9:00 AM - 9:10 AM

5257 - TNF-alpha antagonist and vascular inflammation in patients with Psoriasis vulgaris: A Randomized placebo-controlled study/Robert Bissonnette

Objective 1: to evaluate the effects of the tumor necrosis factor alpha (TNF-?) antagonist adalimumab on vascular inflammation in patients with psoriasis.

Objective 2: included in the Objective 1

Objective 3: None

ABSTRACT

Background: Vascular inflammation is increased in patients with psoriasis vulgaris. The main objective of this randomized, double-blind, multicenter study was to evaluate the effects of the tumor necrosis factor alpha (TNF-?) antagonist adalimumab on vascular inflammation in patients with psoriasis. Approach: A total of 107 patients were randomized (1:1) to receive adalimumab for 52 weeks OR placebo for 16 weeks followed by adalimumab for 52 weeks. Vascular inflammation was assessed with 18-fluorodeoxyglucose positron emission tomography-computed tomography. Results: There were no differences in the change from baseline in vessel wall target to background ratio (TBR) from the ascending aorta [adalimumab: 0.002, 95% confidence Interval (CI) (-0.048, 0.053); placebo: -0.002, 95% CI (-0.053, 0.049); p=0.916] and the carotid arteries (p=0.629) at week 16 between adalimumab and placebo. After 52 weeks of treatment with adalimumab there was no significant change from start of treatment in TBR from the ascending aorta (p=0.796) but there was an increase in TBR in carotid arteries [0.027, 95% CI: 0.000, 0.054), p=0.046].

Innovation: This is the largest randomized placebo-controlled study on the effect of a TNF-alpha antagonist on vascular inflammation. Relevance: The relevance of this study stems from the increase in vascular inflammation reported in patients with psoriasis.

9:10 AM - 9:20 AM

5077 - Certolizumab Pegol Treatment for Chronic Plaque Psoriasis: 16-Week Primary Results from two Phase 3, Multicenter, Randomized, Placebo-Controlled Studies/Alice B. Gottlieb

Objective 1: To investigate the efficacy and safety of certolizumab pegol (CZP)--an Fc-free, PEGylated, anti-TNF biologic--for the treatment of moderate-to-severe chronic plaque psoriasis in adults.

Objective 2: To assess the results from the initial 16-week treatment period of two ongoing, 144-week, phase 3 trials: CIMPASI-1 and CIMPASI-2.

Objective 3: None

ABSTRACT

Background: CZP, an FDA-approved medication for psoriatic arthritis, has demonstrated improvements in chronic plaque psoriasis in phase 2 trials.[1] Methods: Adults with moderate-to-severe plaque psoriasis of ≥6 months (PASI≥12, BSA≥10%, PGA≥3), enrolled in CIMPASI-1(NCT02326298) or CIMPASI-2(NCT02326272) phase 3, multicenter, double-blind, placebo-controlled trials, were randomized 2:2:1 to Q2W CZP 400mg or 200mg (following 400mg loading doses at Week0/2/4), or placebo. Week16 endpoints: PASI75, PGA 0/1, and PASI90 response rates. Analyses used logistic regression models with multiple imputation. Results: For CZP 400mg, 200mg, and placebo groups: 88, 95, and 51(CIMPASI-1), 87, 91, and 49(CIMPASI-2) patients were randomized. Baseline PASI and BSA were comparable across treatment groups within both studies. Week16 PASI75 response rates: 75.8%, 66.5%, and 6.5%(CIMPASI-1), 82.6%, 81.4%, and 11.6%(CIMPASI-2); PGA 0/1 response rates: 57.9%, 47.0%, and 4.2%(CIMPASI-1), 71.6%, 66.8%, and 2.0%(CIMPASI-2); PASI90 response rates: 43.6%, 35.8%, and 0.4%(CIMPASI-1), 55.4%, 52.6%, and 4.5%(CIMPASI-2); p<0.0001 for all comparisons of CZP versus placebo. Most frequent AEs in both studies were in upper respiratory tract infections; serious AEs were infrequent (<4%, with 1 patient with serious infection). Conclusions: 16-week CZP therapy was associated with statistically significant, clinically-meaningful improvements in moderate-to-severe chronic plaque psoriasis. AEs were consistent with the known safety profile of anti-TNF therapy.
9:20 AM - 9:30 AM

