also a not statistically significant increase of the capillary length in patients compared to controls (normal vs increased, $P = 0.45$). No differences were found in the capillary density, morphology, intercapillary distance or presence of hemorrhages.

Conclusion: Our data suggest that C1-INH-HAE patients present morphological alterations of the capillary microcirculation. The qualitative anomalies (loop size or distribution) rather than quantitative (intercapillary distance or number) support the hypothesis that the loss of capillaries, described in connective tissue diseases, is absent in C1-INH-HAE patients. This high prevalence of morphological alterations may represent a substrate that predisposes to the angioedema attacks. Further studies are needed to clarify the role of such alterations in patients with angioedema.

0521 | Fixed-dose subcutaneous (SC) C1 inhibitor liquid for prophylactic treatment of hereditary angioedema attacks: results from the phase 3 SAHARA study

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Background: Hereditary angioedema with C1 inhibitor deficiency (C1-INH-HAE) is a rare disorder associated with painful, potentially fatal attacks characterized by swelling of subcutaneous and/or submucosal tissues. Long-term prophylactic treatment (LTP) of these attacks is a primary goal for many patients. SHP616, a subcutaneously-administered (SC) C1 inhibitor liquid, is a convenient to administer, well-tolerated, and reliably effective prophylactic agent. Findings from the phase 3, double-blind partial crossover SAHARA study evaluating safety and efficacy of fixed dosage (2000 IU, 4 mL) SHP616 twice weekly for attack prevention (NCT02584959) are reported here.

Method: Subjects were randomized to 1 of 3 treatment sequences, received over two 14-week periods—SHP616 with crossover to placebo; placebo with crossover to SHP616; or SHP616 to SHP616. Eligibility included confirmed diagnosis of C1-INH-HAE type I/II, age ≥12 years, and baseline HAE attacks ≥2/month (prior to screening or initiation of LTP). The primary efficacy endpoint was normalized number of attacks (NNA) vs placebo. Additional efficacy endpoints were proportion of subjects achieving NNA reduction ≥50%, and percentage of subjects with no attacks during the treatment period.

Results: Of 81 subjects screened, 75 were randomized (60 for crossover; 15 for the SHP616–SHP616 treatment sequence) and 59 (79%) completed study treatment. The mean age was 41 years; 88% of subjects had HAE type I Most subjects (91%) had received acute or prophylactic treatment within the last year; 51% had received LTP with C1-INH or androgens previously. Treatment with SHP616 reduced attack frequency throughout the study period. Least square means of NNA were reduced from 3.9 with placebo to 1.6 with SHP616 from Day 1 ($P < 0.0001$; median percent reduction 79%), and from 3.8 with placebo to 1.5 with SHP616 from Day 15 (median percent reduction 85%). Most subjects (78%) had ≥50% NNA reduction with SHP616, and 38% were attack free (vs 9% with placebo) throughout the 14-week period. Treatment emergent adverse event (TEAE) rates were similar between treatment groups (52% vs 56% for SHP616 crossover group vs placebo, respectively). Only 13% of subjects experienced TEAEs within 24 hours post SHP616. No treatment-related serious or severe TEAEs occurred and no anti-C1 INH antibodies were detected.

Conclusion: Fixed-dose 2000 IU SC SHP616 was superior to placebo in preventing HAE attacks and demonstrated a favorable safety profile.

0522 | Intramuscular administration of recombinant human c1-inhibitor could be an alternative for the treatment of acute attacks in patients with hereditary angioedema: A 3 year experience

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Background: Recombinant human C1-inhibitor (rhC1-INH) is registered for intravenous treatment of hereditary angioedema (HAE) attacks in adults and adolescents. In some cases, patients have compromised veins and/or difficulties accessing medical facilities. Intramuscular administration of C1-INH is not investigated in clinical trials but could be a feasible alternative in some cases for its ease of administration. Bioavailability of the C1-INH should be superior via the intramuscular administration compared to the sub-cutaneous administration.

Method: Data collected from five different HAE Type 1 patients, who use off-label on-demand (OD) intramuscular (IM) administration of rhC1-INH, the first subject: since 2015. After discussion of all ethical implications, the dose used per administration was either 1 or 2 vials (reconstituted in 10 mL WFI, each) injected IM in different locations (m. gluteus maximus or m. quadriceps femoris). Patient diaries were analyzed, which included documentation for pain by the visual analogue scale (VAS).