SUPPLEMENTARY MATERIAL

Table S1. Summary of hierarchical testing procedure of primary and key secondary efficacy variables

Efficacy variables presented in order of hierarchical testing	p-value	Significant [a]
Step 1: ASAS20 responder rate at Week 12 for CZP 200mg vs PBO	0.004 [b]	Yes
Step 2: ASAS20 responder rate at Week 12 for CZP 400mg vs PBO	<0.001 [b]	Yes
Step 3: ASAS20 responder rate at Week 24 for CZP 200mg vs PBO	<0.001 [b]	Yes
Step 4: ASAS20 responder rate at Week 24 for CZP 400mg vs PBO	<0.001 [b]	Yes
Step 5: Change from Baseline in BASFI at Week 12 for CZP 200mg+400mg vs PBO	<0.001 [c]	Yes
Step 6: Change from Baseline in BASDAI at Week 12 for CZP 200mg+400mg vs PBO	<0.001 [c]	Yes
Step 7: Change from Baseline in BASFI at Week 24 for CZP 200mg+400mg vs PBO	<0.001 [c]	Yes
Step 8: Change from Baseline in BASDAI at Week 24 for CZP 200mg+400mg vs PBO	<0.001 [c]	Yes
Step 9: Change from Baseline in BASMI at Week 12 for CZP 200mg+400mg vs PBO	<0.001 [c]	Yes
Step 10: Change from Baseline in BASMI at Week 24 for CZP 200mg+400mg vs PBO	<0.001 [c]	Yes

ASAS20: Assessment in Axial Spondyloarthritis International Society 20% response criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI linear: Bath Ankylosing Spondylitis Metrology Index linear; a Statistical significance was assessed in the context of the hierarchical testing procedure. Each step was tested at 0.05 two-sided. If the result was not significant at any step, then all steps after that were considered not statistically significant. b p-value was estimated from standard 2-sided Wald asymptomatic test with a 5% alpha level. c p-value was estimated from the ANCOVA model with treatment, region, mNY criteria (Y/N), and prior TNF inhibitor exposure (Y/N) as factors, and baseline score as a covariate.

Table S2: Baseline characteristics of the AS and nr-axSpA subpopulations by treatment group

	AS			nr-axSpA		
	Placebo (n=57)	**CZP 200mg Q2W (n=65)**	**CZP 400mg Q4W (n=56)**	**Placebo (n=50)**	**CZP 200mg Q2W (n=46)**	**CZP 400mg Q4W (n=51)**
Demographic characteristics						
Age, mean yrs (SD)	41.6 (12.8)	41.0 (10.8)	41.9 (11.5)	38.0 (11.8)	36.6 (13.0)	37.5 (10.8)
Male, %	71.9	72.3	73.2	48.0	43.5	52.9
AxSpA characteristics						

Symptom duration, median, yrs (min, max)	10.2 (0.3, 50.9)	8.8 (0.3, 32.7)	8.8 (0.3, 44.8)	4.5 (0.5, 41.5)	4.8 (0.3, 34.2)	7.3 (0.3, 25.3)
Symptom duration < 5 years, n (%)	16 (28.1)	26 (40.0)	15 (26.8)	26 (52.0)	24 (52.2)	19 (37.3)
Definitive sacroiliitis on X-ray	57 (100.0)	65 (100.0)	56 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Positive for HLA-B27, n (%)	48 (84.2)	53 (81.5)	44 (78.6)	39 (78.0)	34 (73.9)	37 (72.5)
CRP mg/L						
Median, (min, max)	16.6 (1.4, 155.6)	14.0 (0.1, 174.8)	12.9 (0.7, 159.9)	13.5 (0.2, 156.2)	10.0 (2.0, 52.0)	12.1 (0.1, 120.0)
> ULN, n (%)	45 (78.9)	48 (73.8)	37 (66.1)	32 (64.0)	27 (58.7)	34 (66.7)
>15 mg/L, n (%)	31 (54.5)	27 (41.5)	22 (39.3)	22 (44.0)	15 (32.6)	16 (31.4)
BASDAI,[#] Mean (SD)	6.4 (1.9)	6.5 (1.7)	6.2 (1.3)	6.4 (1.5)	6.5 (1.4)	6.6 (1.6)
BASFI,[#] Mean (SD)	6.0 (2.0)	5.6 (2.3)	5.7 (2.3)	4.9 (2.2)	4.8 (2.2)	5.1 (2.4)
BASMI,[#] Mean (SD)	4.7 (1.6)	4.2 (1.6)	4.3 (1.8)	3.1 (1.6)	3.1 (1.4)	3.3 (1.5)
ASDAS,[#] Mean (SD)	4.1 (0.9)	4.0 (1.0)	3.8 (0.8)	3.8 (0.9)	3.7 (0.8)	3.8 (0.8)
Arthritis,[†] n (%)	30 (52.6)	39 (60.0)	27 (48.2)	31 (62.0)	23 (50.0)	26 (51.0)
Prior and concomitant medication						
Concomitant NSAIDs, n (%)	51 (89.5)	59 (90.8)	51 (91.1)	41 (82.0)	38 (82.6)	44 (86.3)
Concomitant DMARDs, n (%)	22 (38.6)	21 (32.3)	20 (35.8)	16 (32.0)	10 (21.7)	11 (21.6)
Prior anti-TNFα exposure, n (%)	16 (28.1)	11 (16.9)	9 (16.1)	10 (20.0)	4 (8.7)	2 (3.9)

