Adalimumab dose reduction in psoriasis: Results in a series of 12 patients
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Background: Adalimumab (ADA) is a fully humanized monoclonal antibody that blocks tumor necrosis factor-a used in patients with moderate to severe psoriasis. It is usually administered subcutaneously at a dose of 40 mg every other week (cow).
Objectives: To evaluate the proportion of psoriasis patients maintaining clinical remission after increasing the interval between doses of ADA, the duration of remission, to relapse, and the efficacy of the reintroduction of ADA if it had been finally discontinued.
Methods: We reviewed the clinical records of 12 patients with severe psoriasis who underwent spaced doses of ADA when Psoriasis Area and Severity Index (PASI) <3 had been achieved with conventional doses. Psoriatic arthritis was an exclusion criterion. To a random ADA withdrawal phase without medication was scheduled, it was usually administered subcutaneously at a dose of 40 mg every 4 weeks and if the response was maintained (PASI <3), it was increased to 40 mg every 4 weeks, and after that every 5 weeks or discontinued. If there was an outbreak, the interval was reduced to the previous one with which the PASI was <3. The average of follow-up was 190 weeks with clinical and analytical evaluation every 12 weeks.
Results: We tried to reduce doses of ADA in 12 patients (9 men and 3 women) with a mean baseline PASI of 24.64. The average duration of the dose of 40 mg cow was 46.5 weeks. In the end of follow-up, dose reduction was possible in 75% of patients, who were able to maintain a PASI <3 and also a BSA 10% improvement in Psoriasis Area and Severity Index (PASI) after 5 weeks. Patients with severe psoriasis who underwent spaced doses of ADA when Psoriasis Area and Severity Index (PASI) <3 had been achieved with conventional doses. Psoriatic arthritis was an exclusion criterion to a random ADA withdrawal phase without medication was scheduled, it was usually administered subcutaneously at a dose of 40 mg every 4 weeks and if the response was maintained (PASI <3), it was increased to 40 mg every 4 weeks, and after that every 5 weeks or discontinued. If there was an outbreak, the interval was reduced to the previous one with which the PASI was <3. The average of follow-up was 190 weeks with clinical and analytical evaluation every 12 weeks.
Conclusion: Maintained clinical remission is possible in a high percentage of patients with psoriasis receiving reduced doses of ADA. After analysing our results, we propose to follow ADA in a protocol for dose reduction according to PASI score in order to reduce the costs and side effects without compromising the clinical response achieved initially.
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Apreamplis, an oral phosphodiesterase 4 inhibitor, in patients with moderate to severe psoriasis: 16-week results of a phase 3, randomized, controlled trial (ESTEEM 2)
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Background: Apreamplis (APR), an oral phosphodiesterase 4 inhibitor, works intracellularly to modulate pro- and anti-inflammatory mediators. The ESTEEM 2 trial compared the efficacy and safety of APR with placebo (PBO) in patients with moderate to severe plaque psoriasis.
Methods: Patients with moderate to severe psoriasis (PASI = 12, BSA 10%, and sPGA = 3; N= 413) were randomized to PBO (n = 118) or APR 30 mg BID (APR30; n = 295) through week 16. All patients were then treated with APR30 through week 32. APR30 responses were generally maintained in patients who not only achieved PASI-75 at week 32 but who continued APR30 through week 52.
Results: At week 16, significantly more patients receiving APR30 achieved PASI-75 (28.8%) and PASI-30 (55.5%) vs. PBO (5.8% and 19.7%, respectively; P <0.0001). Mean/median changes from baseline PASI were -15.8%/ -18.0% (PBO) and -50.9%/-59.0% (APR30) (P <0.0001). Significantly more patients receiving APR30 (20.4%) achieved an NAPSI-50: 44.6% vs. 18.7%; P <0.0001). PASI responses were generally maintained through wk 32. Similar PASI responses were achieved at wk 32 in PBO pts switched to APR30 at wk 16. In the randomized treatment withdrawal phase, 61.0% of 77 pts randomized to receive APR30 vs. 32.7% of 50 pts randomized to PBO achieved PASI-75 at wk 32; and 75.3% had 70% improvement in PASI from baseline. APR vs. PBO median percent change from baseline PASI score was -81% to -88% between wks 32 and 52. In pts re-randomized to APR30 at wk 32 (n = 77), 11% had PASI-75 at wk 52. The median time to PASI-75 loss in pts randomized to PBO was 5.1 wks. Of 32 pts re-randomized to PBO who lost response and restarted APR30, 70.8% regained PASI-75 after reintiation of treatment. APR was generally well tolerated for up to 52 wks, with no increase in AE incidence over time. Over the entire APR exposure period, AEs in < 5% of patients were diarrhea (3.6%), URTI (17.8%), nausea (15.3%), nasopharyngitis (13.4%), tension headache (9.6%), and headache (6.5%). Most AEs were mild or moderate in severity and did not lead to discontinuation. Serious AEs (including serious infections, malignancies, and cardiovascular events) and laboratory value changes were consistent with prior APR studies.
Conclusion: APR was effective for moderate to severe psoriasis. In the randomized treatment withdrawal phase, PASI responses were generally maintained in patients randomized to APR30. APR30 maintained an acceptable safety profile and was generally well tolerated for up to 52 wks.
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Autoimmunity in psoriasis patients in the treatment with ustekinumab
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Background: Apremilast (APR), an oral phosphodiesterase 4 inhibitor, works intracellularly to modulate pro- and anti-inflammatory mediators. The objective of the study is to determine the presence of ANA and autoimmune diseases in psoriasis patients in the treatment with ustekinumab.
Methods: A prospective, longitudinal, observational study was performed. Inclusion criteria: 1. Patients with moderate to severe psoriasis treatment with ustekinumab 2. Duration of treatment of ANA at least baseline and at fourth month. 3. Lack of connective disease previously: ANA were identified via indirect immunofluorescence technique, using human epithelial (HEp2) cells and via ELISA. If one of this was positive (>1/160), titres were calculated, pattern was informed and Anti-dsDNA and DNA, screening via ELISA technic were performed. All these determinations were carried out at baseline, at fourth month and sometimes at months 12 and 24.
Results: A total of 76 patients were included; the demographic data were as follows: 46 males and 30 female, mean age 45.5 years and mean psoriasis duration of 20 years. 53 patients (69%) had received anti-TNF therapy previously. At baseline, 15 patients (19%) were ANA-positive and as to the autoimmune diseases there were only 2 patients, 1 case of alopecia areata and another 1 of vitiligo. At months 4, 12, and 24, differences were observed in patients ANA, both at baseline, and at months 12 and 24, statistically significant differences in age, sex, psoriasis duration, arthritis and previous anti-TNF therapy. Regarding the patients who were ANA-positive pretreatment, 15 remained ANA-positive and 2 became ANA-negative on treatment. No anti-dsDNA antibodies were at baseline and there were no new occurrences of dsDNA, nor connective diseases while on treatment.
Conclusions: This study suggests that ustekinumab does not seem to induce ANA, anti-dsDNA antibodies or autoimmune diseases during treatment.