Patients' experience and tolerability with canakinumab and anakinra for the treatment of adult-onset Still's disease

Sirs,

Adult-onset Still's disease (AOSD) is a rare inflammatory disease with protean systemic and articular manifestations (1). The pathogenesis of this autoinflammatory syndrome features interleukin-1 (IL-1) as a key player, and pharmacological blockade of this cytokine has shown remarkable clinical efficacy in the treatment of AOSD patients (2). Both the recombinant receptor antagonist anakinra and the monoclonal antibody canakinumab have proven effective in dampening systemic inflammation and controlling clinical manifestations in severe and steroid-dependent AOSD patients (3-7). Unfortunately, given the relapsing and chronic nature of the disease, the use of these drugs is usually maintained for several years to keep a satisfactory disease control (7). As a consequence, AOSD patients are exposed to prolonged treatments and need to adapt their daily habits. The impact of these drugs on patients' quality of life in AOSD patients has not yet been investigated. Herein, we report a preliminary evaluation of patients' perspective of IL1-inhibitors in a monocentric cohort of AOSD patients treated with both anakinra and canakinumab.

Among the 78 AOSD patients currently actively followed-up at our Autoinflammatory Disease Clinic, 14 patients who had been initially treated with anakinra and subsequently treated with canakinumab were identified and included in the analysis. Our study was approved by San Raffaele Ethical Committee – PanImmuno Protocol; informed consent to take part in the study and for publication was obtained from participants.

At canakinumab start, patients were asked to fill a questionnaire investigating their experience with anakinra; the same questionnaire was submitted again six months later to evaluate their personal perspective on canakinumab. The questionnaire included four different domains assessed by means of a visual analogue scales (VAS) ranging from 1 to 10. The following domains were considered: injection-related pain, satisfaction with the frequency of administration, concern for drug-related adverse events, and overall drug tolerability. VAS values for each of the domains were compared between anakinra and canakinumab with Mann-Whitney U-test.

Demographic and disease characteristics of the study population are shown in Table I. Anakinra was discontinued due to either inefficacy (n=10, 71%) or adverse reactions (n=4, 29%); the median duration of treatment was 3 (IQR 0-6) months. As shown in Figure 1, the overall tolerability of canakinumab was significantly higher compared to the one of anakinra (median 9, IQR 8–10 *vs*. median 5, IQR 4–7; p=0.002). Only one AOSD patient reported a greater tolerability with anakinra compared to canakinumab because she felt more comfortable with pre-filled syringes. Higher canakinumab tolerability was due to lower pain at injection site (median 1, IQR 1–1 *vs*. median 6, IQR 2 - 8; p<0.001) and greater level of satisfaction with the frequency of administration (median 10, IQR 9–10 *vs* median 3, IQR 2 - 4; p<0.001). Conversely, patients' concerns for drug-related adverse events were not significantly different between the two drugs (p=0.270). Canakinumab was associated with clinical benefit and a reduction in Pouchot score (8) in all but one patient. In conclusion, in our cohort of refractory AOSD patients, canakinumab proved not only to effectively control systemic inflammation in most patients that developed secondary anakinra resistance, but its use was also associated with greater patients' tolerability.

Table I. Clinical and treatment characteristics of study population.

	Sex and age (years)	Disease duration (months)	Disease manifestations	Sequential biologic therapies	Steroid dosage variation (mg/day)*	Pouchot score variation*	ESR variation (mm/hour)*	CRP variation (mg/L)*
Patient 1	Male, 70	22	Arthritis, fever rash	TCZ, ANK, CNK	25 → 5	2 → 0	120 → 13	55 → 1
Patient 2	Female, 72	11	Arthritis, fever rash	TCZ, ANK, CNK	5 → 0	4 → 0	60 → 24	265 → 6
Patient 3	Male, 32	48	Fever, rash	ANK, CNK	15 → 0	1 → 0	29 → 11	27 → 1
Patient 4	Male, 71	12	Arthralgia, fever	ANK, CNK	20 → 5	1 → 0	120 → 2	180 → 1
Patient 5	Female, 58	72	Arthralgia, fever	ANK, CNK	0 → 5	1 → 1	27 → 36	5 → 83
Patient 6	Female, 48	5	Arthritis, fever rash	ANK, CNK	10 → 0	0 → 0	8 → 10	2 → 1
Patient 7	Female, 74	180	Arthritis, fever, rash, MAS	ETN, ANK, CNK	5 → 5	1 → 0	33 → 1	1 → 25
Patient 8	Male, 78	180	Arthritis, fever rash, myocarditis pleuropericarditis	ANK, CNK	40 → 20	1 → 0	46 → 10	58 → 40
Patient 9	Male, 22	144	Arthritis, fever	ETN, TCZ, ANK, CNK	20 → 10	0 → 0	86 → 67	135 → 28
Patient 10	Male, 43	24	Arthritis, fever rash	ANK, CNK	15 → 5	2 → 0	15 → 10	4 → 1
Patient 11	Female, 18	18	Fever, rash	ANK, CNK	7.5 → 2.5	1 → 0	14 → 2	8 → 1
Patient 12	Female, 59	42	Arthritis, rash	ANK, CNK	5 → 0	0 → 0	48 → 40	5 → 3
Patient 13	Male, 41	84	Arthritis, fever, hepatosplenomegaly rash	IFX, TCZ, ANK, CNK	25 → 0	3 → 0	45 → 9	6 → 1
Patient 14	Male, 50	240	Arthritis, fever, hepatosplenomegaly	ANK, CNK	0 → 0	2 → 0	77 → 15	38 → 5

*Before and after starting canakinumab.

