BUR-CL207: An open-label, multicentre, non-randomised study to assess the safety, tolerability, pharmacokinetics and efficacy of burosumab in paediatric patients from birth to less than 1 year of age with XLH

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INTRODUCTION

• X-linked hypophosphataemia (XLH) is a hereditary disorder caused by genetic variants in the phosphate-regulating endopeptidase homolog X-linked (PHRX) gene that increase serum fibroblast growth factor 23 (FGF23) concentrations, leading to phosphate wasting, chronic hypophosphataemia and rickets/osteomalacia.1,2

• Early initiation of treatment in children with XLH is known to improve height and prevent skeletal deformities, and may also improve dental and musculoskeletal outcomes.3,4,5

• Burosumab is a recombinant fully human immunoglobulin G1 monoclonal antibody licensed by the European Medicines Agency for the treatment of XLH in children aged >1 year and adults.6,7

• By selectively inhibiting FGF23, burosumab improves serum phosphate and active vitamin D levels as well as radiographic evidence of rickets severity, and has been shown to prevent skeletal deformities and may also improve dental and musculoskeletal outcomes.2,8-10

• The safety profile assessed in clinical trials is favourable for burosumab, with the most common adverse reactions reported in children with XLH aged >1 year across three clinical trials included injection-site reactions, headache, cough and pyrexia.7,8

AIM

• This is a multicentre, open-label, non-randomised phase III study designed to evaluate the safety, tolerability, pharmacology and efficacy of burosumab in paediatric patients aged <1 year

STUDY METHOD

• This study is currently enrolling (in Europe only) and will include approximately 20 infants with XLH (<1 year old) with confirmed PHRX genetic variants

• Infants receiving conventional therapy will discontinue medications >1 week before commencing burosumab treatment and for the duration of the study

• All enrolled patients will receive burosumab (the trial does not contain a placebo arm), across three cohorts

• The duration of treatment will be 48 weeks, with a follow-up of 8 weeks after completion of treatment on study – enrolled patients will be offered long-term follow-up in the Kyowa Kirin Registry upon consent

• A Data Safety Monitoring Board will review safety and efficacy data accrued in each cohort after completion of 4 weeks of treatment by the last enrolled patient, and additionally on an ad hoc basis throughout the study if deemed appropriate

• The study commenced with cohort 1; as no safety issues were identified in at least three patients enrolled after at least 4 weeks of treatment, cohorts 2 and 3 were initiated in parallel (Figure 1)

TRIAL DESIGN

- Patients: 1,25(OH)2D, 1,25-dihydroxyvitamin D; AE, adverse event; ECG, electrocardiogram; echo, echocardiography; FGF23, fibroblast growth factor 23; LH, lower limit of normal; PHRX, phosphate-regulating endopeptidase homolog, PK, pharmacokinetics; RGI, Radiographic Global Impression of Change; Ri, renal ultrasound; SAE, serious adverse event; Sc, subcutaneous; XLH, X-linked hypophosphataemia.

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REFERENCES


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CONTACT INFORMATION

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Figure 1: Trial design for BUR-CL207 including patient populations, treatment schedules and endpoints.

Figure 2: Current status study of the BUR-CL207 trial.