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REVIEW article

Safety and efficacy of Burosumab in patients with X-linked hypophosphatemia: A systematic review

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Abstract: X-linked hypophosphatemia is a rare genetic disorder caused by a loss-of-function mutation in the phosphate-regulating gene with homologies to endopeptidases on the X chromosome. It is characterized by early-onset skeletal deformities, hypophosphatemia, and elevated fibroblast growth factor 23 levels. The following mutations lead to recurrent fractures, osteoarthritis, joint stiffness, and a reduced life expectancy. Burosumab, a human monoclonal antibody, is considered a breakthrough in the treatment of X-linked hypophosphatemia. MEDLINE, Cochrane Library, CENTRAL, Google Scholar, and clinicaltrials.gov were searched from inception through March 3rd, 2025. Overall, eight clinical trials investigating the effectiveness and safety of Burosumab in patients with X-linked hypophosphatemia were identified using the PRISMA guidelines. Out of which two randomized controlled trials exhibited a significant increase in serum phosphate. The other five single-arm studies reported instability in serum phosphate levels with variability in the dosing regimen. Furthermore, other primary outcomes; 1,25 dihydroxy vitamin D, serum calcium, and tubular maximum reabsorption of phosphate to glomerular filtration markedly optimized. Secondary outcomes assessing bone pain and ambulation indicated lower scores on the Brief Pain Inventory and Western Ontario and McMaster Universities Arthritis Index. Burosumab was well-tolerated by all participants, with only mild to moderate adverse events reported. The findings indicate significant improvement in levels of key biochemical markers; serum phosphate concentration, tubular maximum reabsorption of phosphate to glomerular filtration, 1,25 dihydroxy vitamin D after Burosumab use. A decrease in the level of pain and stiffness in joints was reported through the Brief Pain Inventory and Western Ontario and McMaster Universities Arthritis Index in most studies. Burosumab was well tolerated by participants from all included studies.

Introduction

X-linked hypophosphatemia (XLH) is a rare genetic disorder caused by loss-of-function in the PHEX gene (phosphate-regulating gene with homologies to endopeptidases on the X chromosome), which results in progressively debilitating lifelong ambulatory difficulties [1, 2]. Furthermore, according to the United Kingdom's XLH prevalence report, the incidence of XLH increased from 1.8 to 13.3 per million in the adult population from 1995-1999 to 2012-2016. Additionally, the analysis exhibited that 6.5% of the XLH-inflicted population died at

the age of 61 compared to the median age of death at 68 years in the control group, indicating an 8-year survival reduction in the XLH population [3].

X-linked hypophosphatemia is biochemically presented with diminished phosphate reabsorption from the kidneys due to an eminent increase in fibroblast growth factor 23 (FGF23) [4]. Elevation of FGF23 is shown to be linked with remarkable amplification in the incidence of chronic kidney disease and cardiovascular diseases like, cardiomyocyte hypertrophy, and vascular calcification leading to stroke and early death [5, 6]. XLH progression leads to lifelong disability along with severe musculoskeletal morbidities which significantly upscales the economic burden of the disease [7]. Additionally, a study by Steel and others [8] analyzing musculoskeletal comorbidities in nine individuals revealed that adults with XLH presented with enthesopathies, specifically prevalent in the cervical spine (87.0%), thoracic spine (75.0%), lumbar spine (88.0%), and Achilles tendon (88.0%). Along with elevated frequency in osteophyte formation and degenerative arthritis, especially, in the hip (88.0%) and knee (100%) joints. It leads to joint pain and stiffness, thus contributing to impaired mobility, and hampering overall quality of life [8]. Moreover, Orlando and others [9] demonstrate that approximately 40.0% of the 26 included adults had compromised mobility and diminished physical activity related to an eminent deficit in lower limb muscle strength.

Until recently, the sole pharmaceutical intervention to manage elevated FGF-23-associated hypophosphatemia and 1,25 dihydroxy vitamin D deficiency was phosphate analogs and vitamin D metabolites [10]. Though, conventional therapy in symptomatic adults has proven to be imperceptibly efficacious [11, 12]. Long-term subjection to conventional therapy is linked to complications like nephrocalcinosis, hypercalciuria, and medullary calcifications [13]. Kato and others [14] report the occurrence of nephrocalcinosis in 72.0% of adults with XLH undergoing chronic phosphate analog use. To avoid the adverse effects of conventional treatments, Burosumab, a monoclonal antibody has emerged as a new treatment for XLH [15, 16]. We have conducted a systematic review compiling the results of all the clinical trials assessing the efficacy and safety of Burosumab compared to placebo in adults with XLH.

Material and methods

This study conducted a comprehensive search of electronic databases including MEDLINE, Cochrane Library, CENTRAL, and clinicaltrials.gov from inception up to March 2025. We aimed to identify clinical trials that investigated the effectiveness and safety of Burosumab in adults with X-linked hypophosphatemia. The search utilized keywords such as X-linked hypophosphatemia, Burosumab, KRN23, and adults. Studies were selected based on predefined eligibility criteria. The unpublished studies that may have been left out in electronic database searches were manually extracted. This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines to ensure methodological rigor and transparency in reporting [17]. This research is registered in Open Science Framework (OSF) (https://doi.org/10.17605/OSF.IO/B2R76).

Eligibility and study selection: Meticulously designated eligibility criteria were used to filter the obtained results after the search. It was ensured that only randomized control trials (RCT) and clinical trials (CT) published up to April 2023, in the English language were considered. The review process involved two independent researchers (ETR & DA) who screened studies based on their titles and abstracts. Studies that were deemed important by either reviewer were then subjected to full-text evaluation. In case of any disagreements, a third independent reviewer (HS) was consulted to reach a consensus. The studies selected for review were randomized controlled trials that used Burosumab as an intervention and compared it to placebo groups and single-arm, dose-escalation clinical trials. All the clinical trials conducted on adults (aged >18 years) diagnosed with XLH backed with confirmed PHEX mutation qualified. Furthermore, it was considered mandatory to report primary and secondary

outcomes to be included in the review. The primary outcomes of interest included serum phosphate levels, the ratio of tubular maximum reabsorption of phosphate to glomerular filtration rate (TmP/GFR), serum calcium level, 1,25 dihydroxy vitamin D, intact parathyroid hormone (iPTH), Alkaline phosphatase (ALP) or Bone Alkaline phosphatase (BALP). The secondary outcomes of interest, related to pain and ambulation were measured using the Western Ontario and McMaster Universities Arthritis Index **(**WOMAC), Brief Pain Inventory-Short Form (BPI-SF), and Brief Pain Inventory (BFI) instruments. Additionally, studies reporting safety-related adverse events were also included. On the contrary, the studies that solely reported enhancement in bone density or as a remedy for fractures were excluded from the review. After careful consideration, a total of eight studies were selected; three Randomized Controlled Trials (RCTs) and five single-arm dose escalation Controlled Trials (CTs) [18-28].

Extraction and appraisal: The data acquired from the selected research were stratified in tabular form by two independent reviewers (ETR & DA). The sorted variables included; publication details, baseline characteristics, study population, follow-up period, and aforementioned primary and secondary outcomes. To assess the risk of bias (RoB) in RCTs Cochrane Risk of Bias 2.0 (RoB 2) was used and the quality of research was assessed on the following domains; randomization, deviation from intended interventions, missing outcome data, selective reporting of outcomes and measurement of outcomes [29]. After a thorough evaluation of methodological quality and potential biases, high-quality studies were regarded for review. In contrast, single-arm studies were assessed using Downs and Black Checklist [30]. The procedural methods of study were judged on the following domains; confounding, selection, classification of intervention bias, missing outcome data, and selective reporting of data.

