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Expression Profiling of Claudin 18.2 in Resected Specimens and Endoscopic Biopsies from Patients with Gastric and Gastroesophageal Junction Adenocarcinoma: A Review

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Abstract

Claudin 18.2 is now a treatment-defining biomarker in gastric and gastroesophageal junction adenocarcinoma, and eligibility turns on a single number: whether at least 75 per cent of tumour cells stain moderately or strongly. That threshold is where the difficulty lies, because expression within a tumour is uneven and a small endoscopic sample may not represent the whole.

Objectives: *To review the published evidence on claudin 18.2 expression in gastric and gastroesophageal junction adenocarcinoma: reported prevalence, agreement between biopsies, resected specimens and metastatic sites, the influence of the positivity threshold on that agreement, and the treatment outcomes that follow a positive result.*

Material and Methods: *Narrative review of randomised trials, trial screening and correlative analyses, and matched-sample immunohistochemistry studies indexed in PubMed and the major oncology and gastroenterology journals. Studies were eligible if they reported claudin 18.2 prevalence in a defined population, concordance between two sample types in the same patients, or outcomes stratified by claudin 18.2 status. No new patient data were generated; every prevalence, concordance and survival figure quoted is one published by the original investigators.*

Results: *Across the screening populations of two phase 3 trials, positivity at the 75 per cent threshold was 38.4 per cent, and was similar between gastric and junctional primaries, between biopsy and resection, and between primary and metastatic samples. Independent series have reported 47.0 and 24.0 per cent. Concordance depends strongly on the threshold applied: between archival and baseline samples it was 61.1 per cent at the 75 per cent cutoff but 88.9 per cent for any staining. Intratumoral heterogeneity was found in 38.5 per cent of surgical specimens and 25.2 per cent of paired primary-metastatic comparisons were discordant, with peritoneal lesions showing the highest positive concordance at 31.4 per cent and liver lesions the lowest at 12.8 per cent. Adding zolbetuximab to first-line chemotherapy extended median overall survival from 15.5 to 18.2 months in one trial and from 12.2 to 14.4 months in the other.*

Conclusion: *Prevalence is stable enough across sample types to make biopsy-based testing reasonable, but concordance in individual patients is not high, and it falls as the threshold rises. Because eligibility rests on a dichotomised cutoff applied to a continuously distributed and spatially uneven marker, a negative result from a small or single-site sample should not be treated as final where the therapeutic question remains open.*

Abbreviations: *CLDN18.2 – Claudin 18 Isoform 2, G/GEJ – Gastric or Gastroesophageal Junction, IHC – Immunohistochemistry, HER2 – Human Epidermal Growth Factor Receptor 2, PD-L1 – Programmed Death-Ligand 1, CPS – Combined Positive Score, MSI – Microsatellite Instability, dMMR – Deficient Mismatch Repair, PFS – Progression-Free Survival, OS – Overall Survival, HR – Hazard Ratio, FFPE – Formalin-Fixed Paraffin-Embedded.*

Keywords: *Claudin 18.2; Gastric Adenocarcinoma; Zolbetuximab; Immunohistochemistry; Tumour Heterogeneity*

Introduction

Gastric cancer remains the fifth most commonly diagnosed malignancy worldwide, and roughly nine in ten cases are adenocarcinoma [1]. For most of the past two decades the only biomarker-directed option in advanced disease was HER2, established by a single randomised trial and confined to the fifth or so of patients whose tumours overexpress the receptor [16,17,18]. Checkpoint inhibition has since added a second axis of selection, based on PD-L1 combined positive score and on mismatch repair status [15,19,20,21].

Claudin 18 isoform 2 is a tight junction protein. In healthy tissue its expression is confined to gastric mucosal epithelium, and it is retained on malignant transformation, at which point epitopes

normally buried within the junction become accessible to antibody binding [3]. That combination, restricted normal expression and preserved tumour expression, is what made it attractive as a therapeutic target rather than merely a descriptive marker.

The alteration also has a genomic dimension. CLDN18 aberrations are enriched in the genomically stable subgroup of gastric cancer, and recurrent CLDN18-ARHGAP fusions occur in diffuse-type and signet-ring cell tumours, where they carry prognostic weight [14,30]. Protein expression, however, is not confined to that subgroup and is found across histological types [9,10].

