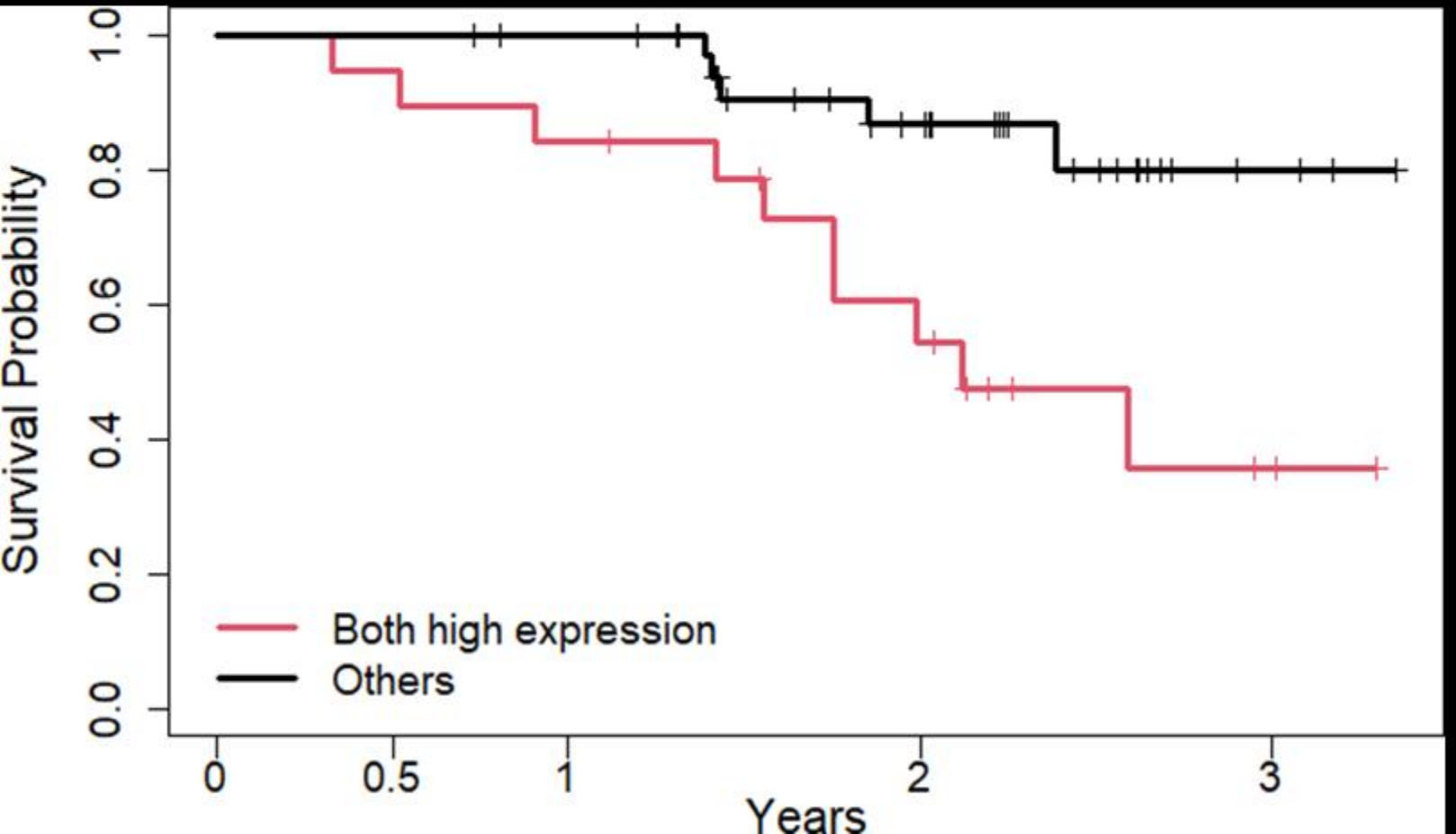
体外診断薬

膵癌NAC-GS効果予測バイオマーカー診断キット



高知大学　谷内恵介

Preoperative Biomarker Kit for Predicting NAC-GS Efficacy in Pancreatic Cancer

- Stratification of Resectable pancreatic cancer using Novel Monoclonal Antibodies for PODXL and ITGB1-

