Efficacy and safety of tirabrutinib, highly selective Bruton’s tyrosine kinase inhibitor, for oral treatment of pemphigus: a multicenter, open-label, uncontrolled and withdrawal study. 1 Yamagami, Y Miyasaka, N Hisi, C Tateshi, I Ishko, T Saito, H Hagiura, K Hashimoto and M Amagai 1 Keio University School of Medicine, Tokyo, Japan, 2 Faculty of Medicine, University of Tokyo School of Medicine, Tokyo, Japan, 3 Kawasaki Medical School, Okayama, Japan, 4 Kurume University School of Medicine, Kurume, Japan, 5 Osaka City University Graduate School of Medicine, Osaka, Japan, 6 School of Medicine, Faculty of Medicine, Toho University, Tokyo, Japan, 7 Ono Pharmaceutical Co., Ltd., Osaka, Japan and 8 Ehime University School of Medicine, Matsuyama, Japan

Bruton’s tyrosine kinase (BTK) enhances BCR-stimulated proliferation, costimulatory molecule expression, and antibody production in B cells. Tirabrutinib is a highly selective oral BTK inhibitor that is expected to inhibit the immunoglobulin G autoantibody-mediated mechanism that plays a central role in the pathophysiology of pemphigus. The aim of this study was to investigate the efficacy and safety of tirabrutinib in patients with refractory pemphigus. In this multicenter, open-label, uncontrolled phase 2 study, patients received posológica oral tirabrutinib 80 mg once daily for 52 weeks. In total, 16 patients were evaluated. The complete remission (CR) rate after 24 weeks of treatment (primary endpoint) was 18.6% (3/16 patients). The cumulative CR rate and cumulative remission rate at 52 weeks of treatment were 50.0% and 62.5%, respectively. Control of disease activity rates were 37.5%, 60%, 76.8%, and 92.9% at weeks 4, 12, 24, and 52, respectively. During the 52 weeks of tirabrutinib administration, decreases in pemphigus disease area index score, auto-dermengin 1 and autoactran levels, and oral corticosteroid exposure were observed. One patient (6.3%) relapsed. The incidence of adverse events (AEs) and serious AEs were 87.5% and 18.8%, respectively. No grade 4 AEs were reported. The patients in this study showed favorable outcomes in response to the treatment with tirabrutinib and did not result in any major safety concerns. Thus, tirabrutinib may be a new treatment option for patients with refractory pemphigus.

Differences in clinical features and comorbidity burden between HLA-C*06:02 carrier groups in more than 9,000 people with psoriasis: A large population-based study. S Kaupp, J Jokeiainen, M Timonen, K Tasanen and J Huijala University of Oulu, Oulu, Finland

Comparison of psoriasis has two distinct ages of onset: early onset (EOP; ≤40 years of age; approx. 25%) and late onset (LOP; >40 years of age; approx. 25%). EOP and LOP appear to be clinically similar but genetically and immunologically separable. There are few clinical trial data and fewer real-world studies comparing drug survival of biologics in EOP against LOP. The aim was to investigate whether age of onset predicts drug survival in a real-world population using BABIR, a long-term pharmacovigilance registry of people on biologic therapies for psoriasis in the UK and Eire. Data from patients registering to BABIR from 2007-2020 on either etanercept, adalimumab, secukinumab or ustekinumab with at least 6 months' follow-up were analysed. Exposure time was calculated from initiation to the discontinuation date, and was censored at the latest follow-up or death. Patients aged 50 years and above at enrolment were categorised into EOP or LOP. Hazard ratio (HR) with 95% confidence interval (CI) was estimated using a flexible parametric model to compare EOP against LOP for drug survival of patients discontinuing therapy due to the lack of effectiveness and/or the occurrence of adverse events. Each model included age of onset (exposure), biologics (modifier) and adjusted for confounders using multiple imputed data. In total, 4677 patients were included; 2137 (69.2%) EOP vs. 1440 (30.8%) LOP. There was no significant difference in proportion of EOP vs. LOP patients between each biologic cohort. There was no significant difference between EOP and LOP for biologic ineffectiveness (HR [95% CI]: 1.1 (1.0-1.3)) or adverse events [1.1 (0.9-1.3)]. Adalimumab and etanercept had higher proportion of discontinuation due to ineffectiveness [1.6 (1.2-2.0) and 6.2 (9.4-24.5)] or adverse events [1.6 (1.2-2.1) and 2.0 (1.4-3.0)] compared with ustekinumab but similar drug survival when compared to secukinumab. There is no evidence that age of onset is a relevant predictor for overall biologic survival in psoriasis.

