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1. ABSTRACT

Title

Non-Interventional Post-Marketing Safety Study on the Long-Term Safety of HYQVIA (Global)

Keywords

HYQVIA, primary immunodeficiency disease, immune globulin, recombinant human hyaluronidase and safety

Rationale and Background

This post-authorisation safety study (PASS) with regular assessment of antibodies against recombinant human hyaluronidase (rHuPH20) was a commitment to the Food and Drug Administration (FDA).

Research Question and Objectives

The purpose of this study was to acquire additional data (including assessment of anti-rHuPH20 antibodies) on the long-term safety of HYQVIA, and to assess the prescribed treatment regimens and treatment administration in routine clinical practice.

Primary Objective:

- To collect and assess additional safety data, in particular the occurrence of long-term changes in incidence and severity of related adverse events (AEs), in subjects treated with HYQVIA.

Secondary Objective:

- To collect data on anti-rHuPH20 antibodies and other laboratory safety assessments, total IgG, further safety assessments that were obtained during the routine clinical management of the subjects, the prescribed treatment regimen and treatment administration, and health-related quality of life (HRQoL) and health resource use (HRU) assessments.

Study Design

This was a non-interventional, prospective, uncontrolled, multicenter, open-label, post-marketing surveillance study with assessment of antibodies against rHuPH20. This study was designed to obtain additional safety and tolerability data on HYQVIA in adult subjects with primary immunodeficiency disease (PIDD) under routine clinical conditions. Further data were collected in subjects with an anti-rHuPH20 antibody titer ≥ 160, measured during study Epoch 1 or documented at any time prior to enrolment.

Each subject was invited to have additional blood samples drawn at the time of routine laboratory assessments approximately every 3 months, but no more than 4 times a year, for the measurement of antibodies against rHuPH20. Antibody characterization was performed for subjects with an anti-rHuPH20 antibody titer ≥ 10,000. If testing for antibodies against rHuPH20 was not done for any reason, all other laboratory data were collected as available.

The study was composed of 2 Epochs:

Epoch 1:

Epoch 1 started at enrolment of the subjects into the study, and the subjects were treated for approximately 1 year with HYQVIA. Subjects who at no time during Epoch 1 tested positive for anti-rHuPH20 antibodies at a titer of ≥ 160, including those who did not undergo testing for anti-rHuPH20 antibodies at least once during Epoch 1, exited the study at the end of Epoch 1.

Epoch 2:

Subjects who at any time during Epoch 1 tested positive for anti-rHuPH20 antibodies at a titer of ≥ 160 continued the study for an additional 2 years from the time of completion of Epoch 1. Additionally, subjects in whom anti-rHuPH20 antibodies at a titer ≥ 160 were measured and documented at any time prior to enrolment, continued in Epoch 2 regardless of any test results for anti-rHuPH20 antibodies that might have been available from Epoch 1. Treatment in Epoch 2 continued as in Epoch 1.

Setting

This study was conducted in the US only. Adult subjects aged ≥ 16 years with PIDD who were prescribed or had initiated treatment with HYQVIA were enrolled. Treatment regimens were prescribed at the discretion of the attending physician in accordance with routine clinical practice. Pregnant or breast-feeding women could continue in the study at the Investigator's discretion. Site visits and all other medical care were performed as per standard for the site and for the subject's healthcare, except for the assessment of antibodies against rHuPH20.

Subject discontinuing HYQVIA treatment during the study who consented for further testing of anti-rHuPH20 antibodies were asked to continue participating in the study and be followed up for anti-rHuPH20 antibody titers and occurrence of AEs. The subject's treating physician prescribed an alternative licensed human normal Ig or any other alternative treatment after discontinuation of HYQVIA.

The planned duration of the study was approximately between 6 to 7 years from the study start, and the planned recruitment period was approximately 3 years. The actual duration of the study was approximately 6 years, from Nov 2015 through Oct 2021, and the actual recruitment period was approximately 3 years, from Nov 2015 through Oct 2018.

Subjects and Study Size, Including Dropouts

Subjects who met ALL the following criteria were eligible for this study:

1. Subject required Ig treatment for PIDD.
2. Subject age was compatible with local package insert requirements (USA ≥ 16, EU ≥ 18years of age).
3. Subject was prescribed or had started treatment with HYQVIA.
4. Subject was willing and able to comply with the requirements of the protocol.