膵癌における術前化学療法（NAC-GS）の治療効果予測バイオマーカー診断キット

-新規モノクローナル抗体を用いたPODXLおよびITGB1発現による切除可能膵癌の層別化-

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Executive Summary

- **Objective**: To identify high-risk patients with resectable pancreatic cancer who may experience rapid progression during neoadjuvant chemotherapy with gemcitabine plus S-1 (NAC-GS), the only approved neoadjuvant treatment for this condition.
- **Current Status**: Following the completion of a prospective multicenter trial and the filing of a basic patent in October 2024, the project is advancing toward clinical implementation. The Research Use Only (RUO) kit is scheduled for launch in March 2026, with the production of monoclonal antibodies for In Vitro Diagnostics (IVD) expected to be completed within the same year. Furthermore, following a PMDA consultation, performance evaluation tests for the diagnostic kit are slated to commence in the second half of 2026.
- **Modality**: Immunohistochemical (IHC) diagnostic kit using novel monoclonal antibodies, optimized for EUS-FNA specimens.
- **Target Disease**: Resectable pancreatic cancer.
- **Competitive Advantage**: This biomarker outperforms TNM staging with a 9.11 Hazard Ratio. It identifies the "Others" group (either/both markers low; score ≦ 3 out of a maximum of 6 points) as optimal NAC-GS candidates (81% 2-year survival). Conversely, the "Both-high" group (both markers high; score ≧ 4 out of a maximum of 6 points) shows high resistance (49% survival). With 94% physician support, it serves as a vital clinical gatekeeper.
- **Collaboration Goal**: Partners for IVD medical device approval, kit sales, and global commercialization.

Backgrounds (1)

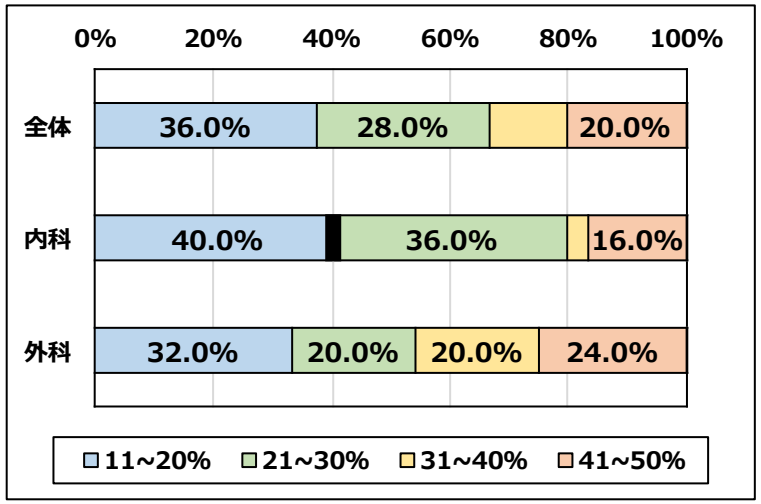
Challenges in the Current Standard Treatment:

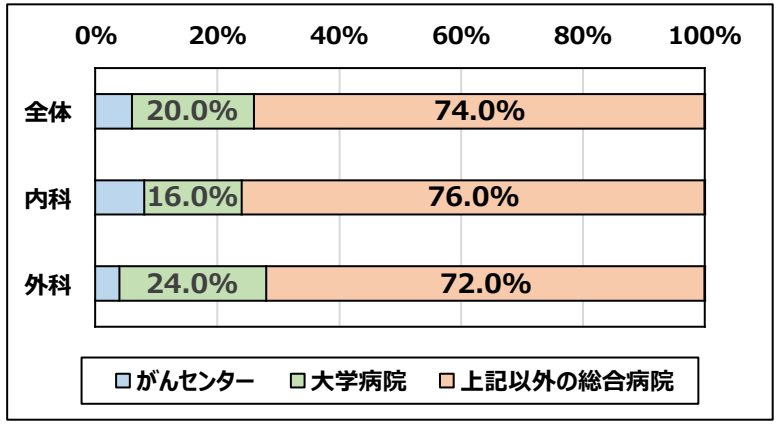
NAC-GS While neoadjuvant chemotherapy with NAC-GS is currently the only approved standard of care for resectable pancreatic cancer, it presents a significant clinical challenge: approximately 10–50% of patients lose the opportunity for curative surgery due to rapid disease progression during the treatment period.

Market Research

- **Target Respondents**: Physicians meeting the following criteria:
  Physicians who have administered NAC-GS therapy to 2 or more cases within one year.
- **Sample Size**: 50 physicians:
  Internal Medicine (Medical Oncology, Gastroenterology): 25.
  Surgery (Gastrointestinal Surgery, Hepato-Biliary-Pancreatic Surgery): 25.
- **Survey Region**: Nationwide (Japan).
- **Survey Schedule**: February 14, 2025 – February 19, 2025.

Q: Percentage of patients whose disease progresses due to the lack of effectiveness of neoadjuvant chemotherapy





In some patients, the therapeutic efficacy of NAC-GS remains limited, and it is not uncommon for individuals to lose the opportunity for curative surgery due to disease progression. The clinical implementation of biomarkers that can accurately predict the response to NAC-GS is highly desired.

Backgrounds (2)

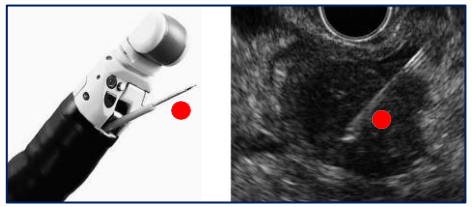
Identification of PODXL and ITGB1 as Prognostic Markers for Resectable Pancreatic Cancer

Increased expression levels of PODXL and ITGB1 in preoperative EUS-FNA specimens independently correlate with poor biological outcomes after surgery.

UMIN000032835： Retrospective clinical study using preoperative biopsy tissue from patients with pancreatic cancer.