Results

Our systematic search yielded a total of 109 studies, out of which 41 studies were analyzed on the basis of title and abstract, the ones considered irrelevant were opted out from the final review. Upon extended assessment, 36 duplicates were found which were subtracted, amounting to a total of 32 studies that were finalized for full-text view. Out of them, two studies did not report complete results, seven had irrelevant outcomes and 15 did not pertain to review of interest. After final selection, it was found that one study, Portale A, had a follow-up period of 24 weeks, and another study, Insogna et al. [18] is an extension of similar studies reporting outcomes up to 96 weeks. Both articles are treated as separate studies. Moreover, a study by Briot K reports secondary outcomes of Insogna K 2018's RCT are completely exempted from our review and only referred for outcomes of interest [20]. Therefore, eight studies were included in the systematic review, with three RCTs and five single-arm studies. The overall search results are summarized in the PRISMA chart **Figure 1**.

Patient characteristics: In the eight included studies, a total of 534 adults diagnosed with XLH were inducted. Adults were defined as ≥18 years of age, while the range was generally regarded as 18-65 years. The main criteria for inclusion defined by all the studies were the diagnosis of XLH through a PHEX gene mutation, alongside other specifications that differed in each study. In two studies all participants were required to have a serum phosphate concentration below LLN; <2.5 mg/dL. Two studies only included patients with a TmP/GFR value of <2.0 mg/dL and in the other two studies with <2.5 mg/dL. Three studies also mandated a BPI worst pain score of ≥4. Participants of two studies were directed to discontinue vitamin D (or its analogs), calcium or phosphate supplements, or aluminum hydroxide for at least 10 days before the screening visit. One study also included participants on the basis of their GFR value; in case GFR was ≥60 mL/min at screening with confirmation that renal insufficiency was not due to nephrocalcinosis. Burosumab was administered over a wide range of doses, with the lowest value of 0.003 mg/kg to 1.0 mg/kg being the highest value throughout all the included clinical trials. Further details of the study and patient characters are provided in **Table 1**.

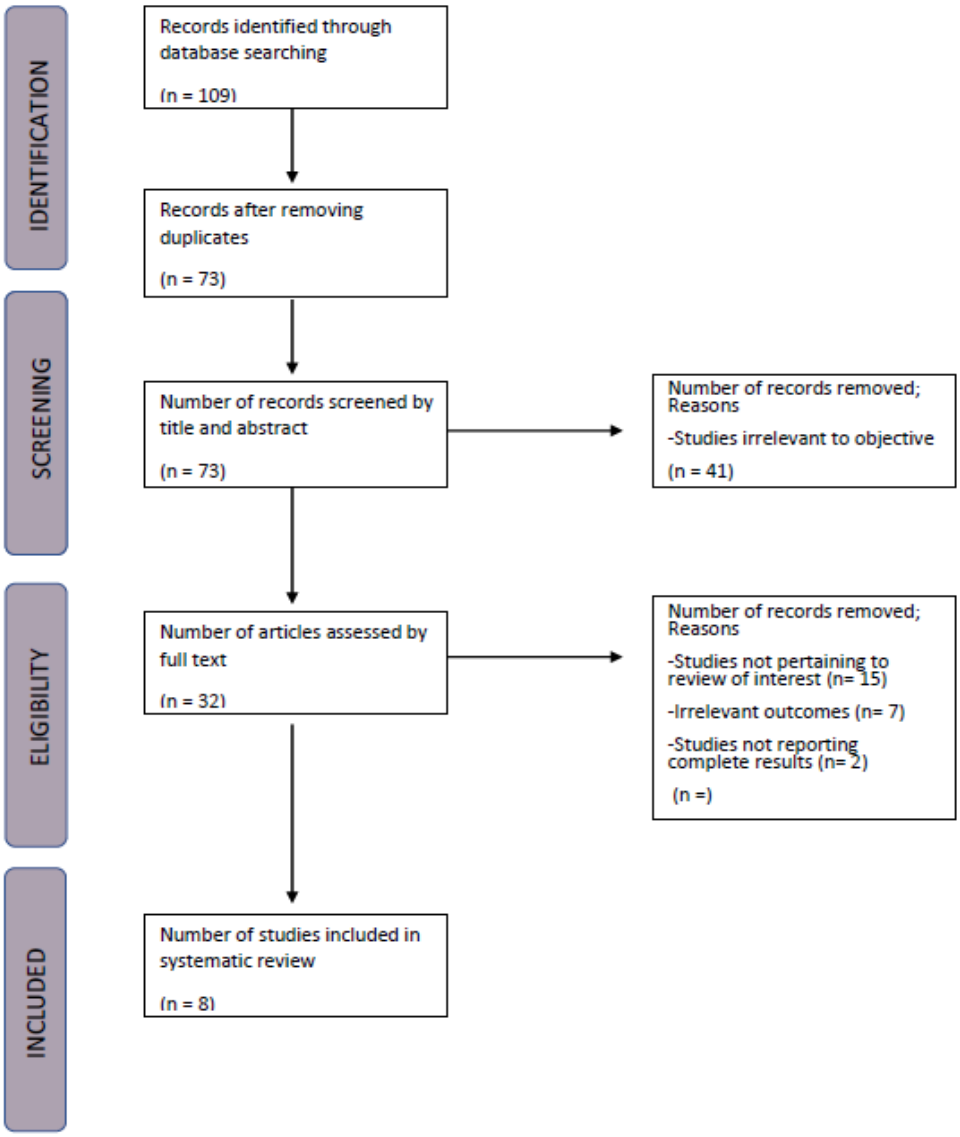

Figure 1: PRISMA flow diagram

Quality Assessment: The three included RCTs; Insogna et al. [18], Carpenter et al. [19], and Portale et al. [20] were assessed via Cochrane RoB 2.0 tool. After thorough consideration; Insogna et al. [18] and Carpenter et al. [19] were interpreted to be low risk overall. However, Portale et al. [20] initially followed the same blinding and randomization protocols as its parent study but after 48 weeks digressed to a single-blinded, open-label study [18]. Since the subjects were unblinded to protocol, it may have caused potential bias in patient-reported, secondary outcomes (WOMAC, BPI-SF), therefore, this study was conclusively marked as having some concerns. The risk of Bias assessment in RCTs is shown in **attached Supplementary**.

Out of the total eight studies; five single-arm studies were assessed via Downs and Black Checklist. The domains which were deemed inapplicable by the reviewers were exempted leading to a total marking score of 22. Four included studies; Weber and others [26] were marked 20, and one study Cheong and others [23]was scored 19 out of 22 by the reviewers. However, these studies are anticipated to have a higher risk of bias due to the absence of a comparative cohort and lack of blinding protocols. The risk of bias assessment in a single-arm dose-escalation study is shown in **Table 2**.

