

SUPPLEMENTARY MATERIAL

Comparative Efficacy of Biologic Disease-Modifying Anti-Rheumatic Drugs for Non-Radiographic Axial Spondyloarthritis: A Systematic Literature Review and Bucher Indirect Comparisons

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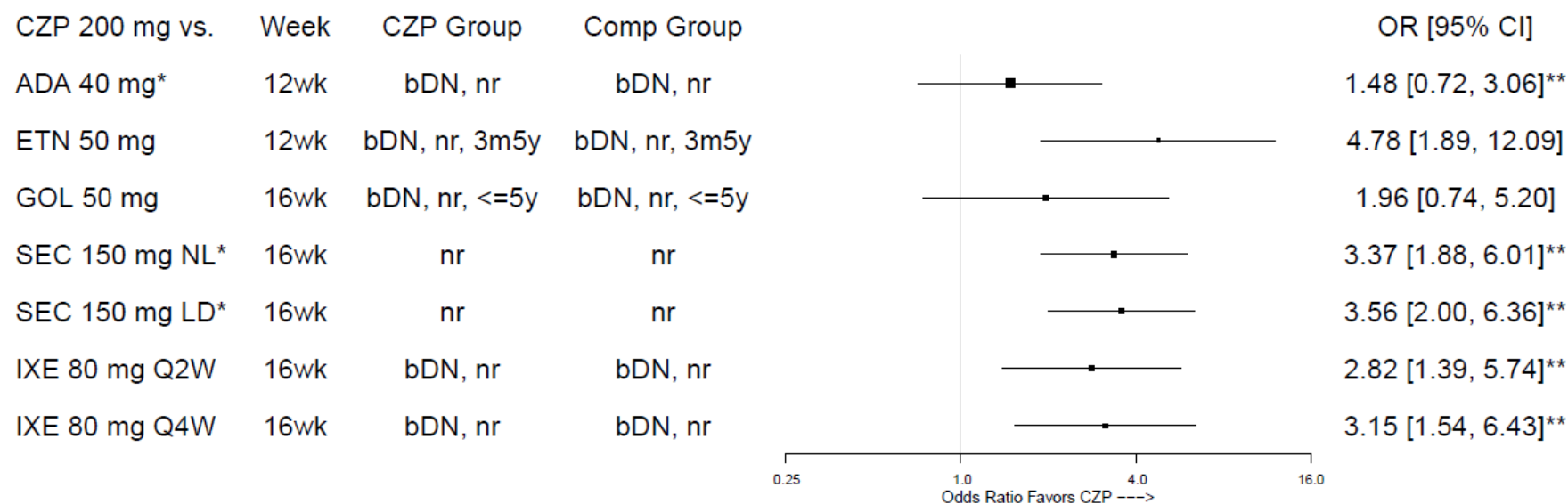
Table S. 1. PICOS Inclusion and Exclusion Criteria