Data refers to the overall patient population (RS). axSpA: axial spondyloarthritis; CZP: certolizumab pegol; Q2W: every 2 weeks; Q4W: every 4 weeks; SD: standard deviation, HLA-B27: human leukocyte antigen B27; CRP: C-reactive protein; ULN: upper limit of normal; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI linear: Bath Ankylosing Spondylitis Metrology Index linear; ASDAS: Ankylosing Spondylitis Disease Activity Score; NSAIDs: Non-steroidal anti-inflammatory drugs; DMARDs: Disease modifying anti-rheumatic drugs; TNFα: tumor necrosis factor alpha; AS: ankylosing spondylitis; nr-axSpA: non-radiographic axial spondyloarthritis. [#] in Full Analysis Set data set; [†]current and/or historical; CRP ULN = 7.9 mg/L.

Table S3. TEAEs by treatment group with an incidence of ≥5% in either CZP group during the 24 week, placebo-controlled, double-blind phase

System Organ Class Preferred Term	Placebo* N=107 n (%)	CZP 200 mg Q2W N=111 n (%)	CZP 400 mg Q4W N=107 n (%)
Infections and infestations	14 (13.1)	19 (17.1)	16 (15.0)
Nasopharyngitis	7 (6.5)	11 (9.9)	11 (10.3)
Upper respiratory tract infections	3 (2.8)	6 (5.4)	4 (3.7)
Investigations	2 (1.9)	7 (6.3)	6 (5.6)
Blood creatine phosphokinase increased	2 (1.9)	7 (6.3)	6 (5.6)
Nervous system disorders	7 (6.5)	7 (6.3)	9 (8.4)
Headache	7 (6.5)	7 (6.3)	9 (8.4)

*Placebo escape at Week 16. Data not adjusted for exposure.

Figure S1. Kinetics of BASFI, BASDAI, BASMI Linear and ASDAS response from Week 0 to Week 24 in axSpA population

Data refers to the full analysis set (FAS) population. **A**, BASFI; **B**, BASDAI; **C**, BASMI linear; and **D**, ASDAS absolute values in the three treatment groups from Week 0 to Week 24. * $p < 0.001$ for CZP vs. PBO.

