Risk of serious infection associated with biologic therapies in psoriasis: A prospective cohort study from the British Association of Dermatologists Biologic Interventions Register (BADDIR)

S Gerdes, P Arenberger, K Kingo, J Wegłowska and H Gerdes

In a prospective cohort study from BADDIR (09/2007-10/2016), we compared the risk of serious infections (SI) associated with the use of biologic therapies in patients with psoriasis against a cohort on non-biologic systemic therapies (non-biologics). Etanercept, adalimumab, and ustekinumab were compared to non-biologics, inclusive of any exposure to methotrexate, ciclosporin, acetimin, fumaric acid esters, psoralen-ultraviolet A, hydroxycarbamide. SI were defined by association with hospitalisation; use of intravenous antimicrobial therapy; and/or led to death. Incidence rates to first SI were measured. Proportion-score weighted Cox proportional hazards models were used to compare the risk of SI and hazard ratios were derived. 1352, 3271 and 994 biologic-naïve participants were included in the etanercept, adalimumab and ustekinumab cohorts respectively and 3421 biologic-naïve participants were included in the non-biologic cohort. In total, 283 patients had a SI: the incidence rates were: non-biologic: 14.2/1000 person-years (95% confidence interval [CI] 11.5 to 17.4); etanercept: 15.3/1000 person-years (11.6 to 20.1); adalimumab: 14.8/1000 person-years (11.4 to 16.6); ustekinumab: 15.1/1000 person-years (10.6 to 21.1). No statistically significant increases in the risk of SI were observed for etanercept (hazard ratio [HR] 1.10; 95% CI 0.75 to 1.60); adalimumab (HR 0.93; 95% CI 0.69 to 1.26) or ustekinumab (HR 0.92; 95% CI 0.60 to 1.43) compared to non-biologics. Our results suggest that the risk of SI should not be a key discriminator when choosing between non-biologics, etanercept, adalimumab and ustekinumab for the treatment of psoriasis.

Crisaborole ointment improves global atopic dermatitis severity: Pooled results from two phase 3 clinical trials

J Fowler, R Sidbury, A Zareaghi, DM Parisier, and FE Cook-Bolden

Crisaborole ointment (C21) is a novel, potent, and selective glucocorticoid receptor (GCR) agonist indicated for the treatment of mild-to-moderate AD. In this analysis, we pooled the results from two Phase 3 RCTs (HEDGEMARK 365 and C21B) to investigate the efficacy of C21 in improving global AD severity in patients with mild-to-moderate AD. All patients were young adults (aged 18-65) with a history of AD for ≥3 months and a Physician’s Global Assessment of Disease Severity (PGA) score of ≥3. Patients were randomized to C21 (0.05% or 0.5% ointment) or vehicle twice daily for 12 weeks. The primary endpoint was the percentage of patients achieving Investigator’s Global Assessment of Disease Severity (IGA) 0 or 1 at Week 12. Additional endpoints included change from baseline inASI and the percentage of patients with ≥50% improvement from baseline in AD-specific quality of life (QoL) measures at Week 12. The per-protocol analysis set included all randomized patients who completed all study visits. At Week 12, 55% of patients achieved an IGA score of 0 or 1 with C21 0.05% ointment compared to 30.3% with vehicle (OR 2.75; 95% CI 2.03-3.76). These improvements were durable at Week 24. C21 0.05% ointment also resulted in clinically meaningful improvements in QoL measures compared to vehicle. In conclusion, these pooled results from two Phase 3 trials indicate that C21 improves global AD severity and QoL in adults with mild-to-moderate AD.

Switching treatments of etanercept biosimilar GP2015 with originator product does not impact efficacy, safety and immunogenicity in patients with chronic plaque psoriasis

CE Griffiths, R Reich, D Thapliyal, S Gerdes, P Arenberger, K Kingo, J Weglowksa and H Gerdes

1 University of Manchester, United Kingdom, Manchester, United Kingdom, 2 University of Manchester, Hamburg, Germany, 3 Medical University of Schleswig-Holstein, Lübeck and Kiel, Germany, 4 Charles University, Prague, Czech Republic, 5 Tartu University Hospital, Tartu, Estonia, 6 Szpital Specjalistyczny w Wroclawiu, Wroclaw, Poland and 7 HELLAX AG&Sandoz, Hofkirchen, Germany

