Supplementary Information

Title: Efficacy and Safety of B-Cell-Targeted and Conventional Immunomodulatory Therapies for IgG4-Related Disease: A Systematic Review and Meta-Analysis of Randomized Trials

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Table S1. Database-specific search strategies

Database	Complete search strategy	Records (n)
PubMed	("Immunoglobulin G4-Related Disease"[Mesh] OR IgG4[tiab] OR "immunoglobulin G4"[tiab] OR "IgG4-RD"[tiab] OR "IgG4-related disease"[tiab]) AND ("Randomized Controlled Trial"[pt] OR "Controlled Clinical Trial"[pt] OR "Random Allocation"[Mesh] OR random*[tiab] OR placebo*[tiab] OR trial[tiab] OR "clinical trial"[tiab] OR "controlled trial"[tiab] OR blind*[tiab])	193
Embase	(igg4:ti,ab,kw OR 'immunoglobulin g4':ti,ab,kw OR 'igg4-rd':ti,ab,kw OR 'igg4-related disease':ti,ab,kw) AND ('randomized controlled trial'/exp OR 'controlled clinical trial'/de OR random*:ti,ab,kw OR placebo*:ti,ab,kw OR trial:ti,ab,kw OR 'clinical trial':ti,ab,kw OR 'controlled trial':ti,ab,kw OR blind*:ti,ab,kw)	622
Web of Science Core Collection	TS=(IgG4 OR "immunoglobulin G4" OR "IgG4-RD" OR "IgG4-related disease") AND TS=(random* OR placebo* OR trial OR "clinical trial" OR "controlled trial" OR blind*)	266
Cochrane CENTRAL	#1 MeSH descriptor: [Immunoglobulin G4-Related Disease] explode all trees #2 (IgG4 OR "immunoglobulin G4" OR "IgG4-RD" OR "IgG4-related disease"):ti,ab,kw #3 #1 OR #2	86

Table S2. GRADE certainty of evidence for the principal efficacy and safety outcomes

Outcome	Trials (N)	Relative effect (95% CI)	Certainty	Reasons for downgrading
Remission	5 (521)	RR 1.81 (1.44–2.28)	Moderate	Risk of bias: serious; indirectness: serious (nonuniform remission definitions).
Relapse or disease flare	5 (521)	RR 0.35 (0.22–0.55)	low	Risk of bias: serious; inconsistency: serious (I^2 = 53.6%); indirectness: serious (relapse versus flare).
Any adverse event	5 (521)	RR 1.28 (0.90–1.83)	low	Risk of bias: serious; inconsistency: serious (I^2 = 77.4%); imprecision: serious.
Serious adverse event	3 (395)	RR 1.00 (0.36–2.74)	Very low	Inconsistency: serious (I^2 = 55.7%); imprecision: very serious (wide interval, sparse events).

Abbreviations: CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; RR, risk ratio.

Figure S1. PRISMA 2020 flow diagram of study selection.

