CO216

Safety and Efficacy of Antibody Drug Conjugate (ADCs) in Pretreated Locally Advanced/Metastatic (LA/m) Triple-negative Breast Cancer (TNBC): Systematic Literature Review (SLR)

P. Dorling [1], S. Bagga [2], V.K. Khurana [2], P. Soni [2], A. Rounak [2], A. Haiderali [3] and T. Keenan [1]

[1] Merck & Co, Rahway, NJ, USA; [2] CHEORS, North Wales, PA, USA; [3] Merck, North Wales, PA, USA

Background

- TNBC is an aggressive subtype defined by the absence of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 (HER2) expression, characterized by limited treatment options and poor prognosis.(1)
- TNBC represents 15-20% of all newly diagnosed breast cancers, with incidence rates in non-Hispanic Black women nearly double that of other racial/ethnic groups.(2)
- TNBC predominantly affects younger women (<50 years) and premenopausal patients, with up to 20% harboring BRCA1/2 mutations.(1,2)
- Despite an overall 5-year survival rate of 78%, prognosis varies dramatically by stage (92% localized vs 15% distant metastatic),(3) with patients facing significant therapeutic challenges in the locally advanced/metastatic settings following progression on standard anticancer therapy.(2)
- The current treatment landscape provides limited effective options for pretreated LA/mTNBC patients,(4) creating an urgent unmet medical need that ADCs aim to address by combining monoclonal antibody specificity with cytotoxic chemotherapy for targeted drug delivery.

Objective

- This SLR was conducted to summarize the evidence on safety and efficacy of ADCs in LA/mTNBC patients previously treated with systemic anticancer therapy.

Methods

- This SLR followed methodological guidelines by Cochrane Collaboration(5) and National Institute for Health and Care Excellence(6), searching across MEDLINE, Embase, and Cochrane databases for English-language ADC studies conducted in solid tumors (Jan 2015-Sept 2024).
- Supplemental searches included trial registries, conference proceedings (American Society of Clinical Oncology [ASCO], European Society for Medical Oncology [ESMO]), bibliography review.
- Study selection was performed in accordance with the eligibility criteria in **Table 1**. For this poster, we focused on LA/mTNBC patients previously treated with systemic anticancer therapy.
- Study selection was performed independently by two reviewers and conflicts were resolved by third reviewer.
- Data extraction was performed into a standardized form by one reviewer and quality checked by a second reviewer.

Table 1: Eligibility Criteria

Parameter	Inclusion Criteria	Exclusion Criteria
Population(s)	Adult patients (≥18 years of age) with any type of solid tumors	Any other disease; pediatric patients
Interventions	ADCs: SG, MIRV, T-DXd, T-DM1, TV, EV, DV, Dato-DXd, and SHR-A1921	Any other ADCs or interventions
Comparators	No restriction	Not applicable
Outcomes	Efficacy; Safety	Any other outcome
Study design	RCTs (phase II, III, II/III, IV); non-RCTs; single-arm trials	Any other study design
Time	Jan 2015-Sept 2024	Prior to 2015
Language	English	Any other language
Country	Global	Not applicable

Abbreviations: ADC: Antibody Drug Conjugate; Dato-DXd: Datopotamab deruxtecan; DV: Disitamab vedotin; EV: Enfortumab vedotin; MIRV: Mirvetuximab soravtansine; RCTs: Randomized Controlled Trials; SG: Sacituzumab govitecan; SHR-A1921: SHR-A1921 (investigational ADC); T-DM1: Trastuzumab emtansine; T-DXd: Trastuzumab deruxtecan; TV: Tisotumab vedotin.

Results

Study Characteristics

- Of 25,206 records identified, 920 were included in the SLR, ultimately yielding 40 citations on pretreated LA/mTNBC patients across 7 unique trials (**Figure 1**).
- Six trials evaluated SG (4 monotherapy, 2 combination) and one trial evaluated EV (KEYNOTE-F21/EV-202).
- All trials used open-label design, with two being multicenter studies across 10 countries.
- All the seven trials enrolled predominantly females with sample sizes ranging between 26-267 patients and median ages ranging between 48-56 years.

Sacituzumab Govitecan (SG)

Efficacy Outcomes

- In a pivotal RCT (ASCENT), SG monotherapy demonstrated significant improvement over chemotherapy in both mPFS (4.8 vs 1.7 months) and mOS (11.8 vs. 6.9 months). SG also reported higher response rates versus chemotherapy (ORR: 31% vs. 4%) (**Table 2**).
- SG monotherapy also demonstrated meaningful clinical activity in single arm trials with median OS of 12.7-14.7 months, median PFS of 5.5-5.6 months, and durable responses (ORR 31-40%; median DoR 9.1-11.6 months) (**Table 2**).
- Furthermore, SG combinations showed promising clinical responses with ORR of 30.1% (SG+talazoparib) and 23.3% (SG+trilaciclib).

