Therapeutic Potential of Bispecific Antibodies in Adenocarcinoma: A targeted literature review

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Presented at ISPOR Europe 2025: November 9-12, 2025; Glasgow, Scotland

INTRODUCTION

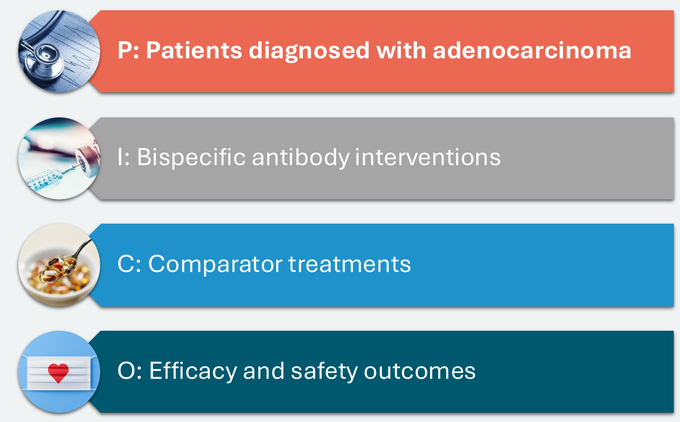
- Adenocarcinoma remains one of the most prevalent solid tumor subtypes, with substantial disease burden and limited long-term outcomes despite advances in targeted and immune-based therapies.
- Established modalities such as chemotherapy, immune checkpoint inhibitors, and monoclonal antibodies have extended survival in select populations but continue to be constrained by tumor heterogeneity and acquired resistance.
- Bispecific antibodies, designed to engage dual antigens or immune pathways, represent a promising therapeutic approach with potential for enhanced cytotoxic precision and immune modulation.
- Their mechanisms of action—encompassing effector immune cell recruitment, T-cell redirection, and tumor microenvironment modulation—align with the evolving paradigm of next-generation immunotherapy.
- However, clinical evidence specific to bispecific antibodies in adenocarcinoma remains scarce, with only three interventional studies currently registered on ClinicalTrials.gov, underscoring the need for a targeted literature review to consolidate existing data and identify critical gaps in the evidence base.
- Strengthening the current understanding through systematic evaluation of available literature can guide future clinical development, optimize target selection, and inform trial design strategies for bispecific antibodies in adenocarcinoma.

OBJECTIVES

To synthesize the clinical evidence supporting bispecific antibodies (BsAbs) in adenocarcinomas, focusing on efficacy outcomes, safety profiles, and therapeutic combinations in early-phase studies.

METHODS

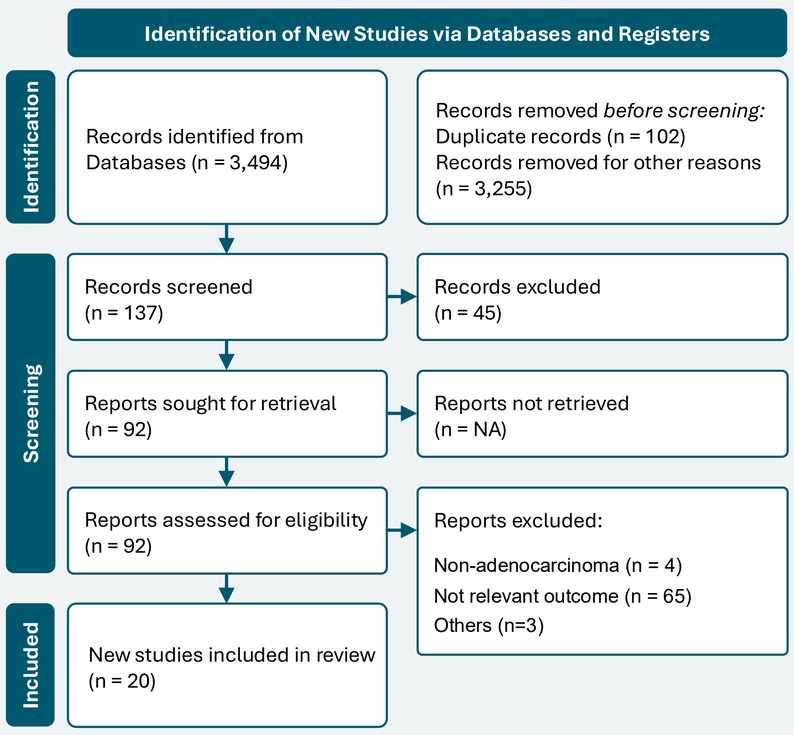
- **Database Search:** Targeted PubMed search using keywords and MeSH terms (e.g., “adenocarcinoma,” “bispecific antibodies,” “dual-target immunotherapy”) to identify studies from the past five years (Jan 2020–Sep 2025).
- **Filters:** Included English-language, human studies focused on clinical and translational research.
- **Clinical Trial Registry:** ClinicalTrials.gov was reviewed for ongoing, completed, and terminated bispecific antibody trials in adenocarcinoma.
- **Data Extracted:** Trial phase, status, intervention type, targets, location, and sponsor.
- **Study Selection Framework (PICO)**
- **Data Synthesis:** Literature and registry data were summarized narratively to outline trends and evidence gaps.



