Dr. Tibaldi, *et al* reply

To the Editor:

We are pleased by the interest of Ozen and colleagues[1] for our work[2] and appreciate their choice to test our predictive model of response to anakinra in their cohort of children with systemic juvenile idiopathic arthritis (sJIA). The authors used the same definition of complete clinical response (CCR) as in our study and quantified the activity of systemic disease through the systemic manifestation score (SMS) that we developed[2].

The frequency of CCR recorded in the study by Ozen, *et al*[1] is higher than that observed in our cohort (62.2% vs. 39%)[2]. This disparity may depend, at least in part, on differences in disease activity and severity, therapeutic protocols, timeline of response evaluation, and concomitant therapies. However, as in our analysis, patients who achieved CCR in the study by Ozen, *et al* had shorter disease duration, fewer active joints, higher ferritin level, and higher SMS at initiation of anakinra than patients who did not achieve CCR, although only the difference for the active joint count was statistically significant, probably owing to the small sample size. Further, a significantly greater proportion of complete responders than nonresponders met all 4 variables included in our predictive model (67.9% vs 8.3%; $p = 0.001$). Interestingly, increased ferritin and an SMS > 3, which are related to the innate immunity mechanisms involved in the early stages of sJIA[3], were the only 2 individual items whose frequency was significantly higher in complete responders than in nonresponders.

Although the difference was not statistically significant, it is worth emphasizing that among patients of Ozen, *et al* the median disease duration at the start of anakinra treatment was shorter in complete responders than in nonresponders (6 mos vs 24 mos). This difference is similar to that observed in our sample (11 mos vs 25 mos). It is currently hypothesized that a window of opportunity may exist in the course of sJIA, whereby early treatment with interleukin (IL)-1 inhibitors may allow rapid remission of systemic disease and avoid the progression of the disease toward the chronic arthritis stage[3,4,5]. In our study, of the 10 patients who started anakinra within 3 months after disease onset, 60% had CCR at 3 months and 70% had CCR at 1 year.

The results of Ozen and co-workers support the validity of our model in the prediction of the effectiveness of IL-1 inhibition in children with sJIA. Further evaluations in larger patient samples are required to establish whether this model may help identify at treatment start the patients who are more likely to benefit from IL-1 blockade.

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