Table 1: Characteristics of the included studies

Study, year	Study design	Sample size	Treatment arms (Interval weeks)	Control	Indication for Burosumab,	Follow up	Endpoints and side effects
Insogna et al. [18]	Double -blind, RCT	134	Burosumab 1.0 mg/kg [4]	Placebo 1.0 mg/kg [4]	Confirmed diagnosis of XLH + serum phosphate LLN; <2.5 mg/dL + TmP/GFR of <2.5 mg/dL, BPI ≥4, 18-65 y.	24 weeks	Mean serum Pi, TmP/GFR, Serum 1,25(OH)2D, WOMAC, BPI, Plasma iPTH
Portale et al. [20]	Double -blind, RCT	134	Burosumab 1.0 mg/kg [4]	Placebo 1.0 mg/kg [4]	Phosphorus < LLN 2.5 mg/dL + TmP/GFR > 2.5 mg/dL + BPI ≥ 4 + serum calcium ≥ 10.8 mg/dL + iPTH ≥2.5 x ULN, 18-65 y.	24 weeks	Serum Pi, TmP/GFR, WOMAC, BPI, iPTH, 1,25(OH)2D, 24-hr urine calcium excretion
Carpenter et al. [19]	Double -blind, RCT	38	Burosumab 0.003, 0.1, 0.3 mg/kg i.v. or 0.1, 0.3, 0.6, 1.0 mg/kg s.c.	Placebo	Confirmed diagnosis of XLH +	50 days	1,25[OH]2D3, Serum Pi, TmP/GFR
Weber et al. [21]	Open-label, Single-arm	20	Burosumab 0.3, 0.6, 0.1 mg/kg [4]	N/A	Confirmed diagnosis of XLH + at least 2 doses of in KRN23-INT-001 or KRN23-INT-002 + GFR ≥60 mL/min	184 weeks	Fasting serum Pi, TmP/GFR, Mean serum 1,25(OH)2D, Serum iPTH, Serum calcium, 24-hour urine calcium excretion, BPI-SF, WOMAC, BALP
Imel et al. [22]	Open-label, single-arm	28	Burosumab 0.05, 0.1, 0.3, 0.6 mg/kg; 4-month dose escalation Burosumab 0.1-1 mg/kg; 12-month extension (28 days)	N/A	Confirmed diagnosis of XLH + TmP/GFR <2.0 mg/dL + CrCl ≥60 mL/min + serum calcium <10.8 mg/dL + serum intact FGF23 >30 pg/mL + discontinuation of vitamin D	64 weeks	Serum Pi, TmP/GFR, 1,25(OH)2D,
Cheong et al. [23]	Open-label, Single-arm	18	Burosumab 0.3 mg/kg; cohort 1 0.6 mg/kg; cohort 2 1 mg/kg cohort 3 (Day 1- Single day)	N/A	Confirmed diagnosis of XLH	29 days	Serum Pi, 1,25(OH)2D, TmP/GFR, Corrected Serum Ca, iPTH, Creatinine, 25OHD, Calcitonin, BALP, Urinalysis, 2-hr urinary parameters (urinary P, Ca, and Cr), 24-hour urine analysis (urinary P, Ca, and Cr)
Zhang et al. [24]	Open-label, single - arm	28	Burosumab 0.05, 0.1, 0.3, and 0.6 mg/kg; step-wise dose escalation (28 days)	N/A	Confirmed diagnosis of XLH + Serum intact serum FGF23 ≥ 30 pg/mL + TmP/GFR < 2.0 mg/dL + creatinine clearance ≥ 60 mL/min + Serum calcium < 10.8 mg/dL	120 days	Serum Pi, TmP/GFR, Mean serum 1,25[OH]2D3, Bone formation and resorption markers, Mean PTH, Mean serum FGF23, Mean serum calcium, 24-hour urine calcium excretion
Insogna et al. [25]	Open-label, single-arm	25	Burosumab 1.0 mg/kg (4 weeks)	N/A	Confirmed diagnosis of XLH + FGF23 level greater than 30 pg/mL + TmP/GFR <2.5 mg/dL + Score of four or more on Question 3, "Worst Pain," of the BPI, 18-65 yrs	96 weeks	TmP/GFR, serum 1,25(OH)2D

Note: FGR23= Fibroblast Growth Factor 23, TmP/GFR= Tubular Maximum Reabsorption of Phosphate (TmP) to Glomerular Filtration Rate, WOMAC= Western Ontario and McMaster Universities Arthritis Index, BPI= Brief Pain Inventory, iPTH= intact parathormone, BALP= Bone Alkaline Phosphatase, PTH= Parathormone, CrCl= Creatinine Clearance, LLN= Lower Limit of Normal, N/A= Not Assigned, i.v= Intravenous, s.c= Subcutaneous

Table 2: Risk of bias assessment in single-arm dose-escalation studies using Downs and Black List

REPORTING	Weber T	Imel E	Cheong H	Zhang X	Insogna K
1. Is the objective of the study clear?	YES	YES	YES	YES	YES
2. Are the main outcomes clearly described in the Introduction or Methods?	YES	YES	YES	YES	YES
3. Are characteristics of the patients included in the study clearly described?	YES	YES	YES	YES	YES
4. Are the interventions clearly described?	YES	YES	YES	YES	YES
5. Are the baseline characteristics or potential confounders of the study participants clearly described?	YES	YES	YES	YES	YES
6. Are the main findings of the study clearly described?	YES	YES	YES	YES	YES
7. Does the study estimate random variability in data for main outcomes?	YES	YES	YES	YES	YES
8. Have all the important adverse events consequential to the intervention been reported?	YES	YES	YES	YES	YES
9. Have characteristics of patients lost to follow-up been described?	YES	YES	YES	YES	YES
10. Have actual probability values been reported for the main outcomes except probability <0.001?	YES	YES	NO	NO	NO
11. Is the source of funding clearly stated?	YES	YES	YES	YES	YES
EXTERNAL VALIDITY	**Weber T**	**Imel E**	**Cheong H**	**Zhang X**	**Insogna K**
12. Were subjects who were asked to participate in the study representative of the entire population recruited?	YES	YES	YES	YES	YES
13. Were those subjects who were prepared to participate representative of the recruited population?	YES	YES	YES	YES	YES
14. Were staff, places, and facilities where patients were treated representative of the treatment most received?	YES	YES	YES	YES	YES
INTERNAL VALIDITY	**Weber T**	**Imel E**	**Cheong H**	**Zhang X**	**Insogna K**
15. Was an attempt made to blind study subjects to the intervention?	N/A	N/A	N/A	N/A	N/A
16. Was an attempt made to blind those measuring the main outcomes?	N/A	N/A	N/A	N/A	N/A
17. If any of the results of the study were based on data dredging was this made clear?	UNCLEAR	UNCLEAR	UNCLEAR	UNCLEAR	UNCLEAR
18. Was the period between intervention and outcome the same for intervention and control groups or adjusted for?	N/A	N/A	N/A	N/A	N/A
19. Were the statistical tests used to assess main outcomes appropriate?	YES	YES	YES	YES	YES
20. Was compliance with the interventions reliable?	YES	YES	YES	YES	YES
21. Were main outcome measures used accurately? (valid and reliable)	YES	YES	YES	YES	YES
22. Were patients in different intervention groups recruited from the same population?	YES	YES	YES	YES	YES
23. Were study subjects in different intervention groups recruited over the same period?	YES	YES	YES	YES	YES
24. Were study subjects randomized to intervention groups?	N/A	N/A	N/A	N/A	N/A
25. Was the randomized intervention assignment concealed from patients and staff until recruitment was complete?	N/A	N/A	N/A	N/A	N/A
26. Was there an adequate adjustment for confounding in the analyses from which the main findings were drawn?	N/A	N/A	N/A	N/A	N/A
27. Was missing data or participant attrition reported?	YES	YES	YES	YES	YES
POWER	**Weber T**	**Imel E**	**Cheong H**	**Zhang X**	**Insogna K**
28. Was the study sufficiently powered to detect clinically important effects where the probability value for a difference due to chance is <5%?	UNCLEAR	NO	NO	NO	NO

FINAL SCORE	Weber T	Imel E	Cheong H	Zhang X	Insogna K
22	20	20	19	20	20

*Domains 5 and 27 were modified according to single-arm studies,
*Domains 15, 16, 18, 24, 25, and 26 were considered not applicable (N/A)

Efficacy: The primary outcomes measured in the RCTs were serum phosphate, serum 1,25(OH)2D concentrations, and TmP/GFR. Insogna et al. [18] intervention with 1.0 mg/kg over a period of a maximum of 24 weeks showed sustained levels of serum phosphate, serum 1,25(OH)2D concentrations, and TmP/GFR. Both in Insogna et al. [18] and Carpenter et al. [19], serum phosphate levels were reported to be significant after the administration of Burosumab. Another study by Portale and others [20] reported an increase in mean serum phosphate concentration above the LLN in 94.1% of subjects. On the other hand, TmP/GFR improved overall in the three studies [18, 19], and the p values were significant. Furthermore, an increase of 0.5 mg/dl in TmP/GFR was documented at 48 weeks in one study [20].

