1058 | Real-world outcomes in C1 inhibitor hereditary angioedema: experience from the icatibant outcome survey in Spain

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Introduction: Hereditary angioedema (HAE) is a rare, potentially fatal, bradykinin-mediated disease. The Icatibant Outcome Survey (IOS; NCT01034969) is a Shire sponsored international observational study monitoring safety and effectiveness of icatibant, a bradykinin B2 receptor antagonist approved for the acute treatment of HAE in adults. Using IOS data from patients (pts) with C1-INH-HAE, we compared disease characteristics and icatibant-treatment outcomes between IOS pts from Spain and other IOS countries.

Objectives: A descriptive, retrospective comparative analyses of IOS data from centers in Spain vs those from centers in Austria, Brazil, Denmark, France, Germany, Greece, Israel, Italy, Sweden and the United Kingdom (July 2009 - August 2016). Icatibant treatment outcomes were retrieved from pts with complete attack outcome data for time to treatment, time to resolution and attack duration.

Results: A total of 666 IOS pts with C1-INH-HAE (84 from Spain and 582 from other IOS countries) provided demographic data. No meaningful differences were identified between pts from Spain and other countries with respect to gender (53.6% vs 60.0% females), median age at enrollment (39.4y vs 39.4y), median age at symptom's onset (14.0y vs 12.0y) and median age at diagnosis (22.2y vs 20.5y). Spanish pts reported fewer severe or very severe HAE attacks (43.1% vs 56.9%) than pts from other countries respectively and differences in the percentage of pts reporting "very mild, mild, or moderate" symptoms (Spain: 251/441; Other: 1171/2714) vs "severe or very severe" symptoms (Spain: 190/441; Other: 1543/2741) were significant ($P < .0001$). Icatibant treatment outcomes were derived from 109 attacks in 84 Spanish pts and 1258 attacks in 582 pts from other IOS countries. The median time to treatment (2.9 h vs 1.0 h; $P = .0049$), time to resolution (17.0 h vs 5.5 h; $P < .0001$), and attack duration (24.0 h vs 8.3 h, $P < .0001$) in Spanish pts vs pts from other countries, were all significantly longer. The majority of pts self-administered icatibant (79.7% in Spain and 89.8% in other countries)

Conclusions: C1-INH-HAE general disease characteristics were similar in Spanish IOS pts and pts from other IOS countries, however Spanish IOS pts report fewer severe attacks, administer icatibant significantly later, and their attacks last longer, perhaps indicating differing HAE management practices, pt selection or reporting procedures.

1059 | A phase 3 open-label extension study of the efficacy and safety of lanadelumab for the prevention of angioedema attacks in patients with hereditary angioedema: trial design

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Introduction: Lanadelumab (DX-2930/SHP-643) is a long-acting, highly-specific, potent, human monoclonal antibody targeting plasma kallikrein that received fast track and breakthrough therapy designations. Results from a Phase 1b study (NCT02093923) did not identify safety signals and supported efficacy of lanadelumab in preventing hereditary angioedema (HAE) attacks. A pivotal randomized, double-blind (DB), placebo-controlled, parallel arm study (NCT02586805) is ongoing, and an open-label extension (OLE; NCT02741596) is currently enrolling patients (pts).

Objectives: To describe the design of a Phase 3 OLE study to evaluate the long-term safety and efficacy of lanadelumab for prevention of angioedema attacks in patients with HAE.

Results: This OLE will include pts (≥12 years old; Type 1/2 HAE) rolling over from the DB study and an additional 50-100 pts who did not participate in the DB study (non-rollover). The non-rollover population will include pts switching to lanadelumab from another prophylactic therapy. Rollover pts will initially receive a single 300 mg subcutaneous dose of lanadelumab and will not receive

another dose until after their first HAE attack. Thereafter, lanadelumab 300 mg q2 weeks will be administered until Day 350, followed by a 4-week safety follow-up. Non-rollover patients will be dosed q2 weeks regardless of their first attack. Pts may qualify to self-administer lanadelumab. The primary objective of the OLE will be to assess long-term safety. In the phase 1b study, 25% pts had local adverse effects following lanadelumab treatment vs 23.1% following placebo. Secondary objectives include evaluation of efficacy (time to first HAE attack to determine outer bounds of the dosing interval, attack rate, number attacks requiring acute treatment, are moderate/severe, or are associated with high-morbidity). Lanadelumab 300 and 400 mg was associated with a 100% and 88% reduction in attacks, respectively, in the Phase 1b study. Immunogenicity, pharmacokinetics/pharmacodynamics, quality of life, characteristics of breakthrough attacks, self-administration and safety/efficacy in pts switching to lanadelumab from another prophylactic therapy will be evaluated. Results of the OLE are expected in 2018.

Conclusions: Results of this study will provide additional important data on the long-term safety, efficacy and dosing frequency of lanadelumab, a first-in-class subcutaneous therapy for prevention of angioedema attacks in patients with HAE.