PREFERENCES FOR AND IMPORTANCE OF EARLY ONCOLOGY TRIAL ENDPOINTS TO CANADIANS WITH EARLY-STAGE CANCER

A QUALITATIVE PATIENT PREFERENCE STUDY

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BACKGROUND

- Overall survival (OS) has been considered the gold standard for measuring efficacy and evaluating the clinical benefits of many treatments in oncology.[1]
- The increasing number of novel therapeutics in early-stage cancers has brought challenges related to relying on early endpoints as surrogates for OS, from the perspective of decision-makers.[2, 3]
- Early-stage oncology trials that assess early, non-OS, endpoints such as recurrence-free survival (RFS), disease-free survival (DFS), event-free survival (EFS), and pathological complete response (pCR) are becoming more frequent.
  - Compared to OS, non-OS endpoints are often assessed at an earlier time point in clinical trials, providing a timely surrogate measure that can demonstrate the value of early-stage cancer therapies in advance of mature OS data.[4,5]
- These endpoints are well-defined in clinical trials and have some acceptance by decision-making bodies that assess new therapies; however, consideration of the value of non-OS endpoints from the patient perspective is currently limited.[6,7]

OBJECTIVE

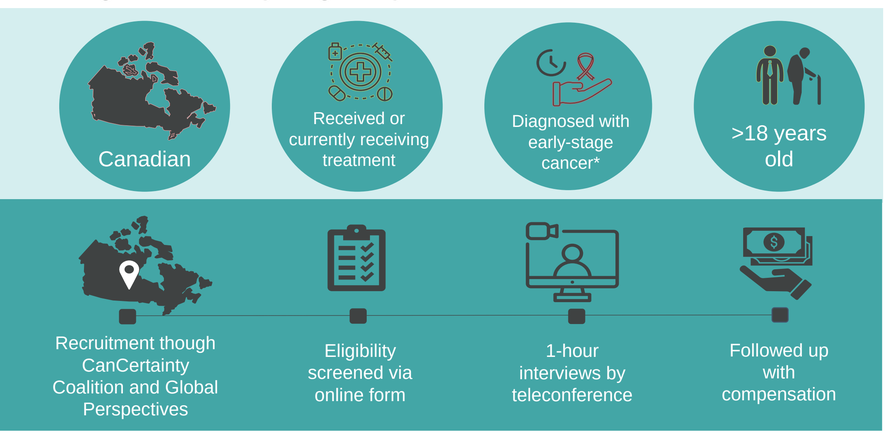
To explore perspectives on early oncology trial endpoints among Canadians with early-stage lung, breast, and liver cancer.

METHODS

DATA COLLECTION

- Canadians living with lung, breast, or liver cancer were recruited through CanCertainty and partner networks.
  - CanCertainty is a coalition of Canadian cancer patient groups, charities, and caregiver organizations that work with cancer care professionals to improve the affordability and accessibility of cancer treatment.
- Eligible individuals participated in one-hour virtual semi-structured interviews (Figure 1) and provided brief demographic details which aligned with Canadian census data collection categories.[8]
  - Recruitment quotas were used to ensure the sample was diverse with respect to cancer type, staging, and time since diagnosis.
- Participants described their cancer journey and provided perspectives on OS, RFS, EFS, DFS, and pCR endpoints.
  - Definitions of endpoints were provided with explanatory graphics to illustrate key constructs (see QR code for examples).
- Ethical approval was granted by the Western Copernicus Group (WCG) Institutional Review Board (IRB); all participants provided consent prior to and were remunerated $100 CAD for the interview.

Figure 1: Study eligibility criteria and recruitment methods



*Self-confirmed diagnosis of stage I-IIIC breast cancer **or** stage IB-IIIA lung cancer **or** stage 0, A, or B liver cancer.

