C1 1412 Ruconest Registry Summary of Results

C1 inhibitor Treatment Registry to assess the Safety and Immunological Profile of Ruconest in the treatment of HAE Attacks

Sponsor:	Pharming Technologies B.V. Darwinweg 24 2333 CR Leiden, The Netherlands
First patient's first visit (screening; date [YYYY-MM-DD]):	2011-10-06
Last patient's last visit (date[YYYY-MM-DD]):	2024-10-18

SUMMARY OF RESULTS

Number of patients (planned and analyzed):

	Adults	Adolescents	Children	Total
No. planned:				300
Enrolled:	172	6	3	181
Did not receive HAE treatment	60	3	3	66
Safety analysis set	112	3	0	115
Treatment received:				
Ruconest only	69 (61.6%)	1 (33.3%)	0	70 (60.9%)
pdC1INH only	7 (6.3%)	1 (33.3%)	0	8 (7.0%)
Firazyr only	10 (8.9%)	0	0	10 (8.7%)
Mixed treatment	26 (23.2%)	1 (33.3%)	0	27 (23.5%)
Males/females	44/68	1/2	0/0	45/70
Mean age (range)	42.9 (18-78)	15.3 (13-17)	-	42.2 (13-78)

Summary of patient disposition (not mentioned above):

For the adults, the mean (standard deviation [SD]) duration of participation in the study was 947.8 (743.3) days for patients who received Ruconest only, 1846.0 (1268.8) days for patients who received Mixed treatment, 1382.0 (980.1) days for those who received Firazyr only, and 952.0 (264.8) days for patients who received pdC1INH only.

Demography and baseline characteristics (not mentioned above):

For the adults, overall, the mean (SD) time since the HAE diagnosis was 206.2 (158.4) months, and the median (range) time was 178.5 (0 to 584) months.

The most common affected location was the peripheral region (77.7% of all patients), followed by the abdominal region (76.8%), the oro-facial pharyngeal region (59.8%), the laryngeal region (34.8%), and the urogenital region (33.9%).

Half of all patients (50.0%), had been treated with Ruconest for their previous acute HAE attacks during the past year, and 39.3% had been treated with pdC1INH.

EFFICACY RESULTS:

- **Insufficient efficacy**

  In total, 40 of the adult patients (35.7%; N=112) reported insufficient efficacy after at least one treatment administration, including 17 patients (24.6%; N=69) treated with Ruconest only, 16 patients (61.5%; N=26) treated with Mixed treatments, 5 patients (50.0%; N=10) treated with Firazyr only, and 2 patients (28.6%; N=7) treated with pdC1INH treatment only.

  Two of the 3 adolescent patients (1 who received Ruconest only and 1 who received Mixed treatments) reported insufficient efficacy after at least one treatment administration.

- **Treatment response (post-hoc)**

  Treatment response was defined if a patient reported improvement within 4 hours after treatment.

  In the subset of the adult patients who administered Ruconest at least once, the response rate was high (>95%) for all treatment locations.

  Response rate was consistent across different attack locations, with continued efficacy of repeated treatments with Ruconest for subsequent acute angioedema attacks.

  The 3 adolescent patients also mainly showed treatment response (>77%).

SAFETY RESULTS:

- **Adverse events**

  In the adults safety analysis set, 21 patients (18.8%; N=112) reported a total of 46 AEs: 14 patients treated with Ruconest only (20.3%; N=69) reported 32 AEs and 7 patients treated with Mixed treatments (26.9%; N=26) reported 14 AEs. None of the patients who received treatment with pdC1INH or Firazyr alone reported any AEs.

  None of the 3 adolescent patients reported any AE.

  For the adults, the most commonly reported AEs (*PT*s) were *Headache*, *Erythema*, *Hospitalisation,* and *Laryngeal oedema*.

  Of the 46 AEs that occurred in the study, 4 AEs (*Erythema* [2 events] and *Headache* [2 events]) in 1 patient, were judged as probably related to the treatment, and 1 AE (*Headache*) in 1 patient was judged as possibly related to the treatment. The other AEs were judged as remote/unlikely related (18 AEs in 9 patients) or unrelated to the treatment (23 AEs in 14 patients).

