BRIEF REPORT

The Perceived Value of Liquid Biopsy: Results From a Canadian Validation Study of Circulating Tumor DNA *T790M* Testing—Patient's Willingness-to-Pay: A Brief Report

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ABSTRACT

Introduction: Liquid biopsy is recommended to diagnose molecular resistance to targeted therapy in patients with lung cancer. Nevertheless, not all jurisdictions provide funding and patient access. We report patients' perceived value of liquid biopsy in targeted therapy resistance.

Methods: Canadian patients participating in a national EGFR T790M liquid biopsy validation study completed structured interviews measuring perceived value and

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willingness-to-pay for plasma circulating tumor DNA testing as an alternative to tumor biopsy using open-ended and iterative bidding approaches.

Results: A total of 60 patients with advanced lung cancer participated with a median age of 64 years (range: 31–87 y); 69% were Asian and 45% female. All had received prior EGFR tyrosine kinase inhibitor; 17% also received chemotherapy. All patients preferred to have plasma testing over repeat tumor biopsy. In the context of the Canadian publicly funded system, patients estimated that a median of 300 (interquartile range: 150–800) Canadian dollars was a reasonable price to pay for liquid biopsy. Patients were personally willing to pay a median 100 (interquartile range: 33–350) Canadian dollars.

Conclusions: In a system that covers the cost of standard diagnostic tests, patients with lung cancer indicated high willingness-to-pay out-of-pocket for liquid biopsy in the setting of acquired targeted therapy resistance. Patients have high perceived value of plasma genotyping and prefer it to repeat tumor biopsy.

Keywords: Non–small cell lung cancer; Willingness-to-pay; T790M; Liquid biopsy

Introduction

Liquid biopsy for genotyping in patients with advanced lung cancer is now routinely recommended.[1,2] These are often preferable for patients as they are minimally invasive, can have rapid turnaround time compared with repeat tissue biopsy and molecular profiling, and can monitor tumor changes in real time with less morbidity than serial biopsies.[3] Willingness-to-pay (WTP) evaluations are used to measure a patient's perceived value or impact of a certain commodity, for example, a new technology, such as liquid biopsies.[4] This is done through surveying individuals and assessing how much they would hypothetically pay for the new technology.[5]

Plasma testing for EGFR T790M resistance mutations after development of resistance to first- and second-generation EGFR kinase inhibitors has been widely validated and found to be highly concordant with tissue genotyping.[6–8] It may also be potentially cost saving and easier for patients.[8] Although osimertinib, a potent EGFR T790M inhibitor, has emerged as the first-line standard for patients with advanced sensitizing EGFR-mutant lung cancer, patients in many countries are unable to afford this and continue to use first- and second-generation EGFR tyrosine kinase inhibitors (TKIs). In addition, EGFR T790M mutations continue to be an important mechanism of resistance to EGFR exon 20 inhibitors and novel EGFR inhibitors, such as zorifertinib.[9–11]

We interviewed Canadian patients with advanced lung cancer about their WTP for liquid biopsies in the setting of EGFR resistance to explore perceived patient value, which may in turn help inform government funding decisions.

Table 1. Demographic Details of the Surveyed Patients (N = 60)

Study Population	N = 60
Age (y)	Median 64 (range: 31–87)
Sex	
Male	55%
Ethnicity	
Asian	67%
Lines of treatment	Median 1 (range: 1–6)
Smoker (active/former)	35%
EGFR mutation (reidentified in biopsy)	31/39
T790M mutation detected	19/44

