# Claudin 18.2 CAR T

Dae Won Kim MD
Moffitt Cancer Center

# What is Claudin 18.2?

- Claudins are the major structural components of the tight junctions present on the membranes of epithelial and endothelial cells
- CLDN18.2 is strictly confined to the inside of gastric mucosa in normal tissues.
- During cancer development, tight junctions are disrupted and CLDN18.2 is exposed on the cell surface.
- CLDN18.2 as a pan-cancer target that is expressed in a diverse variety of epithelial tumor types

| Tumor type | Any labeling | ≥2+ in ≥60% of cells significant labeling | No labeling |
|---|---|---|---|
| Primaries | | | |
| Gastric AC | 51/66 (77%) | 37/66 (56%) | 15/66 (23%) |
| Diffuse | | 15/20 (75%) | |
| Intestinal | | 21/45 (46%) | |
| Esophagus AC | 17/22 (78%) | 11/22 (50%) | 5/22 (22%) |
| Esophagus SCC | 0/7 | 0/7 | 7/7 |
| Pancreatic AC, ductal | 8/10 (80%) | 6/10 (60%) | 2/10 (20%) |
| Pancreatic islet cell carcinoma | 0/5 | 0/5 | 5/5 |
| Ovarian AC | 4/42 (10%) | 4/42 (10%) | 38/42 (90%) |
| Serous | 0/25 | 0/25 | 25/25 |
| Mucinous | 4/17 (24%) | 4/17 (24%) | 13/17 (76%) |

Expression of CLDN18.2 in human cancer tissues as determined by IHC

Sahin U, et al. CCR 2008

# Claudin 18.2 CAR T

nature medicine

Article

https://doi.org/10.1038/s41591-024-03037-z

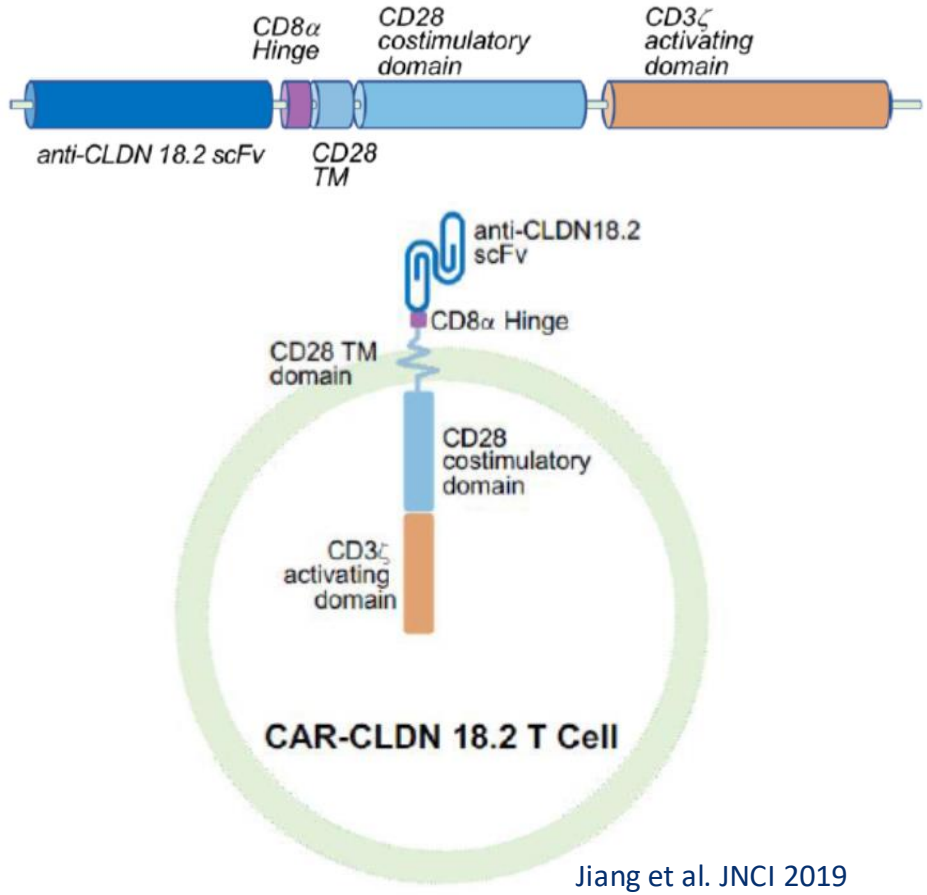
## Claudin18.2-specific CAR T cells in gastrointestinal cancers: phase 1 trial final results

## Claudin-18 isoform 2-specific CAR T-cell therapy (satri-cel) versus treatment of physician's choice for previously treated advanced gastric or gastro-oesophageal junction cancer (CT041-ST-01): a randomised, open-label, phase 2 trial

*Changsong Qi*, Chang Liu*, Zhi Peng*, Yanqiao Zhang*, Jia Wei*, Wensheng Qiu*, Xiaotian Zhang, Hongming Pan, Zuoxing Niu, Meng Qiu, Yanru Qin, Weijia Fang, Feng Ye, Ning Li, Tianshu Liu, Anwen Liu, Xizhi Zhang, Changlu Hu, Jun Zhang, Jiuwei Cui, Xiaoyan Lin, Shubin Wang, Jian Zhang, Tongyu Lin, Xiujuan Qu, Xianglin Yuan, Jifang Gong, Jian Li, Wanwan Gao, Lun Gai, Yumeng Wang, Daijing Yuan, Zonghai Li, Lin Shen*