Subjects who met ANY of the following criteria were not eligible for this study:

1. Subject had known hypersensitivity to any of the components of the medicinal product.
2. Subject had participated in an interventional clinical study involving a medicinal product or device within 30 days prior to enrolment or was scheduled to participate in an interventional clinical study involving a medical product or device during this study.
3. Subject was a family member or employee of the Investigator.

Any subject who provided informed consent (signed and dated the informed consent form [ICF]) was considered enrolled in the study.

A total of 253 adult subjects with PIDD under routine clinical conditions were enrolled and analyzed. All subjects were required to complete Epoch 1 as per protocol.

Variables and Data Sources

Safety variables included treatment emergent incidence of all serious adverse events (SAEs; related and non-related), treatment emergent incidence of non-serious AEs (related and not related; and local and systemic) including/excluding infections, incidence of binding and neutralizing antibodies to rHuPH20, quantitative value of the titer of binding antibodies to rHuPH20, the presence of neutralizing antibodies to rHuPH20, and the characterization of antibodies to rHuPH20 in positive samples of a titer ≥ 10,000 (to include neutralizing antibodies and antibodies cross-reacting with Hyal 1, 2 and 4).

Additional safety variables included laboratory tests such as (but not limited to) clinical chemistry, hematology, urinalysis, total IgG, seroconversion results for human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) and pregnancy testing, physical examination, and vital signs.

Treatment administration variables included treatment regimen (Ig dose and infusion interval) and other variables (actual volume per infusion, maximum infusion rate, mean rate of infusion, duration of infusion, and number of infusion sites (needle sticks) per infusion).

Additional variables included HRQoL questionnaires: Short Form-36 version 2 (SF-36v2); the 3-level version of EuroQoL 5-Dimension (EQ-5D-3L); and Treatment Satisfaction Questionnaire for Medication-9 (TSQM-9) questionnaires. The HRU variables included hospitalizations and length of stay, acute care visits, emergency room (ER) visits, and days missed from work/school.

Results

Subject disposition:

A total of 253 subjects were screened, enrolled and analyzed: 190 subjects (75.1%) completed Epoch 1 and 50 subjects (19.8%) discontinued from Epoch 1 permanently. Overall, 14 subjects had an anti-rHuPH20 antibody titer of ≥ 160 at Screening and/or during Epoch 1; however, 1 subject discontinued the study during Epoch 1 with the reason being discontinuation by subject (withdrawal of consent). Thirteen subjects entered Epoch 2. Among these 13 subjects, 9 subjects completed an additional 2 years in the study from the time of completion of Epoch 1, one subject discontinued the study during the first year of Epoch 2, and 3 subjects discontinued during the second year of Epoch 2.

Overall, 21.3% of subjects (n=54) discontinued the study prematurely, primarily due to lost to follow-up (n=21) and subject withdrawal (n=20). Two subjects (3.7%) discontinued the study due to an AE.

Demographic and baseline characteristics:

The median age was 57.0 years, 30.4% (n=77) were 65 years or older and 79.1% (n=200) were female, 22.5% (n=45) of whom were of childbearing potential. Most subjects identified as White race (92.5% [n=234]), and non-Hispanic or Latino ethnicity (94.9% [n=240]). The most common (>10%) PIDD type was common variable immunodeficiency (n=182, 71.9%). Among the 253 subjects with available information, only 3 subjects (1.2%) reported previous participation in another Baxter Study. The median body mass index (BMI) at Baseline was 28.176 kg/m^2.

Most subjects had a prior history of Ig treatment (95.7% [242 of 253 subjects]), and HYQVIA was the most common prior Ig treatment (69.8% [n=169]).

HYQVIA treatment:

Overall, 2230 HYQVIA infusions were reported in 227 subjects during the follow-up period: 2122 infusions during Epoch 1 (60.7% (1287 infusions) were administered at home, and 39.3% (835 infusions) were administered at study site) while all 108 infusions during Epoch 2 (67 infusions during first year and 41 infusions during second year) were administered at home.

The mean (SD) duration of exposure to HYQVIA treatment was 8.13 (4.976) months overall (n=227): 8.28 (4.954) months during Epoch 1 (n=225), 6.87 (5.237) months during Epoch 2-Year 1 (n=8), and 4.00 (4.122) months during Epoch 2-Year 2 (n=6).

