POST-AUTHORISATION SAFETY STUDY (PASS)

Annual Progress Report

STUDY OVERVIEW

Title	Non-interventional Post-Authorisation Safety Study of Burosumab in the Treatment of Children with X-linked Hypophosphataemia (XLH)
Version of the progress report	Version 2.0
Date of last version of the progress report	11 Oct 2019
European Union electronic Register of Post-Authorisation Studies (EU PAS)/ European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) register number	EUPAS32190
Active substance	Active substance: burosumab - recombinant human IgG1 monoclonal antibody to fibroblast growth factor 23 ATC code: M05BX05: Drug for the treatment for bone diseases, other drugs affecting bone structure and mineralization
Medicinal product	Invented name: Crysvita Pharmaceutical form and strength: 10, 20 and 30 mg/mL solution for injection in vials

This study was conducted in accordance with all relevant regulatory requirements, including, where applicable, the Declaration of Helsinki (and its amendments), the guideline on good pharmacovigilance practices (GVP) Module VIII – post-authorisation safety studies, and the guidelines for good pharmacoepidemiology practice (GPP) (ISPE).

Product reference	Not Available
Procedure number	EMEA/H/C/004275
Joint PASS	No
Research question and objectives	**Primary objectives:** 1. To evaluate the frequency and severity of safety outcomes in paediatric patients with XLH and radiographic evidence of bone disease who are aged 1 year of age and older and adolescents with growing skeletons, treated with burosumab, including but not limited to: death, hospitalizations, cardiovascular disease, cancer [all sites], hyperphosphataemia and its complications, ectopic mineralization and increased parathyroid hormone levels 2. To prospectively evaluate the frequency and outcomes of pregnancies in female patients treated with burosumab 3. To prospectively evaluate the frequency and severity of safety outcomes in patients with mild to moderate chronic kidney disease at baseline treated with burosumab **Secondary objective:** To perform a retrospective cohort study using data from the registry to compare the safety outcomes of interest in patients exposed to burosumab to those in patients receiving alternative treatments for XLH
Author	IQVIA on behalf of the Marketing Authorisation Holder

MARKETING AUTHORISATION HOLDER(S)

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PASS PROGRESS INFORMATION

<table>
<tr><td>Protocol version and date</td><td>Version 1.0; 15-August-2018
(Sub-study to the parent XLH Registry Protocol-Version 3.0; 15-February-2019)</td></tr>
<tr><td>Approval date/s (approved by Committee for Medicinal Products for Human Use [CHMP])</td><td>13-December-2018</td></tr>
<tr><td>Study initiated (FPI)</td><td>24-APR-2019</td></tr>
<tr><td>Data cut-off date</td><td>18-August-2020</td></tr>
<tr><td>Country(-ies) of Study</td><td>Planned: EU countries, Norway and UK
Currently enrolling: UK, Sweden, France, Italy, Norway, Spain, The Netherlands,</td></tr>
<tr><td>Patient Disposition</td><td>204 patients enrolled as of 18-August-2020
<table><tr><th></th><th>UK</th><th>Sweden</th><th>France</th><th>Italy</th><th>Norway</th><th>Spain</th><th>NL</th><th>Total</th></tr><tr><td>PASS</td><td>80</td><td>6</td><td>81</td><td>10</td><td>7</td><td>7</td><td>13</td><td>204</td></tr><tr><td>PASS under Burosumab</td><td>51</td><td>1</td><td>43</td><td>3</td><td>2</td><td>3</td><td>8</td><td>111</td></tr></table></td></tr>
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	The overall patient disposition (till date) can be found in the End-of-text SAP Table 1.1.1
Recruitment	Active, recruiting
Adverse event (AE)	Table from SAP, End-of-text Table 1.28.1 provides the summary overview of ALL AEs by Age Group and treatment for XLH (Crysvita and other treatment) Till the cut-off date (i.e. 18-August-2020): • None of the AEs for the patients were of serious category • There were 9 patients with AE out of whom 4 patients (039002-007, 039007-001, 046004-001, 047001-006) recovered from the AEs and for the rest 5 patients (see below), AEs were ongoing at the cut-off date • Out of the 5 patients with ongoing AEs, 2 patients (033002-001 and 033005-001) had 4 AEs which were 'Possibly related' to Burosumab). None of the patients' burosumab dose was altered. o Patient 033002-001- had hyperthyroidism (mild AE) o Patient 033005-001- had abdominal pain, fatigue and fluctuating pain at ankle level (all moderate AEs)
Protocol deviation/s	There were 10 protocol deviations in the PASS, till the cut-off date (i.e. 18-August-2020): • Most of the deviations were related to the informed consent and related procedures and were of 'major' severity • Out of these 2 deviations were of 'critical' severity: o Patient 034005-003 - Initial ICF missing. Reconsent missing. o Patient 034005-004- Initial ICF missing.

Problems/ Bottlenecks encountered	**Triggers for PASS eligibility:** • Registry amended protocol approved, protocol v3.0 dated 15-February-2019 • Sites to receive adequate training on protocol v3.0 for the Registry and the PASS • Patients to sign the last informed consent form (ICF) (re-consent for already enrolled patients) last ICFs v3.0 04-February-2019 for Parents and Adults and v2.0 10-January-2019 for minors • Burosumab to be available at country level. Not all countries have burosumab available – burosumab launch dates to be followed accurately and any Early Access Program to be known at site level • Only children and adolescents are now in the PASS whatever their treatment (Burosumab AND conventional Therapy), not the adult population **Regarding Adverse Event (AE) reporting:** Sites should actively solicit for any AE (including SAE and AESI) since the last interaction with the patient by means of an open question. During every interaction with patients, the EDC system will prompt sites to enter data on any AEs solicited and recorded during interactions with the patient. Sites are required to report all AEs in the EDC regardless of treatment or relatedness to the treatment. For patients not participating in the PASS, only unsolicited AEs reported by patients are recorded in EDC. **Bottlenecks:** • As of 11th March 2020, the XLH Registry and the PASS were impacted by the COVID-19 Pandemic:

