Deucravacitinib, an oral, selective tyrosine kinase 2 inhibitor, in moderate to severe plaque psoriasis: 52-week efficacy results from the Phase 3 POETYK PSO-1 and POETYK PSO-2 trials

R. B. Warren1, A. Armstrong2, M. Gooderham3, B. Strober4, D. Thaci5, S. Imafuku6, H. Sofen7, L. Spelman8, N. J. Korman9, M. Zheng10, E. Colston11, J. Thourup12, S. Kundi13, R. Kiss14, S. Banerje15, A. Blauvelt15, 1Dermatology Centre, Salford Royal NHS Foundation Trust, Manchester NIHR Biomedical Research Centre, The University of Manchester, Dermatology, Manchester, United Kingdom; 2University of Southern California, Dermatology, Los Angeles, United States of America; 3SKIN Center for Dermatology, Research, and Prophy Research, Medical Research, Peterborough, Canada; 4Yale University, New Haven, and Central Connecticut Dermatological Research Center, Dermatology, Cromwell, United States of America; 5University of Lübeck, Dermatology, Lübeck, Germany; 6Fukuoka University Hospital, Dermatology, Fukuoka, Japan; 7UCLA School of Medicine, Dermatology, Los Angeles, United States of America; 8Veracity Clinical Research, Dermatology, Queensland, Australia; 9Case Western Reserve University and University Hospitals, Dermatology, Cleveland, United States of America; 10Second Affiliated Hospital, Zhejiang University, School of Medicine, Dermatology, Zhejiang, China; 11Bristol Myers Squibb, Dermatology, Princeton, United States of America; 12Bristol Myers Squibb, Rheumatology and Dermatology, Princeton, United States of America; 13Bristol Myers Squibb, Dermatology, Princeton, United States of America; 14Oregon Medical Research Center, Dermatology, Portland, United States of America.

Background: Tyrosine kinase 2 (TYK2) is an intracellular kinase that mediates signaling of key cytokines (e.g., interleukin [IL]-23 and Type I interferons) involved in the pathogenesis of immune-mediated diseases including plaque psoriasis and psoriatic arthritis (PsA). Deucravacitinib is a novel, oral, selective, allosteric inhibitor of TYK2 that achieves high selectivity by uniquely binding to the regulatory domain of the enzyme, rather than to the more conserved active domain. Deucravacitinib showed superior efficacy compared with placebo at 16 weeks in a Phase 2 trial in patients with PsA (NCT03881059). Results from the 16-week, placebo-controlled periods of two 52-week, Phase 3 trials in psoriasis (POETYK PSO-1 and POETYK PSO-2) previously showed that deucravacitinib was significantly more efficacious than placebo and apremilast based on the coprimary endpoints of ≥75% reduction from baseline in Psoriasis Area and Severity Index (PSI75) and a static Physician's Global Assessment (sPGA) score index of 0 or 1 (clear or almost clear) at Week 52.

Objectives: To evaluate the efficacy of deucravacitinib over 52 weeks in the POETYK PSO-1 and POETYK PSO-2 trials.

Methods: POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03617151) were double-blinded trials that randomised patients with moderate to severe plaque psoriasis (body surface area involvement ≥10%, PASI ≥12, sPGA score ≥3) to: 1) deucravacitinib 6 mg once daily, placebo, or apremilast 30 mg twice daily. Patients receiving placebo were switched to deucravacitinib at Week 16 in both trials. Patients randomised to deucravacitinib in PSO-1 received deucravacitinib continuously through Week 52. PSO-2 included a randomised withdrawal phase in which patients originally randomised to deucravacitinib who had achieved PASI 75 response at Week 24 were rerandomised 1:1 to placebo or deucravacitinib, whereas those who did not achieve PASI 75 response at Week 24 continued receiving deucravacitinib. The proportions of patients achieving PASI 75 and sPGA 0/1 responses were evaluated up to Week 52. Secondary efficacy endpoints evaluated over this period included PASI 90, PASI 100, percentage change from baseline in PASI, sPGA score (0 or 1), change from baseline in the Psoriasis Area and Severity Index (PSI75) and a static Physician’s Global Assessment (sPGA) score index of 0 or 1 (clear or almost clear) at Week 52.