The mean (SD) actual Ig dose administered was 369.9 (112.82) mL. HYQVIA was infused every 4 weeks in 54.4% (1197 of 2201 infusions) of infusions and every 3 weeks in 21.7% (478 of 2201 infusions) of infusions throughout the study. Almost all infusions were administered in full volume (99.5% overall, 2149 of 2160 infusions, n=211). 31 infusions (of the 2125 infusions with available data, n=212) had either a change in infusion rate or an interruption due to an AE, all of which occurred during Epoch 1. The mean (SD) number of infusion sites was 1.9 (0.53) overall (2008 infusions, n=203).

The mean (SD) infusion duration was 3.1 (1.03) hours overall (1267 infusions with available data on start and end date/time, n=148): 3.0 (1.02) hours during Epoch 1 (1231 infusions, n=148), 3.9 (1.14) hours during Epoch 2-Year 1 (24 infusions, n=2), and 4.3 (1.14) hours during Epoch 2-Year 2 (12 infusions, n=2). The mean (SD) infusion rate was 127.34 (52.031) mL/h and the mean maximum infusion rate was 248.1 (77.23) mL/h, respectively.

Safety:

Overall, 67.2% of subjects (n=170) reported any AE (total of 945 events) during the study, of which 411 AEs were mild (15.8% [n=40]), 462 AEs were moderate (35.6% [n=90]), and 72 AEs were severe (15.8% [n= 40]) in intensity. Infections and infestations were the most common AEs according to the SOC (43.9% [n=111], 322 events). Sinusitis (13.0% [n=33], 57 events), bronchitis (11.1% [n=28], 35 events), and upper respiratory tract infection (11.1% [n=28], 39 events) were the most commonly reported AEs by PT. AEs reported in 21.3% (n=54, 286 events) of subjects were considered related to HYQVIA treatment. Common treatment emergent related AEs were headache (5.1% [n=13], 37 events), infusion site pain (4.7% [n=12], 24 events), infusion site swelling (3.6% [n=9], 23 events) and fatigue (3.6% [n=9], 20 events) by PT. The majority of AEs related to HYQVIA were mild (n=40, 153 events) or moderate (n=22, 126 events) in intensity. Four subjects (7 events) reported AEs related to HYQVIA that were classified as severe.

Serious AEs were reported in 14.6% of subjects (n=37, 61 events) with infections and infestations (5.9% [n=15], 22 events) being the most common SAE by SOC, and pneumonia (2.4% [n=6], 8 events), and cellulitis (1.2% [n=3], 4 events) as the most common SAE by PT. Only 0.8% (n=2, 2 events) of the subjects experienced SAEs that were related to HYQVIA treatment. Meningitis aseptic and deep vein thrombosis (0.4% each [n=1], 1 event each) were SAEs related to HYQVIA treatment by PT.

There were 2 fatal AEs reported (n=2, 0.8%): multiple organ dysfunction syndrome and chronic lymphocytic leukemia (1 subject each, 0.4%). Both events occurred in Epoch 1, and neither was related to HYQVIA treatment.

Non-serious AEs were reported in 64.4% (n=163, 884 events) of subjects.

Incidence of SAEs and non-serious AEs are summarized below:

- Incidence rate of SAEs related to HYQVIA treatment was 0.007 (95% Confidence Interval [CI]: 0.001 to 0.025) during Epoch 1. There was no SAE related to HYQVIA during Epoch 2.
- The overall incidence rate of all SAEs was 0.208 (95% CI: 0.159 to 0.268, 61 events): 0.215 (95% CI: 0.163 to 0.278) in Epoch 1 and 0.132 (95% CI: 0.027 to 0.386) in Epoch 2, respectively.
- The overall incidence rate of all non-serious AEs, including infections, was 3.018 (95% CI: 2.823 to 3.224) and incidence rate excluding infections was 1.994 (95% CI: 1.836 to 2.162).
  - The incidence rate of all non-serious AEs, including infections in Epoch 1 was 3.176 (95% CI: 2.967 to 3.396) and incidence rate excluding infections was 2.121 (95% CI: 1.951 to 2.302).
  - The incidence rate of all non-serious AEs, including infections in Epoch 2 was 1.055 (95% CI: 0.676 to 1.570) and incidence rate excluding infections was 0.396 (95% CI: 0.181 to 0.751).
- The overall incidence rate of non-serious AEs related to HYQVIA treatment, both including and excluding infections, was 0.970 (95% CI: 0.860 to 1.089): 1.036 (95% CI: 0.919 to 1.165) in Epoch 1, and 0.132 (95% CI: 0.027 to 0.386) in Epoch 2, respectively.
- The overall incidence proportion of all local non-serious AEs, related to HYQVIA treatment was 11.07% (28 of 253 subjects, 95% CI: 7.77 to 15.53). During Epoch 1 the incidence proportions of all local related non-serious AEs, was 10.67% (27 of 253 subjects, 95% CI: 7.44 to 15.08) while there was no local non-serious AEs related to HYQVIA in Epoch 2.

