

Management of Biliary Tract Cancer – A Delphi (Consensus) Survey of UK Clinical Experts

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Background

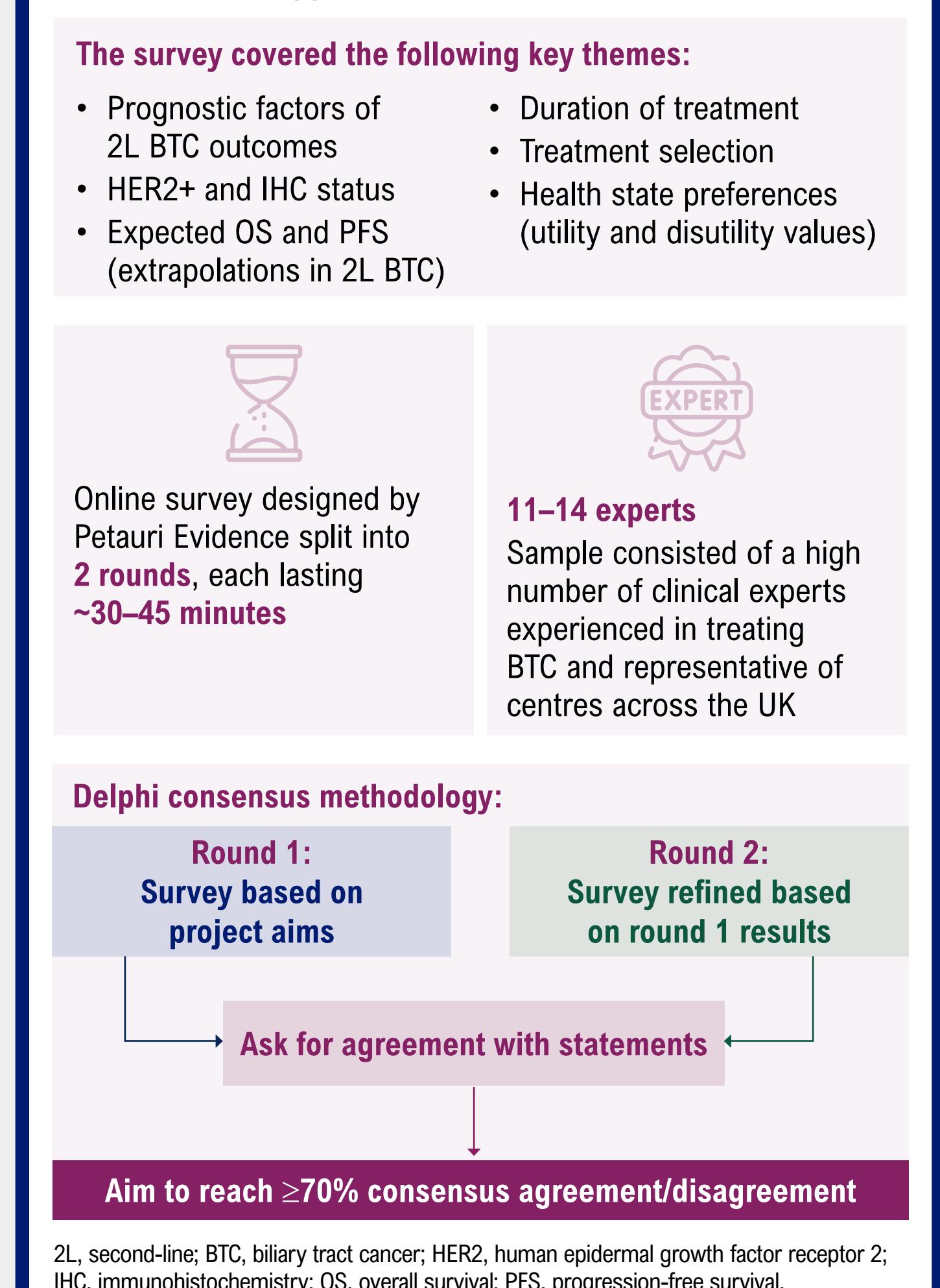
- Biliary tract cancer (BTC) is a rare and aggressive cancer, with poor prognosis and limited treatment options¹
- Current standard of care (SoC) for patients who progress after first-line (1L) chemotherapy is treatment with FOLFOX or modified FOLFIRI, yet patients continue to experience poor survival outcomes²
- Treatment with human epidermal growth factor receptor 2 (HER2)-targeted therapies have been shown to improve outcomes in other cancers and may improve patient survival outcomes in BTC
- To date there are no Health Technology Assessment (HTA)-approved HER2-targeted treatments for BTC in the UK
 - In July 2025, zanidatamab, a dual HER2-targeted bispecific antibody, received conditional authorisation from the European Commission for the treatment of adults with unresectable locally advanced or metastatic HER2-positive (immunohistochemistry [IHC] 3+) BTC previously treated with at least 1 prior line of systemic therapy
- Several aspects concerning the UK treatment pathway and patient care for second-line (2L) BTC lack consensus
- Structured expert elicitation protocols, such as the Delphi methodology, are increasingly accepted by HTA bodies, including the National Institute for Health and Care Excellence, and can be used to improve transparency and consistency of judgements from experts while limiting the effect of heuristics and research biases

