

Longterm Followup of Quality of Life in Patients with Cryopyrin-associated Periodic Syndrome Treated with Canakinumab, an Anti-interleukin 1 β Monoclonal Antibody

To the Editor:

Cryopyrin-associated periodic syndrome (CAPS) is an inherited auto-inflammatory disorder that comprises a clinical spectrum of 3 distinct phenotypes increasing in severity: familial cold autoinflammatory syndrome, Muckle-Wells syndrome (MWS), and chronic infantile neurological cutaneous and articular syndrome (CINCA). Urticarial rash, fever, arthralgia, and intense fatigue are the main clinical signs¹. CINCA is the most severe form, with mental and physical disability. Some patients are difficult to classify because they present intermediate phenotypes. The effect of CAPS on quality of life is significant in all phenotypes, with limitation in ability to work (78%) and in participation in outdoor activities (95%)².

The NOD-like receptor 3 (*NLRP3*) gene mutation is responsible for overproduction of interleukin 1 β (IL-1 β)³. Three IL-1 inhibitors have shown efficacy in CAPS: anakinra, rilonacept, and canakinumab⁴. The approval of canakinumab by the US Food and Drug Administration was based on a 48-week, double-blinded study showing rapid and sustained remission of symptoms under treatment⁵.

Our objective with this monocentric longitudinal study was to evaluate quality of life and socioprofessional effects of longterm treatment with canakinumab in patients with CAPS, who were among the first in the world to be treated with canakinumab.

Patients were those first included in the canakinumab/CAPS study (D2304/2306)⁵ and followed in our reference center and who were still taking the treatment after the end of the study in January 2010. All carried the *NLRP3* mutation and had received 150 mg of canakinumab every 8 weeks. Patients had been prospectively evaluated with 3 generic health-related quality of life (HRQOL) questionnaires during trial and in June 2012 and at last visit: Functional Assessment of Chronic Illness Therapy-fatigue (FACIT-F), the Medical Outcomes Study Short Form-36 survey (SF-36), and the Health Assessment Questionnaire (HAQ). Questions regarding social and professional activities and how patients deal with treatment were added. All patients gave informed consent. Adverse events were reported at every visit.

Seven patients were included (age 24 to 63 years). Six of them had MWS, but 1 had the intermediate MWS/neonatal-onset multisystem inflammatory disease phenotype. Patients belonged to 3 different families. Three patients had received anakinra before the canakinumab trial. The mean time of followup was 4.8 \pm 0.8 years. All were in remission at last visit, defined as a minimal/absent physician global assessment of disease activity, with minimal/absent rash, and normal range of C-reactive protein/serum amyloid A protein. Doses or intervals of injections were modified for 4 patients because of incomplete remission.

At baseline, FACIT-F and SF-36 mean scores were significantly inferior to those obtained in the American general population (Table 1). A significant and sustained improvement in FACIT-F and in physical SF-36 scores was found in comparison to baseline ($p < 0.05$) and they approached scores of the American general population at last visit. Mental SF-36 and

HAQ scores improved but not significantly. The most important gains in SF-36 domains compared to baseline were observed for body pain (+36.4), social functioning (+32.1), and vitality (+28.6; Figure 1).

Patients reported that relief from chronic fatigue allowed them to have an active social life and participate in physical activities. Five patients returned to work, 4 started regular physical activity, 1 stopped smoking; a long-time single patient started a relationship, and another divorced.

Canakinumab was well tolerated, with no injection site reaction. No serious adverse events attributable to treatment were reported. Despite the long duration of treatment, only 2 patients were able to manage the injections on their own.

Longterm followup allowed us to confirm the sustained improvement of HRQOL with canakinumab in patients with CAPS, also observed after 48 weeks of the extension trial⁶. Three scores were used to assess various domains of quality of life because no specific questionnaire exists for autoinflammatory diseases. HAQ questionnaires did not reveal significant results in our study. This score is used for osteoarticular diseases with physical limitation and effect on daily activities. Perhaps it is not very discerning for the symptoms of patients with CAPS.

