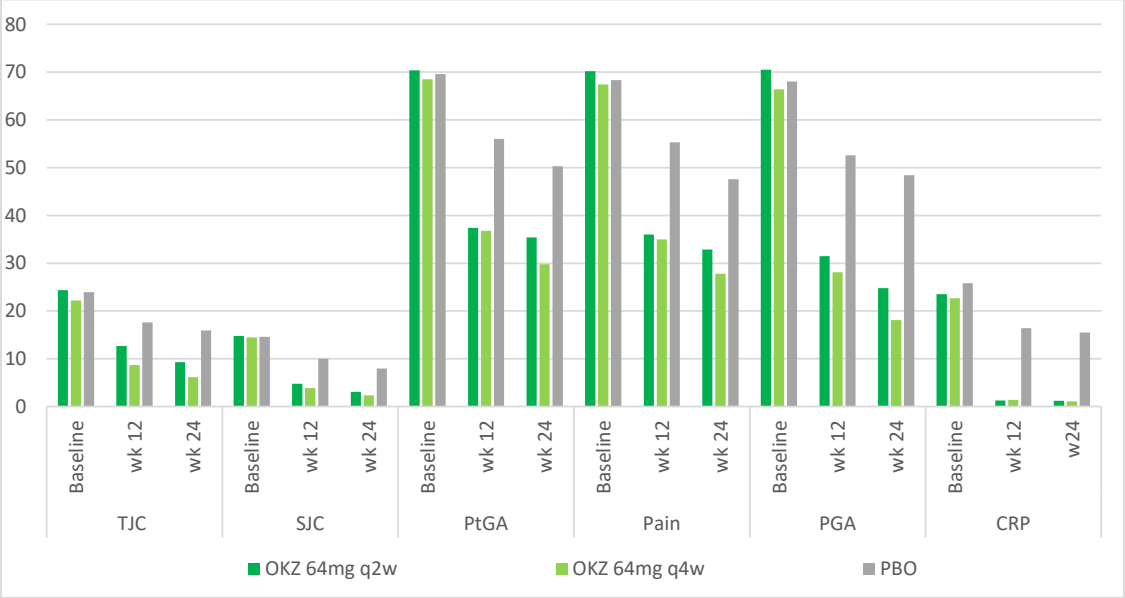
- Sulfasalazine: 3 g per day
- Hydroxychloroquine: 400 mg per day

Nonresponders at Week 14 remained blinded to their assigned treatment. Rescue medication was administered as open-label treatment. The choice of rescue medication (sulfasalazine, hydroxychloroquine, or both) had been made according to local practice, and the assigned rescue medication regimen was maintained throughout the study.

For subjects who receive rescue medication, periodic safety evaluations for toxicity resulting from sulfasalazine and/or hydroxychloroquine were undertaken as per the drug label and local guidelines.

SUPPLEMENTARY FIGURE

Figure S1. **Percent mean changes in ACR response criteria parameters and CDAI score parameters during the double-blind treatment period (ITT population)**



CRP, C-reactive protein; ITT, intention-to-treat; OKZ, olokizumab; PBO, placebo; PGA, physicians' global assessment of disease activity; PtGA, patient's global assessment of disease activity; q2w, every 2 weeks; q4w , every 4 weeks; SJC, swollen joint count (66); TJC, Tender joint count (68); wk, week

SUPPLEMENTARY TABLES

Table S1. **Number of missing observations for key efficacy outcomes (ITT population)**

		OKZ 64mg q2w	OKZ 64mg q4w	Placebo
	Missing data for	N=143	N=142	N=143
Wk 2	ACR20, n(%)	9 (6.3)	6 (4.2)	6 (4.2)
	DAS28-CRP, n(%)	10 (7.0)	9 (6.3)	9 (6.3)
	HAQ-DI, n(%)	8 (5.6)	6 (4.2)	6 (4.2)
	CDAI, n(%)	8 (5.6)	7 (4.9)	6 (4.2)
Wk 4	ACR20, n(%)	7 (4.9)	9 (6.3)	12 (8.4)
	DAS28-CRP, n(%)	8 (5.6)	12 (8.4)	17 (11.9)
	HAQ-DI, n(%)	5 (3.5)	9 (6.3)	12 (8.4)
	CDAI, n(%)	5 (3.5)	9 (6.3)	14 (9.8)
Wk 8	ACR20, n(%)	11 (7.7)	9 (6.3)	18 (12.6)
	DAS28-CRP, n(%)	10 (7.0)	12 (8.4)	24 (16.8)
	HAQ-DI, n(%)	9 (6.3)	9 (6.3)	18 (12.6)
	CDAI, n(%)	11 (7.7)	9 (6.3)	18 (12.6)
Wk 12	ACR20, n(%)	15(10.5)	19(13.3)	18(12.6)
	DAS28-CRP, n(%)	13(9.1)	21(14.7)	18(12.6)
	HAQ-DI, n(%)	13(9.1)	18(12.6)	18(12.6)
	CDAI, n(%)	17(11.9)	20(14.0)	18(12.6)
Wk 18	ACR20, n(%)	18 (12.6)	28 (19.6)	23 (16.1)
	DAS28-CRP, n(%)	26 (18.2)	35 (24.5)	35 (24.5)
	HAQ-DI, n(%)	16 (11.2)	28 (19.6)	23 (16.1)
	CDAI, n(%)	16 (11.2)	29 (20.3)	24 (16.8)