- The overall incidence proportion of all systemic related non-serious AEs was 14.23% (36 of 253 subjects, 95% CI: 10.46 to 19.07): 13.83% (35 of 253 subjects, 95% CI: 10.12 to 18.63) in Epoch 1 and 7.69% (1 of 13 subjects, 95% CI: 1.37 to 33.31) in Epoch 2.
- A total of 14 subjects developed positive anti-rHuPH20 antibodies defined as titer ≥ 160 during the study. Thirteen of these 14 subjects continued HYQVIA treatment in Epoch 2 despite their positive anti-rHuPH20 titer (≥ 160).
  - the overall incidence proportions of positive anti-rHuPH20 binding antibody titers was 7.140% (14 of 196 subjects, 95% CI: 4.302 to 11.631).
  - the incidence rates of all SAEs were 0.355 (95% CI: 0.009 to 1.980) before and 0.133 (95% CI: 0.043 to 0.310) after the first positive anti-rHuPH20 antibody titer, respectively.
  - none of the subjects who developed anti-rHuPH20 antibodies during the study experienced any SAE related to HYQVIA treatment, neither before or after the first positive anti-rHuPH20 antibody test.
  - the incidence rates of all non-serious AEs were 4.619 (95% CI: 2.459 to 7.898) before, and 1.221 (95% CI: 0.894 to 1.629) after the first positive anti-rHuPH20 antibody titer, respectively.
  - the incidence rates of all non-serious AEs related to HYQVIA treatment were 3.198 (95% CI: 1.462 to 6.070) before, and 0.186 (95% CI: 0.075 to 0.383) after the first positive anti-rHuPH20 antibody titer, respectively.
  - there was no neutralizing anti-rHuPH20 antibody development throughout the study.

Health-related quality of life:

A total of 186 subjects had SF-36v2 scores at Baseline (except for the General Health [GH] component, where 187 subjects had scores), 76 subjects at Epoch 1-Month 12 and 6 subjects at Epoch 2-Year 2. At Baseline, the mean (SD) physical health component summary score (PCS) score was 39.8 (10.78): 65.0 (28.34) for physical functioning (PF), 56.7 (31.92) for role-physical (RP), 51.5 (24.33) for bodily pain (BP) and 37.9 (20.25) for GH. At Month 12, the mean (SD) PCS score was 39.2 (11.26): 62.4 (31.29) for PF, 56.4 (32.14) for RP, 53.1 (27.17) for BP and 40.2 (20.19) for GH. At Epoch 2-Year 2, the mean (SD) PCS score was 32.8 (10.33): 44.2 (17.72) for PF, 55.6 (31.83) for RP, 39.7 (15.19) for BP and 35.5 (17.14) for GH.

The mean (SD) mental health component summary score (MCS) score at Baseline was 47.7 (10.29): 43.1 (24.29) for vitality (VT), 64.0 (25.49) for social functioning (SF), 77.0 (25.33) for role emotional (RE), and 70.6 (19.21) for mental health (MH). The mean (SD) MCS score at Month 12 was 49.4 (9.80): 44.6 (24.54) for VT, 64.3 (24.89) for SF, 78.2 (29.12) for RE, and 75.3 (17.72) for MH. The mean (SD) MCS score at Epoch 2-Year 2 was 52.8 (5.60): 44.8 (23.19) for VT, 52.1 (9.41) for SF, 87.5 (19.54) for RE, and 78.3 (8.16) for MH.

EuroQoL 5-Dimension three-level version (EQ-5D-3L): the EQ-5D-3L and the EQ-5D-3L VAS were administered every 3 months during Epoch 1 and annually during Epoch 2.