Results: A total of 666 and 1020 patients were randomised in PSO-1 and PSO-2, respectively. Demographic and baseline disease characteristics were balanced across treatment groups; mean age was 46.6 years, mean disease duration was 18.6 years, 18.4% of patients had PsA, and 34.8% had previously used biologic therapy. PASI 75, PASI 90, and PASI 100 responses were maintained from Week 16 to Week 52 in PSO-1 (Figure 1). Additionally, sPGA responses were maintained during this period with 53.7% to 52.7% (0-17.5% to 23.5%, respectively), Patients who switched from placebo to deucravacitinib at Week 16 demonstrated PASI 75 and sPGA 0/1 responses at Week 52 (68.3% and 53.8%, respectively) comparable to those observed in patients who received continuous deucravacitinib treatment from Day 1 (65.1% and 52.7%, respectively). In PSO-2, among deucravacitinib-treated patients who achieved PASI 75 at Week 24 and were rerandomised to continue treatment, responses were maintained at Week 52 in the majority of patients (PASI 75, 80.4% [119/148]; sPGA 0/1, 70.3% [83/117]). Results for percentage change from baseline in PASI, change from baseline in the PSSD symptom score, and DLQI 0/1 were consistent with those reported for PASI and sPGA responses.
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Conclusion: Results from the Phase 3 POETYK PSO-1 and PSO-2 trials demonstrated that deucravacitinib was efficacious through 52 weeks in patients with moderate to severe plaque psoriasis. Clinical responses were maintained in patients who received continuous deucravacitinib treatment and were improved in patients who switched from placebo at Week 16 to deucravacitinib treatment.

Acknowledgements: This study was sponsored by Bristol Myers Squibb. Professional medical writing assistance was provided by Julienne Hatfield, PhD at Peloton Advantage, LLC, an OPEN Health company, Parsippany, NJ, USA, and funded by Bristol Myers Squibb.

Disclosure of Interests: Richard B. Warren Consultant of: Consulting fees: AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Celgene, DICE, Eli Lilly, Janssen, Leo Pharma, Novartis, Pfizer, Sanofi, UCB, Biogen, and UNION. Grant/research support from: Research grants: AbbVie, Almirall, Amgen, Celgene, Eli Lilly, Janssen, Leo Pharma, Novartis, Pfizer, and UCB.; April Armstrong Grant/research support from: Grants and personal fees: AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Leo Pharma, and Novartis; Personal fees: Boehringer Ingelheim/Parke-Davis, Celgene, Dermavant, Genentech, GlaxoSmithKline, Menlo Therapeutics, Merck, Modernizing Medicine, Ortho Dermatologists, Pfizer, Regeneron, Sanofi Genzyme, Science 37, Sun Pharma, and Valeant; Grants: Dermira, Kyowa Hakko Kirin, and UCB, outside the submitted work. Melinda Gooderham Consultant of: Advisory board, principal investigator, and lecture fees: Arcutis, Galderma, Leo Pharma, Pfizer, and Regeneron; Principal investigator and consulting fees: Akros Pharma and Kyowa Kirin; Advisory board, principal investigator, lecture fees, and consulting fees: AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Novartis, Sanofi Genzyme, and Valeant; Principal investigator: Asian, Bristol Myers Squibb, Dermavant, Dermira, GlaxoSmithKline, MedImmune, Merck, Roche Laboratories, and UCB. Bruce Strober Consultant of: Consultant (honoraria): AbbVie, Almirall, Amgen, Arcutis, Arena, Arista, Asana, Boehringer Ingelheim, Immucologics, Bristol Myers Squibb, Connect Biopharma, Dermavant, Eli Lilly, Equillium, Janssen, Leo Pharma, Merck, Novartis, Pfizer, Sanofi Genzyme, Kisseiya Pharma, Likor, and Sandoz; Employee of: Bristol Myers Squibb, Genentech, Merck, Sanofi, and UCB. Howard Sofen Consultant of: Advisory board, principal investigator, and talk fees: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Leo Pharma, Novartis, and Pfizer; Howard Sofen Consultant of: Clinical investigator: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Janssen, Leo Pharma, Novartis, and Sun Pharma.; Lynda Spielman Consultant of: Consultant, paid investigator, and/or speaker: AbbVie, Amgen, Anacor, Ascend, Astellas, AstraZeneca, Blaze Bioscience, Boehringer Ingelheim, Botanix, Bristol Myers Squibb, Celgene, Dermira, Eli Lilly, Galderma, Genentech, GlaxoSmithKline, HemaLink, Janssen, Leo Pharma, Mayne, MedImmune, Merck, Merck-Serono, Novartis, Otsuka, Pfizer, Phosphagenics, Photon MD, Regeneron, Roche, Samumed, Sanofi Genzyme, SHR, Sun Pharma, Trius, UCB, and Zai Lab.; Neil J Korman Speakers bureau: Advisory board, consulting fees: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Leo Pharma, Novartis, Principia, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB; Grant/research support from: Grant support/principal investigator: AbbVie, Amgen, Argenx, Bristol Myers Squibb, Celgene, Chemocentric, Eli Lilly, Galderma, Kyowa Hakko Kirin, Leo Pharma, Menlo, Principia, Prothera, Rhizen, Syntimmune, Trevi, and Xbiotech.; Min Zheng Speakers bureau: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly China, Leo Pharma China, Novartis China, Pfizer, Sanofi China, and Xian-Janssen, Consultant of: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly China, Leo Pharma China, Novartis China, Pfizer, Sanofi China, and Xian-Janssen, Elizabeth Colston Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, John Throup Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Sudeep Kundu Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Subhasish Banerjee Shareholder of: Employees and shareholders: Bristol Myers Squibb, Andrew Blauvelt Consultant of: Scientific advisor and/or clinical study investigator: AbbVie, Abcentra, Aligos, Almirall, Amgen, Arcutis, Arena, Aslan, Atomoxetine, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Ecol7, Eli Lilly, Evommune, Forte, Galderma, Incyte, Janssen, Landos, Leo Pharma, Novartis, Pfizer, Rapt, Regeneron, Sanofi Genzyme, Sun Pharma, UCB, and Vbiome.; DOI: 10.1136/annrheumdis-2022-eular.1377

