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Journal Watch

Reviewed by CW Chow 周志榮, CC Koh 許招財, AHW Wong 王慶榮, CK Wong 黃之鍵

The oral Janus kinase/spleen tyrosine kinase inhibitor ASN002 demonstrates efficacy and improves associated systemic inflammation in patients with moderate-to-severe atopic dermatitis: results from a randomized double-blind placebo-controlled study

Bissonnette R, Maari C, Forman S, Bhatia N, Lee M, Fowler J, et al.
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Spleen tyrosine kinase (SYK) and Janus kinase (JAK) are tyrosine kinases (TYKs) which have an important role in inflammatory processes of atopic dermatitis (AD) through cytokine pathway. ASN002 is an oral, dual Janus kinase and spleen tyrosine kinase inhibitor. This was a randomised, double-blind, placebo-controlled study conducted in 10 centres in Canada and U.S.A. between April 2017 to November 2017. Thirty-six patients (aged 18-75 years old) with moderate-to-severe AD were recruited in this study. Patients enrolled were randomised (3:1) into different dosage (orally daily for 28 days) and placebo group: doses of 20 mg, 40 mg and 80 mg and placebo group. Patients were assessed at baseline, day 15, day 29 for safety, efficacy, pruritus and serum biomarkers.

ASN002 has better therapeutic response than placebo. The proportion of patients achieved Eczema Area and Severity Index (EASI 50) at day 29 were as follows: (20 mg: 20%, 40 mg: 100%, 80 mg: 83%, placebo: 22%).The proportion of patients achieved EASI 75 were as follows: (20 mg: 0%, 40 mg: 71%, 80 mg: 33%, placebo: 22%). The proportion of patients achieved Investigator's Global Assessment (IGA) score 0/1 with at least a two-grade reduction from baseline at day 29 were as follows: (20 mg: 0%, 40 mg: 43%, 80 mg: 17%, placebo: 11%). Besides, ASN002 showed a significant better changes in single weekly pruritus numeric rating scale (NRS) for patients with treatment: 20 mg (-1.3±2.1), 40 mg: -3.1±2.7, 80 mg: -4.7±2.1, placebo: -1.6±1.8. Side effect of ASN002 were mild and as follows: lymphopaenia, headache, nasopharyngitis, back pain. In conclusion, ASN002 40 mg and 80 mg dose were effective in treatment of moderate-to-severe AD.

Conjunctivitis in dupilumab clinical trials

Akinlade B, Guttman Y, Bruin W, Simpson EL, Blauvelt A, Cork MJ, et al.
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Dupilumab is a fully human VelocImmune-derived monoclonal antibody that inhibits interleukin (IL)-4 and IL-13. It is indicated to treat moderate-to-severe atopic dermatitis (AD) and as maintenance treatment of moderate-to-severe asthma for patients ≥12 years old. Ocular surface disease (e.g. allergic conjunctivitis, blepharitis and keratitis) is a common comorbidity of severe AD and other atopic disorders e.g. asthma and allergic rhinitis. It was found that ocular surface disorders (e.g. conjunctivitis, blepharitis, keratitis, eye pruritus, dry eyes) are also commonly reported adverse events in dupilumab-treated patients with AD.

Randomised, placebo-controlled trials of dupilumab treatment in AD (2629 patients), asthma (2876 patients), chronic rhinosinusitis (60 patients) with nasal polyps and eosinophilic oesophagitis (47 patients) group were studied for the occurrence and risk factors of conjunctivitis.

The incidence of treatment-related conjunctivitis was higher in the dupilumab (8.6%) group than placebo group (2.1%) after 16 weeks treatment of AD patients. The incidence of conjunctivitis was similar between placebo and dupilumab in patients with asthma, chronic rhinosinusitis with nasal polyps and eosinophilic oesophagitis. Conjunctivitis were mostly mild to moderate with only <0.5% patients developing severe conjunctivitis. Conjunctivitis was mostly resolved at the end of treatment. Patients with high-level efficacy outcomes were less likely to develop conjunctivitis. Patients with more severe baseline AD, high levels of certain biomarkers (thymus and activation-regulated chemokine, IgE and eosinophils) or previous conjunctivitis history were more likely to develop conjunctivitis.

In conclusion, dupilumab group has higher incidence of conjunctivitis than placebo group in treatment of AD.

Accuracy of PCR and serological testing for the diagnosis of primary syphilis: Both tests are necessary

Noda A, Rodriguez IG, Grillova L, Bosshard P, Lienhard R.
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Laboratory diagnosis of syphilis remain challenging especially during early disease. Rapid and accurate diagnosis is crucial to ensure patients and their contacts receive timely treatment to eradicate infection and prevent transmission.

This was a prospective observational study conducted in Cuba which studied the performance of polymerase chain reaction (PCR) and serological testing for the diagnosis of primary syphilis by evaluating anogenital swabs and sera from 178 male patients (median age 28 years) presenting with anogenital ulcers, attending a specialist clinic for sexually transmitted infections from 2012 to 2016. Three loci: polA, tpp47 and 16S rDNA were evaluated by PCR, while serology was assessed with venereal disease research laboratory (VDRL) and *T. pallidum* hemagglutination (TPHA) assays.