A total of 146 subjects had data for EQ-5D-3L at Baseline, 85 subjects at Epoch 1-Month 3, 75 subjects each at Epoch 1-Month 6 and Epoch 1-Month 9 and 67 subjects at Epoch 1-Month 12. At Baseline, the majority of subjects reported no problems for mobility (64.4%), self-care (87.7%), and anxiety/depression (61.0%), while some problems were reported for activities and pain/discomfort, 49.3% and 54.1% respectively. During Epoch 1, among subjects reporting anxiety/depression, the proportion who reported some problem decreased during the follow-up period as compared to baseline (anxiety/depression: from 33.6% at Baseline to 23.9% at Epoch 1- 12 months). The proportion of subjects reporting some problems with activities during Epoch 1, also saw a decrease over time as compared to baseline (activities: from 49.3% at Baseline to 43.3% at Epoch 1-12 months). In contrast, the proportion of subjects reporting some problems with pain/discomfort increased over time (from 54.1% at Baseline to 62.7% at Epoch 1-12 months). The mean change in EQ-5D-3L VAS score (n=50) from Baseline to Epoch 1-Month 12 was 2.5 (15.88).

From the 13 subjects that entered Epoch 2, 6 subjects had data at Baseline, 4 subjects at Epoch 2-Year 1, and 5 subjects at Epoch 2-Year 2. At Baseline, for activities and pain/discomfort, 4 (66.7%) and 3 (50.0%) subjects reported some problems, while for mobility (n=2 [33.3%]), self-care and anxiety/depression (n=1 [16.7% each]), these numbers were comparatively lower. The majority of subjects reported some problems during Epoch 2-Year 1 and Epoch 2-Year 2 for mobility (n=3 [75.0%] and n=3 [60.0%]), activities (n=3 [75.0%] and n=4 [80.0%]) and pain/discomfort (n=2 [50.0%] and n=4 [80.0%]), while for self-care none of the subjects had problems during Epoch 2. For anxiety/depression 1 subject in each year of Epoch 2 reported some problems (25.0%). Only one subject completed Epoch 2-Year 1 and Epoch 2-Year 2 assessments for the EQ-5D-3L VAS and for this one subject the mean change in EQ-5D-3L VAS from Baseline to Epoch 2-Year 2 was -5.0.

Treatment Satisfaction Questionnaire for Medication-9:

During Epoch 1, the mean (SD) TSQM-9 questionnaire score for effectiveness at Baseline was 70.8 (21.30, [n=146]). The mean changes of this score were -5.7 at Month 3 (n=70), -0.5 at Month 6 (n=59), 1.1 at Month 9 (n=60) and 5.5 at Month 12 (n=51). The mean (SD) TSQM-9 questionnaire score for convenience at Baseline was 66.4 (17.76, [n=148]). The mean changes of this score were 2.7 at Month 3 (n=71), 4.7 at Month 6 (n=61), 3.7 at Month 9 (n=61) and 3.8 at Month 12 (n=52). The mean (SD) TSQM-9 questionnaire score for satisfaction at Baseline was 76.8 (18.83). The mean changes of this score were -1.9 at Month 3 (n=71), 1.4 at Month 6 (n=61), 1.6 at Month 9 (n=61) and 2.6 at Month 12 (n=52).

During Epoch 2, the change from baseline TSQM-9 questionnaire score data were available for only 1 subject at Epoch 2-Year 1 and 2 subjects at Epoch 2-Year 2.

Health resource use:

The mean (SD) number of hospitalizations per subject was 1.6 (1.07) during Epoch 1 (n=32) and 1.0 during Epoch 2-Year 2 (n=3). There were no hospitalizations in the first year of Epoch 2. The mean (SD) number of days per subject in the hospital was 8.1 days (13.25) during Epoch 1 (n=32) and 4.3 days (1.15) during Epoch 2-Year 2 (n=3). The mean (SD) length of stay per hospitalization was 5.2 (7.35) days during Epoch 1 (n=53) and 4.3 (1.15) days during Epoch 2-Year 2 (n=3).

The mean (SD) number of acute care visits per subject was 1.5 (3.15) in Epoch 1 (n=204), 0.8 (1.25) in Epoch 2-Year 1 (n=11) and 1.2 (1.81) Epoch 2-Year 2 (n=10). The mean (SD) number of emergency room (ER) visits per subject was 0.3 (0.78) in Epoch 1 (n=217), 0.3 (0.65) in Epoch 2-Year 1 (n=11) and 0.3 (0.48) in Epoch 2-Year 2 (n=10). The mean (SD) number of missed days from school/work per subject was 3.3 (16.96) days in Epoch 1 (n=171), 9.4 (24.95) days in Epoch 2-Year 1 (n=7), and 14.2 (32.31) days in Epoch 2-Year 2 (n=6).