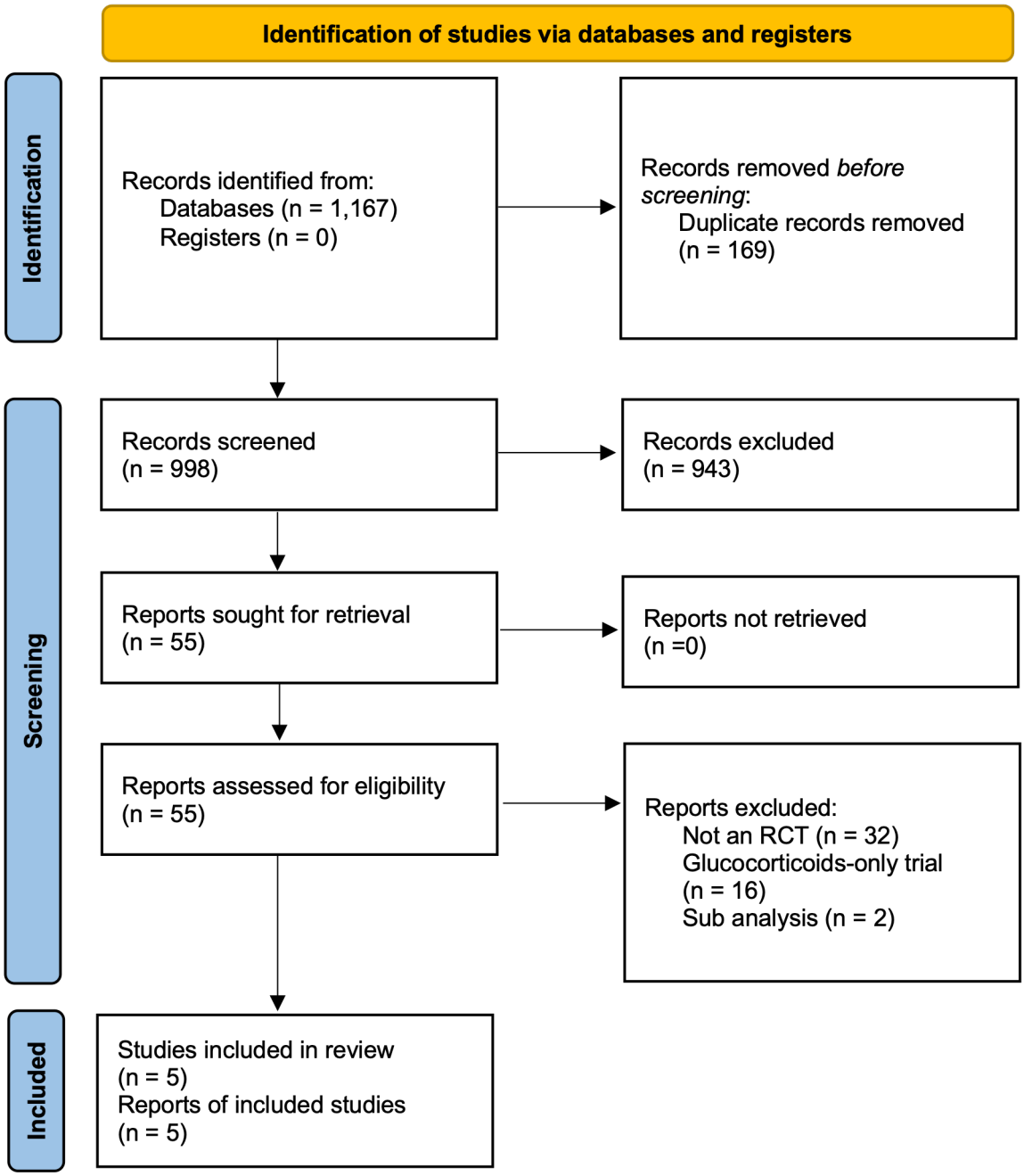


Figure S2. Risk of serious adverse events with active treatment versus respective control

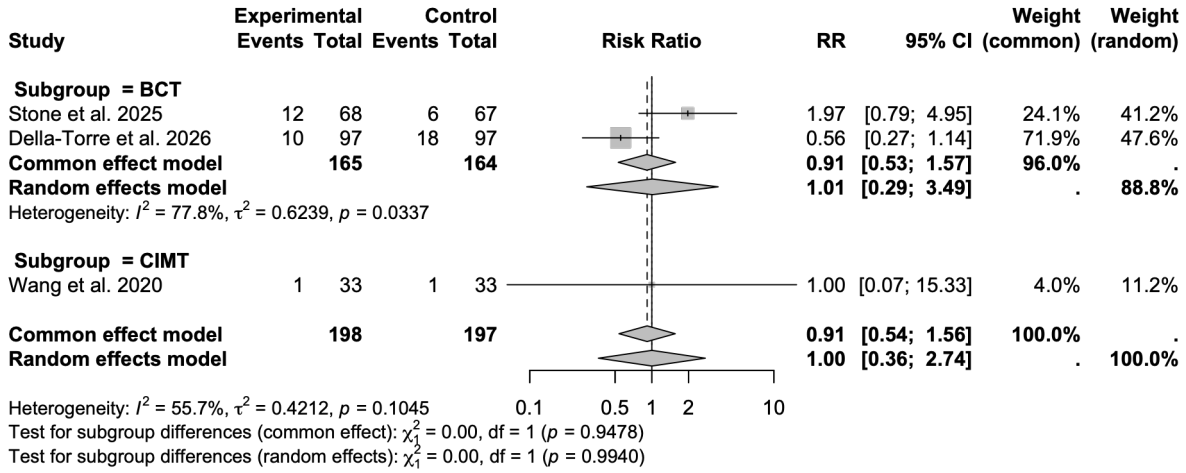
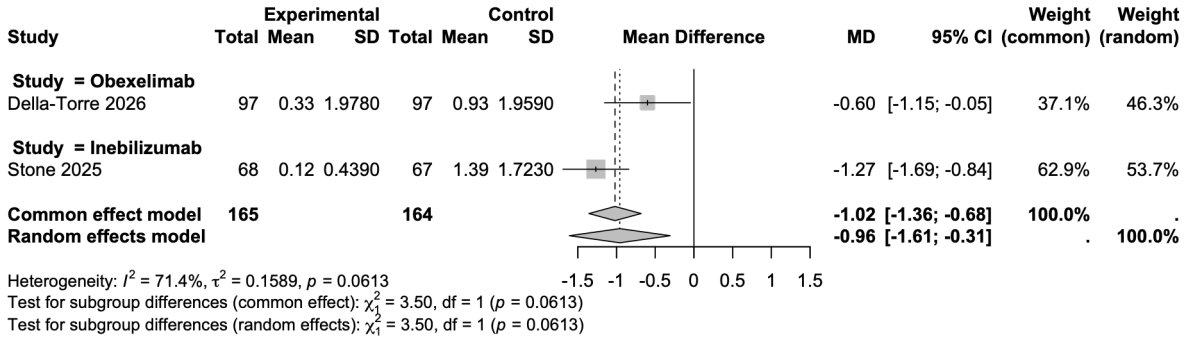