ANALYSIS AND SYNTHESIS OF DATA

- Interview content was transcribed, and transcripts independently reviewed for data familiarization by two analysts.
- Reflexive thematic analysis was used to explore patterns in responses, and alignment of trial endpoints with patient treatment goals, priorities, and preferences.
  - Analysis was conducted in accordance with the principles and guidelines described by Braun and Clarke.[9]
- Codes were assigned to all aspects of the data describing treatment experiences, priorities, and views on the individual endpoints; coding was iterative, with continuous addition of new codes and refinement in existing codes.
- Codes were grouped into categories that formed the basis for constructed themes. Supportive quotes were identified, and themes visualized using a thematic map.
- All analyses were conducted in NVIVO and Excel.

RESULTS

- Disease characteristics of the 28 participants are provided in Table 1. Most participants were White (86%, n=24); 82% reported having surgery (n=23), 75% received systemic therapy (n=21), and 54% had received radiation (n=15).
- 50% of participants were from the province of Ontario (n=14); 75% had at least a university degree (n=21); and 39% worked full-time (n=11).

Table 1: Participant and disease characteristics

	Overall (n=28)	Diagnosed with: Breast cancer (n=12)	Lung cancer (n=11)	Liver cancer (n=5)*
Age (SD)	53.6 (11.7)*	46.3 (9.3)	62.9 (8.9)	49.0 (3.6)*
n (%) female	20 (71%)	12 (100%)	8 (72%)	0
Disease stage, n(%)				
Lung and breast/ liver				
I / 0	9 (32%)	6 (50%)	2 (18%)	1 (20%)
II / A	8 (29%)	3 (25%)	2 (18%)	3 (60%)
III / B	7 (25%)	1 (8%)	5 (45%)	1 (20%)
Unknown	4 (14%)	2 (18%)	2 (18%)	0
Recurrence status				
No evidence of disease	14 (50%)*	6 (50%)	8 (73%)	0 (0%)*

PERSPECTIVES ON ENDPOINTS

- All participants highly valued survival and found OS to be an important endpoint. However, they also noted that OS alone does not capture the whole patient experience (Figure 2).
- Participants regularly indicated their assumption that achieving improved clinical benefits measured by early endpoints, would translate to longer overall survival, even when told there was presently limited evidence to support that assertion.

Figure 2: Perspectives on the value of OS

Strengths

Easily understood endpoint

"…it's information that we've been conditioned to want to know. Everyone wants to know, with a diagnosis, 'Well, what does that mean for me? In terms of longevity, …what am I dealing with here?' "- ID02, breast cancer

Provides valuable benchmarks and lets one understand how different therapies perform

"It helps you plan for the rest of your life. If somebody says to you, 'You have one year to still be alive' or 'You have 10 years to be alive' I think you would behave differently. You would pack these 10 years in one year. [laughs] And do everything you wanted to do…[OS] has some importance for the quality of life and what you want to achieve in your life" -ID11, lung cancer

One of the main goals of treatment

"Yes…That was a biggie for me, just to survive as long as possible… do anything you can to make sure that you survive." -ID 22, lung cancer

Limitations

Measures length but not quality of life; survival without 'good' quality of life isn't desirable by most

"It's a funny word, 'survival,' because that …captures the essence of everything you're asking, really. Are you just looking to 'survive'? Are you looking to really lead a completely normal and healthy life going forward, and where is the gap between those two things?" - ID26, liver cancer

Can be misleading in early-stage cancers where it does not account for competing risks of mortality

