

PLUTO: A randomised clinical trial comparing PlasmaLyte fluid to standard care for children receiving a kidney transplant

Submission date 20/12/2019	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered
		<input checked="" type="checkbox"/> Protocol
Registration date 10/01/2020	Overall study status Completed	<input checked="" type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
Last Edited 14/12/2023	Condition category Injury, Occupational Diseases, Poisoning	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

In the first few days after a kidney transplant, many children develop dangerous changes in the amount of salt and water in the bloodstream. This is because doctors give very large volumes of artificial fluids into the veins to keep the new kidney working. If the main salt in the blood (sodium) falls too far, serious problems including brain damage and even death can occur.

Because of this, blood samples are taken every 2-4 hours for the first day after the transplant operation to check sodium levels and change them if necessary.

This research aims to compare the standard fluid used after the transplant operation with an alternative that may reduce dangerous changes in salt (sodium) levels and help the transplanted kidney to work better.

The alternative fluid is called PlasmaLyte. It matches the normal composition of blood more closely than standard fluid. PlasmaLyte is already used in other sick children, including those in intensive care units. Although there are good reasons to believe that PlasmaLyte may be a safer choice of fluid for children after kidney transplant, there is no evidence comparing PlasmaLyte with standard fluid for children.

Who can participate?

Patients aged under 18 years receiving a kidney transplant

What does the study involve?

This research will work out which of the two fluids is better by looking at children's kidney transplants in the UK, half using standard fluid and half using PlasmaLyte. The choice of fluid will be made randomly by a computer. No additional blood samples will be required. Children who participate in the study will continue to have all the usual care that they would otherwise receive.

What are the possible benefits and risks of participating?

This research has the potential to improve the treatment and outcomes of children and young people receiving kidney transplants. Plasma-Lyte may reduce the risk of developing abnormalities in salt (sodium) levels after a transplant operation. Plasma-Lyte may also help the transplanted kidney to work better, but at present, we do not know if this will be the case. The

PLUTO study will help to find out whether Plasma-Lyte is better than current standard care. There are few risks to taking part in this study (above the risk of kidney transplantation). Abnormal levels of salts and minerals in the bloodstream can be experienced by children and young people receiving any fluid. We do not expect these to be more common with Plasma-Lyte but will monitor all children's blood levels closely to check for this.

Where is the study run from?

1. NHS Blood and Transplant Clinical Trials Unit, UK
2. Belfast City Hospital, UK
3. Birmingham Women's and Children's NHS Foundation Trust, UK
4. University Hospitals Bristol NHS Foundation Trust, UK
5. Great Ormond Street Hospital, UK
6. Guy's and St Thomas' NHS Foundation Trust, UK
7. Leeds Teaching Hospitals NHS Trust, UK
8. Manchester University NHS Foundation Trust, UK
9. The Newcastle Upon Tyne Hospitals NHS Foundation Trust, UK
10. Nottingham University Hospitals NHS Trust, UK

When is the study starting and how long is it expected to run for?
February 2020 to November 2022

Who is funding the study?

National Institute for Health Research (NIHR), UK

Who is the main contact?

Fotini Kaloyirou (public)

PLUTO@nhsbt.nhs.uk

Dr Wesley Hayes (scientific)

wesley.hayes@gosh.nhs.uk

Study website

<https://www.nhsbt.nhs.uk/clinical-trials-unit/current-trials-and-studies/pluto/>

Contact information

Type(s)

Public

Contact name

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ORCID ID

<http://orcid.org/0000-0001-7290-6934>

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Type(s)
Scientific

Contact name
Dr Wesley Hayes

Contact details
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Additional identifiers

EudraCT/CTIS number
2019-003025-22

IRAS number
270431

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
18IA31; CPMS 43031; IRAS 270431

Study information

Scientific Title
PlasmaLyte Usage and assessment of kidney Transplant Outcomes in children: the PLUTO trial