	Patients	Interventions	Comparators	Outcomes	Study Design
Inclusion Criteria	Studies that include adult patients with clearly defined nr-axSpA who failed at least one NSAID agent	TNF inhibitors: ADA, CZP, GOL, IFX, ETN, biosimilars (including, but not limited to, Cipla or Zydus Cadila) IL inhibitors: SEC, IXE	TNF inhibitors: ADA, CZP, GOL, IFX, ETN, biosimilars (including but not limited to Cipla or Zydus Cadila) IL inhibitors: SEC, IXE Conventional DMARDs: cyclosporine, sulfasalazine, MTX, leflunomide, HCQ NSAIDs: celecoxib, etoricoxib, ibuprofen, naproxen, ketoprofen, flurbiprofen, indomethacin/indomethacin, etodolac, diclofenac, aceclofenac, sulindac, piroxicam, meloxicam, tenoxicam PBO/usual care*	<ul style="list-style-type: none"> ASAS 20% and 40% response rate (ASAS 20, 40) BASDAI (pre-, post-, or mean change scores; measure of dispersion; number of patients assessed) and the BASDAI 50 responder rate BASFI (pre-, post-, or mean change scores; measure of dispersion; number of patients assessed) ASDAS-ID and ASDAS-MI Total spine pain 	PBO- and active-controlled RCTs with at least one arm randomized to one of the select TNF inhibitors alone or in combination with other comparator agents in adult patients with active nr-axSpA who failed at least one NSAID; randomized trials in parallel design of at least 12 weeks' duration, or those with crossover happening after 12 weeks
Exclusion Criteria	Studies of non-nr-axSpA patients, those naïve to or on their first NSAID, or studies with mixed populations in which outcomes for nr-axSpA patients are not reported separately	Studies that do not include a treatment arm with any of the bDMARDs of interest	Studies that do not include a treatment arm with any of the selected comparators of interest	Studies lacking relevant data on any of the outcomes of interest	Studies that are not randomized; letters to the editor; citations with no abstract; open-label extensions of RCTs (i.e., the extension phase where previous randomization has been broken); pooled analyses or meta-analyses; animal or in vitro studies; pharmacokinetic or pharmacodynamic studies; randomized trials with crossover happening before 12 weeks; dose-finding studies with no active or PBO comparator; randomized trials with fewer than 10 patients per treatment arm; studies with intended treatment duration fewer than 12 weeks

*Usual care: trials with treatment defined as “usual care” or “standard of care” will be included as active comparators in this review; studies comparing specific treatment regimens that are not on this list, such as non-pharmacologic interventions, will not be considered “usual care” unless they are defined as such by study investigators.

Abbreviations: ADA = adalimumab; CZP = certolizumab pegol; DMARD = disease-modifying anti-rheumatic drug; ETN = etanercept; GOL = golimumab; HCQ = hydroxychloroquine; IFX = infliximab; IXE = ixekizumab; MTX = methotrexate; NSAID = non-steroidal anti-inflammatory drug; nr-axSpA = non-radiographic axial spondyloarthritis; PBO = placebo; PICOS = population, intervention/comparators, outcomes and study design; PRO = patient-reported outcome; RCT = randomized controlled trial; SEC = secukinumab; SLR = systematic literature review; TNF = tumor necrosis factor