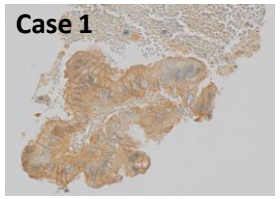
This study included 24 patients with resectable pancreatic cancer and was conducted between 2018 and 2019, prior to the establishment of NAC-GS as the standard neoadjuvant treatment. We used residual pancreatic cancer tissue originally obtained by EUS-FNA for diagnosis.

Preoperative EUS-FNA

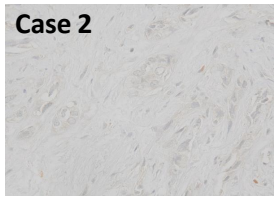


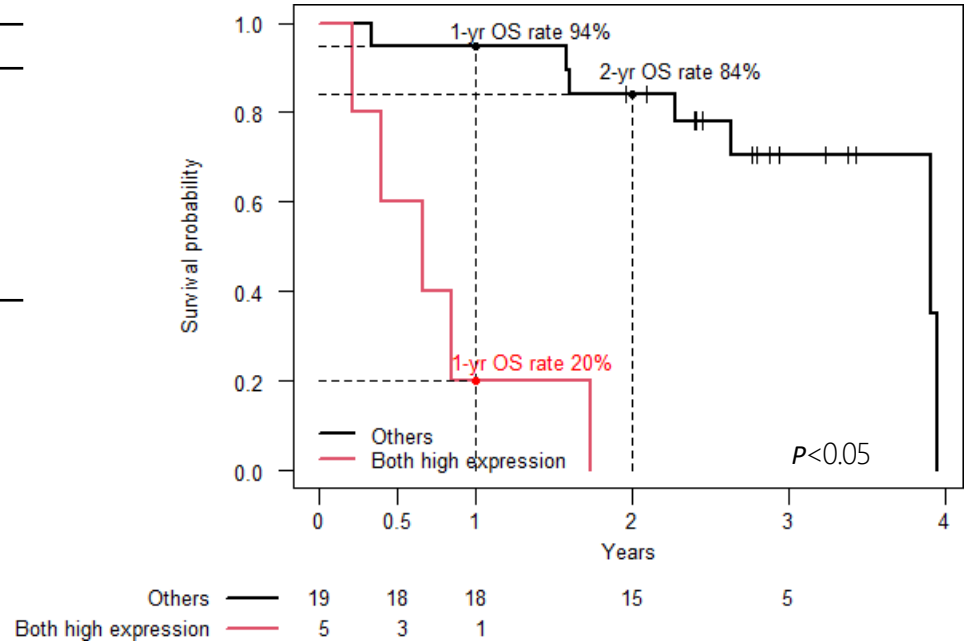
Stage	
IA	n = 4
IB	n = 5
IIA	n = 9
IIB	n = 5
III	n = 1

High expression of PODXL



Low expression of PODXL





Japanese Patent No. 7246731

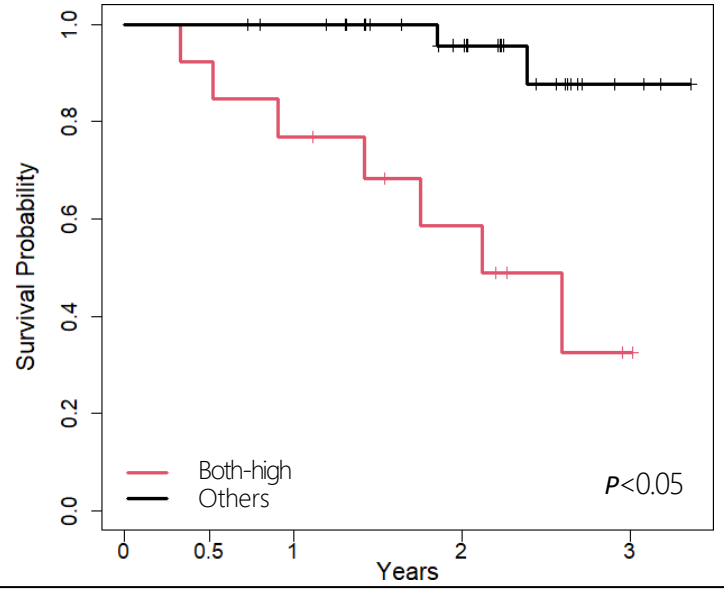
Others: Low expression of either or both biomarkers
Both high expression: Concurrent high expression of both biomarkers

The combination of PODXL and ITGB1 can accurately predict postoperative prognosis at the preoperative stage.

Current Issue; NOT select potential responded patients for preoperative chemotherapy

If the general condition is stable, preoperative chemotherapy is indicated for all cases of resectable pancreatic cancer
➔ If patient selection becomes possible, treatment measures appropriate for each patient can be implemented

UMIN000034022： Prospective study on the clinical utility of preoperative and postoperative prognostic markers in pancreatic cancer.