Figure S3. Additional glucocorticoid exposure in the inebilizumab and obexelimab trials.



The inebilizumab outcome reflects post-taper, disease-related treatment or maintenance exposure, whereas the obexelimab outcome reflects rescue therapy requirement through week 52.

Figure S4. Risk-of-bias assessment for remission using RoB 2.

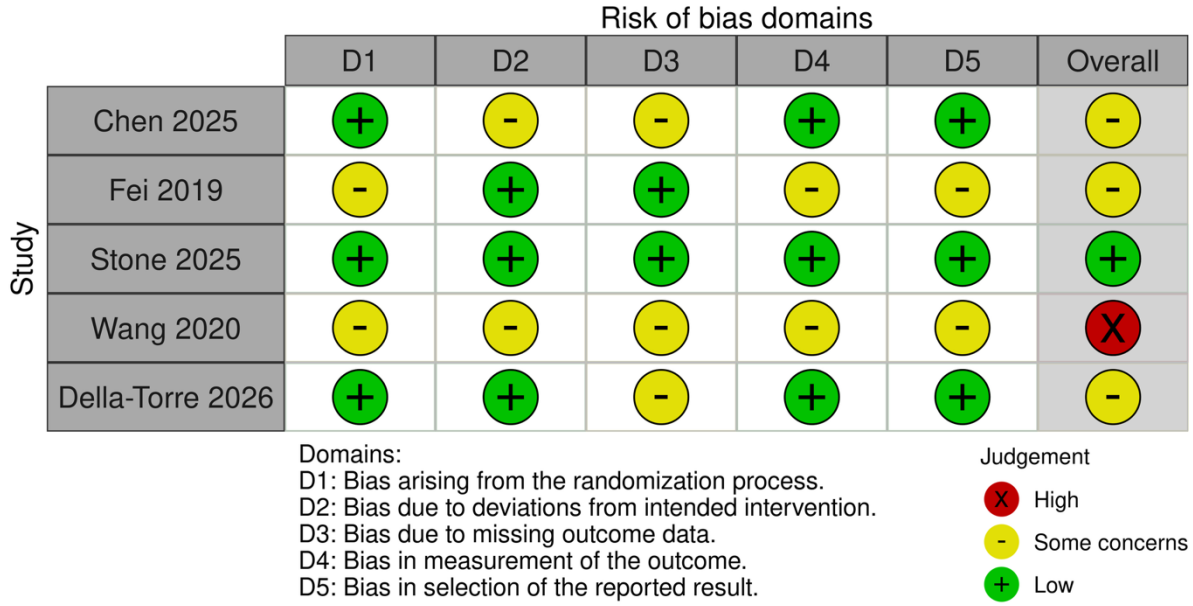


Figure S5. Risk-of-bias assessment for relapse using RoB 2.

