

Background & Aim

- Pancreatic cancer, a leading cause of cancer deaths in developed countries, is one of the most fatal cancers¹⁻². Chemotherapies are recommended in the NCCN Guidelines³ as a treatment for metastatic pancreatic cancer (mPC) which is the most advanced stage of pancreatic cancer.
- Several treatment regimens exist in Japan that can be used for the treatment of MPC. The main purpose of these treatment regimens for mPC are to prolong prognosis and improve health related quality of life (HRQoL)⁴. Therefore, there is a need for evidence that quantitatively evaluates the impact of chemotherapy on HRQoL.
- On the other hand, few studies have evaluated HRQoL in pancreatic cancer disease status or specific adverse events associated with chemotherapy. Additionally, mPC is a severe disease with a limited prognosis, making it difficult to conduct a large-scale HRQoL evaluation study in patients.
- We evaluated Japanese societal-based health related utility values for mPC and different grade toxicities commonly associated with chemotherapy treatments using composite time trade-off (cTTO) based on vignette-based approach (VBA).

Method

DEVELOPMENT HEALTH STATUS SCENARIOS

[Overall process]

- We developed a disease state scenario for patients with mPC, referring to the previous study on VBM methodology by Louis S et al⁵⁻⁶.
- The development of the disease state scenario consisted of three steps.
- Developing the disease state scenarios in this study was developed by referring to the ISPOR PRO Good Research Practices Task Force Report⁷⁻⁸.

[Step 1: Literature review]

- Rapid literature identifying symptom and HRQL burden of mPC conducted.
- Literature review and discussion findings are used to develop an interview script.

[Step 2: Exploratory interviews]

- 7 oncology experts are recruited to take part in an interview on the nature of Stable disease and progressive disease of mPC in terms of symptom, HRQoL burden and adverse events by chemotherapy.
- 11 health states are developed to reflect symptoms and HRQoL burden in stable disease and progressive disease in mPC (Table 1).

[Step 3: Content validation]

- 7 oncology experts are recruited to take part in depth debriefing interviews and asked to consider the health states in terms of accuracy and appropriateness and suggestions are incorporated.
- Health states are reviewed by a QOL expert and suggestions are incorporated.
- Health states are piloted with 5 members of the general public in 'think aloud' and cognitive de-briefing interviews.

Table 1 : List of health status scenario.

No	Health status	AE Grade
1	No adverse effects	-
2	Neutropenia	1/2
3	Neutropenia	3/4
4	FN	-
5	Stable disease	1/2
6	Diarrhea	3/4
7	Nausea/Vomiting	1/2
8	Nausea/Vomiting	3/4
9	Neuropathy	1/2
10	Neuropathy	3/4
11	Progressive disease	-

MAIN STUDY

[Research method]

- The participants were Japanese nationals aged 20 years or older, except for medical professionals such as doctors, dentists, pharmacists, and nurses, who could agree to the consent form.
- We recruited equally in terms of gender and age group, and we designed two methods, cTTO and EQ-VAS, which conducted the survey face-to-face using PC platform(Figure 1).
- Respondents were asked to answer the following questions
 - IC confirmation
 - Background information (gender, age, employment status, education, marital status)
 - Three example cTTO questions
 - Wheelchair status, B: Better than wheelchair status, C: Worse than dead status).
 - cTTO and VAS production answers (11 scenarios)
 - Three comprehension questionnaires (To check the respondents' understanding)

[Statistical analysis]

- In this study, we calculated descriptive utility statistics from cTTO and VAS.
- Since we do not conduct hypothesis testing, there is no clear criterion for calculating the sample size. However, based on the previous study by Nafee et al., we assumed that a sample size of 100 would allow us to calculate descriptive statistics.
- We included in our analysis a population that excluded the following;
 - Participants who gave inconsistent responses to cTTO exercises 1 and 2.
 - Participants who responded to all scenarios with a QOL value = -1, 0, or 1.

Result

PARTICIPANTS BACKGROUND

- Of the 220 participants recruited, all 220 answered all questions, and of the All participants, 201 were eligible for analysis.
- We tabulated the number of respondents by sex and age, employment status, education, and marital status as background information of the respondents in Table 2.

Table 2 : Calculated Cost, QALY and ICER.

Characteristics	N	%	Characteristics (Continue)	N	%
Gender					
Male	110	50.0%	Retired	1	0.5%
Female	110	50.0%	Student	14	6.4%
			Other	0	0.0%
Age			Education		
20-29	44	20.0%	Junior high school	1	0.5%
30-39	44	20.0%	Senior high school	55	25.0%
40-49	44	20.0%	Vocational school / technical college	36	16.4%
50-59	44	20.0%	Junior college	15	6.8%
60-64	44	20.0%	University	104	47.3%
Employment status			Master's Degree	9	4.1%
Full-time employee	133	60.5%	Other	0	0.0%
Temporary worker	13	5.9%	Marital status		
Part-time worker	28	12.7%	Unmarried	74	33.6%
Self-employed	9	4.1%	Married	131	59.5%
Unemployed	22	10.0%	Other	15	6.8%

HEALTH STATUS UTILITY VALUES

- The stable disease with no adverse events (our reference state) had a mean utility value of 0.63 by cTTO. Lowest mean utility scores in stable states were 0.24 (stable disease + grade 3/4 vomiting) (Table 3). VAS results ranged from 0.19 to 0.47 depending on the type and grades of side effects in the stable disease.