Objective

- To gain consensus through structured expert elicitation from UK clinicians on disease outcomes and optimal patient management to support UK HTAs of zanidatamab (referred to as Product X in this study) for 2L BTC

Methods

Figure 1. Overview of Modified Delphi Methodology



- A total of 14 clinicians working in the UK National Health Service in England and Scotland with expertise in managing BTC were identified and invited to participate in a 2-round, web-based consultation using a modified Delphi methodology
- Round 1 consisted of 96 multiple-part, scaled, open and closed-ended statements and questions; round 2 was formed of 33 multiple-part, scaled statements. The survey was divided into 6 themes of interest

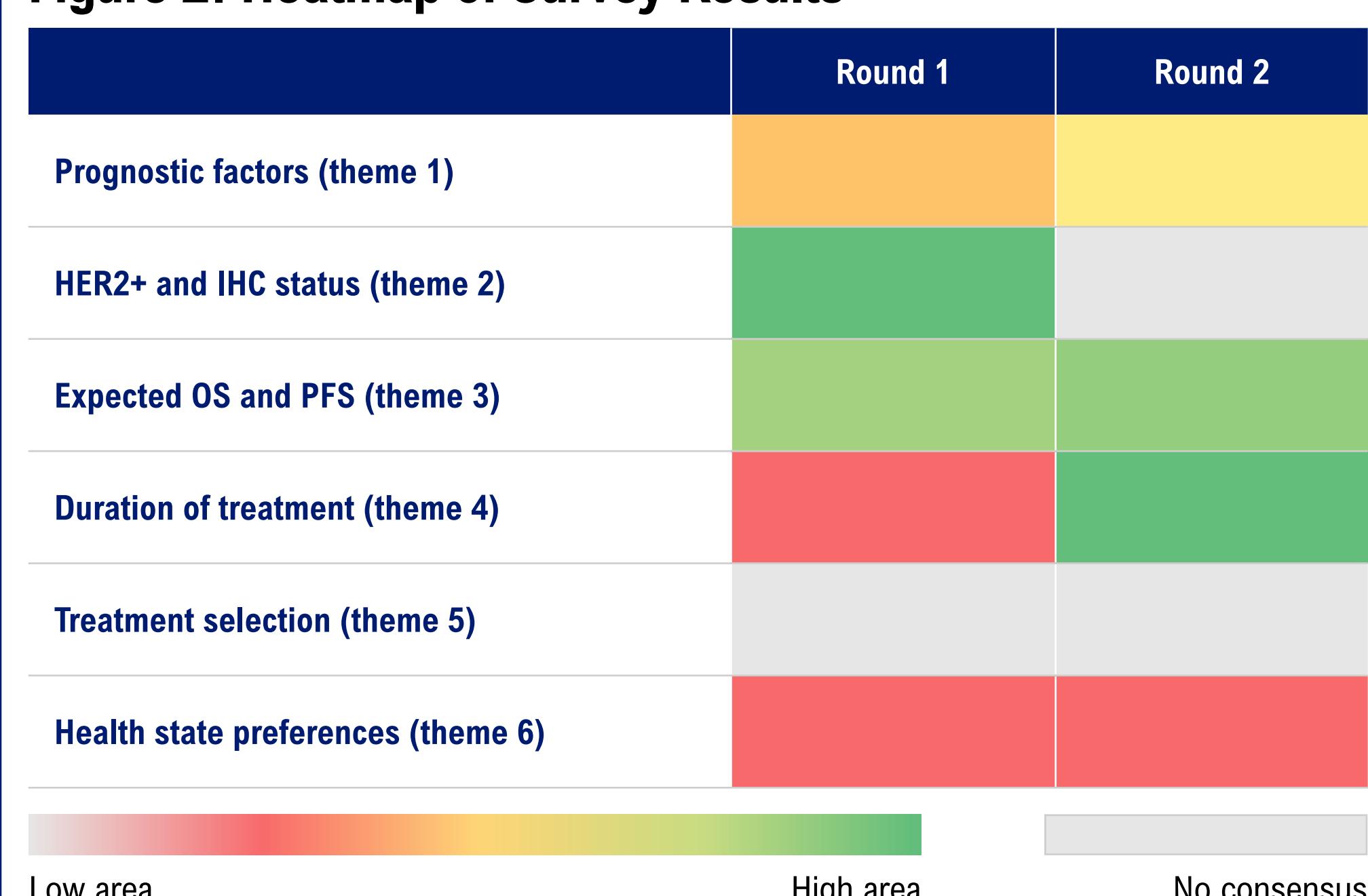
Table 1. Interpretation of Likert Scale Ratings Used for Statements

Rating Scale	Value	Grouping	Interpretation
Strongly Disagree	1	1-2	Negative consensus: Strongly disagree/disagree with the statement in this population
Disagree	2		
Neither Disagree nor Agree	3	3	Uncertain: Uncertain/do not disagree or agree with statement in this population
Agree	4	4-5	Positive consensus: Strongly agree/agree with statement in this population
Strongly Agree	5		

- Expert consensus was determined using 5-point Likert scaled questions, ranging from “strongly disagree” to “strongly agree” and interpreted using numerical value assignment
- Appropriate measures of percentage calculations, central tendency (ie, average, median), and qualitative themed analysis were employed to analyse closed-ended, multiple choice, and open-ended responses, respectively
- Based on previous literature, a cutoff value of ≥70% was used to identify consensus^{3,4}

Results

Figure 2. Heatmap of Survey Results



Heatmap displaying survey results (level of consensus by experts) across key themes. Consensus across key themes was calculated based on percentage of Likert statements achieving ≥70% agreement of the total statements presented. Themes where consensus agreement was achieved across all statements in round 1 or included no Likert statements were not included for analysis.

HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; OS, overall survival; PFS, progression-free survival.

- Round 1 and round 2 achieved 93% (n = 13) and 85% (n = 11) survey completion rates, respectively
- The integration of insights across both Delphi survey rounds enabled reporting on areas of consensus, as well as topics of remaining uncertainty
- Experts were unable to determine the relative importance of impact of prognostic factors upon overall survival (OS) and progression-free survival (PFS)
- Key prognostic factors for OS and PFS achieving ≥70% consensus included Eastern Cooperative Oncology Group performance status, stage at initial diagnosis (I–V), and metastasis/site of metastasis
- Of note, serological and inflammatory markers were unable to be validated for prognostic value during this research
- Other areas of uncertainty, where no consensus was determined, included patient health-related quality of life (HRQoL)/health state utility in the 2L setting for patients with BTC vs the age-matched population (theme 6)

