18540

Real-world evidence of secukinumab in psoriasis treatment: A meta-analysis of 43 studies

Matthias Augustin, University Medical Center Hamburg-Eppendorf; Denis Jullien, MD, PhD, Université Claude Bernard Lyon 1, Hospices Civils de Lyon; Antonio Martin, Carlos Peralta

Introduction: Meta-analyses of real-world evidence (RWE) studies provide valuable insights from unselected patient populations in routine clinical practice. Secukinumab, the first fully human monoclonal antibody that selectively neutralizes IL-17A, has shown long lasting effectiveness and safety in moderate to severe plaque psoriasis (PsO). Since its license approval in 2015, many RWE studies have been published. Here, we reviewed all available literature on RWE studies involving secukinumab in patients with moderate to severe PsO to evaluate its effectiveness, drug survival and safety. Materials and methods https://www.embase.com and https://clinicaltrials.gov databases were searched using pre-specified inclusion criteria from 1/1/2015 to 31/5/2019. Outcomes were measured at 3, 6, and 12 months, and analyzed using a meta-package and R statistical software.

Results: In total, 43 studies were included. Secukinumab drug survival was 90% at 3 and 6 months, and 80% at 12 months. At 12 months, 8% of patients had discontinued treatment due to lack of effectiveness. At 3, 6, and 12 months, Psoriasis Area Severity Index (PASI) 90 scores were 50%, 53%, and 58% and PASI 100 scores were 36%, 46%, and 51%, respectively. At 3, 6, and 12 months, 57%, 55%, and 65% of patients achieved a Dermatology Life Quality Index score of 0 or 1, respectively. Adverse events were consistent with rates observed in clinical trials, with no new safety signals. Discussion This meta-analysis strengthens existing evidence on the effectiveness of secukinumab in patients with moderate to severe PsO, demonstrating high drug survival rates, clinical effectiveness and good tolerance.

Commercial disclosure: This abstract was fully sponsored by Novartis.

18572

Relevant skin exposure after topical application of the pan-PI3K/mTOR inhibitor bimiralisib

Debora Schmitz-Rohmer, PhD, Piqur Therapeutics; Henk Johann Streefkerk, MD PhD, Melanie Rolli, MD, Raphael Legouffe, Robert Rissmann, Maarten Vermeer

Background: Bimiralisib is a dual pan-PI3K/mTOR inhibitor currently in clinical development for oral treatment of human malignancies. A topical formulation of bimiralisib has now been developed to treat human diseases with cutaneous manifestations. We used matrix-assisted laser desorption/ionization mass spectrometry imaging (MALDI-MSI) to generate human skin penetration profiles of topical bimiralisib in a quantitative manner, including bimiralisib exposure of the different skin compartments (stratum corneum, epidermis and dermis). The MALDI-MSI approach circumvents the challenges of surface contamination (active substance adhering to the skin surface or biopsy edges) and allows for spatial resolution of analyte distribution.

Methods: Skin samples from human subjects were collected after multiple applications of topical bimiralisib and subjected to MALDI-MSI. For each biopsy sample, 1 10-μm-thick section containing stratum corneum, epidermis and dermis was collected. For MSI acquisitions, sections were mounted on ITO slides and sprayed with MALDI matrix. MSI was performed at 50 μm of spatial resolution.

Results: Topical bimiralisib penetrates into the epidermis and the upper dermis. Exposure levels in the epidermis are within the range of the IC90's for pAKT and pS6, which are key components of the PI3K/mTOR pathway. Spatial bimiralisib exposure profiles in skin will be presented.

Conclusions: Topical bimiralisib, a novel pan-PI3K/mTOR inhibitor, achieves skin exposures likely to be relevant for the local treatment of human diseases with cutaneous manifestations with an up-regulated PI3K/mTOR pathway.

Commercial disclosure: The lead author is a full-time employee of Piqur Therapeutics.

18557

Assessment of retinal vessel density by optical coherence tomography angiography in patients with psoriasis

Giuseppe Micali, MD, Maria Letizia Musumeci, MD PhD, Antonio Longo, MD, Francesco Lacarrubba, MD, Anna Elisa Verzì, MD, Dermatology Clinic, University of Catania, Italy

Background: Psoriasis is a chronic inflammatory disease characterized by vascular modifications of superficial cutaneous microcirculation. Optical coherence tomography angiography (OCT-A) is a technique currently used in ophthalmology to evaluate the retinal vascularization.

Objective: To assess the superficial and deep retinal vessels density in patients with plaque psoriasis.

Methods: In a prospective study, 64 psoriatic patients (mean age 52 $\pm$ 14 years) without ocular involvement and 30 healthy controls (mean age 55 $\pm$ 8 years) underwent retinal OCT-A. Foveal avascular zone (FAZ), superficial and deep retinal vessels density in parafoveal and foveal areas and central retinal thickness were evaluated. Statistical analysis was performed by unpaired *t* test.

Results: Compared with controls, psoriatic patients had a significant greater FAZ (0.276 ± 0.116 mm^2 vs 0.224 ± 0.065 mm^2, $P = .008$), and superficial retinal vessel density in parafoveal area ($48.0 \pm 4.8\%$ vs $44.9 \pm 5.7\%$, $P = .018$). No significant difference was seen between the two groups in the remaining parameters.

Conclusions: Our results indicate that psoriatic patients show overall retinal vascular alterations including a greater superficial vessel density in parafoveal area compared with healthy controls. These findings may likely reflect those observed in histopathology, videodermatoscopy and reflectance confocal microscopy of psoriatic skin showing vascular alteration, namely dilated and convoluted capillaries in the dermal papillae. Further studies are needed to confirm our preliminary results that could provide new insights in the systemic involvement of the disease.

Commercial disclosure: None identified.

18574

A comparison of the cantharidin blister model and suction blister model in healthy male subjects

John Connell, PhD, MAC Clinical Research; Rob Greenhalgh, Cory Iverson, MSc, Nihar Bhakta, MD, Scott Baumgartner, DeAnne Reid, John P. Montana, Aristea Therapeutics; James Mackay, Sara McCutchan

Introduction: Collection of blister fluid (BF) from induced blisters represent a noninvasive clinical model to detect mediators of inflammation. The cantharidin-induced blister model (CM) and suction-induced blister model (SM) are standardized techniques that allow investigation of inflammation.

Objective: The purpose of this study was to compare the BF from CM and SM to assess differential white blood cell count and inflammatory biomarker levels at various timepoints.

Methods: 12 healthy volunteers had blisters induced on their anterior forearms with one forearm designated for each model. Post application BF was obtained at 12-30 hours in the SM and at 18-36 hours in the CM.

Results: Mean age of volunteers was 29 years. At 12 h in the SM there was a peak in absolute neutrophil count (ANC) and neutrophil percentage (NP) (mean ANC = 23898 and mean NP = 68.73%). At 30 h in the SM the mean ANC = 916. At 30 h in the CM there was a peak in absolute neutrophil count (ANC) and neutrophil percentage (NP) (mean ANC = 62054 and mean NP = 64.8%). At 36 h in the CM the mean ANC = 54519 and the NP = 60.9%. VEGF-A, CXCL1, 2, and 5, IL-1a and b, TNF-α, IL-36, and IL-8 levels were increased in the CM model compared with SM. No adverse events were observed.

Conclusions: This study demonstrates for the first time in the same subjects that there are clear differences in both neutrophils and inflammatory biomarkers at the site of inflammation between CM and SM. CM is most suitable to evaluate anti-inflammatory interventions and elucidate mechanisms of action.

Commercial disclosure: Tthis research was 100% sponsored by Aristea Therapeutics.