Zolbetuximab, a chimeric monoclonal antibody directed at claudin 18.2, progressed from a phase 1 dose-escalation study through single-agent and combination phase 2 work to two positive phase 3 trials [4,5,6,7,8]. Both trials selected patients using the same definition: moderate to strong membranous staining in at least 75 per cent of tumour cells [7,8,9]. That definition now determines who receives the drug.

Which raises the question this review addresses. A dichotomised threshold applied to a marker that is continuously distributed and spatially uneven will misclassify some patients, and the direction and size of that error depend on what tissue was examined. The aim here is to set out what has been reported on claudin 18.2 prevalence, on agreement between endoscopic biopsies, resected specimens and metastatic deposits, and on what a positive result delivers therapeutically.

Material and Methods

Search strategy: PubMed and the archives of the major oncology, pathology and gastroenterology journals were searched for studies of claudin 18.2 in gastric and gastroesophageal junction adenocarcinoma. Search terms combined claudin 18.2, CLDN18.2 and zolbetuximab with gastric adenocarcinoma, gastroesophageal junction, immunohistochemistry, prevalence, concordance, heterogeneity, biopsy, resection and peritoneal metastasis. Reference lists of retrieved trials and reviews were screened by hand for further primary sources.

Eligibility: Studies were included if they reported the prevalence of claudin 18.2 positivity in a defined gastric or gastroesophageal population using a stated threshold and antibody clone; matched comparison of two sample types from the same patients; the spatial distribution of staining within tumours; or clinical outcomes stratified by claudin 18.2 status. Randomised trials and their screening or correlative analyses were included preferentially. Studies in non-gastroesophageal primaries are cited only where they bear on assay interpretation.

Data extraction and handling: Design, sample size, antibody clone, positivity threshold, sample type and reported prevalence, concordance and efficacy estimates were extracted as published. Prevalence and concordance figures are reported together with the threshold used, because the two are not separable in this literature. No pooling, re-analysis or recalculation was performed and no patient-level data were obtained. Figures 1 to 5 and Tables 1 and 2 reproduce published values only. This is a narrative synthesis and was not registered as a systematic review.

Results

How common a positive result is: The largest and most consistent prevalence data come from the screening populations of the two phase 3 trials. Across both, positivity at the 75 per cent threshold, assessed by immunohistochemistry with the 43-14A clone, was 38.4 per cent. Prevalence was similar in gastric compared with junctional adenocarcinoma, similar regardless of whether the sample was a biopsy or a resection, and similar whether it came from the primary or a metastasis. Positivity was most frequent in diffuse-type tumours [9].

Independent series have reported figures on either side of that. A Korean cohort of 166 patients with metastatic disease reported 47.0 per cent using the same clone and threshold [10], while a Japanese cohort of 408 evaluable patients with advanced disease reported 24.0 per cent, as summarised in the trial screening analysis (Figure 1) [9]. The spread is wide enough that prevalence quoted from one population should not be assumed to transfer to another.

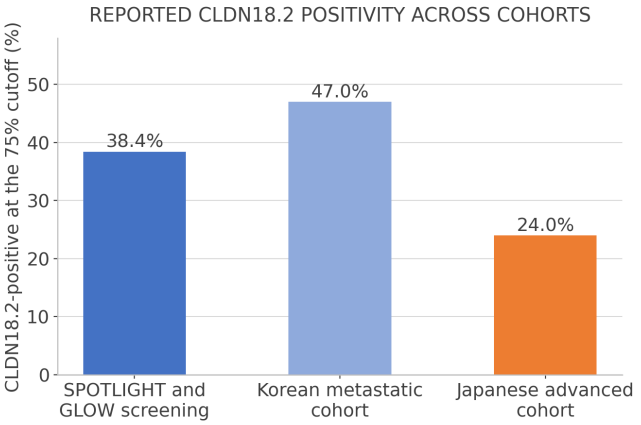

Figure 1: Reported claudin 18.2 positivity at the 75 per cent threshold across three populations [9,10]

The threshold determines the agreement: The headline finding that prevalence is stable across sample types is reassuring at the population level and misleading at the level of the individual patient. In pair-matched samples from the phase 1 and phase 2 zolbetuximab studies, concordance of claudin 18.2 positivity between archival and baseline samples was 61.1 per cent at the 75 per cent cutoff. Applying the far looser definition of any moderate-to-strong staining in at least 1 per cent of cells, concordance rose to 88.9 per cent [9].

