Lipid and cardiovascular effects of statin therapy in patients with and without psoriasis: A post hoc analysis of 3 large cardiovascular endpoint trials

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Background: Psoriasis is associated with increased risk of cardiovascular (CV) events and changes in CV risk factors (eg, elevated LDL-C). This exploratory post hoc analysis compared baseline characteristics and lipid and CV disease response to statins in patients with and without psoriasis in three randomized CV event prevention trials. Methods: Analyses evaluated any treatment effects on lipid levels or CV events (myocardial infarction, coronary heart disease [CHD] death, revascularization, angina, stroke, transient ischemic attack, peripheral vascular disease, congestive heart failure) in the presence or absence of psoriasis. The trials: one primary prevention trial of atorvastatin 10 mg (atorv 10) vs placebo in patients with type 2 diabetes (CARDS,[1] N = 2,838); pooled data (N = 18,889) from two secondary prevention trials of high-dose atorvastatin 80 mg (atorv 80) vs atorv 10 (TNT,[2] N = 10,219) and simvastatin 20-40 mg (LDL-IDEAL,[3] N = 8,888) in patients with CHD. Median follow-up across the trials ranged from 3.9-4.9 yrs.

Results: Baseline characteristics were generally well-balanced between patients with (CARDS, n = 52; TNT/IDEAL, n = 495) and without (CARDS, n = 2,766; TNT/IDEAL, n = 5,963) psoriasis. In the pooled TNT/IDEAL population, there were no differences in rates of CV events between patients with and without psoriasis (incidence rate: 25.9% and 24.3%, respectively). CV events were significantly reduced in patients overall and in those without psoriasis with atorv 80 vs low/standard-dose statin; a nonsignificant reduction was seen in patients with psoriasis. Analysis of treatment by psoriasis interactions for reductions in LDL-C and CV events did not demonstrate any significant differences.

Conclusion: In this exploratory post hoc analysis, atorvastatin had similar reductions in LDL-C and CV events in patients with and without psoriasis. Prospective research would be needed to confirm CV risk reduction with statin therapy in patients with psoriasis.

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Long-term safety and tolerability of brodalumab, an oral phosphodiesterase 4 inhibitor, in patients with moderate to severe plaque psoriasis: Results from a phase III, randomized, controlled trial (ESTEE1)

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Introduction: Brodalumab (AMG 827), an anti-interleukin-17 (IL-17) monoclonal antibody, has demonstrated efficacy for treatment of moderate to severe plaque psoriasis.

Objective: To examine long-term efficacy and safety of brodalumab in subjects undergoing follow-up from a phase 2 dose-ranging study.

Methods: This open-label extension (OLE) study enrolled subjects who had received placebo or active treatment with brodalumab (70, 140, or 210 mg every 2 weeks [Q2WK] or 280 mg every 4 weeks with loading dose at week 1) in a parent phase 2 study. Subjects enrolled in the OLE initially received brodalumab 210 mg Q2WK. Following a protocol amendment (enacted approximately a year after the first subject was enrolled), subjects >100 kg were switched to 140 mg Q2WK at a subsequent visit. Subjects >100 kg remained on 210 mg Q2WK. Measurements of efficacy included static Physician Global Assessment (sPGA) at week 12. Safety was assessed by monitoring adverse events (AE).

Results: Of 181 subjects enrolled at OLE baseline, 165 remained on study at week 48 (48 on 140 mg; 117 on 210 mg); 153 subjects remained on study and had an assessment at week 96 (105 on 140 mg including dose reductions; 48 on 210 mg). Complete skin clearance (sPGA = 0) was achieved in 65% (N = 175; 95% CI: 55-70) of subjects at week 12 of OLE, in 62% (54,70) of subjects at week 48 of OLE, and in 52% (44,60) of subjects at week 96. Responses of Clear/Almost Clear (sPGA 0 or 1) were achieved in 90% (N = 175; 95% CI: 85-95) of subjects at week 12 of OLE, in 86% (79,90) of subjects at week 48 of OLE, and in 76% (68-82) of subjects at week 96. AEs were reported by 93% of subjects through week 96 of the OLE. The most frequently reported AEs (=10% of subjects) were nasopharyngitis (95%), upper respiratory tract infection (91%), and arthralgia (91%). Grade 3 or higher AEs were reported in 22% of 210 mg Q2WK and 12% of 140 mg Q2WK. AEs reported in ≥3% of subjects for 210 mg Q2WK included alanine aminotransferase increased, pyrexia, and peripheral neuropathy.

Conclusion: At all measured time points from weeks 8 to 96 of therapy, the majority of subjects achieved complete skin clearance. The most frequently reported AEs consistent with common conditions (eg, upper respiratory tract infection), and were predominantly grade 2 or less.

Long-term safety of ustekinumab: 5 years of follow-up from the psoriasis anti–IL-12/23 pathway clinical development program

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Background: Ustekinumab (UST) is a human anti–interleukin-12/23 monoclonal antibody that has been approved for the treatment of moderate to severe plaque psoriasis (PsO). The drug is administered subcutaneously at doses of 45 mg or 90 mg every 12 weeks. The drug demonstrated safety and efficacy over 52 weeks in phase 3 trials. The aim of this study was to assess the long-term safety and tolerability of UST in patients with moderate to severe PsO who participated in previous UST phase 2/3 trials and were continued on UST treatment for up to 5 years.

Methods: UST was included. Data from UST dose groups were analyzed as a combined group. Results are expressed in events per 100 pt-years of follow-up (PY) and compared between the PsA subgroup and Overall Population. Conclusions: With continuous UST exposure for up to 5 yrs and approximate 9000 PY in the PsO program, long-term safety in the Overall Population was consistent with previous reports at earlier follow-up; event rates were generally comparable to other currently approved biologic agents. Long-term safety in the PsA subgroup was generally comparable to those in the overall study population.

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Maintenance of clinical response with long-term brodalumab (AMG 827) therapy for psoriasis: Week 96 results from an open-label extension study

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Introduction: Brodalumab (AMG 827), an anti-interleukin-17 (IL-17) monoclonal antibody, has demonstrated efficacy for treatment of moderate to severe plaque psoriasis.

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Methods: This open-label extension (OLE) study enrolled subjects who had received placebo or active treatment with brodalumab (70, 140, or 210 mg every 2 weeks [Q2WK] or 280 mg every 4 weeks, with loading dose at week 1) in a parent phase 2 study. Subjects enrolled in the OLE initially received brodalumab 210 mg Q2WK. Following a protocol amendment (enacted approximately a year after the first subject was enrolled), subjects >100 kg were switched to 140 mg Q2WK at a subsequent visit. Subjects >100 kg remained on 210 mg Q2WK. Measurements of efficacy included static Physician Global Assessment (sPGA) at week 12. Safety was assessed by monitoring adverse events (AE).

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Conclusion: At all measured time points from weeks 8 to 96 of therapy, the majority of subjects achieved complete skin clearance. The most frequently reported AEs consistent with common conditions (eg, upper respiratory tract infection), and were predominantly grade 2 or less.

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