Materials and Methods

The conduct of this study was approved at all participating centers by their institutional research ethics boards and conducted in accordance with the Principles of Helsinki. All patients provided written informed consent before participating. Patients were recruited to a national validation study of plasma EGFR T790M testing at six Canadian sites. Validation of liquid biopsy using digital droplet polymerase chain reaction (ddPCR) or next-generation sequencing (NGS) was undertaken and reported elsewhere.[8] Consenting patients also underwent a short structured interview (Supplementary Appendix) to assess their perceived value of blood-based circulating tumor DNA, a testing in comparison to repeat tissue biopsies. All patients were to have undergone repeat tissue biopsy before participation in the study, but before liquid biopsies were obtained. In brief, the patients were read a hypothetical scenario in which they were given a choice between a biopsy or blood draw for genomic diagnosis of cancer resistance. Each procedure was described along with the potential risks and time required. If patients expressed preference for the blood draw, they were surveyed on how much they would be willing to pay for the test using an iterative bidding approach. The interviewer would increase the price of the bid until the respondents said "no" and then decrease the cost by increments to identify the cutoff value. The patients were then asked what a reasonable price for the test should be.

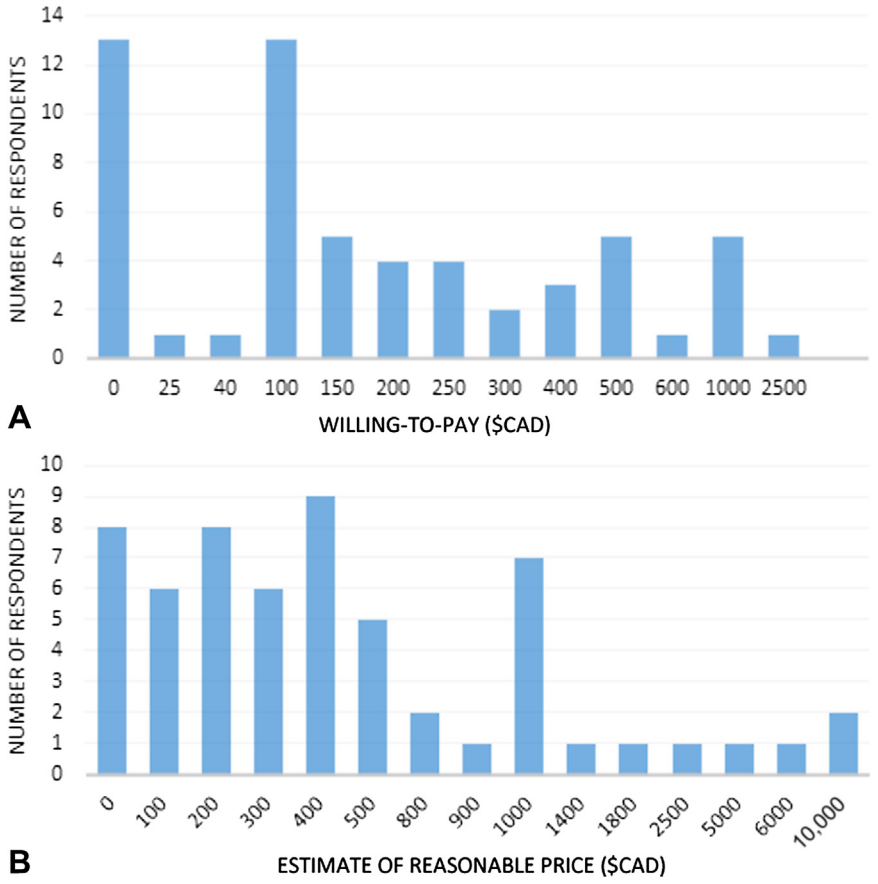

Figure 1. Perceived value and willingness-to-pay for plasma ctDNA T790M testing. (*A*) Patient willingness-to-pay; (*B*) Patient estimate of reasonable price to pay for plasma testing. CAD, Canadian dollar; ctDNA, circulating tumor DNA.

Demographic data were collected, but data on income and employment were not collected owing to previous studies in which patients declined to disclose this information.[12]

Results

All 60 participants in the plasma validation study at the six participating sites completed the WTP interview. Demographics of the cohort are found in Table 1. The median age of the patients was 64 years (31–87 y), and most patients were Asian and never smokers. All patients received prior EGFR TKI, 67% having received gefitinib and 17% also received chemotherapy.