  Most of the 46 AEs were of mild (25 AEs in 14 patients) or moderate (13 AEs in 10 patients) intensity, however, there were 4 severe AEs (in 2 patients), 1 life-threatening AE (in 1 patient), and 3 fatal AEs (in 2 patients) reported during the Registry.

- **Deaths, other serious adverse events, and other significant adverse events**

  In the adults safety analysis set, 2 patients (1.8%; N=112) who received Ruconest only treatment died during the Registry (PTs; *Death* [caused by SARS-CoV-2 infection] and *Laryngeal oedema*).

  A total of 7 non-fatal SAEs (*PTs*: *Breast cancer* [2 SAEs in 1 patient], *Hospitalisation:* [3 SAEs in 2 patients], *Pyelonephritis acute*, and *Vestibular disorder*) occurred in 5 patients (4.5%; N=112).

  None of the deaths or SAEs were considered as related to the treatment.

  No AEs of special interest (AEOSIs) including hypersensitivity reactions and thrombotic/thrombo-embolic events, or AEs related to self-administration of Ruconest, were reported during the Registry study.

  None of the patients that self-administered Ruconest reported any medication errors or AEs related to the self-administration.

- **Hereditary angioedema attacks**

  In total, the mean (SD) number of attacks was 44.5 (75.1) attacks, and varied from 2.3 (1.6) attacks in the Firazyr only group to 56.0 (107.4) attacks in the Mixed treatment group.

For all patients, the mainly affected locations were the abdominal region (77.7% affected; N=112), the peripheral region (75.9% affected) and the oro-facial pharyngeal region (63.4% affected).

- **Immunological test findings**

  No immunological tests were performed, as there was no suspected hypersensitivity or suspected neutralizing antibodies observed in any of the patients treated with Ruconest only or Mixed treatment including Ruconest.

- **Pregnancies**

  Three patients that participated in the Registry study were exposed to Ruconest during pregnancy. The outcomes of all three pregnancies were full-term live births (two vaginal deliveries, and one cesarian section). There were no reported complications before, during or after any of the deliveries.

OVERALL CONCLUSIONS:

- Few AEs were reported in the Registry study. Most AEs were of mild or moderate intensity and assessed as unlikely/unrelated to the treatment.

  None of the SAEs that occurred was judged as related to the treatment.

  No safety concerns were raised regarding AEOSI including hypersensitivity reactions, and thrombotic/thromboembolic events.

  A total of 46 AEs were reported by 20.3% of the patients who received Ruconest only (N=69) and by 26.9% of the patients who received Mixed treatment (N=26). None of the patients who received treatment with pdC1INH (N=7) or Firazyr alone (N=10) reported any AEs.

- In the subset of the adult patients that administered Ruconest at least once, the response rate was high (>95%) for all treatment locations.

  The 3 adolescent patients also mainly showed treatment response (>77%).

- Post-hoc analysis showed a consistent response rate across different attack locations, with continued efficacy of repeated treatments with Ruconest for subsequent acute angioedema attacks.

- Insufficient efficacy after at least one treatment administration, was reported by 24.6% of the patients treated with Ruconest only, 28.6% of the patients treated with pdC1INH only, 50.0% of the patients treated with Firazyr only, and by 61.5% of the patients treated with Mixed treatments.

- There were no suspected hypersensitivity or suspected neutralizing antibodies observed in any of the patients treated with Ruconest only or Mixed treatment including Ruconest, thus, no immunological tests were performed.

- There were no reported AEs or medication errors related to self-administration of Ruconest.

- No evidence was found of an increase in the percentages of patients with AEs or AEOSIs, or in the seriousness or severity of AEs, with Ruconest dosing and number of administrations.

- Data did not suggest any safety signal regarding the use of Ruconest during pregnancy.

- Overall, the safety evaluation of this Registry did not reveal any potential new safety signal or additional risks and confirmed the favorable safety profile of Ruconest, and data are consistent with the results seen in several clinical studies with different subject populations.

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