INPLASY

Disitamab Vedotin-Based Neoadjuvant or Bladder-Sparing Therapy for Muscle-Invasive Bladder Cancer: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - No support.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202690113

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 September 2026 and was last updated on 25 September 2026.

INTRODUCTION

Review question / Objective What are the pooled efficacy and safety of disitamab vedotin-based neoadjuvant or bladder-sparing therapy in patients with MIBC, and do outcomes differ according to HER2 expression level, combination partner, and treatment strategy?

Rationale Disitamab vedotin (RC48) is a HER2-directed antibody-drug conjugate carrying a monomethyl auristatin E payload and has been approved in China for HER2-expressing locally advanced or metastatic urothelial carcinoma. HER2 is expressed in a considerable proportion of urothelial carcinomas. Recently, several phase II trials and multicenter real-world studies have evaluated disitamab vedotin, alone or combined with PD-1 inhibitors, chemotherapy, or radiotherapy, as neoadjuvant therapy before radical cystectomy or as bladder-sparing therapy for MIBC, reporting encouraging pathological and clinical complete response rates. However, these studies are mostly single-arm, have small sample sizes, and use heterogeneous regimens. To date, no systematic review and meta-analysis has specifically summarized the evidence for disitamab vedotin in the perioperative or bladder-sparing management of MIBC.

Condition being studied Non-metastatic muscle-invasive bladder cancer (MIBC; clinical stage T2-T4a, M0) treated with disitamab vedotin (RC48)-based therapy in the neoadjuvant setting before radical cystectomy or as part of a bladder-sparing strategy.

METHODS

Search strategy PubMed:
("disitamab vedotin"[tiab] OR RC48[tiab] OR "RC48-ADC"[tiab] OR Aidixi[tiab]) AND ("Urinary Bladder Neoplasms"[Mesh] OR "bladder cancer"[tiab] OR "bladder carcinoma"[tiab] OR "bladder neoplasm*"[tiab] OR urothelial[tiab] OR "muscle-invasive"[tiab])

Embase:
('disitamab vedotin'/exp OR 'disitamab vedotin':ti,ab OR rc48:ti,ab OR 'rc48-adc':ti,ab) AND ('bladder cancer'/exp OR 'urothelial carcinoma'/exp OR 'bladder cancer':ti,ab OR urothelial:ti,ab OR 'muscle-invasive':ti,ab)
Web of Science:
TS=("disitamab vedotin" OR RC48 OR "RC48-ADC") AND TS=("bladder cancer" OR "bladder carcinoma" OR urothelial OR "muscle-invasive")
Cochrane Library:
("disitamab vedotin" OR RC48):ti,ab,kw AND (bladder OR urothelial):ti,ab,kw
CNKI / Wanfang (Chinese):
(维迪西妥单抗 OR RC48 OR 爱地希) AND (膀胱癌 OR 尿路上皮癌).

Participant or population Adult patients (aged 18 years or older) with histologically confirmed, non-metastatic muscle-invasive urothelial carcinoma of the bladder (clinical stage T2-T4a, M0), regardless of HER2 expression status.

Intervention Disitamab vedotin-based therapy, given alone or in combination with PD-1/PD-L1 inhibitors, chemotherapy, and/or radiotherapy, either (1) as neoadjuvant therapy before radical cystectomy or partial cystectomy, or (2) as part of a bladder-sparing strategy (with or without maximal transurethral resection of bladder tumor and/or radiotherapy).

Comparator No comparator is required for single-arm studies. Where comparative studies are available (e.g., disitamab vedotin-based therapy versus gemcitabine-cisplatin plus immunotherapy), comparative outcomes will be analyzed separately.

Study designs to be included Prospective clinical trials (single-arm or randomized), and prospective or retrospective cohort studies including at least 10 patients who received disitamab vedotin-based therapy for MIBC.

Eligibility criteria Inclusion criteria: (1) patients with histologically confirmed non-metastatic MIBC; (2) disitamab vedotin-based therapy given in the neoadjuvant or bladder-sparing setting; (3) reporting of at least one efficacy outcome (pathological complete response, clinical complete response, pathological downstaging, or bladder-intact rate) or safety outcome; (4) at least 10 patients treated with disitamab vedotin; (5) articles published in English or Chinese.
Exclusion criteria: (1) reviews, case reports, case series with fewer than 10 patients, letters, editorials, study protocols, and preclinical studies; (2) studies of metastatic disease or non-muscle-invasive bladder cancer only; (3) studies without extractable outcome data; (4) overlapping patient populations, in which case the most complete or most recent report will be included. Conference abstracts will be included only if sufficient data are available.