# Claudin 18.2 CAR T (CT041)

- CT041 CAR T: autologous CLDN18.2 CAR T
- CD28 costimulatory domain and CD3ζ signaling domain




Jiang et al. JNCI 2019

# Phase 1 trial of CLDN 18.2 CAR T (CT041)

## Baseline Characteristics

**Table 1 | Baseline characteristics of all patients**

| | Dose-escalation/ de-escalation (*n*=15) | Dose expansion (*n*=83) | | | | Total (*n*=98) |
|---|---|---|---|---|---|---|
| | | Cohort 1 (*n*=61) | Cohort 2 (*n*=15) | Cohort 3 (*n*=5) | Cohort 4 (*n*=2) | |
| Median age (range), year | 56.0 (38–74) | 49.0 (25–74) | 50.0 (29–65) | 50.0 (30–55) | 50.0 (39–61) | 50.0 (25–74) |
| Male, *n* (%) | 11 (73.3) | 33 (54.1) | 8 (53.3) | 1 (20.0) | 1 (50.0) | 54 (55.1) |
| Disease type, *n* (%) | | | | | | |
| GC/GEJ cancer | 12 (80) | 40 (65.5) | 14 (93.3) | 5 (100) | 2 (100) | 73 (74.5) |
| Pancreatic cancer | 2 (13.3) | 8 (13.1) | 0 | 0 | 0 | 10 (10.2) |
| Intestinal cancer | 0 | 8 (13.1) | 0 | 0 | 0 | 8 (8.2) |
| BTC | 1 (6.7) | 3 (4.9) | 0 | 0 | 0 | 4 (4.1) |
| Other | 0 | 2 (3.3) | 1 (6.7) | 0 | 0 | 3 (3.1) |
| ECOG, *n* (%) | | | | | | |
| 0 | 1 (6.7) | 3 (4.9) | 0 | 1 (20.0) | 1 (50.0) | 6 (6.1) |
| 1 | 14 (93.3) | 58 (95.1) | 15 (100) | 4 (80.0) | 1 (50.0) | 92 (93.9) |
| CLDN18.2 expression, *n* (%)[a] | | | | | | |
| Low expression | 0 | 5 (8.2) | 0 | 0 | 0 | 5 (5.1) |
| Medium/high expression | 15 (100) | 56 (91.8) | 15 (100) | 5 (100) | 2 (100) | 93 (94.9) |
| No. of previous lines, *n* (%) | | | | | | |
| 1 | 2 (13.3) | 19 (31.1) | 2 (13.3) | 5 (100) | 0 | 28 (28.6) |
| 2 | 10 (66.7) | 28 (45.9) | 6 (40.0) | 0 | 0 | 44 (44.9) |
| ≥3 | 3 (20.0) | 14 (23.0) | 7 (46.7) | 0 | 2 (100) | 26 (26.5) |

**CLDN18.2 expression**

Low: 1+ or <40%

Medium: 2+ or 40%-70%

High: 3+ or >70%

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# Phase 1 trial of CLDN 18.2 CAR T (CT041)

## Safety Profile: no DLTs, no high-grade CRS

| SOC PT[a], n (%) | ≥Grade 3 | Any |
|---|---|---|
| Any adverse event[b] | 98 (100) | 98 (100) |
| Hematology | 98 (100) | 98 (100) |
| Lymphopenia | 97 (99.0) | 97 (99.0) |
| Leukopenia | 83 (84.7) | 97 (99.0) |
| Neutropenia | 71 (72.4) | 93 (94.9) |
| Anemia | 43 (43.8) | 91 (92.9) |
| Thrombocytopenia | 13 (13.3) | 47 (48.0) |
| GI disorders | 19 (19.4) | 91 (92.9) |
| Nausea | 1 (1.0) | 66 (67.3) |
| Vomiting | 3 (3.1) | 52 (53.1) |
| Abdominal pain | 1 (1.0) | 39 (39.8) |
| Diarrhea | 2 (2.0) | 38 (38.8) |
| Abdominal distension | 0 | 30 (30.6) |
| Intestinal obstruction | 5 (5.1) | 8 (8.2) |
| Gastric mucosal injuries[c] | 1 (1.0) | 8 (8.2) |
| GI hemorrhage | 1 (1.0) | 4 (4.1) |
| Intra-abdominal fluid collection | 1 (1.0) | 4 (4.1) |
| Small intestinal obstruction | 2 (2.0) | 2 (2.0) |
| Abdominal adhesions | 1 (1.0) | 2 (2.0) |
| GI perforation | 1 (1.0) | 2 (2.0) |
| Duodenal obstruction | 1 (1.0) | 1 (1.0) |
| Duodenogastric reflux | 1 (1.0) | 1 (1.0) |
| Intussusception | 1 (1.0) | 1 (1.0) |
| Lower GI hemorrhage | 1 (1.0) | 1 (1.0) |
| Obstructive pancreatitis | 1 (1.0) | 1 (1.0) |

