



# Prognostic impact of TROP2 in adenocarcinoma of the esophageal junction and stomach

Anselm Pitrof<sup>1</sup> · Alexander Arnold<sup>2</sup> · Severin Daum<sup>3</sup> · Jonas Staudacher<sup>3</sup> · Erika Berg<sup>2</sup> · Michael Hummel<sup>2</sup> · David Horst<sup>2</sup> · Beate Rau<sup>4</sup> · Ulrike Stein<sup>5</sup> · Lisa Marie Eich<sup>2</sup> · Christoph Treese<sup>3</sup>

Received: 2 November 2025 / Accepted: 22 December 2025

© The Author(s) 2026

## Abstract

**Introduction** Adenocarcinoma of the esophageal junction and stomach (AEG/S) remains one of the deadliest cancers worldwide. New treatment options are urgently needed. A new target could be trophoblast cell surface protein 2 (TROP2), which is expressed in a variety of solid tumors and can be targeted, e.g., by sacituzumab govitecan, which has shown promising results in triple-negative breast cancer. This study investigates the expression of TROP2 in patients with AEG/S and correlates its expression with clinical and histopathological endpoints.

**Methods** TROP2 expression was assessed in a cohort of 250 patients who underwent primary surgery for AEG/S. Immunohistochemistry was performed on tissue microarrays constructed from primary tumors and lymph node metastases to quantify TROP2 expression intensity. Clinical variables, including overall survival and patient demographics, as well as tumor-specific characteristics such as stage and grade, were correlated with TROP2 expression to evaluate its potential prognostic relevance in AEG/S.

**Results** TROP2 was expressed in 86% of primary tumors and 81.3% of lymph node metastases. The intensity of TROP2 expression (low vs. medium vs. high) was correlated negatively with overall survival ( $p < 0.05$ , 70.9 months vs. 54.2 months vs. 39.5 months), lymphatic invasion ( $p = 0.05$ ,  $V = 0.138$ ), and higher grading ( $p = 0.037$ ,  $V = 0.143$ ). The intensity of TROP2 expression in lymph node metastases and primary tumors correlated significantly ( $p < 0.001$ ,  $\rho = 0.444$ ). There was a non-significant increase in positive lymphonodal status ( $p = 0.093$ ,  $V = 0.138$ ) in patients with higher TROP2 expression.

**Conclusion** In Caucasian AEG/S patients, TROP2 is expressed in the majority of cases. TROP2 expression intensity itself has an impact on survival, which could be explained by a more aggressive phenotype, which leads to lymphatic invasion and lymph node metastasis.

**Keywords** TROP2 · Trophoblast cell surface antigen 2 · Gastric cancer · Esophageal cancer · AEG/S · Sacituzumab govitecan

L. M. Eich and C. Treese—these authors are equally contributed.

Anselm Pitrof  
anselm.pitrof@charite.de

<sup>1</sup> Department of Hematology, Oncology and Cancer Immunology, Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin, Berlin, Germany

<sup>2</sup> Institute of Pathology, Charité - Universitätsmedizin Berlin, Berlin, Germany

<sup>3</sup> Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin, Berlin, Germany

<sup>4</sup> Department of Surgery, Charité - Universitätsmedizin Berlin, Campus Virchow-Klinikum and Campus Mitte, Berlin, Germany

<sup>5</sup> Experimental and Clinical Research Center, Charité – Universitätsmedizin Berlin and Max-Delbrück-Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany

## Introduction

Adenocarcinomas of the esophagogastric junction and stomach (AEG/S) remain a major global health burden, accounting for more than one million deaths annually, with the highest incidence observed in Asian populations [1]. Despite the introduction of targeted therapies—including anti-HER2 [2], anti-VEGFR2 [3], anti-Claudin 18.2 [4, 5], and anti-PD-L1 agents [6]—prognosis remains poor, with approximately half of the patients surviving beyond 1 year after diagnosis [7].

Trophoblast cell surface antigen 2 (TROP2) is a transmembrane glycoprotein involved in calcium signaling and essential physiological processes such as fetal lung development [8]. In cancer, TROP2 is frequently overexpressed and implicated in tumorigenesis, proliferation, lymphatic invasion, and metastatic spread. Elevated TROP2 expression has been reported across multiple epithelial malignancies, including breast, thyroid, and prostate cancer, where it is associated with more aggressive clinical behavior and worse outcomes [9].