Supplementary Figure S. 1. ASAS 20 – Forest Plot

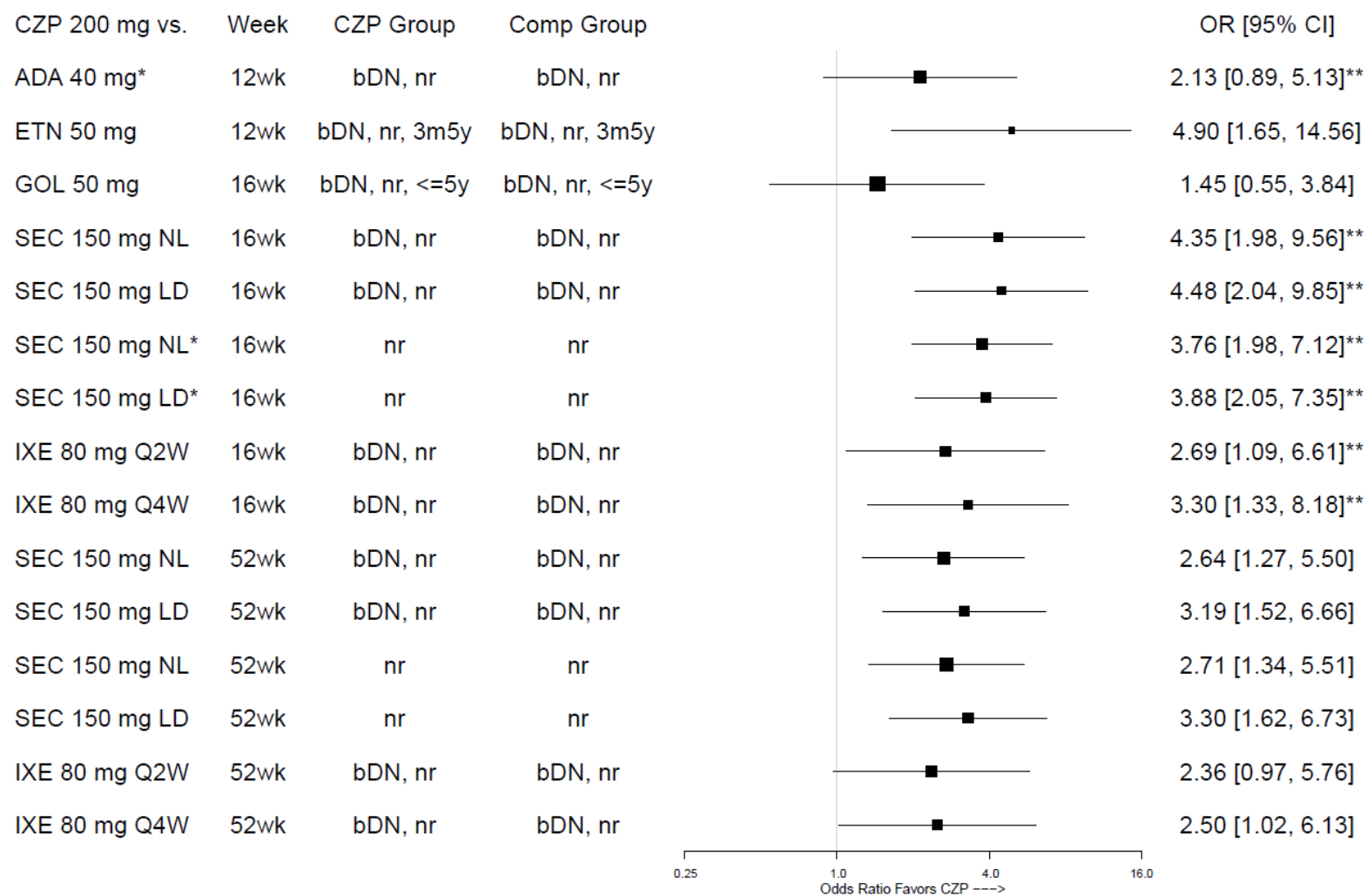


* CZP Pooled (CZP 200 Q2W + CZP Q4W) is analyzed instead of CZP 200 mg

** Random-effect model (analyses are otherwise fixed-effect models)

List of abbreviations: 3m5y = disease duration between three months and five years; <=5y = disease duration of less than or equal to five years; ADA = adalimumab; bDN = biologic Disease-modifying antirheumatic drug-naïve; CI = confidence interval; comp = comparator; CRP = C-reactive protein; CZP = certolizumab pegol; ETN = etanercept; GOL = golimumab; IXE = ixekizumab; LD = loading dose; MD = mean difference in change from baseline; mg = milligram; MRI = magnetic resonance imaging; NL = no loading dose; nr = non-radiographic axial spondyloarthritis; OR = odds ratio; Q2W = every two weeks; Q4W = every 4 weeks; SEC = secukinumab; wk = week