Information sources PubMed/MEDLINE, Embase, Web of Science Core Collection, the Cochrane Library, China National Knowledge Infrastructure (CNKI), and Wanfang Data will be searched from inception to the date of the final search. Abstracts from major oncology and urology meetings (ASCO, ASCO GU, ESMO, AUA, and EAU) will also be screened. The reference lists of included studies and relevant reviews will be manually checked.

Main outcome(s) Pathological complete response (pCR; ypT0N0) rate in patients who underwent cystectomy, and clinical complete response (cCR) rate in patients receiving bladder-sparing therapy. Pooled proportions with 95% confidence intervals (CIs) will be calculated.

Additional outcome(s) Pathological downstaging rate (ypT1N0 or lower), objective response rate, bladder-intact rate, event-free survival, progression-free survival, overall survival, incidence of treatment-related adverse events (any grade and grade 3 or higher), and perioperative complications.

Data management Search results will be imported into EndNote, and duplicates will be removed. Two reviewers will independently screen titles and abstracts, followed by full-text assessment. Data will be extracted independently by two reviewers using a standardized form, including first author, publication year, country, study design, number of centers, sample size, age, sex, clinical stage, HER2 expression level (IHC score), treatment regimen and combination partner, number of cycles, treatment strategy (neoadjuvant or bladder-sparing), follow-up duration, and all efficacy and safety outcomes. Disagreements will be resolved by discussion or by consultation with a third reviewer.

Quality assessment / Risk of bias analysis Non-comparative studies will be assessed using the Methodological Index for Non-Randomized Studies (MINORS); comparative cohort studies using the Newcastle-Ottawa Scale (NOS); and randomized controlled trials using the Cochrane Risk of Bias 2 (RoB 2) tool. Assessment will be performed independently by two reviewers. The certainty of evidence will be rated using the GRADE approach.

Strategy of data synthesis Pooled proportions and 95% CIs will be calculated using the Freeman-Tukey double arcsine transformation with a random-effects model. For comparative studies, odds ratios (ORs) or risk ratios (RRs) with 95% CIs will be pooled for dichotomous outcomes, and hazard ratios (HRs) for time-to-event outcomes. Heterogeneity will be assessed using Cochran's Q test and the I^2 statistic. Statistical analyses will be performed using R software (meta package) or Stata. A two-sided P value < 0.05 will be considered statistically significant.

Subgroup analysis Where data allow, subgroup analyses will be performed according to HER2 expression level (IHC 2+/3+ versus 0/1+), combination partner (disitamab vedotin plus PD-1/PD-L1 inhibitor, plus chemotherapy, or plus radiotherapy), treatment strategy (neoadjuvant before cystectomy versus bladder-sparing), study design (prospective versus retrospective), and publication type (full text versus conference abstract).

Sensitivity analysis Leave-one-out sensitivity analyses will be conducted by sequentially removing each study. Additional sensitivity analyses will exclude conference abstracts and studies at high risk of bias. Publication bias will be assessed using funnel plots and Egger's test when at least 10 studies are available for an outcome.

Language restriction English and Chinese.

Country(ies) involved China.

Other relevant information This review will be conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. Any amendments to this protocol will be documented and reported in the final publication.

Keywords disitamab vedotin; RC48; muscle-invasive bladder cancer; neoadjuvant therapy; bladder preservation; meta-analysis.

Dissemination plans The results will be submitted to a peer-reviewed journal for publication.

Contributions of each author

Author 1 - Guowei Liu - conceived the review, designed the search strategy, performed literature screening and data extraction, conducted the statistical analysis, and drafted the manuscript.conceived the review, designed the search strategy, performed literature screening and data extraction, conducted the statistical analysis, and drafted the manuscript.

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Author 3 - Jinsheng Wu - Supervised the study, resolved disagreements as the third reviewer, and critically revised the manuscript.

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