P7775

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 the 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 (eow).

Objectives: To evaluate the proportion of psoriasis patients maintaining clinical remission after increasing the interval between doses of ADA, the duration of remission, time 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. The interval of ADA doses was increased to 40 mg every 3 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 eow was 46.5 weeks. In the end of follow-up, dose reduction was possible in 75% of patients, who maintained a PASI <3 with a follow-up of 46.5 weeks after the last dose modification. In all patients in which increasing the interval triggered an outbreak of psoriasis, PASI <3 was obtained after recovering the standard regimen. Average time to relapse in those who achieved discontinuation was 36.75 weeks, obtaining a satisfactory clinical response after reintroduction of ADA. The impact of cost saving because of the avoided doses was significantly high.

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 a new algorithm as guidance for dose reduction according to PASI score in order to reduce the costs and side effects without compromising the clinical response achieved initially.

Commercial support: None identified.

P8412

Apremilast, 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: Apremilast (APR), an oral phosphodiesterase 4 inhibitor, works intracellularly to modulate pro- and antiinflammatory 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 = 138) or APR 30 mg BID (APR30; n = 275) through week 16. All patients were then treated with APR30 through week 32, followed by a randomized withdrawal phase through week 52.

Results: At week 16, significantly more patients receiving APR30 achieved PASI-75 (28.8%) and PASI-50 (55.5%) vs. PBO (5.8% and 19.7%, respectively; $P < .0001$). Mean/median changes from baseline PASI were -15.8%/-18.0% (PBO) and -50.9%/-56.0% (APR30). Significantly more patients receiving APR30 (20.4%) achieved an sPGA score of clear (0) or almost clear (1) vs. PBO (4.4%; $P < .0001$). APR30 demonstrated significantly higher response rates vs. PBO for psoriasis affecting nails (NAPSI-50: 44.6% vs. 18.7%; $P < .0001$), scalp (ScPGA 0-1: 40.9% vs. 17.2%; $P < .0001$), and palmoplantar areas (PPPGA 0-1: 65.4% vs. 31.3%; $P = .0315$) among patients with nail involvement, ScPGA = 3, and PPPGA = 3 at baseline, respectively. Adverse events (AEs) reported during weeks 0-16 in = 5% of either group were nausea (PBO: 6.6%; APR30: 18.4%), diarrhea (PBO: 5.9%; APR30: 15.8%), nasopharyngitis (PBO: 4.4%; APR30: 7.4%), tension headache (PBO: 1.5%; APR30: 7.4%), headache (PBO: 0.7%; APR30: 6.3%), and vomiting (PBO: 3.7%; APR30: 5.1%). The majority of AEs were mild or moderate in severity and discontinuation rates because of AEs during weeks 0-16 were low (PBO: 5.1%; APR30: 5.5%). Psoriasis (flare or rebound) was reported more frequently by PBO (5.1%) vs. APR30 (1.5%) patients during weeks 0 to 16. In patients receiving APR30, diarrhea and nausea were predominantly mild in severity, had the highest incidence during the first week of dosing, and generally resolved within 1 month, with few patients reporting use of concomitant medications. Serious AEs (including serious infections, malignancies, and cardiovascular events) and laboratory value changes were consistent with prior APR studies; serious AEs were low across treatment groups.

Conclusion: Apremilast significantly reduced the severity of moderate to severe psoriasis, including nail, scalp, and palmoplantar involvement, and was generally well tolerated with no new safety or laboratory findings.

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P8359

Apremilast, an oral phosphodiesterase 4 inhibitor, in patients with moderate to severe psoriasis: Results from the randomized treatment withdrawal phase of a phase 3, randomized, controlled trial (ESTEEM 1)

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Background: Apremilast (APR), an oral phosphodiesterase 4 inhibitor, works intracellularly to modulate pro- and antiinflammatory mediators.

Methods: In ESTEEM 1, pts with moderate to severe plaque psoriasis (PASI = 12, BSA = 10%, sPGA = 3) were randomized 2:1 to APR 30 mg BID (APR30) or placebo (PBO). At wk 16, all PBO pts switched to APR30 (PBO/APR30) through wk 32. At wk 32, all APR30 pts who achieved PASI-75 were randomized (1:1, blinded) to continue APR30 or receive PBO. Upon loss of PASI-75, pts re-randomized to PBO resumed APR30.

Results: 844 pts were randomized to PBO (n = 282) or APR30 (n = 562) (mean PASI score, 19.0; mean BSA, 24.7%; >20% BSA involvement, 49.2%; PASI >20, 29.0%; prior systemic therapy and/or phototherapy, 65.0%). At wk 16, significantly more pts receiving APR30 achieved PASI-75 (33.1%) and PASI-50 (58.7%) vs. PBO (5.3% and 17.0%; $P < .0001$). Mean/median percent change from baseline (BL) in PASI score was -52.1%/-59.0% for APR30 vs. -16.8%/-14.0% for PBO ($P < .0001$). 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 at wk 32 were PASI-75 responders at wk 52, and 75.3% had = 70% improvement in PASI from BL; mean percent change from BL in PASI score ranged from -81% to -88% between wks 32 and 52. In pts re-randomized to PBO at wk 32 (n = 77), 11.7% had PASI-75 at wk 52. The median time to PASI-75 loss in pts rerandomized to PBO was 5.1 wks. Of pts rerandomized to PBO who lost response and restarted APR30, 70.3% regained PASI-75 response after reinitiation 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 (18.7%), 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 rerandomized to APR30. APR demonstrated an acceptable safety profile and was generally well tolerated for up to 52 wks.

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P8340

Autoimmunity in psoriasis patients in the treatment with ustekinumab

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Introduction: Anti−tumor necrosis factor (TNF) therapy has been associated with the induction of antinuclear antibodies (ANA) 15-40 % and autoimmune disease. The induction of ANA has been linked recently with loss of response to anti-TNF therapy in psoriasis. There is a lack of information about autoimmunity and ustekinumab. 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. Determination of ANA at least baseline and at fourth month. 3. Lack of connective disease previously."ANA were identified via indirect immunofluorescence technic 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 ENA 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, ANA were induced in 2, 2, and 1 patients, respectively; without any statistically significant differences in age, sex, psoriasis duration, arthritis and previous anti-TNF therapy. Regarding the patients who were ANA-positive pretreatment, 13 remained ANA-positive and 2 became ANA-negative on treatment. No anti-dsDNA antibodies were at baseline and there were neither cases of developed anti-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 therapy.

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