**TABLES & SUPPLEMENTAL TABLES**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Weight (kg) | Duration of disease (months) | Atopy | Profylactic treatment1 | Attack intervention1 | Attack frequency (attacks/month) | Baseline C1-INH function (U/ml) | Baseline  C4 level (g/L) | Baseline total IgE (kU/L) | Dose of rhC1INH administered |
| Patient 1  31 y/o female | **100** | **47** | **Asthma**  **Eczema**  **Rhinitis** | **Levocetirizine 4dd** | **ER - 1x**  **Adrenalin 1x**  **Prednisolone** | **2.8** | **1.25** | **0.30** | **275** | **4200 U** |
| Patient 2  37 y/o  Female | **72** | **6** | **Rhinitis** | **Levocetirizine 4dd** | **ER – 1x**  **Adrenalin 1x**  **Clemastine**  **Dexamethasone** | **3.7** | **0.95** | **0.15** | **163** | **3615 U** |
| Patient 3  56 y/o  Male | **85** | **103** | **-** | **Levocetirizine 4dd** | **Prednisolone** | **2.6** | **1.19** | **0.27** | **254** | **4200 U** |
| Patient 4  33 y/o  Male | **74** | **8** | **-** | **Desloratadine 4dd**  **Clemastine 1dd** | **Prednisolone** | **15.8** | **1.54** | **0.52** | **98** | **3715 U** |
| Patient 5  25 y/o  Female | **85** | **84** | **-** | **Levocetirizine 4dd**  **Montelukast 1dd** | **-** | **2.8** | **1.70** | **0.34** | **87** | **4200 U** |
| Patient 6  60 y/o  Female | **116** | **21** | **-** | **Levocetirizine 4dd** | **Desloratadine**  **Clemastine** | **4.2** | **1.21** | **0.23** | **95** | **4200 U** |

**Table 1.** **Demographic and clinical characteristics of included patients.**   
**Legend:**1 six months before start. Reference values for C1-INH function: 0.63-1.82 U/mL. C4 level: 0.1-0.47 g/L. IgE level: 0-100 kU/L.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Observation 1** | | | | **AAS28** | **Observation 2** | | | | **AAS28** |
| **Patient 1** | 18 | 26 | 0 | 14 | **58** | 30 | 48 | 44 | 53 | **175** |
| **Patient 2** | 33 | 10 | 0 | 33 | **76** | 10 | 13 | 0 | 48 | **71** |
| **Patient 3** | 0 | 0 | 6 | 12 | **18** | 0 | 0 | 0 | 7 | **7** |
| **Patient 4** | 8 | 13 | 19 | 24 | **64** | 17 | 9 | 12 | 0 | **38** |
| **Patient 5** | 25 | 3 | 11 | 9 | **48** | 1 | 5 | 0 | 10 | **16** |
| **Patient 6** | 19 | 31 | 0 | 3 | **53** | 0 | 0 | 9 | 0 | **9** |
|  | **Treatment 1** | | | | **AAS28** | **Treatment 2** | | | | **AAS28** |
| **Patient 1** | 8 | 0 | 0 | 0 | **8** | 12 | 9 | 0 | 0 | **21** |
| **Patient 2** | 12 | 15 | 0 | 0 | **27** | 67 | 35 | 36 | 0 | **138** |
| **Patient 3** | 8 | 31 | 0 | 9 | **48** | 9 | 22 | 0 | 18 | **49** |
| **Patient 4** | 38 | 19 | 14 | 0 | **71** | 8 | 4 | 3 | 2 | **17** |
| **Patient 5** | 3 | 7 | 16 | 12 | **38** | 0 | 4 | 6 | 0 | **10** |
| **Patient 6** | 17 | 7 | 34 | 22 | **80** | 1 | 0 | 22 | 13 | **36** |

**Table 2. Angioedema Activity Score (AAS) during the observational and treatment months**.

**Legend**: AAS7 accumulated into AAS28 are presented for the observational and treatment months.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Post-study drug | Max dose | Total time of use in months | Effectiveness |
| Patient 1 | pdC1INH  rhC1INH  Omalizumab  Tranexaminic acid  Prednisolone | 1000IE  4200IE  300mg/4wks  3dd1000mg  60mg | 12  19  3  3  Attack use only | Very effective  Very effective  Poor  Poor  Poor |
| Patient 2 | Omalizumab  Dexamethasone | 600mg/3wks  10mg | 33 months  Attack use only | Yes, after 28 doses  Yes |
| Patient 3 | Prednisolone | 20mg | Attack use only | Yes |
| Patient 4 | Desloratadine  Tranexamic acid | 1dd5mg  3dd500mg | 23 months  23 months | Good, near complete response |
| Patient 5 | - |  |  |  |
| Patient 6 | Omalizumab | 300mg/4wks | 2 months | Good, near complete response |