Glucagon-like peptide-1 analogues and sodium-glucose co-transporter-2 inhibitors do not increase risk of bullous pemphigoid. O Vargulisa, J Jokeiainen, J Huijala and K Tasanen 1 PEDEGO Research Unit, University of Oulu, 2 Department of Dermatology and a Medical Research Center, Oulu University Hospital, Oulu, Finland, 3 Infrastructure for Population Studies, Faculty of Medicine, University of Oulu, Oulu, Finland and 4 Unit of General Practice, Oulu University Hospital, Oulu, Finland

Glucagon-like peptide-1 (GLP-1) analogues and sodium-glucose co-transporter 2 (SGLT2) inhibitors, glucagon-like peptide-1 (GLP-1) analogues or thiazolidinediones were associated with increased risk of BP. The present study strengthens the view of DPP-4 inhibitors being the most evident risk factor for BP among DM drugs. Also, it offers novel data showing GLP-1 analogues and SGLT2 inhibitors not being associated with increased risk of BP.

Efficacy of continuous dosing, down-dository, or treatment withdrawal after successful treatment with baricitinib in patients with moderate-to-severe atopic dermatitis. K Reich, B Sinn, A Weillenborg, F Raiman, I Gullotta, J Bon, E Staud, M Eberle, C Kaspers and M Simpson 1 Department of Medical and Molecular Genetics, School of Basic & Medical Biosciences, Faculty of Life Sciences & Medicine, King’s College London, London, United Kingdom, 2 St John’s Institute of Dermatology, School of Basic & Medical Biosciences, Faculty of Life Sciences & Medicine, King’s College London, London, United Kingdom, 3 St John’s Institute of Dermatology, Guy’s and St Thomas’ NHS Foundation Trust, London, United Kingdom and 4 Health Data Research UK, London, United Kingdom

Corticosteroids have an established role in the treatment of moderate-to-severe atopic dermatitis (AD) with oral prednisolone (PSL) or prednisone (PRED) the reference standard. This study was conducted to compare the efﬁcacy and safety of baricitinib, a selective JAK1/2 inhibitor, with continuous dosing (CD), down-dository (DD), and treatment withdrawal (TW) in the extension phase of an ongoing, double-blind, phase 3 long-term study (BADBIR) with AD patients who had achieved a ≥0/1/2 (P < 0.001, PBO vs BARI 2mg); 41% (continuous 2mg), 41%, and 64% of pts were retreated and of these, 71%, 45% and 30% for vIGA-AD 0/1 (P < 0.001). This study showed that the efficacy and safety of baricitinib were not affected by varying the treatment strategy. Baricitinib 4mg is associated with an increased risk of bullous pemphigoid and other cardiometabolic comorbidities. This study reveals striking new differences in clinical features and comorbid burden between HLA-C*06:02-stratified subgroups. HLA-C*06:02 status is therefore a candidate biomarker for the delineation of important psoriasis endotypes.

Efficacy with continuous dosing, down-dository, or treatment withdrawal after successful treatment with baricitinib in patients with moderate-to-severe atopic dermatitis. K Reich, E Simpson, A Weillenborg, R Raiman, I Gullotta, J Bon, E Staud, M Eberle, C Kaspers and M Simpson 1 Department of Medical and Molecular Genetics, School of Basic & Medical Biosciences, Faculty of Life Sciences & Medicine, King’s College London, London, United Kingdom, 2 St John’s Institute of Dermatology, School of Basic & Medical Biosciences, Faculty of Life Sciences & Medicine, King’s College London, London, United Kingdom, 3 St John’s Institute of Dermatology, Guy’s and St Thomas’ NHS Foundation Trust, London, United Kingdom.

A candidate biomarker for the delineation of important psoriasis endotypes.

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