Successful initiation of an international pediatric investigator initiated trial- EuroNet-PHL-C1

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First pan-European HL study in young people

EuroNet-PHL-C1

EuroNet-Paediatric Hodgkin's Lymphoma Group

First international Inter-Group Study for classical Hodgkin's Lymphoma in Children and Adolescents

- No radiotherapy in patients with adequate response at first restaging after two cycles of chemotherapy
- Randomised comparison of Procarbazine versus Dacarbazine (within COPP versus COPDAC) in patients in intermediate and advanced stages
- Standardised risk- and response-adapted salvage strategy

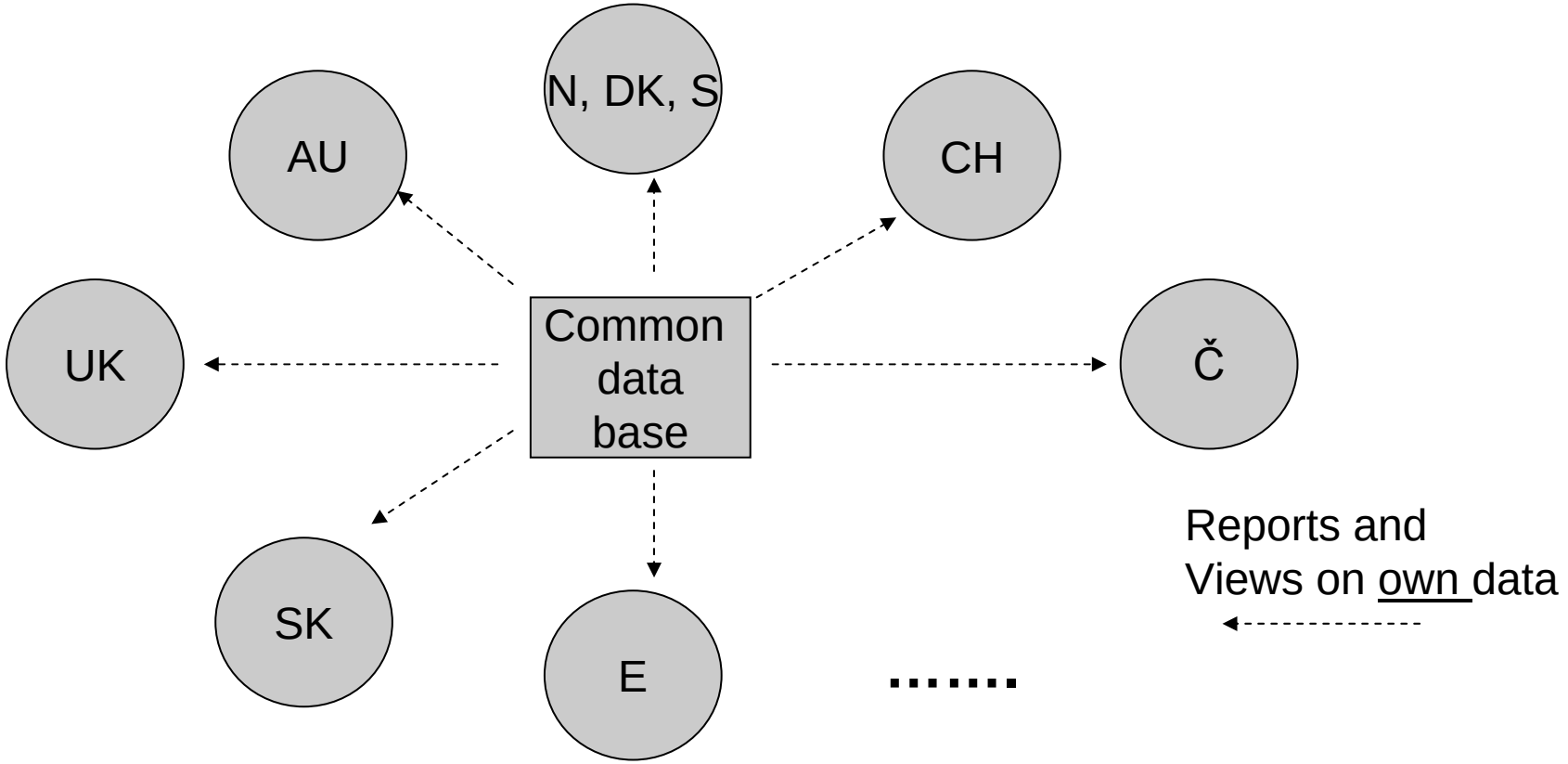
EudraCT-No.: 2006-000995-33

Study initiation process

