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Pharmacokinetic variation and toxicity in Ewing's sarcoma

Submission date	Recruitment status	[_] Prospectively registered
14/01/2014	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
25/02/2014	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
26/06/2025	Cancer	[X] Record updated in last year

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-blood-levels-of-chemotherapy-drugs-in-people-with-ewings-sarcoma-pk201301

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2013-000052-17

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
PK 2013 01

Study information

Scientific Title
Pilot study to investigate the early prediction of toxicity following induction chemotherapy in Ewing's sarcoma by blood-borne biomarkers and correlation with age-dependent pharmacokinetic variation

Study objectives
The main objective behind this study is to test the hypothesis that the variation seen in the exposure to vincristine, ifosfamide, cyclophosphamide, doxorubicin and etoposide in patients is related to the age of the patient (children, adolescents and adults). This may explain differences in toxicity and/or survival response to these drugs.

Ethics approval required
Old ethics approval format

Ethics approval(s)
National Research Ethics Service committee North East - Newcastle and North Tyneside 1, 07/10/2013, Ref: 13/NE/0225

Study design
Five-year observational pharmacology study

Primary study design
Observational

Secondary study design
Other

Study setting(s)
Hospital

Study type(s)
Diagnostic

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

Health condition(s) or problem(s) studied
Ewing's sarcoma

Interventions
The study will involve 120 male and female Ewing's sarcoma patients recruited at 20 clinical cancer centres across the UK. Participation will be over a five-year period.

Blood sampling for pharmacokinetic studies will taken over a maximum period of 24 h or 54 h depending on the treatment arm. Blood sampling for biomarkers will be collected on 4 separate study days. Patients will be followed up clinically for a period of 3 years.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
1. To establish pharmacokinetic profiles for vincristine, ifosfamide, doxorubicin, etoposide and cyclophosphamide in adolescent Ewing's sarcoma patients and to compare profiles between children, adolescents and adults. Pharmacokinetic measurements will be performed on one course of treatment using established methods for the measurement of vincristine, ifosfamide, doxorubicin, etoposide and cyclophosphamide by liquid chromatography/mass spectrometry (LC /MS).
2. To validate in young people a panel of blood-borne biomarkers which have been shown to be predictive of bone marrow and mucosal toxicity in adults. Blood samples for biomarker analysis will be taken on cycles 1, 2 and the last cycle of induction chemotherapy. M30 and M65 ELISA assays will be performed as biomarkers for mucosal toxicity. The FLT 3 ligand assay will be performed as a biomarker for bone marrow toxicity.

Secondary outcome measures
1. To examine polymorphisms associated with drug metabolism and identify loci associated with the major acute and late toxicities associated with VIDE or VDC/IE chemotherapy.
2. To investigate potential relationships between pharmacokinetics, biomarkers of toxicity and pharmacogenetics in Ewing's sarcoma patients.

A single blood sample for pharmacogenetic analysis taken prior to the first course of VIDE or VDC/IE treatment, will be used to investigate whether genetic variation in the expression of key enzymes could underlie individual differences in drug metabolism and exposure.

Overall study start date
01/02/2014

Completion date
31/12/2025

Eligibility

Key inclusion criteria
1. Age 0 - 24 years
2. Diagnosis of histologically confirmed Ewing sarcoma
3. Receiving VIDE or VDC/IE as part of standard clinical treatment
4. Single or double lumen central venous catheter in place
5. Written informed consent
6. Protocol approval by national and local ethics committee, regulatory authority and Trust R&D Departments

Participant type(s)

Patient

Age group
Mixed

Lower age limit
0 Years

Upper age limit
24 Years

Sex
Both

Target number of participants
120

Total final enrolment
139

Key exclusion criteria
1. Receiving nonstandard dose chemotherapy.
2. Glomerular filtration rate <60 ml/min/1.73m2.

Date of first enrolment
01/02/2014

Date of final enrolment
20/11/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Northern Institute for Cancer Research
Newcastle upon Tyne
United Kingdom
NE2 4HH

Sponsor information

Organisation
The Newcastle Upon Tyne Hospitals NHS Foundation Trust (UK)

Sponsor details
c/o Andrew Johnston (RM&G Manager)
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (C27826/A15994)

Alternative Name(s)
CR_UK, Cancer Research UK - London, CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date
30/06/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Professor Gareth Veal (g.veal@nhs.net).

Participants have not given consent for sharing of data – therefore, only selected anonymised individual participant data that underlie the results reported in the article will be available. The trial protocol will also be available.

Data will be available following article publication.

Only investigators whose proposed use of the data has been approved by an independent review committee will be granted access to the data via 'password protected' documents sent to an individual email account. Proposals shall be directed to Professor Gareth Veal. To gain access requestors will need to sign a data access agreement.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Plain English results			26/06/2025	No	Yes