We thank Xu et al for their interesting observations focussed on response-guided therapy in the era of directly acting antivirals. We support their view that strategies proposed to date to select those patients who may be cured with 4 weeks (ultrashort) treatment are still not able to offer high enough cure rates to be recommended routinely. However, it is worth noting that the 80% SVR12 rates in those selected for 4 weeks' treatment in this trial, based on day 7 (D7) viral load under the lower limit of quantification (LLOQ), are the highest of studies to date.

Of potential next steps, they highlight two. Using the same diagnostic strategy as our trial with 6 rather than 4 weeks therapy for those below LLOQ at D7 would undoubtedly yield better results: whether this would reach the 98% cure rate seen with 8 weeks' therapy in those between LLOQ-250 IU/mL at D7 deserves prospective validation in appropriate settings. Whether a more complex diagnostic approach, e.g. with viral loads at D7 and D14, would help is less clear - taking an additional sample at D14 would add complexity (an extra visit) and it is less likely that D14 viral load would add value to decision making, given 85% were already <250 IU/mL at D7 in our trial.

Another longer-term approach is to address the unmet need in diagnostic testing, namely biomarkers that can reliably establish cure whilst on treatment. This is a significant challenge but may be possible with a combination of ultrasensitive viral detection and identification of relevant host markers.

Ultimately, it is possible that the greatest value in understanding cure rates for ultrashort treatment courses will not be in choosing that specific duration of therapy but rather helping clinicians and patients decide whether to start treatment at all in those at high risk of being unable to complete 12 weeks of therapy.