URTICARIA, ANGIOEDEMA

EVALUATION OF A LOW-DOSE METHOTREXATE ADDED TO H1-ANTIHISTAMINES REGIMEN FOR SEVERE CHRONIC SPONTANEOUS URTICARIA: A PHASE III, RANDOMIZED, PLACEBO-CONTROLLED TRIAL

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Introduction: H1-antihistamines (anti-H1) are the first-line treatment for chronic spontaneous urticaria (CSU). Immunosuppressive drugs may be proposed in case of incomplete improvement of CSU.

Objective: To evaluate the efficacy of a low-dose methotrexate added to H1-antihistamines regimen for CSU resistant to anti-H1 treatment, compared with anti-H1 monotherapy in a randomized, placebo-controlled trial.

Materials and Methods: Patients with CSU resistant to at least a 3 month-period of anti-H1 were randomly assigned to receive either low-dose methotrexate (0.2 mg/kg/week) or placebo in addition to anti-H1. Primary outcome was the proportion of patient with complete remission of CSU after 18 weeks (W18), defined as no urticarial lesion within the previous

30 days. Intention to treat analyses were performed (failure was considered when data on primary outcome were missing).

Results: From November 2011 to May 2016, 75 patients were randomized: 39 were allocated to methotrexate and 36 to placebo. In the intention to treat population, 3 patients in the methotrexate group (7.9%) and 0 patient in the placebo group (0.0%) had a complete remission at W18 (difference, 7.9 percentage points, [95% confidence interval (CI) -4.0 to 20.8], p=0.24). Eleven patients in the methotrexate group (29.0%) and 6 patients in the placebo group (18.8%) had less than 7 days with urticarial lesions within the 30 days before W18 (difference, 10.2 percentage points, [95% CI -10.2 to 28.8], p=0.40). Clinical adverse events occurred in 56.4% of patients in the methotrexate group and 50.0% in the placebo group (p=0.58), mostly gastrointestinal symptoms. Biological adverse events occurred in 59.0% of patients in the methotrexate group and 30.6% in the placebo group (p=0.01), mainly increased blood level of transaminases.

Conclusions: We did not evidence any superiority of a low dose methotrexate added to anti-H1, compared with anti-H1 monotherapy, for patients with chronic spontaneous urticarial.