Acronym
PLUTO

Study objectives
To determine whether the incidence of abnormal and potentially dangerous plasma electrolyte levels in paediatric kidney transplant recipients will be different with the use of Plasma-Lyte-148 compared to intravenous fluid with current standard composition

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 20/12/2019, London Central Research Ethics Committee (Health Research Authority, Skipton House, 80 London Road, London, SE1 6LH; +44 (0)207 104 8208; NRESCommittee. London-Central@nhs.net), ref: 19/LO/1866

Study design

Interventional randomized controlled trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Prevention

Participant information sheet

Provided upon request. Please email the PLUTO team at PLUTO@nhsbt.nhs.uk

Health condition(s) or problem(s) studied

Prevention of hyponatremia in children undergoing kidney transplant

Interventions

SCREENING

All paediatric patients awaiting kidney transplantation will be screened for participation in PLUTO. Data will be collected on the Patient Log. Also as part of this study, a Qualitative Sub-Study will be undertaken to find out more about patients/families opinions of the screening and consent process. To facilitate this, all patients/families who are given the study information sheet will also be given a short questionnaire to complete (whether or not they decide to participate).

The screening data will be regularly reviewed by the Trial Management Group, as well as feedback from the process evaluation.

RANDOMISATION

Informed consent will take place during the pre-transplant preparation period, which typically takes several months. This will allow adequate time for patients and families to consider participating in the study. Randomisation will take place on the day of the transplant (after study consent is re-confirmed verbally by a member of the clinical or Research Team).

Participants will be randomised using an online randomisation service, called SealedEnvelope, and given a unique Randomisation Number. The treatment allocation will also be provided and communicated to all relevant members of the clinical care team at that site.

TREATMENT

The study treatment is Plasma-Lyte 148 (+/- 5% glucose). This will be compared to standard intravenous fluid therapy. Standard therapy varies across the participating sites, which will be accounted for in the trial analysis. The fluid will be administered as required throughout the operation and for 72 hours afterwards as per routine clinical care.

FOLLOW-UP OF PARTICIPANTS

Patients will be reviewed as per standard clinical care. Data will be collected for the trial (e.g. results of blood tests taken as part of standard clinical care). A symptom assessment will be carried out once daily (for 3 days) for headaches, nausea, vomiting and seizures. A proportion of the follow-up data will be obtained the routinely collected data (on the UK Transplant Registry, which is held by NHS Blood and Transplant). No additional study visits or blood tests outside routine clinical care will be required for the trial.

Intervention Type

Drug

Phase

Phase IV

Drug/device/biological/vaccine name(s)

Plasma-Lyte 148 & Glucose 5% w/v

Primary outcome measure

Acute hyponatraemia in the first 72 hours post-transplant (defined as plasma sodium concentration < 135mmol/l)

Secondary outcome measures

1. Symptoms of acute hyponatraemia (nausea, vomiting, headache, seizures) within the first 72 hours post-transplant
2. The degree of fluid overload experienced (defined as proportional increase in patient weight between pre-transplant weight and maximum weight in the 72 hours post-transplant weight)
3. Time to discharge from hospital (measured from transplant operation start time ("knife to skin")), measured in days
4. Transplant kidney function at 1, 3, 7 and 90 days (using creatinine-based univariate Schwartz formula(24) to determine eGFR)
5. Other electrolyte abnormalities within the first 72 hours post-transplantation:
 - 5.1. Hypernatraemia (defined as plasma sodium concentration > 145mmol/l)
 - 5.2. Hyperkalaemia (defined as plasma potassium concentration > 5.5mmol/L)
 - 5.3. Hypokalaemia (defined as plasma potassium concentration < 3.5mmol/L)
 - 5.4 Non anion-gap acidosis (defined as plasma bicarbonate < 20mmol/L and anion gap < 20mmol/L)
 - 5.5. Hyperglycaemia (defined as random blood glucose > 5.5 mmol/L)
 - 5.6. Hypomagnesaemia (defined as plasma magnesium concentration < 0.7 mmol/L)
 - 5.7. Hyperchloraemia (defined as plasma chloride concentration > 107mmol/L)
 - 5.8. Excessive rate of reduction in plasma sodium concentration (defined as >1mmol/L/hour averaged over 6 hours)
 - 5.9. Excessive magnitude of reduction in plasma sodium concentration (defined as > 10mmol/L from pre-transplant level)
6. Maximum and minimum systolic blood pressure (normalised to age and height percentile) sustained on 3 repeated values on each day, for 3 days post-transplant
7. Number of changes in intravenous fluid composition and rationale for change within the first 72 hours post-transplant

