INPLASY

Anti-EGFR monoclonal antibodies in potentially resectable metastatic colorectal cancer: Updated systematic review and meta-analysis

INPLASY2025120079
doi: 10.37766/inplasy2025.12.0079
Received: 22 December 2025
Published: 22 December 2025

Li, S.

Corresponding author:
Shun Li

tk56@mail.ccmu.edu.cn

Author Affiliation:
National Clinical Research Center for Digestive Diseases, State Key Lab of Digestive Health, Beijing Friendship Hospital, Capital Medical University, Beijing, China; 2. Clinical Epidemiology and EBM Unit, Beijing Clinical Research Institute, Beijing, China.

ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Data extraction.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2025120079

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 December 2025 and was last updated on 22 December 2025.

INTRODUCTION

Review question / Objective Objective: The present study focused on the efficacy and safety of adding anti-EGFR targeted agents in patient with potentially resectable mCRC.
Population: patients with potentially esectable mCRC
Intervention: anti-EGFR targeted agents combination with chemotherapy (cetuximab/ panitumumab)
Comparison: chemotherapy only
Outcomes: Primary outcomes: progression-free survival (PFS) and overall survival (OS), R0 resection rate
Secondary outcomes: objective response rate (ORR), disease control rate (DCR), total adverse events (AE), treatment-emergent adverse event (TEAE), treatment-related adverse event (TRAE).
Study design: randomized controlled trial (RCT)
language: Chinese and English.

Rationale A comprehensive meta-analysis published in 2023 summarized RCTs evaluating the efficacy of anti-EGFR monoclonal antibodies in potentially resectable mCRC15. That study concluded that, although anti-EGFR therapy significantly improved objective response and R0 resection rates, no survival benefits were observed in terms of progression-free survival (PFS) or OS. However, the previous analysis was limited by the small number of available trials, relatively short follow-up periods, and lack of detailed subgroup analyses that might identify patient populations deriving the greatest benefit.
Since then, several new RCTs with larger cohorts, longer follow-up, and more detailed molecular classification, particularly within the RAS wild-type population have been published, providing an opportunity to reappraise the efficacy of anti-EGFR therapy in this setting16. Moreover, emerging evidence suggests that treatment outcomes may vary according to clinical and molecular characteristics, such as age, sex, presence of liver-

limited metastases, and specific RAS mutation subtypes.
Therefore, we performed an updated systematic review and meta-analysis that incorporates both newly published English-language RCTs and all relevant Chinese-language studies from database inception. This updated analysis not only expands the evidence base but also explores clinically meaningful subgroups to define better which patients may derive the greatest benefit from anti-EGFR–based conversion therapy.

Condition being studied
Patients with potentially resectable mCRC.

METHODS

Search strategy A systematic search will be conducted in the following databases: PubMed, EMBASE, Cochrane library, WoS, CNKI, Wanfang and CBM. For English-language literature, we will conduct a new search for studies published from 2023 onward, whereas eligible studies published prior to 2023 will be identified based on previously published meta-analyses to ensure comprehensive inclusion without unnecessary redundancy15. In addition, we will perform an independent and exhaustive search of Chinese-language databases from their inception, which represents a novel aspect of our study, as previous meta-analyses did not incorporate evidence from Chinese sources.
Pre-search strategy
#1.pubmed
#2. EGF receptor inhibitor*[tw] OR EGFR inhibitor*[tw] OR epidermal growth factor receptor inhibitor*[tw] OR epidermal growth factor receptor protein tyrosine kinase inhibitor*[tw] OR epidermal growth factor receptor tyrosine kinase inhibitor*[tw] OR epidermal growth factor receptor kinase inhibitor*[tw] OR "anti-EGFR" [tw] OR "Panitumumab"[Mesh] OR panitumumab[tw] OR Vectibix[tw] OR panitumab[tw] OR vectibex[tw] OR "Cetuximab"[Mesh] OR cetuximab[tw] OR "IMC-C225"[tw] OR "IMC-225"[tw] OR Erbitux[tw] 21,627
#3. colo-rectal metastas*[tw] OR colorectal metastas*[tw] OR metastatic colo-rectal[tw] OR metastatic colo-rectal cancer*[tw] OR metastatic colorectal[tw] OR colorectal liver metastas*[tw] OR metastatic colon[tw] OR metastatic rectal[tw] OR metastatic colonic cancer*[tw] OR metastatic rectum[tw] OR colonic metastas*[tw] OR colonic metastas*[tw] OR rectal metastas*[tw] OR rectum metastas*[tw] 22,779
#4. #1 AND #2 and ("2023/01/01"[Date – Publication] : "3000"[Date – Publication]) 466
#5. ("controlled clinical trial"[pt] OR "Controlled Clinical Trials as Topic"[MeSH] OR "Random Allocation"[MeSH] OR "Double-Blind Method"[MeSH] OR "single-blind method"[MeSH] OR "Control Groups"[MeSH] OR "cross-over studies"[MeSH] OR random*[tiab] OR placebo[tiab] OR trial[tiab] OR groups[tiab] OR crossover[tiab] OR cross-over[tiab] OR single blind*[tiab] OR double blind*[tiab] OR triple blind*[tiab] OR Factorial design*[tiab]) NOT ("Animals"[Mesh] NOT ("Humans"[Mesh] AND "Animals"[Mesh])) 4,193,148
#6. #3 and #4 234
CNKI(期刊、学位、会议，中英文扩展：是，中文)
#1. (SU%=抗EGFR药物+ EGFR抑制剂+ "anti-EGFR" +西妥昔单抗+西沱昔单抗+cetuximab+ Erbitux+爱必妥+帕尼单抗+ panitumumab+ Vectibix OR TKA % 抗EGFR药物+ EGFR抑制剂+ "anti-EGFR" +西妥昔单抗+西沱昔单抗+cetuximab+ Erbitux+爱必妥+帕尼单抗+ panitumumab+ Vectibix) AND (SU%=转移*(结直肠癌+结肠癌+直肠癌) OR TKA % 转移*(结直肠癌+结肠癌+直肠癌)) 932
#2. #1 and (SU%=随机+盲法+双盲+单盲+三盲+交叉+RCT OR TKA % 随机+盲法+双盲+单盲+三盲+交叉+RCT) 134.