32 cases in the Others group: Cases where the efficacy of NAC-GS is expected.
→ **Indication for NAC-GS followed by surgery.**

Current Issues: Preoperative chemotherapy is currently administered to all patients with resectable pancreatic cancer, provided their general condition is favorable.

13 cases in the Both-high group: Cases where the efficacy of NAC-GS is not expected.
→ **Indication for upfront surgery or alternative neoadjuvant chemotherapy.**

N＝45 (11 cases were excluded due to comorbidities, etc.)

	Both-high	Others
1 year survival rate	0.77 (95%CI 0.57-1.00)	1.00(-)
2 year survival rate	0.59 (0.36-0.95)	0.96(0.88-1.00)

Patent Application No. 2025-130317

Survival rates were comparable to those of surgery-only cases reported in previous literature.

Key Data (1): High expression of both PODXL and ITGB1 could have a potential as a strong predictor of resistance to NAC-GS

A Strong Independent Prognostic Factor for Resectable Pancreatic Cancer (Multivariate Analysis)

"Both-high" status (concurrent high expression of PODXL and ITGB1) serves as a potent predictor of resistance to NAC-GS; this group exhibits significantly poorer survival (HR 9.11) and minimal therapeutic benefit compared to conventional clinical staging.

We confirmed the absence of multicollinearity among the following eight variables using the Variance Inflation Factor (VIF) criterion: age, sex, the biomarker (combination of PODXL and ITGB1), clinical stage, ITGB1 alone, preoperative chemotherapy, resectable pancreatic cancer, and CA19-9. Furthermore, variable selection was performed based on the Akaike Information Criterion (AIC).

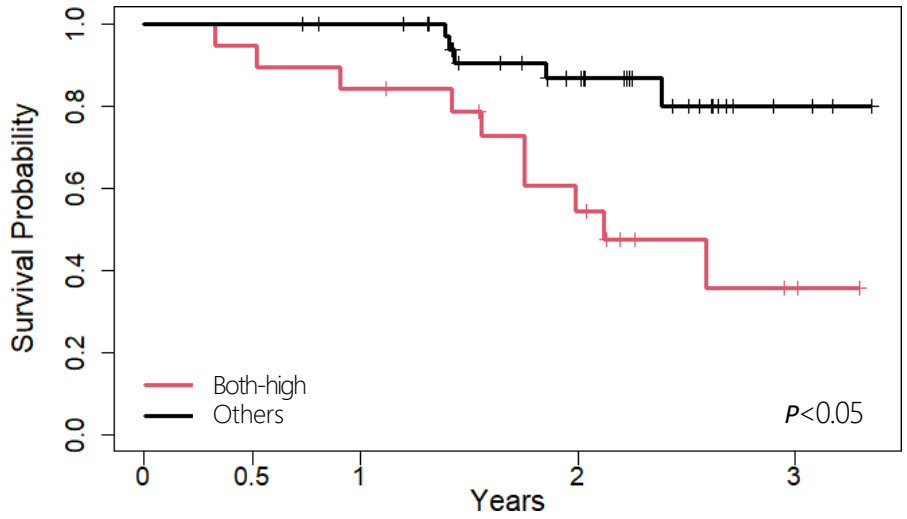
	Hazard Ratio	95%CI	*P* value
PODXL and ITGB1	9.11	[2.58-32.1]	0.0006
Clinical stage	3.29	[1.12-9.67]	0.03
NAC-GS	4.53	[0.87-6.08]	0.09

Patent Application No. 2025-130317

Key Data (2)

Survival Stratification of Resectable Pancreatic Cancer by PODXL/ITGB1 Status

Kaplan-Meier analysis highlights that the "Others" group (patients with low expression of either or both biomarkers) achieves a superior 2-year survival rate of 81% with NAC-GS.
This demonstrates that NAC-GS is highly effective for the "Others" phenotype, whereas the "Both-high" group shows limited benefit with a survival rate of only 49%.



In the 'Others' group, which excludes double-high expression, approximately 70% of patients survived.

N = 56 (including patients who underwent upfront surgery)

Patent Application No. 2025-130317

	Both-high	**Others**
1-year survival rate	0.88 (95%CI 0.75-1.00)	1.00(-)
2-year survival rate	0.49 (0.32-0.74)	0.81(0.69-0.96)
Median OS	1.98 (1.75 – 3.13)	NA (NA-NA)

