MATERIALS AND METHODS

The study was a 2-centre, randomized, double-blind, 3-way crossover, placebo-controlled study in which patients with a confirmed diagnosis of ColdU of at least 6 months’ duration were recruited from the Departments of Dermatology Charité-Universitätsmedizin, Berlin and Hospital del Mar, Barcelona. The study was approved by the ethics committee and regular authorities of Berlin and Barcelona (EudraCTnumber: 2011-004094-93) and was conducted according to the Declaration of Helsinki and applicable local and European laws and regulations. The clinicaltrials.gov number is NCT01605487. All participants signed informed consent at the beginning of the study.

Patients

Patient recruitment began in June 2012 and the study was completed in September 2013. A total number of 24 patients (6 males and 18 females, mean age 45 years, age range 19–68 years) participated in the study. The group size was estimated based on the significance level of 0.05 and a power of 80% and a medium effect of 1.2 standard deviations (SD). All women of childbearing potential were required to use effective contraception for the duration of the study. Exclusion criteria included a history of significant gastroenterological, neurological, cardiac, oncological, psychiatric, renal, or liver diseases that could have interfered with patient safety or the conduct of the study. Patients with a history of hypersensitivity or an allergic reaction to rupatadine or other H1-antihistamines were also excluded. Before the start of the study, the participants followed washout periods of 7 days for H1-antihistamines or anti-leukotrienes, 28 days for oral or 3 months for depot corticosteroids and 28 days for immunosuppressants/immunomodulators, such as cyclosporine A, dapsone, methotrexate, mycophenolate, and chloroquine. The administration of ketoconazole, erythromycin or potential inhibitors of the isoenzyme CYP3A4 of the cytochrome P450 was also forbidden.

Study design

Patients with ColdU were randomized according to a balanced experimental design. Each of the 6 possible sequences of placebo, rupatadine 20 mg, or rupatadine 40 mg was applied to an equal number of patients once daily (morning intake) for one week with a 2-week washout period before crossing over to the next treatment group (Fig. 1). The study medication was provided by J. Uriach & Co.: S.A. The tablets of placebo and rupatadine were enclosed in identical blisters. During the treatment phase 4 tablets of placebo, or 2 tablets of rupatadine each of 10 mg and 2 tablets of placebo, or 4 tablets of rupatadine each of 10 mg daily were given. Tablets were taken each morning on a daily basis during the treatment period.

Statistical analysis

The results for CTT and CsTT are expressed as median (with range) and the significance of differences calculated using Wilcoxon non-parametric test. The significance values for the numbers of individual patients responding or not responding to treatments were calculated using Fisher’s exact test.