Table 2. Experts' Perceptions of HER2-Targeted Therapies and HER2 IHC Testing in UK Clinical Practice

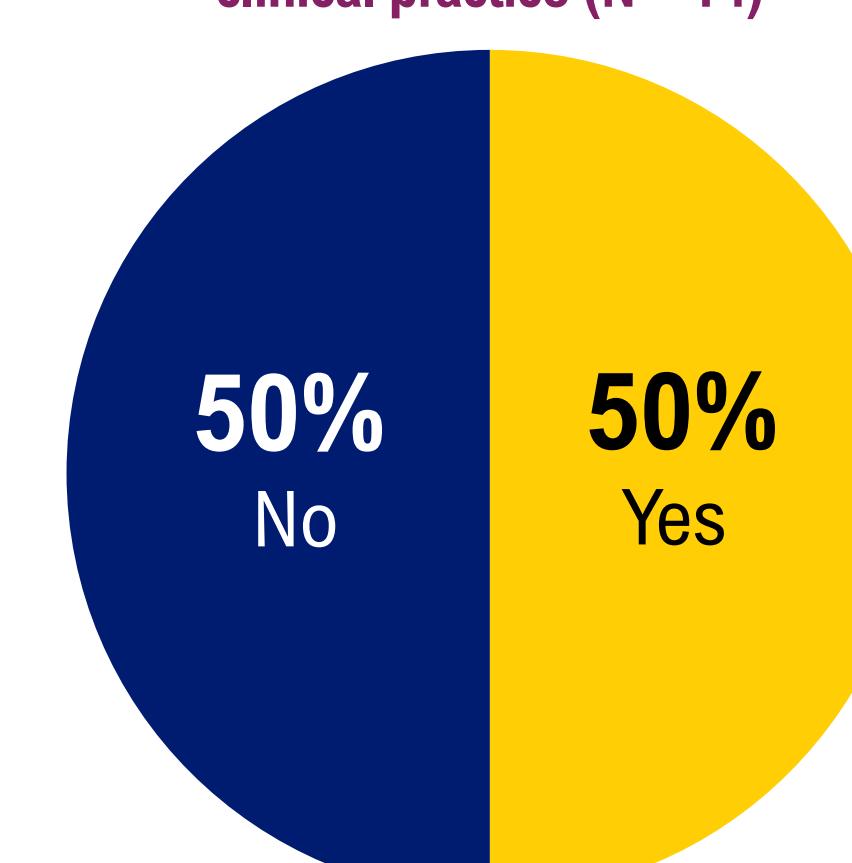
	Consensus, %	Round in Which Consensus Was Achieved
From my clinical experience, I believe conducting HER2/IHC scoring is important in improving a patient's treatment options, in particular for patients who have unresectable locally advanced or metastatic BTC (2L+)	100	Round 1
If a HER2-targeted therapy was approved for the treatment of BTC, how likely would you test for the expression or amplification of HER2/IHC status?	100	Round 1
I believe HER2-targeted therapies have the potential to improve treatment outcomes for 2L HER2+ (defined as IHC 3+ or equivalent) BTC patients, with unresectable locally advanced or metastatic disease who have received prior gemcitabine and cisplatin chemotherapy	100	Round 1

2L, second-line; BTC, biliary tract cancer; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry.