The same pattern appears in comparisons across anatomical sites. In gastric cancer with peritoneal dissemination, concordance between primary tumour and peritoneal deposit was 79.8 per cent at a 40 per cent cutoff and 75.0 per cent at 75 per cent, and expression in the disseminated lesions was significantly lower than in the primary [11]. In the Korean metastatic series, 25.2 per cent of paired primary-metastatic comparisons were discordant for positivity (Figure 2) [10]. Comparable divergence between primary tumours and lymph node metastases has been described [12].

Read together, these figures say that the marker itself is reasonably stable but the dichotomy applied to it is not. The proportion of tumours sitting near the threshold is large enough that small differences in which part of the tumour was sampled will move a meaningful number of patients across the line.

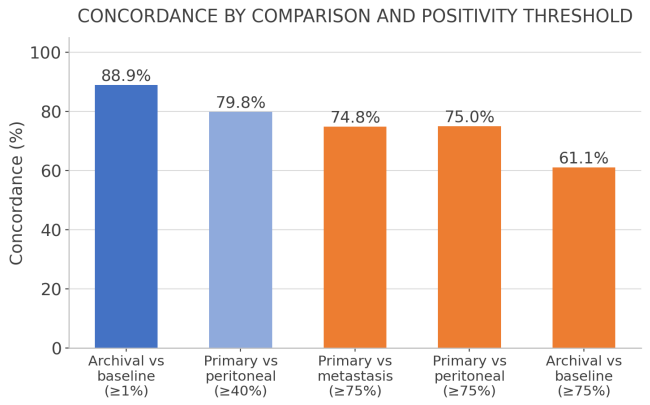

Figure 2: Reported concordance of claudin 18.2 status by the comparison made and the positivity threshold applied [9,10,11]

Study	n	Material	Principal reported finding
Sahin et al. 2021 [6]	246	Trial	Zolbetuximab plus EOX improved survival at a 40% cutoff
Shitara et al. 2023 [7]	565	Trial	SPOTLIGHT: median OS 18.2 vs 15.5 months
Shah et al. 2023 [8]	507	Trial	GLOW: median OS 14.4 vs 12.2 months
Shitara et al. 2024 [9]	Screening	Biopsy and resection	Positivity 38.4%; archival-baseline concordance 61.1%
Choi et al. 2024 [10]	166	Paired specimens	Intratumoral heterogeneity in 38.5%; 25.2% discordant
Ogawa et al. 2024 [11]	84	Primary and peritoneal	Concordance 75.0% at the 75% cutoff

Table 1: Principal studies reviewed, with the material examined and the finding as reported by the original investigators

Where the sample is taken from matters: The Korean series examined this directly. Intratumoral heterogeneity was present in 38.5 per cent of surgical specimens, meaning that staining varied appreciably between regions of the same tumour. Across metastatic organ categories, peritoneal lesions had the highest positivity rate at 44.3 per cent and the highest positive concordance with the primary at 31.4 per cent, while liver lesions had the lowest at 17.9 and 12.8 per cent respectively (Figure 3) [10]. Claudin 18.2-positive tumours were also more likely to present with peritoneal metastasis and less likely with hepatic or distant nodal involvement, while survival did not differ by claudin 18.2 status [10]. That absence of a prognostic effect is worth noting against earlier work reporting that loss of claudin-18 correlated with poor outcome in gastric cancer [13]; the marker appears to be predictive of benefit from zolbetuximab rather than prognostic in its own right.

For a clinician choosing which lesion to biopsy in a patient with metastatic disease, that is directly actionable. Sampling a liver metastasis is technically easier than sampling peritoneum, and it is the site least likely to reflect the claudin 18.2 status of the disease as a whole.