Additionally, the levels of serum 1,25(OH)2D3 concentrations did not prove to be an effective marker of the efficacy of Burosumab since only Carpenter and associates [20] reported a significant p-value of <0.05 and an increase to 7.1 pg/ml at 48 weeks was reported. No significant change was observed in the study conducted by Insogna and others [18]. The secondary outcome measures were reported by three included studies [18, 20] among which a significant improvement in the WOMAC score was reported by all. BPI-SF worst pain score also had a significant in the research by Insogna et al. [18] and Portale et al. [20]. Single-arm studies had a range of reported results that varied considerably. The serum phosphate concentration was significant in one study [26]. Imel and Zhang [21] reported a fluctuating level of serum phosphate, with the maximum levels being attained on the 7th day and then lowering by the 28th day. Insogna and associates [25] achieved a serum phosphorus concentration above LLN (2.5 mg/dl) in 13 subjects.

The value of TmP/GFR remained significant throughout the period of the study conducted by Imel and others [22] after the fourth dose. Weber et al. [26] reported an increase in the value from baseline but below LLN overall. An increase in value was observed by Zhang et al. [24] and Insogna et al. [25] but it returned to the baseline by day 28 in the latter study, thus not providing any significant results. While the values did increase in the studies by Weber et al. [25], they eventually decreased to the baseline by 36, 28, and 4 weeks respectively. The secondary outcomes examining the bone pain levels were only assessed by Insogna et al. [25] and Weber et al. [26] and reported an overall improvement in pain severity. The summary of the findings of the single-arm dose-escalation study is provided in **Table 3** and a summary of the findings of RCTs is provided in **Table 4**.

Table 3: Findings of single-arm dose-escalation studies

Author	Follow-up (weeks)	Phosphate Levels (mg/dL)		1,25(OH)2D (pg/mL)		TmP/GFR (mg/dL)	
		Baseline	Post-treatment	Baseline	Post-treatment	Baseline	Post-treatment
Imel E	17.3	1.9	2.16	36.6	36.3	1.6	2.13
Weber J	69	1.9	2.65	32	36.5	1.6	2.0
Zhang X	16	1.77	2.3	47.99	42.0	1.51	1.98
Insogna L	48	2.2	2.65	37	39.4	1.9	2.4
Cheong H	7	1.77	2.8	47.99	55.0	1.51	1.7

Table 4: Findings of Randomized Controlled Trials

Author	Follow-up (weeks)	Phosphate Levels (mg/dL)		1,25(OH)2D (pg/mL)		TmP/GFR (mg/dL)		WOMAC (physical function impairment)		BPI Worst Pain score	
		Baseline	*LS Mean Change*	*Baseline*	*LS Mean Change*	*Baseline*	*LS Mean Change*	*Baseline*	*LS Mean Change*	*Baseline*	*LS Mean Change*
Insogna L	24										
Placebo		1.9±0.32	N/R	33.5±15.6	25.5±3.52	1.6±0.37	0.43±0.067	43.0±19.97	−4.9±2.48	43	−0.5±0.28
Burosumab		2.0±0.30		32.4±13.0		1.7±0.40		50.8±19.7		53	
Anthony A	24-96										
Placebo-Burosumab		1.9±0.32	0.4	33.5±15.6	7.1	1.6±0.37	0.5	43.9±19.9	−7.76	6.5±1.4	−1.09± 0.216
Burosumab-Burosumab		2.0±0.30		32.4±13.0		1.7±0.40		50.8±19.7		6.8±1.3	
Carpenter T	7										
Placebo		1.7±0.2	0.79	29±10	41.7	1.43±0.25	1.00	N/R	N/R	N/R	N/R
Burosumab		1.9±0.5		42±18		1.59±0.33		N/R		N/R	

Note: N/R=Not Reported

Whereas, another single-arm dose escalation study [26] provided doses of 0.3, 0.6, or 1.0 mg/kg given by subcutaneous injection every four weeks which led to a rise of 1,25(OH)2D concentration at 24 weeks but a vigorous decline after 24 weeks. Likewise, in a study conducted by Zhang X, doses were escalated from 0.05, 0.1, 0.3, and 0.6 mg/kg sequentially for up to 28 days; nonetheless, serum phosphate and TmP/GFR returned to baseline on the 7th day and serum 1,25(OH)2D declined after three days. Analogously, in study of Insogna et al. [25], a dose of 1.0 mg/kg every four weeks for 96 weeks was administered but serum 1,25(OH)2D level dropped to near baseline at week four. As reported in double-arm studies, the levels of serum 1,25(OH)2D3 concentration did not prove to be an effective marker in single-arm studies as well. **Figures 2-4** provide a visual representation of changes in serum phosphate, TmP/GFR, and 1,25(OH)2D with varying levels of dosage over different periods in the included studies.

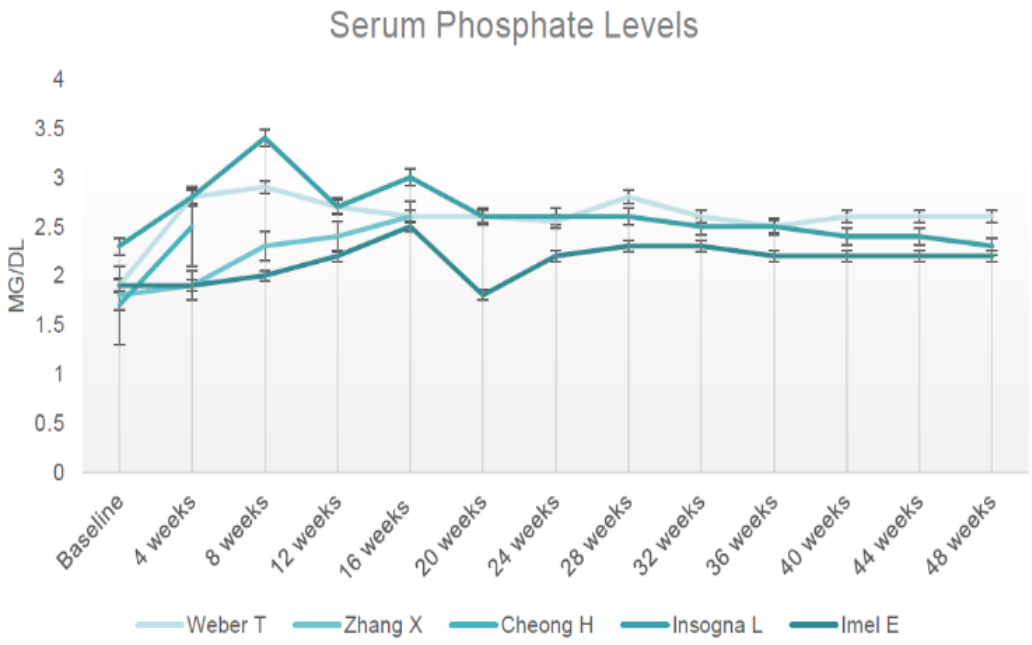

Figure 2: Changes in serum phosphate levels with variable Burosumab dosage over different periods in included single-arm dose-escalation studies

