

One of the major advantages of ozanimod is drug selectivity, which might lead to a more acceptable risk-benefit profile. Although theoretically sphingosine 1-phosphate receptor subtype 1 modulators can increase the risk of bradycardia and atrioventricular conduction effects, in the 12-week STEPSTONE trial only a few safety issues of ozanimod were noted, mainly related to disease activity and infections. A future well powered, long-term study is necessary to further investigate possible side-effects with a special interest for cardiovascular and pulmonary disease.⁴ Furthermore, the additive value of trough levels for timely identification of overtreatment and undertreatment is of clinical interest.

Overall, to optimise management of Crohn's disease, there is still a need for large prospective observational studies to assess the real-world effectiveness and safety profiles of new drugs, as only 30% of patients are eligible for participation in registration trials.⁶ Subsequently, comparative effectiveness research using propensity score matching of comparable cohorts could be used to determine the drug's position relative to others in treatment strategies. Although restrictions on concomitant medication and dose optimisation increase the internal validity of the STEPSTONE trial, valuable information can also be extracted from use in daily care.

A great strength of the STEPSTONE trial is the inclusion of histological outcomes in addition to clinical and endoscopic endpoints. Clinical and endoscopic endpoints define the emerging concept of deep remission in Crohn's disease; however, early histological response might be a stronger predictor of disease remission 1 year after ozanimod initiation and of lower complication rates. Challenges remain in translating these data to specific subgroups of patients, such as those who are refractory to multiple treatments, and those with complicated disease, extensive surgical

history, and specific comorbidities. The development of prediction models and immunological profiles of the various Crohn's disease phenotypes will help to characterise patients who may respond preferentially to sphingosine 1-phosphate receptor modulators and support treating physicians in the challenges presented by the expanding choice of new options for Crohn's disease.

To conclude, the promising results of the uncontrolled phase 2 STEPSTONE study warrant further research, not only of the long-term efficacy and safety of ozanimod, but also the predictive value of histological improvement, potential for drug optimisation, and the translation to both the overall Crohn's disease population and specific subgroups.

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Jasmijn A M Sleutjes, Annemarie C de Vries,
*C Janneke van der Woude
c.vanderwoude@erasmusmc.nl

Department of Gastroenterology and Hepatology, Erasmus Medical Center, 3015GD Rotterdam, Netherlands

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The impact of COVID-19 on hepatitis elimination

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Around the world, the communities most underserved by health systems have been among the hardest hit by the COVID-19 pandemic.¹ Often, these are the same groups that are disproportionately affected by viral hepatitis. With just 10 years to achieve WHO's target,

adopted in 2016, to eliminate hepatitis by 2030,² has the COVID-19 pandemic put reaching that goal in greater doubt?

The World Hepatitis Alliance (WHA), a global umbrella organisation representing more than 300 member

organisations across 99 countries, did a global survey to assess the effects of the COVID-19 crisis on viral hepatitis services and on people living with viral hepatitis. A 13-question online questionnaire (appendix pp 1–2) was distributed by email to WHA members and stakeholders, on the WHA social media accounts, and by civil society networks in organisational communications. From March 30 to May 4, 2020, 132 self-selecting individuals responded to the survey from 32 countries across all WHO global regions (appendix p 3). Respondents represented civil society organisations and other frontline hepatitis service providers. The survey had an over-representation of participants from the USA, with 64 (48%) responses, which was due to the promotion of the survey by civil society networks there.

Civil society organisations are a key contributor to national hepatitis elimination programmes³ and 123 (94%) of 131 analysable responses reported that their services had been affected by the crisis. One participant from the USA stated that effects included a halt to in-person events, including community-based education and screening programmes. As a result, the respondent reported that many fewer people who are at high risk of viral hepatitis will be tested this year.

Only 47 (36%) of all 132 respondents reported that people were able to access viral hepatitis testing. 101 respondents gave reasons for lack of access to testing, with the main reason (indicated by 46 [46%] respondents) being closure of testing facilities. Testing facilities being closed was reported by 16 (30%) of 54 respondents outside the USA. 66 (65%) of the 101 respondents believed another key reason people were not accessing testing was because the public were avoiding going to testing facilities due to COVID-19.

23 (34%) of 68 respondents outside the USA reported that people on treatment for hepatitis were unable to access their medications at this time. Lack of access to medications was more common in low-income and middle-income countries (LMICs), with 15 (52%) of 29 respondents from those countries reporting that people were unable to access treatment. Only five (8%) of 64 respondents from the USA reported that people living with viral hepatitis were unable to access treatment during the pandemic. Inability to access medications will undoubtedly cause increased anxiety among people living with viral hepatitis,

many of whom might have been left with gaps in their hepatitis B medication or a delay to starting hepatitis C curative treatment. Participants in India and Nigeria reported that travel restrictions were particularly difficult for remote communities, in which people living with viral hepatitis were unable to access medications because of government restrictions on movement.

