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PARADIGHM™: A Natural History Registry for Patients With Chronic Hypoparathyroidism

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HYPOPARATHYROIDISM

- A rare endocrine disorder caused by absent or insufficient parathyroid hormone (PTH), a critical regulator of serum calcium, phosphate, and active vitamin D levels[1]
- An estimate of the overall prevalence of hypoparathyroidism in Europe is not available, however the prevalence in Denmark has recently been estimated at 25/100,000 individuals[2]
- Patients with hypoparathyroidism suffer from symptoms of hypocalcemia (eg, numbness, paresthesias, tetany, cognitive difficulties, seizures, cardiac arrhythmias, and laryngospasm/bronchospasm) and complications such as skeletal abnormalities, renal calcifications potentially leading to renal failure, and soft tissue calcifications[3]
- Most commonly caused by injury to the parathyroid gland during surgery[4]
- Current management aims for symptom control with calcium and calcitriol/alfacalcidol supplementation[1]
- No PTH replacement treatment has been approved to treat hypoparathyroidism

RATIONALE FOR THE REGISTRY

- PARADIGHM™: Physicians Advancing Disease Knowledge in Hypoparathyroidism
- Limited published data are available regarding the natural history and epidemiology of chronic hypoparathyroidism, including
  - Descriptive epidemiology
  - Risk factors
  - Modifying factors
  - Comorbidities and long-term consequences including nephrocalcinosis, renal failure, and mortality
  - Management strategies
- Results from the registry are intended to assist healthcare providers in optimizing their clinical decision making through enhanced understanding of the variability, progression, and natural history of chronic hypoparathyroidism

OBJECTIVE OF THE REGISTRY

- To characterize the natural history and epidemiology of chronic hypoparathyroidism in patients under conditions of normal clinical practice, regardless of disease origin and management
- Aspects of hypoparathyroidism to be examined include
  - Etiology
  - Treatment patterns
  - Clinical course and outcomes
  - Comorbidity
  - Mortality
  - Patients' quality of life (SF-36 Survey)
  - Impact of hypoparathyroidism on patients' work productivity
  - Hospital, emergency room, and physician visits

PATIENT ELIGIBILITY

Inclusion Criteria
Patients with a diagnosis of chronic hypoparathyroidism are eligible for inclusion into the registry, regardless of hypoparathyroidism etiology and management
Diagnosed with chronic hypoparathyroidism (≥6 months)
Signed informed consent and medical records release
Patients who participated or are currently enrolled in NPS Pharmaceuticals, Inc.–sponsored recombinant human parathyroid hormone (rhPTH[1-84]) clinical trials and investigator-initiated trials are also eligible for registry entry
Exclusion Criteria
Transient hypoparathyroidism within 6 months of enrollment
Diagnosed with hypoparathyroidism <6 months ago

PARADIGHM™ STUDY DESIGN

- Patients will be enrolled at participating study centers
  - Approximately 7 years of patient recruitment
  - Global target enrollment is 900 patients
  - Estimated study completion date: June 2032
  - ClinicalTrials.gov identifier: NCT01922440
  - Follow-up for each patient will be a minimum of 10 years
- Patient care and follow-up will be according to routine care by the patients' physicians
  - Except for patient questionnaires, no study-defined procedures will be required

DATA COLLECTION

Table 1. Registry Data to Be Collected

Data Field	Baseline	Follow-Up
Informed consent and medical records release	X	
Inclusion/exclusion criteria	X	
Demographic information	X	
Family history of hypoparathyroidism	X	
Hypoparathyroidism history	X	
Medical history	X	
Prior and concomitant medications (including over-the-counter medications)	X	X
Hypoparathyroidism management	X	X
Height and weight	X	X
Laboratory and imaging evaluations	X	X
Patient- or investigator-reported questionnaires (eg, quality of life, social history, hospitalizations)	X	X
New concomitant diseases		X
Mortality and cause of death		X

DATA COLLECTION (cont'd)

- Patient data collected from routine medical care will be recorded in electronic case report forms (eCRFs) using an electronic data capture system
- To ensure quality control and source data verification of eCRFs, 10% of study centers will be visited by a monitor; additional data monitoring may be conducted based on periodic data review
- Although no predetermined patient follow-up requirements are specified by the registry protocol, investigators are expected to update patient data in the registry at each patient visit and at a minimum of every 12 months

DATA ANALYSIS

- All analyses will be based on the entire enrolled population using an observed case approach
- Data will be summarized using descriptive statistics
- Cumulative incidence and incidence rates of prospective events will be calculated
  - Patients lost to follow-up will have their person-time contribution to the registry included in the analyses
- As the database grows, protocol-driven specific research questions and hypothesis testing will be done

SCIENTIFIC STEERING COMMITTEE

- Steering committee composed of 9 members (6 independent medical experts, 3 representatives of the study sponsor)
  - Membership is currently based in the United States, but will be expanded internationally within the year
  - Independent medical experts are all physicians involved in both clinical practice and research
- Provides scientific guidance and oversight
- Advises on ethical policy decisions
- Develops and/or approves proposed research projects
- Evaluates all requests for analyses and publications
- Coordinates the formation of and provides the oversight for research topic working groups
- Coordinates and guides publications and presentations

CONCLUSIONS

- **PARADIGHM™ will provide previously unavailable long-term, prospective data from a large sample of patients with chronic hypoparathyroidism**
- **Physicians' contributions of patient data to PARADIGHM™ will benefit all registry participants, since data are pooled to study trends or address specific questions**
- **The hypoparathyroidism community will gain important information on a rare condition that affects a small patient population, and its treatment**

REGISTRY PARTICIPATION

- Registry enrollment began in the United States in July 2013
- Targeted to begin in Canada and Europe in late 2014 to early 2015
  - Canada
  - Denmark
  - France
  - Germany
  - Italy
  - Sweden
  - United Kingdom

More information about the PARADIGHM™ Registry	
Physicians or other healthcare providers may find out more by scanning the QR code at the bottom of this poster, or by one of these other methods:	
Contact the Registry Coordination Center at 1-888-472-6735 or paradighm@mapigroup.com	Visit www.clinicaltrials.gov NCT01922440

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DISCLOSURES

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TJV and MM have served as advisory group members for NPS Pharmaceuticals, Inc.
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Scan this QR code with your reader to receive a PDF file of the poster and/or more information regarding the PARADIGHM™ registry.
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