5174 - Efficacy and safety of ixekizumab compared to ustekinumab after 24 weeks of treatment in patients with moderate-to-severe plaque psoriasis: Results from IXORA-S, a randomized head-to-head trial/Kristian Reich

Objective 1: Assess the efficacy of ixekizumab versus ustekinumab at 24 weeks

Objective 2: Assess the safety of ixekizumab versus ustekinumab at 24 weeks

Objective 3: None

ABSTRACT

Introduction & Objectives: Ixekizumab (IXE) is a high-affinity monoclonal antibody that selectively targets interleukin-17A and has demonstrated superiority to ustekinumab (UST) at 12 weeks. Here we present the efficacy and safety of IXE versus UST at 24 weeks. Methods: In this trial (IXORA-S, NCT02561806), patients were randomized (1:1) to receive either IXE (160-mg starting dose, then 80-mg every 2 weeks for 12 weeks followed by 80-mg every 4 weeks; N=136) or UST (45-mg/90-mg weight-based dosing per label; N=166). At Week 24, categorical data were assessed using logistic regression (NRI). Incidence of TEAEs between groups was compared using Fisher’s exact test. Results: At Week 24, IXE-treated patients had significantly better response rates than UST-treated patients for PASI 100 (IXE: 49.3%, UST: 23.5%; p=.001), PASI 90 (IXE: 83.1%, UST: 59.0%; p<.001), PASI 75 (IXE: 91.2%, UST: 81.9%; p=.015), sPGA (0) (IXE: 53.7%, UST: 24.1%; p<.001), sPGA (0,1) (IXE: 86.6%, UST: 69.3%; p<.001), DLQI (0,1) (IXE: 66.2%, UST: 53.0%; p=.030), and itch NRS >4-point improvement (IXE: 85.5%, UST: 72.1%; p=.018). There were no deaths and no significant differences in rates of overall TEAEs between treatment groups. Conclusions: This study demonstrated the continued superiority of IXE to UST after 24 weeks of treatment.

9:30 AM - 9:40 AM

5095 - Dose-Finding Study of GSK2894512 Cream for Treatment of Plaque Psoriasis/Tomoko Maeda-Chubachi

Objective 1: To evaluate the efficacy of GSK2894512 topical cream (0.5% and 1%, BID and QD) for the treatment of plaque psoriasis. GSK2894512 is a synthetic hydroxylated stilbene molecule that is a novel anti-inflammatory agent.

Objective 2: To evaluate the safety of both concentrations of GSK2894512 topical cream for the treatment of psoriasis.

Objective 3: None

ABSTRACT

Methods: Randomized, Evaluator-Blinded study (#203120, funded by GSK), 3 periods: screening, 12 weeks treatment, 4 weeks follow-up, adults with psoriasis. Primary endpoint: Proportion of subjects with Physician Global Assessment (PGA) score of clear or almost clear (0 or 1) at Week 12 and minimum 2-grade improvement in 5-point PGA score from baseline to Week 12. Secondary endpoint: Proportion of subjects with 75% improvement in Psoriasis and Severity Index (PASI75). Results: 227 subjects enrolled, 174 subjects completed the study. Mean PGA and PASI at baseline were 2.7-3.0, and 7.88-10.56, respectively, across the treatment arms. 65% (15/23), 56% (14/25), 46% (12/26), 36% (10/28), 11% (2/19), and 5% (1/20) of subjects receiving 1%BID, 1%QD, 0.5%BID, 0.5%QD, vehicle (VC) BID, and VC QD, respectively, achieved the primary endpoint. PASI75 was achieved faster in 1% cream than 0.5% with Week 12 rates of 65, 56, 46, 46, 16, and 5% for 1%BID, 1%QD, 0.5%BID, 0.5%QD, VC BID, and VC QD, respectively. Efficacy was maintained for 4 weeks after discontinuation of treatment. 3-13% of subjects withdrew due to adverse events (AE), most common AE (6/227) leading discontinuation was contact dermatitis. Conclusion: GSK2894512 is an efficacious topical treatment for plaque psoriasis with an acceptable safety profile.
9:40 AM - 9:50 AM

5269 - Efficacy and safety of topical 1% benvitimod cream for the treatment of mild to moderate plaque psoriasis: A randomized, multi-center, placebo- and comparator-controlled phase III study/Jianzhong Zhang

Objective 1: A phase III clinical trial was performed to study the efficacy of 1% benvitimod cream for the treatment of mild to moderate plaque psoriasis.

