EU Clinical Trials Register

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Home & Search | Joining a trial | Contacts | About

Clinical trials

The European Union Clinical Trials Register allows you to search for protocol and results information on:

- interventional clinical trials that are conducted in the European Union (EU) and the European Economic Area (EEA);
- clinical trials conducted outside the EU / EEA that are linked to European paediatric-medicine development.

Learn more about the EU Clinical Trials Register including the source of the information and the legal basis.

The EU Clinical Trials Register currently displays **23180** clinical trials with a EudraCT protocol, of which **3069** are clinical trials conducted with subjects less than 18 years old.
The register also displays information on **17724** older paediatric trials (in scope of Article 45 of the Paediatric Regulation (EC) No 1901/2006).

Please enter search term... X Search

Examples: Cancer AND drug name. Pneumonia AND sponsor name.
How to search [pdf]

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< Back to search results

Summary	
EudraCT Number:	2013-004137-32
Sponsor's Protocol Code Number:	111-202
National Competent Authority:	UK - MHRA
Clinical Trial Type:	EEA CTA
Trial Status:	Ongoing
Date on which this record was first entered in the EudraCT database:	2014-02-17
Trial results	

Index

A. Protocol Information		
A.1	Member State Concerned	UK - MHRA
A.2	EudraCT number	2013-004137-32
A.3	Full title of the trial	A Phase 2, Open-label, Sequential Cohort Dose-escalation Study of BMN 111 in Children with Achondroplasia
A.3.1	Title of the trial for lay people, in easily understood, i.e. non-technical, language	A Study to Evaluate Safety, Tolerability, and Efficacy of BMN 111 in Children with Achondroplasia
A.4.1	Sponsor's protocol code number	111-202
A.7	Trial is part of a Paediatric Investigation Plan	No
A.8	EMA Decision number of Paediatric Investigation Plan	

B. Sponsor Information		
B.Sponsor: 1		
B.1.1	Name of Sponsor	BioMarin Pharmaceutical Inc.
B.1.3.4	Country	United States
B.3.1 and B.3.2	Status of the sponsor	Commercial
B.4 Source(s) of Monetary or Material Support for the clinical trial:		
B.4.1	Name of organisation providing support	BioMarin Pharmaceutical Inc.
B.4.2	Country	United States
B.5 Contact point designated by the sponsor for further information on the trial		
B.5.1	Name of organisation	BioMarin Pharmaceutical Inc.
B.5.2	Functional name of contact point	Clinical Trials Information
B.5.3	Address:	
B.5.3.1	Street Address	105 Digital Drive
B.5.3.2	Town/ city	Novato

B.5.3.3	Post code	94949
B.5.3.4	Country	United States
B.5.6	E-mail	clinicaltrials@bmrn.com

D. IMP Identification

D.IMP: 1		
D.1.2 and D.1.3	IMP Role	Test
D.2	Status of the IMP to be used in the clinical trial	
D.2.1	IMP to be used in the trial has a marketing authorisation	No
D.2.5	The IMP has been designated in this indication as an orphan drug in the Community	Yes
D.2.5.1	Orphan drug designation number	EU/3/12/1094
D.3 Description of the IMP		
D.3.1	Product name	modified recombinant human C-type natriuretic peptide
D.3.2	Product code	BMN 111
D.3.4	Pharmaceutical form	Lyophilisate for solution for injection
D.3.4.1	Specific paediatric formulation	Yes
D.3.7	Routes of administration for this IMP	Subcutaneous use
D.3.8 to D.3.10 IMP Identification Details (Active Substances)		
D.3.8	INN - Proposed INN	TBD
D.3.9.2	Current sponsor code	BMN 111
D.3.9.3	Other descriptive name	MODIFIED RHCNP
D.3.9.4	EV Substance Code	SUB120857
D.3.10	Strength	
D.3.10.1	Concentration unit	mg/ml milligram(s)/millilitre
D.3.10.2	Concentration type	range
D.3.10.3	Concentration number	0.2 to 10
D.3.11 The IMP contains an:		
D.3.11.1	Active substance of chemical origin	No
D.3.11.2	Active substance of biological/ biotechnological origin (other than Advanced Therapy IMP (ATIMP)	Yes
	The IMP is a:	
D.3.11.3	Advanced Therapy IMP (ATIMP)	No
D.3.11.3.1	Somatic cell therapy medicinal product	No
D.3.11.3.2	Gene therapy medical product	No
D.3.11.3.3	Tissue Engineered Product	No
D.3.11.3.4	Combination ATIMP (i.e. one involving a medical device)	No
D.3.11.3.5	Committee on Advanced therapies (CAT) has issued a classification for this product	No
D.3.11.4	Combination product that includes a device, but does not involve an Advanced Therapy	No
D.3.11.5	Radiopharmaceutical medicinal product	No
D.3.11.6	Immunological medicinal product (such as vaccine, allergen, immune serum)	No
D.3.11.7	Plasma derived medicinal product	No
D.3.11.8	Extractive medicinal product	No
D.3.11.9	Recombinant medicinal product	Yes
D.3.11.10	Medicinal product containing genetically modified organisms	No
D.3.11.11	Herbal medicinal product	No
D.3.11.12	Homeopathic medicinal product	No
D.3.11.13	Another type of medicinal product	No