	▪ All study activities were forced to slow down as site selection, regulatory submission, contract negotiation, site initiation, patient enrollment, site monitoring, data cleaning and analysis timelines were impacted by the Pandemic restrictions. ▪ This resulted in the PASS 1st Interim Analysis being delayed by 6months. The iCSR is now expected in October 2021 instead of April 2021. ▪ COVID-19 may have prevented sites from reporting safety events in a timely fashion (e.g. SAEs should be reported within 24 hours of becoming aware). This can result in Protocol Deviations. This may also contribute to an increase in missing data on safety events due to limited contact with patients as a result of local restrictions. ▪ Patients treated with burosumab were impacted by changes in routine practice due to the pandemic. Patients were able to visit sites to have their injection administered however a full routine assessment may not have been possible, therefore it would not be guaranteed that adverse event reporting would be assessed. Where patients were not able to visit the site directly to receive their injection, home visits were utilized, or parents were trained to administer the injection to their child. • For the patients who were initially enrolled into the XLH Registry in a participating country where burosumab is available (UK, France, Italy, Sweden) reconsenting is required to allow the patient to participate in the PASS and PASS participation was not explicitly included in the original informed consent form (ICF) for the study. • The re-consenting process takes considerable time and may need some months to have this re-consent in place. The option of remote re-consenting has been proposed, however many sites wanted to have a face to face visit with their patients to re-consent them. With the COVID-19 impact, sites have been encouraged to use remote consenting as much as possible. • Some physicians have declined to be part of the PASS. All sites are invited and encouraged to be part of the PASS.

Planned interim/ final Analysis report	• First interim report of study results to be submitted after 50 patients under burosumab have achieved at least 6 months of time in the PASS. • Milestone met on 28-February 2020, but due to the impact of the Covid-19 pandemic, analysis has been delayed by 6 months to allow sites to review their patients and record the reported AEs appropriately. • Interim Clinical Study Report, prior to COVID-19 impact, was expected in Apr 2021. With COVID-19 impact, the first interim analysis has been delayed by 6 months and is expected in October 2021. • Second interim report of study results to be submitted after 5 years, i.e. December 2023 • December 2028 is anticipated for the final analysis

APPENDIX: END-OF- TEXT TABLES

Table 1.1.1: Patient Disposition by XLH Treatment, Gender and Country (All Screened Patients)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
ALL COUNTRIES					
OVERALL					
Patients screened, n	179	80	99	194	373
Patients included in SAF[a], n (%)	170 (95.0)	77 (96.3)	93 (93.9)	80 (41.2)	250 (67.0)
Follow-up time (years)[b]					

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
n	170	77	93	80	250
Mean (SD)	1.3 (0.76)	1.3 (0.71)	1.4 (0.81)	1.3 (0.68)	1.3 (0.74)
Median	1.2	1.3	1.2	1.3	1.3
Q1 : Q3	0.7:2.0	0.7:2.0	0.7:2.1	0.7:1.9	0.7:2.0
Min : Max	0:3	0:2	0:3	0:3	0:3
Missing	0	0	0	0	0
Study ongoing[c], n (%)	168 (98.8)	76 (98.7)	92 (98.9)	80 (100.0)	248 (99.2)
Study discontinued[c], n (%)	2 (1.2)	1 (1.3)	1 (1.1)	0 (0.0)	2 (0.8)
Reason[d], n (%)					
n	2	1	1	0	2
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	2 (100.0)	1 (100.0)	1 (100.0)	0 (0.0)	2 (100.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	170 (100.0)	77 (100.0)	93 (100.0)	0 (0.0)	170 (68.0)
Phosphate	58 (34.1)	0 (0.0)	58 (62.4)	76 (95.0)	134 (53.6)
Active Vitamin D	60 (35.3)	0 (0.0)	60 (64.5)	66 (82.5)	126 (50.4)
Growth hormone	11 (6.5)	0 (0.0)	11 (11.8)	5 (6.3)	16 (6.4)
Other	40 (23.5)	0 (0.0)	40 (43.0)	36 (45.0)	76 (30.4)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
MALE					
Patients screened, n	76	37	39	61	137
Patients included in SAF[a], n (%)	72 (94.7)	35 (94.6)	37 (94.9)	29 (47.5)	101 (73.7)
Follow-up time (years)[b]					
n	72	35	37	29	101
Mean (SD)	1.2 (0.72)	1.2 (0.72)	1.2 (0.72)	1.4 (0.68)	1.3 (0.71)
Median	1.0	1.1	1.0	1.6	1.2
Q1 : Q3	0.7:2.0	0.5:2.0	0.7:1.9	0.9:1.9	0.7:1.9
Min : Max	0:3	0:2	0:3	0:3	0:3
Missing	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Study ongoing[c], n (%)	71 (98.6)	35 (100.0)	36 (97.3)	29 (100.0)	100 (99.0)
Study discontinued[c], n (%)	1 (1.4)	0 (0.0)	1 (2.7)	0 (0.0)	1 (1.0)
Reason[d], n (%)					
n	1	0	1	0	1
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	1 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	1 (100.0)
Missing	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
XLH treatments[c], n (%)					
Crysvita	72 (100.0)	35 (100.0)	37 (100.0)	0 (0.0)	72 (71.3)
Phosphate	24 (33.3)	0 (0.0)	24 (64.9)	27 (93.1)	51 (50.5)
Active Vitamin D	22 (30.6)	0 (0.0)	22 (59.5)	22 (75.9)	44 (43.6)
Growth hormone	4 (5.6)	0 (0.0)	4 (10.8)	2 (6.9)	6 (5.9)
Other	14 (19.4)	0 (0.0)	14 (37.8)	12 (41.4)	26 (25.7)
FEMALE					
Patients screened, n	103	43	60	133	236
Patients included in SAF[a], n (%)	98 (95.1)	42 (97.7)	56 (93.3)	51 (38.3)	149 (63.1)
Follow-up time (years)[b]					