| SOC PT[a], n (%) | ≥Grade 3 | Any |
|---|---|---|
| Immune system disorders | 1 (1.0) | 96 (98.0) |
| CRS | 0 | 95 (96.9) |
| Anaphylactic shock | 1 (1.0) | 1 (1.0) |
| Infections and infestations | 5 (5.1) | 22 (22.4) |
| Pneumonia | 2 (2.0) | 6 (6.1) |
| Abdominal infection | 1 (1.0) | 5 (5.1) |
| Bacteremia | 1 (1.0) | 1 (1.0) |
| Sepsis | 1 (1.0) | 1 (1.0) |
| Other[d] | | |
| Pyrexia | 5 (5.1) | 95 (96.9) |
| Hypoproteinemia | 2 (2.0) | 81 (82.7) |
| Occult blood positive | 0 | 75 (76.5) |
| Hypoalbuminemia | 0 | 73 (74.5) |
| Alanine aminotransferase increased | 9 (9.2) | 67 (68.4) |
| Activated partial thromboplastin time prolonged | 0 | 64 (65.3) |
| Bilirubin conjugated increased | 22 (22.4) | 62 (63.3) |
| Aspartate aminotransferase increased | 8 (8.2) | 61 (62.2) |
| Hyponatremia | 5 (5.1) | 61 (62.2) |
| Sinus tachycardia | 2 (2.0) | 54 (55.1) |
| Hypokalemia | 12 (12.2) | 52 (53.1) |
| Hypotension | 1 (1.0) | 49 (50.0) |
| Prothrombin time prolonged | 0 | 48(49.0) |
| Blood bilirubin increased | 14 (14.3) | 47 (48.0) |
| Blood glucose increased | 0 | 45 (45.9) |

| SOC PT[a], n (%) | ≥Grade 3 | Any |
|---|---|---|
| Proteinuria | 0 | 44 (44.9) |
| Weight decreased | 4 (4.1) | 43 (43.9) |
| Lipase increased | 5 (5.1) | 33 (33.7) |
| Temperature intolerance | 0 | 32 (32.7) |
| Hypophagia | 0 | 31 (31.6) |
| Rash | 3 (3.1) | 29 (29.6) |
| Edema peripheral | 0 | 25 (25.5) |
| Blood fibrinogen decreased | 4 (4.1) | 25 (25.5) |
| Blood bilirubin unconjugated increased | 4 (4.1) | 19 (19.4) |
| Weight increased | 1 (1.0) | 19 (19.4) |
| Decreased appetite | 1 (1.0) | 14 (14.3) |
| Amylase increased | 1 (1.0) | 13 (13.3) |
| Pleural effusion | 1 (1.0) | 9 (9.2) |
| Blood potassium increased | 1 (1.0) | 3 (3.1) |
| Hepatic function abnormal | 2 (2.0) | 3 (3.1) |
| Jaundice cholestatic | 2 (2.0) | 2 (2.0) |
| Partial pressure of oxygen decreased | 1 (1.0) | 2 (2.0) |

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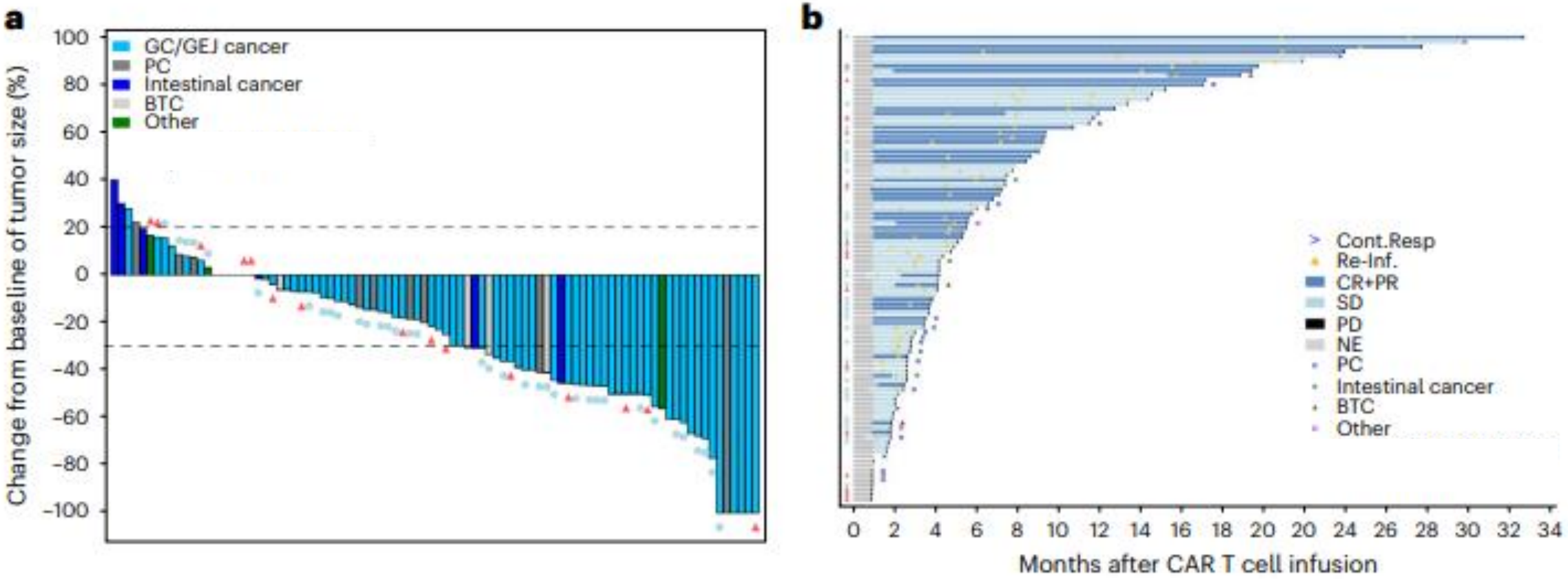
# Phase 1 trial of CLDN 18.2 CAR T (CT041)




