GENOMIC® TESTING COOPERATIVE

25371 Commercentre Drive, Lake Forest, CA 92630
Tel: 1-866-484-8870 www.genomictestingcooperative.com
CLIA #: 05D2111917 CAP #: 9441574

Immunohistochemistry Study

Patient Name:		Ordering Physician:	
Date of Birth:		Accession #:	
Gender (M/F):	F	Specimen Type:	Tissue
Client:	Cancer Hope	Specimen ID:	
Case #:			
Body Site:	LEFT ADNEXAE		

Collected Date:	05/05/2024	Time:	12:00 AM	Tumor Type:	stomach, adeno neuroendocrine gastric carcinoma
Received Date:	01/21/2025	Time:	01:44 PM		
Reported Date:	01/24/2025	Time:	05:33 PM		

Results

CLDN18.2 FDA (Zolbetuximab™) testing by immunohistochemistry (IHC): Positive. Percentage of cells with 2+/3+ membrane staining: 100.

CLDN18		
Clone	**Result_CLDN18**	**2+/3+ membrane staining %**
CLDN18 (43-14A)	Positive	100

CLDN18 Methodology and Test Background

CCLDN18 (43-14A) Scoring Guide:

VENTANA CLDN18 (43-14A) Assay staining in gastric adenocarcinoma including gastroesophageal junction (GEJ) tissue follows a cytoplasmic and membranous pattern. The signal is classified as strong, moderate, weak, or negative based on membrane localization only. Negative (0) signal intensity is characterized by an absence of any detectable signal. Negative cases may still exhibit pale grey cytoplasmic and/or membranous discoloration. Weak (1+) signal intensity is characterized by a faint gold/light brown hue that may be partial or circumferential. Moderate (2+) or Strong (3+) signal intensity is characterized by a chocolate brown to thickened dark brown, black hue that may be partial or circumferential. CLDN18 results are measured by Tumor Cell Percentage (TC%), which corresponds to the total number of viable cancer cells showing CLDN18 staining of moderate and strong intensity divided by the total number of viable cancer cells. CLDN18 positivity is defined as ≥ 75% of tumor cells demonstrating moderate to strong membrane CLDN18 staining as measured by the VENTANA CLDN18 (43-14A) RxDx Assay. In SPOTLIGHT and GLOW clinical studies, approximately 38% of gastric/GEJ cancer patients expressed high levels of CLDN18 and were considered CLDN18 positive by the VENTANA CLDN18 (43-14A) RxDx Assay. Patients who received a combination of zolbetuximab and chemotherapy experienced a 25-31% reduction in disease progression or death.

CLDN18 (43-14A) Background:

The VENTANA CLDN18 (43-14A) RxDx Assay is a qualitative immunohistochemical assay intended to be used in the assessment of Claudin 18 (CLDN18) protein in gastric adenocarcinoma including gastroesophageal junction (GEJ) adenocarcinoma. The OptiView DAB IHC Detection Kit is used for staining on a BenchMark ULTRA instrument. The assay is indicated as an aid in identifying patients with gastric or GEJ adenocarcinoma who may be eligible for treatment with VYLOY® (zolbetuximab) or PT886 in accordance with the approved therapeutic product labelling. The Roche test measures expression of both variants of the CLDN18 protein (18.1 and 18.2 isoforms). CLDN18.2 is the predominant variant expressed in gastric and GEJ cancers.

The VENTANA CLDN18 RxDx assay is a CE-marked IHC test for gastric cancer patients in the EU, identifying those eligible for zolbetuximab treatment. This assay is also FDA approved as a companion diagnostic device to identify patients with gastric or GEJ

adenocarcinoma who may be eligible for treatment with zolbetuximab.

CLDN18 (43-14A) Methodology:

Tissues should be fixed in 10% neutral-buffered formalin for 12-72 hours; other fixatives are not recommended. This assay has not been validated on decalcified tissues. Paraffin-embedded tissue sections were stained with VENTANA CLDN18 (43-14A) on the Ventana BenchMark Ultra Automated staining platform and visualized using OptiView DAB IHC Detection Kit which utilizes a hapten conjugated secondary antibody that is recognized by an anti-hapten-HRP multimer and is visualized using 3, 3'-diaminobenzidine tetrahydrochloride (DAB). Normal gastric epithelial tissue FFPE samples were used as positive tissue control for high intensity positive CLDN18 staining. Normal gastric stromal and muscular FFPE samples were used as negative tissue controls for CLDN18. In addition, patient tissue was stained with a non-specific mouse monoclonal negative antibody to determine presence of non-specific (background) staining. All three of these controls were run in concert with each patient sample. The test results of the VENTANA CLDN18 (43-14A) RxDx Assay were interpreted by a qualified pathologist in conjunction with histological examination, relevant clinical information, and proper controls.

Reference

• PT886 for treatment of patients with advanced gastric, gastroesophageal junction and pancreatic adenocarcinoma. ClinicalTrials.gov. Updated March 1, 2024. Accessed March 24, 2023.

• Roche. VENTANA CLDN18 (43-14A) RxDx Assay, CE Package Insert, 2024. 2008;26:677-704.

• Saito, T. Matsuda, D. Moran, P-114 Claudin 18 isoform expression in gastric adenocarcinoma and pancreatic adenocarcinoma, Annals of Oncology, Volume 32, Supplement 3, 2021, Page S138, ISSN 0923-7534, https://doi.org/10.1016/j.annonc.2021.05.169.

• Astellas press release, Astellas Announces Positive Findings from Phase 3 GLOW Trial of Zolbetuximab during March ASCO Plenary Series. https://www.astellas.com/en/news/27481. Accessed September 19, 2024.

Electronic Signature

Ahmad Charifa, M.D.

The test was performed at Genomic Testing Cooperative, LCA, Genomic Testing Cooperative, LCA, 25371 Commercentre Drive, Lake Forest, CA 92630. Medical Director Maher Albitar, M.D. Analysis of the data was performed at Genomic Testing Cooperative, LCA, 25371 Commercentre Drive, Lake Forest, CA 92630. Medical Director: Maher Albitar, M.D.