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Dose-ranging study of AVI-4658 to induce dystrophin expression in selected duchenne muscular dystrophy (DMD) patients

Submission date
23/04/2010

Recruitment status
No longer recruiting

Registration date
23/04/2010

Overall study status
Completed

Last Edited
10/09/2019

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.mdex.org.uk

Contact information

Type(s)
Scientific

Contact name
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Institute of Child Health
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00844597

Secondary identifying numbers
6420

Study information

Scientific Title
Dose-ranging study of AVI-4658 to induce dystrophin expression in selected duchenne muscular dystrophy (DMD) patients : a non-randomised interventional screening treatment trial

Acronym
AVI-4658

Study objectives
AVI BioPharma is developing AVI-4658, a phosphorodiamidate morpholino oligomer (PMO), for administration to patients with duchenne muscular dystrophy (DMD). It is believed that treatment with AVI-4658 will increase production of a truncated form of dystrophin, such as seen in patients with Becker muscular dystrophy (BMD), and consequently result in improved muscle function and overall quality of life for patients with DMD.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Gene Therapy Advisory Committee (GTAC) approved on the 5th December 2008 (ref: GTAC157)

Study design
Non-randomised interventional screening treatment trial

Primary study design
Interventional

Secondary study design
Non randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Screening

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Medicines for Children Research Network; Subtopic: All Diagnoses; Disease: All Diseases

Interventions
1. Muscle biopsy: dystrophin production will be determined by comparing results of immunohistological staining and Western blots of muscle homogenates between baseline and

after the completion of 12 weekly doses of AVI-4658 (at week 14)
2. Quantitive Muscle Testing (QMT) (i.e., myometry assessments): obtain isometric strength assessments using a hand held myometer. This assessment entails measure of force of right and left knee extension, right and left knee flexion, right and left elbow flexion

Follow up length: 3 months.

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
AVI-4658

Primary outcome measure
Safety of escalating doses of AVI-4658, measured throughout the trial

Secondary outcome measures
1. Pharmacokinetics, measured at 1st, 6th and 12th dosing
2. Efficacy (dystrophin expression) of AVI-4658 at week 14

Overall study start date
01/02/2009

Completion date
30/06/2010

Eligibility

Key inclusion criteria
Candidates will be included in the study only if all of the following conditions are met:
1. Has provided written informed assent (as required by IRB) and parents/guardians have provided written informed consent
2. Has an out of frame deletion(s) that could be corrected by skipping exon 51 (45 - 50; 47 - 50; 48 - 50; 49 - 50; 50; 52), based on DNA sequencing data
3. Is male and between the ages of greater than or equal to 5 years and less than or equal to 15 years
4. Has a muscle biopsy analysis showing less than 5% revertant fibers present
5. DNA sequencing of exon 51 confirms that no DNA polymorphisms occur that could compromise PMO duplex formation or there is confirmation of in vitro dystrophin production after AVI-4658 exposure to fibroblast or myoblast in vitro cultures
6. Intact right and left bicep muscles or alternative arm muscle group
7. Is able to walk independently
8. Has a forced vital capacity (FVC) greater than or equal to 50% of predicted and does not require night time ventilatory support or supplemental oxygen
9. Receives the standard of care for DMD as recommended by the Muscular Dystrophy Association or the United Kingdom Board of Paediatrics
10. The parent(s) or legal guardian and Subject have undergone counselling about the

expectations of this protocol and agree to participate
11. The parent(s) or legal guardian and Subject intend to comply with all study evaluations and return for all study activities

Participant type(s)
Patient

Age group
Child

Sex
Male

Target number of participants
Planned sample size: 18; UK sample size: 18

Total final enrolment
19

Key exclusion criteria
Candidates will be excluded from the study if any of the following conditions are present:
1. A DNA polymorphism within exon 51 that may compromise PMO duplex formation
2. Antibodies to dystrophin
3. Lacks intact right and left bicep muscles or alternative arm muscle group
4. A calculated creatinine clearance less than 70% of predicted normal for age based on the Cockroft and Gault Formula (See the Clinical Study Operations Manual)
5. A left ventricular ejection fraction (LVEF) of less than 35% and/or fractional shortening less than 30% based on echocardiography (ECHO) prior to or during screening
6. A history of respiratory insufficiency as defined by a need for intermittent, night time, or continuous supplemental oxygen
7. A severe cognitive dysfunction rendering the potential Subject unable to understand and comply with the study protocol
8. Any immune deficiency or autoimmune disease
9. A known bleeding disorder or has received chronic anticoagulant treatment within three months of study entry
10. Receipt of pharmacologic treatment, apart from corticosteroids, that might affect muscle strength or function within 8 weeks of study entry (viz., growth hormone, anabolic steroids, and /or creatine protein supplementation)
11. Surgery within 3 months of study entry or planned for anytime during the duration of the study
12. Another clinically significant illness at time of study entry
13. Subject or parent has active psychiatric disorder, has adverse psychosocial circumstances, recent significant emotional loss, and/or history of depressive or anxiety disorder that might interfere with protocol completion or compliance
14. Use of any experimental treatments or has participated in any DMD interventional clinical trial within 4 weeks of study entry

Date of first enrolment
01/02/2009

Date of final enrolment

30/06/2010

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Institute of Child Health
London
United Kingdom
WC1N 1EH

Sponsor information

Organisation
AVI Biopharma, Inc (USA)

Sponsor details
3450 Monte Villa Parkway Suite 101
Bothell
United States of America
WA 98021

Sponsor type
Industry

Website
http://www.avibio.com/

ROR
https://ror.org/054f2wp19

Funder(s)

Funder type
Research organisation

Funder Name
MRC Clinical Sciences Centre (UK)

Funder Name
AVI Biopharma, Inc (USA)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	13/08/2011		Yes	No
Basic results			10/09/2019	No	No