Dear Editor, Half of patients with RA, who are in sustained low disease activity (LDA) or remission, can discontinue TNF-inhibitor successfully, without experiencing a flare within 1 year after stopping [1]. This implies that 50% does have flare; unfortunately, we are not yet able to predict at the moment of stopping TNFi which patient is at high risk of flaring. However, soon after restarting TNFi again, at least LDA is achieved [1]. The aim of our study was to establish whether flaring in this situation would be associated with more radiographic progression [2], compared with no flaring.

This is a sub-analysis of the POET-US study [3], in which patients had been included who had RA (ACR 1987 OR 2010 criteria), were older than 18 years, had been using TNFi and csDMARD >1 year and had DAS28 < 3.2 for 6 months prior to inclusion. The study was approved by a central ethics commission and participants gave their written informed consent according to the Declaration of Helsinki. TNFi was stopped and patients were followed for 52 weeks thereafter. In case of a flare, TNFi was restarted within a short period in most patients. Flare was defined as >0.6 increase of DAS28 since study start AND (Boolean) an actual DAS28 ≥ 3.2, according to OMERACT [4]. X-rays of hands and feet were made at, or <12 months before, inclusion and at 12 and 24 months after stopping TNFi. These were scored by two independent readers using the Sharp van der Heijde score (SvdH); their inter-rater reliability was 0.97 (95%CI: 0.96, 0.98) and their average score was used, unless only one reading was available. Cumulative probability plots of radiographic joint progression for those flaring vs those not flaring were drafted [5].

Complete X-ray data were available of 141 of 256 POET-US patients at 12 months after stopping TNFi, and of 84 at 24 months. During the first year, 69 (49%) patients experienced a flare. Baseline characteristics did not differ between patients with or without complete X-ray data. Linear regression (outcome: radiographic progression over 1 year, predictors baseline SvdH-score and flare y/n) was performed to establish whether flare would independently predict radiographic progression, but it did not. In contrast, a higher baseline SvdH-score predicted more radiographic progression (R^2 0.123, P = 0.0000). After one year there was no significant difference in mean (s.d.) radiographic progression between RA patients who flared and those who did not: respectively 0.74 (3.0) and 0.53 (2.8) SvdH units, P = 0.94 (Mann–Whitney U test). The cumulative probability plot (Fig. 1a) shows that 86% (121/141) of patients in both groups had no radiographic progression over one year. Although at 24 months a major part of X-rays were missing, we also plotted a cumulative probability plot for

![Cumulative probability plots of radiographic progression](https://academic.oup.com/rheumatology/article/59/5/1170/5607342/fig1.png)

Cumulative radiographic progression plots showing the change in Sharp van der Heijde score (y-axis) during the first year after stopping TNFi and continuing csDMARD (a, n = 141) and during the first two years after stopping TNFi and continuing csDMARD (b, n = 84). No flare: patients who did not experience a flare of RA during the first year after stopping TNFi, Flare: patients who experienced a flare of RA during the first year after stopping TNFi.
radiographic progression over two years with similar results (Fig. 1b).

Although these outcomes are reassuring, it should be noted that flare occurred after a mean (s.d.) of 21 (14) weeks after stopping TNFi, leaving a relatively short period in which progression could be increased, but in both groups, we found minor radiological progression also over two years. Minor radiological progression has been reported before in patients with LDA; it might be explained by subclinical disease activity in some [6]. In conclusion: flare in the first year after TNFi cessation in RA patients with LDA seems not to cause additional radiographic progression.

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**References**