- **09/2004** formation of the EuroNet-PHL group: D, A, CH, UK, S, NO, DK, F, PL, CZ, SK, I, E, B, GR
- Consensus decision on study protocol based on DAL-GPOH-HD studies
- **12/2005** notification of funding by DKH (Germany)
- **05/2006** study protocol finalised
- **08/2006** application process through main sponsor`s (University of Halle) authorities (EC, CA) and affiliated EC`s of 65 German trial sites
- **01/2007** start of EuroNet-PHL-C1 in Germany
- **09/2007** start of EuroNet-PHL-C1 in Czech republic
- **10/2007** start of EuroNet-PHL-C1 in Switzerland
- **01/2008** start of EuroNet-PHL-C1 in Norway
- **In 2008**: rest of participating countries to follow

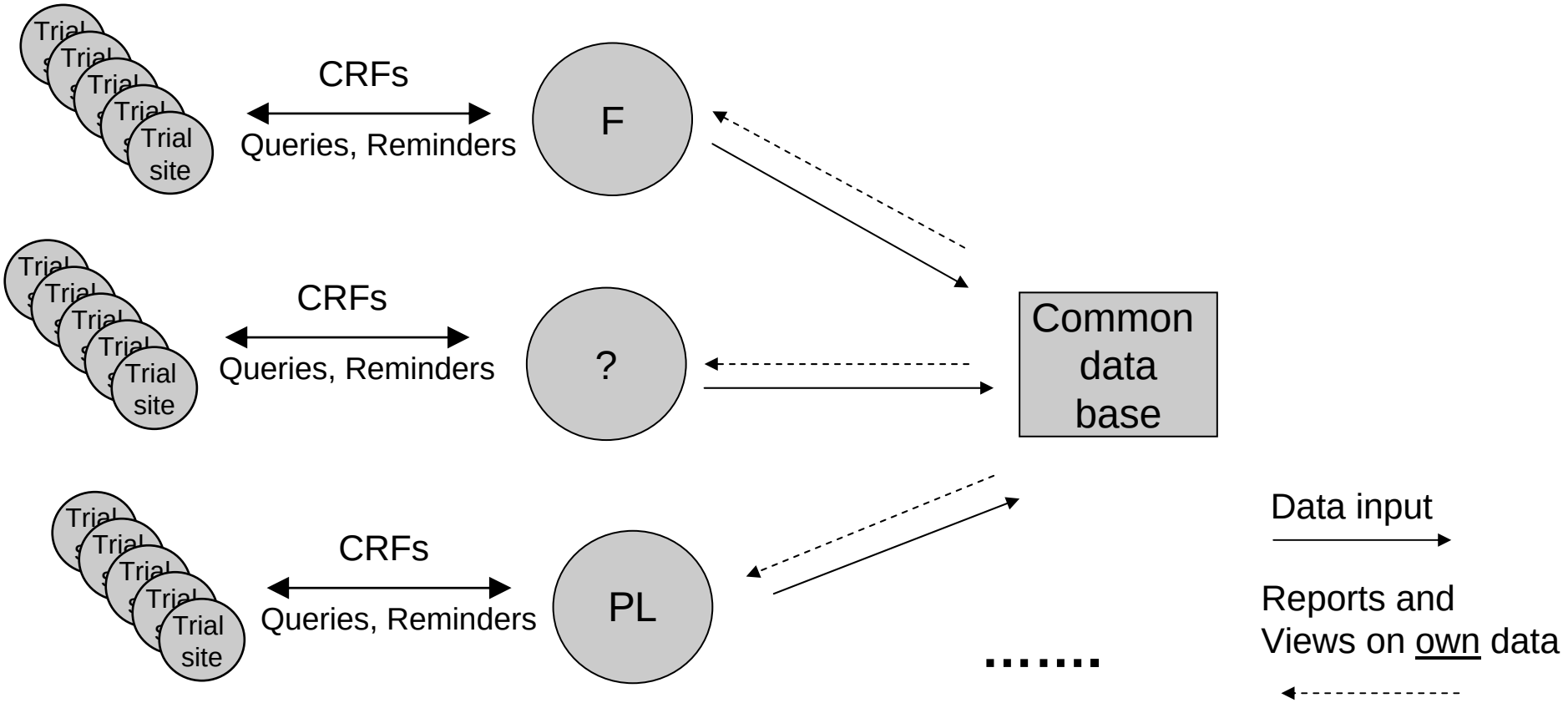
CSRA countries: Regional study offices (RSOs)