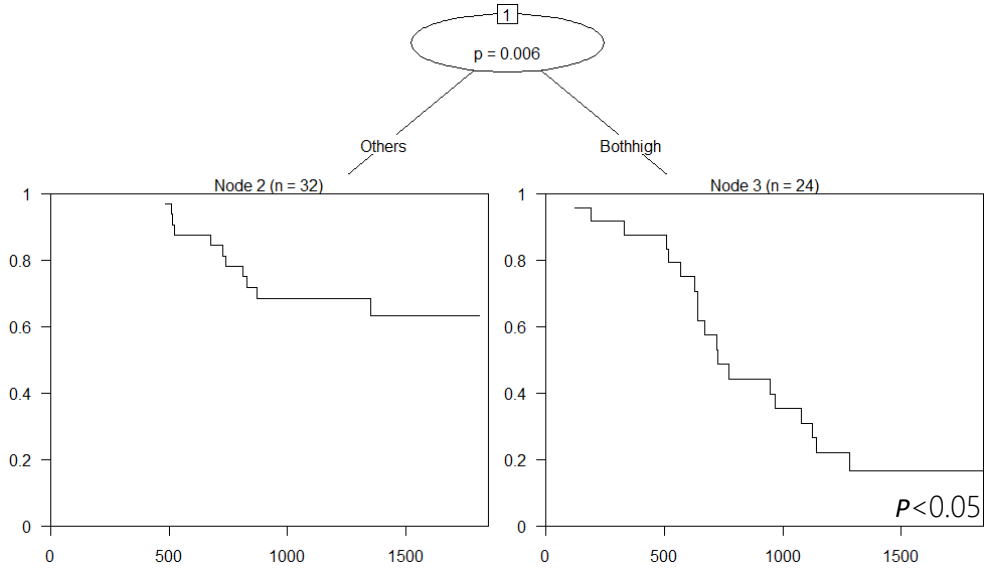
Key Data (3)

Integrated Risk Stratification in Resectable Pancreatic Cancer using CART Analysis

Decision tree (CART) analysis confirms that PODXL/ITGB1 status is the primary predictor of NAC-GS efficacy; it precisely identifies the "Others" group as those most likely to benefit from NAC-GS, while simultaneously isolating the "Both-high" group at the highest risk of treatment failure.

CART analysis was performed using the following eight factors: the combination of PODXL and ITGB1, clinical stage, preoperative chemotherapy, resectable pancreatic cancer, tumor size, tumor location within the pancreas, and CA19-9.

Others: NAC-GS is expected to be effective.



Both-high: No therapeutic effect of NAC-GS is expected.

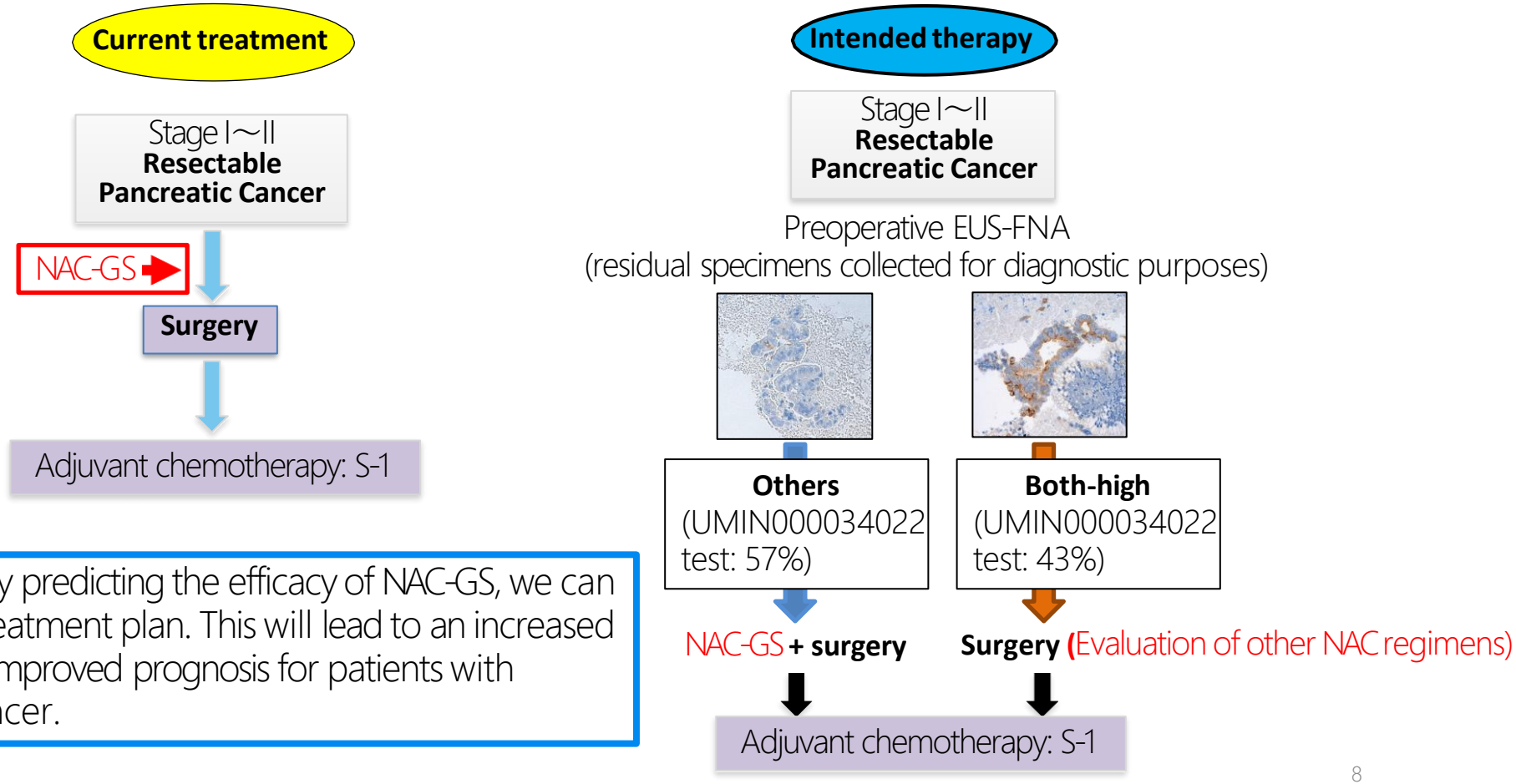
Patent Application No. 2025-130317

The combination of PODXL and ITGB1 most closely correlated with survival after NAC-GS and successfully stratified treatment efficacy.