Sacituzumab govitecan, an antibody–drug conjugate targeting TROP2, delivers the cytotoxic payload SN-38 directly to TROP2-expressing tumor cells, exerting potent antitumor activity and enabling a bystander effect on neighboring cells [10, 11]. Clinical trials, including ASCENT [12] and IMMU-132-01 [13], have demonstrated substantial efficacy across several epithelial cancers, resulting in regulatory approval by the U.S. Food and Drug Administration and the European Medicines Agency for metastatic triple-negative breast cancer and urothelial carcinoma.

Although the IMMU-132-01 trial included only a limited number of gastric ( $n=5$ ) and esophageal ( $n=19$ ) cancers, emerging evidence indicates that most gastric and esophageal adenocarcinomas express TROP2, with moderate-to-high expression detected in more than half of cases [14]. A large Chinese cohort comprising 600 gastric cancer patients similarly demonstrated high TROP2 expression, which correlated with poorer survival, advanced TNM stage, larger tumor size, and increased rates of lymph node and distant metastasis [15]. Preclinical data further suggest a link between TROP2 expression and therapeutic response to sacituzumab govitecan, underscoring its potential relevance as both a prognostic biomarker and therapeutic target in AEG/S [16].

To better define the prognostic significance of TROP2 and assess its potential therapeutic implications in Caucasian patients with AEG/S, robust survival data are needed. In this study, a cohort of 250 patients with AEG/S was analyzed, assessing TROP2 expression by immunohistochemistry and correlating its expression with detailed clinical and histopathological parameters.

## Materials and methods

### Patients

Clinical data from 250 patients with AEG/S of all tumor stages, primarily treated by surgery between 1992 and 2004 at the Charité—Universitätsmedizin Berlin, were collected retrospectively. The mean follow-up was 121.7 months (95% CI 113.9–129.5). The data including patient characteristics and follow-up information were retrieved from the patient management software (SAP) and the regional population-based cancer registry (“Gemeinsames Krebsregister”) and are summarized in Table 1. This study was approved by the Institutional Review Board of the Charité (EA4/115/10).

### Tissue samples

Out of formalin-fixed, paraffin-embedded (FFPE) tumor samples from 414 patients (primary tumors  $n=314$ , synchronous lymph node metastasis  $n=151$ ), tissue microarrays (TMA) were engineered and analyzed histomorphologically as described before [17]. Two hundred fifty primary tumor samples and one hundred seven lymph node metastases were evaluable after processing.

TMA blocks were sectioned at 2- $\mu$ m thickness for immunohistochemical staining. Antigen retrieval was performed using either “CC1 mild buffer” (Ventana Medical Systems) with heat treatment at 100 °C for 30 min or enzymatic digestion with protease 1 for 8 min. Following antigen retrieval, tissue sections underwent primary antibody incubation for 60 min at room temperature using anti-TROP2 (clone EPR20043; Abcam, diluted 1:1000). Signal detection was achieved through the avidin–biotin complex methodology with 3,3'-diaminobenzidine as chromogen. All immunohistochemical procedures were carried out using the BenchMark XT automated immunostainer (Ventana Medical Systems).

Expression was evaluated by an immunoreactivity score (H-score) [18, 19] which incorporates the percentage of tumor cells showing membranous staining and the intensity of that staining: The percentage of positive tumor cells is estimated and assigned a value from 0 to 100. The intensity of staining is scored as 0 (none), 1 (weak), 2 (moderate), or 3 (strong):

$$\begin{aligned} H\text{- score} = & [(\% \text{ of cells with weak intensity}) \times 1] \\ & + [(\% \text{ with moderate intensity}) \times 2] \\ & + [(\% \text{ with strong intensity}) \times 3] \end{aligned}$$

The results ranged from 0 to 300. Values over 0 were evaluated as positive TROP2 expression. The intensity of TROP2 expression was divided into three groups: low expression (0–100), moderate expression (101–200) and

**Table 1** Patient characteristics of the analyzed patient cohort and distribution of TROP2-positive and -negative primary tumors