AB0891 DEUCRAVACITINIB EFFICACY IN PSORIATIC ARTHRITIS BY BASELINE DMARD USE: EXPLORATORY ANALYSIS FROM A PHASE 2 STUDY

A Dech暂停,1 M. Nowak,2 J. Ye,3 T. Lehman,4 L. Wei,5 S. Banerjee,5 P. J. Mease,6 1Oregon Health & Science University, Arthritis and Rheumatic Diseases, Portland, United States of America; 2Bristol Myers Squibb, Clinical R&D, Princeton, United States of America; 3Bristol Myers Squibb, Medical Affairs, Princeton, United States of America; 4Bristol Myers Squibb, WW Medical Immunology, Princeton, United States of America; 5Bristol Myers Squibb, Medical Immunology, Princeton, United States of America; 6Bristol Myers Squibb, Rheumatology and Dermatology, Princeton, United States of America; 7Swedish Medical Center/Providence St. Joseph Health and University of Washington, Rheumatology Research, Seattle, United States of America

Background: Psoriatic arthritis (PsA) treatment guidelines recommend that patients (pts) inadequately responding to conventional synthetic DMARDs (csDMARDs) can be treated with targeted synthetic DMARDs with or without background use of csDMARDs. Deucravacitinib (DEUC) is a novel, oral, selective, allosteric inhibitor of tyrosine kinase 2 (TYK2) that binds to the unique TYK2 regulatory domain, thereby suppressing signaling of key cytokines (eg, IL-23) involved in PsA pathogenesis. In a Phase 2 trial in pts with active PsA, DEUC was well tolerated and significantly more efficacious than placebo (PBO) after 16 weeks of treatment.1

Objectives: This analysis further evaluated the effect of DEUC in this Phase 2 trial in pts treated with and without background csDMARDs for 16 weeks.

Methods: This double-blind trial (NCT03881059) enrolled pts with active PsA who had either failed or were intolerant to ≥1 nonsteroidal anti-inflammatory drug, corticosteroid, csDMARD, and/or 1 TNF inhibitor (TNFi; up to 30%). Pts were randomised: 1:1:1 to DEUC 6 mg once daily (QD) or 12 mg QD, or PBO. A post hoc subgroup analysis in pts with and without background csDMARD use assessed improvements in select clinical outcomes (ACR 20 response, and change from baseline in ACR components, Psoriasis Area and Severity Index total score, and Psoriatic Arthritis Disease Activity Score) at Week 16.

Results: Baseline (BL) demographics, clinical characteristics, and disease activity were generally similar among pts with and without background csDMARD use. At BL, background csDMARD use was 64.3%, 64.2%, and 66.7% and methotrexate use was 50.0%, 55.2%, and 59.1% in the DEUC 6 mg QD, 12 mg QD, and PBO groups, respectively. Pts with and without background csDMARD use showed similar improvements at Week 16 with DEUC treatment versus PBO.