Safety Outcomes

- Grade ≥3 AEs were common with acceptable discontinuation rates enabling continued treatment.
- AE-related deaths remained low supporting favorable safety profile (**Table 3**).
- Combination with trilaciclib, a cyclin-dependent kinase 4/6 inhibitor approved to reduce bone marrow suppression caused by chemotherapy, demonstrated an enhanced safety profile with lower toxicity rates.

Enfortumab Vedotin (EV)

Efficacy Outcomes

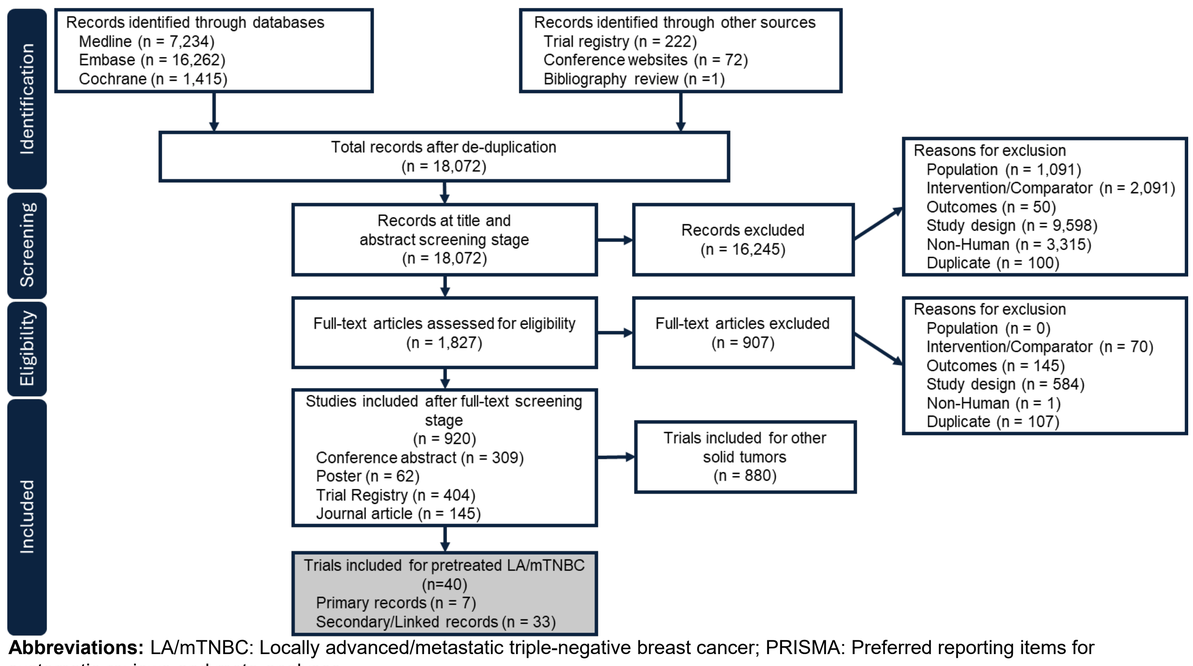
- EV showed modest clinical responses in TNBC with ORR of 19% and median DoR of 3.8 months (**Table 2**).

Safety Outcomes

- Safety data was not comprehensively reported in the available literature.

Scan QR for Digital Copy

Figure 1: PRISMA Flowchart



Abbreviations: LA/mTNBC: Locally advanced/metastatic triple-negative breast cancer; PRISMA: Preferred reporting items for systematic reviews and meta-analyses.