	Trop2 low	%	Trop2 mid	%	Trop2 high	%	p value* (2x)	N	Cramer's V
Gender male	91	57	40	25	28	18	0.195	159	0.114
Gender female	54	59	15	16	22	24		91	
Alter <65	82	60	27	20	28	20	0.627	137	0.061
Age ≥65	63	56	28	25	22	19		113	
Localization AEG	29	67	7	16	7	16	0.381	43	0.088
Localization GC	116	56	48	23	43	21		207	
Death by tumor	Yes	71	50	36	25	35	25	142	<b>0.189</b>
	No	70	69	18	18	14	14	102	
	Unknown							4	
Grading	1	0	0	1	100	0	0	1	<b>0.143</b>
	2	35	57	19	31	7	11	61	
	3	109	59	34	18	43	23	186	
	Unknown							2	
Lauren	Intestinal	51	57	25	28	13	15	89	0.110
	Diffuse	74	58	22	17	32	25	128	
	Mixed	19	61	7	23	5	16	31	
	Unknown							2	
T	1	24	73	7	21	2	6	33	0.154
	2	61	59	18	17	25	24	104	
	3	25	39	23	36	16	25	64	
	4	17	57	6	20	7	23	30	
	Unknown							17	
N	0	41	60	19	28	8	12	68	0.114
	1	44	56	19	24	16	20	79	
	2	31	58	9	17	13	25	53	
	3	29	58	8	16	13	26	50	
Nodal status	Negative	41	60	19	28	8	12	68	0.138
	Positive	104	57	36	20	42	23	182	
M	M0	119	62	38	20	35	18	192	0.079
	M1	34	52	17	26	15	23	66	
	Unknown							2	
L	L0	55	68	16	20	10	12	81	<b>0.161</b>
	L1	81	54	30	20	38	26	149	
	Unknown							20	
V	V0	93	62	28	19	28	19	149	0.099
	V1	41	53	17	22	20	26	78	
	Unknown							23	
CPS	<5	113	59	44	23	33	17	190	0.070
	≥5	28	56	10	20	12	24	50	
	Unknown							10	
Claudin 18.2	Negative	96	59	31	19	35	22	162	0.101
	Positive	48	55	24	28	15	17	87	
	Unknown							44	
Her2neu	Negative	111	59	45	24	32	17	188	0.105
	Positive	7	44	4	25	5	31	16	
	Unknown							46	
MSI	dMMR	12	46	8	31	6	23	26	0.087
	pMMR	131	59	46	21	44	20	221	
	Unknown							3	

Positive tumors were divided by H-score in three groups (low expression 0–100, medium expression 101–200, high expression 201–300). Significant differences between the groups ( $p$ -value  $\leq 0.05$ ) are written in bold

“AEG” = adenocarcinoma of the esophagogastric junction; “GC” = gastric cancer; “T” = tumor, “N” = node, “M” = metastasis, “L” = lymphatic invasion, “V” = vascular invasion from the TNM staging system; “CPS” = combined positivity score of PD-L1 expression on tumor and immune cells; “MSI” = microsatellite instability, “pMMR” = proficient mismatch repair, “dMMR” = deficient mismatch repair

**Table 1** (continued)

Significance calculated by  $\chi^2$  or Fisher's exact test when appropriate

high expression (201–300) (For different expression levels, see Fig. 1).

The expression profiles of Claudin 18.2, HER2, and PD-L1, as well as the MSI status were previously analyzed by Arnold et al. [5].

## Statistics

Statistical analysis was performed using IBM SPSS Version 29. Overall survival was defined as time from diagnosis to death or last follow-up and was compared using Kaplan–Meier method with the log-rank test for assessment of statistical significance.

Associations of TROP2 expression in primary tumor samples with tumor size, distant and lymph node metastasis, lymphonodal status, vascular and lymphatic infiltration, TROP2 expression in lymphonodal samples, Lauren classification, grading, combined positivity score of PD-L1 expression on tumor and immune cells (CPS), Her2-neu positivity, Claudin 18.2 positivity and mismatch-repair-status (MSI) were tested using the  $\chi^2$  test. If the expected frequency in a cell was less than 5, Fisher's exact test was used. Effect size of nominal correlations was evaluated using Cramer's V. Correlations of categorical variables were tested by Spearman correlation.

## Results

### TROP2 expression in primary tumors samples and correlation with survival

Of 314 primary tumor samples, 250 (79.6%) were evaluable after staining with Anti-TROP2. Low expression was observed in 145 samples (58%), moderate expression in 55 samples (22%) and high expression in 50 samples (20%). Thirty-five patients showed no TROP2 expression (14%), which resulted in an overall TROP2 positivity of 86%.

There was a significant difference in survival between the low- and high-TROP2-expressing patients (70.9 months (95% KI 58.4–83.4) versus 39.5 months (95% KI 23.9–55.0)  $p=0.009$ ) (Fig. 2).

