

# Pharmacokinetic variation and toxicity in Ewing's sarcoma

<b>Submission date</b> 14/01/2014	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 25/02/2014	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 26/06/2025	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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

### Contact name

Dr Gareth Veal

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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 be 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/1.73m<sup>2</sup>.

**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)  
Joint Research Office  
Level 6 Leazes Wing  
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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?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Plain English results</a>			26/06/2025	No	Yes