PLEASE NOTE: *This study has been imported from ClinicalTrials.gov without additional data checks.*

Trial Description

Title

Phase II Pharmacokinetic Study to Assess the Age-dependency in the Clearance of Doxorubicin in Paediatric Patients With Solid Tumours and Leukaemia

Trial Acronym

Doxo

URL of the trial

[---]*

Brief Summary in Lay Language

Analyze pharmacokinetics of doxorubicin in children with cancer. Furthermore investigate the predictive role of troponin and natriuretic peptides for anthracycline-induced cardiotoxicity .

Brief Summary in Scientific Language

- Paediatric patients up to the age of 17 years will be included. Number and time points of PK sampling will depend on age and tumour type.

- PK samples will be collected from two doxorubicin administrations. Analyzing samples from two doxorubicin administrations will allow distinguishing between interindividual, intraindividual and residual variability.

- Doxorubicin and its major metabolite doxorubicinol will be measured in plasma using HPLC

- In addition, the natriuretic peptide BNP and the precursors NT-pro ANP and NT-proBNP as well as troponin T will be measured in plasma up to 28 days after doxorubicin administration to evaluate their use as clinical markers for cardiotoxicity.

- A data set of max 5 samples (3 +2 (in the 1st + 2nd Doxorubicin sampling periods)) will be collected in the younger children (< 3 years) and a data set of max. 8

**samples (5 +
3) will be collected in the older children. Samples will be taken at predefined time
points/ time intervals.**

**- An additional DNA sample will be taken and analyzed for genetic polymorphisms. The
influence of genotype on pharmacokinetics and metabolism will be investigated by
appropriate statistical methods, including population pharmacokinetic analyses. Genes
to study would include MDR1 and SLC22A16, both involved in the transport of doxorubicin
and AKR1A1 and CBR1, both involved in the reduction of doxorubicin to doxorubicinol.
Selected genotypes will be incorporated as covariates into the population
pharmacokinetic models developed. The potential impact of genetic variation will be
evaluated in the context of other sources of variability such as age, weight, gender
etc**

Do you plan to share individual participant data with other researchers?

[---]*

Description IPD sharing plan

[---]*

Organizational Data

- DRKS-ID: **DRKS00003787**
- Date of Registration in DRKS: **2012/05/04**
- Date of Registration in Partner Registry or other Primary Registry: **2010/03/22**
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **[---]***
- (leading) Ethics Committee Nr.: **[---]***

Secondary IDs

- EudraCT-No.
(for studies acc. to Drug Law): **2009-011454-17**
- Primary Registry-ID: **NCT01095926 (ClinicalTrials.gov)**
- Sponsor-ID: **EPOC-MS-001 (University Hospital Muenster)**
- Other Secondary-ID: **2009-011454-17**

Health condition or Problem studied

- Free text: **Wilms Tumor**
- Free text: **Neuroblastoma**
- Free text: **Soft Tissue Sarcoma**
- Free text: **Acute Lymphoblastic Leukemia**
- ICD10: **C91.0 - Acute lymphoblastic leukaemia**
- ICD10: **C64 - Malignant neoplasm of kidney, except renal pelvis**

Interventions/Observational Groups

- Arm 1: **Drug: doxorubicin**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Single arm study**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Uncontrolled/Single arm**
- Purpose: **Treatment**
- Assignment: **Single (group)**
- Phase: **II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

- Assess age-dependency in pharmacokinetics of doxorubicin in paediatric patients with solid tumours and leukaemia; time frame: 24h; Measure doxorubicin and doxorubicinol concentration in blood plasma. Collect samples at two different doxorubicin infusions.

Secondary Outcome

- Assess interindividual, intraindividual and residual variability of PK parameters in children; time frame: 24h; Measure doxorubicin and doxorubicinol concentration in blood plasma. Collect samples at two different doxorubicin infusions.

- Assess relationship between PK parameters and patient characteristics; time frame: 24h; Measure doxorubicin and doxorubicinol concentration in blood plasma. Collect samples at two different doxorubicin infusions.
- Explore in a preliminary fashion genetic polymorphisms that may influence doxorubicin clearance; time frame: 5 years; Obtain one whole blood sample per patient, if separate consent was given.
- Evaluate the potential role of natriuretic peptides and troponin as indicators for subclinical cardiotoxicity; time frame: 1 month; Measure troponin T, troponin I, BNP, NT-proBNP, NT-proANP. Collect samples at two different doxorubicin infusions before and up to 1month after doxorubicin administration.

Countries of recruitment

- FR **France**
- DE **Germany**
- IT **Italy**
- UK **United Kingdom**

Locations of Recruitment

- **Universitätsklinikum Essen, Essen**
- **Universitätsklinikum Frankfurt, Frankfurt**
- **Universitätsklinikum Freiburg, Freiburg**
- **Universitätsklinikum Kiel, Kiel**
- **Universitätsklinikum Münster, Münster**
- **Klinikum Stuttgart, Stuttgart**

Recruitment

- Planned/Actual: **[---]***
- (Anticipated or Actual) Date of First Enrollment: **2010/05/31**
- Target Sample Size: **100**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **International**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **no minimum age**
- Maximum Age: **17 Years**

Additional Inclusion Criteria

- patients ≤ 17 years of age

- plan to receive at least two cycles of doxorubicin

- must be enrolled in a national or European protocol for treatment of Wilms Tumours,
Neuroblastoma, Soft tissue sarcoma, Ewing Sarcoma or Acute lymphoblastic leukaemia
and must be treated with doxorubicin according to that protocol Or
Patients < 3 years
enrolled or listed in any national or European study protocol for any paediatric
malignancy. Treatment with doxorubicin has to be according to that protocol.

- Parents or legal representative(s) must provide written informed consent to
participate in the trial according to national regulations. Patients that are able to
understand should provide assent to participate in the trial.

- Life expectancy of at least 3 month

- Karnofsky performance status of ≥ 70%

- Additional blood withdrawal is acceptable for the patient. The decision is left to
the investigator

Exclusion criteria

- prior cardiac problems

Addresses

■ **Primary Sponsor**

University Hospital Muenster

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

■ **Contact for Scientific Queries**

University Hospital Muenster
Joachim Boos, MD, Prof.

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- **Contact for Public Queries**

University Hospital Muenster
Joachim Boos, MD, Prof.

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URL: **[---]***

Sources of Monetary or Material Support

- **[---]***

Bitte wenden Sie sich an den Sponsor / Please refer to primary sponsor

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

Status

- Recruitment Status: **Recruiting complete, follow-up complete**
- Study Closing (LPLV): **2013/05/01**

Trial Publications, Results and other documents

- Further trial documents **Information about the study**

The parameters in ClinicalTrials.gov and DRKS are not identical. Therefore the data import from ClinicalTrials.gov required adjustments. For full details please see the DRKS FAQs.

- Translation on version: 53

- Last processed date by ClinicalTrials.gov: 2013/10/30

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*