Prevalence of Claudin18.2 Expression in Gastric/gastroesophageal Junction Adenocarcinoma among Patients in TranStar101 and TranStar102 Clinical Trials

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TranStar

Poster# 3629

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ABSTRACT

Background: Claudin18.2 (CLDN18.2) is a tight junction protein highly specific to gastric mucosa, and a validated target for gastric cancer (GC) treatment[1]. Immune checkpoint therapy targeting PD-1 combined with chemotherapy has been approved as the first line therapy of GC[2]. Understanding the expression profiles of CLDN18.2 and PD-L1 could guide the development of combination therapies to maximize the benefits of these two agents. This study investigated the prevalence of CLDN18.2 expression in gastric/gastroesophageal junction adenocarcinoma (G/GEJC) screening samples from studies Transtar101 (NCT04396821 in US) and TranStar102 (NCT04495296 in China), and its correlation with various clinical characteristics and PD-L1 expression.

Methods: CLDN18.2 expression in formalin-fixed, paraffin-embedded (FFPE) G/GEJC tissue samples was prospectively detected by an immunohistochemistry-based LDT using an in-house anti-CLDN18.2 antibody (Clone14G11) on the Leica Bond III stainer. CLDN18.2 expression was assessed by scoring the staining intensity (0, 1+, 2+, 3+) and the percentage of positive tumor cells. Positive CLDN18.2 expression is defined as the cutoff at ≥10% of tumor cell with ≥1+ staining intensity for this evaluation. PD-L1 expression was assessed by combined positive score (CPS) using Agilent's PD-L1 IHC 28-8 pharmDx. Both assays were conducted in CAP/CLIA certified LabCorp central lab.

Results: Out of 562 screened patient samples, 550 G/GEJC patient samples had CLDN18.2 results as part of the screening procedures for the clinical trials. Of these patients (454 GC/96 GEJC), 440 (80%) were Asian, 31 (6%) were Caucasian, 8 (1%) were other ethnic group, and 71 (13%) were not recorded; 437 (79%) were primary tumors and 113 (21%) were metastasis; 201 (37%) were core needle biopsies (CNB), 108 (20%) were surgical resections (SR) and 241 (44%) had no information.

314 (57%) samples had positive CLDN18.2 expressions (≥10%/≥1+). No significant difference in CLDN18.2 positive rates were found between TranStar101 and TranStar102 studies (p=0.643), Asian and Caucasian (p=0.690), GC and GEJC (p=0.524), or core needle biopsies and surgical resection (p=0.715). Out of 83 TranStar102 specimens that had both CLDN18.2 and PD-L1 results, 15 (18%) had PD-L1 CPS≥5, 59 (71%) had positive CLDN18.2, and 10 (12%) had both positive CLDN18.2 and PD-L1 CPS≥5. No correlation (p=0.393) was observed between PD-L1 scores (CPS<5 or CPS≥5) and CLDN18.2 expression (≥10%/≥1+ or <10%/≥1+).

CONCLUSIONS

Data suggested CLDN18.2 expression levels were independent of PD-L1 status, and support the use of Transcenta 14G11 antibody for CLDN18.2 detection regardless of sample collection methods, location, and patient demographics. An anti-CLDN18.2 companion diagnostic device based on 14G11 is being developed (CLDN18.2 IHC 14G11 pharmDx, Agilent Technologies, Inc.)

Clinical Features by CLDN18.2 Status

Table 1. Correlation between CLDN18.2 expression and clinicopathological features or PD-L1 expression. * p<0.05

Characteristics	N (%)	CLDN18.2<10%&≥1+	CLDN18.2≥10%&≥1+	Unknown
All samples	562 (100%)	236 (42%)	314 (56%)	12 (2%)
RACE		Chi-square, p-Value 0.6903		
Asian	450 (80%)	189 (42%)	251 (56%)	10 (2%)
Caucasian	31 (6%)	11 (35%)	20 (65%)	0 (0%)
Mixed/Other	8 (1%)	3 (38%)	5 (63%)	0 (0%)
Unknown	73 (13%)	33 (45%)	38 (52%)	2 (3%)
Diagnosis		Chi-square, p-Value 0.5240		
GC	465 (83%)	192 (41%)	262 (56%)	11 (2%)
GEJ	97 (17%)	44 (45%)	52 (54%)	1 (1%)
Tumor sample site		Chi-square, p-Value 0.0425*		
Primary	444 (79%)	178 (40%)	259 (58%)	7 (2%)
Metastatic	118 (21%)	58 (49%)	55 (47%)	5 (4%)
Collection method		Chi-square, p-Value 0.7151		
Core Needle Biopsy	206 (37%)	85 (41%)	116 (56%)	5 (2%)
Surgical Resection	112 (20%)	48 (43%)	60 (54%)	4 (4%)
Unknown	244 (43%)	103 (42%)	138 (57%)	3 (1%)
Study		Chi-square, p-Value 0.6427		
TranStar101	119 (21%)	48 (40%)	69 (58%)	2 (2%)
TranStar102	443 (79%)	188 (42%)	245 (55%)	10 (2%)
PD-L1 status	89	Correlation analysis, P value 0.3929		
CPS≥5	15 (17%)	5 (33%)	10 (67%)	0 (0%)
CPS<5	68 (76%)	19 (28%)	49 (72%)	0 (0%)
Unknown	6 (7%)	4 (67%)	1 (17%)	1 (17%)

CLDN18.2 Expression in First-line and Later-line Patients

Table 2. Correlation between CLDN18.2 expression and treatment lines.

