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Using Structured Expert Elicitation in Cost-Effectiveness analysis: An Exploratory Case Evaluating Selpercatinib for Thyroid Cancer in Norway

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INTRODUCTION

RET mutant Medullary Thyroid Cancer (MTC) is a **rare disease** with approximately 2 diagnosed patients in Norway annually.

• The **standard of care** is cabozantinib and vandetanib.

Selpercatinib is an innovative treatment for RET



This study focuses on the execution of two CUAs:

1. The **phase II CUA**, which is based on LIBRETTO-001 (single-arm) and SEE.

RESULTS

Experiences of the pragmatic approach

This study emphasizes the importance of **behavioural aggregation** in a situation where **between-expert** variation is present.

Address the knowledge gap surrounding SEE as a method

- mutant MTC. **Single Arm Trial** "LIBRETTO-001" &
- Randomized Controlled Trial "LIBRETTO-531"
- Reimbursement decisions have been made in the **UK** and **CA** based on LIBRETTO-001 using common methods for **indirect comparisons**.
- \rightarrow However, in the field of rare diseases, **Structured Expert Elicitation (SEE)** might be a suitable alternative or supplement to these methods.

OBJECTIVE

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- 2. The **phase III CUA**, which is based on LIBRETTO-531 (RCT).
- Model design: a Partitioned Survival Model with 3 health states (PF, PD and D) and monthly cycles over a time horizon of 25 years.

Gathering and integrating SEE

- SEE was conducted with **3 Norwegian clinicians** experienced in treating MTC.
- The exercise aimed to elicit the **PFS** and **OS** of patients treated with • the intervention or comparator at three timepoints (i.e., 12 months, 24 months and 60 months).
- **Beta** distributions were fitted to the expert estimations.
- **Behavioral aggregation** was not performed due to time constraints.

Mathematical aggregation

- \rightarrow Initially, **linear pooling** with equal weights for all experts.

PFS

- Additionally, the **effect** of including **enough experts** is • stressed as the inclusion of fewer experts than recommended places a **high weight** on individual estimates.
- Lastly, challenges emerged regarding the **combination** of SEE and trial data leading to conflicting courses in the first few cycles of the Markov trace, with OS (SEE) exceeding PFS (trial data).

		Costs	Inc		Inc	
	Strategy	(in NOK)	costs	QALYs	QALYs	ICER
Phase II	Intervention	11,677,362	4,302,743	6.07	1.91	2,249,739
	Comparator	7,374,620	_	4.16	_	-
Phase III	Intervention	11,218,979	5,104,565	5.71	2.49	2,053,354
	Comparator	6,114,414	-	3.23	_	-

Comparisons of the CUAs

Regarding the **clinical treatment effects**,

discrepancies between of SEE and trial data were

for **indirect comparison**, exploring the ability to inform reimbursement decisions.

- Describe the **experiences** of a pragmatic application of SEE.
- **Compare** the outcomes of a decision-analytic model based on SEE to one that is based on RCT data.







		ion arma Dha	
Jpper bound	100.00	90.00	7
ower bound	85.00	70.00	3.
Nedian (p50)	92.10	80.20	5
Beta	7.41	12.93	2
Alpha	82.94	51.29	2
OS S			
Jpper bound	80.00	65.00	3.
ower bound	55.00	35.00	
Nedian (p50)	67.60	50.00	1
Beta	28.81	34.96	2
Alpha	59.67	34.96	

12 m

	Intervention arm Phase II			
OS	12 m	24 m	60 m	
Alpha	64.95	55.42	40.23	
Beta	3.91	8.46	26.88	
Median (p50)	94.70	87.10	60.10	
Lower bound	85.00	75.00	45.00	
Upper bound	100.00	95.00	75.00	

Between- expert variation was present.

- Preliminary analysis included the estimates of **expert 2** on the **PFS** at 12 months & **experts 1 and 2** on the **OS** do not fall within the expected ranges and were probably altered if **behavioral aggregation** had taken place.
- \rightarrow Therefore, PFS was informed by expert 1 and 3 while OS was informed only by expert 3.

Control arm

24 m

hase	e II
60) m
96	5.77
96	27.39
00	16.70
00	5.00
00	35.00
29	29.82
23	26.28
20	53.20
00	35.00
00	70.00
ո Pho	ase II
	_

found.

- This led to a **divergence in state occupancy** of PD between the phase II and phase III models.
- However, **similarity** in the cost-effectiveness outcomes of the two analyses was found.

In both CUAs there is a **0% probability** of selpercatinib to be cost-effective compared to cabozantinib and vandetanib at e WTP threshold of NOK 825,000 per QALY.



DISCUSSION

• This study demonstrates that SEE can be used in decision analysis with the **potential** to support reimbursement recommendations.

- The pragmatic approach facilitated a **quick and easily understandable** application of SEE in decision analysis.
- Varation and bias will be present in SEE, and care should be exercised in conducting, analyzing and deciding based on SEE.
- o **Incorporating uncertainty** into decision analysis will be increasingly important for situations similar to this study.
- Significant differences existed between the phase II and phase III trials in terms of design and patient characteristics.
- A **pragmatic approach** was taken to conduct this study, limiting the **generalisability** of the results.

This research presents an example of an especially **rare patient group**, in a relatively **small country**.



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Further research

Should target **varied settings** (e.g., near-cost-effective interventions) and examine options for **cross-country** expert sharing. Furthermore, it would *be interesting to investigate SEE as a* supplementary method to other methods for **indirect comparisons**, or in combination with real-world data. Additionally, a better understanding of systematic biases in SEE, and the propagation of **uncertainty** into decision models, would be valuable.