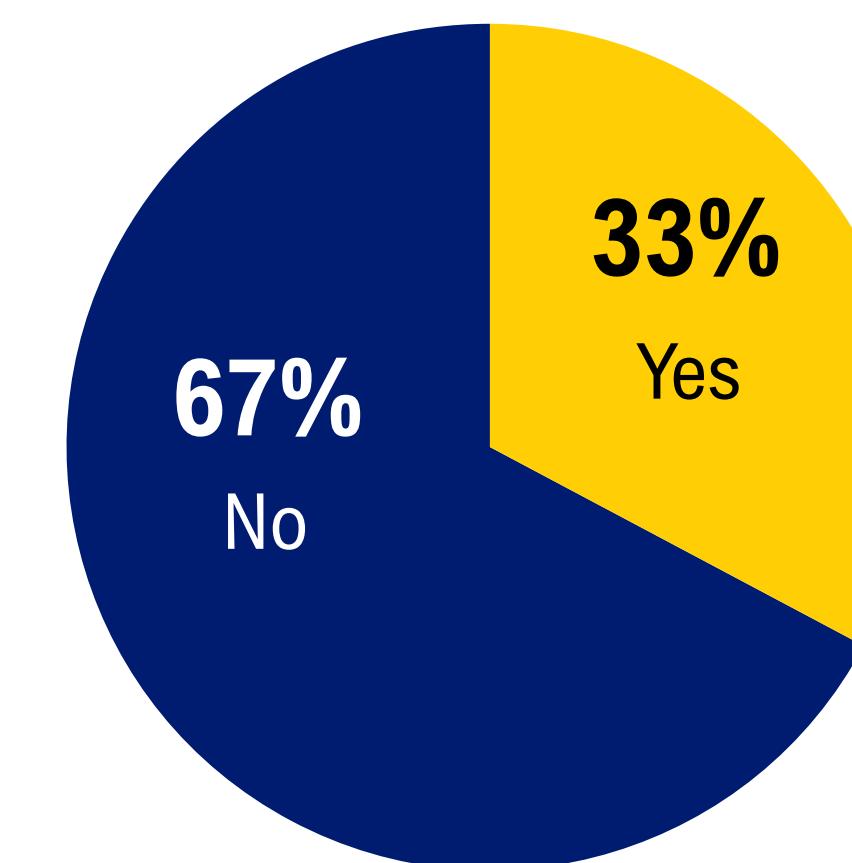
- All experts agreed that 2L HER2-targeted monotherapies had the potential to improve current outcomes for patients with BTC and would likely increase HER2 testing as part of routine care, if treatments were approved

Figure 5. Experts' Responses to Yes/No Questions About HER2 IHC Testing and HER2-Targeted Therapies

Please indicate whether HER2 IHC scoring is routinely undertaken within your clinical practice (N = 14)



Would you expect the treatment effect of a HER2-targeted monotherapy to reduce the likelihood of death (OS) to an extent equal to that of patients receiving FOLFOX + ASC? (n = 9)



Would you expect the treatment effect of a HER2-targeted monotherapy to reduce the likelihood of disease progression (PFS) to an extent equal to that of patients receiving FOLFOX + ASC? (n = 9)

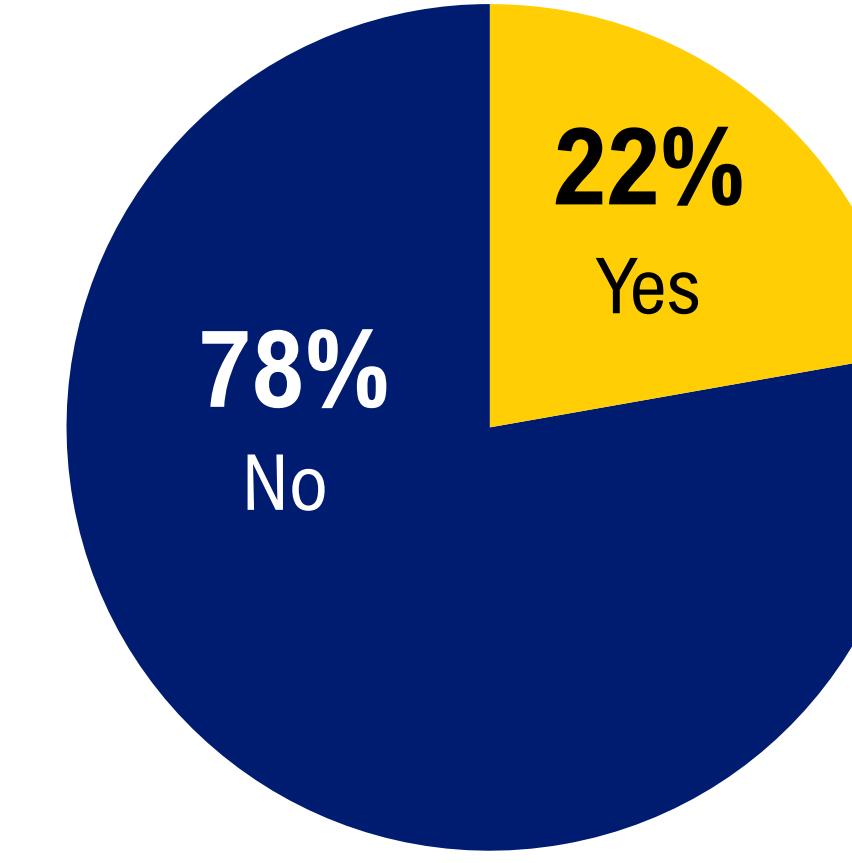
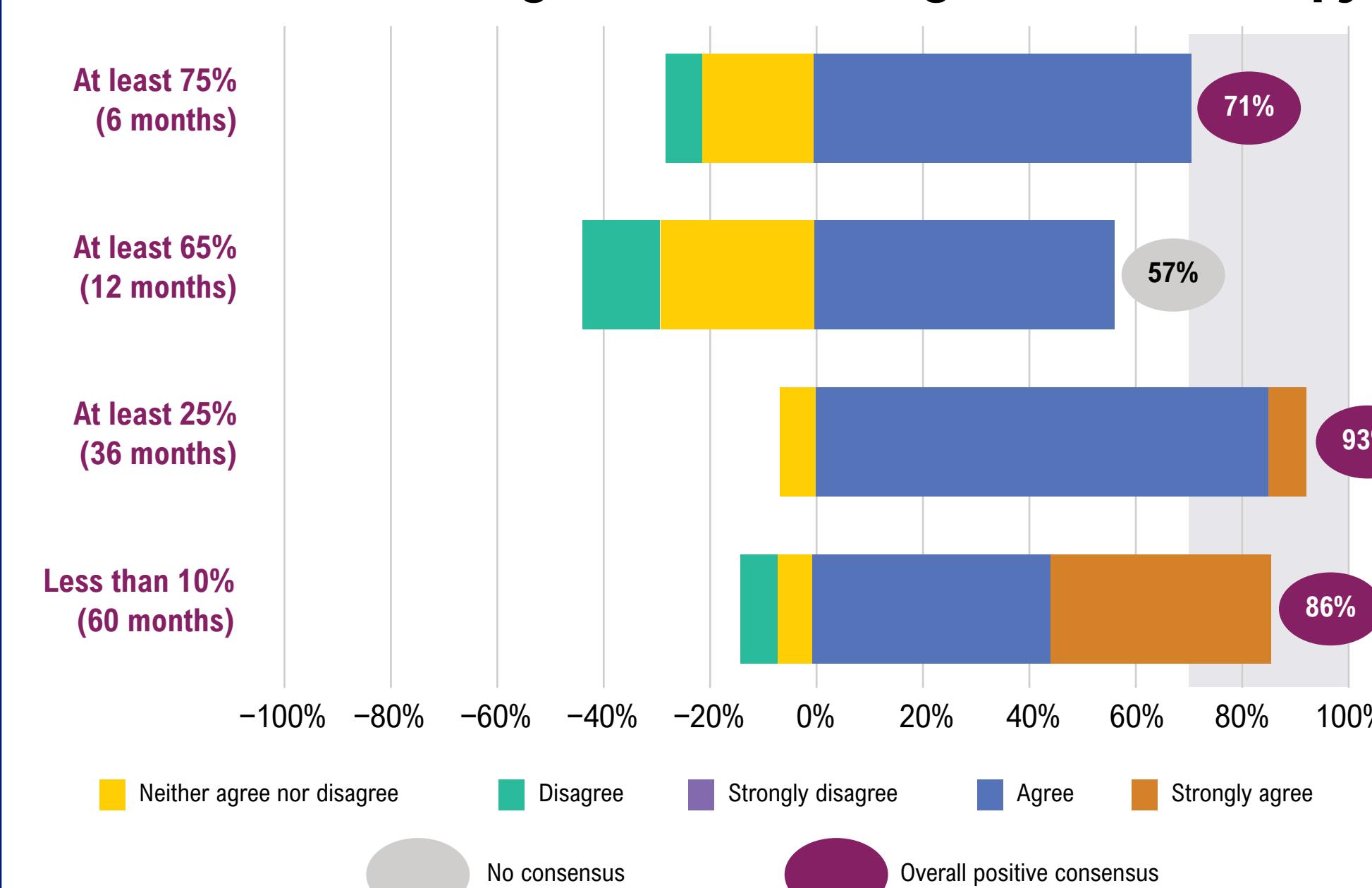
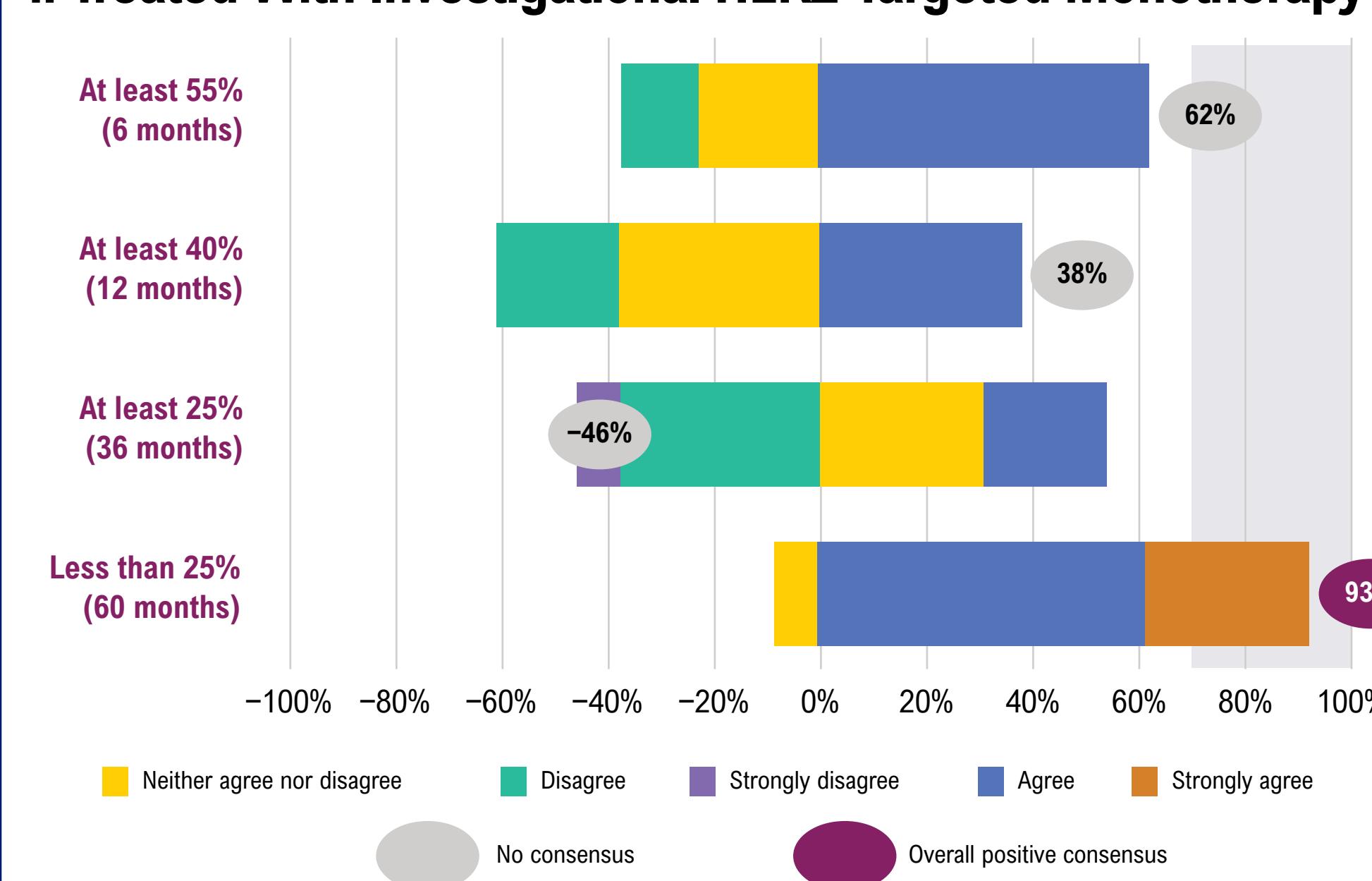


Figure 3. Estimated OS Rates Over Time for Patients With 2L+ Unresectable Locally Advanced or Metastatic HER2+ BTC if Treated With Investigational HER2-Targeted Monotherapy



Positive values on the x-axis represent overall agreement (agree or strongly agree) by experts; negative values indicate negative agreement (disagree or strongly disagree) with the given statement(s). Based on my clinical experience with targeted therapies and considering the data, I believe that for patients with unresectable locally advanced or metastatic HER2+ (defined as IHC 3+ or equivalent) BTC, treated 2L+ with the investigational HER2-targeted product monotherapy, the percentage survival rate of patients would be...
2L, second-line; BTC, biliary tract cancer; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; OS, overall survival.

Figure 4. Estimated PFS Rates Over Time for Patients With 2L+ Unresectable Locally Advanced or Metastatic HER2+ BTC if Treated With Investigational HER2-Targeted Monotherapy



Positive values on the x-axis represent overall agreement (agree or strongly agree) by experts; negative values indicate negative agreement (disagree or strongly disagree) with the given statement(s). Based on my clinical experience with targeted therapies and considering the data, I believe that for patients with unresectable locally advanced or metastatic HER2+ (defined as IHC 3+ or equivalent) BTC, treated 2L+ with the investigational HER2-targeted product monotherapy, the proportion of patients progression free would be...
2L, second-line; BTC, biliary tract cancer; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; OS, overall survival; PFS, progression-free survival.

- A ≥70% consensus agreement was achieved for OS outcomes for HER2-targeted monotherapies across different time points; however, no consensus around the precise level of PFS benefit was agreed for 6, 12, and 36 months

Conclusions

- To our knowledge, this is the first UK Delphi survey conducted in BTC
- Results from this study showed ≥70% consensus across HER2 testing, expected survival outcomes, and duration of treatment measure themes and highlighted some uncertainties, including the precise PFS benefit, relative impact of prognostic factors, and HRQoL
- An inconsistency in HER2 testing in UK clinical practice was identified for BTC
- As a rare cancer, some uncertainties are expected. A structured expert elicitation method, like the Delphi survey, can help reassure payer decision-making, enabling patient access to innovative treatments in areas of high unmet need

References: 1. Jansen H, et al. *J Gastrointest Oncol*. 2020;11(4):770-89. 2. Vogel A and Ducreux M. *ESMO Open*. 2025;10(1):104003. 3. National Guideline Centre (UK). Preoperative tests (update). In: NICE Guideline, No. 45. National Institute for Health and Care Excellence (NICE); 2016. 4. Junger S, et al. *Palliat Med*. 2017;31(8):684-706.

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Disclosures: MO, BC, JN, MJ, SB, JS, and AS are employees of Jazz Pharmaceuticals and own stock or stock options in Jazz Pharmaceuticals. MJ and SG are employees of Petauri Evidence Ltd.

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