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
n	98	42	56	51	149
Mean (SD)	1.4 (0.79)	1.4 (0.70)	1.5 (0.86)	1.3 (0.68)	1.4 (0.76)
Median	1.6	1.5	1.7	1.3	1.3
Q1 : Q3	0.7:2.0	0.7:2.0	0.7:2.2	0.7:1.8	0.7:2.0
Min : Max	0:3	0:2	0:3	0:3	0:3
Missing	0	0	0	0	0
Study ongoing[c], n (%)	97 (99.0)	41 (97.6)	56 (100.0)	51 (100.0)	148 (99.3)
Study discontinued[c], n (%)	1 (1.0)	1 (2.4)	0 (0.0)	0 (0.0)	1 (0.7)
Reason[d], n (%)					
n	1	1	0	0	1
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	1 (100.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	98 (100.0)	42 (100.0)	56 (100.0)	0 (0.0)	98 (65.8)
Phosphate	34 (34.7)	0 (0.0)	34 (60.7)	49 (96.1)	83 (55.7)
Active Vitamin D	38 (38.8)	0 (0.0)	38 (67.9)	44 (86.3)	82 (55.0)
Growth hormone	7 (7.1)	0 (0.0)	7 (12.5)	3 (5.9)	10 (6.7)
Other	26 (26.5)	0 (0.0)	26 (46.4)	24 (47.1)	50 (33.6)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
BELGIUM					
OVERALL					
Patients screened, n	0	0	0	1	1
Patients included in SAF[a], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
Follow-up time (years)[b]					
n	0	0	0	1	1
Mean (SD)	-	-	-	0.2 (-)	0.2 (-)
Median	-	-	-	0.2	0.2
Q1 : Q3	-	-	-	0.2:0.2	0.2:0.2
Min : Max	-	-	-	0:0	0:0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Missing	0	0	0	0	0
Study ongoing[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
MALE					
Patients screened, n	0	0	0	0	0
Patients included in SAF[a], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Follow-up time (years)[b]					
n	0	0	0	0	0
Mean (SD)	-	-	-	-	-
Median	-	-	-	-	-
Q1 : Q3	-	-	-	-	-
Min : Max	-	-	-	-	-
Missing	0	0	0	0	0
Study ongoing[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
FEMALE					
Patients screened, n	0	0	0	1	1
Patients included in SAF[a], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
Follow-up time (years)[b]					
n	0	0	0	1	1
Mean (SD)	-	-	-	0.2 (-)	0.2 (-)
Median	-	-	-	0.2	0.2
Q1 : Q3	-	-	-	0.2:0.2	0.2:0.2
Min : Max	-	-	-	0:0	0:0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Missing	0	0	0	0	0
Study ongoing[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
DENMARK					
OVERALL					
Patients screened, n	0	0	0	9	9

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Patients included in SAF[a], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.1)	1 (11.1)
Follow-up time (years)[b]					
n	0	0	0	1	1
Mean (SD)	-	-	-	2.5 (-)	2.5 (-)
Median	-	-	-	2.5	2.5
Q1 : Q3	-	-	-	2.5:2.5	2.5:2.5
Min : Max	-	-	-	2:2	2:2
Missing	0	0	0	0	0
Study ongoing[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
MALE					
Patients screened, n	0	0	0	4	4
Patients included in SAF[a], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (25.0)
Follow-up time (years)[b]					
n	0	0	0	1	1
Mean (SD)	-	-	-	2.5 (-)	2.5 (-)
Median	-	-	-	2.5	2.5

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Q1 : Q3	-	-	-	2.5:2.5	2.5:2.5
Min : Max	-	-	-	2:2	2:2
Missing	0	0	0	0	0
Study ongoing[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
FEMALE					
Patients screened, n	0	0	0	5	5

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Patients included in SAF[a], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Follow-up time (years)[b]					
n	0	0	0	0	0
Mean (SD)	-	-	-	-	-
Median	-	-	-	-	-
Q1 : Q3	-	-	-	-	-
Min : Max	-	-	-	-	-
Missing	0	0	0	0	0
Study ongoing[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
FRANCE					
OVERALL					
Patients screened, n	46	6	40	52	98
Patients included in SAF[a], n (%)	44 (95.7)	6 (100.0)	38 (95.0)	25 (48.1)	69 (70.4)
Follow-up time (years)[b]					
n	44	6	38	25	69

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Mean (SD)	0.6 (0.29)	0.9 (0.38)	0.6 (0.25)	0.9 (0.31)	0.7 (0.31)
Median	0.7	0.8	0.7	0.8	0.7
Q1 : Q3	0.4:0.8	0.7:1.3	0.4:0.8	0.7:1.1	0.5:0.8
Min : Max	0:1	0:1	0:1	0:1	0:1
Missing	0	0	0	0	0
Study ongoing[c], n (%)	44 (100.0)	6 (100.0)	38 (100.0)	25 (100.0)	69 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	44 (100.0)	6 (100.0)	38 (100.0)	0 (0.0)	44 (63.8)
Phosphate	12 (27.3)	0 (0.0)	12 (31.6)	24 (96.0)	36 (52.2)
Active Vitamin D	12 (27.3)	0 (0.0)	12 (31.6)	25 (100.0)	37 (53.6)
Growth hormone	10 (22.7)	0 (0.0)	10 (26.3)	3 (12.0)	13 (18.8)
Other	35 (79.5)	0 (0.0)	35 (92.1)	23 (92.0)	58 (84.1)
MALE					

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Patients screened, n	21	4	17	10	31
Patients included in SAF[a], n (%)	20 (95.2)	4 (100.0)	16 (94.1)	6 (60.0)	26 (83.9)
Follow-up time (years)[b]					
n	20	4	16	6	26
Mean (SD)	0.7 (0.30)	1.0 (0.48)	0.6 (0.21)	0.8 (0.15)	0.7 (0.28)
Median	0.7	1.0	0.7	0.8	0.7
Q1 : Q3	0.5:0.8	0.6:1.3	0.5:0.8	0.7:1.0	0.5:0.8
Min : Max	0:1	0:1	0:1	1:1	0:1
Missing	0	0	0	0	0
Study ongoing[c], n (%)	20 (100.0)	4 (100.0)	16 (100.0)	6 (100.0)	26 (100.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Crysvita	20 (100.0)	4 (100.0)	16 (100.0)	0 (0.0)	20 (76.9)
Phosphate	5 (25.0)	0 (0.0)	5 (31.3)	6 (100.0)	11 (42.3)
Active Vitamin D	5 (25.0)	0 (0.0)	5 (31.3)	6 (100.0)	11 (42.3)
Growth hormone	4 (20.0)	0 (0.0)	4 (25.0)	1 (16.7)	5 (19.2)
Other	13 (65.0)	0 (0.0)	13 (81.3)	6 (100.0)	19 (73.1)
FEMALE					
Patients screened, n	25	2	23	42	67
Patients included in SAF[a], n (%)	24 (96.0)	2 (100.0)	22 (95.7)	19 (45.2)	43 (64.2)
Follow-up time (years)[b]					
n	24	2	22	19	43