Wk 24	ACR20/50/70, n(%)	42(29.4)	44(30.8)	38(26.6)
	DAS28-CRP, n(%)	43(30.1)	44(30.8)	38(26.6)
	HAQ-DI, n(%)	42(29.4)	44(30.8)	38(26.6)
	CDAI, n(%)	43(30.1)	44(30.8)	38(26.6)

Missing observations are defined as number of missing data and/or number of case "out of Window". ACR, American College of Rheumatology response; CDAI, clinical disease activity index; DAS28-CRP, Disease Activity Score 28 based on C-reactive protein; ITT, Intention-to-treat; HAQ-DI, Health Assessment Questionnaire Disability Index; N, Number of subjects in the analysis population; n (%), Number of subjects with missing data and/or with cases "out of Window"; OKZ, olokizumab; q2w, every 2 weeks; q4w, every 4 weeks; Wk, week

Table S2. **Changes from baseline at months 3 (12 week) and 6 (24 week) for WPS-RA (patient-reported outcome measures)[1]**

	Week 12			**Week 24**		
	OKZ q2w N=143	**OKZ q4w N=142**	**Placebo N= 142**	**OKZ q2w N=143**	**OKZ q4w N=142**	**Placebo N= 142**
WPS-RA Missed Work Days	-11.14(3.6) -10.3(5.2) -22.0,1.4	-13.5(3.3) -12.7(5.1) -24.0,-1.3	-0.9(3.7)	-10.5(3.0) -2.9(4.4) -12.8,6.9	-12.8(3.1) -5.2(4.5) -15.3,4.8	-7.6(3.3)
WPS-RA Missed Household Days	-15.4(1.7) -7.5(2.5) -13.0,-2.0	-17.9(1.7) -10.0(2.5) -15.5,-4.6	-7.8(1.8)	-17.2(2.0) -10.0(2.7) -16.1,-3.8	-18.0(1.9) -10.8(2.8) -17.0,-4.6	-7.2(1.9)
WPS-RA Work Impairment	-21.5(3.2) -12.9(4.6) -23.3,-2.6	-23.8(3.0) -15.2(4.4) -25.0,-5.3	-8.6(3.3)	-22.5(3.3) -12.8(4.8) -23.6,-2.0	-30.1(3.3) -20.4(4.8) -31.2,-9.6	-9.7(3.6)
WPS-RA Household Impairment	-25.1(1.9) -13.7(2.7) -19.8,-7.6	-29.1(1.9) -17.7(2.7) -23.8,-11.6	-11.3(1.9)	-31.6(2.2) -16.1(3.1) -23.0,-9.2	-36.2(2.2) -20.6(3.1) -27.6,-13.7	-15.5(2.2)
WPS-RA Work Day Productivity	-16.7(4.3) -8.3(62) -22.1,5.5	-18.6(3.9) -10.2(5.9) -23.4,3.0	-8.4(4.4)	-14.7(4.2) -7.3(6.0) -20.7,6.1	-22.6(4.1) -15.2(6.0) -28.6,-1.9	-7.4(4.4)
WPS-RA Household Day Productivity	-17.5(2.0) -8.4(2.8) -14.7,-2.0	-19.6(2.0) -10.4(2.8) -16.7,-4.1	-9.2(2.0)	-19.2(2.2) -11.2(3.0) -18.0,-4.4	-22.2(2.1) -14.2(3.1) -21.0,-7.4	-8.0(2.1)

Changes were analyzed using ANCOVA model adjusted for the baseline value of the corresponding parameter; missing data resulted from study withdrawal imputed based on the return to baseline assumption; 1, LSM change from baseline (SE), treatment comparison vs placebo LSM difference (SE), 97.5% confidential interval for LSM difference are presented. CI, confidence interval; LSM, least squares mean; N, number of subjects in the analysis population; n, number of responders; OKZ, olokizumab; q2w, every 2 weeks; q4w, every 4 weeks; SE, standard error; Wk, week; WPS-RA, Work Productivity Survey-Rheumatoid Arthritis.

