SUPPLEMENTARY DATA

Table S1. Patient characteristics at baseline split by disease duration (FAS)

Mean (SD), unless otherwise stated	RA≤1 year N=29	RA>1 to 2 years N=59	RA>2 years N=43
Age, years	56.9 (12.6)	52.6 (13.8)	56.3 (12.6)
Female, n (%)	23 (79.3)	51 (86.4)	33 (76.7)
Disease duration, median (min; max)	0.6 (0; 1)	1.7 (1; 2)	3.9 (2; 5)
With extra-articular features, n (%)	6 (20.7)	6 (10.2)	4 (9.3)
Duration of morning stiffness, median hours (min; max)	1.0 (1; 24)	1.0 (1; 24)	1.0 (0; 10)
<2 hours, n (%)	19 (65.5)	45 (76.3)	28 (65.1)
≥2 hours, n (%)	10 (34.5)	14 (23.7)	15 (34.9)
DAS28(ESR)	5.8 (1.2)	5.8 (0.9)	6.2 (1.1)
DAS28(CRP)	5.2 (1.1)	5.1 (0.9)	5.5 (1.1)
HAQ-DI	1.4 (0.8)	1.3 (0.6)	1.3 (0.8)
PtAAP	58.5 (24.6)	53.9 (23.1)	58.8 (23.1)
PtGADA	58.6 (23.2)	54.0 (23.7)	61.0 (22.4)
PhGADA	56.0 (17.6)	53.6 (19.7)	61.1 (19.0)
mTSS, median (min; max)	12.0 (0; 44)	31.0 (0; 121)	7.0 (2; 12)
ESR, median mm/h (min; max)	36.0 (2; 105)	34.0 (4; 80)	39.0 (4; 140)
CRP median mg/L (min; max)	8.2 (0; 200)	5.0 (0; 66)	9.0 (0; 97)
Bone erosion at BL, n (%)	7 (24.1)	36 (61.0)	2 (4.7)

BL baseline, *CRP* C-reactive protein, *DAS28* disease activity score in 28 joints, *ESR* erythrocyte sedimentation rate, *FAS* full analysis set, *HAQ-DI* health assessment questionnaire disability index, *mTSS* modified total Sharp score, *PDUS* Power Doppler ultrasound score, *PtAAP* patient's assessment of arthritis pain, *PtGADA* patient's global assessment of disease activity, *PhGADA* physician's global assessment of disease activity, *SD* standard deviation

Table S2. Prior and concomitant medications (SS)

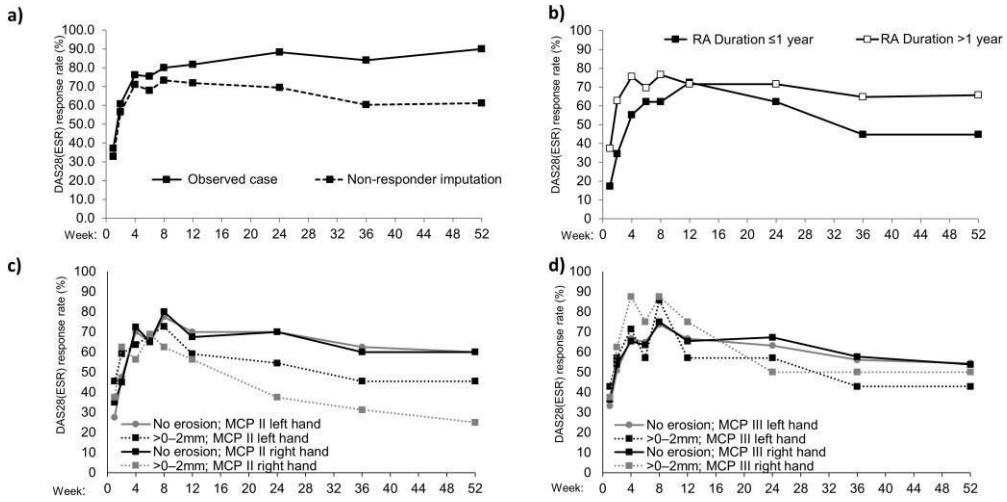
Safety set, n=132	**n (%)**
Corticosteroids for systemic use	73 (55.3)
Prednisone	43 (32.6)
Methylprednisolone	34 (25.8)
Betamethasone sodium phosphate	2 (1.5)
Triamcinolone	1 (0.8)
Anti-inflammatory and anti-rheumatic products	48 (36.4)
Etoricoxib	12 (9.1)
Diclofenac	9 (6.8)
Ibuprofen	6 (4.5)
Aceclofenac	5 (3.8)
Celecoxib	4 (3.0)
Naproxen	4 (3.0)
Ketoprofen	3 (2.3)
Analgesics	31 (23.5)
Paracetamol	21 (15.9)
Panadeine Co	4 (3.0)
Acetysalicyclic acid	3 (2.3)
Pregabalin	2 (1.5)
Tramadol Hydrochloride	2 (1.5)
Frovatriptan	1 (0.8)
Oxycocet	1 (0.8)
Oxycodone	1 (0.8)
Oxycodone hydrochloride	1 (0.8)
Tapentadol hydrochloride	1 (0.8)
Targin	1 (0.8)
Tramadol	1 (0.8)
Ultracet	1 (0.8)