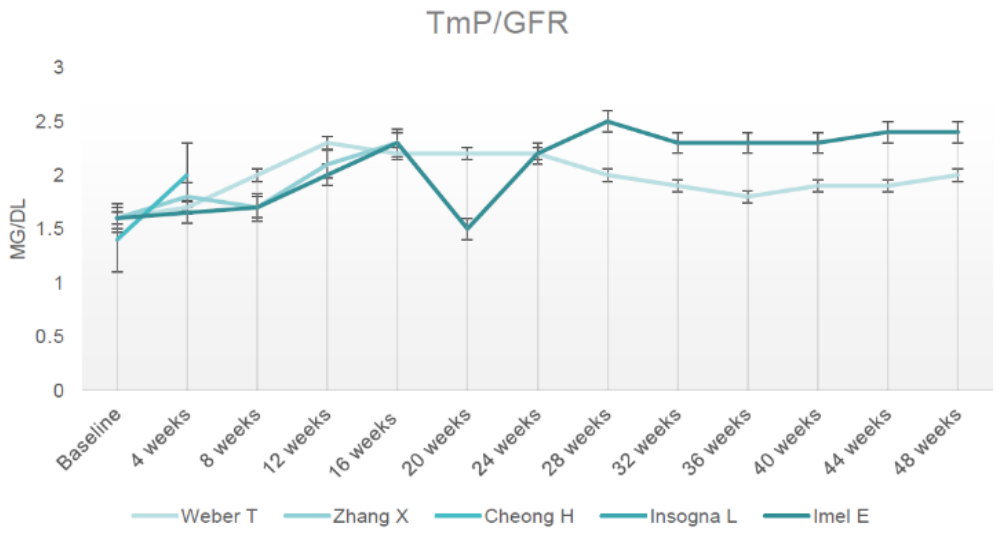

Figure 3: Changes in TmP/GFR levels with variable Burosumab dosage over different periods in included single-arm dose-escalation studies

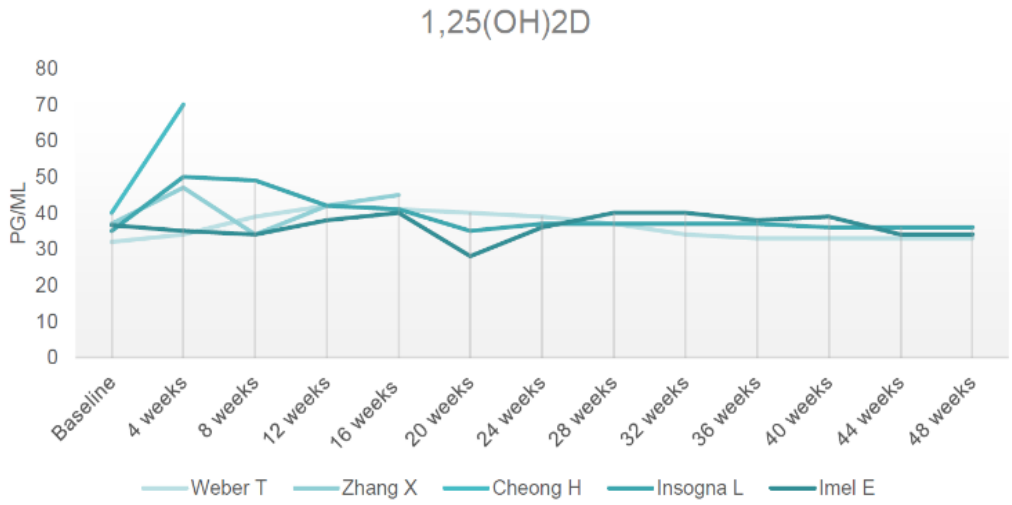

Figure 4: Changes in 1,25(OH)2D levels with variable Burosumab dosage over different time periods in included single-arm dose-escalation studies

Safety: Burosumab was generally well tolerated across participants of all included studies as no study reported deaths or adverse effects (AE) that may have led to the discontinuation of the study. Portale A did not report any adverse effects the second time since all the details were mentioned in the 24-week RCT by Insogna and associates [18]. The remaining six researches described a heterogeneous cluster of mild AEs while only one research [25] included serious AEs. Among the mild to moderate AEs, the most common AE was the injection site urticarial/reaction [18, 25]. Other AEs included nausea, headache, back pain, extremity pain, dizziness, sinusitis, nasopharyngitis, pyrexia, diarrhea, abnormal white blood cell count, restless leg syndrome, and dysgeusia. Insogna and others [18] reported hyperphosphatemia in 5.9% of subjects in the treatment group as compared to 0.0% in the control group. Even though it is a mild but clinically significant effect with regards to the pharmacodynamics of Burosumab. In the research conducted, an increase in nephrocalcinosis was not observed in renal ultrasound from baseline to the end of treatment for any subject [27]. However, five subjects experienced ectopic mineralization treatment-emergent adverse effects (TEAEs). Two of these had mild nephrolithiasis and one of them already had a history of nephrolithiasis.

Discussion

We conducted a systematic review assessing the efficacy and safety of Burosumab in adults diagnosed with XLH. After thorough contemplation of various clinical trials, it was found that Burosumab was indeed successful in sustaining higher levels of serum phosphate throughout the treatment. It was also shown to improve ambulation and proved to be effective in ameliorating debilitating effects of the disease; thereby enhancing overall quality of life. Additionally, it was observed that Burosumab favorably had minimal adverse effects throughout the follow-up period in most studies which conferred its pharmacovigilance. However, considering that most of the clinical trials were not placebo-controlled, the need for more randomized clinical trials with larger population sizes persists. The comparative analysis of primary outcomes in our systematic review suggests that Burosumab significantly improved serum phosphate, serum 1,25(OH)2D, and TmP/GFR concentrations, which is majorly consistent with the findings of the existing literature [31-33]. A study collectively evaluated Burosumab to the conventional therapy (Vitamin D and Phosphate analogs) and reported that Burosumab had more vigilance in trapping FGF-23 and improving the primary outcomes than the conventional therapy. Although the data supporting its efficacy in adults were limited, it was found that Burosumab not only sustained serum phosphate levels but also improved rickets-related skeletal deformities in children. However, in the context of adults, no considerable improvement was reported in regard to enthesopathy, osteoarthritis, osteomalacia, and fractures [34]. On the contrary, one of our included RCTs, Insogna and others [25], showed enhancement in makers of bone remodeling indicators; osteoid volume/bone volume (-54.0%), osteoid thickness (-32.0%), osteoid surface/bone surface (-26.0%), and a substantial decrease in mineralization lag time (-83.0%) [34]. Indicating improvement in osteomalacia-related histomorphometric measures at week 48. Also, documented complete recovery of four patient-reported pseudofractures.

Secondary patient-reported outcomes; WOMAC and BPI-SF used to determine improvement in mobility have improved throughout all the clinical trials. Similarly, a review done by Schindeler and others [33] assented with our findings, reporting considerable improvement in ambulatory functions not only in adults but in children as well compared to conventional therapy. A substantial increase in Radiographic Global Impression score (RGI) and Thacher rickets severity score at 40 weeks was observed, in one of the included RCTs. Moreover, a substantial improvement in the 6-minute walk test was noted in children, contrary to our included RCT, Insogna and associates [18] in adults, showing no significant improvement compared to placebo [35]. So far multiple clinical trials have been conducted with varying periods and quantity of doses. In our systematic review, it was shown in multiple-dose escalation studies; Zhang et al. [24] and Weber and others. [26] TmP/GFR, serum phosphate, and serum 1,25(OH)2D increased after the first few doses but declined back to baseline after a certain period. This pattern shows that an optimum effective period for Burosumab has not yet been discovered. Furthermore, this could be inferred that long-term usage does not transcribe to augmentation of its efficacy; as recorded, whilst Burosumab increases phosphate levels it concurrently diminishes serum 1,25(OH)2D concentration which could hinder physiological calcium-phosphate homeostasis in the longer run. In regard to research by Imel E, it was also pointed out that a lapse exists in the development of treatment regimens for a systematic transition from adolescence to adulthood for patients in need of life-long treatment [36].