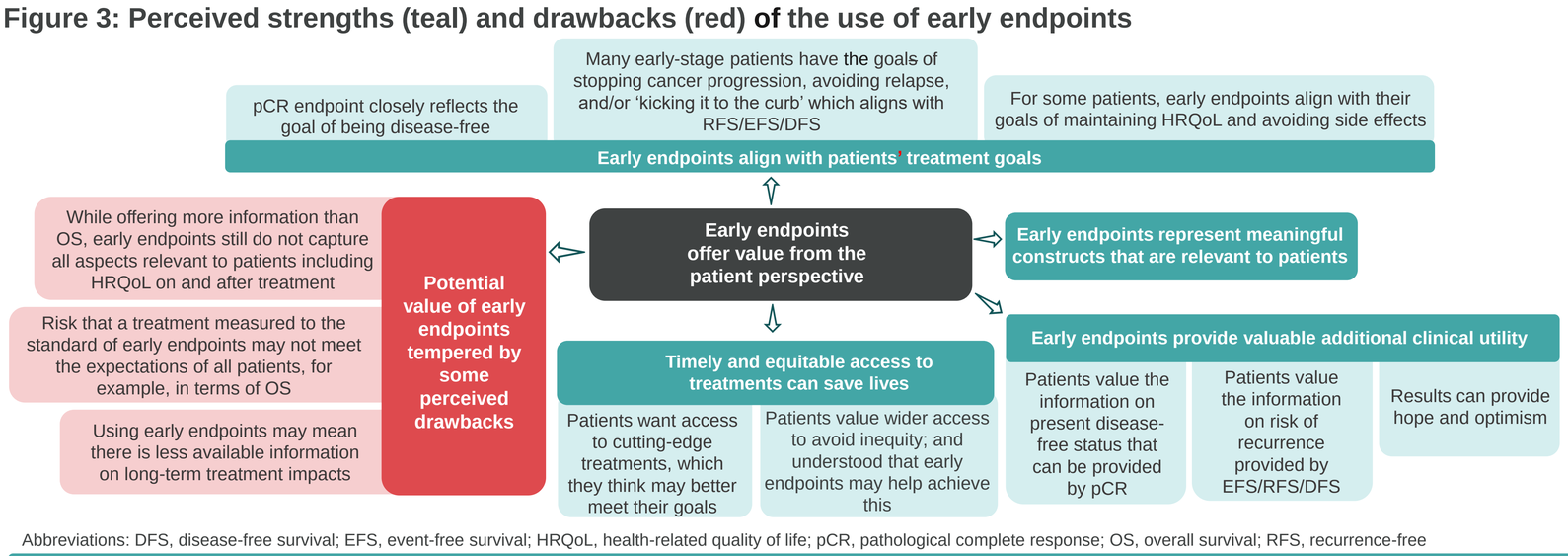
"Also, there's just that random factor of all the other things that could lead to death. That, to me, feels like a huge variable that is not at all controlled….Anyone could die at any point in time for any measurable thing, but knowing that the cancer isn't coming back means that that is one thing that I can eliminate from the everything else in life that I need to stress about." – ID08, breast cancer

Can take a long time to measure

"Just because of the length, it means that we're still evaluating things that came out 10+ years ago. That scares me that if we're waiting on certain metrics of overall survival that drugs that can save people's lives aren't going to be getting into people's bodies in time." – ID23, lung cancer

- Participants also noted that early endpoints offer value from a patient's perspective (Figure 3).
  - Participants viewed RFS, DFS, EFS, and pCR as reflective of their treatment priorities, including maintaining health-related quality-of-life (HRQoL), getting back to 'normal', and being disease-free.
  - Non-OS endpoints represent meaningful constructs and provided valuable clinical benefits beyond survival; participants considered early endpoints sufficient evidence of efficacy to want access to new treatments.
  - Participants placed high value on having treatment options; and equated having more options with better options, and timely access as critical for saving and improving lives.