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Mean (SD)	0.6 (0.28)	0.8 (0.09)	0.6 (0.28)	0.9 (0.35)	0.7 (0.34)
Median	0.7	0.8	0.6	0.8	0.7
Q1 : Q3	0.3:0.8	0.7:0.9	0.2:0.8	0.6:1.2	0.5:0.9
Min : Max	0:1	1:1	0:1	0:1	0:1
Missing	0	0	0	0	0
Study ongoing[c], n (%)	24 (100.0)	2 (100.0)	22 (100.0)	19 (100.0)	43 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	24 (100.0)	2 (100.0)	22 (100.0)	0 (0.0)	24 (55.8)
Phosphate	7 (29.2)	0 (0.0)	7 (31.8)	18 (94.7)	25 (58.1)
Active Vitamin D	7 (29.2)	0 (0.0)	7 (31.8)	19 (100.0)	26 (60.5)
Growth hormone	6 (25.0)	0 (0.0)	6 (27.3)	2 (10.5)	8 (18.6)
Other	22 (91.7)	0 (0.0)	22 (100.0)	17 (89.5)	39 (90.7)
GERMANY					

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
OVERALL					
Patients screened, n	32	17	15	7	39
Patients included in SAF[a], n (%)	32 (100.0)	17 (100.0)	15 (100.0)	6 (85.7)	38 (97.4)
Follow-up time (years)[b]					
n	32	17	15	6	38
Mean (SD)	1.4 (0.67)	1.1 (0.59)	1.8 (0.59)	2.3 (0.44)	1.6 (0.71)
Median	1.5	1.1	1.7	2.3	1.7
Q1 : Q3	1.1:1.8	0.7:1.5	1.4:2.5	1.8:2.6	1.1:1.8
Min : Max	0:3	0:2	0:3	2:3	0:3
Missing	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Study ongoing[c], n (%)	31 (96.9)	16 (94.1)	15 (100.0)	6 (100.0)	37 (97.4)
Study discontinued[c], n (%)	1 (3.1)	1 (5.9)	0 (0.0)	0 (0.0)	1 (2.6)
Reason[d], n (%)					
n	1	1	0	0	1
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	1 (100.0)
Missing	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
XLH treatments[c], n (%)					
Crysvita	32 (100.0)	17 (100.0)	15 (100.0)	0 (0.0)	32 (84.2)
Phosphate	8 (25.0)	0 (0.0)	8 (53.3)	6 (100.0)	14 (36.8)
Active Vitamin D	15 (46.9)	0 (0.0)	15 (100.0)	5 (83.3)	20 (52.6)
Growth hormone	1 (3.1)	0 (0.0)	1 (6.7)	0 (0.0)	1 (2.6)
Other	0 (0.0)	0 (0.0)	0 (0.0)	2 (33.3)	2 (5.3)
MALE					
Patients screened, n	12	6	6	4	16
Patients included in SAF[a], n (%)	12 (100.0)	6 (100.0)	6 (100.0)	4 (100.0)	16 (100.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Follow-up time (years)[b]					
n	12	6	6	4	16
Mean (SD)	1.4 (0.66)	1.0 (0.48)	1.9 (0.52)	2.1 (0.38)	1.6 (0.68)
Median	1.4	1.1	1.7	2.1	1.6
Q1 : Q3	1.1:1.7	0.8:1.2	1.4:2.5	1.8:2.4	1.2:2.1
Min : Max	0:3	0:1	1:3	2:3	0:3
Missing	0	0	0	0	0
Study ongoing[c], n (%)	12 (100.0)	6 (100.0)	6 (100.0)	4 (100.0)	16 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	12 (100.0)	6 (100.0)	6 (100.0)	0 (0.0)	12 (75.0)
Phosphate	4 (33.3)	0 (0.0)	4 (66.7)	4 (100.0)	8 (50.0)
Active Vitamin D	6 (50.0)	0 (0.0)	6 (100.0)	4 (100.0)	10 (62.5)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (6.3)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
FEMALE					
Patients screened, n	20	11	9	3	23
Patients included in SAF[a], n (%)	20 (100.0)	11 (100.0)	9 (100.0)	2 (66.7)	22 (95.7)
Follow-up time (years)[b]					
n	20	11	9	2	22
Mean (SD)	1.4 (0.69)	1.2 (0.66)	1.7 (0.65)	2.6 (0.49)	1.5 (0.75)
Median	1.6	1.1	1.7	2.6	1.7
Q1 : Q3	0.9:1.8	0.7:1.7	1.7:1.8	2.3:3.0	1.1:1.8
Min : Max	0:3	0:2	0:3	2:3	0:3
Missing	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Study ongoing[c], n (%)	19 (95.0)	10 (90.9)	9 (100.0)	2 (100.0)	21 (95.5)
Study discontinued[c], n (%)	1 (5.0)	1 (9.1)	0 (0.0)	0 (0.0)	1 (4.5)
Reason[d], n (%)					
n	1	1	0	0	1
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	1 (100.0)
Missing	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
XLH treatments[c], n (%)					
Crysvita	20 (100.0)	11 (100.0)	9 (100.0)	0 (0.0)	20 (90.9)
Phosphate	4 (20.0)	0 (0.0)	4 (44.4)	2 (100.0)	6 (27.3)
Active Vitamin D	9 (45.0)	0 (0.0)	9 (100.0)	1 (50.0)	10 (45.5)
Growth hormone	1 (5.0)	0 (0.0)	1 (11.1)	0 (0.0)	1 (4.5)
Other	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	1 (4.5)
IRELAND					
OVERALL					
Patients screened, n	0	0	0	1	1

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Patients included in SAF[a], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
Follow-up time (years)[b]					
n	0	0	0	1	1
Mean (SD)	-	-	-	0.3 (-)	0.3 (-)
Median	-	-	-	0.3	0.3
Q1 : Q3	-	-	-	0.3:0.3	0.3:0.3
Min : Max	-	-	-	0:0	0:0
Missing	0	0	0	0	0
Study ongoing[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
MALE					
Patients screened, n	0	0	0	0	0
Patients included in SAF[a], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Follow-up time (years)[b]					
n	0	0	0	0	0
Mean (SD)	-	-	-	-	-
Median	-	-	-	-	-
Q1 : Q3	-	-	-	-	-