The objective of the phase III ECG study was to show equivalence in efficacy, safety and immunogenicity of the etanercept biosimilar GP2015 and the originator product (ETN) in patients with chronic plaque psoriasis. We present the 30-week data comparing repeated switching between continued treatments (n=531) with moderate to severe plaque psoriasis were randomized to receive 50 mg GP2015 or ETN twice weekly s.c. up to week 12. Patients with ≥50% improvement in psoriasis area and severity index (PSI) at week 12 were re-randomized to continue with the same treatment or to undergo 3 consecutive switches to the alternative product until week 30 each at 50 mg once-weekly. The primary endpoint of equivalence in PSI 75 response at week 12 was met. At week 30, the pooled continued and pooled switched treatment groups (n=446, per-protocol set) showed similar PSI 75 response rates of 86.6% and 85.9%. The proportion of patients with ≥1 treatment-emergent adverse event (AE) and the types of AEs reported were similar between groups (continued 34.9%; switched 36.7%). Similar proportion of patients experienced injection site reactions with continued (4.3%) or switched treatments (4.6%). The incidence of serious adverse events over 30 weeks was low (1.9%, n=5, all in ETN group). At week 36, 12 weeks after the last of multiple switches, another patient switching from ETN to GP2015 found ADA positive. All ADAs were transient and non-neutralizing. Equivalence in efficacy of GP2015 and ETN was observed in moderate to severe psoriasis patients. Multiple switching between treatments did not impact efficacy, safety, or immunogenicity. AEs were consistent with previous ETN trials in psoriasis.

Patients with hidradenitis suppurativa have a high psychiatric disease burden

L Huillaia, H Tiri, J Jokelaenen, M Timonen and K Jass elasticity

1 Department of Dermatology, University of Oulu, Oulu, Finland

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease of hair follicles which is associated with various comorbidities. The aim of our study was to clarify the associations between HS and psychiatric disorders. We conducted a nationwide retrospective study that included 4381 patients with HS and 39554 psoriasis and 43248 melanocytic nevi (MN) patients as controls. Patient data were obtained from the statutory Finnish Care Register for Health Care. Statistical analyses were performed using STATA and the SAS software package. The incidence of HS in Finland was 2.7/100,000 persons/year. At least one psychiatric diagnosis was found in 24.1% of the HS patients compared with 19.1% of those with psoriasis (OR 1.41; 95% CI 1.30-1.53) and 14.6% of those with MN (OR 1.28; 95% CI 1.17-1.41). The prediction prevalence psychotic disorders was 4.7% in the HS group compared with 3.8% of those with psoriasis (OR 1.26; 95% CI 1.12-1.43) and 1.9% of those with MN (OR 1.33; 95% CI 1.14-1.55). The prevalence of bipolar disorder, dysthymia, and personality disorders were: non-biologic 14.2/1000 person-years (95% confidence interval [CI] 11.5 to 17.4); etanercept: 15.3/1000 person-years (11.6 to 20.1); adalimumab: 14.8/1000 person-years (11.4 to 16.6); ustekinumab: 15.1/1000 person-years (10.6 to 21.1). No statistically significant increases in the risk of SI were observed for etanercept (hazard ratio [HR] 1.10; 95% CI 0.75 to 1.60); adalimumab (HR 0.93; 95% CI 0.69 to 1.26) or ustekinumab (HR 0.92; 95% CI 0.60 to 1.43) compared to non-biologics. Our results suggest that the risk of SI should not be a key discriminator when choosing between non-biologics, etanercept, adalimumab and ustekinumab for the treatment of psoriasis.

Abdominal obesity and insulin resistance are strongly associated with liver fibrosis in people with severe psoriasis

C Macbury, WF Porter, C Lewis, R Miquel, T Wong, CH Smith and J Barker

1 St John’s Institute of dermatology, Kings College London, London, United Kingdom, 2 Guys and St Thomas Hospital, London, United Kingdom and 3 Kings College London, London, United Kingdom

People with severe psoriasis are at risk of developing liver fibrosis due to obesity, alcohol and methotrexate. In Europe only people taking methotrexate are screened for liver fibrosis. Aims were: (1) To identify the proportion of patients attending our service with liver fibrosis (2) Identify the most important risk factors associated with fibrosis (3) Evaluate non-invasive tests for fibrosis.400 adults with severe psoriasis were recruited 2012-2015. Data collection to assess risk factors included a questionnaire, PASI, anthropometric indices and fasting blood draw. Abdominal ultrasound was performed. Fatty liver disease. Diagnosis made by transient elastography (Fibroscan). Diagnostic accuracy of blood tests and clinical measures were compared to Fibroscan results. Characteristics at enrolment were: age (years): 49.5±13, 27% female, body mass index: 29.2±6.7, waist (cm): 102±26, and PASI: 16.7±2.8. 27% had fatty liver disease, 20% liver fibrosis (Fibroscan≥16.7 kPa). 14% had advanced fibrosis (Fibroscan≥27.0 kPa). Prognostic risk factors significantly associated with fibrosis on univariate analysis included age >60, female, waist, fatty liver disease and HOMA-IR (HOMA-IR: 7.2 ± 6.5). The association of Insulin Resistance calculated from (fasting glucose and insulin). Sex, methotrexate duration, psoriasis duration and alcohol use were not significantly associated with fibrosis. Multivariate analysis identified the model of waist measurement, HOMA-IR and AST as the best predictors of liver fibrosis (R² = 0.21). For both fibrosis and advanced fibrosis, HOMA-IR and waist measurements provided the strongest predictive measures with all AUCs > 0.78. One fifth of our patient population have liver fibrosis. Metabolic parameters were the most important factors associated with fibrosis. We should now only screen restricting people taking methotrexate but should screen according to waist measurement.