D.8 Information on Placebo

E. General Information on the Trial

E.1 Medical condition or disease under investigation		
E.1.1	Medical condition(s) being investigated	achondroplasia
E.1.1.1	Medical condition in easily understood language	dwarfism
E.1.1.2	Therapeutic area	Body processes [G] - Bones and nerves physological processes [G11]
MedDRA Classification		
E.1.2 Medical condition or disease under investigation		
E.1.2	Version	16.1
E.1.2	Level	LLT
E.1.2	Classification code	10000452
E.1.2	Term	Achondroplasia
E.1.2	System Organ Class	100000004850
E.1.3	Condition being studied is a rare disease	Yes
E.2 Objective of the trial		
E.2.1	Main objective of the trial	To evaluate the safety and tolerability of daily SC injections of BMN 111 administered for 6 months
E.2.2	Secondary objectives of the trial	

• To evaluate change in annualized growth velocity, of daily SC injections of BMN 111 administered for 6 months
• To evaluate the changes in growth following daily SC injections of BMN 111 administered for 6 months
• To evaluate changes in body proportions following daily SC injections of BMN 111 administered for 6 months

E.2.3 Trial contains a sub-study: No

E.3 Principal inclusion criteria

• Parent(s) or guardian(s) are willing and able to provide written, signed informed consent after the nature of the study has been explained and prior to performance of any research-related procedure. Also, subjects under the age of 18 are willing and able to provide written assent (if required) after the nature of the study has been explained and prior to performance of any research-related procedure.
• 5 to 14 years old, inclusive at study entry
• Have ACH, documented by clinical grounds and confirmed by genetic testing
• Have at least a 6-month period of pretreatment growth assessment in Study 111-901 immediately before study entry
• Females of childbearing potential must have a negative pregnancy test at the Screening Visit and be willing to have additional pregnancy tests during the study. If sexually active, willing to use an acceptable method of contraception while participating in the study
• Are ambulatory and able to stand without assistance
• Are willing and able to perform all study procedures as physically possible
• Parents or caregivers are willing to administer daily injections to the subjects