Overall study start date

01/08/2019

Completion date

17/11/2022

Eligibility

Key inclusion criteria

1. Children expected to be under 18 years of age at the time of transplantation
2. Children undergoing preparation for living or deceased donor kidney only transplantation, or active on the deceased donor transplant waiting list for a kidney only transplant at participating UK paediatric transplant centres either pre-emptively (not currently receiving dialysis) or patients on dialysis

Participant type(s)

Patient

Age group

Child

Upper age limit

18 Years

Sex

Both

Target number of participants

Planned Sample Size: 144; UK Sample Size: 144

Total final enrolment

144

Key exclusion criteria

1. Multi-organ transplant recipients

Date of first enrolment

03/02/2020

Date of final enrolment

09/08/2022

Locations

Countries of recruitment

England

Northern Ireland

United Kingdom

Study participating centre
NHS Blood and Transplant Clinical Trials Unit (lead centre)
Long Road
Cambridge
United Kingdom
CB2 0PT

Study participating centre
Belfast City Hospital
51 Lisburn Road
Belfast
United Kingdom
BT9 7AB

Study participating centre
Birmingham Women's and Children's NHS Foundation Trust
Steelhouse Lane
Birmingham
United Kingdom
B4 6NH

Study participating centre
University Hospitals Bristol NHS Foundation Trust
Trust Headquarters
Marlborough Street
Bristol
United Kingdom
BS1 3NU

Study participating centre
Great Ormond Street Hospital
Great Ormond Street
London
United Kingdom
WC1N 3JH

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
Great Maze Pond

London
United Kingdom
SE1 9RT

Study participating centre

Leeds Teaching Hospitals NHS Trust

St. James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre

Manchester University NHS Foundation Trust

Cobbett House
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre

The Newcastle Upon Tyne Hospitals NHS Foundation Trust

Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Sponsor information

Organisation

Great Ormond Street Hospital for Children NHS Foundation Trust

Sponsor details

Great Ormond St
London
England
United Kingdom

WC1N 3JH
+44 (0)207 905 2271
vanshree.patel@gosh.nhs.uk

Sponsor type

Hospital/treatment centre

Website

<http://www.gosh.nhs.uk/>

ROR

<https://ror.org/03zydm450>

Funder(s)

Funder type

Government

Funder Name

NIHR Central Commissioning Facility (CCF); Grant Codes: NIHR200512

Funder Name

National Institute for Health Research (NIHR) (UK)

Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Planned publication in a high-impact peer-reviewed journal.

Intention to publish date

31/07/2024

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from the PLUTO Trial Manager (PLUTO@nhsbt.nhs.uk) or the PLUTO Chief Investigator Dr Wesley Hayes (wesley.hayes@gosh.nhs.uk).

The type of data: full dataset, anonymised.

When the data will become available and for how long: no later than 18 months after the last participant has been recruited.

By what access criteria data will be shared including with whom: submit a request to the CI/Trial Manager for review by the Sponsor. A full Data Sharing Request form will be required.

For what types of analyses, and by what mechanism: to be agreed before data is shared

Whether consent from participants was obtained: full informed consent obtained

Comments on data anonymisation: data will be anonymised prior to sharing

Any ethical or legal restrictions: none

Any other comments: a contract is mandatory before any data is shared with a third party

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	14/03/2022	25/03/2022	Yes	No
HRA research summary			28/06/2023	No	No
Results article		31/10/2023	05/12/2023	Yes	No
Statistical Analysis Plan	version 1.1	20/12/2022	14/12/2023	No	No