ANK: anakinra; CNK: canakinumab; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; ETN: etanercept; IFX: infliximab; MAS: macrophage activation syndrome; MTX: methotrexate; PDN: prednisone; TCZ: tocilizumab.

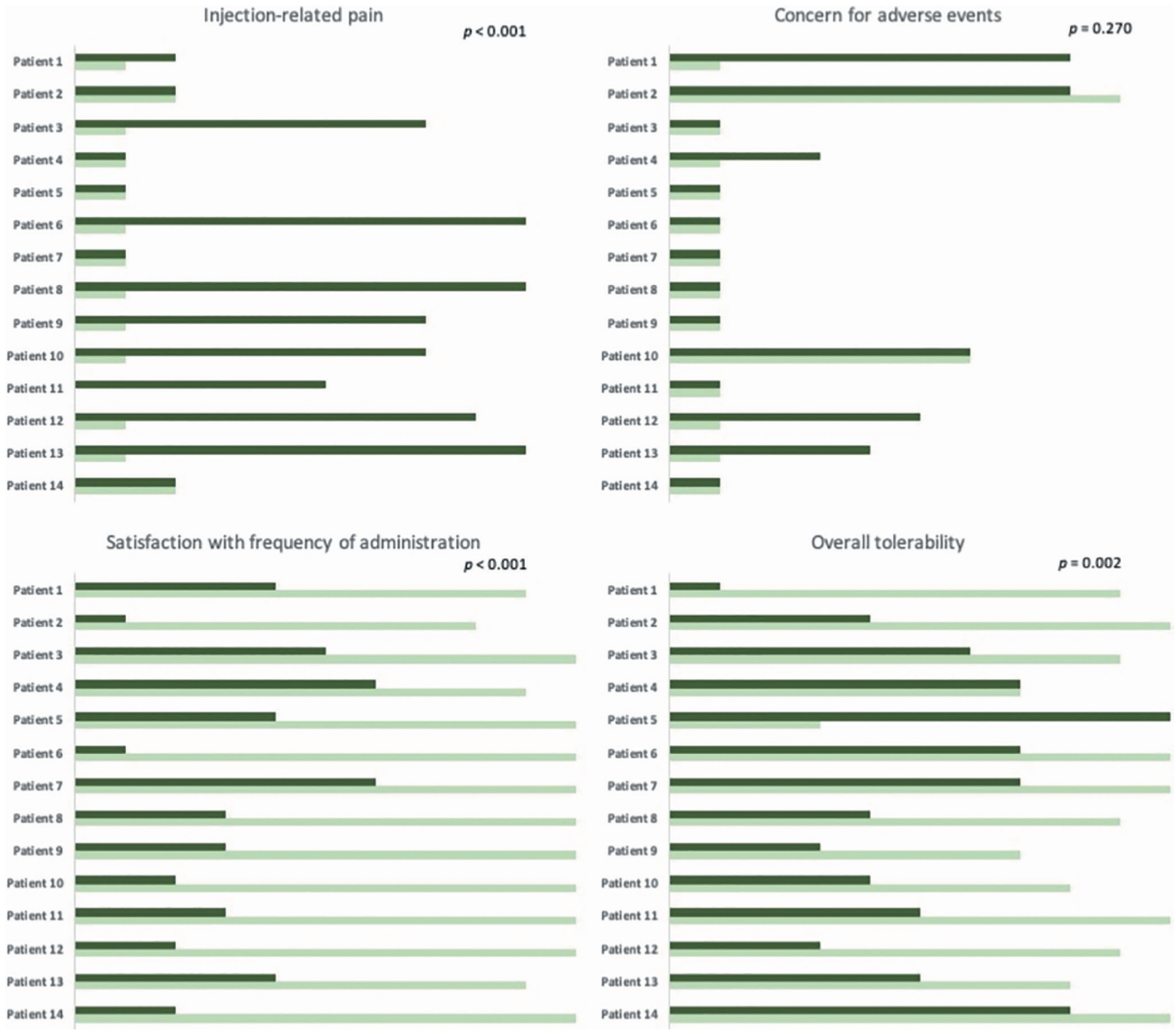

Fig. 1. Comparative tolerability of anakinra (dark green line) and canakinumab (light green line) in our study population, expressed as visual analogue scale values (range from 1 to 10). Reported *p*-values refer to the comparative analysis with Mann-Whitney U-test between the two drugs.

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