Table 3 : Utility values for all health status of metastatic pancreas cancer from cTTO and VAS.

Health status	AE Grade	N	cTTO	AVG	STE	MIN	MED	MAX	N	VAS	AVG	STE	MIN	MED	MAX
SD (Reference)	-	201	0.63	0.02	-1.00	0.80	1.00	105	0.47	0.02	0.06	0.44	0.89		
SD + Neutropenia	G1/2	201	0.65	0.03	-1.00	0.80	1.00	105	0.44	0.02	0.06	0.44	0.80		
SD + Neutropenia	G3/4	105	0.51	0.04	-1.00	0.65	0.95	105	0.35	0.02	-0.14	0.35	0.80		
SD + FN	G3/4	201	0.32	0.04	-1.00	0.45	0.95	105	0.20	0.02	-0.43	0.20	0.63		
SD + Diarrhea	G1/2	105	0.50	0.04	-1.00	0.60	0.95	105	0.30	0.02	-0.43	0.33	0.67		
SD + Diarrhea	G3/4	201	0.31	0.04	-1.00	0.50	1.00	105	0.19	0.02	-0.43	0.15	0.63		
SD + Vomiting	G1/2	201	0.42	0.04	-1.00	0.50	0.95	105	0.30	0.02	-0.43	0.30	0.70		
SD + Vomiting	G3/4	105	0.24	0.06	-1.00	0.40	0.95	105	0.19	0.02	-0.43	0.17	0.60		
SD +Neuropathy	G1/2	105	0.54	0.04	-1.00	0.65	0.95	105	0.33	0.02	-0.07	0.31	0.83		
SD +Neuropathy	G3/4	201	0.37	0.04	-1.00	0.50	0.95	105	0.25	0.02	-0.13	0.25	0.63		
PD	-	201	-0.12	0.04	-1.00	0.00	0.95	105	0.11	0.02	-0.40	0.06	0.85		

PARTICIPANT UNDERSTANDING

- Most of the participants answered "Strong agree" or "Agree" to three questions of the comprehension questionnaire. (Table 4).

Table 4 : Three comprehension questionnaires.

Contents	N	%
ALL participants	220	
Questioner (Conducted after answering cTTO and VAS)		
Q1, "I found it easy to imagine the scenarios I was asked"		
Strongly agree	101	45.9%
Agree	110	50.0%
Disagree	8	3.6%
Strongly disagree	1	0.5%
Q2, "I found it easy to tell the difference between the lives I was asked to think about"		
Strongly agree	147	66.8%
Agree	71	32.3%
Disagree	2	0.9%
Strongly disagree	0	0.0%
Q3, "I found it difficult to decide on my answers to the questions"		
Strongly agree	57	25.9%
Agree	117	53.2%
Disagree	44	20.0%
Strongly disagree	2	0.9%

Discussion

- Creating the health status scenario in this study was based on VBM. The selected factors and the scenario text were validated in terms of the impact of the disease on HRQoL and the participants' cognition.
- The utility of the scenario in SD was based on previous studies on QOL in metastatic breast cancer and metastatic lung cancer, suggesting consistency with previous studies^{5,9}.
- Utility in PD status by cTTO was the same as that in worse than death. It is suggested that the serious scenario of PD in mPC strongly affected the Disutility.
- In the future, it is desirable to conduct a QOL survey of a small number of healthcare professionals and patients to examine the consistency with the present study.

Conclusion

- We clarified health state utility values based on the general population for metastatic pancreatic cancer in Japan.

Example : cTTO question screen (PC platform)

QX

You will be asked to think about the "Full health" and the "Impaired health" shown below.
After reading all the statements on the screen, imagine how you would feel if you were in such a health condition.

	Full health	Impaired health
Summary	Physically and mentally, the healthiest state.	You have a life-threatening disease, but his condition has been stabilized by treatment.
Physical symptoms	Appetite You have the same appetite as usual.	You do not have enough appetite to lose weight.
	Fatigue You can eat as usual.	You are more tired than when you were healthy.
	Body aches You have not pain.	Sometimes you have strong pain. You take medication to relieve it.
Daily life at home and outside	You can live freely on your own.	You can live by yourself at home, but you can only go out for a couple of hours.
Mental	You have no worries or concerns about your health.	You are very anxious about the possibility of dying from the disease.
Adverse effects	None.	Due to the side effects of the treatment, you have persistent tingling pain and numbness in your hands and feet, which is uncomfortable.

QX_yy

We created two cases by combining two health conditions and years of survival.
When do you imagine the two cases in your own life, which one you think is more preferable for you, Case 1 or Case 2, as shown below?

Case 1

Case 2

Full health

Impaired health

Case 1: Live only 10 years in "perfect health".

Case 1 and Case 2 are the same for you.

Case 2: Live for 10 years in "perfect health" and then live for 10 years in the "specific health condition" described above.

Reference) ¹Ferlay J, et al. Int J Cancer 2015; March 1; 136(5): E359-86. ²Noone AM, et al. SEER Cancer Statistics Review (CSR) 1975–2015. ³Tempero MA, et al. J Natl Compr Canc Netw. 2021 April 1;19(4):439-457.

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