Objective 2: A phase III clinical trial was performed to study the safety of 1% benvitimod cream for the treatment of mild to moderate plaque psoriasis.

Objective 3: None

ABSTRACT

Objective: A phase III clinical trial was performed to study the efficacy and safety of 1% benvitimod cream for the treatment of mild to moderate plaque psoriasis. Methods: Patients with mild to moderate plaque psoriasis were randomized into three groups, receiving 1% Benvitimod cream (n=344), 0.005% calcipotriol ointment (n=169) or placebo (n=173) twice daily for 12 weeks. Primary endpoints included the percentage of patients with a reduction of PASI75% and of patients with PGA score of clear or almost clear at the end of the treatment. Safety profiles were also analyzed. Results: At the end of treatment, 51.2% patients in benvitimod group achieved PASI75, which was higher than calcipotriol group (37.9%, p<0.05) or placebo group (14.5%, p<0.001). 66.3% patients in benvitimod group and 63.9% patients in calcipotriol group achieved PGA score of clear or almost clear, higher than in placebo group (33.5%, p<0.001). Treatment-related adverse events were found in 44.5% patients in benvitimod group, 19.5% in calcipotriol group and 20.2% in placebo group. Most were mild to moderate and transient erythema, sting and warming sensation at the sites of application. No clinical-relevant systemic abnormality was reported. Conclusion: Benvitimod cream is effective and safe for mild to moderate plaque psoriasis.

9:50 AM - 10:00 AM

5220 - Results From Phase II Study of Nitric Oxide-Releasing SB206 Once Daily Administration Show Favorable Efficacy and Safety in Genital Warts/Stephen Tyring

Objective 1: To evaluate the efficacy of an investigational nitric oxide-releasing topical gel, SB206 in subjects with external genital or perianal warts.

Objective 2: To evaluate the tolerability and safety of SB206 in subjects with external genital or perianal warts.

Objective 3: None

ABSTRACT

A multi-center, double-blind, vehicle-controlled study (NI-WA201) to assess efficacy and safety of SB206, a novel, investigational, nitric oxide-releasing topical gel in the treatment of genital warts was conducted at 15 US centers. Eligible subjects had 2-20 external genital/perianal warts (EGW/PAW). Subjects were randomized to either once- or twice-daily treatments of SB206 or vehicle gel for up to 12 weeks. A total of 108 subjects were randomized; 73% completed the study. Thirty-three percent of subjects treated with SB206 12% once daily achieved complete clearance of all baseline warts by Week 12 versus 4.3% of vehicle treated subjects (p=0.0099, ITT). Analyses of the per protocol set and total wart clearance also demonstrated a statistically significant difference between SB206 12% and vehicle. Application site adverse events were reported in 5% of vehicle treated subjects, 16.7% of subjects treated with SB206 12%, and rarely led to treatment discontinuation (3%). In this Phase 2 study, topical application of SB206 once daily in adults with EGW/PAW appeared to be safe and well tolerated. Treatment with SB206 12% once daily for up to 12 weeks led to a statistically significant difference from vehicle in clearance of both baseline and total warts.
F056 – Late-breaking Research Forum
Clinical Trials
Saturday, March 4 - 9:00 AM – 11:00 AM
Room W415D

10:00 AM - 10:10 AM

5221 - Positive Efficacy and Safety Outcomes from a Randomized, Double-Blind, Placebo-Controlled Phase 2b Study of Four Oral VT-1161 Regimens in the Treatment of Patients with Moderate-Severe Distal-Lateral Subungal Onychomycosis (DLSO)/Boni Elewski

