Dr. Reggia, *et al,* reply

To the Editor:

We are pleased that our article[1] has aroused interest from colleagues and we thank them for providing us valuable input for further analysis.

We have considered the data presented by Monti, *et al*[2] in their Letter to the Editor regarding the good outcome obtained in a cohort of 21 patients after the switch from the intravenous (IV) to the subcutaneous (SC) formulation of abatacept (ABA). In their study, the risk of disease relapse appears to be lower than in our experience, even though about 40% of their patients presented moderate disease activity at the end of followup (6 mos after the switch). Within these, 21 patients (10%) showed an objective disease worsening. However, in general terms, the disease activity achieved during IV therapy has been maintained and no patients needed to return to parenteral administration for clinical reasons.

Since our study was first published[1], we have extended the followup of our cohort to better analyze the outcome of the patients switched to SC formulation.

We have retrospectively included 49 patients: 15 of them (30.6%) returned to IV administration because of a disease flare [mean 28-joint Disease Activity Score (DAS28): 4.8 vs 2.1, $p < 0.001$], after a mean of 15 injections (range 4-48). To obtain a more objective evaluation of the disease flare, we have made a subanalysis of the objective components of the DAS28 index [C-reactive protein (CRP) values and number of involved joints], removing the pain evaluation made by the patient, which could be influenced by the eventual presence of alterations in pain perception, such as in fibromyalgia.

We observed a significant increase in CRP values (mean 0.29 vs 0.86 mg/dl, $p = 0.004$) and in the number of painful (mean 0.6 vs 4.9, $p < 0.001$) and swollen joints (mean 0.5 vs 4.2, $p < 0.001$), confirming the clinical suspicion of disease flare. The remaining 34 patients (69.4%) continued with the SC formulation. As in published data[1], no differences were observed between demographic and clinical features of the 2 groups of patients, nor in the previous therapeutic history (Table 1). Regarding the short-term outcome, we observed that in patients with an arthritis flare, disease activity decreased again (mean DAS28: 4.16 vs 2.43, $p < 0.001$) after returning to the IV infusion (mean: 45 days), with a significant decrease in the CRP values (mean 0.9 vs 0.4 mg/dl, $p = 0.04$) and in the number of painful (mean 4.9 vs 1.7, $p = 0.003$) and swollen joints (mean 4.2 vs 1.2, $p = 0.003$). However, 12 months after the switch, we registered that 32 of the 34 patients (94%) who maintained the SC formulation were still treated with SC ABA (1 withdrawn from therapy for sustained remission and 1 for the onset of repeated infections), while only 10 (67%) of the 15 patients who needed to return to IV infusion were still treated with IV ABA. Five of them had been switched to other biologics because of a new reactivation of arthritis ($p = 0.0368$). This finding could be explained by assuming that those patients who experienced a first arthritis flare at the formulation switch probably had higher disease activity or were not in sustained remission, so that the return to IV administration was not enough to guarantee a prolonged control of the disease. From this point of view, we can assume that the switch failure seems to predict a reduced persistence of ABA efficacy over time. The safety profile of the SC ABA was maintained also in the longterm followup.

Table 1. Comparison between the clinical and serological features of patients with and without the need to return to the intravenous (IV) administration of abatacept (ABA) after the switch to the subcutaneous (SC) formulation. Values are n (%) unless otherwise specified. No p values were significant.

Analyzed Features	Patients Who Maintained the SC Formulation, n = 34 (69.4%)	Patients Who Returned to IV Infusions, n = 15 (30.6%)
Mean age, yrs (SD)	58.8 (14.4)	57.1 (13.1)
Positivity for RF	31/34 (91.2)*	9/12 (85.7)*
Positivity for ACPA	20/27 (74.1)*	9/11 (81.8)*
Mean disease duration, mos (SD)	132 (116.5)	111.9 (86.4)
Previous IV therapy duration, mos (SD)	22.4 (20)	16.4 (17)
BMI, mean (SD)	24.6 (4.9)	25.2 (5)
Smokers	4 (11.8)	2 (12.5)
DMARD in association	31 (91.2)	13 (86.7)
Previous use of biological agents	24 (66.7)	11 (73.3)
No. different biological agents used in the past, mean (SD)	1.4 (1.4)	2.2 (2.2)
ABA as first biological agent	12 (33.3)	4 (26.7)
Remission at SC therapy start, DAS28 < 2.6	27 (79.4)	11 (73.3)
DAS28 at SC therapy start, mean (SD)	1.9 (0.8)	2.1 (0.9)

* Percentage based on available data. RF: rheumatoid factor; ACPA: anti-citrullinated protein antibodies; BMI: body mass index; DMARD: disease-modifying antirheumatic drug; DAS28: 28-joint Disease Activity Score.

ROSSELLA REGGIA, MD; ANGELA TINCANI, MD; FRANCO FRANCESCHINI, MD; ILARIA CAVAZZANA, MD; Rheumatology and Clinical Immunology, Spedali Civili and University of Brescia, Brescia, Italy. Address correspondence to Dr. R. Reggia, Piazzale Spedali Civili 1, 25123 Brescia, Italy. E-mail: rossella.reggia@gmail.com

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