Table 2: Efficacy Outcomes

Trial Name/Study Name (NCT id)	Study arm (N)	Median OS, months (95% CI)	Median PFS, months (95% CI)	ORR/CR/PR (%)	Median DoR, months (95% CI)
ASCENT (NCT02574455)(7)	SG (267)	**11.8 (10.5-13.8)[a]**	**4.8 (4.1-5.8)[a]**	31[a]/4[a]/27[a]	6.3 (5.5-9.0)[a] **7.0 (5.7-8.4)**
	PC (262)	6.9 (5.9-7.7)[a]	1.7 (1.5-2.5)[a]	4[a]/1[a]/3[a]	3.6 (2.8-NE)[a] 2.9 (2.8-4.2)
IMMU-132-01 (NCT01631552)(8, 15)	SG (108)	13 (11.2-14.0)	5.6 (4.8-6.6)	34.3[a]/NR/NR 33.3/2.8/30.6	9.1 (4.6-11.3)[a] 7.7 (4.9-10.8)
Bardia et al. 2018 (NR)(9)	SG (110)	12.7 (10.8-13.6)	5.5 (4.8-6.6)	31[a]/5.5[a]/25.5[a] 34/2.7/30.9	9.1 (4.1-14.3)[a] 7.6 (4.8-11.3)
EVER-132-001 (NCT04454437)(10, 16)	SG (80)	14.7 (10.3-18.3)	5.6 (4.1-8.3)[a] 5.6 (4.2-7.0)	40[a]/2.5[a]/36.3[a] 37.5/2.5/35	11.6 (7.0-13.8)[a] 5.6 (5.6-NE)
Abelman et al. 2024 (NCT04039230)(11)	SG + Tal (26)	18 (10.7-NE)	6.2 (3.7-12.8)	30.1/NR/NR	-
Seneviratne et al. 2024 (NCT05113966)(12)	SG + Tri (30)	17.9 (9.9-NE)	4.1 (2.2-7.3)	23.3/NR/NR	9.1 (4-NE)
KEYNOTE-F21/EV-202 (NCT04225117)(13)	EV (42)	12.9 (10.3-NE)	3.5 (2.1-4.6)	19/NR/NR	3.8 (1.9-3.9)

[a]Values assessed by Independent Review Committee (IRC).
Bold values indicate statistically significant results (p<0.05).
Abbreviations: CI: Confidence interval; CR: Complete response; DoR: Duration of response; EV: Enfortumab vedotin; NCT: National Clinical Trial identifier; NE: Not estimable; NR: Not reported; ORR: Overall response rate; OS: Overall survival; PC: Physician's choice; PFS: Progression-free survival; PR: Partial response; SG: Sacituzumab govitecan; Tal: Talazoparib; Tri: Trilaciclib

Table 3: Safety Outcomes

Trial Name/Study Name (NCT id)	Study arm (N)	Grade ≥3 AEs (%)	SAEs (%)	Grade ≥3 TRAEs (%)	Discont. Due to AEs (%)	Death Due to TRAEs (%)
ASCENT (NCT02574455)(7, 14)	SG (267)	73	27	70.2	4.7	0
	PC (262)	65	29	46.4	5.4	0.4
IMMU-132-01 (NCT01631552)(8, 15)	SG (108)	-	30.6	-	2.8	-
Bardia et al. 2018 (NR)(9)	SG (110)	-		-	1.8	0
EVER-132-001 (NCT04454437)(10, 16)	SG (80)	79	21.3	71.3	8	1.3
Abelman et al. 2024 (NCT04039230)(11)	SG + Tal (26)	-	38.5	-	-	-
Seneviratne et al. 2024 (NCT05113966)(17, 18)	SG + Tri (30)	-	20	-	3.3	-
KEYNOTE-F21/EV-202 (NCT04225117)(13)	EV (42)	-	-	-	-	-

[a]Values assessed by Independent Review Committee (IRC).
Bold values indicate statistically significant results (p<0.05).
Abbreviations: AEs: Adverse events; Discont.: Discontinuation; EV: Enfortumab vedotin; NCT: National Clinical Trial identifier; NR: Not reported; PC: Physician's choice; SAEs: Serious adverse events; SG: Sacituzumab govitecan; Tal: Talazoparib; TRAEs: Treatment-related adverse events; Tri: Trilaciclib

Conclusion

- ADCs demonstrated meaningful clinical benefits in pretreated LA/mTNBC, with varying safety profiles.
- SG monotherapy showed consistent clinical activity with acceptable safety across studies.
- Moreover, combination approaches with SG also showed promise, particularly with trilaciclib (approved to reduce bone marrow suppression caused by chemotherapy), demonstrating enhanced safety profiles.
- Ongoing research into combination therapies and biomarker-driven patient selection is essential to optimize ADC integration into clinical practice for pretreated LA/mTNBC patients.