Table S3. Summary of adverse events in the CZP-SPEED study

Safety set, n=132	**n (%) [#]**
Any TEAEs	94 (71.2) [301]
Serious TEAEs	16 (12.1) [25]
Most common serious TEAEs in ≥2% of patients	
Infections and infestations	3 (2.3) [4]
Malignancies[a,b]	3 (2.3) [3]
Renal and urinary disorders	3 (2.3) [3]
Discontinuation due to TEAEs	15 (11.4) [17]
TEAEs requiring dose change[c]	26 (19.7) [54]
Drug-related TEAEs[d]	35 (26.5) [55]
Severe TEAEs	12 (9.1) [13]
Deaths	0

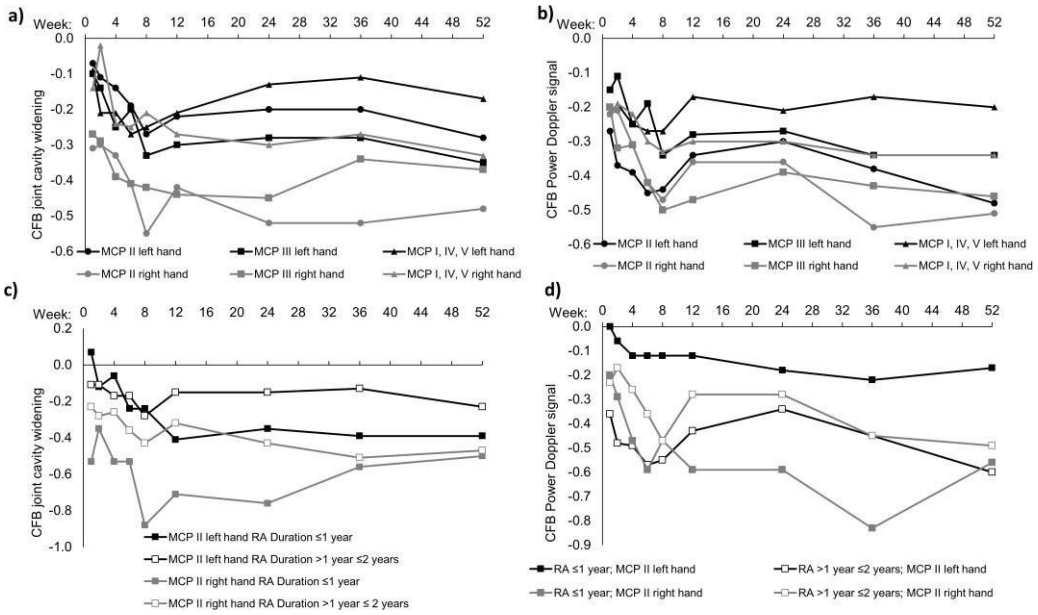
Data are reported for the Safety Set (n=132), which is defined as all patients in the study who received at least one dose of CZP. # number of individual occurrences of the TEAEs in each respective category. Serious TEAEs occurring in ≥2% of patients are reported, according to MedDRA SOC. [a]Malignancies are reported as none of the reported neoplasms were benign. [b]Malignancies were reported in 4 patients, however 1 case was confirmed as a bladder cancer after the database lock. [c]Dose reduction, increase or temporary interruption, [d]TEAEs considered related to CZP treatment or those with missing responses regarding relationship to CZP treatment.
CZP certolizumab pegol, *MedDRA* Medical Dictionary of Regulatory Activities, *SOC* system organ class, *TEAEs* treatment emergent adverse events.