All cohorts (N=98): ORR- 38.8%, DCR- 91.8%, mDOR-6.2mo, mPFS- 4.4mo, mOS- 8.8mo

Upper GI cancer (N=59): ORR- 54.9%, DCR- 96.1%, mDOR-6.4mo, mPFS- 5.8mo, mOS- 9.0mo

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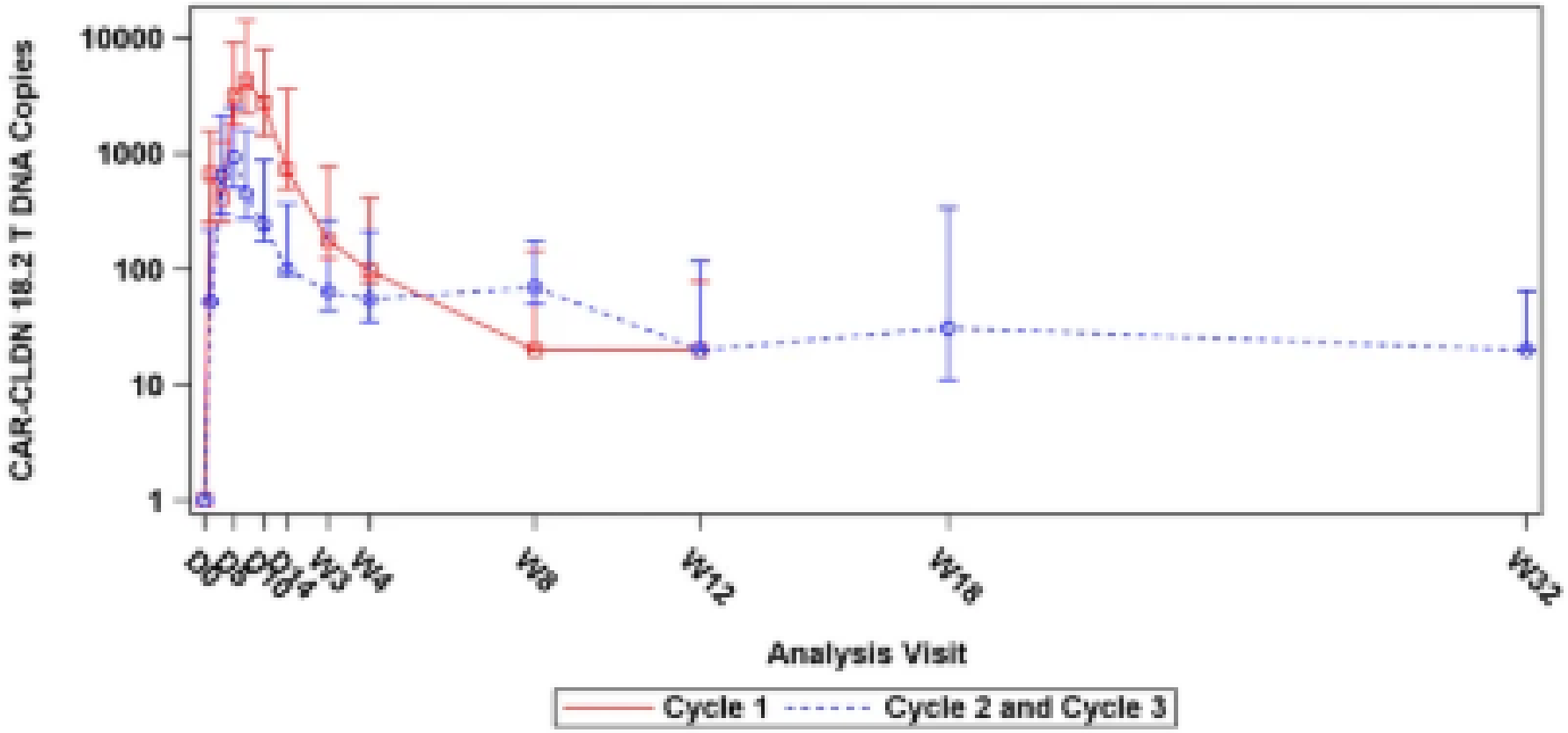
# Phase 1 trial of CLDN 18.2 CAR T (CT041)




