Original Article

Subcutaneous Icatibant for the Treatment of Hereditary Angioedema Attacks: Comparison of Home Self-Administration with Administration at a Medical Facility

Iris M. Otani, MD[a], William R. Lumry, MD[b,c], Shelley Hurwitz, PhD[d], Huamin Henry Li, MD, PhD[e], Timothy J. Craig, DO[f], Niki S. Holtzman, BA[a], Matthew I. Iandoli, MS[a], Julie Tucker, CCRC[b,c], Marc A. Riedl, MD, MS[g], Bruce L. Zuraw, MD[g], and Aleena Banerji, MD[a] *Boston, Mass; Dallas, Texas; Chevy Chase, Md; Hershey, Pa; and La Jolla, Calif*

What is already known about this topic? Icatibant, a subcutaneous bradykinin-B2-receptor antagonist, is an effective on-demand therapy for treating hereditary angioedema attacks.

What does this article add to our knowledge? This is the first prospective, multicenter comparison of icatibant self-administration and HCP-administration (administration by health care professionals at medical facilities) in the United States showing that self-administration is comparable to HCP-administration with regard to efficacy and safety.

How does this study affect current management guidelines? Current US and World Allergy Organization guidelines recommend a home-based treatment plan for hereditary angioedema. This study provides prospective evidence that icatibant can be used as an effective on-demand therapy for home-based treatment plans.

BACKGROUND: Hereditary angioedema (HAE) is a life-threatening disorder characterized by recurrent angioedema. Icatibant, a subcutaneous bradykinin-B2-receptor antagonist, is an effective on-demand therapy. Data outside the United States suggest that self-administration is tolerated and patient-preferred compared with administration by health care professionals at medical facilities (HCP-administration).

OBJECTIVE: A prospective, multicenter study was conducted in the United States to compare icatibant self-administration and HCP-administration.

METHODS: Subjects 18 years or older with type I or II HAE were recruited. The first 2 HAE attacks after enrollment were treated at medical facilities. Subjects were instructed by a health care professional on self-administration during icatibant treatment for the second HAE attack. Icatibant was self-administered

[a]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Mass
[b]Allergy Asthma Research Associates Research Center, Dallas, Texas
[c]Allergy and Asthma Specialists, Dallas, Texas
[d]Biostatistics Core, Center for Clinical Investigation, Department of Medicine, Brigham and Women's Hospital, Boston, Mass
[e]Institute for Asthma and Allergy, Chevy Chase, Md
[f]Division of Pulmonary, Allergy and Critical Care, Department of Medicine and Pediatrics, Penn State University, Hershey, Pa
[g]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, University of California, San Diego, La Jolla, Calif

The project described was supported by grant number 1UL1TR001102-03 and Shire (ClinicalTrials.gov Identifier: NCT01457430).

Conflicts of interest: W. R. Lumry has received research support from Shire, Viropharma, Biocryst, and CSL Behring; is on the US Hereditary Angioedema Association (HAEA) Medical Advisory Board; has received consultancy fees from Shire/Viropharma, Salix/Valeant, Biocryst, and CSL Behring; has received lecture fees from Shire/Viropharma and CSL Behring; and has received travel support from the US Hereditary Angioedema Association. H. H. Li has received research support, personal fees, and nonfinancial support from Shire/Dyax/ViroPharma, CSL Behring, and Salix/Pharming and has received research support and nonfinancial support from BioCryst. T. J. Craig is a past Interest Section Leader for American Academy of Allergy, Asthma & Immunology; is an American Lung Association of Pennsylvania board member; is a US HAEA Advisory Board member; is on the Alpha-1 Foundation Clinical Research Center Board; has received consultancy fees from CSL Behring, Dyax, Shire, Merck, Biocryst, Bellrose, Merck, and Novartis; has received research support from CSL Behring, Shire, Dyax, Pharming, Merck, Genentech, GlaxoSmithKline, Grifols, Novartis, Sanofi Aventis, Boehringer Ingelheim, and Biocryst; has received lecture fees from CSL Behring, Dyax, Shire, and Grifols; and is a coinvestigator for Asthmanet, the National Heart, Lung, and Blood Institute. M. A. Riedl is on the US HAEA Medical Advisory Board; has received consultancy fees from Shire, Dyax, CSL Behring, Salix, Arrowhead, BioCryst, Ionis, and Global Blood Therapeutics; has received research support from Shire, Dyax, CSL Behring, BioCryst, Pharming, and Ionis; and has received lecture fees from Shire, Dyax, Salix, and CSL Behring. B. L. Zuraw has received consultancy fees from Alnylan, Arrowhead, BioCryst, CSL Behring, Dyax, Ionis, Nektar, Shire, and Salix and has received travel support from US HAEA. A. Banerji has received research support from Shire and CSL and is on the Alnylam Advisory Board. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication June 23, 2016; revised August 3, 2016; accepted for publication September 12, 2016.
Available online ■■

Corresponding author: Iris M. Otani, MD, Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, 55 Fruit St, Cox 201, Boston, MA 02114. E-mail: iris.m.otani@gmail.com.