Objective 1: Design and develop VT-1161, a first in-class, orally administered novel fungal CYP51 inhibitor (tetrazole) for treatment dermatophyte and candida skin and nail infections

Objective 2: Conduct a 48-week, multi-center, double blind, randomized, placebo controlled phase 2b trial in the treatment of moderate to severe onychomycosis

Objective 3: Report that VT-1161 achieved its primary endpoint of complete cure rates at 48 weeks with excellent safety and tolerability profile

ABSTRACT

BACKGROUND: Current therapies for onychomycosis are inadequate due to low efficacy rates and poor safety profile. APPROACH: VT-1161 is a selective inhibitor of fungal CYP51. In this multicenter study, patients with great target toenail with 25%-75% nail involvement received 300 or 600 mg once-weekly oral VT-1161 or matching placebo for either 10 or 22 weeks, following a two-week daily loading dose. The primary efficacy endpoint was complete cure of the target toenail at Week 48, a composite endpoint requiring 100% clear nail with negative culture and negative KOH. RESULTS: In the intent-to-treat analysis, complete cure rates were 0% in the placebo arm compared to 32 – 42% across all VT-1161 arms (p<0.001 vs. placebo). In patients who completed through 48-Weeks, the complete cure rates were as high as 51%. The incidence of adverse events was similar across treatment arms relative to placebo. No patient discontinued due to a laboratory abnormality. The drug was well tolerated with no evidence of an adverse effect on liver function. INNOVATION: VT-1161 is a novel oral antifungal agent with a very favorable efficacy, safety and pharmacokinetic profile suggesting it can be a highly effective new treatment for onychomycosis. RELEVANCE: VT-1161’s clinical profile warrants evaluation in phase 3 trials.

10:10 AM - 10:20 AM

5267 - Long-term management of moderate-to-severe atopic dermatitis (AD) with dupilumab up to 1 year with concomitant topical corticosteroids (TCS): a randomized, placebo-controlled phase 3 trial (CHRONOS)/Andrew Blauvelt

Objective 1: Evaluate efficacy of long-term treatment with dupilumab plus concomitant topical corticosteroids in moderate-to-severe AD

Objective 2: Evaluate safety of long-term treatment with dupilumab plus concomitant topical corticosteroids in moderate-to-severe AD

Objective 3: None

ABSTRACT

Background: In previous 16-week (Wk) monotherapy studies, dupilumab (anti-interleukin-4-receptor-alpha mAb), significantly improved signs and symptoms of moderate-to-severe AD, with acceptable safety. Methods: Adults with moderate-to-severe AD and inadequate TCS response were randomized 3:1:3 to dupilumab 300mg-once-weekly (qw):300mg-every-2 Wks (q2w):placebo for 52 wks; all received low-/medium-potency TCS, which could be tapered/stopped, or topical calcineurin inhibitors in areas inadvisable for TCS (ClinicalTrials.gov: NCT02260986). Results: Efficacy data were available for 740 (Wk16) and 623 (Wk52) patients; safety for 740 (Wk52). More dupilumab+TCS-treated patients achieved Investigator’s Global Assessment score=0/1 and 72-point improvement from baseline (qw+TCS/q2w+TCS vs placebo+TCS: Wk16: 39.2%/38.7% vs 12.4%; Wk52: 40.0%/36.0% vs 12.5%), Eczema Area and Severity Index-75% improvement (Wk16: 63.9%/68.9% vs 23.2%; Wk52: 64.1%/65.2% vs 21.6%), and peak pruritus numerical rating scale?4-point improvement (Wk16: 50.8%/58.8% vs 19.7%; Wk52: 39.0%/51.2% vs 12.9%) (P<0.0001 vs placebo+TCS, each comparison). Treatment groups had similar adverse/serious adverse event rates, and no significant laboratory abnormalities. Dupilumab+TCS-treated patients reported numerically higher rates of conjunctivitis (19.4%/13.6% vs 7.9%) and injection-site reactions (20.0%/16.4% vs 7.9%); placebo+TCS-treated patients reported more non-herpetic skin infections (8.3%/10.9% vs 17.8%) and AD flares (12.7%/13.6% vs 41.3%). Conclusions: Long-term treatment with dupilumab with concomitant topical medications significantly improved AD signs and symptoms, including pruritus, with acceptable safety.
10:20 AM - 10:30 AM