64 respondents gave reasons for lack of access to treatment, 32 (50%) of whom (14 [64%] of 22 in LMICs) felt that the cause was people avoiding health-care facilities due to COVID-19. Of 40 respondents from outside the USA, 22 (55%) felt that travel restrictions were the main reason people were unable to access treatment. To overcome this challenge, organisations have adapted their services. A participant in India reported mobilising volunteers to deliver medication to people living in rural communities who were unable to attend medical facilities. 26 (41%) of the 64 respondents felt that services being redeployed to combat COVID-19 was a contributing factor in the reduction in access to treatment. A participant from Australia reported that they had to reduce their testing service because of this change, and not proactively seek to test people due to health staff being redeployed to the COVID-19 response.

A lack of specific information on COVID-19 for people living with viral hepatitis was also a concern. Only 39 (30%) of 131 analysable responses indicated adequate information on COVID-19 had been provided to people living with viral hepatitis in their country. One participant from the Ukraine said that no specific information had been provided for people living with viral hepatitis, although information had been provided for people living with HIV.

Despite the important role that civil society organisations have in their communities, a survey by the Civil Society Engagement Mechanism for UHC2030 found that most respondents reported minor involvement or no input of civil society organisations in the COVID-19 response of their country.⁴ Civil society organisations are experts on their communities because they are part of those communities. They often represent the most underserved in society and those disproportionately affected by COVID-19. If governments do not use civil society organisations in their COVID-19 responses, they are likely to fail in their response for these communities.

See Online for appendix

For the open letter of NOhep see <https://www.nohep.org/2020whdletter/>

Civil society has a central role to play in the pandemic response. Even if the numbers of deaths and new infections decrease, the fear of attending a traditional health-care setting might persist. The decentralisation of services will become a crucial method of service delivery. In November, 2019, the leading liver societies made a joint call for action to explore the ways in which hepatitis prevention, testing, and treatment services can be decentralised.⁵ This pandemic is an opportunity to accelerate this call to action. However, many civil society organisations face an uncertain future. In the WHA survey, one participant from the USA expressed concern over their organisation's funding situation and uncertainty over what services will look like in the future.

Every opportunity should be seized to identify the 290 million people living with viral hepatitis who are unaware of their status.⁶ As countries look to increase testing capacity for COVID-19, they must consider existing programmes led by civil society networks, to enable the rapid scale-up needed. Hepatitis community organisations can test for both COVID-19 and viral hepatitis in settings that are already trusted by their communities. From this crisis, we have an opportunity to evolve health systems to better serve us all. Hepatitis elimination must not be left behind. This World Hepatitis Day, the global community is calling on all governments to honour the commitment they made at the World Health Assembly in 2016 to

eliminate viral hepatitis by 2030. An open letter led by the campaigning body NOhep is available to sign to urge governments to keep their promise of eliminating hepatitis. Civil society and the affected community stand ready to combat the dual threats of COVID-19 and viral hepatitis together.

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*Chris Wingrove, Lucy Ferrier, Cary James, Su Wang
chris.wingrove@worldhepatitisalliance.org

World Hepatitis Alliance, London SE1 3YD, UK (CW, LF, CJ, SW); Center for Asian Health, Florham Park, NJ, USA (SW); and Hepatitis B Foundation, Doylestown, PA, USA (SW)

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Immune therapies in ulcerative colitis: are we beyond anti-TNF yet?

In the past 5 years, three new drugs of different classes have been licensed for the treatment of ulcerative colitis. Vedolizumab, a humanised IgG1 antibody that binds $\alpha 4\beta 7$ integrin and disrupts immunocyte trafficking;¹ tofacitinib, a small molecular inhibitor of Janus kinase-mediated intracellular signal transduction;² and ustekinumab, a humanised IgG1 antibody that binds to the interleukin-12/23p40 subunit.³ These drugs join monoclonal antibodies targeting tumour necrosis factor (TNF) as therapeutic options for moderate-to-severe disease, heralding an era of choice, previously unknown to physicians treating ulcerative colitis.

Registration trials for these drugs shared certain key design aspects. Patients were randomly assigned to induction trials with placebo comparator groups, using almost identical disease severity definitions. Following 6–8-week induction periods, identical disease response definitions were used to determine eligibility for re-randomisation to active drug or placebo with maintenance endpoints determined at 1 year and in long-term extension trials. Baseline characteristics were similar, but not identical; in particular, induction trials of vedolizumab included a lower proportion of patients with previous anti-TNF failure (41%), compared with