- Each participating **study group (CSRA)** has a **study office**
- The study offices are **linked** through internet to a **common data base**



LSRA countries: Regional study offices (RSOs)

- Each participating **study group (LSRA)** has a **study office**
- The study offices are **linked** through internet to a **common data base**



Sponsorship and transfer of sponsor duties

- **Sponsor of EuroNet-PHL-C1**

  Martin-Luther-University Halle

- **Transfer of sponsor duties** via **contract** to the **national chairperson** (resp. to the corresponding/authorized insitution)

  - **Mandatory** for **submission** of the trial to the competent authorities in other EU-countries

  - **Mandatory** for the **start of the trial in other EU-countries**

Transfer of sponsor duties

Agreement
between the
University of Halle
represented by the Dean of the Medical Faculty,
who is represented by the Coordinating Chairman of the EuroNet-PHL-C1 Study
(Prof. Dr. D. Körholz)
(in the following **sponsor**)

and
(external scientific institution / trial site)

.....

National Chairperson -<*country X*>

.....

(in the following **authorised institution**)

on the **transfer of sponsor duties**.

Subject of the agreement

Preamble

The University of Halle is the sponsor of the international clinical trial EuroNet-PHL-*C1* in the legal sense as defined by the Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001.

The sponsor internally transfers his duties to the authorised institution, as stated in the following. The sponsor transfers the mandate as representative for the sponsor for *country X* vis-à-vis third parties to the National Chairperson-*country X*.

§ 1

Subject of the agreement

Subject of this agreement is the part of the clinical trial EuroNet-PHL-C1, which is performed in *country X.*

Authorisation

§ 2
Authorisation

The sponsor authorises the national chairperson-*country X* to perform the sponsor duties also to third parties on behalf of the University of Halle. Authority is limited to sponsor duties, which arise in the context of the performance of the clinical trial in *country X* stated in § 1.

The certificate of authority will be drawn up separately, see enclosure 1.

Concerning publication of results, the authorised institution of *country X* complies with regulations of the EuroNet-PHL-group. The voting members decide on proposals for publications of all trials results coming out of multinational activities within the EuroNet-PHL. National trial data belong to the country-specific societies. No participating country shall be allowed to publish national trial data without permission of the inter-group chairpersons of EuroNet-PHL-C1.

Duties of the authorised institution

§ 3
Duties of the authorised institution

In the scope of the part of the clinical trial stated in § 1 which is performed in *country X* the sponsor has to carry out duties according to the applying legal provisions. The sponsor partially transfers these duties to the authorised institution.

In detail the duties transferred to the authorised institution and those remaining with the sponsor arise from enclosure 2 of this contract (catalogue of sponsor duties according to national law of *country X*). Enclosure 2 is part of the contract.

The authorised institution assures that enclosure 2 contains all sponsor duties, which have to be considered in the scope of the part of the clinical trial stated in § 1 which is performed in *country X* according to applicable law in *country X*. Furthermore the authorised institution assures that the transfer of the duties assigned to the authorised institution is permitted.

The authorised institution will fulfil the transferred duties for the sponsor and warrants the compliance with all the statutory provisions relevant for the sponsor in the current version. The authorised institution will point out the duties not transferred to the authorised institution to the sponsor timely and support the sponsor in fulfilling these duties as required.

...

Duties of the authorised institution

§ 3
Duties of the authorised institution

...

Beginning with the date of the agreement the authorised institution will semi-annually draw up a written report on the progress of the clinical trial, the fulfilment of the transferred duties and the compliance with legal requirements. In addition the authorised institution will on demand provide all documents (if applicable as copy) necessary for the Trial Master File for the sponsor.

The sponsor reserves the right to audit the authorised institution for the purpose of control of compliance with all legal requirements.

The authorised institution takes responsibility for financing the clinical trial in *country X,* including patient insurance and on-site monitoring as required by the protocol.

Term of contract

§ 4
Term of contract

The term of this contract begins with the last signature and ends with the termination of the sponsor duty.

The contract can only be terminated for a grave cause.