### TROP2 expression and clinicopathological features

Patients were stratified by H-score into three subgroups and were correlated with clinicopathological features (Table 1). Patients with high TROP2 expression showed statistically significant more tumor-related deaths ( $p=0.013$ ,  $V=0.189$ ),

a worse tumor grading ( $p=0.037$ ,  $V=0.143$ ), and higher rates of lymphatic invasion ( $p=0.05$ ,  $V=0.161$ ). In addition, there was a non-significant trend towards increased positive nodal status ( $p=0.093$ ,  $V=0.138$ ) in patients with higher TROP2 expression. There were no significant differences in TROP2 expression and sex, age, TNM stage, localization, Lauren classification, vascular invasion, CPS, Claudin 18.2 expression, Her2/neu expression, and MSI.

### TROP2 expression in lymph node metastasis

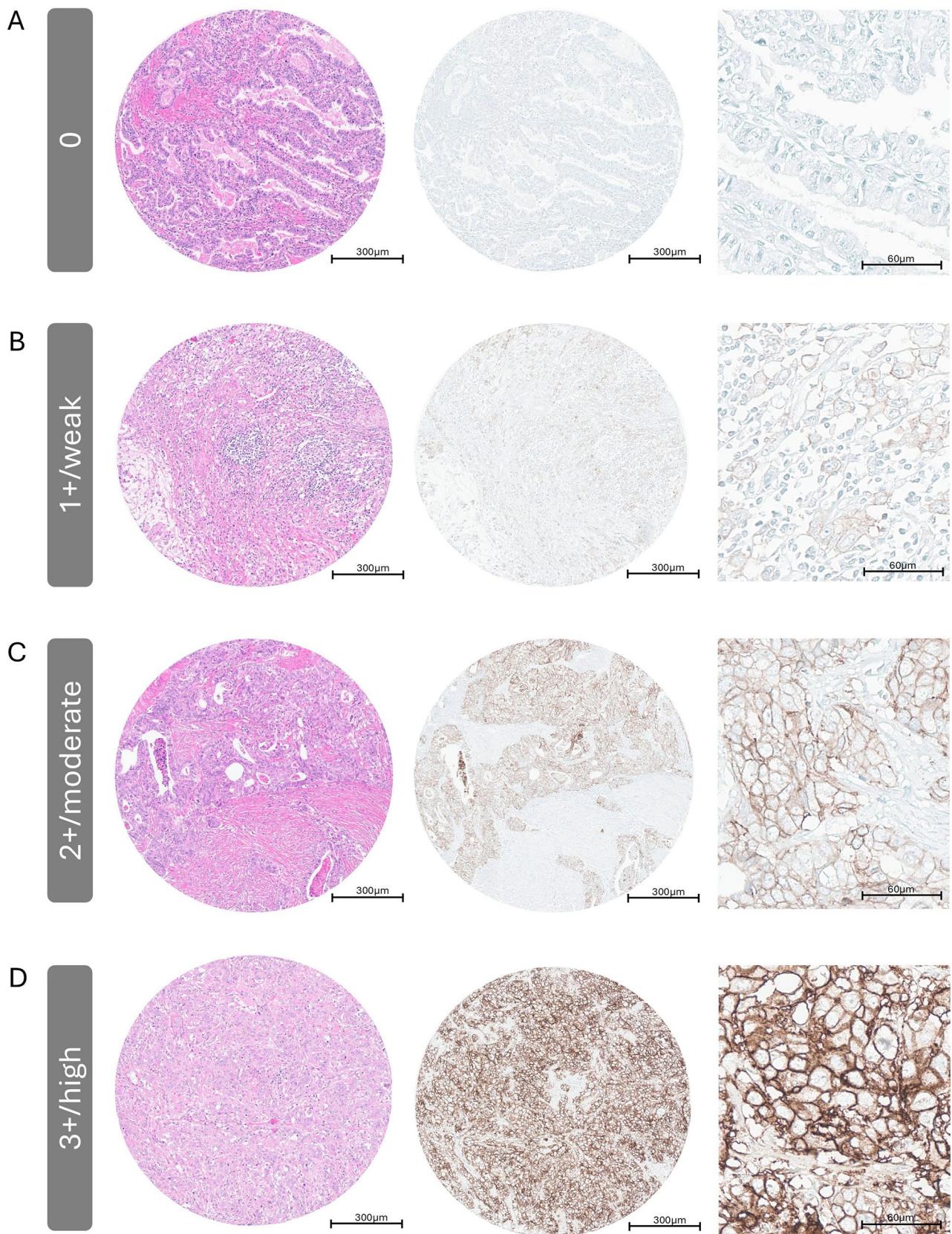
Of 151 lymph node metastasis specimens, TROP2 immunohistochemistry was assessable in 107 (70.9%). Overall, 81.3% of evaluable samples demonstrated TROP2 positivity. Low-, medium-, and high-TROP2 expression levels were observed in 55 (51.4%), 30 (28.0%), and 22 (20.6%) patients, respectively. Sixty-two lymph node specimens were matched with corresponding primary tumor samples from the same individuals. The intensity of TROP2 expression showed a strong correlation between primary tumors and their corresponding lymph node metastasis (Table 2; Spearman's  $\rho=0.495$ ;  $p<0.001$ ).

