INTRODUCTION

- Hypophosphatasia (HPP) is a rare, inherited metabolic disease caused by inactivating mutations in the gene encoding tissue-nonspecific alkaline phosphatase (TNSALP).
- Low TNSALP activity leads to extracellular accumulation of inorganic pyrophosphate (Pi), pyridoxal 5'-phosphate (PLP [active form of vitamin B6]), and phosphoethanolamine (PEA), resulting in bone mineralization defects, rickets, osteomalacia, and multiple systemic complications.
- The clinical expression of signs and symptoms of HPP may vary depending on when it presents to the clinician and may include:
  - Infant – severe hypomineralization of the skeleton, failure to thrive, respiratory failure and/or respiratory compromise requiring ventilator support, vitamin D deficiency, seizures, hypercalcemia, nephrocalcinosis, fractures, high risk of mortality.
  - Juvenile – premature loss of deciduous teeth, skeletal and skin deformities resulting from rickets and craniofacial dysostoses, respectively, and fractures, muscle weakness, poor growth, pain, compromised physical function including diminished ambulation.
  - Adult – osteomalacia, recurrent, poorly healing and/or nontraumatic fractures, pain, muscle weakness, ectopic calcification in the joints, compromised mobility, and nephrocalcinosis.
- Osteoarthropathyphosphatasia – dental syndromes only, such as premature tooth loss, discolddation of teeth, and poor dental health (although dental symptoms may be the presenting features of systemic HPP).
- Additional research is required to fully understand the presentation, current management, and clinical course of the disease.

OBJECTIVE

- To establish a prospective patient registry study that will document demographics, biochemical, laboratory and radiologic phenotypes, clinical course, and functional impact of HPP in patients of all ages.

METHODS

Design

- Multicenter, multinational, observational, prospective, registry study.
- Planned duration of ≥5 years.
- Planned enrollment of ≥500 patients across all ages.
- Compliance with all local regulations and guidelines governing medical practice and ethics.
- Compliance with all relevant data protection and privacy regulations, including patient anonymity.
- Study registered with ClinicalTrials.gov: NCT02306720.
- Sponsored by Alesion Pharmaceuticals, Cheshunt, CT, USA.

- The registry will be conducted in 2 phases:
  - In the pilot phase, all patients will fill out a 6-site phase to ensure appropriate endpoints are collected.
  - In the second phase, any changes from the pilot phase will be incorporated, and the registry will be broadened to include additional global sites.

PATIENTS

- Inclusion criteria:
  - Male or female patients of any age with a confirmed diagnosis of HPP.
  - The confirmed diagnosis of HPP is based on the judgement of the physician.
  - Signed informed consent and medical records release by the patient or the patient’s legal guardian.

- Exclusion criteria:
  - Ongoing participation in an Alesion-sponsored clinical trial or received asfoate alfa, an investigational drug in development for HPP.
  - Enrolment in the registry will not exclude a patient from participation in a future clinical trial.

Data Collection

- Data concerning patients’ treatment and clinical condition will be collected and analyzed from medical records and patient registry entry (baseline) and at a minimum of a 6-months’ period thereafter.
- Patients may choose to link their records with those of family members also participating in the HPP Registry Study.
- Data will be collected in the course of routine clinical care.
- Performance of specific clinical procedures is not mandated.
- Follow-up visits will occur at least every 6 months and at registry study termination.

Table: Patient-reported outcome assessments

<table>
<thead>
<tr>
<th>Domain</th>
<th>Instrument</th>
<th>Pediatric Age Group</th>
<th>Adult Age Group</th>
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<tbody>
<tr>
<td>Outcomes</td>
<td>BF-5F</td>
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<td></td>
</tr>
<tr>
<td>Pain</td>
<td>PDI-VAS</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Physical function</td>
<td>HAQ-DI</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>SF-36</td>
<td>SF-36 Short Form Health Survey (0-100)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>CRF</td>
<td>eCRF</td>
<td></td>
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</tbody>
</table>

CONCLUSIONS

- The HPP Registry Study will provide a comprehensive, real-life, longitudinal profile of patients with HPP, including:
  - Demographics
  - Diagnosis patterns
  - Genotype-phenotype correlations
  - HPP-associated complications or disease characteristics
  - Country-specific findings
  - Impact of HPP on activities of daily living and quality of life.

- Analysis of information gathered by the HPP Registry Study will lead to a better understanding of HPP which, in turn, will increase awareness, ad diagnosis, and improve patient care.

- The HPP Registry Study is open for additional sites to participate. For more information about participation in the HPP Registry Study, contact: HPPRegistry@quintiles.com.

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DISCLOSURES

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REFERENCES