In case of termination the duties of the authorised institution stated in enclosure 2 *(archiving!)* will persist. If the authorised institution should not be able to fulfil these duties the parties will agree on the further proceedings, especially on the whereabouts of the study documents, in a separate agreement.

Enclosure 1: Certificate of authority

CERTIFICATE OF AUTHORITY

The Martin Luther University of Halle-Wittenberg is sponsor for the clinical trial

EuroNet-PHL-C1.

.....
(National Chairperson - country X)

is hereby given authority to represent the sponsor for country X vis-à-vis third parties and to perform all sponsor duties from all applicable legal provisions in the recent version, as far as the clinical trial stated above is concerned.

Authority is given until its revocation, at the most until the completion of clinical trial.

Halle, ...

.....
Dean of Medical Faculty, Martin Luther University of Halle-Wittenberg

Enclosure 2: Catalogue of sponsor duties

Allocation of sponsor duties

Legal basis

European Community

Fig. 1. Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001

Fig. 2. Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial, October 2005, Rev. 2

Fig. 3. Detailed guidance on the application format and documentation to be submitted in an application for an Ethics Committee opinion on the clinical trial on medicinal products for human use, February 2006, Rev. 1

Fig. 4. Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use, April 2006, Rev. 2

Fig. 5. Commission directive 2005/28/EC of 8 April 2005

Country X

To be added

Enclosure 2: Catalogue of sponsor duties

List of sponsor duties

The list is to be completed according to the legal provisions of country X

EuroNet-PHL-C1

Duties of the sponsor	Sponsor	Authorised institution
Request of authorisation to the competent authorities		
Application EudraCT-No.	x	
Provision of all documents required by German law According to (2), Attachement 1	x	
Request of authorisation to the competent authority of country X According to (1), art. 9, 2		x
Application for an Ethics Committee opinion		
Provision of all documents required by German law According to (3), Attachement 2	x	
Application for an Ethics committee opinion in country X According to (1), art. 7, 6		x

Enclosure 2: Catalogue of sponsor duties

Duties of the sponsor	Sponsor	Authorised institution
<u>Notification of substantial amendments</u>		
Provision of all documents required According to (2), cp. 4.2 and (3), cp. 5.1	x	
Request of authorisation to the competent authority of country X According to (1), art. 10a		x
Application for an Ethics committee opinion in country X According to (1), art. 10a		x
<u>Declaration of the end of trial</u>		
Provision of all documents required According to (2), cp. 4.3.3 and (3), cp. 6	x	
Declaration to the competent authority of country X According to (1), art. 10c		x
Declaration to the Ethics committee of country X According to (1), art. 10c		x

Enclosure 2: Catalogue of sponsor duties

Duties of the sponsor	Sponsor	Authorised institution
<u>Pharmacovigilance</u>		
Immediate report of serious adverse events to the sponsor According to (4), cp. 5		x
Evaluation of serious adverse events According to (4), cp. 4.2	x	
Provision of the required documents on Suspected Unexpected Serious Adverse Reactions (SUSARs) or other safety issues requiring expedited reporting According to (4), cp. 5	x	
Reporting of SUSARS to all competent authorities concerned According to (1), art. 17, 1	x	
Reporting of SUSARS to the Ethics Committee of country X According to (1), art. 17, 1		x
Reporting of other safety issues to competent authority and the Ethics Committee of country X According to (1), art. 17, 1		x
Preparation of annual safety reports According to (4), cp. 5.2	x	
Submission of the annual safety reports to the competent authority and the Ethics Committee of country X According to (1), art. 17,2		x
Preparation of safety reports for the investigators According to (4), cp. 5.3	x	
Transmission of safety reports to the investigators in country X According to (4), cp. 5.3		x

Enclosure 2: Catalogue of sponsor duties

Duties of the sponsor	Sponsor	Authorised institution
Further duties		
Translation of all relevant documents of the trial, incl. the patients' informed consent form in national language		x
Selection of qualified investigators and trial sites in country X		x
Selection of further trial sites in country X during the course of the trial in consideration of all legal regulations		x
Written agreements for trial participation with trial sites in country X		x
Provision of an insurance for the trial subjects in country X According to (1), art. 3		x
Assuring the financing of the clinical trial in country X		x
Setup of adequate procedures for quality control and quality assurance in country X According to (5), cp. 2, art. 2		x
Archiving According to (5), cp. 4		x
Further duties according to national laws to be detailed		