Discussion

This study was a prospective, non-interventional PASS aimed to acquire additional data on the long-term safety of HYQVIA, with regular assessment of antibodies against rHuPH20, and was a commitment to the Food and Drug Administration (FDA). The primary objective of the study was to collect and assess additional safety data, in particular the occurrence of long-term changes in incidence and severity of related AEs in subjects treated with HYQVIA. The secondary objective was to collect data on anti-rHuPH20 antibodies and other laboratory safety assessments, total IgG, further safety assessments that were obtained during the routine clinical management of the subjects, the prescribed treatment regimen and treatment administration, and HRQoL and HRU assessments.

The study was conducted in the US, and the study population consisted of adult subjects aged ≥ 16 years with PIDD who were prescribed or had initiated treatment with HYQVIA. The study comprised 2 Epochs: Epoch 1 started at enrolment of the subjects into the study, and the subjects were treated for approximately 1 year with HYQVIA, and Epoch 2 that included subjects who at any time during Epoch 1 tested positive for anti-rHuPH20 antibodies at a titer of ≥ 160. Subjects in Epoch 2 continued the study for an additional 2 years from the time of completion of Epoch 1.

A total of 253 subjects met eligibility criteria, were enrolled and analyzed in the study. Of the 253 subjects, 14 subjects had an anti-rHuPH20 antibody titer of ≥ 160 during Epoch 1. Thirteen subjects entered Epoch 2. The mean actual Ig dose administered was 369.9 mL in the study.

The most common HYQVIA treatment interval was every 4 weeks (54.4% of infusions), with a total observation time of 162.57 person-years. The subjects used a mean of 1.9 infusion sites. The mean maximum infusion rate was 248.1 mL/h. From the 253 enrolled subjects, 170 subjects reported at least one AE over the course of the study, with a total of 945 reported AEs. Of the total AEs, 286 AEs reported by 54 subjects were assessed as related to HYQVIA treatment. The most frequently reported related AEs according to the SOC were general disorders and administration site conditions, with headache, infusion site pain, infusion site swelling, and fatigue reported as the most frequent related AEs by PT. Only two related AEs qualified as SAEs, meningitis aseptic and deep vein thrombosis. No related AEs were fatal. The incidence proportion of the SAEs related to HYQVIA treatment during the entire study duration was 0.79%, the incidence rate was 0.007 per person-year, and the event rate per infusion was 0.001.

A total of 7.14% of the subjects (n=14) developed positive anti-rHuPH20 antibodies during the study. None of the subjects who developed positive anti-rHuPH20 antibodies during the study experienced any SAE related to HYQVIA treatment, neither before nor after the first positive anti-rHuPH20 antibody test. Among the subjects who developed positive anti-rHuPH20 antibodies, few had AEs which were non-serious and related to HYQVIA treatment: 1 subject before the first positive anti-rHuPH20 antibody test (incidence rate: 3.198, 95% CI: 1.462 to 6.070, 9 events) and 3 subjects after the first positive anti-rHuPH20 antibody test (incidence rate: 0.186, 95% CI: 0.075 to 0.383, 7 events). However, the incidence rates of non-serious AEs related to HYQVIA treatment were 3.198 before, and 0.186 after the first positive anti-rHuPH20 titer, respectively. No neutralizing antibodies were detected at any time during the study.

With respect to the HRQoL, the results of the present study suggest that HRQoL measurements remained generally stable among the participating subjects over the course of Epoch 1. The HRQoL results from Epoch 2 must be interpreted with care due to very low sample sizes.

As for HRU, low rates of events were observed for hospitalizations, acute care visits, and ER visits, with no hospitalizations in the first year of Epoch 2. Considering the long follow-up of the study and the large proportion of elderly subjects in the study population, the results can be considered highly favorable.

The study findings presented in this report support the conclusion that long-term repeated self-administration of HYQVIA is generally safe and well-tolerated in adult subjects with PIDD. The development of antibodies against rHuPH20 is rare. No neutralizing antibodies were detected in the study, consistent with previous observations. These long-term safety data show that HYQVIA can be administered safely at home. The results of this study confirm the known safety profile of HYQVIA and provide valuable insights into HYQVIA treatment and product administration in the US. While the study population is presumed to be representative of the broader population of subjects using HYQVIA, the results can only be generalized to populations with access to health care in countries where HYQVIA is authorized.

Marketing Authorisation Holder(s)

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EU: Baxalta Innovations GmbH*, Industriestrasse 67, A-1221 Vienna, Austria

* Note: Baxalta is now part of Takeda.

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