AB0609

DESIGN OF A PHASE 2, DOUBLE-BLIND, PLACEBO-CONTROLLED, GLOBAL TRIAL OF DEUCRAVACITINIB, AN ORAL, SELECTIVE, ALLOSTERIC TYROSINE KINASE 2 (TYK2) INHIBITOR, IN PATIENTS WITH ACTIVE DISCOID AND/OR SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Clinical trials

V. P. Werth1, J. F. Merola2, J. Wenzel3, N. Delev4, H. Kothari5, R. Meier6, S. Singh7, M. Madireddi8, S. Korish9,1. University of Pennsylvania and the Michael J. Crescenz VA Medical Center, Dermatology, Philadelphia, United States of America; 2Brigham and Women’s Hospital, Harvard Medical School, Dermatology and Immunology, Boston, United States of America; 3University Hospital of Bonn, Germany, Dermatology and Immunology, Bonn, United States of America; 4Bristol Myers Squibb, Clinical Development, Princeton, United States of America; 5Bristol Myers Squibb, Global Biometrics and Data Sciences, Princeton, United States of America

Background: Deucravacitinib is a first-in-class, oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor approved in multiple countries for the treatment of adults with plaque psoriasis [1,2]. Deucravacitinib demonstrated efficacy across multiple outcome measures, including achievement of ≥50% reduction in Cutaneous Lupus Erythematous Disease Area and Severity Index-Activity score (CLASI-A-50), in a phase 2 trial in patients with systemic lupus erythematosus (SLE) [3] and is being investigated in two phase 3 trials (NCT05617877; NCT05620407). Patients with discoid and/or subacute cutaneous lupus erythematosus (DLE/SCLE) have elevated expression of Type I interferons (IFN) [4]. Deucravacitinib mediates signaling of Type I IFN, IL-12, and IL-23 and may be an effective treatment for patients with DLE/SCLE [5].

Objectives: Results of this ongoing phase 2 trial (NCT04857034) will characterize the efficacy and safety of deucravacitinib compared in placebo in patients with active DLE/SCLE with or without SLE.

Methods: This phase 2, global, randomized, double-blind, placebo-controlled trial is enrolling adults (aged 18-75) with biopsy-confirmed clinical diagnosis of DLE/SCLE. Key eligibility criteria and study design are depicted below (Figure 1). Eligible patients will be randomized (1:1:1) to treatment with placebo or deucravacitinib (dose 1 or 2) for 16 weeks. At week 16, all patients randomized to placebo will be re-randomized (1:1:1) to treatment with deucravacitinib dose 1 or 2 until week 52. Patients originally randomized to deucravacitinib will continue treatment until week 52. The primary and secondary endpoints are depicted below (Table 1). This trial will also assess the safety and tolerability of 2 doses of deucravacitinib, exploratory efficacy endpoints, patient-reported outcomes, and pharmacodynamics.

Results: Planned enrollment is 75 total patients (25 per double-blind treatment group) in 8 countries in North and South America, Europe, and Asia-Pacific regions.

Conclusion: This phase 2 trial will characterize the efficacy, safety, and tolerability of deucravacitinib in patients with active DLE/SCLE.

REFERENCES:

Table 1. Primary and Secondary Endpoints Assessed at Week 16

<table>
<thead>
<tr>
<th>Primary Endpoint</th>
<th>Secondary Endpoints</th>
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<tbody>
<tr>
<td>Mean percentage change from baseline in CLASI-A score</td>
<td>Percentage of patients who achieve a ≥ 50% reduction in CLASI-A score (CLASI-A-50) from baseline</td>
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<tr>
<td>Percentage of patients who achieve a ≥ 4-point improvement in CLASI-A from baseline</td>
<td>Percentage change from baseline in CLASI-A score</td>
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<tr>
<td>Percentage of patients who achieve a complete response (defined as a CLASI-A score of 0)</td>
<td>Percentage of patients who achieve a ≥ 50% reduction in CLASI-A score</td>
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AB0610