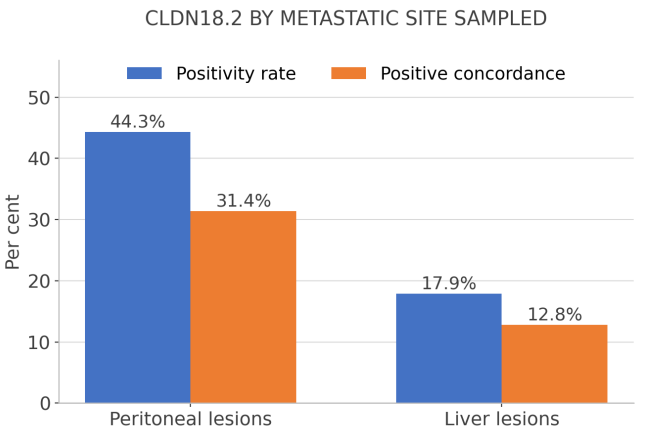

Figure 3: Claudin 18.2 positivity and concordance with the primary tumour, by metastatic site sampled [10]

What a positive result delivers: The therapeutic case rests on two randomised trials with consistent results. In the first, 565 patients with claudin 18.2-positive, HER2-negative advanced disease received zolbetuximab or placebo with mFOLFOX6; median overall survival was 18.2 against 15.5 months, with hazard ratios of 0.75 for both progression-free and overall survival [7]. In the second, 507 patients received zolbetuximab or placebo with CAPOX; median progression-free survival was 8.21 against 6.80 months (HR 0.687, 95% CI 0.544-0.866, p = 0.0007) and median overall survival 14.39 against 12.16 months (HR 0.771, 95% CI 0.615-0.965, p = 0.0118) (Figures 4 and 5) [8].

Grade 3 or worse treatment-emergent events were comparable between arms in the second trial, at 72.8 against 69.9 per cent [8], though nausea and vomiting associated with the infusion have required specific management guidance [28]. Objective response rates differed little between arms, 53.8 against 48.8 per cent, so the benefit lies in duration rather than in depth of response [8].

These outcomes are the reason the threshold matters. Earlier work had used a looser definition: the randomised phase 2 study enrolled patients with moderate-to-strong expression in at least 40 per cent of tumour cells and still showed benefit [6], while single-agent activity had been established in a phase 2a study and dose selection in a phase 1 study [4,5]. The 75 per cent cutoff adopted for the phase 3 programme was a pragmatic choice to enrich for benefit, not a biologically derived boundary [7,8,9].

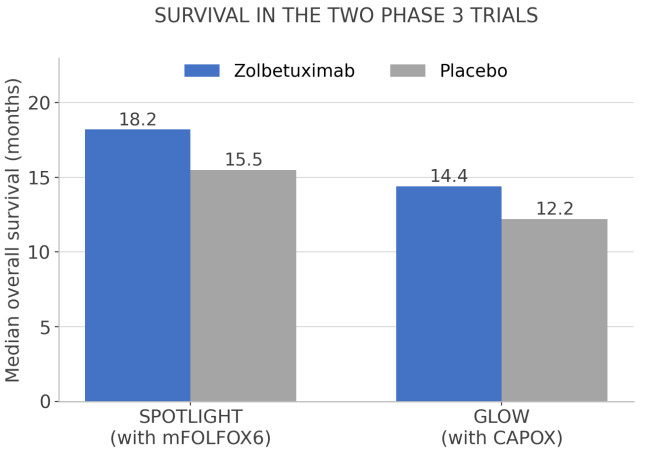

Figure 4: Median overall survival with zolbetuximab against placebo in the two phase 3 trials [7,8]

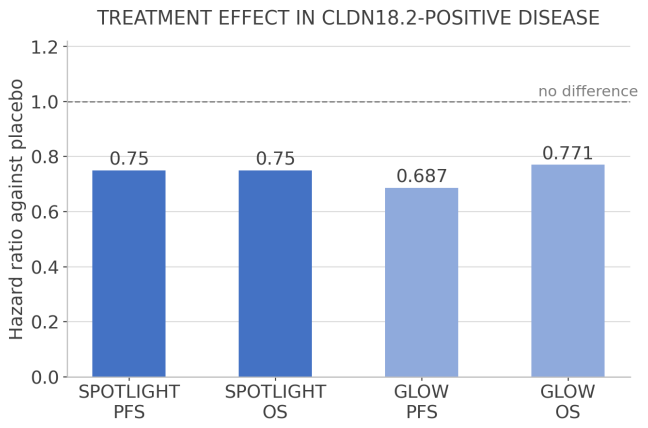

Figure 5: Hazard ratios for progression-free and overall survival in the two phase 3 trials [7,8]

Claudin 18.2 alongside the other biomarkers: Testing in this disease no longer involves a single marker. HER2 status has been assessed since the ToGA trial, and that experience is directly relevant here because HER2 staining in gastroesophageal tumours is itself heterogeneous, with variability observed in almost half of centrally assayed cases [16,17]. Mismatch repair status carries both prognostic and predictive weight, with the chemotherapy interaction reported from a perioperative trial and compatible findings from an adjuvant trial [22,23,24], and it identifies patients for checkpoint inhibition where response rates far exceed those in unselected disease [20,31]. PD-L1 combined positive score guides first-line immunotherapy [15,19,21]. European and North American guidance now folds these markers into a single recommended diagnostic workup rather than treating them as sequential questions [2,15].