Median persistence of CAR T in peripheral blood: 28 days

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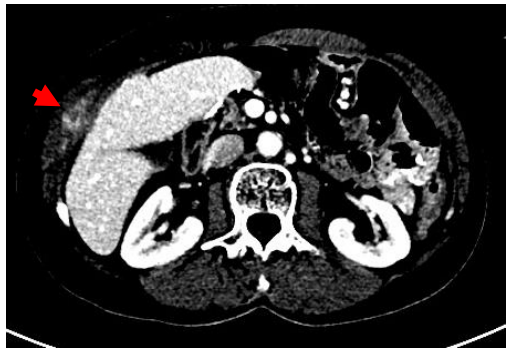
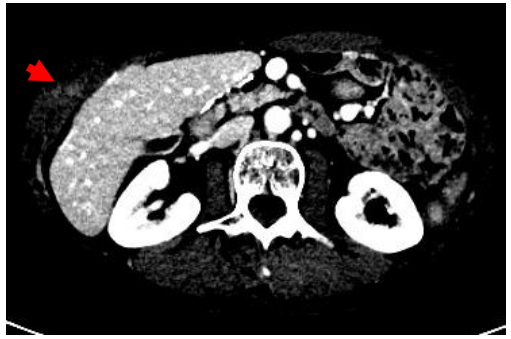
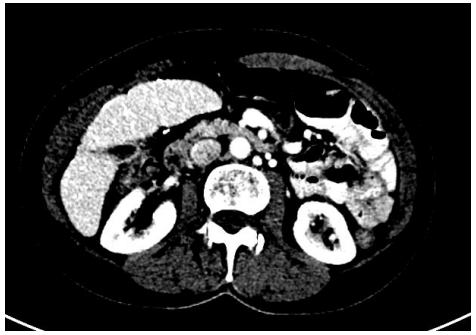
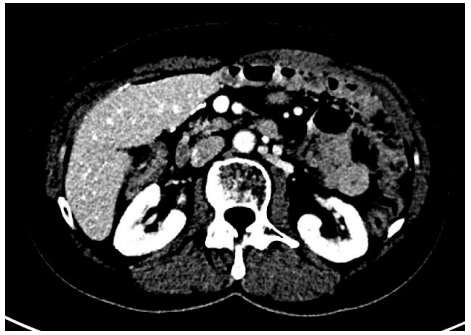
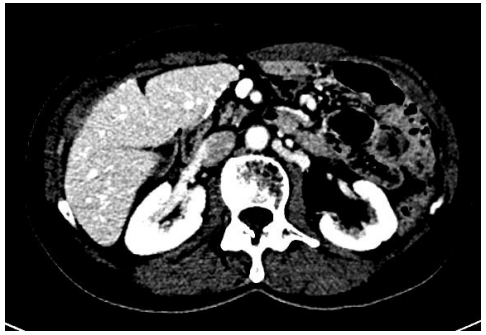
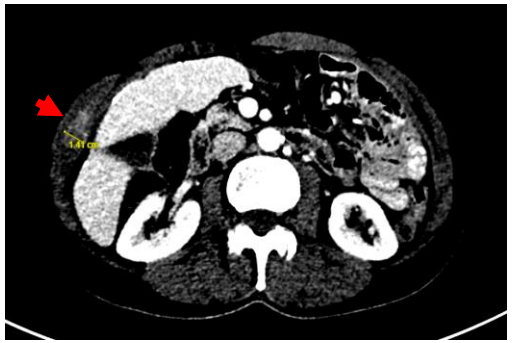
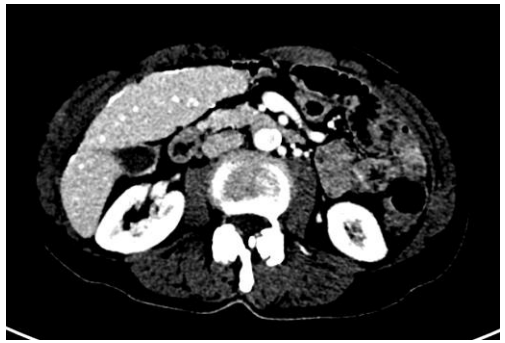
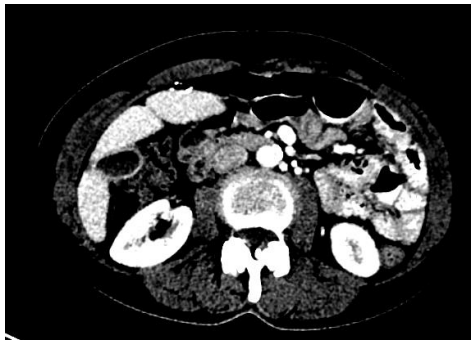
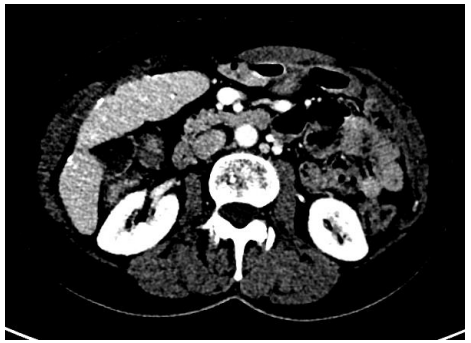
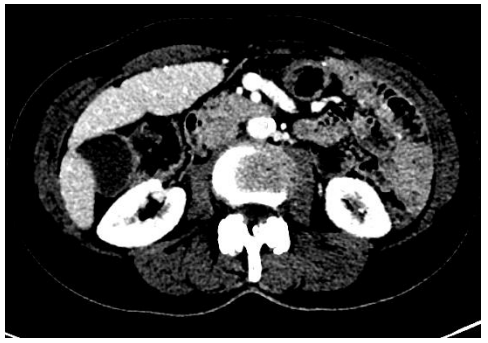
# Claudin 18.2 CAR T

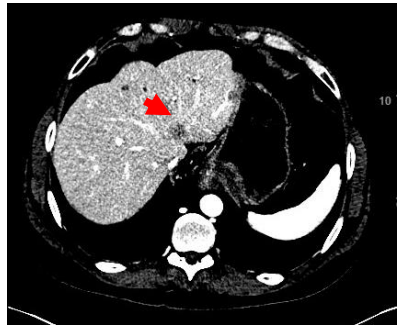
66 YO F with metastatic gastric adenocarcinoma involving abdominal wall muscle. Previous treatment: FOLFOX/pembrolizumab/trastuzumab, fam-trastuzumab deruxtecan

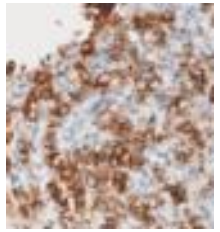
| Baseline | Week 8 | Week 12 | Month 6 | Month 12 |
|---|---|---|---|---|
|  |  |  |  |  |
|  |  |  |  |  |
| | **PR** | **CR** | **CR** | **CR** |