**Table 3. Real-world post-study Inh-AAE treatment.**

**Legend:** Antihistamine use shown only for patient 4 due to the reported positive treatment response in combination with tranexamic acid.

|  |  |  |  |
| --- | --- | --- | --- |
| A2M  ACE  ANGPT1  BDKRB1  BDKRB2  CPB2  CPM  CPN1  CPN2  DPP4  F11  F12  F13B | F2  HRH1  HRH3  HRH4  KLK1  KLK10  KLK11  KLK12  KLK13  KLK14  KLK15  KLK2  KLK3 | KLK4  KLK5  KLK6  KLK7  KLK8  KLK9  KLKB1  KNG1  MASP1  MASP2  PLAU  PLAUR  PLG | PTGS1  PTGS2  SERPINA1  SERPINA4  SERPINB2  SERPINE1  SERPINF2  SERPING1  TFPI  VEGFA  XPNPEP1  XPNPEP2  MYOF  HS3ST6 |

**Supplemental table 1. Gene panel analysed in patient 1 (rhC1-INH responder).**

**Legend:** No mutation was found in any of the 53 genes.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Functioning | | | | | | Fatique/Mood | | | | | |
|  | O1 | O2 | **Final O** | T1 | T2 | **Final T** | O1 | O2 | **Final O** | T1 | T2 | **Final T** |
| **Patient 1** | 12 | 12 | **8** | 4 | 4 | **0** | 10 | 13 | **6.5** | 10 | 13 | **6.5** |
| **Patient 2** | 16 | 12 | **10** | 4 | 12 | **4** | 10 | 7 | **3.5** | 9 | 6 | **2.5** |
| **Patient 3** | 7 | 4 | **1.5** | 10 | 9 | **5.5** | 7 | 8 | **2.5** | 8 | 8 | **3** |
| **Patient 4** | 7 | 5 | **2** | 4 | 4 | **0** | 16 | 8 | **7** | 10 | 9 | **4.5** |
| **Patient 5** | 13 | 7 | **6** | 14 | 12 | **9** | 12 | 7 | **4.5** | 14 | 13 | **8.5** |
| **Patient 6** | 9 | 4 | **2.5** | 14 | 4 | **5** | 19 | 14 | **11.5** | 18 | 12 | **10** |
|  | Fear/Shame | | | | | | Nutrition | | | | | |
|  | O1 | O2 | **Final O** | T1 | T2 | **Final T** | O1 | O2 | **Final O** | T1 | T2 | **Final T** |
| **Patient 1** | 14 | 14 | **8** | 9 | 12 | **4.5** | 5 | 6 | **3.5** | 4 | 3 | **1.5** |
| **Patient 2** | 24 | 18 | **15** | 20 | 23 | **15.5** | 7 | 7 | **5** | 2 | 8 | **3** |
| **Patient 3** | 17 | 16 | **10.5** | 15 | 16 | **9.5** | 5 | 5 | **3** | 4 | 5 | **2.5** |
| **Patient 4** | 20 | 15 | **11.5** | 12 | 14 | **7** | 4 | 3 | **1.5** | 2 | 2 | **0** |
| **Patient 5** | 24 | 20 | **16** | 23 | 23 | **17** | 2 | 2 | **0** | 2 | 2 | **0** |
| **Patient 6** | 22 | 19 | **14.5** | 26 | 17 | **15.5** | 7 | 5 | **4** | 9 | 3 | **4** |

**Supplemental table 2. Angioedema quality of life score.**

**Legend:**O1: Observational month 1, O2: Observational month, T1: Treatment month 1, T2: Treatment month 2.

Minimum/Maximum scores for each domain: Functioning: 4/20. Fatique/Mood: 5/25. Fear/Shame: 6/30. Nutrition: 2/10.

Final QoL scores calculated as: Entered score for the two observational or two treatment months minus twice the minimum score, divided by two.