P8321

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

William Ports, Pfizer Inc, Groton, CT, United States; David DeMicco, Pfizer Inc, New York, NY, United States; Rachel Laskey, Pfizer Inc, New York, NY, United States; Rana Fayyad, Pfizer Inc, New York, NY, United States; Robert Wolk, Pfizer Inc, Groton, CT, United States

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 (atorva 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; atorva 80) vs. atorva 10 (TNT,[2] N = 10,001) or standard-dose simvastatin (20−40 mg; 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 = 2,786; TNT/IDEAL, n = 18,394) psoriasis. Similar and significant LDL-C reductions from baseline were observed in patients with and without psoriasis with atorva 10 in CARDS (mean % change: -32.8 and -28.9 respectively, vs. 0.6 and 4.5 with placebo) and atorva 80 in the pooled TNT/IDEAL population (mean % change: -23.4 and -22.4 respectively, vs. -7.7 and -2.1 with low/standard-dose statin). 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 event risk was significantly reduced in patients overall and in those without psoriasis with atorva 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.

This study was sponsored by Pfizer Inc. All authors are employees of Pfizer Inc. Editorial assistance was provided by Erin Bekes, PbD, of CMC and funded by Pfizer Inc.

P8296

Long-term safety and tolerability of apremilast, an oral phosphodiesterase 4 inhibitor, in patients with moderate to severe psoriasis: Results from a phase III, randomized, controlled trial (ESTEEM 1)

Kristian Reich, MD, SCIderm Research Institute and Dermatologikum Hamburg, Hamburg, Germany; Christopher Griffiths, MD, Dermatology Centre, University of Manchester, Manchester, United Kingdom; Craig Leonardi, MD, Saint Louis University School of Medicine, St. Louis, MO, United States; Kim Papp, MD, Probity Medical Research, Waterloo, Canada; Leon Kircik, MD, Physicians Skin Care, PLLC, Louisville, KY, United States; Robert Day, PhD, Celgene Corporation, Warren, NJ, United States; Sergio Chimenti, MD, University of Rome Tor Vergata, Rome, Italy

Background: Apremilast (APR), an oral phosphodiesterase 4 inhibitor, works intracellularly to modulate inflammatory mediators. The ESTEEM 1 trial compared the efficacy and safety of APR with placebo (PBO) in pts with moderate to severe psoriasis. The safety profile of APR was assessed over 52 wks.

Methods: Pts with moderate to severe plaque psoriasis (PASI = 12, BSA = 10%, sPGA = 3) were randomized 2:1 to APR 30 mg BID (APR30) or 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 PASI-75 loss, pts rerandomized to PBO resumed APR30 treatment.

Results: 844 pts were randomized (mean psoriasis duration, 19.4 yrs; mean PASI score, 19.0; mean BSA, 24.7%; >20% BSA involvement, 49.2%; PASI >20, 29.0%; and previous systemic therapy and/or phototherapy, 65.0%). The APR-exposure period (all pts who received APR, despite when initiated [wks 0-52]) included 804 pts treated with APR30 (567.8 pt-yrs). During the APR exposure period, adverse events (AEs) in = 5% of pts were diarrhea (18.7%), URTI (17.8%), nausea (15.3%), nasopharyngitis (13.4%), tension headache (9.6%), and headache (6.5%). These AEs did not appear to increase over time and no new significant AEs emerged with continued exposure to APR. AEs were predominantly mild or moderate in severity. Severe AEs occurred in 6% of patients with no clear trend or pattern observed. Discontinuation rates because of AEs were low across all study phases and the APR exposure period. Diarrhea, nausea, and headache tended to occur in greater numbers during the first wk of APR exposure with decreased frequency over time. Serious AEs were infrequent, reported in <3% of pts in any phase of the study and in 4.2% in the APR exposure period. No imbalance in rates of major adverse cardiac events, serious infections including systemic opportunistic infection, or malignancies between APR and PBO was observed. No cases of TB (new infection/reactivation) were reported. Over the APR exposure period, there were no clinically meaningful effects on laboratory measurements except those associated with comorbidities. No cases meeting Hy's law were reported.

Conclusion: APR demonstrated an acceptable safety profile and was generally well tolerated for up to 52 wks with no new or unexpected safety findings compared with previous phase II studies. Current data do not indicate a need for laboratory monitoring with APR.

Sponsored 100% by Celgene Corporation.