Burosumab is a Food and Drug Authority (FDA) approved drug for the treatment of XLH [38]. Nevertheless, its limitations in implication on the general population are noteworthy. To begin with, Burosumab being a monoclonal antibody is supremely expensive which subsequently designates it as an unattainable entity, also, exacerbating the socioeconomic disparity among the deserving subjects. In addition, it is informed by Canadian drug regulatory authorities that an amount of approximately $1,119,456 is required to treat adults with XLH which means that affordability of treatment through a lifetime would be nearly impossible [37]. Furthermore, due to the

potential adverse effects of Burosumab on the physiological process of the body, it requires constant monitoring and therefore can only be given in clinical settings. This will eventually raise the cost and decrease the ease with which a prospective beneficial medicine can be administered.

Nephrolithiasis is the term that is used to describe calculi which are formed within the kidney and are most commonly referred to as 'kidney stones. Most patients that are diagnosed with nephrolithiasis have calcium stone formation that consists of calcium oxalate or calcium phosphate while other types may also include struvite, uric acid, and cysteine [38] It is important to consider that nephrolithiasis and nephrocalcinosis are both renal calcification disorders but the localization of calculi largely differs. In nephrocalcinosis, calcium deposition is within the renal parenchyma whereas in nephrolithiasis, it is mainly within the collecting system [39]. Hyperphosphaturia and subsequent hypophosphatemia are both independent risk factors in the development of renal calcification and are specifically seen in XLH which exposes patients to the risk of nephrocalcinosis and nephrolithiasis [40]. Even though the prevalence of nephrocalcinosis is more common [41]. Alongside the mutation in the FGF23 gene, the conventional therapies used to treat XLH such as calcitriol and phosphate analogs also cause hypercalciuria and thus contribute to a declining kidney function [29, 42].

Research suggests that in contrast to conventional therapies, Burosumab has proven to be a novel treatment since it reduces the underlying renal phosphate wasting and has not been linked with renal complications [43]. Weber T however reported the incidence of nephrolithiasis as a TEAE in three subjects which pointed towards the possible complications of Burosumab therapy that require monitoring and research. A study also concluded that over-treatment with Burosumab may result in hyperphosphatemia which likely poses a risk for nephrocalcinosis [44]. In this review, seven studies reported a series of mild to moderate side effects with no deaths and/or withdrawals from the study which elevates the safety factor of Burosumab. Injection site reactions were the most common AE reported alongside headache, restless leg syndrome, and arthralgia. The treatment groups in the study conducted by Carpenter and associates [19] were divided on the basis of the method of Burosumab administration. 82.0% of AEs were reported in the intravenous group as compared to 83.0% in the subcutaneous group. This goes on to depict that different routes of drug administration have no significant effect on its safety. Furthermore, Insogna et al. [25] was the only study to report serious AEs which were grade three paresthesia and migraine headache. These were not related to Burosumab and were resolved on their own.

The risk of nephrocalcinosis or nephrolithiasis due to Burosumab treatment is still a major impediment in determining its safety. Even though the frequency of nephrocalcinosis is variable in patients with XLH, the further risks that it entails could become a serious cause of concern for healthcare professionals. Nephrocalcinosis may be associated with left ventricular hypertrophy and hypertension [45]. Furthermore, if Burosumab is administered above the required amount, hyperphosphatemia may be observed which manifests through a series of consequential symptoms such as muscle cramps and tetany. This systematic review has a few potential limitations. Firstly, six out of the nine studies included in this review had a sample size of <50 which implies that there is a need for multi-center research with a greater patient population. An increased sample size will be a better predictor of the efficacy of Burosumab and will help in formulating efficacious diagnosing regimens. The effect of Burosumab may also differ in patients across geographical locations and ethnicities thus a diverse patient population will assist in inferring region-specific administration guidelines. Furthermore, two studies did not report any adverse effects that raise ambiguity regarding researcher bias and may not be representative of the true outcomes. It is also important to note that the inducted subjects in the studies that were pooled for analysis had differing baseline characteristics. Certain characteristics, such as serum phosphate, 1,25(OH)2D3 concentration, and TmP/GFR, were disclosed in the studies, shedding light on specific aspects. However, crucial factors like the duration from the onset of diagnosis and details regarding prior therapies were left undisclosed. This lack of

information poses a potential confounding bias, influencing the reliability and comprehensiveness of the study results. Additionally, a more detailed description of the patient demographics, comorbidities, and treatment adherence would have provided a more nuanced understanding of the observed outcomes. Addressing these gaps in future research could enhance the overall validity and applicability of the findings.

Conclusion: Burosumab was proven to be widely effective in regulating debilitating symptoms caused by XLH. Burosumab administration resulted in an overall increase in the serum phosphate concentration which was the primary measure of efficacy. The number of adverse effects noted throughout various clinical trials was minimal and was significantly overridden by its beneficial effects. The present data is obtained from single-arm studies and more placebo-controlled trials are needed to confirm its long-term impact. For a more rigorous analysis of the efficacy of Burosumab, physicians should consider the impact of different dosing regimens on the levels of serum phosphate concentration and should therefore include subsets of varying doses as the primary intervention. It will also be beneficial in devising the transitional dosing regimen from childhood to adolescence and adulthood.

References

1. Francis F, Hennig S, Korn B, Reinhardt R, De Jong PJ, Poustka AJ, et al. A gene (PEX) with homologies to endopeptidases is mutated in patients with X-linked hypophosphatemic rickets. Nature Genetics. 1995; 11(2): 130-136. doi: 10.1038/ng1095-130
2. Gattineni J, Bates CM, Twombley K, Dwarakanath V, Robinson ML, Goetz R, et al. FGF23 decreases renal NaPi-2a and NaPi-2c expression and induces hypophosphatemia in vivo predominantly via FGF receptor 1. American Journal of Physiology-Renal Physiology. 2009; 297(2): F282-F291. doi: 10.1152/ajprenal.90742.2008
3. Hawley S, Shaw N, Delmestri A, Prieto-Alhambra D, Cooper C, Pinedo-Villanueva R, et al. Prevalence and mortality of individuals with X-linked hypophosphatemia: A United Kingdom Real-World Data Analysis. The Journal of Clinical Endocrinology and Metabolism. 2019; 105(3): e871-878. doi: 10.1210/clinem/dgz203
4. Lee JY. The changing face of hypophosphatemic disorders in the FGF-23 era. Pediatric Endocrinology Review. 2013; 10 Suppl 2(0 2): 367-379. PMID: 23858620; PMCID: PMC4170520.
5. Beck-Nielsen SS, Mughal Z, Haffner D, Nilsson O, Levtchenko E, Ariceta G, et al. FGF23 and its role in X-linked hypophosphatemia-related morbidity. Orphanet Journal of Rare Diseases. 2019; 14(1): 58. doi: 10.1186/s13023-019-1014-8
6. Panwar B, Jenny NS, Howard VJ, Wadley VG, Muntner P, Kissela BM, Judd SE, Gutiérrez OM. Fibroblast growth factor 23 and risk of incident stroke in community-living adults. Stroke. 2015; 46(2): 322-328. doi: 10.1161/STROKEAHA.114.007489
7. Verge CF, Lam A, Simpson JM, Cowell CT, Howard NJ, Silink M. Effects of therapy in X-Linked hypophosphatemic rickets. The New England Journal of Medicine. 1991; 325(26): 1843-1848. doi: 10.1056/nejm199112263252604
8. Steele A, González R, Garbalosa JC, Steigbigel K, Grgurich T, Parisi EJ, et al. Osteoarthritis, osteophytes, and enthesophytes affect biomechanical function in adults with x-linked hypophosphatemia. The Journal of Clinical Endocrinology and Metabolism. 2020; 105(4): e1798-814. doi: 10.1210/clinem/dgaa064
9. Orlando G, Bubbear J, Clarke S, Keen R, Roy M, Anilkumar AP, et al. Physical function and physical activity in adults with X-linked hypophosphatemia. Osteoporosis International. 2022; 33(7): 1485-1491. doi: 10.1007/s00198-022-06318-w
10. Harrell RM, Lyles KW, Harrelson JM, Friedman N, Drezner MK. Healing of bone disease in X-linked hypophosphatemic rickets/osteomalacia. Induction and maintenance with phosphorus and calcitriol. Journal of Clinical Investigation. 1985; 75(6): 1858-1868. doi: 10.1172/jci111900
11. Linglart A, Duplan MB, Briot K, Miller C, Esterle L, Guillaume-Czitrom S, et al. Therapeutic management of hypophosphatemic rickets from infancy to adulthood. Endocrine Connections. 2014; 3(1): R13-30. doi: 10.1530/ec-13-0103
12. Mäkitie O, Doria A, Kooh SW, Cole WG, Daneman A, Sochett E. Early treatment improves growth and biochemical and radiographic outcome in X-Linked hypophosphatemic rickets. The Journal of Clinical Endocrinology and Metabolism. 2003; 88(8): 3591-3597. doi: 10.1210/jc.2003-030036

