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LETTER TO THE EDITOR



Response to "Need to minimize bias when surveying patient attitudes to stopping CML treatment"

The Editor,
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We thank Villemagne *et al.* for their comments, and we will address some of the issues that they raised.

It is important that clinicians understand patient concerns and values before key treatment decisions are made. Hypothetical scenarios such as "what if" or "when this occurs" are discussed routinely in close patient–physician relationships, and for that reason, we reject the assertion that our sample is not representative of patients with chronic myeloid leukemia (CML) who might be eligible for stopping tyrosine kinase inhibitors (TKIs). We contend that it is not necessary for patients to have achieved a sustained deep molecular response (Bcr-Abl $\leq$ 0.0032%) to make informed responses to a hypothetical scenario. It is unknown whether a group of patients who have achieved a deep molecular response would respond differently than would patients whose molecular response might have not been optimal.

For the second point, consecutive patients with CML being treated by the investigators were approached for participation in the study during the study period.

We agree with the third comment that our single-centre study might have allowed for the opinion or influence of a small number of clinicians to have a significant impact on patient responses, which is explicitly stated in the Discussion section of the article. The reference cited by Villemagne *et al.* to support the statement that "studies of compliance in CML have shown a much more complex array of behaviours and choices" is also a single-centre study and subject to the same limitations[1].

In response to the measurement tool, Villemagne *et al.* suggest that the first two measures of patient preference for relapse rates are confounded with willingness to stop treatment. Again, it is important to understand that the patient scenario is laid out with the remarks that the questions are hypothetical, that the response will not affect current clinical care, and that the very first question is asking about willingness to stop. There is no assumption of willingness to stop in the first question. It was not our intention to use only patients who are in deep molecular response and who are willing to stop to assess risk acceptability. Rather, we wanted to gauge the response of the general CML population who might or might not be faced with that decision. The visual analog scales were not modified from their original formats (with a 0 labelled the worst imaginable health state and a "sad face"). That presentation did cause some difficulty in interpretation of the question by the patients, but it was clarified by the interviewer in a standardized fashion.

We agree that patient compliance is complex, that our choices do not make a distinction between unintentional and deliberate noncompliance, and that self-reported measures of compliance are notoriously unreliable. The two references listed by Villemagne *et al.* as having validated measures for patient-reported outcomes of compliance and toxicity specific to CML have no documentation of the inclusion of CML patients in the studies[2,3]. The first study, by Morisky *et al.*[2], dealt with adherence in hypertensive patients, and the second study, by Cleeland *et al.*[3], categorized only 7 of 527 patients as having chronic leukemia in the outpatient setting, without clarifying the type of chronic leukemia. We agree that the evidence suggests that patients are more likely to misrepresent their treatment adherence in clinical settings; however, we conducted an interviewer-led study using an independent surveyor who had no involvement in patient care to minimize such bias. As discussed, conveying risk in treatment decisions is complex and is influenced by patient–physician communication and relationship[4]. Those interactions are also affected by physician beliefs about the quality of evidence, which influences how information about risk is conveyed to patients. Objective standardized patient education and decision tools can be useful adjuncts in such circumstances[5].

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We have outlined the various limitations of our study, but it nevertheless represents real-life discussions that can arise with patients who are generally well informed and interested in taking greater ownership of their health. Larger studies of stopping TKIs are being done, and we anticipate that the question of stopping will arise for some patients. Our study offers a glimpse of how patients might approach this issue. Thus, the average patient with CML on a TKI approaching this hypothetical question based on a personal opinion of "compliance" and a personal view of side effects might or might not be willing to stop. Larger multicentre studies can be performed, but ultimately each patient makes a personal decision based on their own perceptions of level of "compliance," severity of side effects, and risk acceptability. The main message of the paper is that patients are capable of balancing risk, and the choice to stop a TKI should involve shared decision-making between the patient and the clinician, which has been reported to be the approach preferred by most patients with cancer[6].

David Sanford MD
Department of Medicine, Division of Hematology
London Health Sciences Centre
University of Western Ontario

Rachel Kyle BSc
Schulich School of Medicine and Dentistry
University of Western Ontario
London, Ontario

Alejandro Lazo–Langner MD MSc
Department of Medicine, Division of Hematology
London Health Sciences Centre
Department of Epidemiology and Biostatistics
University of Western Ontario
London, Ontario

Anargyros Xenocostas MD
Department of Medicine, Division of Hematology
London Health Sciences Centre
University of Western Ontario
London, Ontario

Ian Chin–Yee MD
Department of Medicine, Division of Hematology
London Health Sciences Centre
University of Western Ontario
London, Ontario

Kang Howson–Jan MD
Department of Medicine, Division of Hematology
London Health Sciences Centre
University of Western Ontario
London, Ontario

Cyrus C. Hsia MD
Department of Medicine, Division of Hematology
London Health Sciences Centre
University of Western Ontario
Victoria Hospital, Room E6-219A
800 Commissioners Road East
London, Ontario
Cyrus.Hsia@lhsc.on.ca

CONFLICT OF INTEREST DISCLOSURES

RK, DS, ICY, AX, and KHJ have no conflicts to disclose. CH has received honoraria from Novartis, and ALL has received honoraria from Pfizer, Leo Pharma, and Boehringer Ingelheim.

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