Participant or population
Patients with potentially resectable mCRC.

Intervention
Anti EGFR targeted agents combination with chemotherapy (cetuximab/panitumumab).

Comparator Chemotherapy only.

Study designs to be included
Randomized controlled trial (RCT).

Eligibility criteria
1. Patients with potentially resectable mCRC
2. Intervention: anti-EGFR targeted agents combination with chemotherapy (cetuximab /panitumumab)
3. Comparison: chemotherapy only
4. Primary outcomes: progression-free survival (PFS) and overall survival (OS), R0 resection rate
Secondary outcomes: objective response rate (ORR), disease control rate (DCR), total adverse events (AE), treatment-emergent adverse event (TEAE), treatment-related adverse event (TRAE).
5. Randomized controlled trial (RCT)
6. Language: Chinese and English.

Information sources A systematic search will be conducted in the following databases: PubMed,

EMBASE, Cochrane library, WoS, CNKI, Wanfang and CBM.

Main outcome(s) Progression-free survival (PFS) and overall survival (OS), R0 resectionrate.

Additional outcome(s)
Objective response rate (ORR), disease control rate (DCR), total adverse events (AE), treatment-emergent adverse event (TEAE), treatment-related adverse event (TRAE).

Quality assessment / Risk of bias analysis Two reviewers will independently assess the quality of the included studies using the risk of bias assessment tool recommended by the Cochrane Handbook for Systematic Reviews of Interventions (RoB 2.0) (Appendix 2)18. Specific items that will be assessed included: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in selection of the reported result. Each domain will be judged as having a low risk of bias, some concerns, or a high risk of bias in accordance with the RoB 2 guidance.

Strategy of data synthesis To statistically analyze the prognosis and surgical resection rate of anti-EGFR targeted agents combined with chemotherapy, hazard ratio (HR) as well as 95% confidence intervals (CI) for PFS and OS will be extracted from the included articles in this study to evaluate the prognostic impact of anti-EGFR targeted agents plus chemotherapy. Furthermore, ORR, DCR, R0 resection, and AEs will be measured by risk ratio (RR) and 95%CI. Statistical heterogeneity will be determined by using chi-square test and I2 statistic, with p50% indicating high heterogeneity. Due to the different conditions of patients and the use of different drugs, the random-effect model will be used to improve the reliability of the results. Sensitivity analysis will be used to verify the stability of the results. All the statistical tests will be performed with RevMan 5.4 and STATA version 10.0 (Stata Corporation, College Station, TX, USA). The p-value is two sided, and the results of $p<0.05$ will be deemed to be statistically significant.

Subgroup analysis Subgroup analyses will be performed according to age (<65 vs. ≥65 years), hepatic metastasis status (yes vs. no), sex (male vs. female), and Genotype (wild-type vs. mutant).

Sensitivity analysis Sensitivity analysis will be used to verify the stability of the results. All the statistical tests will be performed with RevMan 5.4 and STATA version 10.0 (Stata Corporation, College Station, TX, USA). The p-value is two sided, and the results of $p<0.05$ will be deemed to be statistically significant.

Country(ies) involved China.

Keywords Efficacy; Safety; Anti-EGFR; resectable mCRC; Meta-Analysis; RCTs.

Contributions of each author
Author 1 - Shun li.
Email: tk56@mail.ccmu.edu.cn