The practical consequence is that a diagnostic biopsy must now support four separate assays, and the tissue available from an endoscopic sample is finite. Evidence from mismatch repair testing in this same setting shows that assay yield on small biopsy fragments is a real constraint and that taking more fragments is a more useful response than running more assays on too few [25,26]. The molecular heterogeneity documented in gastroesophageal adenocarcinoma more broadly points the same way [27,30,32], and local against central assessment has been shown to diverge for HER2 in routine practice [29].

Comparison	Threshold	Concordance	Source
Archival vs baseline sample	Any staining	88.9%	[9]
Archival vs baseline sample	75%	61.1%	[9]
Primary vs paired metastasis	75%	74.8%	[10]
Primary vs peritoneal deposit	40%	79.8%	[11]
Primary vs peritoneal deposit	75%	75.0%	[11]
Within a single resected tumour	75%	Heterogeneous in 38.5%	[10]

Table 2: Reported concordance of claudin 18.2 status, by comparison and by the positivity threshold applied

Discussion

The evidence supports a position that is more qualified than the trial results alone suggest. Claudin 18.2 identifies a large minority of patients, close to four in ten, who derive a real survival benefit from adding zolbetuximab to first-line chemotherapy [7,8]. Prevalence is stable enough across biopsy and resection, and across primary and metastatic samples, that testing on whatever tissue is available is defensible at the population level [9].

At the level of the individual patient the picture is less comfortable. Agreement between two samples from the same person is in the region of 61 to 75 per cent at the threshold that governs eligibility, and rises to near 90 per cent only when the definition is loosened to any staining at all [9,10,11]. That gap is the signature of a continuously distributed marker being forced into a binary, with a substantial number of tumours sitting close to the line.

Implications for practice

Three points follow. Where the disease is metastatic and a choice of biopsy site exists, the reported concordance data favour peritoneal over hepatic sampling, since liver deposits showed both the lowest positivity and the lowest agreement with the primary [10]. Where a biopsy returns a negative result but the clinical question remains open, repeating the assessment on a different or larger sample is reasonable rather than excessive, given documented heterogeneity within single resected tumours [10,11]. And where a biopsy is being taken for molecular workup, the number of fragments obtained matters, because four biomarkers now compete for the same tissue [15,25,26].

A further consideration concerns timing. Concordance between archival and recent samples was only 61.1 per cent at the operative threshold [9], which suggests that a result generated years earlier should not be relied on when a current treatment decision depends on it.

Study limitations

The limitations belong to the underlying literature. The concordance data come from retrospective analyses of samples collected for other purposes, and the pair-matched trial subset is small relative to the screening population from which it was drawn [9]. The heterogeneity series are single-institution and predominantly East Asian, and prevalence in that setting differs from that reported in Japanese and Western cohorts, so generalisation is uncertain [9,10]. Efficacy data derive from two trials that enrolled only patients above the 75 per cent threshold, so nothing is known from randomised evidence about whether patients below it would benefit, which is precisely the group that misclassification affects [6,7,8]. Reported concordance also depends on the antibody clone and staining protocol, and figures generated on different platforms are not directly comparable [9,11,12].

Two gaps deserve naming. No study has reported outcomes for patients treated on the basis of a result that later proved discordant with a second sample, which is the clinically relevant endpoint for a threshold-based selection assay. And no prospective study has compared systematic multi-fragment biopsy sampling against standard practice for claudin 18.2 assessment, although the analogous question in mismatch repair testing has been examined and favoured taking more fragments [25,26].