E.4 Principal exclusion criteria

• Have hypochondroplasia or short stature condition other than ACH (e.g., trisomy 21, pseudoachondroplasia)
• Have any of the following: Hypothyroidism, Insulin-requiring diabetes mellitus, Autoimmune inflammatory disease, Inflammatory bowel disease, Autonomic neuropathy, Acute illness associated with volume dehydration (e.g., nausea, vomiting, diarrhea)
• Have an unstable condition likely to require surgical intervention during the study (including progressive cervical medullary compression)
• Growth plates have fused
• Have a history of any of the following: Renal insufficiency, Anemia, Baseline systolic blood pressure (BP) < 75 millimeters of mercury (mm Hg) or recurrent symptomatic hypotension (defined as episodes of low BP generally accompanied by symptoms i.e., dizziness, fainting) or recurrent symptomatic orthostatic hypotension, Cardiac or vascular disease, including the following: Cardiac dysfunction (abnormal echocardiogram [ECHO] including left ventricle [LV] mass) at Screening Visit, Hypertrophic cardiomyopathy, Congenital heart disease with ongoing cardiac dysfunction, Cerebrovascular disease, aortic insufficiency, Clinically significant atrial or ventricular arrhythmias
• Have an ECG showing any of the following: Right or left atrial enlargement or ventricular hypertrophy, PR interval > 200 msec, QRS interval > 110 msec, Corrected QTc > 440 msec, Second- or third-degree atrioventricular block
• Demonstrate vitamin D deficiency (i.e., concentration of 25-hydroxy-vitamin D in the blood serum occurs at 12 ng/mL or less)
• Require any investigational agent prior to completion of study period
• Have received another investigational product or investigational medical device within 30 days before the Screening Visit
• Have used any other investigational product or investigational medical device for the treatment of ACH or short stature
• Current treatment with antihypertensive medications, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, diuretics, beta-blockers, calcium-channel blockers, cardiac glycosides, systemic anticholinergic agents, any medication that may impair or enhance compensatory tachycardia, drugs known to alter renal function
• Have been treated with growth hormone, insulin-like growth factor 1 (IGF-1), or anabolic steroids in the previous 6 months or long-term treatment (> 3 months) at any time
• Have had regular long-term treatment (> 1 month) with oral corticosteroids (low-dose ongoing inhaled steroid for asthma is acceptable)
• Concomitant medication that prolongs the QT/QTc interval within 14 days or 5 half-lives, whichever is longer, before the Screening Visit
• Unwilling to temporarily discontinue CPAP use for 2 days prior to Screening Visit if applicable
• Pregnant or breastfeeding at the Screening Visit or planning to become pregnant (self or partner) at any time during the study
• Have had bone-related surgery or expected to have bone-related surgery during the study period. Subjects with previous bone-related surgery may enroll if surgery occurred at least 18 months prior to the study and healing is complete without sequelae.
• Have aspartate aminotransferase (AST) or alanine aminotransferase (ALT) at least 3x upper limit of normal (ULN) or total bilirubin at least 2x ULN
• Have known hypersensitivity to BMN 111 or its excipients
• Have a condition or circumstance that, in the view of the Investigator, places the subject at high risk for poor treatment compliance or for not completing the study
• Concurrent disease or condition that, in the view of the Investigator, would interfere with study participation or safety evaluations, or would predispose the subject to hypotension (such as recent gastroenteritis or dehydration for any reason)

E.5 End points

E.5.1 Primary end point(s)

Safety will be evaluated by the incidence of AEs, SAEs, and clinically significant changes in vital signs, ECG results, imaging, echocardiographic results, physical examination, anti-BMN 111 immunogenicity assessments, and laboratory test results (urinalysis, chemistry, hematology). Additionally, imaging, biomarker, and physical measurement data, including a flexion-extension measure of elbow joint range of motion measured with goniometer, will be utilized for safety-related reviews and analysis.

E.5.1.1 Timepoint(s) of evaluation of this end point

AEs, SAEs, vital signs - Screening, Days 1, 2, 3, 4, 15, 10, 22, 29, 43, 85, 127, 183, 208, Early Term
ECG - Screening, Days 10, 29, 85, 183, 208, Early Term
ECHO - Screening, Day 183
Anti-BMN 111 immunogenicity - Days 1, 10, 29, 85, 183, 208, Early Term
Laboratory tests - Screening, Days 1, 4, 10, 15, 29, 43, 85, 127, 183, 208, Early Term
Anthropometric measurements - Screening, Days 43, 85, 127, 183
Imaging:
-QCT of forearm and tibia - Screening, Days 43, 183
-Bone age x-ray (wrist) and lateral lumbar spine x-ray, and anterior-posterior x-ray of spine - Screening and Day 183

E.5.2 Secondary end point(s)

Efficacy will be assessed by change from baseline in height growth velocity (annualized to cm/year), absolute growth, subject growth compared with ACH and non-ACH standardized pediatric growth curves, and