Correspondence: Patricia Dorling (patricia.dorling@merck.com)

References:

1. Sukumar J, Gast K, Quiroga D, Lustberg M, Williams N. Triple-negative breast cancer: promising prognostic biomarkers currently in development. Expert review of anticancer therapy. 2021 Feb 1;21(2):135-48.
2. Adel NG. Current treatment landscape and emerging therapies for metastatic triple-negative breast cancer. American journal of managed care. 2021 Apr 2;27.
3. Triple-negative breast cancer: details, diagnosis, and signs. American Cancer Society. June 2025. Available from: https://www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer/triple-negative.html
4. Riaz F, Gruber JJ, Telli ML. New Treatment Approaches for Triple-Negative Breast Cancer. American Society of Clinical Oncology Educational Book. 2025 Jun 3;45(3):e481154.
5. Higgins JP, Green S. Cochrane handbook for systematic reviews of interventions. 4 ed. John Wiley & Sons. 2011.
6. National Institute for Health and Care Excellence. NICE guide to the methods of technology appraisal. 2013.
7. Bardia A, Hurvitz SA, Tolaney SM, Loirat D, Punie K, Oliveira M, et al. Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer. The New England journal of medicine. 2021;384(16):1529-41.
8. Bardia A, Messersmith WA, Kio EA, Berlin JD, Vahdat L, Masters GA, et al. Sacituzumab govitecan, a Trop-2-directed antibody-drug conjugate, for patients with epithelial cancer: final safety and efficacy results from the phase I/II IMMU-132-01 basket trial. Annals of oncology : official journal of the European Society for Medical Oncology. 2021;32(6):746-56.
9. Bardia A, Vahdat LT, Diamond J, Kalinsky K, O'Shaughnessy J, Moroose RL, et al. Sacituzumab govitecan (IMMU-132), an anti-Trop-2-SN-38 antibodydrug conjugate, as ≥3rd-line therapeutic option for patients with relapsed/refractory metastatic triple-negative breast cancer (mTNBC): efficacy results. Cancer research. 2018;78(4).
10. Ma F, Wang S, Tong Z, Li W, Wu X, Sun T, et al. Overall survival results from EVER-132-001, a phase 2b single-arm study of sacituzumab govitecan in Chinese patients with metastatic triple-negative breast cancer. Cancer Research. 2024;84(9 Supplement).
11. Abelman RO, Spring L, Niemierko A, Abraham E, McNeice M, Goff J, et al. Sequential combination of sacituzumab govitecan and talazoparib in metastatic triple negative breast cancer (mTNBC): Results from a phase II study. Journal of Clinical Oncology. 2024;42(16 Supplement).
12. Seneviratne LC, Harnden KK, Blau S, Danso MA, Berz D, Guaqueta DC, et al. Trilaciclib combined with sacituzumab govitecan (SG) in metastatic triple-negative breast cancer (mTNBC): Updated phase 2 safety and efficacy results. Journal of Clinical Oncology. 2024;42(16 Supplement).
13. Giordano A, Awan AAA, Bruce JY, Rugo HS, Diamond JR, Novik Y, et al. Enfortumab vedotin (EV) in triple-negative breast cancer (TNBC) and HR+/HER2- breast cancer (BC) cohorts of EV-202. Journal of Clinical Oncology. 2024;42(16 Supplement).
14. Bardia A, Rugo HS, Tolaney SM, Loirat D, Punie K, Oliveira M, Brufsky A, Kalinsky K, Cortés J, Shaughnessy JO, Diéras V. Final results from the randomized phase III ASCENT clinical trial in metastatic triple-negative breast cancer and association of outcomes by human epidermal growth factor receptor 2 and trophoblast cell surface antigen 2 expression. Journal of Clinical Oncology. 2024 May 20;42(15):1738-44.
15. Study of sacituzumab govitecan-hziy (IMMU-132) in adults with epithelial cancer. National Library of Medicine (US); ClinicalTrials.gov Identifier: NCT01631552. Available from: https://clinicaltrials.gov/study/NCT01631552
16. Xu B, Ma F, Wang T, Wang S, Tong Z, Li W, Wu X, Wang X, Sun T, Pan Y, Yao H. A Phase IIb, single arm, multicenter trial of sacituzumab govitecan in Chinese patients with metastatic triple-negative breast cancer who received at least two prior treatments. International Journal of Cancer. 2023 May 15;152(10):2134-44.
17. Seneviratne L, Harnden KK, Mardones M, Blau S, Gillespie-Twardy A, Danso MA, Berz D, Guaqueta D, Schwerkoske J, O'Shaughnessy J, Patt D. 201P trilaciclib combined with sacituzumab govitecan (SG) in metastatic triple-negative breast cancer (mTNBC): preliminary phase II results. ESMO Open. 2023 May 1;8(1).
18. Trilaciclib in Patients Receiving Sacituzumab Govitecan-hziy for Triple Negative Breast Cancer. National Library of Medicine (US); ClinicalTrials.gov Identifier: NCT05113966. Available from: https://clinicaltrials.gov/study/NCT05113966

Presented at the Professional Society for Health Economics and Outcomes Research (ISPOR) European Congress; November 09–12, 2025; Glasgow, Scotland, UK