SATURDAY

124 Subgroup Analyses From the Phase 3 HELP Study of Lanadelumab for the Prevention of Hereditary Angioedema Attacks

Aleena Banerji, MD[1], Michael E. Manning, MD, FAAAAI[2], Inmaculada Martinez-Saguer, MD[3], Lawrence B. Schwartz, MD, PhD, FAAAAI[4], Andrew M. Smith, MD, FAAAAI[5], William H. Yang, MD, FAAAAI[6], Peng Lu, MD, PhD[7], James Hao, PhD[7], and Bruce L. Zuraw, MD[8]; [1]Division of Rheumatology, Allergy and Immunology, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, [2]Medical Research of Arizona, Scottsdale, AZ, [3]Haemophilia Centre Rhine Main, Mörfelden-Walldorf, Germany, [4]Division of Rheumatology, Allergy and Immunology, Department of Internal Medicine, Virginia Commonwealth University, Richmond, VA, [5]Allergy Associates of Utah, Murray, UT, [6]Ottawa Allergy Research Corporation and University of Ottawa Medical School, Ottawa, ON, Canada, [7]Shire, Lexington, MA, [8]Division of Rheumatology, Allergy & Immunology, University of California, San Diego, San Diego.

RATIONALE: Treatment with the plasma kallikrein inhibitor lanadelumab significantly reduced hereditary angioedema (HAE) attack rate versus placebo over 26 weeks in the HELP Study (NCT02586805). Here we report findings from subgroup analyses for the primary endpoint.

METHODS: Patients ≥12 years old with HAE type I/II and ≥1 attack/month at baseline were randomized 2:2:2:3 to lanadelumab 150 mg every 4 weeks (q4wks), 300 mg q4wks, 300 mg q2wks, or placebo. Exploratory analyses were planned for subgroups with adequate numbers of patients for Poisson regression.

RESULTS: Overall, 125 patients were treated. Mean monthly attack rates were consistently reduced with lanadelumab versus placebo across all subgroups analyzed. Percentage reductions from placebo (n=41) were observed for the following demographic and disease characteristic subgroups with lanadelumab 300 mg q4wks (n=29) and 300 mg q2wks (n=27) respectively: age <18 years (20.5% and 62.3%), 18–<40 years (80.3% and 84.5%), 40–<65 years (71.5% and 89.8%); male (82.4% and 90.3%), female (69.6% and 85.8%); weight 50–<75 kg (78.4% and 93.1%), 75–<100 kg (74.0% and 84.0%), ≥100 kg (61.3% and 82.7%); HAE type I (73.4% and 87.8%), type II (60.1% and 69.8%); prior laryngeal attacks (64.2% and 85.7%), no prior laryngeal attacks (85.8% and 88.0%). Subgroups treated with 150 mg q4wks (n=28) also experienced attack rate reductions versus placebo (data not shown).

CONCLUSIONS: Patients with HAE type I/II treated with lanadelumab 300 mg q2wks or q4wks experienced clinically meaningful and persistent reductions in HAE attack rate compared with placebo regardless of age, sex, weight, and baseline HAE clinical characteristics.

125 Cleaved High Molecular Weight Kininogen Correlates With Hereditary Angioedema Due To C1-Inhibitor Deficiency

Adriana Moreno, PhD[1], Fernanda L. Nunes, MD[1], Yunan C. Januario, MSc[1], Luana S. M. Maia, MSc[1], Mariana P. L. Ferriani, MD, PhD[1], Marina M. Dias, Chem[1], Davi C. Aragon, PhD[1], Chiara Suffritti, PhD[2], Marco Cicardi[2], Luis L. P. da Silva, PhD[1], and Luisa Karla P. Arruda, MD PhD FAAAAI[1]; [1]University of São paulo, Ribeirão Preto Medical School, Ribeirão Preto, Brazil, [2]Department of Biomedical and Clinical Sciences "Luigi Sacco", University of Milan, ASST Fatebenefratelli Sacco, Milan, Italy.