Supplementary Figure S1. Improvements in DAS28(ESR) response over time evaluated across different RA durations and levels of bone erosion in MCP II and MCP III



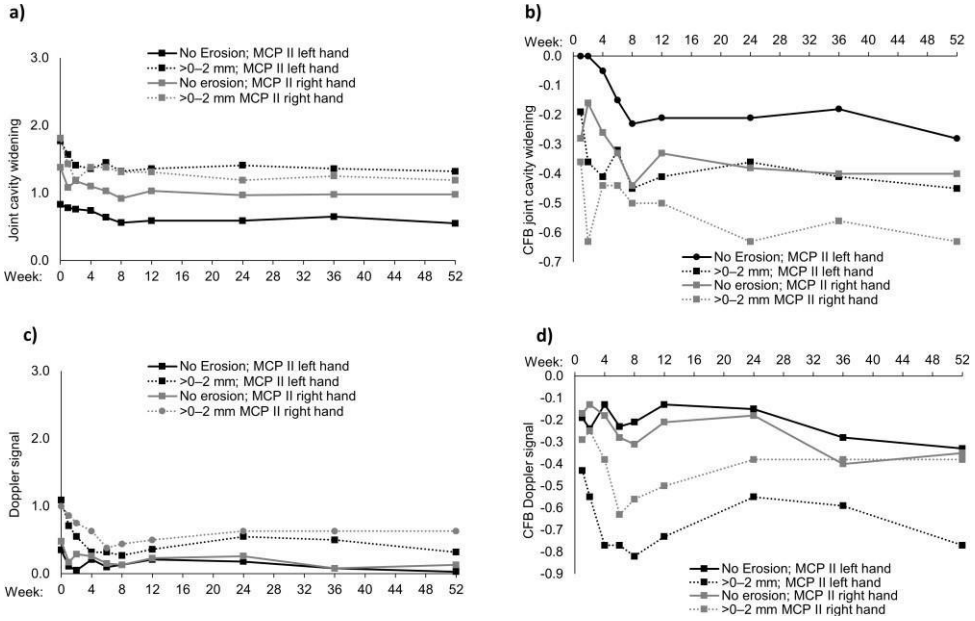
a–b: Data are reported for the full analysis set (n=131). c–d: Data are reported for the PDUS subset (n=66). Missing data were imputed using non-responder imputation (NRI) in Figures S2b, S2c, and S2d. *DAS28* 28-joint Disease Activity Score, *ESR* erythrocyte sedimentation rate, *MCP* metacarpophalangeal joints, *NRI* non-responder imputation, *PDUS* Power Doppler ultrasound, *RA* rheumatoid arthritis.

Supplementary Figure S2. Mean change from baseline (CFB) in joint cavity widening (a, c) and PD signal (b, d) measured with PDUS over time in MCPs. Groups are analyzed by MCP joint (a, b) and duration of RA (c, d).



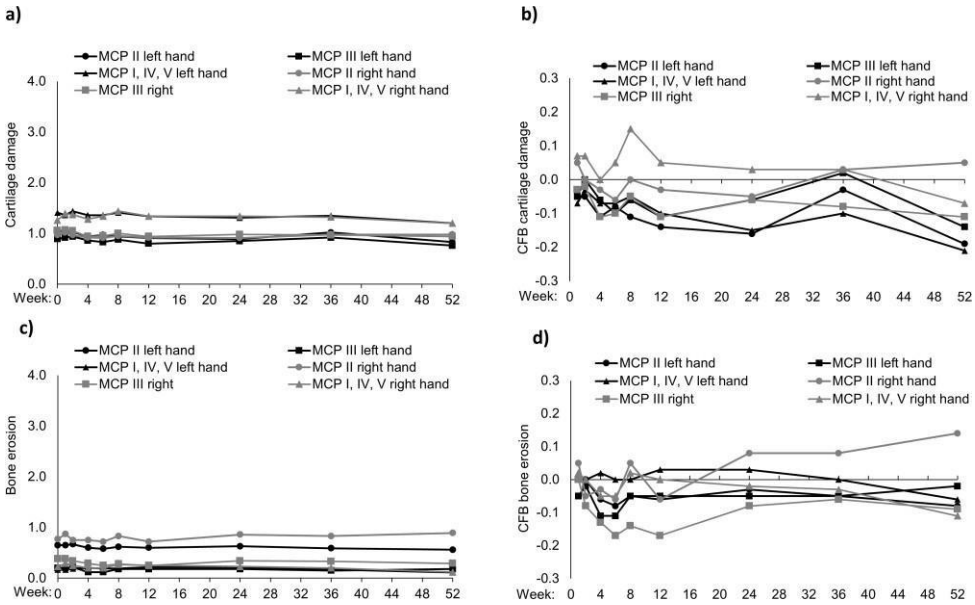
Data are reported for the full analysis set, in the patients eligible for inclusion in the PDUS subgroup (n=66). Missing data were imputed using last observation carried forward (LOCF); LOCF data are shown. *CFB* change from baseline, *PD* Power Doppler, *PDUS* Power Doppler ultrasound, *MCP* metacarpophalangeal joints, *RA* rheumatoid arthritis.