2213-2198
© 2016 American Academy of Allergy, Asthma & Immunology
http://dx.doi.org/10.1016/j.jaip.2016.09.023

Abbreviations used
AE- Adverse event
HAE- Hereditary angioedema
HCP-administration- Administration by health care professionals at medical facilities
ISR- Injection-site reaction
PSS- Patient symptom score
VAS- Visual analog scale

for all subsequent attacks. For each treated HAE attack, efficacy, safety, and tolerability data were recorded.
RESULTS: Nineteen patients with HAE received icatibant for 79 distinct HAE attacks. Mean attack duration was significantly shorter with self-administration (n = 50; 547 ± 510 minutes) than with HCP-administration (n = 29; 968 ± 717 minutes; $P = .006$). Mean time to treatment was significantly shorter with self-administration (143 ± 226 minutes) than with HCP-administration (361 ± 503 minutes; $P < .0001$). Shorter times to treatment were associated with shorter time from treatment to symptom resolution ($r = 0.35$; $P = .02$). Improvements in visual analog scale score and patient symptom score from pretreatment to 4 hours postinjection were comparable between self-administration and HCP-administration. There were no serious adverse events or discontinuations due to adverse events with self-administration or HCP-administration.
CONCLUSIONS: Icatibant self-administration shortened attack duration and time to treatment, with no difference in safety or local tolerability compared with HCP-administration. These findings support icatibant as an effective on-demand option for home-based treatment. © **2016 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2016;■:■-■)**

Key words: *Hereditary angioedema; Icatibant; Home-based treatment; Bradykinin-receptor antagonist*

Hereditary angioedema (HAE) is a potentially life-threatening disease that is characterized by recurrent angioedema of cutaneous (face, genitalia, extremities) and mucosal (abdomen, oropharynx, larynx) tissues. HAE attacks are painful, unpredictable, and vary in severity, frequency, and anatomical location between patients.[1] As a result, attacks can be debilitating and result in significant and multifaceted disease burden.[2]

Historically, treatment options for HAE have been limited, but newly approved and emerging therapies appear to provide safe and effective relief for a significant proportion of patients with HAE.[3] Despite advances in HAE treatment, the need to travel to a health care facility for on-demand treatment can subject patients to the inconvenience of travel and prolonged wait times in the emergency department and delay treatment after attack onset.[3] Home administration of on-demand treatment with C1-inhibitor concentrate has been shown to decrease attack duration and pain medication use.[4,5] Therefore, efforts have been focused on emphasizing home-based treatment to decrease the burden of disease and improve quality of life.[3,6] Current clinical HAE guidelines and consensus recommend a home-based treatment plan, where patients receive self-administration training and have at least 2 doses of HAE medications with them at all times for on-demand treatment.[7-12]

Icatibant is a bradykinin-B2-receptor antagonist with efficacy in treating acute attacks of HAE that was approved by the Food and Drug Administration in 2011 for patients 18 years or older.[13,14] Data from outside the United States suggest that icatibant self-administration has a comparable safety and efficacy profile to administration by health care professionals at medical facilities (HCP-administration).[15,16] Importantly, previous studies have reported that icatibant self-administration is patient-preferred and improves quality of life compared with HCP-administration, suggesting that self-administration would decrease disease burden.[15,17] Self-administration has also been shown to lower health care costs in Spain.[18] US data are needed to investigate the applicability of previous data to US patients. To our knowledge, this is the first prospective, multicenter study in the United States evaluating icatibant self-administration for HAE attacks.

METHODS

Study subjects

Subjects 18 years or older with documented HAE were recruited at 5 separate sites in different states. A documented diagnosis of type I or II HAE was based on the presence of all of the following: (1) family and/or medical history, (2) characteristic and recurrent attacks, and (3) low C4 with normal C1q and low C1 inhibitor function. Subjects who met the following exclusion criteria were excluded from the study: (1) participation in another clinical therapeutic trial within the past month; (2) diagnosis of angioedema other than type I or type II HAE; (3) comorbidities: symptomatic coronary artery disease, congestive heart failure New York Heart Association class 3 and 4, stroke within the past 6 months; (4) treatment with angiotensin-converting enzyme inhibitor; (5) pregnant and/or breast-feeding; (6) mental condition rendering patient unable to understand possible consequences of study; and (7) inability to comply with protocol. Recruitment was initiated after Food and Drug Administration approval of icatibant and previous use of icatibant was not specified as part of the exclusion criteria.

Study design

The first 2 HAE attacks after entry into the study were treated at a medical facility (HCP-administration). The medical facilities used for the study were the recruiting physician's offices at all 5 sites. During the first HAE attack treated at a medical facility, icatibant was administered by a health care professional while the technique was explained to the subject. Subjects were instructed on self-administration during icatibant treatment for the second HAE attack. HAE attacks treated at a medical facility were included in the HCP-administration group. Subsequent HAE attacks were treated with self-administration and were included in the self-administration group. All HAE attacks were treated according to icatibant prescribing guidelines (30 mg in 3 mL solution).

At the onset of each HAE attack, attack location site(s) and Patient Global Clinical Impression scores were recorded. The Patient Global Clinical Impression asks patients to answer the question "How severe do you consider your attack to be?" on a scale of 1 (very mild) to 5 (very severe). For each treated attack, efficacy and safety and tolerability data were recorded. Time of onset of HAE attack, time icatibant was administered, and time to complete relief of symptoms were recorded in hours and minutes. Time to complete relief of symptoms was defined as time from onset of symptoms to complete or near-complete resolution as reported by the patient.

Download English Version:

https://daneshyari.com/en/article/5647388

Download Persian Version:

https://daneshyari.com/article/5647388

Daneshyari.com