The PCR sensitivities, specificities, positive and negative predictive values were 76.1%, 100%, 100% and 57.9%, respectively, while that of serology were 62.5%, 100%, 100% and 45.2% respectively, indicating that there was poor correlation between the two methods (agreement=52.3%, kappa 0.0512, 95% CI=-0.0928 to 0.1951, p=0.496). It can be associated with the variation in sensitivity of both tests with regard to the timing of the diseases e.g. PCR can be positive during the early serological window period while positive serology with negative PCR can occur in healing ulcers.

The authors concluded that combined complementary use of both investigations was recommended for patients presenting with anogenital ulceration.

Self-collected versus clinician-collected samples for HSV-2 and HSV-2/HPV screening in HIV-infected and uninfected women in the Tapajos region, Amazon, Brazil

Rodrigues LLS, Pilotto JH, Lima LRP, Gaydos CA, Hardick J, Morgado MG, et al.
Int J STD & AIDS 2019;30:1055-62.

This cross-sectional study compared self-collected samples and clinician-collected samples in the evaluation of the prevalence of herpes simplex virus 2 (HSV-2) and HSV-2/human papillomavirus (HPV) co-infection by in human immunodeficiency virus 1 (HIV-1)-infected and uninfected women from the Tapajos region, Amazon, Brazil. In the study, 439 anal and cervical scrapings and cervico-vaginal self-collected samples from 153 HIV infected and uninfected women were analysed with real time PCR for HSV-2 and nested PCR for HPV.

The prevalence was as follows: anogenital HSV-2: 9.2% (14/153); HPV: 67.3% (103/153); HSV-2/HPV co-infection: 6.5% (10/153). There overall agreement between the self-collected and clinician-collected samples was significant (95.5%, 11/133, kappa 0.64, 95% CI 0.38-0.90, $p<0.0001$) for HSV-2 detection. Multivariate analysis to identify risk factors for HSV-2/HPV co-infection showed that, in all cases, HSV-2 genital infection was more prevalent than anal infection. There was a higher prevalence of HSV-2 and HSV-2/HPV in HIV-infected women. HSV-2/HPV co-infection was not detected in any of the cases of cervical squamous intraepithelial lesion. Risk factors for HSV-2/HPV were as follows: age 25 years or less (aOR=10.07) and being single (aOR=3.79). Young, single women in general, had a higher risk of HSV-2/HPV infection. It was concluded that cervico-vaginal self-collection can be a useful for the screening of HSV-2 and HPV in limited-resource settings where early STI diagnosis is hampered by the unavailability of laboratory STI testing and difficult access to medical facilities.

Association of hidradenitis suppurativa with inflammatory bowel disease: A systematic review and meta-analysis

Chen WT, Chi CC.
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The MEDLINE, Cochrane Central Register of Controlled Trials, and Embase databases were searched for studies to conduct a meta-analysis investigating the association between hidradenitis suppurativa (HS) and inflammatory bowel disease (IBD). Case-control, cross-sectional, or cohort studies were selected. The odds ratios (ORs) and hazard ratios (HRs) of IBD, Crohn disease, and ulcerative colitis in association with HS were studied.

A total of 93,601 unique participants from one cohort study, five case-control studies and two cross-sectional studies were included. In the meta-analysis of case-control and cross-sectional studies, there was a significantly increased odds of Crohn disease in patients with HS (pooled OR, 2.12; 95% CI: 1.46-3.08). A significantly increased odds of ulcerative colitis in patients with HS (pooled OR, 1.51; 95% CI: 1.25-1.82) was demonstrated by the meta-analysis of cross-sectional and case-control studies. In one cohort study of 14136 participants, there was an increased risk of IBD in patients with HS (HR, 5.6; 95% CI not reported; $P<0.002$). A significantly increased odds of IBD in subjects with HS (ORs, 2.16; 95% CI: 1.40-3.34) and 10.00 (95% CI: 1.94-51.50) was seen in two case-control studies.

It was concluded that there is evidence to support an association of HS with IBD and that

gastroenterology consultation should be sought in cases of HS presenting with weight loss, chronic diarrhoea, bloody stools, and recurrent abdominal pain.

Factors associated with complete remission after rituximab therapy for pemphigus

Kushner CJ, Wang S, Tovanabutra N, Tsai DE, Werth VP, Payne AS.
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The study investigated the rates of complete remission off therapy (CROT) and relapse and prognostic factors for achieving CROT in pemphigus cases treated with rituximab. This was a single-centre, retrospective, cohort study of 112 patients with pemphigus treated with rituximab followed up for least 12 months after rituximab therapy. The primary study outcome was complete remission off therapy (CROT) after one cycle and secondary study outcomes consisted of median time to relapse, rate of CROT or the composite end point of CROT or complete remission on minimal therapy after one or more cycle.

A total of 112 patients with pemphigus with followed for a median 37.8 months (range, 12.1-130.7) after rituximab infusion were studied. Of these, 79 patients (70.5%) achieved CROT at any time during the study period, which was reached at a median 10.5 months (range, 2.0-49.8 months). Relapse occurred within 23.3 months (interquartile range, 10.8-50.4 months) after achieving CROT in 36 out of 72 (50%) patients studied analyzed.