Supplementary Figure S. 2. ASAS 40 – Forest Plot



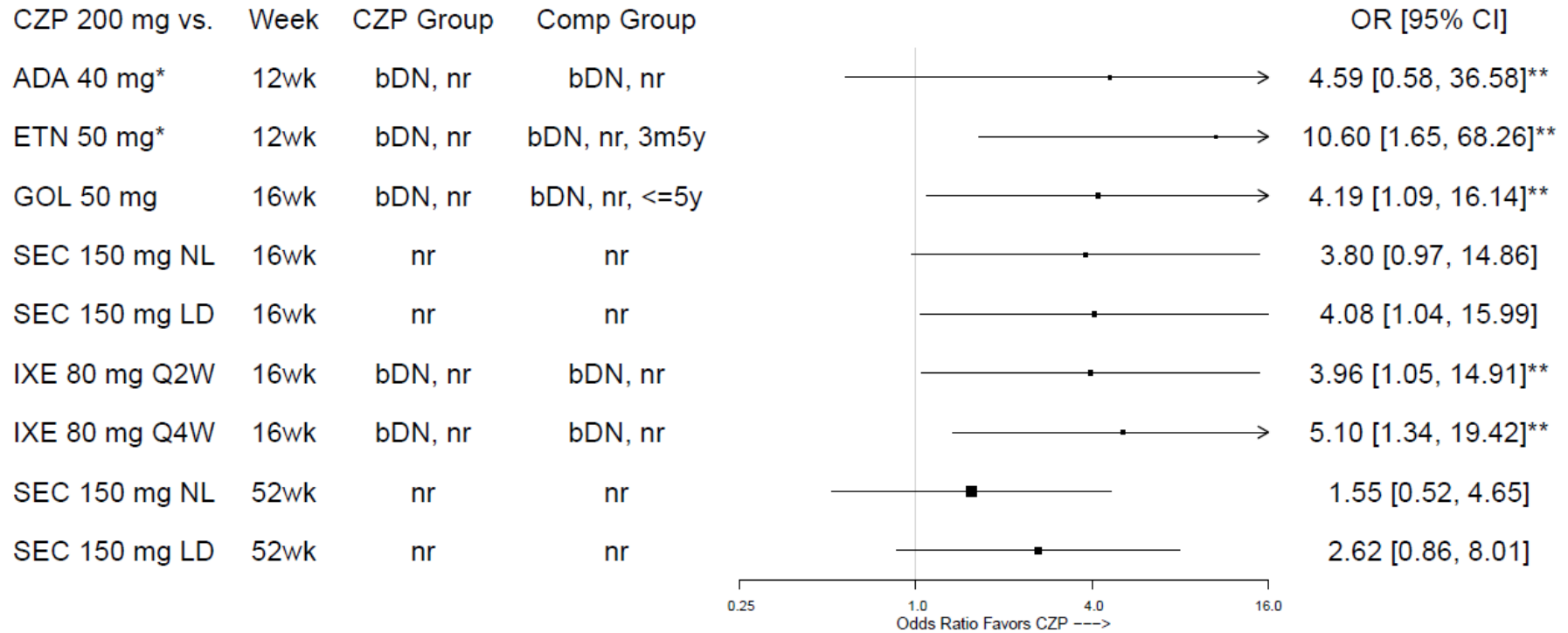
* CZP Pooled (CZP 200 Q2W + CZP Q4W) is analyzed instead of CZP 200 mg

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golimumab; IXE = ixekizumab; LD = loading dose; MD = mean difference in change from baseline; mg = milligram; MRI = magnetic resonance imaging; NL = no loading dose; nr = non-radiographic axial spondyloarthritis; OR = odds ratio; Q2W = every two weeks; Q4W = every 4 weeks; SEC = secukinumab; wk = week