13. Miyamoto J, Koto S, Hasegawa Y. Final height of Japanese patients with X-linked hypophosphatemic rickets: Effect of vitamin d and phosphate therapy. Endocrine Journal. 2000; 47(2): 163-167. doi: 10.1507/endocrj.47.163
14. Katô H, Koga M, Kinoshita Y, Taniguchi Y, Kobayashi H, Fukumoto S, et al. Incidence of complications in 25 adult patients with X-linked hypophosphatemia. The Journal of Clinical Endocrinology and Metabolism. 2021; 106(9): e3682-3692. doi: 10.1210/clinem/dgab282
15. Costa T, Marie PJ, Scriver CR, Cole DEC, Reade TM, B N, et al. X-linked hypophosphatemia: Effect of calcitriol on renal handling of phosphate, serum phosphate, and bone mineralization. The Journal of Clinical Endocrinology and Metabolism. 1981; 52(3): 463-472. doi: 10.1210/jcem-52-3-463
16. Dahir K, Roberts MS, Krolczyk S, Simmons JH. X-Linked Hypophosphatemia: A new era in management. Journal of the Endocrine Society. 2020; 4(12): bvaa151. doi: 10.1210/jendso/bvaa151
17. Takkouche B, Norman G. PRISMA Statement. Epidemiology. 2011; 22(1): 128. doi: 10.1097/ede.0b013e318 1fe7999
18. Insogna K, Briot K, Imel EA, Kamenicky P, Ruppe MD, Portale AA, et al. A randomized, double-blind, placebo-controlled, phase 3 trial evaluating the efficacy of burosumab, an anti-FGF23 antibody, in adults with X-linked hypophosphatemia: Week 24 primary analysis. Journal of Bone and Mineral Research. 2018; 33(8): 1383-1393. doi: 10.1002/jbmr.3475
19. Carpenter TO, Imel EA, Ruppe MD, Weber TJ, Klausner MA, Wooddell MM, et al. Randomized trial of the anti-FGF23 antibody KRN23 in X-linked hypophosphatemia. Journal of Clinical Investigation. 2014; 124(4): 1587-1597. doi: 10.1172/jci72829
20. Portale AA, Carpenter TO, Brandi ML, Briot K, Cheong HI, Cohen-Solal M, et al. Continued beneficial effects of burosumab in adults with X-linked hypophosphatemia: Results from a 24-Week treatment continuation period after a 24-week double-blind placebo-controlled period. Calcified Tissue International. 2019; 105(3): 271-284. doi: 10.1007/s00223-019-00568-3
21. Weber TJ, Imel EA, Carpenter TO, Peacock M, Portale AA, Hetzer J, et al. Long-term burosumab administration is safe and effective in adults with X-linked hypophosphatemia. The Journal of Clinical Endocrinology and Metabolism. 2022; 108 (1): 155-165. doi: 10.1210/clinem/dgac518
22. Imel EA, Zhang X, Ruppe MD, Weber TJ, Klausner MA, Ito T, et al. Prolonged correction of serum phosphorus in adults with X-Linked hypophosphatemia using monthly doses of KRN23. The Journal of Clinical Endocrinology and Metabolism. 2015; 100(7): 2565-2573. doi: 10.1210/jc.2015-1551
23. Cheong HI, Yoo HW, Adachi M, Tanaka H, Fujiwara I, Hasegawa Y, et al. First-in-Asian phase I study of the anti-fibroblast growth factor 23 monoclonal antibody, burosumab: Safety and pharmacodynamics in adults with X-linked hypophosphatemia. Journal of Bone and Mineral Research. 2018; 3(2): e10074. doi: 10.1002/jbm4.10074
24. Zhang X, Imel EA, Ruppe MD, Weber TJ, Klausner MA, Ito T, et al. Pharmacokinetics and pharmacodynamics of a human monoclonal anti-FGF23 antibody (KRN23) in the first multiple ascending-dose trial treating adults with X-linked hypophosphatemia. The Journal of Clinical Pharmacology. 2015; 56(2): 176-185. doi: 10.1002/jcph.570
25. Insogna K, Rauch F, Kamenicky P, Ito N, Kubota T, Nakamura A, et al. Burosumab improved histomorphometric measures of osteomalacia in adults with X-linked hypophosphatemia: A phase 3, single-arm, international trial. Journal of Bone and Mineral Research. 2019; 34(12): 2183-2891. doi: 10.1002/jbmr.3843
26. Weber TJ, Imel EA, Carpenter TO, Peacock M, Portale AA, Hetzer J, et al. Long-term Burosumab administration is safe and effective in adults with X-linked hypophosphatemia. The Journal of Clinical Endocrinology and Metabolism. 2019; 34(12): 2183-2191. doi: 10.1210/clinem/dgac518
27. Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The cochrane collaboration's tool for assessing risk of bias in randomized trials. British Medical Journal. 2011; 343: d5928. doi: 10.1136/bmj.d5928
28. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomized and non-randomized studies of health care interventions. Journal of Epidemiology and Community Health. 1998; 52(6): 377-384. doi: 10.1136/jech.52.6.377
29. Imel EA. Burosumab for pediatric X-Linked hypophosphatemia. Current Osteoporosis Reports. 2021; 19(3): 271-277. doi: 10.1007/s11914-021-00669-9
30. Yuasa T, Toyokawa K, Oda N, Muta Y, Yokomizo H, Fukumoto S, et al. Combined treatment by burosumab and a calcimimetic can ameliorate hypophosphatemia due to excessive actions of FGF23 and PTH in adult XLH with tertiary hyperparathyroidism: A case report. Frontiers in Endocrinology. 2022; 13. doi: 10.3389/fendo.2022. 1004624
31. Imel EA. Burosumab for pediatric X-Linked hypophosphatemia. Current Osteoporosis Reports. 2021; 19(3): 271-277. doi: 10.1007/s11914-021-00669-9

