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Title: Study to evaluate the efficacy and safety of Anakinra in the treatment of articular manifestations refractory to conventional therapy in Systemic Lupus Erythematosus patients

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SUMMARY OF RESULTS:

Background & Aims

Joint involvement in Systemic Lupus Erythematosus is frequent (90%). Although usually is symmetrical and transient, in some patients it can become chronic and disabling due to the deformities (Jaccoud's artropathy). Low-dose steroids, anti-malarial and disease-modifying anti-rheumatic drugs (DMARDS) is the conventional treatment. However, approximately 25-30% of patients will be refractory, and for them there are no established guidelines. Most of the recent studies include heterogeneous patients and none of them focus in the management of more selected clinical manifestations. Biological therapy with anti-TNF agents has been administered in some cases, but its use is limited by the known risk to develop autoantibodies or even the lupus-like syndrome. Treatment with the IL-1 receptor antagonist (IL-1Ra), Anakinra, has proven its efficacy in rheumatoid arthritis and systemic juvenile idiopathic arthritis, improving inflammation and development of erosions.

The objective of the study was to assess the efficacy and safety of the interleukin-1 receptor antagonist, Anakinra, in Systemic Lupus Erythematosus (SLE) patients with refractory arthritis. Secondary objectives included evaluating the effect of this drug in other systemic manifestations of lupus disease (SLEDAI, BILAG and 28-joint count), the adverse effects, the frequency of flare after withdrawal, the sequelae, and the effect on the inflammatory and immunological laboratory parameters.

Methods

Twenty patients with arthritis refractory to at least six-month treatment with one DMARD were included. Anakinra (subcutaneously) was started at 100mg/day for 6 months. Complete remission was defined by a complete resolution of the arthritis (28-jount count=0). Blood and radiological tests and clinical controls were performed monthly, according to protocol.

Only 15 patients were finally studied, since 5 discontinued the treatment due to local administration site effects.

Results

Primary endpoint:

Local adverse effects were observed in 47% of patients. They were moderate, with no improvement after topic corticosteroid treatment, or ice application locally. No other adverse events were reported.

Secondary endpoints:

Efficacy: From the 10 patients that continued treatment until the 6th month, only 3 (30%) reached the criterion of complete remission, 2 (20%) had some improvement, and 5 (50%) did not show any improvement at all.

SLEDAI score: A non-significant improvement was obtained in patients following the treatment in the SLEDAI score (initial 7.2 ±1.9 vs final 6.23 ±2.3, p= 0.229). Only 3 patients reduced more than 4 points this score, due to the articular component. No improvement was obtained in skin or pleural manifestations.

Quality of Life (SF36): Improvement was very limited, and parallel to VAS pain score by patient or PGA score by physician. At 6 months, no differences were obtained (average VAS: initial 54±30; final 52 ±25).

From the 3 patients with total remission, all presented with a new flare, in average 5±3 weeks after drug retrieval. This suggest the beneficial effects are directly derived from long-term, continuous administration of the drug.

Conclusions

Anakinra treatment did not show efficacy in this pilot study in treating SLE patients with refractory arthritis, and showed an important number of local adverse events in the site of administration. Thus, it does not bring benefits compared to present treatments.

In patients with good response, this was impaired after drug retrieval, thus suggesting the need for even longer treatments. During follow-up, even when this was short, no impacts were observed on systemic disease, or anti-dsDNA or complement (C3, C4) levels.