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Min : Max	-	-	-	-	-
Missing	0	0	0	0	0
Study ongoing[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
FEMALE					
Patients screened, n	0	0	0	1	1

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Patients included in SAF[a], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
Follow-up time (years)[b]					
n	0	0	0	1	1
Mean (SD)	-	-	-	0.3 (-)	0.3 (-)
Median	-	-	-	0.3	0.3
Q1 : Q3	-	-	-	0.3:0.3	0.3:0.3
Min : Max	-	-	-	0:0	0:0
Missing	0	0	0	0	0
Study ongoing[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
ITALY					
OVERALL					
Patients screened, n	4	4	0	18	22
Patients included in SAF[a], n (%)	3 (75.0)	3 (75.0)	0 (0.0)	13 (72.2)	16 (72.7)
Follow-up time (years)[b]					
n	3	3	0	13	16
Mean (SD)	1.2 (0.74)	1.2 (0.74)	-	1.5 (0.61)	1.4 (0.62)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Median	1.6	1.6	-	1.7	1.6
Q1 : Q3	0.3:1.6	0.3:1.6	-	1.6:1.8	1.5:1.8
Min : Max	0:2	0:2	-	0:2	0:2
Missing	0	0	0	0	0
Study ongoing[c], n (%)	3 (100.0)	3 (100.0)	0 (0.0)	13 (100.0)	16 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	3 (100.0)	3 (100.0)	0 (0.0)	0 (0.0)	3 (18.8)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	13 (100.0)	13 (81.3)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	11 (84.6)	11 (68.8)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	3 (23.1)	3 (18.8)
MALE					

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Patients screened, n	4	4	0	6	10
Patients included in SAF[a], n (%)	3 (75.0)	3 (75.0)	0 (0.0)	5 (83.3)	8 (80.0)
Follow-up time (years)[b]					
n	3	3	0	5	8
Mean (SD)	1.2 (0.74)	1.2 (0.74)	-	1.3 (0.68)	1.3 (0.65)
Median	1.6	1.6	-	1.6	1.6
Q1 : Q3	0.3:1.6	0.3:1.6	-	1.4:1.7	0.9:1.7
Min : Max	0:2	0:2	-	0:2	0:2
Missing	0	0	0	0	0
Study ongoing[c], n (%)	3 (100.0)	3 (100.0)	0 (0.0)	5 (100.0)	8 (100.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	3 (100.0)	3 (100.0)	0 (0.0)	0 (0.0)	3 (37.5)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	5 (100.0)	5 (62.5)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	4 (80.0)	4 (50.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	1 (20.0)	1 (12.5)
FEMALE					
Patients screened, n	0	0	0	12	12
Patients included in SAF[a], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	8 (66.7)	8 (66.7)
Follow-up time (years)[b]					
n	0	0	0	8	8
Mean (SD)	-	-	-	1.6 (0.58)	1.6 (0.58)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Median	-	-	-	1.7	1.7
Q1 : Q3	-	-	-	1.6:2.0	1.6:2.0
Min : Max	-	-	-	0:2	0:2
Missing	0	0	0	0	0
Study ongoing[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	8 (100.0)	8 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	8 (100.0)	8 (100.0)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	7 (87.5)	7 (87.5)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	2 (25.0)	2 (25.0)
NETHERLANDS					

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
OVERALL					
Patients screened, n	8	7	1	2	10
Patients included in SAF[a], n (%)	8 (100.0)	7 (100.0)	1 (100.0)	2 (100.0)	10 (100.0)
Follow-up time (years)[b]					
n	8	7	1	2	10
Mean (SD)	0.4 (0.07)	0.4 (0.07)	0.5 (-)	0.5 (0.01)	0.4 (0.07)
Median	0.4	0.4	0.5	0.5	0.4
Q1 : Q3	0.3:0.5	0.3:0.5	0.5:0.5	0.4:0.5	0.3:0.5
Min : Max	0:0	0:0	0:0	0:0	0:0
Missing	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Study ongoing[c], n (%)	8 (100.0)	7 (100.0)	1 (100.0)	2 (100.0)	10 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
XLH treatments[c], n (%)					
Crysvita	8 (100.0)	7 (100.0)	1 (100.0)	0 (0.0)	8 (80.0)
Phosphate	1 (12.5)	0 (0.0)	1 (100.0)	2 (100.0)	3 (30.0)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	2 (20.0)
MALE					
Patients screened, n	6	5	1	2	8
Patients included in SAF[a], n (%)	6 (100.0)	5 (100.0)	1 (100.0)	2 (100.0)	8 (100.0)
Follow-up time (years)[b]					