# Claudin 18.2 CAR T

44 YO M with metastatic esophageal adenocarcinoma involving liver. Previous treatment FOLFOX/pembrolizumab/trastuzumab, FOLFIRI/ramucirumab and carboplatin/paclitaxel

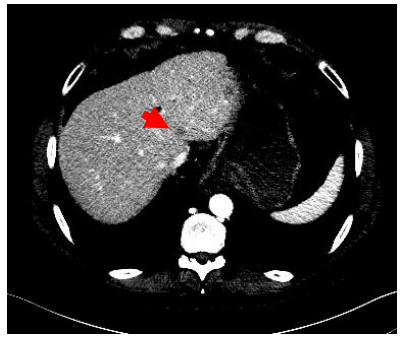
Baseline





| TDx Number | LB1908 CLDN18 P IHC |
|---|---|
| | CLDN18 Status at 50% |
| 193-0001-0113-B0-2 | Positive |

Week 4

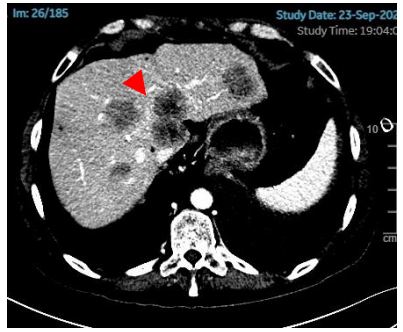


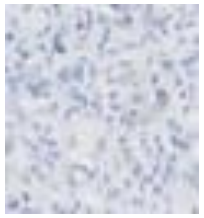
**Final Diagnosis:**

A. Distal esophagus mass biopsy:

Microscopic focus of poorly differentiated adenocarcinoma.
Over 90% of the specimen is represented by necrotic material.

Week 16

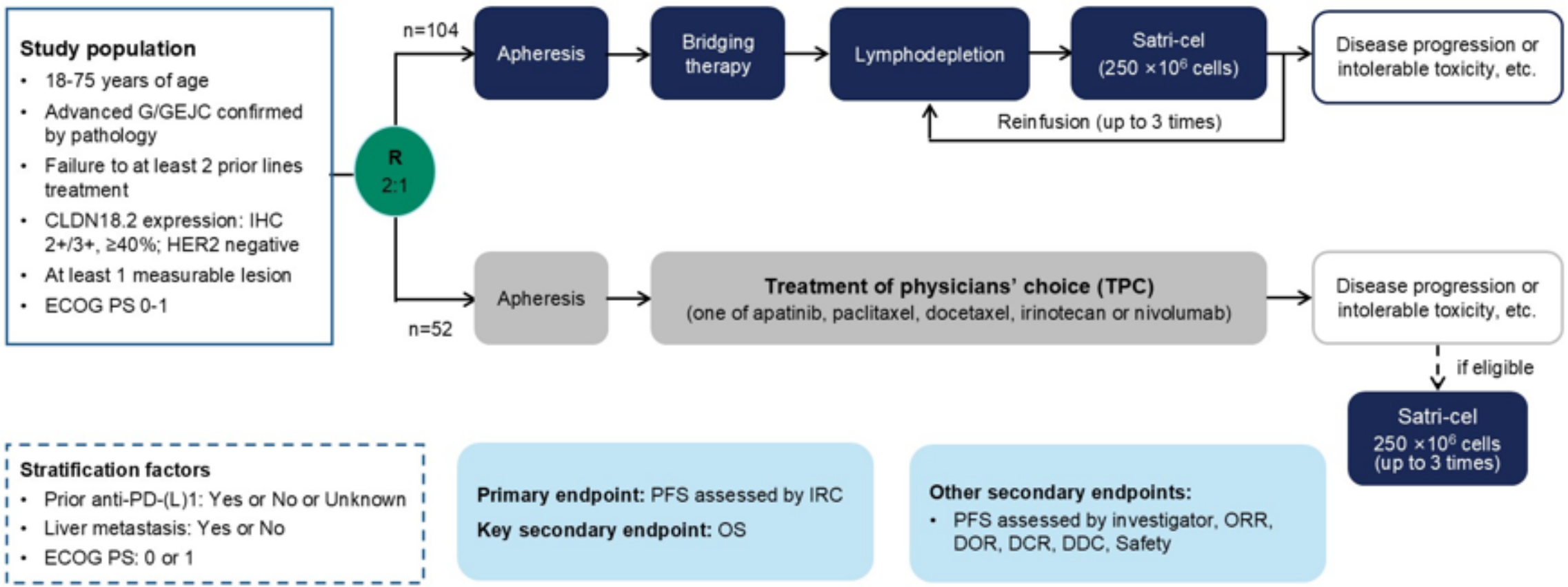


**IHC: CLDN18 (43-14A) RxDx IHC Report Ver3**

| | |
|---|---|
| Specimens: | A: Liver Lesion |
| Immunohistochemical stains are performed on blocks designated below with appropriate controls showing appropriate reactivity. Results on the population(s) of interest are as indicated in the table(s) below. | |
| | Block: A1 |
| Assay Results: | |
| Assay Results: | Negative |
| Percentage of tumor cells positive: | 0 % |

# Phase 2 trial of CLDN 18.2 CAR T (CT041)

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# Phase 2 trial of CLDN 18.2 CAR T (CT041)