Figure 3: Perceived strengths (teal) and drawbacks (red) of the use of early endpoints



Abbreviations: DFS, disease-free survival; EFS, event-free survival; HRQoL, health-related quality of life; pCR, pathological complete response; OS, overall survival; RFS, recurrence-free

Align with patients' treatment goals

"To a cancer patient, clear margins are extremely important for your [physical] health and mental health…because if you can say, 'Okay, there's no more cancer in me,' that gives you a very positive outlook on the future. So, yes, if a doctor offered me another treatment …that would say, '80% of people did very well with this. They had clear margins afterwards,' yeah, I absolutely would." – ID14, lung cancer

"I wanted ...treatment to essentially make me disease-free; …[so] I don't have to go through the same thing in a few years time... sometimes when you've just climbed that mountain and there's another peak which you have to climb again, it's just like, 'Not again. I can't do this again.'... So, yeah, that was very important for me to... kind of anticipate what's in the future for me when it comes to this disease."– ID29, liver cancer

Provide valuable information

"I am most interested in [RFS] because it weighs very heavily on me, and many cancer patients live with that sort of threat or fear for the rest of their lives, of recurrence…Knowing the rates of recurrence-free survival would be very useful information for me." – ID02, breast cancer

"I like [the] DFS [endpoint]. I don't want to think about it in terms of a decade or 15-20 years. I really want to focus on something more achievable and relevant to me in the short-term." – ID25, liver cancer

Access to treatment

"Definitely I would say to decision makers that, at the speed at which the science is going, if you're waiting, as you wait, the cost is lives of people. And yes, there is uncertainty [with e.g., DFS], and I would put some boundary of certainty in the goodness and the challenges of treatment. But waiting for a very long time to make drugs appear, as somebody who has cancer, it's kind of a little bit crazy [laughs]." – ID11, lung cancer

"I think that our system, drug approvals and clinical trials take way too long to be able to get approved. It's hard to see things that are available to people in other countries that should be available to us here, but you can't have access unless you have money. It's frustrating." – ID07, breast cancer

Perceived drawbacks

"There are some long-term use impacts associated with a drug that are just unknown at the time of [early endpoints] that only in time would become evident. And so that is a risk that you would have to consider before agreeing to the treatment. But I think in most circumstances, and certainly in my circumstance, the risk of the cancer killing you is greater, so you kind of take those risks and hope for the best." – ID02, breast cancer

"Well, faster access would mean less information and less reassurance to offer people because there wouldn't be the data." – ID07, breast cancer

- While participants agreed that achieving pCR was a priority in their own treatment journey, they predominantly valued medium- to long- term outcomes like HRQoL and remaining cancer-free over time.
- The relative importance of being recurrence-free versus maximizing the length of life may differ based on age, recurrence status, prognosis, cancer type, and life stage.

DISCUSSION

- Limited research exists exploring the relative importance of non-OS endpoints from an early-stage cancer patient perspective, compared to OS as a traditional measure in oncology;
  - This research highlights that non-OS endpoints are of value to patients as they are personally meaningful and may be impactful on their treatment decisions and journey.[10,11]
- Canadians with early-stage lung, breast, or liver cancer found early endpoints highly related to their treatment priorities and believed they provided meaningful clinical information that would augment their understanding of one's status and prognosis compared to OS alone.
  - This is corroborated by other quantitative studies in oncology which have reported that patients value pCR and other early, non-OS, endpoints; in that study, the relative importance of treatment characteristics varied by age, time since diagnosis, and disease stage.[12]
- Participants also valued timely access to innovative treatments, which can be facilitated through the use of non-OS endpoints to inform reimbursement decisions while awaiting mature trial data.[13]
- Study limitations include a high concentration of participants living in the province of Ontario (although nearly 40% of Canadians live in that province),[14] and who are White. Additionally, lung cancer patients were mostly female, despite a high incidence of lung cancer in both men and women.

CONCLUSION

These findings support the relevance and importance of early, non-OS, oncology endpoints – such as DFS, RFS, EFS and pCR – to Canadians with early-stage lung, breast, and liver cancer. Participants found the clinical information provided by non-OS endpoints to be valuable; that they align with treatment goals focusing on avoiding events like recurrence or progression to more advanced stages of disease; and that they provide optimism for better survival. Participants emphasized the need for timely access to new treatments that demonstrate meaningful clinical improvements in HRQoL and non-OS endpoints, even in the absence of OS data.

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