## Discussion

### TROP2 is strongly expressed in AEG/S and correlates with worse outcome

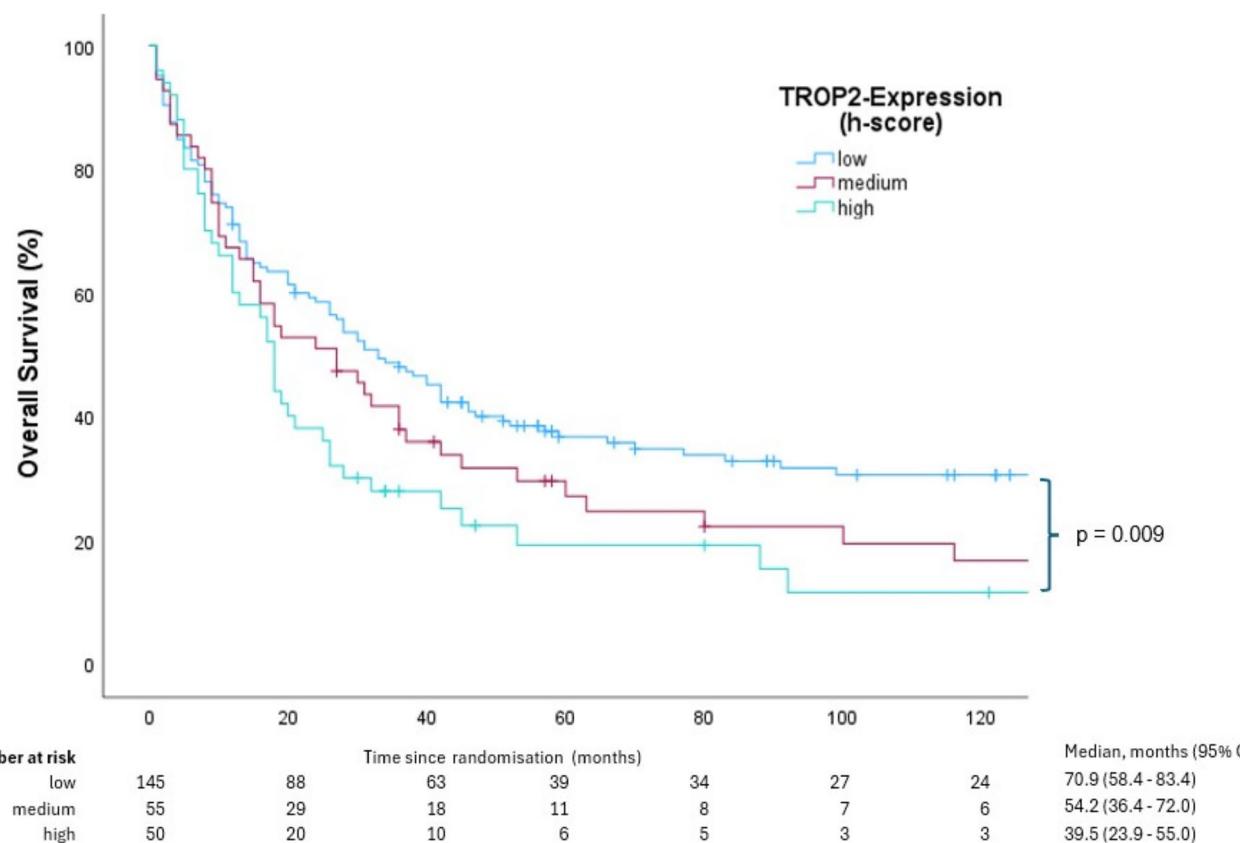
To our knowledge, this study represents the first large Caucasian AEG/S cohort comprehensively profiled for TROP2 expression and correlated with detailed clinicopathological parameters. TROP2 was expressed in majority of primary tumors as well as in lymph node metastases. Higher TROP2 expression was significantly associated with increased lymphatic invasion, poorer tumor differentiation, a greater number of tumor-related deaths, and reduced overall survival. Although lymph node positivity was more frequent in cases with elevated TROP2 expression, this difference did not reach statistical significance.