All patients preferred liquid biopsy over repeat tissue biopsy. Patients were willing to pay a median of 100 Canadian dollars in the setting of the Canadian health care system (mean $281, $0–$2500, interquartile range $33–$350) (Fig. 1*B*). They estimated a reasonable price to pay at 300 Canadian dollars median (mean $954, $0–$10,000, interquartile range $150–$800) (Fig. 1*A*). Nearly one-quarter of the patients (22%) said that they would not or could not pay for the liquid biopsy procedure.

Conclusions

Current guidelines recommend plasma testing in the setting of EGFR TKI resistance, but this is not funded in all jurisdictions, for example, in Canada. In our study, patients preferred and perceived high value for liquid biopsies. They were willing to pay a median $100 and estimated $300 as a reasonable price despite being in the context of a universal public system in which diagnostic tests are routinely funded. The current cost of tissue biopsies is approximately $2350 in the Canadian public system, whereas ddPCR testing for plasma EGFR T790M testing is approximately $375.[13]

WTP studies reveal societal preferences and help with better understanding risk and reward tradeoffs an individual will make for their own health. Tissue biopsies are more expensive, more likely to yield complications, and are more inconvenient for patients. Public systems such as Canada could save money and conserve precious biopsy resources through the use of liquid biopsy. Despite this, Canada has not proceeded with public funding of liquid biopsy despite positive HTA recommendations.[14]

There are limitations to the generalizability of our results owing to the relatively small sample size. In addition, data on individual income were not collected owing to patient reluctance on a previous survey.[12] Nonetheless, it is worth noting that results from WTP studies in this context are likely correlated with an individual's financial capacity, as it is known that patients with lung cancer often experience high financial toxicity and lower income.[15] Although this study predates implementation of osimertinib for first-line treatment of EGFR-mutated lung cancer, T790M testing remains globally relevant in countries where patients can only afford gefitinib and afatinib. Detection of T790M mutations is also associated with resistance to exon 20 inhibitors and novel agents such as zorifertinib.[9–11] In our clinical validation study, all patients had plasma testing with ddPCR, although some also had NGS testing. Osimertinib resistance is more genomically complex and requires more complex technology such as NGS to elucidate the spectrum of molecular resistance.[16] In our study, we did not specify the testing method for resistance, but rather patient preference and WTP for liquid biopsy in this setting. Furthermore, given that patient WTP is often limited by their ability to pay, we would not expect major differences in WTP whether we specified ddPCR versus NGS in the context of this study.

On the basis of clinical benefit and improved system efficiency, cost, patient preferences, and perceived value for liquid biopsies, we believe that plasma testing should be funded in more jurisdictions. More WTP studies may help health care payers better understand the utility and importance of investing in novel diagnostic methods such as liquid biopsy.

CRediT Authorship Contribution Statement

Kaitlin H. Chen: Writing—original draft, Writing—review and editing, Visualization.

Tristan A. Barnes: Writing—original draft, Investigation, Visualization, Data curation.

Janessa Laskin: Data curation.

Parneet Cheema: Resources, Data curation.

Geoffrey Liu: Resources, Data curation, Formal analysis.

Mussawar Iqbal: Data curation.

Jeffrey Rothenstein: Formal analysis, Data curation.

Ronald Burkes: Resources, Data curation.

Ming-Sound Tsao: Conceptualization, Funding acquisition, Project administration, Resources, Data curation, Formal analysis.

Natasha B. Leighl: Writing—original draft, Writing—review and editing, Supervision, Conceptualization, Project administration, Resources, Data curation, Formal analysis.

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Supplementary Data

Note: To access the supplementary material accompanying this article, visit the online version of the *JTO Clinical and Research Reports* at www.jtocrr.org and at 10.1016/j.jtocrr.2023.100615.

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