Conclusion

Claudin 18.2 positivity is found in roughly 38 per cent of advanced gastric and gastroesophageal junction adenocarcinomas at the threshold used to grant access to zolbetuximab, and that access is worth having: median survival improved by between two and three months in both phase 3 trials. Prevalence is stable across sample types, which makes biopsy-based testing sound at the level of a population. Agreement between two samples from the same patient is not stable, falling from near 90 per cent when any staining counts

to around 61 per cent at the 75 per cent cutoff. The practical consequences are modest but real: prefer peritoneal to hepatic sampling where there is a choice, take more fragments rather than fewer, treat an old result with caution, and do not read a single negative biopsy as closing the question.

Acknowledgements

This article rests on cohorts assembled by trial groups and pathology departments elsewhere; what appears below is a summary of their published measurements.

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Conflict of Interest

No author has a competing interest in this subject.

Ethics Statement

This is a review of studies that were published beforehand. It involved no new collection of patient data and no enrolment of participants, so no ethical approval was needed.

References

1. Sung H, Ferlay J, Siegel RL, et al. "Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries". CA Cancer J Clin 71(2021):209-249.
2. Lordick F, Carneiro F, Cascinu S, et al. "Gastric cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up". Ann Oncol 33(2022):1005-1020.
3. Sahin U, Koslowski M, Dhaene K, Usener D, Brandenburg G, Seitz G, et al. "Claudin-18 splice variant 2 is a pan-cancer target suitable for therapeutic antibody development". Clin Cancer Res 14(2008):7624-7634.
4. Sahin U, Schuler M, Richly H, Bauer S, Krilova A, Dechow T, et al. "A phase I dose-escalation study of IMAB362 (zolbetuximab) in patients with advanced gastric and gastro-oesophageal junction cancer". Eur J Cancer 100(2018):17-26.
5. Türeci O, Sahin U, Schulze-Bergkamen H, et al. "A multicentre, phase IIa study of zolbetuximab as a single agent in patients with recurrent or refractory advanced adenocarcinoma of the stomach or lower oesophagus: the MONO study". Ann Oncol 30(2019):1487-1495.
6. Sahin U, Türeci Ö, Manikhas G, Lordick F, Rusyn A, Vynnychenko I, et al. "FAST: a randomised phase II study of zolbetuximab (IMAB362) plus EOX versus EOX alone for first-line treatment of advanced CLDN18.2-positive gastric and gastro-oesophageal adenocarcinoma". Ann Oncol 32(2021):609-619.
7. Shitara K, Lordick F, Bang YJ, Enzinger P, Ilson D, Shah MA, et al. "Zolbetuximab plus mFOLFOX6 in patients with CLDN18.2-positive, HER2-negative, untreated, locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma (SPOTLIGHT): a multicentre, randomised, double-blind, phase 3 trial". Lancet 401(2023):1655-1668.
8. Shah MA, Shitara K, Ajani JA, et al. "Zolbetuximab plus CAPOX in CLDN18.2-positive gastric or gastroesophageal junction adenocarcinoma: the randomized, phase 3 GLOW trial". Nat Med 29(2023):2133-2141.
9. Shitara K, Xu RH, Ajani JA, Moran D, Guerrero A, Li R, et al. "Global prevalence of claudin 18 isoform 2 in tumors of patients with locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma". Gastric Cancer 27(2024):1058-1068.
10. Choi E, Shin J, Ryu MH, Kim HD, Park YS. "Heterogeneity of claudin 18.2 expression in metastatic gastric cancer". Sci Rep 14(2024):17648.
11. Ogawa H, Abe H, Yagi K, Seto Y, Ushiku T. "Claudin-18 status and its correlation with HER2 and PD-L1 expression in gastric cancer with peritoneal dissemination". Gastric Cancer 27(2024):802-810.
12. Rohde C, et al. "Comparison of claudin 18.2 expression in primary tumors and lymph node metastases in Japanese patients with gastric adenocarcinoma". Jpn J Clin Oncol 49(2019).
13. Jun KH, Kim JH, Jung JH, Choi HJ, Chin HM. "Expression of claudin-7 and loss of claudin-18 correlate with poor prognosis in gastric cancer". Int J Surg 12(2014):156-162.