RATIONALE: Hereditary angioedema with C1 inhibitor deficiency (HAE-C1-INH) is characterized by recurrent episodes of angioedema of cutaneous and submucosal tissue, and gastrointestinal and respiratory tracts. Our group has described the mutation c.351delC in *SERPING1* gene, causing HAE type I in a large Brazilian family. Prospective follow-up revealed that there are currently 33 members diagnosed by genetic analysis. We aimed to compare the cleavage of high-molecular-weight kininogen (HMWK) both during HAE attacks and in remission among HAE patents in this family.

METHODS: Whole blood was collected from 24 HAE-C1-INH patients, 13F/11M, aged 8-80 years-old, during remission; 6 HAE-C1-INH patients up to 12 hours after the onset of an acute attack (10 attacks), and 5 normal controls. Cleavage of HMWK was assessed by SDS-PAGE and immunoblot analysis. HMWK was identified using goat polyclonal anti-HMWK light chain antibody and biotinylated rabbit anti-goat antibody. Native HMWK appears as a single band with M_r 130,000, and upon cleavage, it is replaced by bands ofM_r 107,000 and 98,000. The density of the bands was measured using Image Lab. Kaolin-incubated plasma was used as control sample. The amount of cleaved HMWK was expressed as a percentage of total HMWK.

RESULTS: Cleaved HMWK was increased in HAE-C1-INH patients during remission, as compared to normal controls (mean 0.44 ±0.05 and 0.38 ±0.03 respectively, p=0.01). Cleaved HMWK was higher in 3/6 patients during 5/10 attacks, as compared to remission period.

CONCLUSIONS: Our results support the evidence that evaluating plasma levels of cleaved HMWK may contribute to identify laboratory markers of disease in HAE-C1-INH patients.

126 Angioedema Due To Acquired C1-Inhibitor Deficiency: Spectrum And Treatment With C1-Inhibitor Concentrate

Konrad Bork, MD[1], Petra Staubach-Renz, MD[1], and Jochen Hardt, PhD[2]; [1]Department of Dermatology, University of Mainz, Mainz, Germany, [2]Department of Medical Psychology and Medical Sociology, University of Mainz, Mainz, Germany.

RATIONALE: The purpose was to describe characteristics and associated disorders of patients with acquired angioedema due to C1-inhibitor deficiency (AAE-C1-INH) and assess the efficacy of plasma derived C1-INH concentrate (pdC1-INH).

METHODS: Fourty-four patients with AAE-C1-INH were assessed for associated disorders. In 32 of the patients, the duration of swelling attacks was measured before and after treatment with pdC1-INH. The time between injection and disappearance of symptoms was recorded and treatment evaluations were provided by the patients.

RESULTS: The following associated disorders were present: monoclonal gammopathy of undetermined significance (47.7%), non-Hodgkin lymphoma (27.3%), anti-C1-INH autoantibodies alone (11.4 %), and other conditions (4.5%). In 9.1% patients, no associated disorder could be found. AAE-C1-INH led to the detection of lymphoma in 75% of patients with the malignancy. Treatment with pdC1-INH shortened attacks by an average 54.4 (±32.8) hours (P<0.0001). The earlier the attack was treated, the shorter the time between injection and disappearance of symptoms (P=0.0149). A total of 3553 (97.7%) of 3636 treated attacks were effectively treated with pdC1-INH as assessed by the patients. pdC1-INH was effective in 1246 (93.8%) of 1329 attacks in 8 patients with anti-C1-INH autoantibodies and in 344 (99.4%) of 346 attacks in 6 patients without autoantibodies. The average dose per effectively treated attack was 1238.4 U in patients with anti-C1-INH autoantibodies and 510.2 U in patients without autoantibodies.

CONCLUSIONS: pdC1-INH is highly effective in treating AAE-C1-INH patients. It reduces attack duration and is fast-acting. It is also effective in the vast majority of attacks in patients with anti-C1-INH autoantibodies.