P7922

Long-term safety of ustekinumab: 5 years of follow-up from the psoriasis clinical development program including patients with psoriatic arthritis

Kim Papp, MD, Probity Medical Research, Waterloo, Ontario, Canada; Kristian Reich, MD, Dermatologikum Hamburg, Hamburg, Germany; Mark Lebwohl, MD, Mount Sinai School of Medicine, New York, NY, United States; Yasmine Wasfi, PhD, Janssen Research & Development, LLC, Spring House, PA, United States

Objective: We report the long-term safety experience of ustekinumab (UST) in the subgroup of psoriasis (PsO) patients with a medical history of psoriatic arthritis (PsA) (PsA subgroup) compared with the overall PsO population (Overall Population) from the PsO development program through up to 5 yrs.

Methods: Pooled safety data across 1 Ph2 and 3 Ph3 [PHOENIX 1, PHOENIX 2, ACCEPT] clinical trials in patients with moderate to severe PsO were analyzed. Patients received UST 45- or 90 mg SC through up to 5yrs. The presence/absence of PsA (history of/current) at baseline was reported. No concurrent treatment for PsO/PsA was permitted, except low potency topical steroids for PsO during open-label long-term extensions of PHOENIX 1&2. All patients who received = 1 dose of UST were 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.

Results: The Overall Population included 3117 pts (8998 PY) who received = 1 dose of UST; with 1482 (47.5%) pts treated for >4 yrs or more (including 838 [26.9%] for >5 yrs). At baseline, 27.5% 858 pts (2490 PY) of pts had concomitant PsA and were included in the PsA subgroup. Through year 5, event rates for overall safety endpoints and AEs of interest (serious infections, NMSC/other malignancies, MACE) were generally comparable between the PsA subgroup and Overall Population. Event rates (per 100PY [95% CI]) for the PsA subgroup vs. Overall Population were as follows: AEs 249.40 (243.23-255.68) vs. 232.59 (229.44-235.76); infections 91.49 (87.77-95.32) vs. 86.52 (84.61-88.47); AEs leading to d/c 2.77 (2.16-3.51) vs. 2.40 (2.09-2.74); serious AEs 8.59 (7.48-9.83) vs. 7.10 (6.56-7.67). For AEs of interest event rates were: serious infections 1.53 (1.08-2.09) vs. 1.10 (0.89-1.34); non-melanoma skin cancers 0.48 (0.25-0.84) vs. 0.52 (0.39-0.70); other malignancies 0.72 (0.43-1.15) vs. 0.60 (0.45-0.78); major adverse cardiovascular events (MACE) 0.56 (0.31-0.94) vs. 0.44 (0.32-0.61).

Conclusions: With continuous UST exposure for up to 5 yrs and approx 9000 PY in the PsO program, long-term safety in the Overall Population were 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 were generally comparable to those in the overall study population.

Sponsored 100% by Janssen Research & Development, LLC.

P8418

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

Kim Papp, Probity Medical Research, Waterloo, Ontario, Canada; Alan Menter, Baylor University Medical Center, Dallas, TX, United States; Cassandra Milmont, Amgen Inc, Thousand Oaks, CA, United States; Criag Leonardi, St. Louis University, St Louis, MO, United States; Jean-Paul Ortonne, Hopital de l'Archet, Nice, France; Paul Klekotka, Amgen Inc, Thousand Oaks, CA, United States

Introduction: Brodalumab (AMG 827), anti−interleukin (IL)-17 receptor A 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 rolling over from a phase 2 dose-ranging study.

Methods: This open-label extension (OLE) study enrolled subjects who had received placebo or 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 clearance (sPGA = 0) was achieved in 63% (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, 85-94) of subjects at week 12 of OLE, in 85% (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 (25%), upper respiratory tract infection (18%), and arthralgia (13%). Grade 3 or higher AEs were reported in 22 subjects (12.2%). Serious AEs (SAEs) were reported in 12 (6.6%) subjects. SAEs reported between weeks 48 and 96 included acute cholecystitis, constipation (considered related), pyelonephritis, and benign parathyroid tumor (n = 1 each). One SAE of esophageal adenocarcinoma was reported and 1 fatal aortic aneurysm rupture occurred, both before week 48.

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 comprised common conditions (eg, nasopharyngitis and upper respiratory tract infection), and were predominantly grade 2 or less.

Sponsored by Amgen Inc. Brodalumab is being codeveloped by Amgen Inc and AstraZeneca/MedImmune.