14. Shu Y, Zhang W, Hou Q, et al. "Prognostic significance of frequent CLDN18-ARHGAP26/6 fusion in gastric signet-ring cell cancer". Nat Commun 9(2018):2447.
15. Shah MA, Kennedy EB, Alarcon-Rozas AE, et al. "Immunotherapy and targeted therapy for advanced gastroesophageal cancer: ASCO guideline". J Clin Oncol 41(2023):1470-1491.
16. Bang YJ, Van Cutsem E, Feyereislova 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 376(2010):687-697.
17. Van Cutsem E, Bang YJ, Feng-Yi F, et al. "HER2 screening data from ToGA: targeting HER2 in gastric and gastroesophageal junction cancer". Gastric Cancer 18(2015):476-484.
18. Gravalos C, Jimeno A. "HER2 in gastric cancer: a new prognostic factor and a novel therapeutic target". Ann Oncol 19(2008):1523-1529.
19. Sun JM, Shen L, Shah MA, et al. "Pembrolizumab plus chemotherapy versus chemotherapy alone for first-line treatment of advanced oesophageal cancer (KEYNOTE-590): a randomised, placebo-controlled, phase 3 study". Lancet 398(2021):759-771.
20. Chao J, Fuchs CS, Shitara K, et al. "Assessment of pembrolizumab therapy for the treatment of microsatellite instability-high gastric or gastroesophageal junction cancer among patients in the KEYNOTE-059, KEYNOTE-061, and KEYNOTE-062 clinical trials". JAMA Oncol 7(2021):895-902.
21. Shitara K, Van Cutsem E, Bang YJ, et al. "Efficacy and safety of pembrolizumab or pembrolizumab plus chemotherapy vs chemotherapy alone for patients with first-line, advanced gastric cancer: the KEYNOTE-062 phase 3 randomized clinical trial". JAMA Oncol 6(2020):1571-1580.
22. Smyth EC, Wotherspoon A, Peckitt C, et al. "Mismatch repair deficiency, microsatellite instability, and survival: an exploratory analysis of the Medical Research Council Adjuvant Gastric Infusional Chemotherapy (MAGIC) trial". JAMA Oncol 3(2017):1197-1203.
23. Cunningham D, Allum WH, Stenning SP, et al. "Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer". N Engl J Med 355(2006):11-20.
24. Choi YY, Kim H, Shin SJ, et al. "Microsatellite instability and programmed cell death-ligand 1 expression in stage II/III gastric cancer: post hoc analysis of the CLASSIC randomized controlled study". Ann Surg 270(2019):309-316.
25. Asesio N, Mhamdi Aloui N, Bonnereau J, Lehmann-Che J, Bouhidel F, et al. "Assessment of the reliability of MSI status and dMMR proteins deficiency screening on endoscopic biopsy material in esophagus and gastric adenocarcinoma". Dig Liver Dis 55(2023):1105-1113.
26. Fornaro L, Lonardi S, Catanese S, Nappo F, Pietrantonio F, et al. "Concordance of microsatellite instability and mismatch repair status in paired biopsies and surgical specimens of resectable gastroesophageal adenocarcinoma: time for a call to action". Gastric Cancer 26(2023):958-968.
27. Maron SB, Chase LM, Lomnicki S, et al. "Circulating tumor DNA sequencing analysis of gastroesophageal adenocarcinoma". Clin Cancer Res 25(2019):7098-7112.
28. Klempner SJ, et al. "Consensus guidance for prevention and management of nausea and vomiting in patients treated with zolbetuximab plus chemotherapy: a RAND/UCLA modified Delphi panel study". ESMO Gastrointest Oncol 7(2024):100131.

29. Huemer F, Weiss L, Regitnig P, et al. "Local and central evaluation of HER2 positivity and clinical outcome in advanced gastric and gastroesophageal cancer: results from the AGMT GASTRIC-5 registry". J Clin Med 9(2020):935.

30. Dulak AM, Stojanov P, Peng S, Lawrence MS, Fox C, et al. "Exome and whole-genome sequencing of esophageal adenocarcinoma identifies recurrent driver events and mutational complexity". Nat Genet 45(2013):478-486.

31. Raimondi A, Lonardi S, Murgioni S, et al. "Tremelimumab and durvalumab as neoadjuvant or non-operative management strategy of patients with microsatellite instability-high resectable gastric or gastroesophageal junction adenocarcinoma: the INFINITY study by GONO". Ann Oncol 36(2025):285-296.

32. Kato S, Okamura R, Baumgartner JM, et al. "Analysis of circulating tumor DNA and clinical correlates in patients with esophageal, gastroesophageal junction, and gastric adenocarcinoma". Clin Cancer Res 24(2018):6248-6256.

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