5268 - Efficacy and safety of nemolizumab over 64 weeks in patients with moderate-to-severe atopic dermatitis: Results from the long-term extension of the Phase 2 study/Kenji Kabashima

**Objective 1:** To assess 64-week efficacy of nemolizumab, a humanized anti-interleukin-31 receptor A monoclonal antibody, in patients with moderate-to-severe atopic dermatitis.

**Objective 2:** To evaluate 64-week safety and tolerability of nemolizumab in patients with moderate-to-severe atopic dermatitis.

**Objective 3:** To examine the effect of nemolizumab in combination with topical corticosteroids for patients with moderate-to-severe atopic dermatitis in the 64-week, long-term extension period.

**ABSTRACT**

Background/Innovation: Nemolizumab, an anti-interleukin-31 receptor A antibody, improved pruritus and atopic dermatitis (AD) scores in a 12-week study in patients with moderate-to-severe AD, but long-term data are also needed. Methods: Following the 12-week, randomized, double-blind, placebo-controlled study (Part A), a long-term extension (Part B) evaluated continuous subcutaneous nemolizumab (0.1, 0.5, or 2.0 mg/kg Q4W, or 2.0 mg/kg Q8W) for 52 weeks (NCT01986933). Results: Of 264 patients randomized, 191 patients enrolled in Part B, 131 (68.6%) completed 52 weeks. Numbers of patients who achieved pruritus visual analogue score <30 mm (no or mild itch) at Weeks 12 and 64 were: 14/45 and 22/29 in nemolizumab 0.1 mg/kg, 30/45 and 25/26 in 0.5 mg/kg, 29/47 and 21/28 in 2.0 mg/kg Q4W, and 23/39 and 14/18 in 2.0 mg/kg Q8W. Numbers of patients who achieved a 75% reduction in Eczema Area and Severity Index (EASI75) were: 13/45 and 21/31, 18/46 and 19/28, 11/46 and 19/29, and 8/37 and 14/19. On-demand concomitant topical corticosteroid use increased EASI75 response. The most common adverse event (AE) was nasopharyngitis (23.1–28.8%); no substantial new AEs were observed. Relevance: Nemolizumab maintained improved pruritus and dermatitis responses to 64 weeks. Nemolizumab represents a potential novel treatment option in moderate-to-severe AD.

10:30 AM - 10:40 AM

5205 - Phase II results of brentuximab vedotin for lymphomatoid papulosis: a subset analysis/Daniel Lewis

**Objective 1:** To determine the safety and preliminary activity of brentuximab vedotin in patients with lymphomatoid papulosis (LyP) requiring systemic therapy

**Objective 2:** To measure the severity and duration of peripheral neuropathy associated with brentuximab vedotin

**Objective 3:** None

**ABSTRACT**

Introduction: Brentuximab vedotin is a monomethyl auristatin E-conjugated monoclonal antibody directed against CD30. It offers potential for use in treating CD30+ lymphoproliferative disorders such as LyP, which currently has no approved or curative treatment available. Patients and Methods: Between 2011 and 2016, 12 LyP patients at MD Anderson Cancer Center received 1.8 mg/kg infusions of brentuximab vedotin every 21 days. Complete response (CR) was zero lesions, and partial response (PR) was a >50% reduction in lesion count. Results: All 12 patients (8 males, 4 females, median age 46) responded, and 7/12 exhibited a CR. All patients responded rapidly, with a time to response of 3 weeks. Duration of response was 20 weeks (range, 6-42). In 5 patients who relapsed, time to relapse was 12 weeks (range, 6-123). One patient who relapsed was retreated and remains in PR over 16 months of follow-up. Grade 1-2 neuropathy occurred in 10/12, lasting for 35 weeks (range, 0.1-124.7), and resolved in 5/10. Grade 3-4 adverse events were neutropenia (n=2) and dizziness/vertigo (n=1). Conclusion: Brentuximab vedotin results in a 100% response rate and 58% CR rate in LyP patients, with an 83% incidence of neuropathy. More work is needed to determine its optimal dosing schedule in treating this chronic, relapsing disorder.
10:40 AM - 10:50 AM