Supplementary Figure S3. Improvement in joint cavity widening (a) and Power Doppler signal (c) and their mean change from baseline (b and d, respectively) measured with PDUS over time in MCPs analyzed by amount of bone erosion.



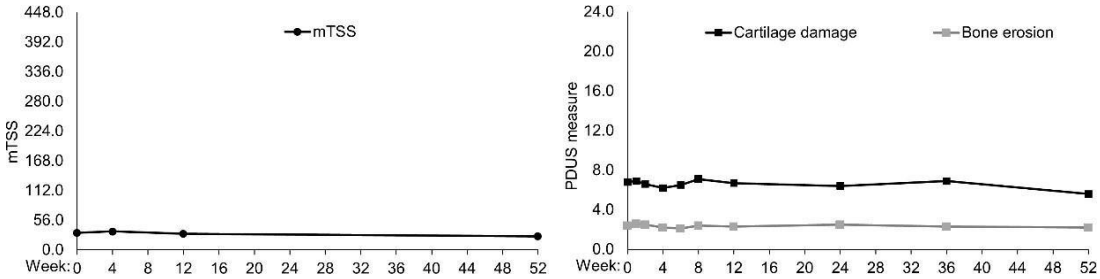
Data are reported for the full analysis set with only patients eligible for inclusion within the PDUS subgroup included (n=66). Joint cavity widening scores (0–3 scale; 0=no effusion/hypertrophy, 1=minimal effusion/hypertrophy, 2=moderate effusion/hypertrophy, 3=extensive effusion/hypertrophy). Power Doppler signal was based on the 4-point scale ranging from 0 (normal/minimal blood flow) to 3 (marked blood flow). Missing data were imputed using last observation carried forward (LOCF). *CFB* change from baseline, *PD* Power Doppler, *PDUS* Power Doppler ultrasound, *MCP* metacarpophalangeal joints.

Supplementary Figure S4. Development of cartilage damage and bone erosion as well as mean change from baseline over time measured with PDUS.



Data are reported for the full analysis set for all patients that were eligible for inclusion within the PDUS subset (n=66). Cartilage damage was based on a 5-point scale ranging from 0–4 for each joint analyzed (0=normal hyaline cartilage, 1=loss of sharpness of the superficial margin of the hyaline cartilage, 2=partial thickness defect of the cartilage layer, 3=full thickness defect of the cartilage layer with a normal subchondral bone profile, 4=complete loss of the cartilage layer and subchondral bone involvement). Bone erosion was scored on a 5-point scale ranging from 0–4 (0=absence of bone erosion, 1=very small bone erosion [<1mm], 2=small erosion [1–2mm], 3=moderate erosion [>2–4mm], 4=large erosion [>4mm]. Missing data were imputed using last observation carries forward (LOCF). *PDUS* Power Doppler ultrasound, *LOCF* last observation carried forward, *MCP* metacarpophalangeal joints.

Supplementary Figure S5. Mean development of joint damage as measured by (a) mTSS and (b) PDUS



Data are reported for the full analysis set for all patients who were eligible for inclusion within the PDUS subset (n=66). For PDUS assessments of cartilage damage and bone erosion, a total of 6 joints (on each hand MCP II, MCP III, and one of MCP I, IV, or V) were assessed by the radiologist, on a 5-point scale ranging from 0–4. For cartilage damage (0=normal hyaline cartilage, 1=loss of sharpness of the superficial margin of the hyaline cartilage, 2=partial thickness defect of the cartilage layer, 3=full thickness defect of the cartilage layer with a normal subchondral bone profile, 4=complete loss of the cartilage layer and subchondral bone involvement). For bone erosion: 0=absence of bone erosion, 1=very small bone erosion (<1 mm), 2=small erosion (1–2 mm), 3=moderate erosion (>2–4 mm), 4=large erosion (>4 mm). Missing data were imputed using last observation carried forward (LOCF). mTSS measurements of joints were scored on a scale ranging from 0–448. *MCP* metacarpophalangeal, *mTSS* modified total Sharp score, *PDUS* Power Doppler ultrasound

Supplementary Figure S6. Representative Power Doppler ultrasound images showing an inflamed II metacarpophalangeal joint of the dominant hand. Images were acquired in dorsal longitudinal (A) and transverse (**B**) scans. **m**=metacarpal bone; **p**=proximal phalanx; **t**=finger extensor tendon.