

Risk of Bias Assessment (Cochrane RoB 2)

Study: **Kolodziej et al. (2025) - DUONEN trial**

Domain	Judgment	Support for judgment
D1: Bias arising from the randomization process	Some concerns	The study is described as a randomized, multicenter phase 3 trial. However, this interim report lacks detailed descriptions of the randomization sequence generation algorithm or allocation concealment mechanism.
D2: Bias due to deviations from intended interventions	Some concerns	The trial is open-label. While blinding is impossible in this context, the safety analysis appears to be conducted on 56 patients who 'completed PRRT according to their randomized assignment' (per-protocol approach), rather than a strict intention-to-treat (ITT) analysis.
D3: Bias due to missing outcome data	Low risk	Safety and toxicity outcomes were fully collected for the 56 patients in the interim cohort. Reasons for early treatment discontinuation (e.g., 3/16 in Arm A) were clearly reported, with no evidence of missing data skewing the results.
D4: Bias in measurement of the outcome	Low risk	Safety outcomes (e.g., complete blood counts, eGFR, creatinine) and dosimetric calculations (Q-DOSE, IDAC 2.1) are highly objective parameters and are unlikely to be influenced by the open-label design of the study.

D5: Bias in selection of the reported result	Low risk	The study protocol was pre-registered (EudraCT 2020-006068-99). All adverse events and dosimetric data were transparently reported without evidence of selective outcome reporting.
Overall Risk of Bias	Some concerns	The main weaknesses stem from the interim nature of the report, resulting in missing details on the randomization process (D1) and a lack of strict ITT analysis (D2).