Characteristics	N (%)	CLDN18.2<10%&≥1+	CLDN18.2≥10%&≥1+	unknown
All Samples	*562* (100%)	236 (42%)	314 (56%)	12 (2%)
Treatment Line		*Chi-square P value 0.9095*		
First line	294 (52%)	119 (40%)	169 (57%)	6 (2%)
Second or later line	161 (29%)	64 (40%)	93 (58%)	4 (2%)
unknown	107 (19%)	53 (50%)	52 (49%)	2 (2%)

Analysis of CLDN18.2 Expression in First-line Patients

Table 3. Correlation between CLDN18.2 expression and clinicopathological features or PD-L1 expression in first-line patients. ** p<0.01

Characteristics	N (%)	CLDN18.2<10%&≥1+	CLDN18.2≥10%&≥1+	Unknown
All samples	294 (100%)	119 (40%)	169 (57%)	6 (2%)
Race		Chi-square P value 0.0083**		
Asian	281 (96%)	119 (42%)	156 (56%)	6 (2%)
Caucasian	10 (3%)	0 (0%)	10 (100%)	0 (0%)
Mixed/Other	3 (1%)	0 (0%)	3 (100%)	0 (0%)
Diagnosis		Chi-square P value 0.5069		
GC	271 (92%)	111 (41%)	154 (57%)	6 (2%)
GEJ	23 (8%)	8 (35%)	15 (65%)	0 (0%)
Tumor sample site		Chi-square P value 0.8437		
Primary	259 (88%)	104 (40%)	149 (58%)	6 (2%)
Metastatic	35 (12%)	15 (43%)	20 (57%)	0 (0%)
Collection method		Chi-square P value 0.3051		
Core Needle Biopsy	183 (62%)	74 (40%)	105 (57%)	4 (2%)
Surgical Resection	83 (28%)	39 (47%)	42 (51%)	2 (2%)
Unknown	28 (10%)	6 (21%)	22 (79%)	0 (0%)
PD-L1 status	83	Correlation analysis P value 0.6477		
CPS≥5	14 (17%)	4 (29%)	10 (71%)	0 (0%)
CPS<5	64 (77%)	19 (30%)	45 (70%)	0 (0%)
Unknown	5 (6%)	3 (60%)	1 (20%)	1 (20%)

CLDN18.2 and PD-L1 Expression in TranStar102 Cases

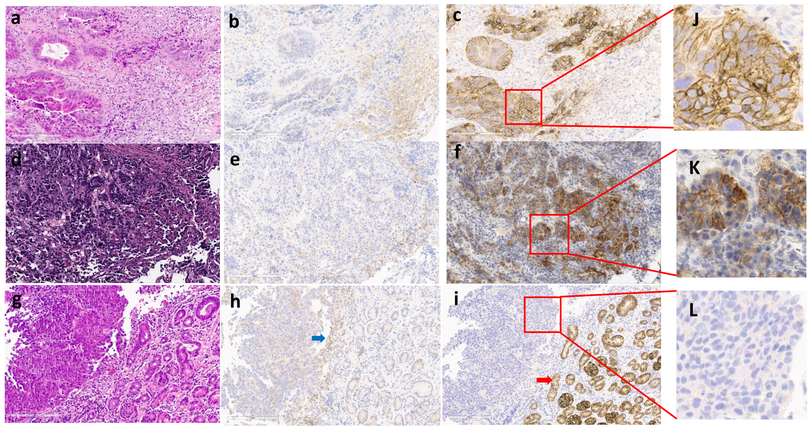

Figure 1 Representative images of CLDN18.2 (c, f, i) and PD-L1 (b, e, h) expression in TranStar102 cases. Hematoxylin and eosin staining (a, d, g). Sample 1, gastric cancer, surgery sample from metastatic site at ureter, with CLDN18.2 expression at 100% ≥ 1+ and 95% ≥ 2+, and PD-L1 CPS=30 (a, b, c, J); Sample 2, gastroesophageal junction cancer, core needle biopsy sample from primary site from esophageal, with CLDN18.2 expression at 45% ≥ 1+ and 15% ≥ 2+, and PD-L1 CPS=2 (d, e, f, K); Sample 3, gastric cancer, core needle biopsy sample from primary site from stomach, with CLDN18.2 expression at 1% ≥ 1+ and 1% ≥ 2+, and PD-L1 CPS=5 (g, h, I, L). Red arrow: CLDN18.2 positive cells in normal mucosa (no CLDN18.2 expression in tumor area); Blue arrow: PD-L1 positive cells at tumor front near normal mucosa area. J, K and L are magnified areas from correspondent CLDN18.2 IHC images c, f, I, respectively. Original magnification 200x (a–i).

REFERENCES

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