32. Insogna K, Rauch F, Kamenicky P, Ito N, Kubota T, Nakamura A, et al. Burosumab improved histomorphometric measures of osteomalacia in adults with X-linked hypophosphatemia: A phase 3, single-arm, international trial. Journal of Bone and Mineral Research. 2019; 34(12): 2183-2191. doi: 10.1002/jbmr.3843
33. Schindeler A, Biggin A, Munns CF. Clinical evidence for the benefits of Burosumab therapy for X-Linked hypophosphatemia (XLH) and other conditions in adults and children. Frontiers in Endocrinology. 2020; 11. doi: 10.3389/fendo.2020.00338
34. Insogna K, Briot K, Imel EA, Kamenicky P, Ruppe MD, Portale AA, et al. A randomized, double-blind, placebo-controlled, phase 3 trial evaluating the efficacy of burosumab, an anti-FGF23 antibody, in adults with X-linked hypophosphatemia: Week 24 primary analysis. Journal of Bone and Mineral Research. 2018; 33(8): 1383-1393. doi: 10.1002/jbmr.3475
35. Lamb YN. Burosumab: First global approval. Drugs. 2018; 78(6):707-714. doi: 10.1007/s40265-018-0905-7
36. Nojaba L, Guzman N. Nephrolithiasis (Kidney Stones) (Archived). 2023. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; PMID: 32644653.
37. Boyce AM, Shawker TH, Hill S, Choyke PL, Hill MC, James RL, et al. Ultrasound is superior to computed tomography for assessment of medullary nephrocalcinosis in hypoparathyroidism. The Journal of Clinical Endocrinology and Metabolism. 2013; 98(3): 989-994. doi: 10.1210/jc.2012-2747
38. Prié D, Friedlander G. Genetic disorders of renal phosphate transport. The New England Journal of Medicine. 2010; 362 (25): 2399-2409. doi: 10.1056/nejmra0904186
39. Cheidde L, Ajzen SA, Langen CHT, Christophalo D, Heilberg IP. A critical appraisal of the radiological evaluation of nephrocalcinosis. Nephron Clinical Practice. 2007; 106(3): c119-124. doi: 10.1159/000102999
40. Letavernier E, Daudon M. Vitamin D, hypercalciuria and kidney stones. Nutrients. 2018; 10(3): 366. doi: 10.3390/nu10030366
41. Reusz G, Hoyer PF, Lucas M, Krohn HP, Ehrich JH, Brodehl J. X-linked hypophosphatemia: treatment, height gain, and nephrocalcinosis. Archives of Disease in Childhood. 1990; 65(10): 1125-1128. doi: 10.1136/adc.65.10.1125
42. Laurent M, De Schepper J, Trouet D, Godefroid N, Boros E, Heinrichs C, et al. Consensus recommendations for the diagnosis and management of X-Linked hypophosphatemia in Belgium. Frontiers in Endocrinology. 2021; 12. doi: 10.3389/fendo.2021.641543
43. Trombetti A, Al-Daghri N, Brandi ML, Cannata-Andía JB, Cavalier E, Chandran M, et al. Interdisciplinary management of FGF23-related phosphate wasting syndromes: A consensus statement on the evaluation, diagnosis and care of patients with X-linked hypophosphatemia. Nature Reviews Endocrinology. 2022; 18(6): 366-384. doi: 10.1038/s41574-022-00662-x
44. Nakamura Y, Takagi M, Takeda R, Miyai K, Hasegawa Y. Hypertension is a characteristic complication of X-linked hypophosphatemia. Endocrine Journal. 2017; 64(3): 283-289. doi: 10.1507/endocrj.ej16-0199
45. Testelli MR, Pilz CG. Massive calcification of the myocardium. The American Journal of Cardiology. 1964; 407-414. doi: 10.1016/0002-9149(64)90086-4

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ATTACHED SUPPLEMENTARY

Studies	D1	D2	D3	D4	D5	Overall
Insogna L, 2018	⊕	⊕	⊕	⊕	⊕	⊕
Portale A	⊖	⊕	⊕	⊕	⊕	●
Carpenter T	⊕	⊕	⊕	⊕	⊕	⊕

Note: D1: Randomization Process D2: Deviation fro the intended interventions D3: Missing outcome data D4: Measurement of outcomes D5: Selection of the reported results

⊕ Low Risk

⊖ High Risk

● Some Concerns

سلامة وفعالية بوروسوماب لدى مرضى نقص فوسفات الدم المرتبط بالكروموسوم X: مراجعة منهجية

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ملخص: نقص فوسفات الدم المرتبط بالكروموسوم X هو اضطراب وراثي نادر ناتج عن طفرة تؤدي إلى فقدان الوظيفة في الجين المنظم للفوسفات، وهو مشابه لإنزيمات الببتيداز الداخلية على الكروموسوم X. يتميز بتشوهات هيكلية مبكرة، ونقص فوسفات الدم، وارتفاع مستويات عامل نمو الخلايا الليفية 23. تؤدي الطفرات التالية إلى كسور متكررة، وهشاشة العظام، وتيبس المفاصل، وانخفاض متوسط العمر المتوقع. يُعتبر بوروسوماب، وهو جسم مضاد وحيد النسيلة بشري، إنجازًا كبيرًا في علاج نقص فوسفات الدم المرتبط بالكروموسوم X. تم البحث في MEDLINE، ومكتبة كوكرين، وCENTRAL، وGoogle Scholar، وclinictrials.gov منذ البداية وحتى 3 مارس 2025. بشكل عام، تم تحديد ثماني تجارب سريرية تبحث في فعالية وسلامة بوروسوماب لدى مرضى نقص فوسفات الدم المرتبط بالكروموسوم X باستخدام إرشادات PRISMA. من بينها تجربتان عشوائيتان محكومة أظهرتا زيادة كبيرة في فوسفات المصل. تشير النتائج إلى تحسن كبير في مستويات المؤشرات الكيميائية الحيوية الرئيسية؛ تركيز الفوسفات في المصل، وإعادة الامتصاص الأنبوبي الأقصى للفوسفات إلى الترشيح الكبيبي، وفيتامين د 1,25 ثنائي هيدروكسي بعد استخدام بوروسوماب. أفادت الدراسات الخمس الأخرى أحادية الذراع بعدم استقرار مستويات الفوسفات في المصل مع تباين في نظام الجرعات. علاوة على ذلك، تحسنت النتائج الأولية الأخرى؛ تركيز فيتامين د 1.25 ثنائي هيدروكسي، والكالسيوم في المصل، وإعادة الامتصاص الأنبوبي الأقصى للفوسفات إلى الترشيح الكبيبي بشكل ملحوظ. أشارت النتائج الثانوية التي قيّمت آلام العظام والمشي إلى درجات أقل في اختبار الألم الموجز ومؤشر التهاب المفاصل لجامعتي غرب أونتاريو وماكماستر. كان بوروسوماب جيد التحمل من قبل جميع المشاركين، مع الإبلاغ فقط عن آثار جانبية خفيفة إلى متوسطة. تشير النتائج إلى تحسن كبير في مستويات العلامات البيوكيميائية الرئيسية؛ تركيز الفوسفات في المصل، وإعادة الامتصاص الأنبوبي الأقصى للفوسفات إلى الترشيح الكبيبي، وفيتامين د 1.25 ثنائي هيدروكسي بعد استخدام بوروسوماب. تم الإبلاغ عن انخفاض في مستوى الألم والتيبس في المفاصل من خلال اختبار الألم الموجز ومؤشر التهاب المفاصل لجامعتي غرب أونتاريو وماكماستر في معظم الدراسات. لقد تم تحمل بوروسوماب بشكل جيد من قبل المشاركين في جميع الدراسات المشمولة.