Competitive Advantage (1);

Superior Accuracy Over Conventional Diagnostic Methods

Unlike CA19-9 or imaging, this IHC-based stratification directly reflects the biological aggressiveness and NAC-GS resistance of the tumor. It provides a robust molecular basis at the time of diagnosis to identify the "Others" group who will benefit from NAC-GS, as well as the "Both-high" group who may require alternative strategies.

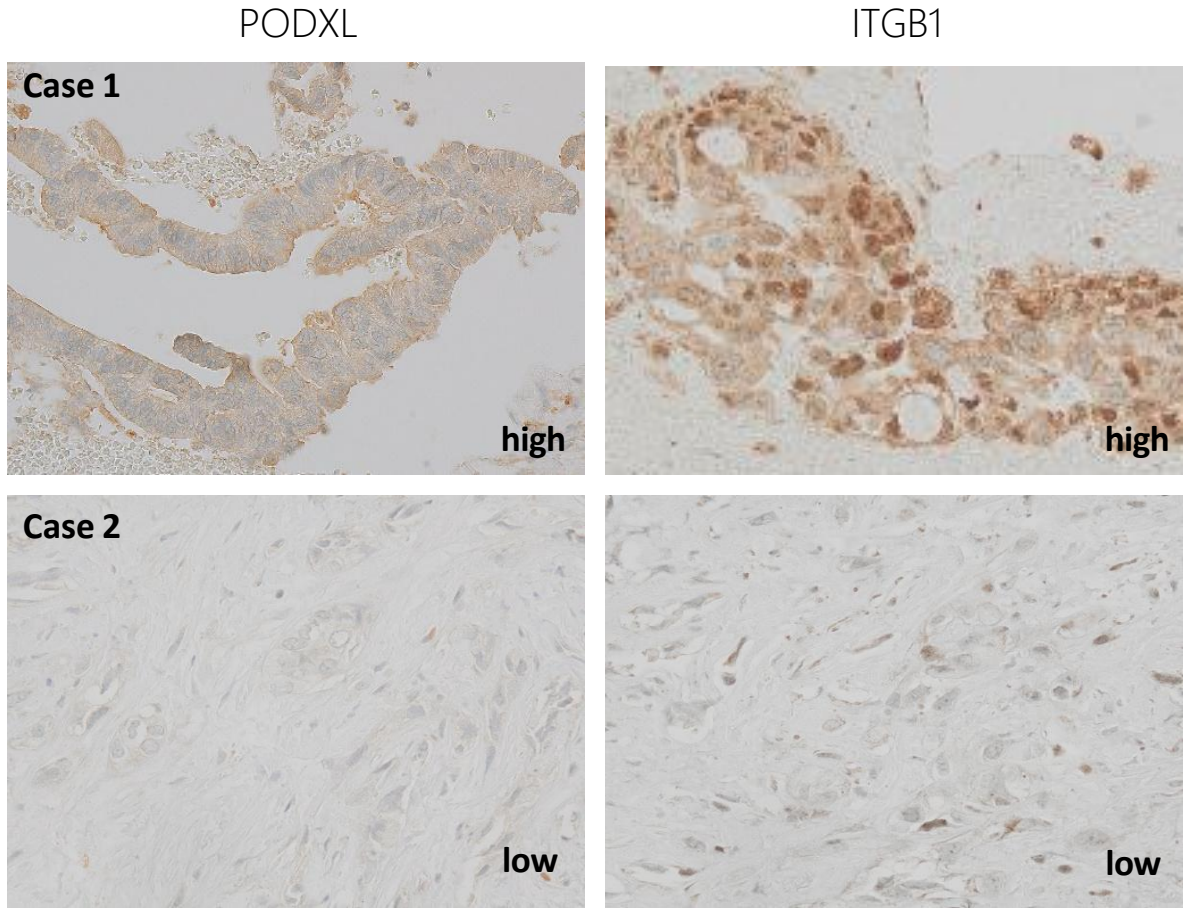


Goal of the Treatment: By predicting the efficacy of NAC-GS, we can determine the optimal treatment plan. This will lead to an increased rate of R0 resection and improved prognosis for patients with resectable pancreatic cancer.

Competitive Advantage (2);

Standardized Workflow and High Clinical Feasibility

The use of novel monoclonal antibodies and automated staining platforms ensures high reproducibility even with small-volume EUS-FNA samples.