The underlying pathobiology of worse outcomes could be explained by gene expression profiles in TROP2-positive cells that contribute to epithelial–mesenchymal transition, migration/invasiveness, and extracellular matrix interaction/remodeling. This mechanism has been observed in colorectal cancer, where TROP2 overexpression leads to lymph node metastases and poor tumor differentiation [20]. Supporting this hypothesis, we observed high TROP2 expression rates in



**Fig. 1** TROP2 expression in patients with adenocarcinomas of the esophagogastric junction and stomach. H&E (left) and low (middle) and high-magnification (right) histopathological images with **A** no

TROP2 expression, **B** TROP2 expression of 1+(weak), **C** TROP2 expression of 2+(moderate) and **D** TROP2 expression of 3+(high)



**Fig. 2** Kaplan-Meier plots of overall survival, divided by intensity of TROP2 expression. A vertical line marks a censored patient. There is a significant ( $\log\text{-rank } X^2 = 6.682$ ,  $df = 1$ ,  $p = 0.009$ ) difference in survival between the low- and high-TROP2-expressing patients. There

was no significant difference between the low- and medium-TROP2-expressing patients and the medium- and high-TROP2-expressing patients, respectively

**Table 2** TROP2 expression in primary tumor samples ( $T$ ) and corresponding lymph node metastasis ( $N$ )

TROP2 expression ( $T$ )	TROP2 expression ( $N$ )				$p$ value	Spearman
	Low	Medium	High	N total		
Low	24	4	4	32 (51.6%)	<0.001	correlation
Medium	7	8	1	16 (25.8%)		0.495
High	2	4	8	14 (22.6%)		
	33 (53.2%)	16 (25.8%)	13 (21%)	62 (100%)		

$H$ -score groups between tumor samples and lymph node samples are correlated

the lymph node metastases that correlated with the intensity of expression in corresponding primary tumor samples.

### Differences of TROP2 expression in Asian and Caucasian cohorts

The present findings are broadly concordant with those reported by Zhao and colleagues [15], who analyzed a Chinese cohort of 600 gastric cancer patients and demonstrated that high TROP2 expression was associated with significantly poorer outcomes, including increased rates of

lymph node or distant metastasis and a higher prevalence of intestinal-type tumors. These discrepancies between cohorts may be influenced by differences in the molecular profile of AEG/S in Asian and Caucasian patients [21] and, at least in part, by differences in *Helicobacter pylori* exposure. In the cohort studied by Zhao et al., 79.2% of patients were infected with *H. pylori*, whereas in Western populations, the prevalence is substantially lower, with only approximately 20% of non-cardia AEG/S cases attributable to *H. pylori* infection [20]. Mechanistically, TROP2—typically absent or minimally expressed in normal gastric mucosa—is upregulated

during the metaplasia–dysplasia transition, a process frequently initiated and sustained by chronic *H. pylori*-induced inflammation [21]. Unfortunately, *H. pylori* infection status was not available for our cohort, precluding direct assessment of its role in modulating TROP2 expression. Moreover, Zhao et al. applied a dichotomous classification of TROP2 expression (high: H-score > 130; low: H-score < 130 or negative), whereas contemporary practice typically employs a three-tiered H-score system (low, medium, high) [18, 19].

Kim et al. [22] were able to show similar findings in their Korean cohort that comprised 412 surgically treated gastric cancer patients. They also found significantly poorer outcomes, higher rates of lymph node or distant metastasis and a higher prevalence of intestinal-type tumors in high TROP2-expressing patients, using a dichotomous H-score system.

## TROP2 expression as a potential biomarker

Kim et al. [22] reported significant associations between TROP2 expression and the predictive biomarkers HER2/neu and PD-L1. In our cohort, despite comparable frequencies of PD-L1-positive and HER2/neu-positive tumors, we were unable to replicate these findings. When applying a dichotomous H-score classification, we observed a trend toward higher PD-L1 expression in TROP2-high tumors ( $p=0.073$ ; data not shown), which may partially account for this discrepancy. Claudin 18.2, another emerging predictive biomarker, has not been shown to correlate with other biomarkers [5, 22], which appears to hold true for TROP2 in our dataset as well. Similarly, MSI status demonstrated no significant association with TROP2 expression, consistent with the observations of Kim et al. [22].