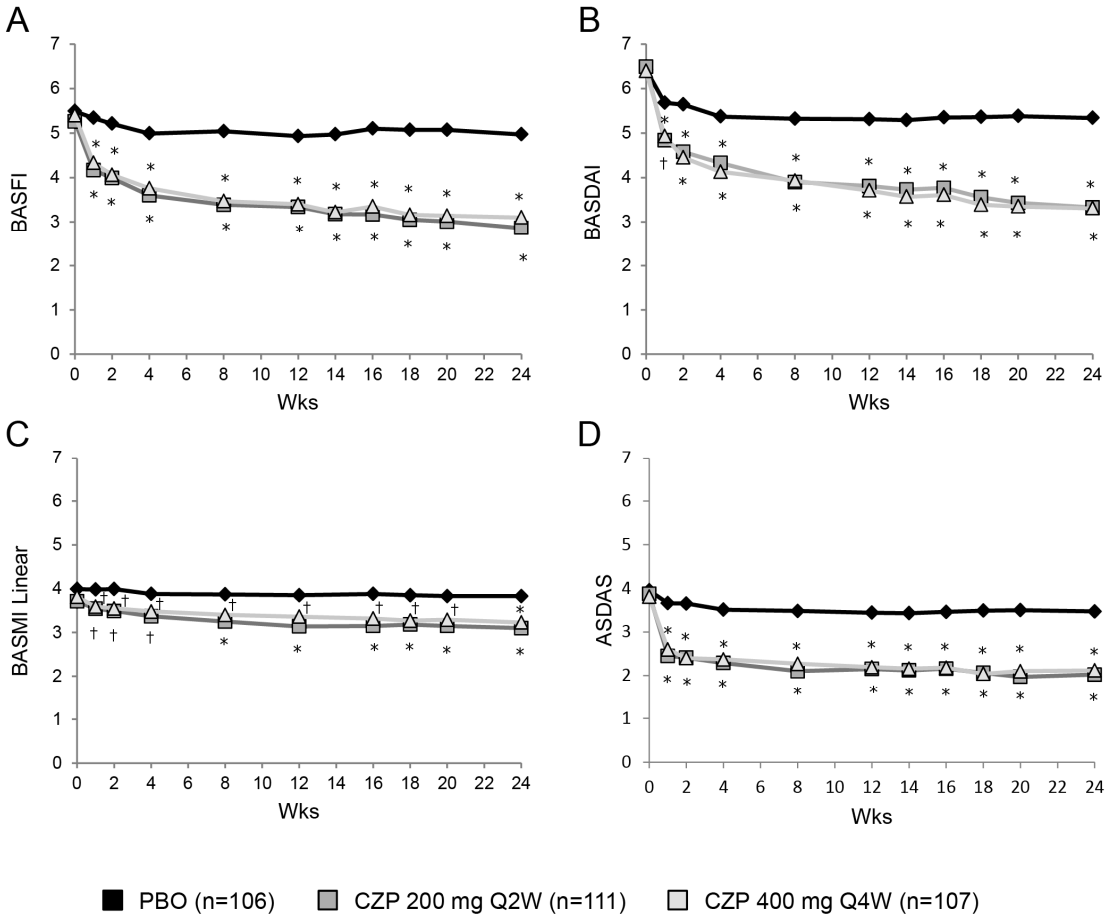
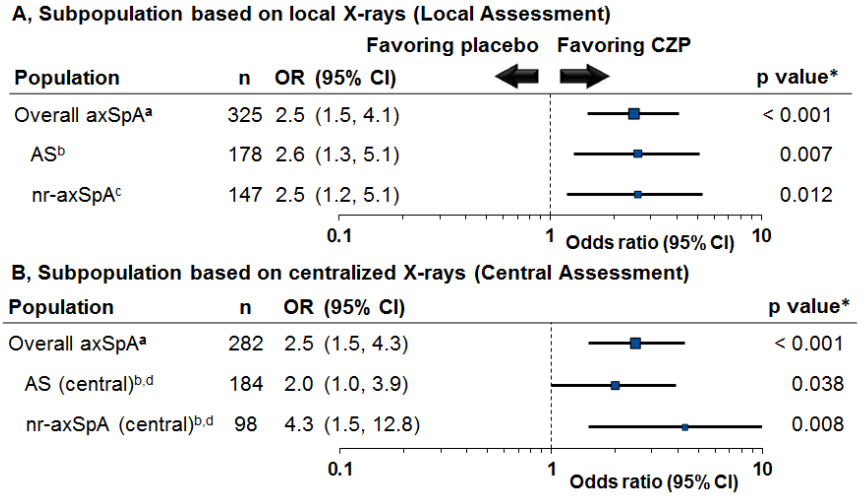


Figure S2. Logistic regression analysis of treatment interaction for AS and nr-axSpA subpopulations as defined by Local Assessment and Central Assessment X-rays.