Supplementary Figure S. 3. ASDAS-ID – Forest Plot

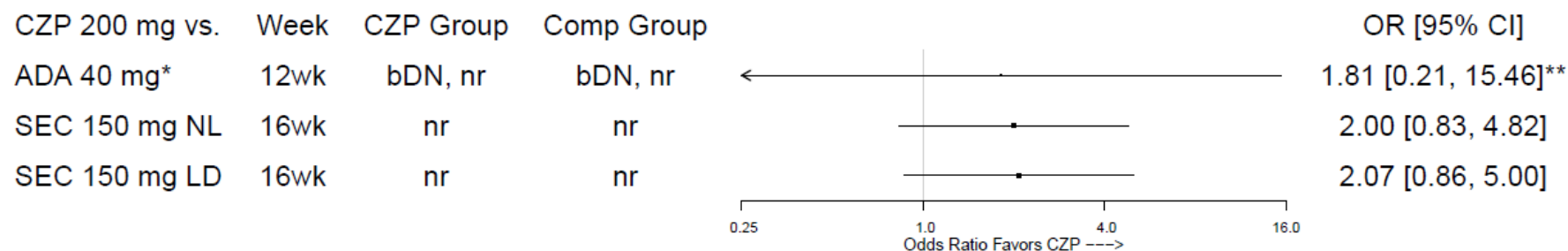


* CZP Pooled (CZP 200 Q2W + CZP Q4W) is analyzed instead of CZP 200 mg

** Random-effect model (analyses are otherwise fixed-effect models)

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Supplementary Figure S. 4. ASDAS-MI – Forest Plot