The benefit of canakinumab treatment in allowing a professional life was one of our most important observations; no patients were out of work during the followup. The gain in vitality scores permitted them to enjoy a social life after work and physical activity, which were impossible without treatment.

One study compared HRQOL in patients treated first with anakinra and then with canakinumab, but the authors did not reveal significant difference between treatments⁷.

Canakinumab had proven its efficacy and safety in treatment of patients with CAPS with rapid clinical and biological remission after the first dose of treatment. We have shown that canakinumab had not only a sustained effect on quality of life, but also allowed dramatic changes in social and work lives. The good tolerance of the injections and the long interval between doses of canakinumab were real benefits for patients requiring lifelong treatment.

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Table 1. Changes in quality of life. Values are expressed in mean \pm SD.

	General Population	Baseline D2304/2306, n = 7	End D2306, n = 7	Last Visit, n = 7
FACIT-F	43.5	25.1 \pm 11.3	42.6 \pm 5.8*	42.3 \pm 6.9*
SF-36 PCS	50	37.7 \pm 4.8	49.7 \pm 4.9*	48.6 \pm 10.6*
SF-36 MCS	50	34.1 \pm 11.4	44.1 \pm 9	43.9 \pm 8.7
HAQ	—	0.64 \pm 0.73	0.32 \pm 0.56	0.52 \pm 0.83

* p value < 0.05 . FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; SF-36: Medical Outcomes Study Short Form-36 survey; PCS: physical component summary; MCS: mental component summary; HAQ: Health Assessment Questionnaire; D2304/2306: canakinumab/CAPS study.

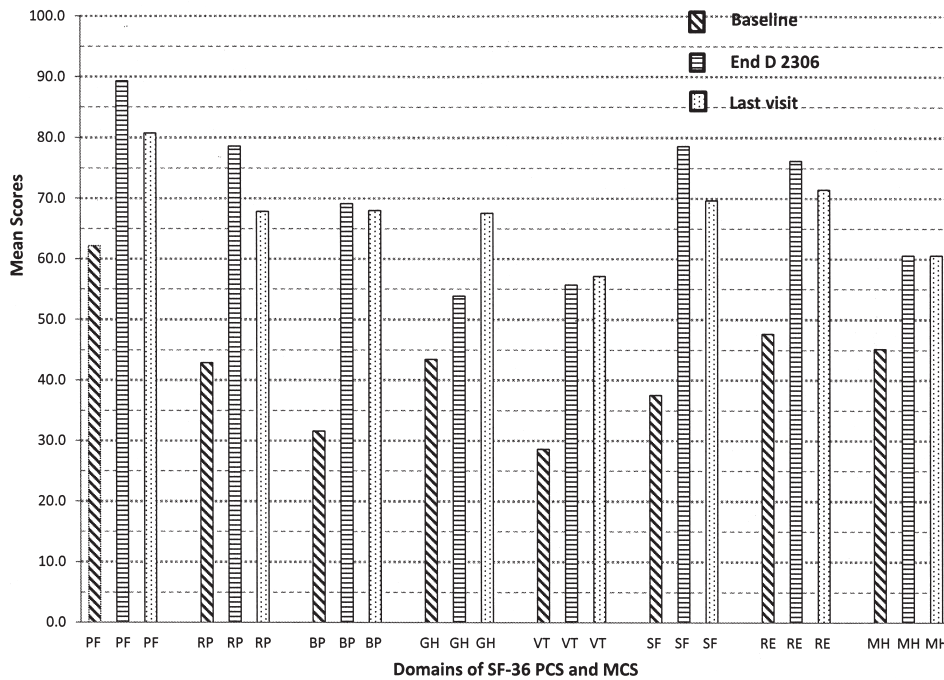


Figure 1. Evolution of mean scores in the 8 domains of Medical Outcomes Study Short Form-36 survey (SF-36) questionnaires. PCS: physical component summary; MCS: mental component summary; PF: physical functioning; RP: role physical; BP: body pain; GH: general health; VT: vitality; SF: social functioning; RE: role emotional; MH: mental health; End D 2306: End values, canakinumab/CAPS study⁵ (June 2012).

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