CHARACTERIZATION OF DISEASE SEVERITY AND ORGAN SYSTEM INVOLVEMENT IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN SRI LANKA: ESTABLISHING A COUNTRY-WIDE LUPUS COHORT

Keywords: Organ damage, Systemic lupus erythematosus, Geographical differences

C. Dandeniya1, D. Munidasa2, K. Deshapriya3, N. Aravinthan4, M. De Silva5, G. Kasthuriratna6, U. Dissanayake7, A. Udagedara7, P. Wanigasekara8, N. Darshana8, B. Parker9, N. Bruce9, A. Edirweera10, University of Peradeniya, Department of Medicine, Kandy, Sri Lanka; 1Rheumatology and Rehabilitation Hospital Ragama, Rheumatology Ragama, Sri Lanka; 2Teaching Hospital Karapitiya, Rheumatology, Galle, Sri Lanka; 3Teaching Hospital Jaffna, Rheumatology, Jaffna, Sri Lanka; 4National Hospital Sri Lanka, Rheumatology. Colombo, Sri Lanka; 5Teaching Hospital Kurunegala, Rheumatology, Kurunegala, Sri Lanka; 6District General Hospital- Polonnaruwa, Rheumatology, Polonnaruwa, Sri Lanka; 7Teaching Hospital Anuradhapura, Rheumatology, Anuradhapura, Sri Lanka; 8University Of Ruhuna, Community Medicine, Galle, Sri Lanka; 9University Of Manchester, Rheumatology, Manchester, United Kingdom; 10District General Hospital Ampara, Rheumatology, Ampara, Sri Lanka

Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune connective tissue disease with varying degrees of disease severity and organ system involvement. Disease phenotype and severity are shown to be different based on ethnicity [1,2] where Asians have been shown to have a more severe disease phenotype compared to Caucasians [2]. Infections, active SLE and cardiovascular involvement are identified as leading causes of death among Asian patients [3]. However, there is no consensus on whether this represents a different disease phenotype or a socioeconomically less fortunate population, owing to lacking of contemporary studies in Asian settings. This study aims to explore the disease severity and organ involvement of Asian counterparts while establishing a lupus cohort in the region for follow up and future studies.

Objectives: To assess the disease severity and organ system involvement among patients with SLE in Sri Lanka based on an ongoing national multicentre lupus database.

Methods: This is a multi-centre descriptive follow-up study with plans to establish a national lupus database in Sri Lanka. 258 patients are recruited so far with a clinical diagnosis of SLE at 14 state hospitals which provide specialist rheumatology services across the country. Disease severity is assessed using the British Isles Lupus Assessment Group-2004 (BILAG-2004).

Results: Of 258 patients, 196 (76%) were females. Mean (SD) age of the sample was 36.1(12.7) years. Majority fulfilled ACR/EULAR 2019 criteria for classification (86.0%). Renal involvement was seen in 42.6% with 25% having active disease at the time of recruitment. Neurological involvement was seen in 18.6%. Percentages of other domain involvement were mucocutaneous 83.7%, musculoskeletal 74.4%, haematological 65.4%, constitutional 61.6%, cardiorespiratory 8.5%, gastrointestinal 2.8% and ophthalmological involvement 1.2%. Nearly 44% had moderate or severe disease involvement (BILAG A or B) in at least one organ system at the time of recruitment. Mean SLICC Damage score was 0.9 (0-8). Disease severity was not significantly determined by the fact that whether the classification criteria were met or not (p=0.17)

Conclusion: Disease severity at time of recruitment and the prevalence of major organ system involvement during the course of illness are commoner among the study population. This is in keeping with higher disease severity and organ involvement reported in the limited available studies among Asians when compared with available data for North American and European populations. This study highlights the importance of early detection and treatment with close