5198 - A Randomized, Double-Blind, Placebo-Controlled, Study of the Neurokinin-1 Receptor (NK1-R) Antagonist Serlopitant in Subjects with Prurigo Nodularis (PN)/Sonja Ständer

Objective 1: To evaluate the efficacy of serlopitant for the treatment on prurigo nodularis

Objective 2: To evaluate the safety and tolerability of serlopitant for the treatment on prurigo nodularis

Objective 3: None

ABSTRACT

Background: Prurigo nodularis (PN) is an intensely pruritic chronic skin condition. NK1-R stimulation has been shown to be an important pathway for pruritus perception. Serlopitant is a small molecule, highly selective NK1-R antagonist. Approach: A randomized, double-blind, placebo-controlled study of 127 subjects (mean age: 57.6 years) at 15 German sites evaluated orally administered serlopitant in subjects with PN. Subjects were assigned (1:1) to serlopitant 5 mg or placebo daily for 8 weeks. Results: Serlopitant was superior to placebo for reducing pruritus in the primary analysis, change from baseline to Weeks 4 and 8 in subject-reported average itch over last 24 hours on a visual analog scale (VAS) (-3.6 cm vs -1.9 cm at Week 8, p = 0.0005). Similarly, serlopitant was superior to placebo in multiple secondary pruritus endpoints. The proportion of serlopitant subjects with ≤4 cm response by Week 8 on average itch VAS was over double that observed in placebo (54.4% vs. 25.0%). Serlopitant was well tolerated. The majority of AEs were mild or moderate and no significant safety signals were detected. Innovation/Relevance: This study represents one of the first randomized placebo-controlled studies in PN. Results support continuing evaluation of serlopitant for treating pruritus in PN.

10:50 AM - 11:00 AM

5143 - Improving the Appearance of Keratosis Pilaris with Ammonia Oxidizing Bacteria/Nicole Lee

Objective 1: To assess the safety and tolerability of ammonia oxidizing bacteria mist relative to placebo in subjects with keratosis pilaris on their arms and legs after twice-a-day application for 4 weeks.

Objective 2: To assess the efficacy of ammonia oxidizing bacteria mist relative to placebo in subjects with keratosis pilaris on their arms and legs after twice-a-day application for 4 weeks, as measured by KP Investigator Score (IGA), Skindex16 (patient reported outcome), and 3D Digital photographs (Primos Lite, 45x30mm, Canfield).

Objective 3: None

ABSTRACT

Keratosis pilaris is a common skin condition presenting as follicular hyperkeratotic papules on proximal extremities. The appearance is disturbing to patients and current therapies are limited. Nitric oxide (NO) is essential in systemic and cutaneous physiologic function, specifically its anti-microbial and anti-inflammatory properties, which evolutionarily may have been maintained by ammonia-oxidizing bacteria (AOB). Modern hygiene has eliminated cutaneous AOB resulting in inflammatory dysregulation [1]. We hypothesized that topical skin application of AOB (Nitrosomonas eutropha), a biological delivery system of nitrite and NO, could benefit KP patients. We evaluated tolerability and efficacy in a double-blind, placebo-controlled, bilateral study in subjects with KP on both arms and legs. Investigator Global Assessment (IGA) success occurred in 29% (7/24; p=0.01) of the active group versus 4% of placebo group (1/24). Skindex16 progressively improved from baseline to week 4 (35%; p<0.0003). Skin smoothness evaluated with 3D imaging showed impressive improvement (>45% reduction versus placebo in Knots Total Count and Knots Total Area). PCR analysis of skin swabs was used to detect the presence of AOB and to follow compliance. In summary, topical Nitrosomonas eutropha offers a safe and effective treatment for improving the appearance of skin afflicted with keratosis pilaris.