Compared with established predictive biomarkers such as HER2/neu and PD-L1, TROP2 appears to function primarily as a prognostic marker, given its association with reduced survival in patients exhibiting higher expression levels. Its potential role as a predictive biomarker is currently under investigation in ongoing clinical trials, including studies of anti-TROP2 antibody–drug conjugates in AEG/S, such as the SAGA trial (AIO-STO-0123/ass).

## Conclusion

TROP2 is highly expressed in AEG/S and is associated with increased lymphatic invasion, poor tumor differentiation, and reduced survival, supporting its role as a prognostic biomarker. Expression patterns in Caucasian cohorts align with findings from Asian populations, though differences in *H. pylori* exposure may contribute to variability. TROP2 showed no consistent correlation with HER2/neu, PD-L1, Claudin 18.2, or MSI, but ongoing trials, including the

SAGA study (AIO-STO-0123/ass), will clarify its potential as a predictive biomarker and therapeutic target.

**Author's contribution** All authors contributed to the study conception and design. Collection of tissue samples and medical history was performed by BR and CT. Material preparation, TMA engineering and immunohistochemistry were performed by LME, MH, and EB. The data collection and analysis were performed by AP, JS, AA, SD, US, and CT. The first draft of the manuscript was written by AP, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

**Funding** Open Access funding enabled and organized by Projekt DEAL. OpenAccess funding enabled and organized by Projekt DEAL.

**Data availability** The data that support the findings of this study are available from the corresponding author, AP, upon reasonable request.

## Declarations

**Conflict of interest** The author(s) declare that they have no conflict of interest.

**Ethics approval** This study was approved by the Institutional Review Board of the Charité (EA4/115/10).

**Consent to participate** Retrospective study, so no consent of participation is possible.

**Consent for publication** Retrospective study, so no consent of participation is possible.

**Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

## References

- Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74:229–63. <https://doi.org/10.3322/caac.21834>.
- Bang Y-J, Cutsem EV, Feyereislova A, Chung HC, Shen L, Sawaki A, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. Lancet. 2010;376:687–97. [https://doi.org/10.1016/S0140-6736\(10\)61121-X](https://doi.org/10.1016/S0140-6736(10)61121-X).
- Wilke H, Muro K, Van Cutsem E, Oh S-C, Bodoky G, Shimada Y, et al. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced

gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial. *Lancet Oncol.* 2014;15:1224–35. [https://doi.org/10.1016/S1470-2045\(14\)70420-6](https://doi.org/10.1016/S1470-2045(14)70420-6).