## Baseline Characteristics

| Characteristics | Satri-cel group (n=104) | TPC group (n=52) |
|---|---|---|
| Age, median (IQR), years | 53.5 (45.0, 60.0) | 50.5 (43.0, 58.0) |
| Sex, n (%) | | |
| Male | 56 (53.8) | 31 (59.6) |
| Female | 48 (46.2) | 21 (40.4) |
| Ethnicity, n (%) | | |
| Chinese | 104 (100%) | 52 (100%) |
| ECOG, n (%) | | |
| 0 | 17 (16.3) | 8 (15.4) |
| 1 | 87 (83.7) | 44 (84.6) |
| Primary tumor site, n (%) | | |
| Gastric | 88 (84.6) | 48 (92.3) |
| Gastroesophageal junction | 16 (15.4) | 4 (7.7) |
| **Signet ring cell carcinoma*** | 41 (**39.4**) | 27 (**51.9**) |
| Lauren type, n (%) | | |
| Intestinal type | 21 (20.2) | 12 (23.1) |
| **Diffuse type** | 45 (**43.3**) | 26 (**50.0**) |
| **Mixed type** | 29 (**27.9**) | 8 (**15.4**) |
| Unknown | 9 (8.7) | 6 (11.5) |
| Previous gastrectomy, n (%) | 49 (47.1) | 31 (59.6) |

| Characteristics | Satri-cel group (n=104) | TPC group (n=52) |
|---|---|---|
| CLDN18.2 expression, n (%)† | | |
| Medium expression | 24 (23.1) | 10 (19.2) |
| High expression | 80 (76.9) | 42 (80.8) |
| Number of prior lines, n (%)‡ | | |
| 2 | 76 (73.1) | 42 (80.8) |
| ≥3 | 28 (26.9) | 10 (19.2) |
| Previous systemic therapies, n (%) | | |
| Fluorouracil/analogs and derivatives§ | 101 (97.1) | 52 (100) |
| Taxanes | 96 (92.3) | 47 (90.4) |
| Platinum | 103 (99.0) | 50 (96.2) |
| Prior anti-PD-(L)1 | 81 (77.9) | 42 (80.8) |
| Number of metastatic organs, n (%) | | |
| ≤2 | 53 (51.0) | 25 (48.1) |
| **≥3** | 51 (**49.0**) | 27 (**51.9**) |
| Metastatic organs, n (%) | | |
| **Peritoneal** | 72 (**69.2**) | 31 (**59.6**) |
| Liver | 21 (20.2) | 10 (19.2) |
| Lung | 9 (8.7) | 7 (13.5) |
| Bone | 8 (7.7) | 9 (17.3) |

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# Phase 2 trial of CLDN 18.2 CAR T (CT041)

## Safety

| | Satri-cel group (n=88) | | TPC group (n=48) | |
|---|---|---|---|---|
| | All grades | Grade ≥3 | All grades | Grade ≥3 |
| All treatment-emergent adverse events | 88 (100%) | 87 (99%) | 44 (92%) | 30 (63%) |
| Treatment-related adverse events | 88 (100%) | 87 (99%) | 44 (92%) | 27 (56%) |
| Leading to discontinuation | 0 | 0 | 2 (4%) | 1 (2%) |
| Leading to death | 1 (1%) | 1 (1%) | 1 (2%) | 1 (2%) |
| Treatment-related adverse events* by preferred terms | | | | |
| Lymphocyte count decreased | 87 (99%) | 86 (98%) | 27 (56%) | 12 (25%) |
| White blood cell count decreased | 86 (98%) | 68 (77%) | 33 (69%) | 14 (29%) |
| Cytokine release syndrome | 84 (95%) | 4 (5%) | 0 | 0 |
| Neutrophil count decreased | 82 (93%) | 58 (66%) | 33 (69%) | 13 (27%) |
| Anaemia | 72 (82%) | 29 (33%) | 22 (46%) | 7 (15%) |
| Hypoalbuminaemia | 70 (80%) | 0 | 8 (17%) | 0 |
| Nausea | 64 (73%) | 3 (3%) | 17 (35%) | 0 |
| Vomiting | 55 (63%) | 4 (5%) | 17 (35%) | 1 (2%) |
| Sinus tachycardia | 50 (57%) | 0 | 0 | 0 |
| Alanine aminotransferase increased | 45 (51%) | 4 (5%) | 9 (19%) | 1 (2%) |
| Platelet count decreased | 45 (51%) | 12 (14%) | 13 (27%) | 2 (4%) |
| Aspartate aminotransferase increased | 44 (50%) | 3 (3%) | 9 (19%) | 1 (2%) |
| Hypokalaemia | 42 (48%) | 9 (10%) | 4 (8%) | 1 (2%) |
| Diarrhoea | 41 (47%) | 1 (1%) | 19 (40%) | 1 (2%) |
| Hyponatraemia | 38 (43%) | 2 (2%) | 2 (4%) | 0 |

