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Efficacy, durability and safety of ampreloxetine, a norepinephrine reuptake inhibitor, given once daily to treat neurogenic orthostatic hypotension (nOH) in subjects with primary autonomic failure

Background: The neurogenic orthostatic hypotension (nOH) is due to failure of the autonomic nervous system to adequately increase synaptic norepinephrine to maintain upright blood pressure (BP). Norepinephrine reuptake inhibitors (NRI) could augment local synaptic concentrations of tonically released norepinephrine, resulting in increased BP and reduced symptoms of OH. Ampreloxetine is a novel NRI being investigated for the treatment of symptomatic nOH.

Methods: This was a phase 2 multicenter, single and multiple-dose study of subjects with nOH. After a single dose escalation phase, responders were enrolled in an open label phase, treated with ampreloxetine taken orally once daily for up to 20 weeks, and followed for 4 weeks thereafter. The primary endpoint was the improvement from baseline in the validated symptom questionnaire OHSA#1 on day 29.

Results: 21 subjects were enrolled (mean age 64yrs), 16(76%) completed day 29. The mean [SD] improvement from baseline in OHSA#1 was 2.4[4.5] in all subjects and 3.8[3.1] in symptomatic subjects (OSHA#1 >4 at baseline). OHSA and OHDAS composite scores improved by 1.0(2.8) and 1.1(2.9), respectively. The most frequently reported adverse events (AE) were urinary tract infection (24%), hypertension (19%) and headache (14%). 2(10%) discontinued treatment due to AE and 5(24%) reported SAEs, none considered related to the study medication.

Conclusion: In subjects with nOH, ampreloxetine demonstrated clinically meaningful improvements in OHSA#1, OHSA and OHDAS composite scores at week 4. The improvement in OHSA#1 was maintained through week 20, with a regression to baseline levels during the 4 week follow-up. Ampreloxetine was generally well-tolerated.

Biography

Horacio Kaufmann is Professor of Neurology, Medicine and Pediatrics and holds the Axelrod Chair for Neurological Research at New York University School of Medicine where he also Heads the Division of Autonomic Disorders and the Dysautonomia Center at NYU Langone Health. He received his Medical Degree from the National University of Buenos Aires, Argentina. He trained in Internal Medicine and completed Neurology residency and fellowship at Mount Sinai School of Medicine in New York City. His research focuses on the autonomic nervous system and its abnormalities in neurological disorders. His research is funded by the National Institute of Health (NIH, NINDS), the US Food and Drug Administration (FDA), The Michael J. Fox Foundation,The MSA Coalition and the Dysautonomia Foundation, Inc.

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