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
n	6	5	1	2	8
Mean (SD)	0.4 (0.07)	0.4 (0.06)	0.5 (-)	0.5 (0.01)	0.4 (0.07)
Median	0.4	0.3	0.5	0.5	0.4
Q1 : Q3	0.3:0.5	0.3:0.4	0.5:0.5	0.4:0.5	0.3:0.5
Min : Max	0:0	0:0	0:0	0:0	0:0
Missing	0	0	0	0	0
Study ongoing[c], n (%)	6 (100.0)	5 (100.0)	1 (100.0)	2 (100.0)	8 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	6 (100.0)	5 (100.0)	1 (100.0)	0 (0.0)	6 (75.0)
Phosphate	1 (16.7)	0 (0.0)	1 (100.0)	2 (100.0)	3 (37.5)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	2 (25.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
FEMALE					
Patients screened, n	2	2	0	0	2
Patients included in SAF[a], n (%)	2 (100.0)	2 (100.0)	0 (0.0)	0 (0.0)	2 (100.0)
Follow-up time (years)[b]					
n	2	2	0	0	2
Mean (SD)	0.5 (0.00)	0.5 (0.00)	-	-	0.5 (0.00)
Median	0.5	0.5	-	-	0.5
Q1 : Q3	0.5:0.5	0.5:0.5	-	-	0.5:0.5
Min : Max	0:0	0:0	-	-	0:0
Missing	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Study ongoing[c], n (%)	2 (100.0)	2 (100.0)	0 (0.0)	0 (0.0)	2 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
XLH treatments[c], n (%)					
Crysvita	2 (100.0)	2 (100.0)	0 (0.0)	0 (0.0)	2 (100.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
NORWAY					
OVERALL					
Patients screened, n	2	1	1	2	4
Patients included in SAF[a], n (%)	2 (100.0)	1 (100.0)	1 (100.0)	2 (100.0)	4 (100.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Follow-up time (years)[b]					
n	2	1	1	2	4
Mean (SD)	0.5 (0.26)	0.3 (-)	0.7 (-)	0.5 (0.24)	0.5 (0.21)
Median	0.5	0.3	0.7	0.5	0.5
Q1 : Q3	0.3:0.7	0.3:0.3	0.7:0.7	0.4:0.7	0.4:0.7
Min : Max	0:1	0:0	1:1	0:1	0:1
Missing	0	0	0	0	0
Study ongoing[c], n (%)	2 (100.0)	1 (100.0)	1 (100.0)	2 (100.0)	4 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	2 (100.0)	1 (100.0)	1 (100.0)	0 (0.0)	2 (50.0)
Phosphate	1 (50.0)	0 (0.0)	1 (100.0)	2 (100.0)	3 (75.0)
Active Vitamin D	1 (50.0)	0 (0.0)	1 (100.0)	1 (50.0)	2 (50.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
MALE					
Patients screened, n	1	1	0	0	1
Patients included in SAF[a], n (%)	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	1 (100.0)
Follow-up time (years)[b]					
n	1	1	0	0	1
Mean (SD)	0.3 (-)	0.3 (-)	-	-	0.3 (-)
Median	0.3	0.3	-	-	0.3
Q1 : Q3	0.3:0.3	0.3:0.3	-	-	0.3:0.3
Min : Max	0:0	0:0	-	-	0:0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Missing	0	0	0	0	0
Study ongoing[c], n (%)	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	1 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	1 (100.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
FEMALE					
Patients screened, n	1	0	1	2	3
Patients included in SAF[a], n (%)	1 (100.0)	0 (0.0)	1 (100.0)	2 (100.0)	3 (100.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Follow-up time (years)[b]					
n	1	0	1	2	3
Mean (SD)	0.7 (-)	-	0.7 (-)	0.5 (0.24)	0.6 (0.20)
Median	0.7	-	0.7	0.5	0.7
Q1 : Q3	0.7:0.7	-	0.7:0.7	0.4:0.7	0.4:0.7
Min : Max	1:1	-	1:1	0:1	0:1
Missing	0	0	0	0	0
Study ongoing[c], n (%)	1 (100.0)	0 (0.0)	1 (100.0)	2 (100.0)	3 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	1 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	1 (33.3)
Phosphate	1 (100.0)	0 (0.0)	1 (100.0)	2 (100.0)	3 (100.0)
Active Vitamin D	1 (100.0)	0 (0.0)	1 (100.0)	1 (50.0)	2 (66.7)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
SPAIN					
OVERALL					
Patients screened, n	3	3	0	14	17
Patients included in SAF[a], n (%)	3 (100.0)	3 (100.0)	0 (0.0)	12 (85.7)	15 (88.2)
Follow-up time (years)[b]					
n	3	3	0	12	15
Mean (SD)	1.1 (0.54)	1.1 (0.54)	-	1.4 (0.65)	1.4 (0.62)
Median	1.3	1.3	-	1.8	1.7

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Q1 : Q3	0.5:1.6	0.5:1.6	-	1.2:1.9	0.8:1.8
Min : Max	1:2	1:2	-	0:2	0:2
Missing	0	0	0	0	0
Study ongoing[c], n (%)	3 (100.0)	3 (100.0)	0 (0.0)	12 (100.0)	15 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	3 (100.0)	3 (100.0)	0 (0.0)	0 (0.0)	3 (20.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	12 (100.0)	12 (80.0)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	7 (58.3)	7 (46.7)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	2 (16.7)	2 (13.3)
Other	0 (0.0)	0 (0.0)	0 (0.0)	3 (25.0)	3 (20.0)
MALE					
Patients screened, n	1	1	0	5	6

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Patients included in SAF[a], n (%)	1 (100.0)	1 (100.0)	0 (0.0)	4 (80.0)	5 (83.3)
Follow-up time (years)[b]					
n	1	1	0	4	5
Mean (SD)	1.6 (-)	1.6 (-)	-	1.5 (0.80)	1.5 (0.69)
Median	1.6	1.6	-	1.8	1.8
Q1 : Q3	1.6:1.6	1.6:1.6	-	1.0:1.9	1.6:1.9
Min : Max	2:2	2:2	-	0:2	0:2
Missing	0	0	0	0	0
Study ongoing[c], n (%)	1 (100.0)	1 (100.0)	0 (0.0)	4 (100.0)	5 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	1 (20.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	4 (100.0)	4 (80.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	2 (50.0)	2 (40.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (20.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
FEMALE					
Patients screened, n	2	2	0	9	11
Patients included in SAF[a], n (%)	2 (100.0)	2 (100.0)	0 (0.0)	8 (88.9)	10 (90.9)
Follow-up time (years)[b]					
n	2	2	0	8	10
Mean (SD)	0.9 (0.51)	0.9 (0.51)	-	1.4 (0.63)	1.3 (0.62)
Median	0.9	0.9	-	1.7	1.6

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Q1 : Q3	0.5:1.3	0.5:1.3	-	1.2:1.8	0.8:1.8
Min : Max	1:1	1:1	-	0:2	0:2
Missing	0	0	0	0	0
Study ongoing[c], n (%)	2 (100.0)	2 (100.0)	0 (0.0)	8 (100.0)	10 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	2 (100.0)	2 (100.0)	0 (0.0)	0 (0.0)	2 (20.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	8 (100.0)	8 (80.0)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	5 (62.5)	5 (50.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	1 (10.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	3 (37.5)	3 (30.0)
SWEDEN					
OVERALL					