The lymphoma-dose regimen was significantly more likely to achieve CROT than those who received the rheumatoid arthritis-dose regimen (OR, 2.70; 95% CI, 1.03-7.12; P=0.04) as suggested by the multivariate analysis. Increasing age was associated with a significantly higher rate of CROT (P=0.01) while the odds of CROT was decreased with a body mass index of greater than or equal to 35 (OR, 0.14; 95% CI, 0.03-0.63; P=0.01).

It was concluded that the odd of achieving CROT in pemphigus with rituximab were increased by lymphoma dosing and older patient age and decreased by body mass index greater than or equal to 35. These findings provide information for predicting outcomes when rituximab is used to treat pemphigus.

Dermal suture only versus layered closure: A randomized, split wound comparative effectiveness trial

Joo JS, Zhuang AR, Tchanque-Fossuo C, Tartar D, Armstrong AW, King TH, et al.
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This was a prospective, randomised, evaluator-blinded, split scar study comparing the conventional bilayered closure technique with the single-layer deep-dermal suturing technique for primary closure of wounds. The primary outcome measure was mean sum Patient and Observer Scar Assessment Scale (POSAS) score at 3 and 12 months. In the POSAS score, there are questionnaires for the patient also another questionnaire for the assessor. Patients were asked to evaluate five scar parameters: color, stiffness, thickness, irregularity, and overall opinion, grading 1 to 10 (1: comparable to normal skin; 10: worst scar imaginable). The same scale was used by the observers. During the study, the wound was labelled as follows: the left half or superior half of the wound being labelled A and the right or inferior half of the wound being labelled B. Half of the wound was then closed with buried vertical mattress sutures with absorbable sutures and over the other half of the wound, an additional cuticular layer of simple running suture was applied or no further intervention depending on the randomization.

There were 49 patients enrolled in the study of which 73.5% were male and the mean age was 65.6 years. The treatment sites were as follows: head and neck (65.3%), trunk (22.4%), extremities (12.2%). At 3-months, the blinded observer mean sum POSAS score was 13.96 for the dermal suture only side and 11.80 for the layered closure side [p=0.02). At the 12-month follow up, there was no statistically significant difference in observer POSAS score or any of the subcategory scar outcomes. At the 3-month follow-up, there was a statistically significant difference in the patient mean sum POSAS score; the dermal suture only side had an average score of 16.53 and the layered closure side a score of 13.31 (p=0.02). However, at the 12-month follow-up, there were no statistically significant differences in scar characteristics as noted by the patient, except for scar color, which appeared better on the layered closure side (p=0.015).

In conclusion, a small but statistically significant better scar was seen at at 3-months after surgery with conventional bilayered suturing compared to a single layer of buried dermal sutures. However, at 12 months, this difference was no longer present.

Prevalence and determinants for xerosis cutis in the middle-aged and elderly population: A cross-sectional study

Mekic S, Jacobs LC, Gunn DA, Mayes AE, Ikram MA, Pardo LM, et al.
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Xerosis cutis is a very common skin condition among the middle-aged and elderly population with prevalence up to 85% reported. Little evidence is available for determinants of xerosis cutis in general middle-aged and older populations, and few studies have investigated a broad range of possible determinants and how they relate to the extent of dry skin.

The authors performed a prospective population-based cohort consisting of 5547 participants between 2010 and 2016. A full-body skin examination was performed on the participants. A dermatology-trained physician examined for dry skin, noting its extent. Dry skin was defined as scaly or rough skin with or without erythema that was not suggestive of any other dermatological condition. Grading was divided into absent, localised (extensor side of the arms, legs), or generalised. Past medical history and usual medications were noted and any co-existing skin diseases were assessed during examination.

The mean age of the participants was 70 years (range 51-101 years) and 57% of which were female. Of these, 60% of the participants had dry skin, of which 1 in 5 were severely affected with generalised xerosis. Dry skin was significantly associated with age. This association was stronger with the generalised type (OR:1.04;95% CI 1.03-1.05) than with the localized type (OR:1.009; 95%CI 1.003-1.016). Dry skin was more common in women and eczema (localized dry skin OR: 2.44; CI 1.85-3.25; generalized dry skin OR 7/04; CI 5.92-8.37) but psoriasis was not associated with dry skin. Diabetes mellitus was associated with localised xerosis (OR: 1.22; 95%CI 1.04-1.45) only. Renal impairment, hypothyroidism, and atopic constitution (asthma, hay fever, or dust mite allergy) were not associated with dry skin. Using statins (OR 1.28; 95%CI 1.05-1.57) and diuretics (OR 1.37; 95%CI 1.06-1.75) were both significantly associated with generalised but not with localised xerosis.

In conclusion, the prevalence of dry skin in people with an average age of 70 years was 60%. Risks factors of skin xerosis included advanced age, female sex, eczema, seborrheic dermatitis, diabetes mellitus and the usage of statins and diuretics.