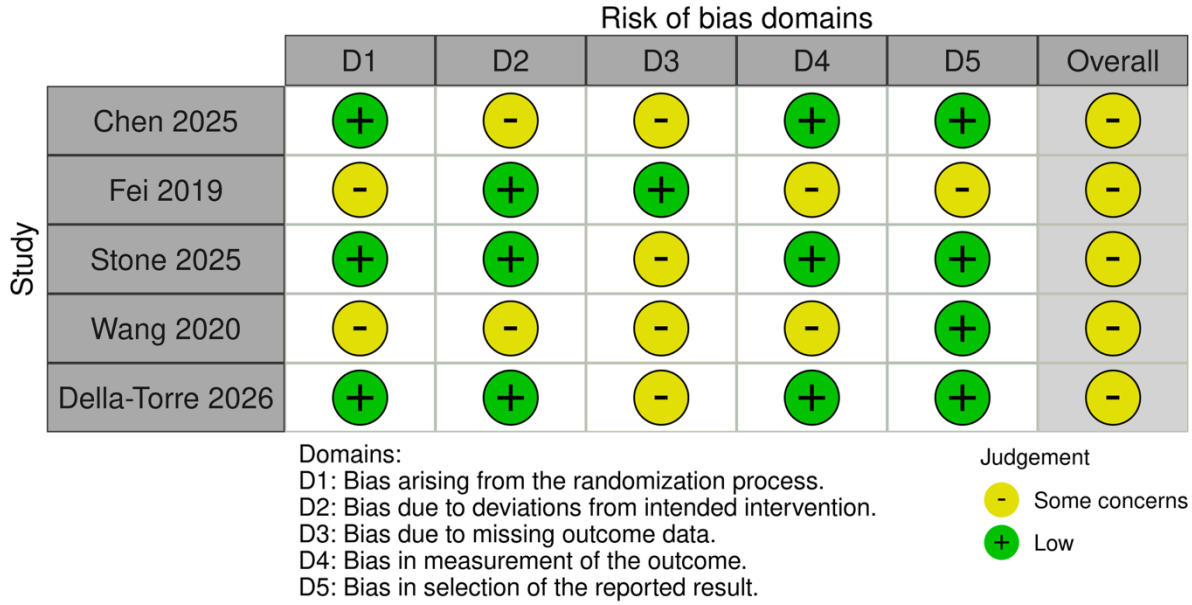


Figure S6. Risk-of-bias assessment for any adverse event using RoB 2.

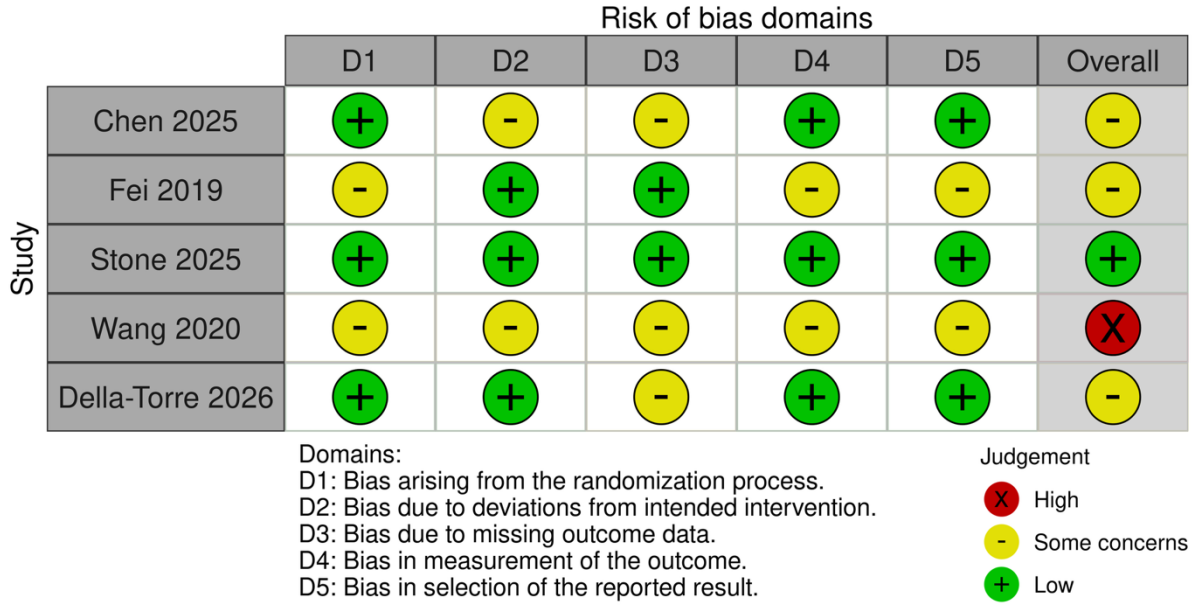


Figure S7. Risk-of-bias assessment for serious adverse event using RoB 2.