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Patients screened, n	1	0	1	27	28
Patients included in SAF[a], n (%)	1 (100.0)	0 (0.0)	1 (100.0)	1 (3.7)	2 (7.1)
Follow-up time (years)[b]					
n	1	0	1	1	2
Mean (SD)	1.2 (-)	-	1.2 (-)	1.3 (-)	1.3 (0.13)
Median	1.2	-	1.2	1.3	1.3
Q1 : Q3	1.2:1.2	-	1.2:1.2	1.3:1.3	1.2:1.3
Min : Max	1:1	-	1:1	1:1	1:1
Missing	0	0	0	0	0
Study ongoing[c], n (%)	1 (100.0)	0 (0.0)	1 (100.0)	1 (100.0)	2 (100.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Crysvita	1 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	1 (50.0)
Phosphate	1 (100.0)	0 (0.0)	1 (100.0)	1 (100.0)	2 (100.0)
Active Vitamin D	1 (100.0)	0 (0.0)	1 (100.0)	1 (100.0)	2 (100.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
MALE					
Patients screened, n	0	0	0	10	10
Patients included in SAF[a], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Follow-up time (years)[b]					
n	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Mean (SD)	-	-	-	-	-
Median	-	-	-	-	-
Q1 : Q3	-	-	-	-	-
Min : Max	-	-	-	-	-
Missing	0	0	0	0	0
Study ongoing[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Phosphate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Active Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
FEMALE					

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Patients screened, n	1	0	1	17	18
Patients included in SAF[a], n (%)	1 (100.0)	0 (0.0)	1 (100.0)	1 (5.9)	2 (11.1)
Follow-up time (years)[b]					
n	1	0	1	1	2
Mean (SD)	1.2 (-)	-	1.2 (-)	1.3 (-)	1.3 (0.13)
Median	1.2	-	1.2	1.3	1.3
Q1 : Q3	1.2:1.2	-	1.2:1.2	1.3:1.3	1.2:1.3
Min : Max	1:1	-	1:1	1:1	1:1
Missing	0	0	0	0	0
Study ongoing[c], n (%)	1 (100.0)	0 (0.0)	1 (100.0)	1 (100.0)	2 (100.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Crysvita	1 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	1 (50.0)
Phosphate	1 (100.0)	0 (0.0)	1 (100.0)	1 (100.0)	2 (100.0)
Active Vitamin D	1 (100.0)	0 (0.0)	1 (100.0)	1 (100.0)	2 (100.0)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
UNITED KINGDOM					
OVERALL					
Patients screened, n	83	42	41	61	144
Patients included in SAF[a], n (%)	77 (92.8)	40 (95.2)	37 (90.2)	16 (26.2)	93 (64.6)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Follow-up time (years)[b]					
n	77	40	37	16	93
Mean (SD)	1.8 (0.62)	1.6 (0.66)	2.1 (0.50)	1.7 (0.53)	1.8 (0.61)
Median	2.0	2.0	2.1	1.9	2.0
Q1 : Q3	1.5:2.2	1.0:2.1	2.0:2.3	1.2:2.0	1.4:2.2
Min : Max	0:3	0:2	1:3	1:3	0:3
Missing	0	0	0	0	0
Study ongoing[c], n (%)	76 (98.7)	40 (100.0)	36 (97.3)	16 (100.0)	92 (98.9)
Study discontinued[c], n (%)	1 (1.3)	0 (0.0)	1 (2.7)	0 (0.0)	1 (1.1)
Reason[d], n (%)					
n	1	0	1	0	1
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	1 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	1 (100.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	77 (100.0)	40 (100.0)	37 (100.0)	0 (0.0)	77 (82.8)
Phosphate	35 (45.5)	0 (0.0)	35 (94.6)	14 (87.5)	49 (52.7)
Active Vitamin D	31 (40.3)	0 (0.0)	31 (83.8)	15 (93.8)	46 (49.5)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	5 (6.5)	0 (0.0)	5 (13.5)	2 (12.5)	7 (7.5)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
MALE					
Patients screened, n	31	16	15	20	51
Patients included in SAF[a], n (%)	29 (93.5)	15 (93.8)	14 (93.3)	7 (35.0)	36 (70.6)
Follow-up time (years)[b]					
n	29	15	14	7	36
Mean (SD)	1.7 (0.60)	1.7 (0.64)	1.7 (0.57)	1.6 (0.44)	1.7 (0.57)
Median	2.0	2.0	2.0	1.9	2.0
Q1 : Q3	1.0:2.2	0.9:2.2	1.0:2.2	1.2:2.0	1.0:2.2
Min : Max	1:2	1:2	1:2	1:2	1:2
Missing	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Study ongoing[c], n (%)	28 (96.6)	15 (100.0)	13 (92.9)	7 (100.0)	35 (97.2)
Study discontinued[c], n (%)	1 (3.4)	0 (0.0)	1 (7.1)	0 (0.0)	1 (2.8)
Reason[d], n (%)					
n	1	0	1	0	1
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	1 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	1 (100.0)
Missing	0	0	0	0	0

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
XLH treatments[c], n (%)					
Crysvita	29 (100.0)	15 (100.0)	14 (100.0)	0 (0.0)	29 (80.6)
Phosphate	14 (48.3)	0 (0.0)	14 (100.0)	5 (71.4)	19 (52.8)
Active Vitamin D	11 (37.9)	0 (0.0)	11 (78.6)	6 (85.7)	17 (47.2)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	1 (3.4)	0 (0.0)	1 (7.1)	2 (28.6)	3 (8.3)
FEMALE					
Patients screened, n	52	26	26	41	93
Patients included in SAF[a], n (%)	48 (92.3)	25 (96.2)	23 (88.5)	9 (22.0)	57 (61.3)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Follow-up time (years)[b]					
n	48	25	23	9	57
Mean (SD)	1.9 (0.63)	1.6 (0.68)	2.3 (0.33)	1.8 (0.60)	1.9 (0.63)
Median	2.0	1.9	2.2	1.9	2.0
Q1 : Q3	1.9:2.2	1.1:2.0	2.0:2.5	1.2:2.0	1.8:2.2
Min : Max	0:3	0:2	2:3	1:3	0:3
Missing	0	0	0	0	0
Study ongoing[c], n (%)	48 (100.0)	25 (100.0)	23 (100.0)	9 (100.0)	57 (100.0)
Study discontinued[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reason[d], n (%)					
n	0	0	0	0	0
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study terminated by sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0	0
XLH treatments[c], n (%)					
Crysvita	48 (100.0)	25 (100.0)	23 (100.0)	0 (0.0)	48 (84.2)
Phosphate	21 (43.8)	0 (0.0)	21 (91.3)	9 (100.0)	30 (52.6)
Active Vitamin D	20 (41.7)	0 (0.0)	20 (87.0)	9 (100.0)	29 (50.9)
Growth hormone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	4 (8.3)	0 (0.0)	4 (17.4)	0 (0.0)	4 (7.0)

	Crysvita (N=179)	Crysvita only (N=80)	Crysvita + alternative XLH treatment (N=99)	Alternative XLH treatment only (N=194)	Total (N=373)

SAF: Safety Analysis Set, XLH: X-linked hypophosphatemia.

