Clinical trial results:
Pharmacokinetics and pharmacogenetics of anticancer drugs in infants and young children

Summary

EudraCT number	2006-002845-36
Trial protocol	GB
Global end of trial date	12 September 2014

Results information

Result version number	v1 (current)
This version publication date	30 March 2019
First version publication date	30 March 2019
Summary attachment (see zip file)	Investigating the pharmacokinetics and dosing of anticancer drugs in infants and young children. (PK 2006 09 Journal of Clinical Oncology Abstract.docx)

Trial information

Trial identification

Sponsor protocol code	PK 2006 09

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00897871
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Newcastle Upon Tyne Hospitals NHS Foundation Trust
Sponsor organisation address	Level 1, Regent Point, Regent Farm Rd, Newcastle upon Tyne, United Kingdom, NE3 3HD
Public contact	Prof. Gareth Veal, Northern Institute for Cancer Research, Newcastle University, 44 01912084332, g.j.veal@newcastle.ac.uk
Scientific contact	Prof. Gareth Veal, Northern Institute for Cancer Research, Newcastle University, 44 01912084332, g.j.veal@newcastle.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 September 2014
Global end of trial reached?	Yes
Global end of trial date	12 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study is designed to :-

•Investigate inter-individual variability in the pharmacokinetics of selected anticancer drugs in infants and children age <2 years on current dosing schedules.

•Compare drug exposures and degree of pharmacokinetic variability in children <2 years with data obtained from published studies in older children.

• Relate inter-individual variability in pharmacokinetics and drug exposure to clinical toxicity and response.

•Use pharmacokinetic data in conjunction with clinical information obtained following treatment to investigate the suitability of current dosing regimens in infants/young children. The feasibility and clinical value of pharmacologically-guided dosing in subsequent studies in this patient population will also be considered.

Protection of trial subjects:

Patients receiving the IMP were doing so as part of their standard clinical treatment. Blood volumes for samples taken as part of this trial were kept to a minimum and were taken from the patients central line to minimise pain and distress. Where possible PK samples were taken at the same time as clinical samples to keep discard volumes to a minimum.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 October 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 63
Worldwide total number of subjects	63
EEA total number of subjects	63

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	63
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period 22/10/07 to 08/01/13 UK wide (NHS Sites only).

Pre-assignment

Screening details:

Patients screened by their treating clinician/research nurses as they attended clinic for their standard care against the inclusion criteria stated in the protocol. Patients only excluded during screening if they fail to meet the study inclusion criteria.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Overall Trial

Arm description:

Overall Trial

Arm type	Experimental
Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IMP dosed according to the dosing regimen detailed in the clinical protocol on which the child is being treated.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

IMP dosed according to the dosing regimen detailed in the clinical protocol on which the child is being treated.

Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	Eposin
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IMP dosed according to the dosing regimen detailed in the clinical protocol on which the child is being treated.

Number of subjects in period 1	Overall Trial
Started	63
Completed	63

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	63	63	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	63	63	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	32	32	
Male	31	31	

End points

End points reporting groups

Reporting group title	Overall Trial
Reporting group description:	
Overall Trial	

Primary: Quantification of Carboplatin, Cyclophosphamide and Etoposide plasma levels in infants

End point title	Quantification of Carboplatin, Cyclophosphamide and Etoposide plasma levels in infants[1]
End point description:	
End point type	Primary
End point timeframe:	
Drug levels measured on a single course of treatment for each patient	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Final data analysis involved determination of pharmacokinetic parameters for this infant patient population. No formal statistical analysis was required relating to the primary endpoint.

End point values	Overall Trial			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: µg/ml				
number (not applicable)	63			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Per patient - adverse events only to be collected for the cycle of treatment that PK sampling takes place on.	
Adverse event reporting additional description:	
Only adverse events directly related to PK sampling were collected for this trial	
Assessment type	Systematic

Dictionary used	
Dictionary name	NCI CTC
Dictionary version	1

Frequency threshold for reporting non-serious adverse events: 5 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: The study was a low risk trial simply involving the collection of blood samples following standard treatment. Adverse events were reported through the main clinical trial on which the patients were being treated.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 November 2009	Change of sponsor from University Hospitals of Leicester NHS Trust to Newcastle upon Tyne Hospitals NHS Foundation Trust. Change in study sponsor accompanied by change in study management to the Northern Institute for Cancer Research, Newcastle University. Changes to protocol relate to change in study sponsor and management only (new protocol version 3.0, 1st October 2009)
22 June 2010	Change of Principal Investigator at St James Hospital, Leeds. No changes to protocol
08 December 2010	Change of Principal Investigator at Sheffield Children's Hospital. No changes to protocol
08 March 2011	Change of Principal Investigator at Alder Hey Children's Hospital, Liverpool. No changes to protocol
15 March 2012	Change of Principal Investigator at John Radcliffe Hospital, Oxford. No changes to protocol
15 March 2012	Change of Principal Investigator at Southampton University Hospital NHS Foundation Trust. No changes to protocol
19 November 2012	Change of Principal Investigator at John Radcliffe Hospital, Oxford. No changes to protocol

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported