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Quantifying the value of progression-free survival in breast cancer treatment among a general population of US women

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Objectives

To identify whether women in the US general population are willing to trade survival certainty in return for longer PFS in metastatic breast cancer treatment.

To quantify the value US general population places on a treatment with greater PFS benefits despite uncertain survival benefits.

Conclusions

Respondents preferred the therapy with longer PFS—despite uncertain OS—over the standard of care with shorter, but certain OS. Although respondents applied a penalty for reduced OS certainty, the PFS therapy was preferred due to longer pre-progression duration and potential for improved survival.

Regulators, payers, and clinicians interested in following patient-centered care should consider both treatment uncertainty and patient preferences when considering the approval, reimbursement and prescribing of new oncology therapies.

Background

- Overall survival (OS) is commonly considered the "gold standard" for assessing clinical efficacy of cancer treatments during regulatory and HTA review.[1]
- Because OS data typically takes years to collect for patients with metastatic breast cancer (mBC), progression-free survival (PFS) often serves as a surrogate endpoint in mBC treatment approvals. Gains in PFS, however, do not always result in OS gains.
- It is unclear whether patients are willing to accept treatments with proven PFS gains but with uncertainty around future OS gains.

Materials and Methods

KEY QUESTIONS

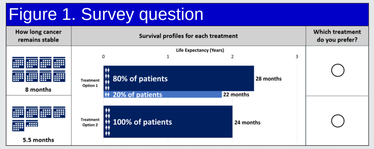
- **Q1:** What share of patients prefer therapy with longer PFS and projected superior but uncertain OS gains?
- **Q2:** How strongly do patients prefer therapy with longer PFS and uncertain OS relative to standard of care (SoC) with known OS data?
- **Q3:** How much heterogeneity is there across individuals?

SURVEY OVERVIEW

- **Purpose:** To measure the value women place on improvements in PFS when using a treatment with uncertain OS
- **Setting:** Online survey
- **Subjects:** US women ≥ 21 years with no history of cancer (Electronic informed consent was required before participation)
- Survey Instrument: Participants were presented with PFS outcomes and survival profiles for two hypothetical mBC treatments. In a sequence of choice tasks, they were then instructed to choose between the treatments, imagining they were a mBC patient (Figure 1).
  - **Option 1 ["Certain OS"]** Offered shorter PFS (5.5 months) and shorter, but certain OS (24 months) compared to Option 2
  - **Option 2 ["Uncertain OS"]** Offered longer PFS than Option 1 (8 months) and uncertain OS, with the possibilities of both longer OS (28 months) and shorter OS (22 months) OS compared to Option 1*

Participants were asked to choose between the treatment options three times, with the expected OS in Option 2 being adjusted each time.

Figure 1. Survey question



Note: In the figure, Option 1 "Certain OS" is the choice on the bottom and Option 2 "Uncertain OS" is the choice at the top.

*At the baseline, expected OS for Option 2 "Uncertain OS" was longer than the certain OS in Option 1

ELICITATION OF PFS-OS TRADEOFF

Elicitation of PFS Outcome Values (Figure 1)

- ***"How long cancer remains stable"* (i.e., PFS):** Determined using a hypothetical scenario
  - **Option 1:** Based on current standard-of-care (SoC) outcomes, the disease is controlled for approximately 5.5 months in median
  - **Option 2:** Based on early trial data in the second-line setting and ESMO guidelines,[2] new treatment extends duration of disease control by approximately 3 months, resulting in a median PFS of 8.3 months, rounded to 8 months.

Elicitation of OS Outcome Values (Figure 1)

- ***"Survival profile"* (i.e., OS) for Option 1 ["Certain OS"]:** SoC OS in FDA drug approvals estimated as 24 months in median[3,4]
- **Base case distribution of *"Survival profile"* for Option 2 ["Uncertain OS"] :** Calculated as an 80% chance of longer OS (28 months) than SoC (24 months) and a 20% chance of shorter OS (22 months) resulting in an expected OS of 26.8 months
  - OS values were calculated from clinical trials investigating mBC treatments[5-9]
    - *Positive* OS benefit: Based on studies with "positive" PFS benefits (hazard ratio (HR) < 1) and "positive" OS benefits (HR < 1)
    - *Negative* OS benefit: Based on studies with "positive" PFS benefits (HR < 1) and "negative" OS benefits (HR ≥ 1)
  - **Base case expected OS value:**
    - The initial probability distribution was estimated based on the proportion of studies in each group (positive vs. negative OS benefit).
    - From the second iteration, the distribution was updated according to the participant's previous choice

Determining the maximum risk of shorter OS (and corresponding minimum expected OS) participant is willing to accept

- This was assessed by identifying the probability of shorter OS (and hence the expected OS) under Option 2 "Uncertain OS" at which a participant is indifferent between the two treatments ("indifference point")
  - Estimated using a multiple random staircase, where participants chose between Option 1 "Certain OS" vs Option 2 "Uncertain OS", with the expected OS for Option 2 "Uncertain OS" adjusted depending on the participant's previous choice.

Estimation of Value of PFS Improvement

- **Step 1:** Determine expected OS of Option 2 "Uncertain OS" at baseline (first-choice iteration) → Base case expected OS
- **Step 2**: Derive the median of the probability range for longer OS from the last choice question and compute the expected OS based on the resulting probability distribution of longer and shorter OS outcomes → Indifference point for expected OS (Figure 2)
- **Step 3:** Calculate the difference between the indifference point for expected OS and the certain OS for Option 1, which is the additional value from the improvement in PFS after accounting for the uncertainty in expected OS

Results

PARTICIPANT CHARACTERISTICS

- The 306 participants had an average age of 51.8 years, 93.7% were insured, 76.1% were white, and 52.5% had a bachelor's degree or higher.

PRIMARY ANALYSIS

- **Q1: Preference for longer PFS benefits with uncertain OS** (Figure 2)
  - In the first iteration, **53%** (n=162) of participants indicated a preference for Option 2 (offering longer PFS with uncertain but longer expected OS).
- **Q2: Improvements in PFS provide value over the SoC** (Figure 3)
  - While expected survival for Option 2 was 26.8 months, individuals valued these survival gains less—due to risk aversion. The survival gains for Option 2 were only valued at 25.84 months, a reduction of 0.96 months.
  - Nevertheless, this valuation was still significantly greater than the OS of Option 1 (offering certain OS of 24 months). Thus, after accounting for uncertainty, the *incremental* PFS value of Option 2 was **1.84 months**.
- **Q3: Preferences were highly heterogeneous** (Figure 2)
  - **24.8% (n=76) always preferred Option 1** with shorter PFS and certain OS, even when the expected OS in Option 2 was 3.7 months longer (27.7 months) than the certain OS of Option 1.
  - **19.6% (n=60) always preferred Option 2** with longer PFS and uncertain OS even when the expected OS was 0.8 months shorter (23.2 months) than the certain OS in Option 1.

Figure 2. Survey Decision Tree with OS Probability Distribution for Option 2

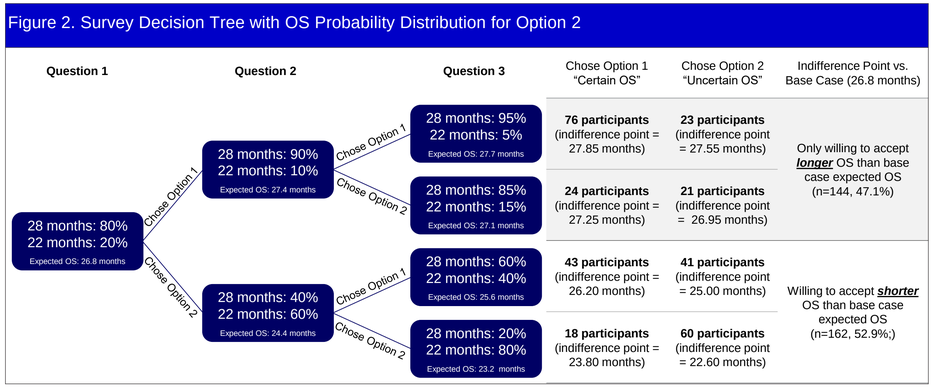
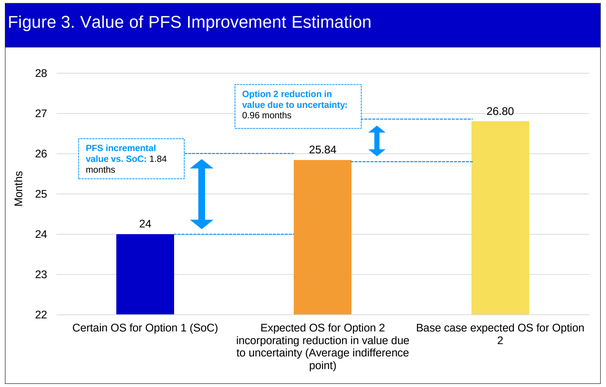


Figure 3. Value of PFS Improvement Estimation



Discussion

- Most participants chose the treatment option with longer PFS even if there was some possibility of shorter OS.
- Preferences varied significantly across individuals in the sample.

Limitations

- The study did not explicitly describe quality of life benefits with PFS and thus may underestimate the value of treatments with increased PFS.
- The study included only women from the US general population at risk of breast cancer, which may limit the generalizability.
- The online survey format required internet access and digital literacy, potentially excluding groups whose preferences may systematically differ.

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