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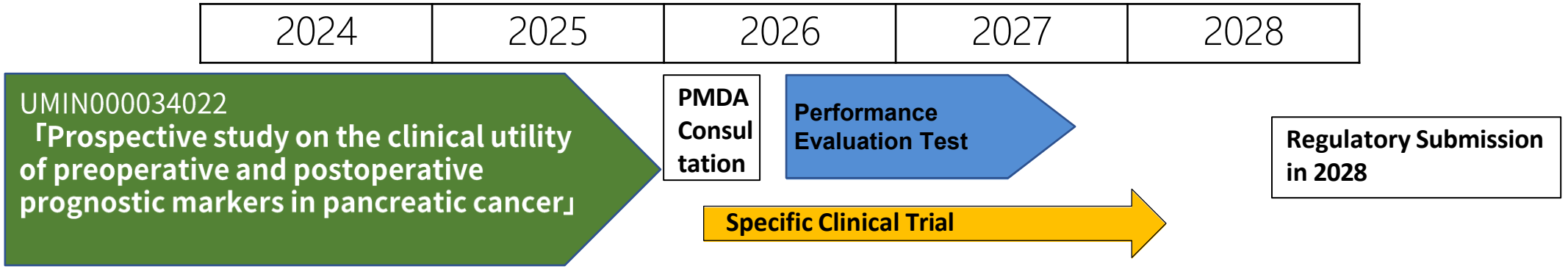
Product Development & Regulatory Roadmap



Key Milestones:

2026: Launch RUO (Research Use Only) kit.

2026: Conducting Specified Clinical Research.

2026: Conduct performance and stability testing for the IVD kit.

2028: Regulatory approval, manufacturing, and marketing.

Reference （Patents / Key Papers）

Patents

1. **Prognostic Biomarker Patent:** A patent titled "Prognostic marker for pancreatic cancer, prognostic diagnostic kit for pancreatic cancer, and method for predicting prognosis of pancreatic cancer" has been filed and registered (**Patent No. 7246731**; Applicant: Kochi University; Inventor: Keisuke Taniuchi). This patent pertains to the use of PODXL+ITGB1 to accurately predict postoperative prognosis for patients with surgically resectable pancreatic cancer at the preoperative stage.
2. **Treatment Efficacy Patent:** In October 2024, a basic patent application was filed titled "Molecular marker for determining the efficacy of Gemcitabine + S-1 therapy (NAC-GS) as neoadjuvant chemotherapy for pancreatic cancer, kit for determining said efficacy, and method for determining said efficacy" (**Patent Application No. 2024-188719**; Applicants: Salus Science and Kochi University; Inventor: Keisuke Taniuchi). This application covers the potential of PODXL+ITGB1 as a biomarker to predict the therapeutic effect of NAC-GS on resectable pancreatic cancer and includes analysis results using research-grade monoclonal antibodies. Furthermore, an updated application incorporating the latest analytical data was filed via a priority claim (**Patent Application No. 2025-130317**; Applicants: Salus Science and Kochi University; Inventor: Keisuke Taniuchi).

Key Paper

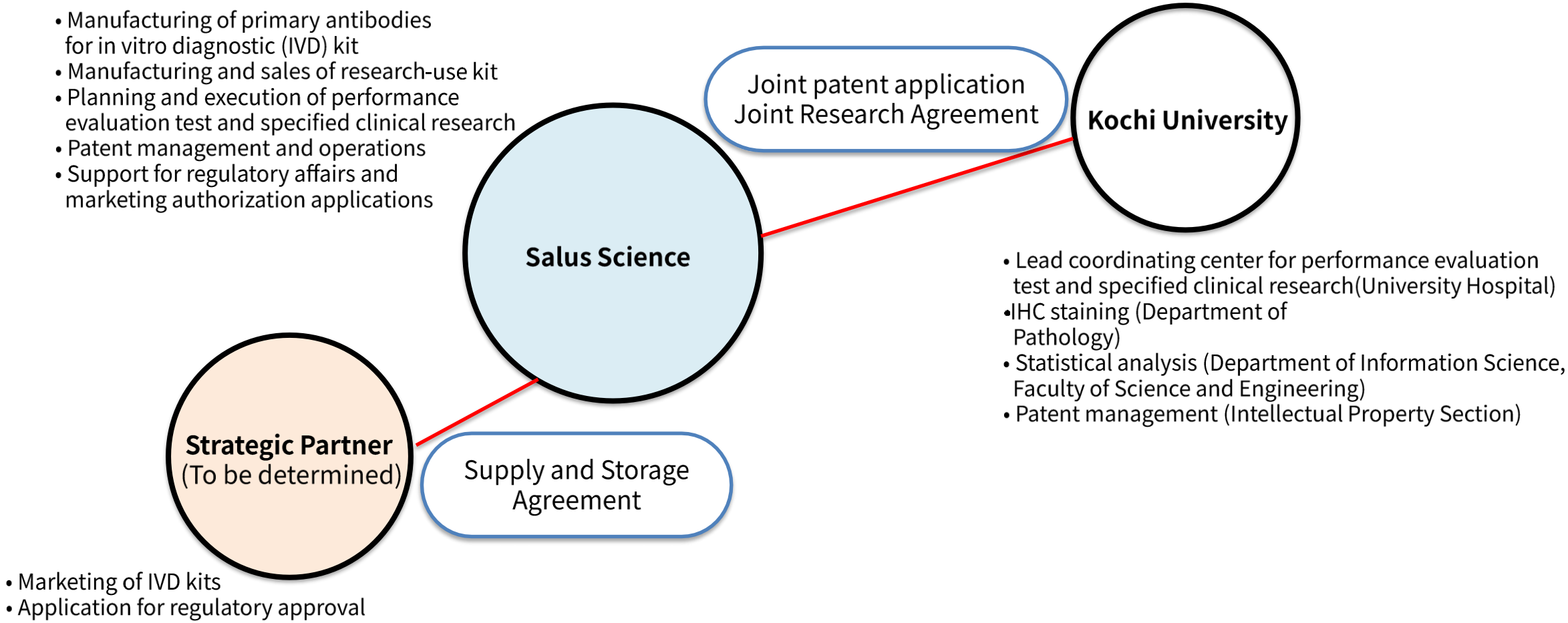
1. Taniuchi K, et al. (Manuscript in preparation) regarding EUS-FNA biomarkers for NAC-GS.
2. Taniuchi K, et al. Upregulation of PODXL and ITGB1 in pancreatic cancer tissues preoperatively obtained by EUS-FNA correlates with unfavorable prognosis of postoperative pancreatic cancer patients. PLoS One. 2022;17:e0265172.
3. Taniuchi K, et al. Overexpression of PODXL/ITGB1 and BCL7B/ITGB1 accurately predicts unfavorable prognosis compared to the TNM staging system in postoperative pancreatic cancer patients. PLoS One. 2019;14:e0217920.