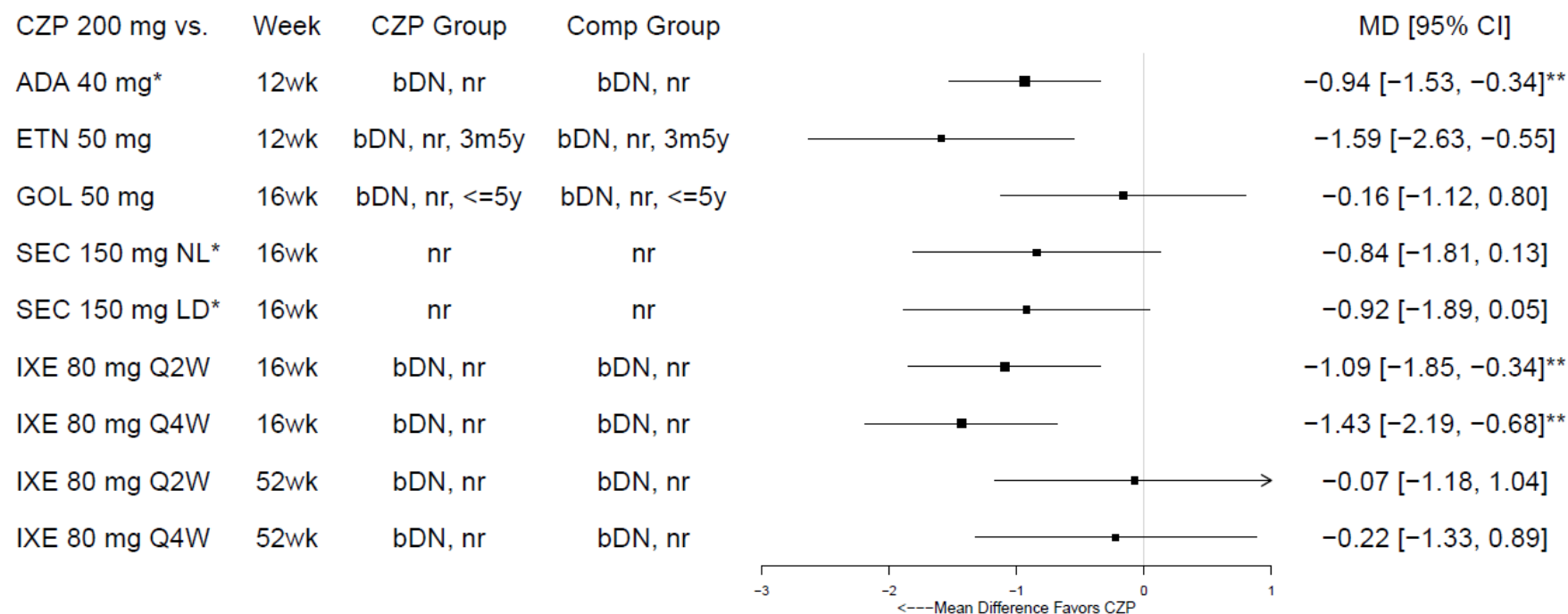


* CZP Pooled (CZP 200 Q2W + CZP Q4W) is analyzed instead of CZP 200 mg

** Random-effect model (analyses are otherwise fixed-effect models)

List of abbreviations: 3m5y = disease duration between three months and five years; <=5y = disease duration of less than or equal to five years; ADA = adalimumab; bDN = biologic Disease-modifying antirheumatic drug-naïve; CI = confidence interval; comp = comparator; CRP = C-reactive protein; CZP = certolizumab pegol; ETN = etanercept; GOL = golimumab; IXE = ixekizumab; LD = loading dose; MD = mean difference in change from baseline; mg = milligram; MRI = magnetic resonance imaging; NL = no loading dose; nr = non-radiographic axial spondyloarthritis; OR = odds ratio; Q2W = every two weeks; Q4W = every 4 weeks; SEC = secukinumab; wk = week

Supplementary Figure S. 5. BASDAI – Forest Plot

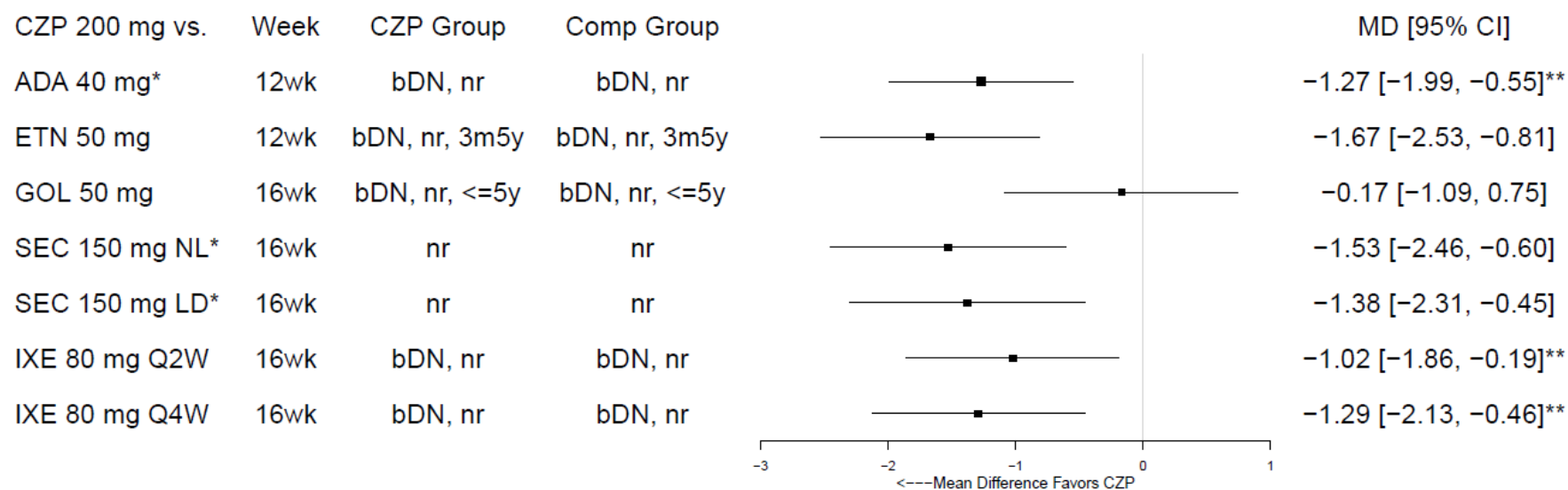


* CZP Pooled (CZP 200 Q2W + CZP Q4W) is analyzed instead of CZP 200 mg

** Random-effect model (analyses are otherwise fixed-effect models)

List of abbreviations: 3m5y = disease duration between three months and five years; <=5y = disease duration of less than or equal to five years; ADA = adalimumab; bDN = biologic Disease-modifying antirheumatic drug-naïve; CI = confidence interval; comp = comparator; CRP = C-reactive protein; CZP = certolizumab pegol; ETN = etanercept; GOL = golimumab; IXE = ixekizumab; LD = loading dose; MD = mean difference in change from baseline; mg = milligram; MRI = magnetic resonance imaging; NL = no loading dose; nr = non-radiographic axial spondyloarthritis; OR = odds ratio; Q2W = every two weeks; Q4W = every 4 weeks; SEC = secukinumab; wk = week