Screened patients: All patients who were included and assigned a seven-digit E-code enrolment number (i.e., Exxxxxxx) in the Electronic Data Capture.

SAF: All screened patients with age ≥ 1 and <18 years who signed informed consent form and received XLH treatment on or after 30 days prior to first informed consent date.

[a] Percentages are calculated using the number of patients screened as denominator.

[b] The follow-up time is calculated as the time from the date of informed consent to the date of study discontinuation or date of cut-off analysis. Follow-up time = (date of discontinuation/cut-off - date of informed consent + 1) / 365.25.

[c] Percentages are calculated using the number of patients in the SAF as denominator.

[d] Percentages are calculated using the number of patients who discontinued the study as denominator.

Table 1.28.1: Summary Overview of All Adverse Events by XLH Treatment and Age Group (Prospective) (Safety Analysis Set)

	Crysvita (N=170)	Crysvita only (N=77)	Crysvita + alternative XLH treatment (N=93)	Alternative XLH treatment only (N=80)	Total (N=250)
TOTAL (N=250)					
Any AE, n (%)	15 (8.8)	7 (9.1)	8 (8.6)	2 (2.5)	17 (6.8)
Any AE possibly/probably related to XLH treatment, n (%)	6 (3.5)	3 (3.9)	3 (3.2)	2 (2.5)	8 (3.2)
Any AE leading to death, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any AE leading to death and possibly/probably related to XLH treatment, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=170)	Crysvita only (N=77)	Crysvita + alternative XLH treatment (N=93)	Alternative XLH treatment only (N=80)	Total (N=250)
Any AE leading to XLH treatment withdrawn, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any AE leading to XLH treatment withdrawn and possibly/probably related to XLH treatment, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any severe AE, n (%)	1 (0.6)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.4)
Any AESI, n (%)	1 (0.6)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.4)
Any AESI possibly/probably related to XLH treatment, n (%)	1 (0.6)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.4)
Any SAE, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=170)	Crysvita only (N=77)	Crysvita + alternative XLH treatment (N=93)	Alternative XLH treatment only (N=80)	Total (N=250)
Any SAE possibly/probably related to XLH treatment, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TODDLER (1-<5years) (N=50)	35	13	22	15	50
Any AE, n (%)	1 (2.9)	0 (0.0)	1 (4.5)	0 (0.0)	1 (2.0)
Any AE possibly/probably related to XLH treatment, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any AE leading to death, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any AE leading to death and possibly/probably related to XLH treatment, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=170)	Crysvita only (N=77)	Crysvita + alternative XLH treatment (N=93)	Alternative XLH treatment only (N=80)	Total (N=250)
Any AE leading to XLH treatment withdrawn, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any AE leading to XLH treatment withdrawn and possibly/probably related to XLH treatment, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any severe AE, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any AESI, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any AESI possibly/probably related to XLH treatment, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any SAE, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=170)	Crysvita only (N=77)	Crysvita + alternative XLH treatment (N=93)	Alternative XLH treatment only (N=80)	Total (N=250)
Any SAE possibly/probably related to XLH treatment, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
CHILDREN (5-<12years) (N=114)	79	36	43	35	114
Any AE, n (%)	7 (8.9)	5 (13.9)	2 (4.7)	0 (0.0)	7 (6.1)
Any AE possibly/probably related to XLH treatment, n (%)	2 (2.5)	2 (5.6)	0 (0.0)	0 (0.0)	2 (1.8)
Any AE leading to death, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any AE leading to death and possibly/probably related to XLH treatment, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=170)	Crysvita only (N=77)	Crysvita + alternative XLH treatment (N=93)	Alternative XLH treatment only (N=80)	Total (N=250)
Any AE leading to XLH treatment withdrawn, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any AE leading to XLH treatment withdrawn and possibly/probably related to XLH treatment, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any severe AE, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any AESI, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any AESI possibly/probably related to XLH treatment, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any SAE, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=170)	Crysvita only (N=77)	Crysvita + alternative XLH treatment (N=93)	Alternative XLH treatment only (N=80)	Total (N=250)
Any SAE possibly/probably related to XLH treatment, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ADOLESCENTS (12-<18years) (N=86)	56	28	28	30	86
Any AE, n (%)	7 (12.5)	2 (7.1)	5 (17.9)	2 (6.7)	9 (10.5)
Any AE possibly/probably related to XLH treatment, n (%)	4 (7.1)	1 (3.6)	3 (10.7)	2 (6.7)	6 (7.0)
Any AE leading to death, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any AE leading to death and possibly/probably related to XLH treatment, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=170)	Crysvita only (N=77)	Crysvita + alternative XLH treatment (N=93)	Alternative XLH treatment only (N=80)	Total (N=250)
Any AE leading to XLH treatment withdrawn, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any AE leading to XLH treatment withdrawn and possibly/probably related to XLH treatment, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any severe AE, n (%)	1 (1.8)	0 (0.0)	1 (3.6)	0 (0.0)	1 (1.2)
Any AESI, n (%)	1 (1.8)	0 (0.0)	1 (3.6)	0 (0.0)	1 (1.2)
Any AESI possibly/probably related to XLH treatment, n (%)	1 (1.8)	0 (0.0)	1 (3.6)	0 (0.0)	1 (1.2)
Any SAE, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Crysvita (N=170)	Crysvita only (N=77)	Crysvita + alternative XLH treatment (N=93)	Alternative XLH treatment only (N=80)	Total (N=250)
Any SAE possibly/probably related to XLH treatment, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE: Adverse Event, AESI: Adverse Event of Special Interest, SAE: Serious Adverse Event, SAF: Safety Analysis Set, XLH: X-linked hypophosphatemia.

Note: Percentages are calculated using the number of patients in the SAF as denominator.

Source Data: ADAE

Database Cut Date: 25AUG2020