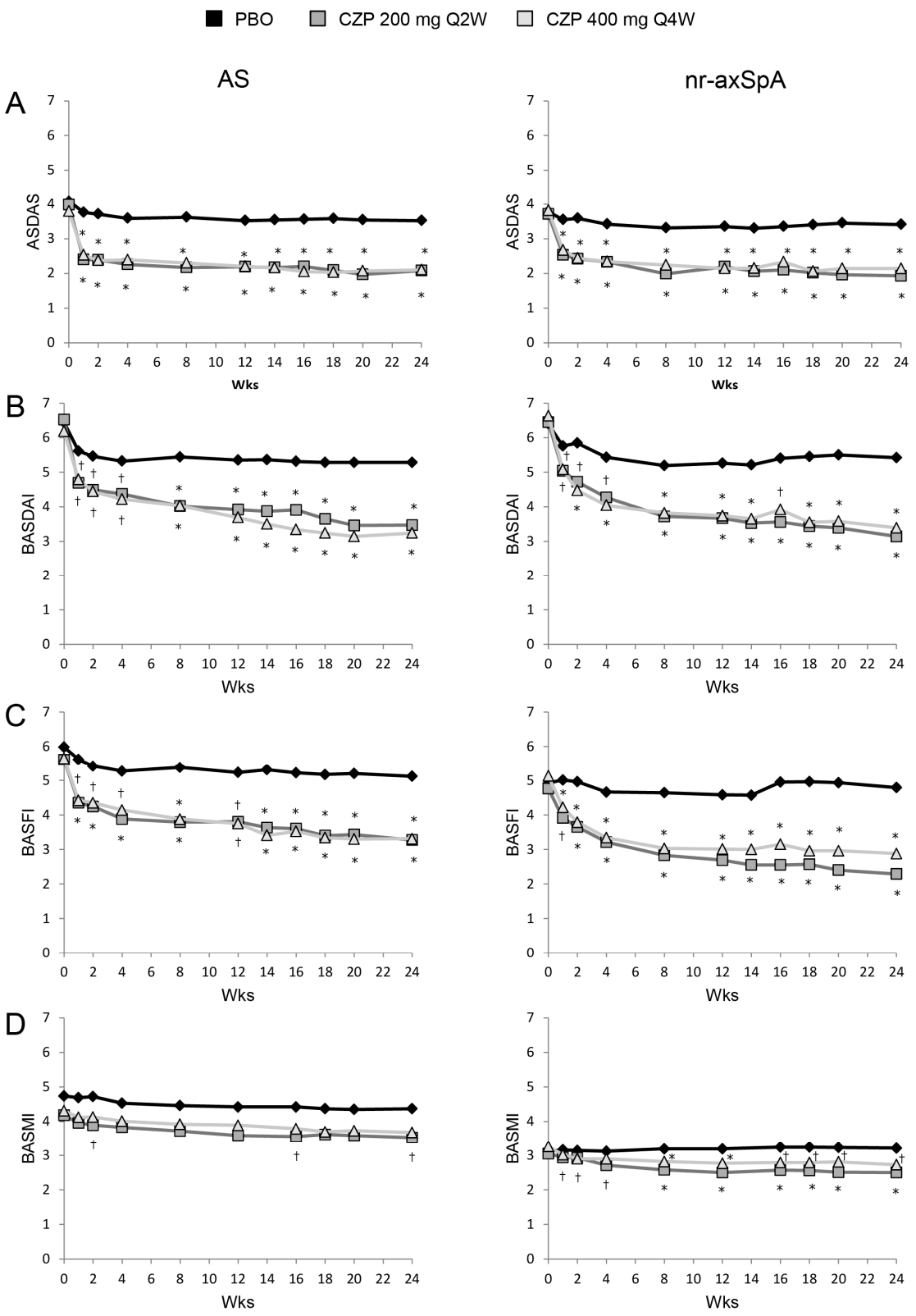
Data refers to the full analysis set (FAS) population. Odds ratios (OR) and confidence intervals (CIs) for achieving ASAS20 response represent all CZP vs placebo groups, respectively. **A**, Subpopulation based on local X-rays (Local Assessment); **B**, Subpopulation based on centralized X-rays (Central Assessment)



[a] With treatment, region, prior TNF exposure, and NY status as factors; [b] With treatment, region, and prior TNF exposure as factors; [c] With treatment and region as factors. [d] Based on central reading of baseline x-rays; * Nominal p value Randomized Set (NRI).

Figure S3. Kinetics of ASDAS, BASDAI, BASFI, and BASMI Linear response from Week 0 to Week 24 in the AS and nr-axSpA subpopulations

Data refers to the full analysis set (FAS) population. **A**, ASDAS; **B**, BASDAI; **C**, BASFI; and **D**, BASMI linear absolute values in the three treatment groups from Week 0 to Week 24. * $p < 0.001$; † $p<0.05$ CZP vs. PBO.


PBO
CZP 200 mg Q2W
CZP 400 mg Q4W
AS
nr-axSpA
A
B
C
D
ASDAS
BASDAI
BASFI
BASMI
Wks