Supplementary Figure S. 6. BASFI – Forest Plot

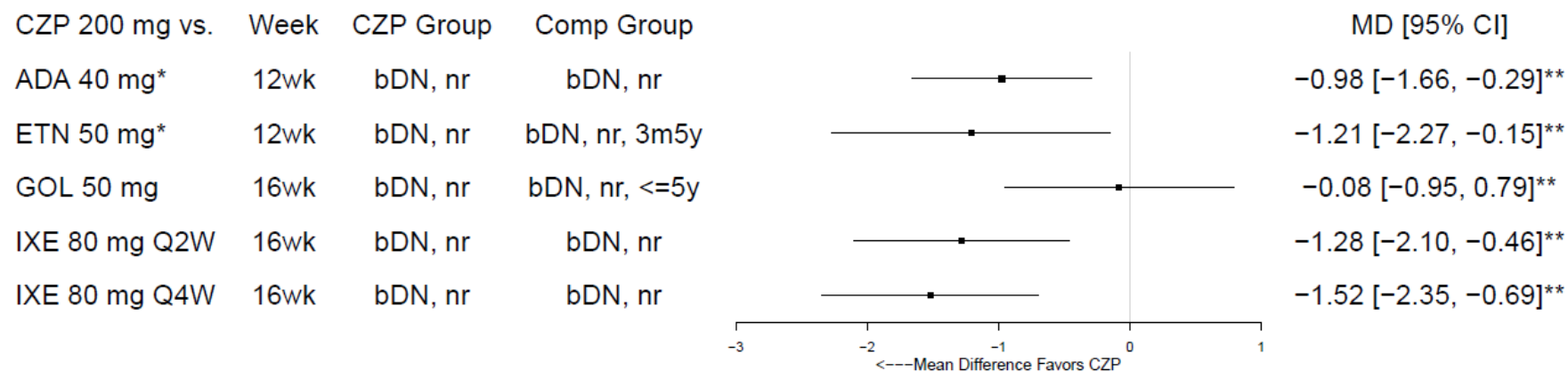


* CZP Pooled (CZP 200 Q2W + CZP Q4W) is analyzed instead of CZP 200 mg

** Random-effect model (analyses are otherwise fixed-effect models)

List of abbreviations: 3m5y = disease duration between three months and five years; <=5y = disease duration of less than or equal to five years; ADA = adalimumab; bDN = biologic Disease-modifying antirheumatic drug-naïve; CI = confidence interval; comp = comparator; CRP = C-reactive protein; CZP = certolizumab pegol; ETN = etanercept; GOL = golimumab; IXE = ixekizumab; LD = loading dose; MD = mean difference in change from baseline; mg = milligram; MRI = magnetic resonance imaging; NL = no loading dose; nr = non-radiographic axial spondyloarthritis; OR = odds ratio; Q2W = every two weeks; Q4W = every 4 weeks; SEC = secukinumab; wk = week