4. Shitara K, Van Cutsem E, Lordick F, Enzinger PC, Ilson DH, Shah MA, et al. Final overall survival results from phase 3 SPOTLIGHT study evaluating zolbetuximab + mFOLFOX6 as first-line (1L) treatment for patients (Pts) with claudin 18 isoform 2 (CLDN18.2)+, HER2–, locally advanced (LA) unresectable or metastatic gastric or gastroesophageal junction (mG/GEJ) adenocarcinoma. *J Clin Oncol.* 2024;42:4036–4036. [https://doi.org/10.1200/JCO.2024.42.16\\_suppl.4036](https://doi.org/10.1200/JCO.2024.42.16_suppl.4036).
5. Arnold A, Daum S, von Winterfeld M, Berg E, Hummel M, Rau B, et al. Prognostic impact of claudin 18.2 in gastric and esophageal adenocarcinomas. *Clin Transl Oncol.* 2020;22:2357–63. <https://doi.org/10.1007/s12094-020-02380-0>.
6. Rha SY, Oh D-Y, Yañez P, Bai Y, Ryu M-H, Lee J, et al. Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for HER2-negative advanced gastric cancer (KEYNOTE-859): a multicentre, randomised, double-blind, phase 3 trial. *Lancet Oncol.* 2023;24:1181–95. [https://doi.org/10.1016/S1470-2045\(23\)00515-6](https://doi.org/10.1016/S1470-2045(23)00515-6).
7. Rau B, Lang H, Koenigsrainer A, Gockel I, Rau H-G, Seeliger H, et al. Effect of hyperthermic intraperitoneal chemotherapy on cytoreductive surgery in gastric cancer with synchronous peritoneal metastases: the phase III GASTRIPEC-I trial. *J Clin Oncol.* 2024;42:146–56. <https://doi.org/10.1200/JCO.22.02867>.
8. Goldenberg DM, Stein R, Sharkey RM. The emergence of trophoblast cell-surface antigen 2 (TROP-2) as a novel cancer target. *Oncotarget.* 2018;9:28989–9006. <https://doi.org/10.18632/oncotarget.25615>.
9. Lombardi P, Filetti M, Falcone R, Altamura V, Paroni Sterbini F, Bria E, et al. Overview of Trop-2 in cancer: from pre-clinical studies to future directions in clinical settings. *Cancers.* 2023;15:1744. <https://doi.org/10.3390/cancers15061744>.
10. Starodub AN, Ocean AJ, Shah MA, Guarino MJ, Picozzi VJ Jr., Vahdat LT, et al. First-in-human trial of a novel anti-Trop-2 antibody-SN-38 conjugate, sacituzumab govitecan, for the treatment of diverse metastatic solid tumors. *Clin Cancer Res.* 2015;21:3870–8. <https://doi.org/10.1158/1078-0432.CCR-14-3321>.
11. Pavone G, Motta L, Martorana F, Motta G, Vigneri P. A new kid on the block: sacituzumab govitecan for the treatment of breast cancer and other solid tumors. *Molecules.* 2021;26:7294. <https://doi.org/10.3390/molecules26237294>.
12. Bardia A, Hurvitz SA, Tolaney SM, Loirat D, Punie K, Oliveira M, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer. *N Engl J Med.* 2021;384:1529–41. <https://doi.org/10.1056/NEJMoa2028485>.
13. 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. *Ann Oncol.* 2021;32:746–56. <https://doi.org/10.1016/j.annonc.2021.03.005>.
14. Dum D, Taherpour N, Menz A, Höflmayer D, Völkel C, Hinsch A, et al. Trophoblast cell surface antigen 2 expression in human tumors: a tissue microarray study on 18,563 tumors. *Pathobiology.* 2022;89:245–58. <https://doi.org/10.1159/000522206>.
15. Zhao W, Zhu H, Zhang S, Yong H, Wang W, Zhou Y, et al. Trop2 is overexpressed in gastric cancer and predicts poor prognosis. *Oncotarget.* 2016;7:6136–45. <https://doi.org/10.18632/oncotarget.6733>.
16. Hoppe S, Meder L, Gebauer F, Ullrich RT, Zander T, Hillmer AM, et al. Trophoblast cell surface antigen 2 (TROP2) as a predictive bio-marker for the therapeutic efficacy of sacituzumab govitecan in adenocarcinoma of the esophagus. *Cancers.* 2022;14:4789. <https://doi.org/10.3390/cancers14194789>.
17. Arnold A, Daum S, von Winterfeld M, Berg E, Hummel M, Horst D, et al. Analysis of NTRK expression in gastric and esophageal adenocarcinoma (AGE) with pan-TRK immunohistochemistry. *Pathol Res Pract.* 2019;215:152662. <https://doi.org/10.1016/j.prp.2019.152662>.
18. Van Bockstal MR, Depelsmaeker M-C, Daoud L, Fontanges Q, Francois A, Guiot Y, et al. Evaluation of trophoblast cell surface antigen-2 (TROP2) protein expression in chemotherapy-resistant and metastatic breast carcinomas. *Pathol Res Pract.* 2024;264:155724. <https://doi.org/10.1016/j.prp.2024.155724>.
19. Henry NL, Somerfield MR, Dayao Z, Elias A, Kalinsky K, McShane LM, et al. Biomarkers for systemic therapy in metastatic breast cancer: ASCO guideline update. *J Clin Oncol.* 2022;40:3205–21. <https://doi.org/10.1200/JCO.22.01063>.
20. Švec J, Šťastná M, Janečková L, Hrčkulák D, Vojtěchová M, Onhajzer J, et al. TROP2 represents a negative prognostic factor in colorectal adenocarcinoma and its expression is associated with features of epithelial-mesenchymal transition and invasiveness. *Cancers.* 2022;14:4137. <https://doi.org/10.3390/cancers14174137>.
21. Jia F, Teer JK, Knepper TC, Lee JK, Zhou H-H, He Y-J, et al. Discordance of somatic mutations between Asian and Caucasian patient populations with gastric cancer. *Mol Diagn Ther.* 2017;21:179–85. <https://doi.org/10.1007/s40291-016-0250-z>.
22. Kim HS, Kim Y, Lee HS. Clinicopathologic characteristics of Trop family proteins (Trop-2 and EpCAM) in gastric carcinoma. *J Gastric Cancer.* 2024;24:391–405. <https://doi.org/10.5230/jgc.2024.24.e32>.

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.