| | Satri-cel group (n=88) | | TPC group (n=48) | |
|---|---|---|---|---|
| | All grades | Grade ≥3 | All grades | Grade ≥3 |
| Activated partial thromboplastin time prolonged | 37 (42%) | 1 (1%) | 1 (2%) | 0 |
| Decreased appetite | 37 (42%) | 2 (2%) | 11 (23%) | 0 |
| Total protein decreased | 35 (40%) | 3 (3%) | 1 (2%) | 0 |
| Asthenia | 34 (39%) | 1 (1%) | 14 (29%) | 2 (4%) |
| Lipase increased | 34 (39%) | 4 (5%) | 1 (2%) | 1 (2%) |
| Weight decreased | 33 (38%) | 1 (1%) | 5 (10%) | 0 |
| Temperature intolerance | 31 (35%) | 0 | 0 | 0 |
| Prothrombin time prolonged | 29 (33%) | 0 | 0 | 0 |
| Abdominal pain | 25 (28%) | 0 | 5 (10%) | 0 |
| Conjugated bilirubin increased | 25 (28%) | 8 (9%) | 2 (4%) | 0 |
| Abdominal distension | 24 (27%) | 0 | 1 (2%) | 0 |
| Blood bilirubin increased | 24 (27%) | 4 (5%) | 5 (10%) | 0 |
| Constipation | 24 (27%) | 0 | 3 (6%) | 0 |
| Proteinuria | 24 (27%) | 0 | 4 (8%) | 0 |
| Chills | 23 (26%) | 0 | 0 | 0 |
| Rash | 23 (26%) | 2 (2%) | 4 (8%) | 0 |
| Blood fibrinogen decreased | 22 (25%) | 2 (2%) | 1 (2%) | 1 (2%) |
| Tachypnoea | 20 (23%) | 0 | 0 | 0 |
| Hypocalcaemia | 19 (22%) | 2 (2%) | 2 (4%) | 0 |

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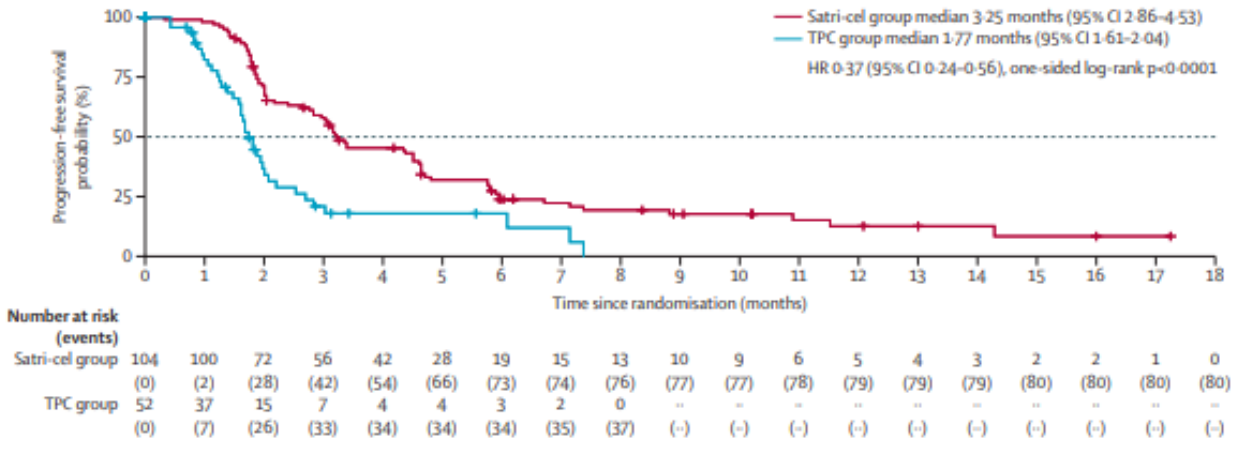
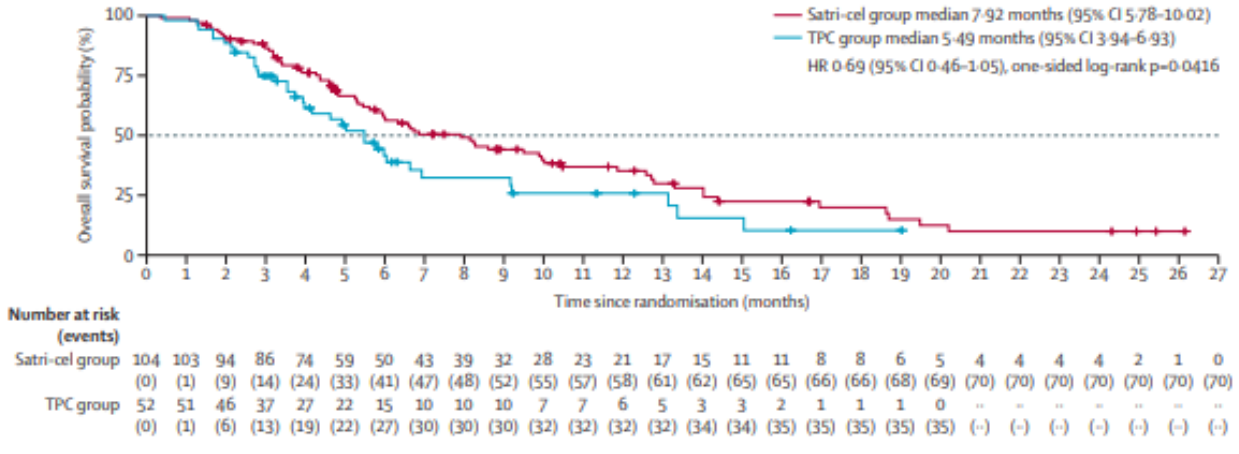
# Phase 2 trial of CLDN 18.2 CAR T (CT041)

PFS




OS




mPFS: 3.25 mo vs 1.77 mo (P<0.0001)

mOS: 7.9 mo vs 5.5mo (P=0.04)

ORR: 26% vs 4%

Qi et al. Lancet 2025

# Ongoing Claudin 18.2 CAR T trials

- 1st line maintenance treatment: LB1908 – Claudin 18.2 CAR T
- Armored CAR T: AZD6422 - Claudin 18.2 CAR T with dominant-negative TGF-β receptor
- Dual target CAR T: BAH2573-102 – Claudin 18.2 and Mesothelin dual- target CAR T

# Questions?