Supplementary Figure S. 7. Total Spine Pain – Forest Plot

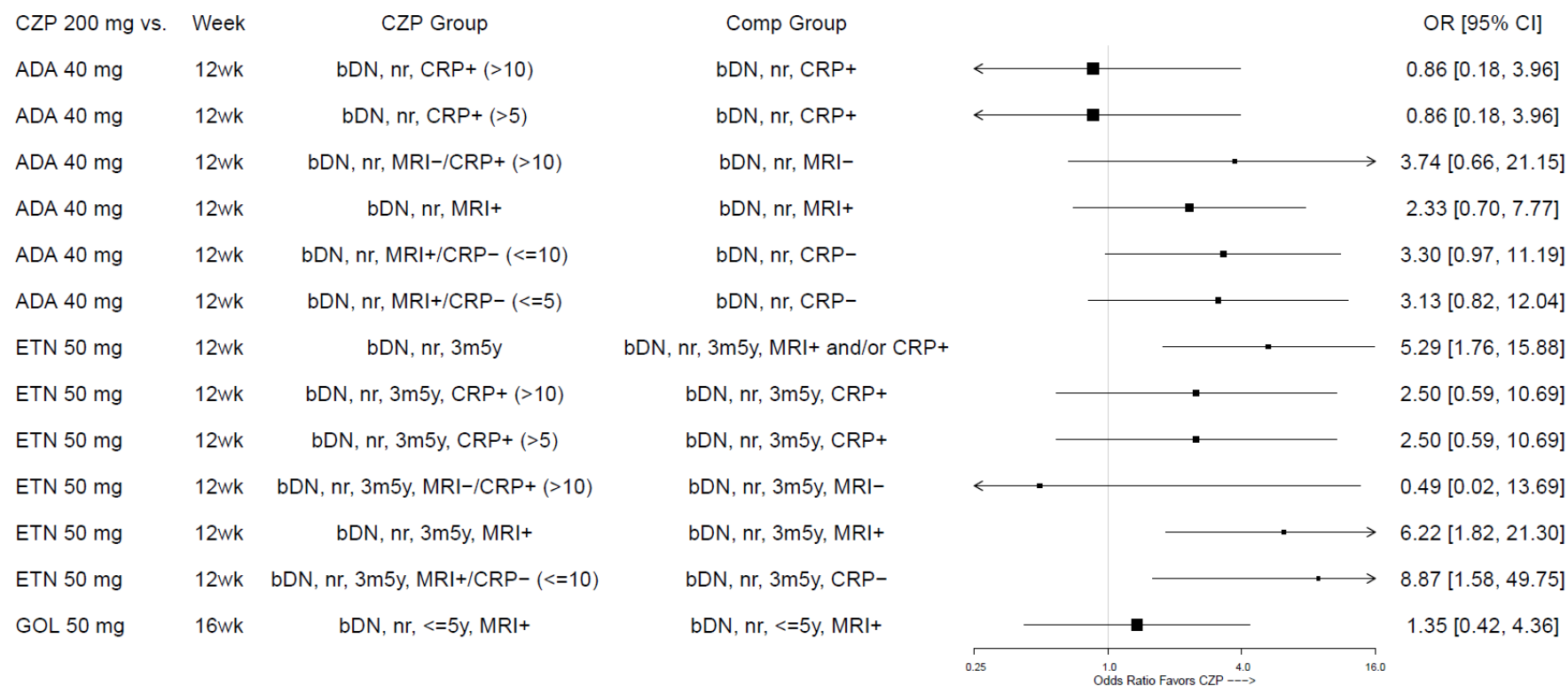


* CZP Pooled (CZP 200 Q2W + CZP Q4W) is analyzed instead of CZP 200 mg

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List of abbreviations: 3m5y = disease duration between three months and five years; <=5y = disease duration of less than or equal to five years; ADA = adalimumab; bDN = biologic Disease-modifying antirheumatic drug-naïve; CI = confidence interval; comp = comparator; CRP = C-reactive protein; CZP = certolizumab pegol; ETN = etanercept; GOL = golimumab; IXE = ixekizumab; LD = loading dose; MD = mean difference in change from baseline; mg = milligram; MRI = magnetic resonance imaging; NL = no loading dose; nr = non-radiographic axial spondyloarthritis; OR = odds ratio; Q2W = every two weeks; Q4W = every 4 weeks; SEC = secukinumab; wk = week

Supplementary Figure S. 8. ASAS 40, Other MRI and CRP Subgroups – Forest Plot



* CZP Pooled (CZP 200 Q2W + CZP Q4W) is analyzed instead of CZP 200 mg

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