## Long-term efficacy and safety of ruxolitinib in polycythaemia vera

In their randomised trial,[1] Jean-Jacques Kiladjian and colleagues reported long-term efficacy and safety of ruxolitinib therapy in polycythaemia vera. The authors found herpes zoster infection as one of the significant adverse events (exposure adjusted rates; 4·7 per patient-years for the ruxolitinib group and 0·0 for the best available therapy group). Notably, a

previous meta-analysis[2] also revealed that ruxolitinib was associated with an increased risk of herpes zoster infection (odds ratio 7·39, 95% CI 1·33–41·07) compared with the control group in three randomised control trials including patients with polycythaemia vera.[3-5]

Herpes zoster infection is caused by reactivation of a latent varicella zoster virus and accompanied by various complications, including post-herpetic neuralgia, neurological complications, and ophthalmological complications. These complications can adversely affect activities of daily living in patients with herpes zoster infection. In particular, patients who are immunocompromised can have severe complications, including disseminated skin disease, acute or progressive outer retinal necrosis, chronic herpes zoster with verrucous skin lesions, and development of acyclovir-resistant varicella zoster virus.[6]

A live-attenuated zoster vaccine is routinely used, but the adjuvanted recombinant zoster vaccine which was recently introduced in 2017, has successfully reduced morbidity and post-herpetic neuralgia not only among older adults, but also among patients who have haematological malignancies with sufficient immunogenicity and safety profiles.[7,8] Thus, we speculate that patients with long-term ruxolitinib therapy should be vaccinated against herpes zoster virus. To affirm this assumption, we would be grateful if Kiladjian and colleagues could provide a detailed history of herpes zoster vaccination among the participants in the RESPONSE study.[1]

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## Authors' reply

I thank Motoharu Shibusawa and Tetsuya Tanimoto for their comments on our RESPONSE study published in *The Lancet Haematology*.[1] Shibusawa and Tanimoto speculate that on long-term treatment with ruxolitinib, patients should be vaccinated against herpes zoster. In this Correspondence we highlight the rationale behind the history of herpes zoster vaccination in the RESPONSE study, and the recommendation on vaccination among patients exposed to ruxolitinib in the long term.

Information on previous vaccination for herpes zoster was not collected for patients enrolled in the RESPONSE study, as this was not part of the study data collection plan. The recommendation that patients should have previous herpes zoster vaccination was not shown on any ruxolitinib drug label or made by any studies exposing the patients to long-term treatment with ruxolitinib.

We understand that herpes zoster infection occurred at a higher rate in our study among the ruxolitinib arm. However, we are not in favour of recommending the herpes zoster vaccination for patients receiving long-term treatment with ruxolitinib, as we currently have no clear data on whether the vaccine can decrease herpes zoster occurrence, which would support this recommendation.[2-5]

The declaration of interests remains the same as in the original Article.

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