		change in body proportions. These changes will be assessed by anthropometric measurements and measurement ratios.
E.5.2.1	Timepoint(s) of evaluation of this end point	Screening, Days 43, 85, 127, and 183
E.6 and E.7 Scope of the trial		
E.6	Scope of the trial	
E.6.1	Diagnosis	No
E.6.2	Prophylaxis	No
E.6.3	Therapy	Yes
E.6.4	Safety	Yes
E.6.5	Efficacy	Yes
E.6.6	Pharmacokinetic	Yes
E.6.7	Pharmacodynamic	Yes
E.6.8	Bioequivalence	No
E.6.9	Dose response	Yes
E.6.10	Pharmacogenetic	No
E.6.11	Pharmacogenomic	No
E.6.12	Pharmacoeconomic	No
E.6.13	Others	Yes
E.6.13.1	Other scope of the trial description	tolerability
E.7	Trial type and phase	
E.7.1	Human pharmacology (Phase I)	No
E.7.1.1	First administration to humans	No
E.7.1.2	Bioequivalence study	No
E.7.1.3	Other	No
E.7.1.3.1	Other trial type description	
E.7.2	Therapeutic exploratory (Phase II)	Yes
E.7.3	Therapeutic confirmatory (Phase III)	No
E.7.4	Therapeutic use (Phase IV)	No
E.8 Design of the trial		
E.8.1	Controlled	No
E.8.1.1	Randomised	No
E.8.1.2	Open	Yes
E.8.1.3	Single blind	No
E.8.1.4	Double blind	No
E.8.1.5	Parallel group	No
E.8.1.6	Cross over	No
E.8.1.7	Other	Yes
E.8.1.7.1	Other trial design description	sequential cohort dose-escalation
E.8.2	Comparator of controlled trial	
E.8.2.1	Other medicinal product(s)	No
E.8.2.2	Placebo	No
E.8.2.3	Other	No
E.8.3	The trial involves single site in the Member State concerned	Yes
E.8.4	The trial involves multiple sites in the Member State concerned	No
E.8.5	The trial involves multiple Member States	Yes
E.8.5.1	Number of sites anticipated in the EEA	2
E.8.6 Trial involving sites outside the EEA		
E.8.6.1	Trial being conducted both within and outside the EEA	Yes
E.8.6.2	Trial being conducted completely outside of the EEA	No
E.8.6.3	If E.8.6.1 or E.8.6.2 are Yes, specify the regions in which trial sites are planned	Australia France United Kingdom United States
E.8.7	Trial has a data monitoring committee	Yes
E.8.8	Definition of the end of the trial and justification where it is not the last visit of the last subject undergoing the trial	LVLS
E.8.9 Initial estimate of the duration of the trial		
E.8.9.1	In the Member State concerned years	
E.8.9.1	In the Member State concerned months	7
E.8.9.1	In the Member State concerned days	
E.8.9.2	In all countries concerned by the trial months	7

F. Population of Trial Subjects

F.1 Age Range		
F.1.1	Trial has subjects under 18	Yes
F.1.1	Number of subjects for this age range:	24
F.1.1.1	In Utero	No
F.1.1.2	Preterm newborn infants (up to gestational age <	No

	37 weeks)	
F.1.1.3	Newborns (0-27 days)	No
F.1.1.4	Infants and toddlers (28 days-23 months)	No
F.1.1.5	Children (2-11years)	Yes
F.1.1.5.1	Number of subjects for this age range:	23
F.1.1.6	Adolescents (12-17 years)	Yes
F.1.1.6.1	Number of subjects for this age range:	1
F.1.2	Adults (18-64 years)	No
F.1.3	Elderly (>=65 years)	No
F.2 Gender		
F.2.1	Female	Yes
F.2.2	Male	Yes
F.3 Group of trial subjects		
F.3.1	Healthy volunteers	No
F.3.2	Patients	Yes
F.3.3	Specific vulnerable populations	Yes
F.3.3.1	Women of childbearing potential not using contraception	No
F.3.3.2	Women of child-bearing potential using contraception	Yes
F.3.3.3	Pregnant women	No
F.3.3.4	Nursing women	No
F.3.3.5	Emergency situation	No
F.3.3.6	Subjects incapable of giving consent personally	No
F.3.3.7	Others	No
F.4 Planned number of subjects to be included		
F.4.1	In the member state	5
F.4.2	For a multinational trial	
F.4.2.1	In the EEA	10
F.4.2.2	In the whole clinical trial	24
F.5	Plans for treatment or care after the subject has ended the participation in the trial (if it is different from the expected normal treatment of that condition)	In order to assess safety and efficacy of BMN 111 over the longer term, subjects may be eligible to continue receiving BMN 111 in an open-label extension study after completing 6 months of treatment in the initial study.

G. Investigator Networks to be involved in the Trial

N. Review by the Competent Authority or Ethics Committee in the country concerned

N.	Competent Authority Decision	Authorised
N.	Date of Competent Authority Decision	2014-02-14
N.	Ethics Committee Opinion of the trial application	Favourable
N.	Ethics Committee Opinion: Reason(s) for unfavourable opinion	
N.	Date of Ethics Committee Opinion	2014-04-03

P. End of Trial

P.	End of Trial Status	Ongoing