Table S3**. Patients with selected hematology assessments outside of the normal range (Safety Population)**

			OKZ q2w	**OKZ q4w**	**PBO**
Number of Subjects with			**N=143**	**N=142**	**N=142**
WBC count < 4000/mm^3 (or < 4 ·10^9/L)	BL	Nx(%) n(%)	143(100.0) 2(1.4)	142(100.0) 2(1.4)	142(100.0) 3(2.1)
	Wk 12	Nx(%) n(%)	125(87.4) 16(12.8)	128(90.1) 15(11.8)	129(90.8) 2(1.6)
	Wk 24	Nx(%) n(%)	111(77.6) 16(14.4)	111(78.2) 17(15.3)	115(81.0) 2(1.7)
ANC count < 1500/mm^3 (or < 1.5 ·10^9/L)	BL	Nx(%) n(%)	143(100.0) 0(0.0)	142(100.0) 0(0.0)	142(100.0) 0(0.0)

	Wk 12	Nx(%) n(%)	115(80.4) 1(0.9)	123(86.6) 5(4.1)	125(88.0) 1(0.8)
	Wk 24	Nx(%) n(%)	101(70.6) 3(3.0)	101(71.1) 3(3.0)	112(78.9) 0(0.0)
Hemoglobin ≤80 g/L	BL	Nx(%) n(%)	143(100.0) 0(0)	142(100.0) 0(0)	142(100.0) 0(0)
	Wk 12	Nx(%)	126(88.1)	128(90.1)	129(90.8)
		n(%)	0(0)	0(0)	0(0)
	Wk 24	Nx(%)	111(77.6)	111(78.2)	116(81.7)
		n(%)	0(0)	0(0)	1(0.9)

ANC < 1000/mm^3 (or < 1.0 ·10^9/L) and ALC < 500/mm^3 (or < 0.5 ·10^9/L): no observations. ALC, absolute lymphocyte count; ANC, absolute neutrophil count; BL, baseline; N, number of subjects in the arm; Nx(%), number and percent of the subjects with non-missing results; n(%), number and percent of the subjects with abnormal parameters; %, percentage of subjects with non-missing results is calculated relative to the total number of subjects in the population, whilst all other percentages are calculated relative to the number of subjects with non-missing results at a given visit; OKZ, olokizumab; PBO, placebo; q2w, every 2 weeks; q4w, every 4 weeks; WBC, white blood cells; Wk, week.

Table S4. **Patients with selected chemistry assessments outside of the normal range (Safety Population)**

		OKZ q2w	**OKZ q4w**	**PBO**
Number of subjects with		N=143	N=142	N=142
ALT, n(%) Baseline	Nx >1xULN to≤3xULN >3xULN to≤5xULN >5xULN	143(100.0) 12(8.4) 0 1(0.7)	142(100.0) 14(9.9) 0 0	142(100.0) 14(9.9) 0 0
ALT, n(%) Post-Baseline	Nx >1xULN to≤3xULN >3xULN to≤5xULN > 5x ULN	141(98.6) 67(47.5) 9(6.4) 4(2.8)	140(98.6) 74(52.9) 8(5.7) 8(5.7)	141(99.3) 38(27.0) 6(4.3) 1(0.7)
Cholesterol, n(%) Baseline	Nx High	142(99.3) 53(37.3)	138(97.2) 57(41.3)	141(99.3) 65(46.1)
Cholesterol, n(%) Post-Baseline	Nx High	141(98.6) 105(74.5)	139(97.9) 95(68.3)	140(98.6) 77(55.0)
Cholesterol shifts from normal to high	Wk 12, n(%) Mean change[1],(SD) Wk 24, n(%) Mean change[1],(SD)	40(30.3) 1.3(0.6) 34(30.9) 1.3(0.6)	33(26.4) 1.5(0.7) 33(29.5) 1.5(0.7)	12(9.2) 0.7(0.5) 12(10.3) 1.3(0.8)
LDL Cholesterol, n(%) Baseline	Nx High	142(99.3) 28(19.7)	138(97.2) 36(26.1)	141(99.3) 47(33.3)
LDLCholesterol, n(%) Post-Baseline	Nx High	141(98.6) 82(58.2)	139(97.9) 73(52.5)	140(98.6) 56(40.0)
LDLCholesterol shifts from normal to high	Wk 12, n(%) Mean change[1],(SD) Wk 24, n(%) Mean change[1],(SD)	40(30.5) 1.1(0.6) 34(30.9) 1.2(0.6)	32(25.8) 1.0(0.6) 24(21.4) 1.2(0.6)	12(9.2) 0.6(0.4) 13(11.1) 1.1(0.9)

1, mmol/L; LDL, low density lipoproteins; N, Number of subjects in the population; Nx(%), number and percent of the subjects with non-missing results; n(%), number and percent of the subjects with abnormal parameters; %, percentage of subjects with non-missing results is calculated relative to the total number of subjects in the population, whilst all other percentages are calculated relative to the number of subjects with non-missing results at a given visit; OKZ, olokizumab; PBO, placebo; q2w, every 2 weeks; q4w, every 4 weeks; SD, standard deviation; ULN, upper limit of normal; Wk, week