RESULTS

Study Distribution

- A total of **20 studies** involving bispecific antibodies were identified.
- The majority focused on **gastric/GEJ adenocarcinoma**.
- Response Rate and PFS was reported in **16 studies**.



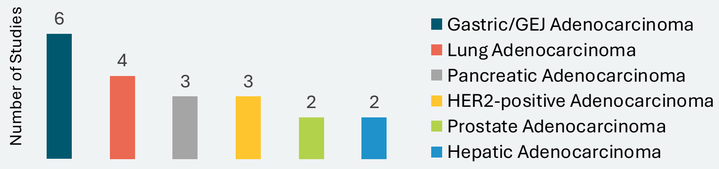
More Frequently Studied Molecules

AK104 (PD-1/CTLA-4)
Zanidatamab (HER2/HER2)
CDX-527 (PD-L1/CD27)

Less Frequently Studied Molecules

KN046 (PD-L1/CTLA-4)
MCLA-128 (HER2/HER3)
EMB-01 (EGFR/cMet)
Zenocutuzumab (HER2/HER3)
Amivantamab (EGFR/MET)
Cadonilimab (PD-1/CTLA-4)
PRS-343 (HER2/4-1BB)
XmAb20717 (PD-1/CTLA-4)

Bispecific Antibody Molecule Landscape in Adenocarcinoma

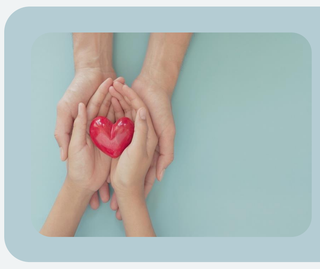


Outcomes Summary

Response Rate Across 16 BSAB studies, **objective response rates (ORR)** ranged from **44% to 73%**.

Complete response rates were generally low (≈2–4%), while **partial responses** accounted for the majority of responders.

Disease control rates (DCR) frequently exceeded **70%**.



Progression-free Survival (PFS)

Across 16 BSAB studies, **median PFS ranged from 5 to 10.9 months**.

In comparative analyses, **median PFS values (≈6–7 months)** were similar between treatment arms.

In some studies, **median PFS was not yet reached**.

Overall Survival

Across BSAB studies, **median overall survival (OS)** ranged from **13 to 31.6 months**.

Several studies reported **median OS around 17–18 months**.

In select cohorts, **OS exceeded 30 months**.

Safety Events

Treatment-related adverse events (TRAEs) were reported in nearly all patients (~98%), most commonly hematologic abnormalities such as decreased platelet, white cell, and neutrophil counts.

Non-hematologic toxicities included fatigue, infusion reactions, diarrhea, and mild transaminase elevations, with most events being **grade 1–2 and manageable**.

Serious AEs like infection or elevated liver enzymes were infrequent.

DISCUSSION

- BsAb-based regimens demonstrated encouraging clinical activity, with ORR ranging from 44–73%, supporting their emerging role in adenocarcinoma.
- Partial responses predominated, and DCR >70% suggested durable disease stabilization across studies.
- Median PFS (5–10.9 months) and OS (up to 31.6 months) indicated sustained benefit, with select cohorts exceeding 30 months.
- Treatment-related AEs were largely grade 1–2, mainly hematologic and infusion-related, and clinically manageable.
- Mild non-hematologic toxicities such as diarrhea, fatigue, and liver enzyme elevations resolved with supportive care.
- Overall, BsAbs exhibited a balanced efficacy–safety profile, reinforcing their potential as a next-generation option for solid tumors.

CONCLUSION

- BsAb therapies showed strong clinical activity in adenocarcinoma, with response rates up to 73% and PFS of 5–10.9 months.
- Safety profile was favorable, mainly grade 1–2 hematologic and infusion-related events.
- Findings support BsAbs as viable targeted immunotherapies offering durable disease control with good tolerability.
- BsAbs hold promise for hard-to-treat adenocarcinoma subsets, especially in combination or biomarker-driven settings.
- Future work should focus on optimized molecule design, adaptive trials, and real-world evidence integration.
- Cross-sector collaboration among developers, CROs, and evidence experts is key to translating BsAb innovation into scalable oncology solutions.

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