Our Team

Multidisciplinary Collaboration for Clinical Implementation

- **Academic**: Kochi University.
- **Industrial**: Salus Science* and Strategic Partner

*: SU company, Co-founder / Dr. Taniuchi



Market Opportunity; **Market survey showed high preference**

Executive Summary of Market Suervey

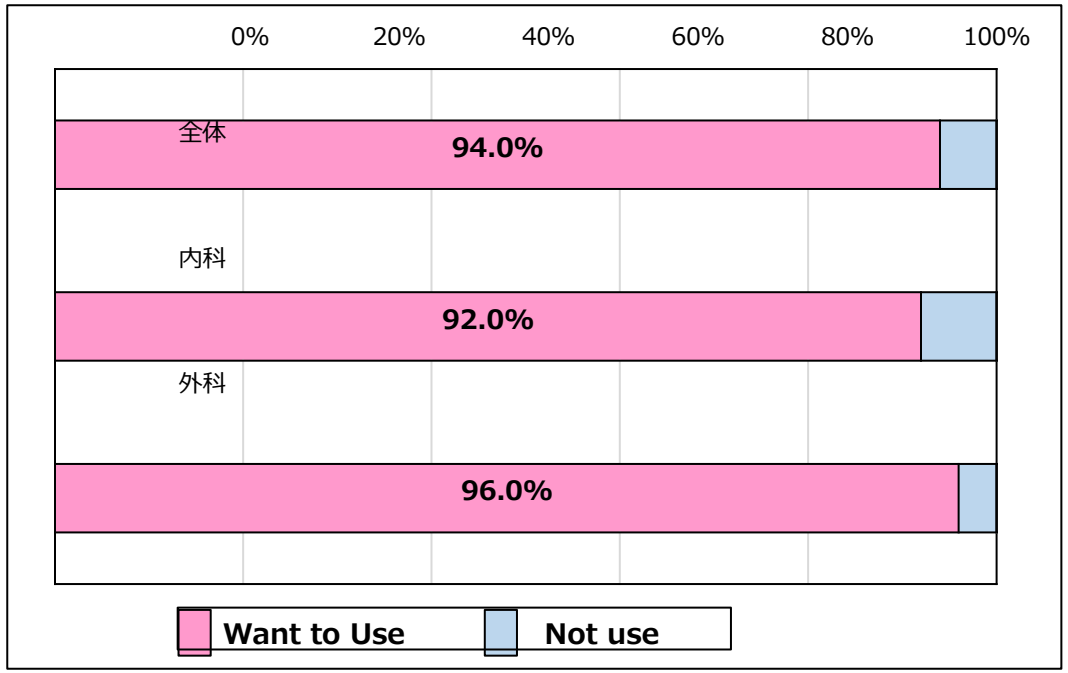
Market research indicates an exceptional clinical need for this biomarker among pancreatic cancer specialists, with nearly universal intent for facility-level adoption.

Clinical Utility

- **94.0%** of all specialists expressed the intent to use this biomarker in a clinical setting.
- High demand across disciplines: **92.0%** in Internal Medicine and **96.0%** in Surgery.

Routine Implementation

- **100%** of respondents who would use the biomarker confirmed they would implement it as a routine diagnostic method at their own facility.



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