Newsletter N°1
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Introduction

The TROPHOS clinical trial is finally starting to move. This is the first multicenter trial on Spinal Muscular Atrophy in Europe and we are sure it will be successful in any case. Besides looking to demonstrate the clinical safety and therapeutic efficacy of olesoxime, the experience that will derive from this clinical trial will surely be invaluable to bring together clinical sites for developing other future multicentre trials in Europe for SMA, increasing efficiency in the recruitment of patients, improving the quality of clinical trials, and promoting interaction with family associations. In addition this trial will be very useful to add knowledge on the variability of outcome measures and correlation of electrophysiological measures with functional outcome measures in SMA patients. We need the active participation of everybody particularly of the participating families, of evaluating physicians and operating monitors to obtain valuable results from this important study.

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Clinical Trial and Sites Status

14 sites are initiated among the 23 sites taking part in the study (see below, sites list). We have encountered three principal issues in getting the trial underway:

1. Regulatory processes have been complex in a certain countries, thus taking longer than planned. In certain other countries the processes are long by their nature.

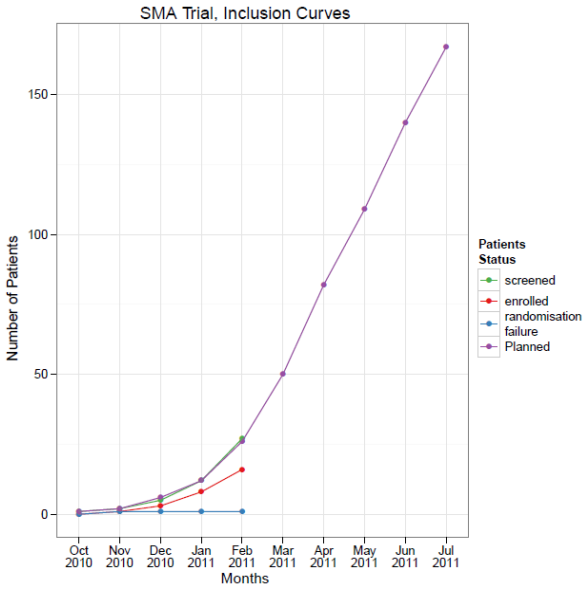
2. Budget and contract negotiations have been complicated. This is increasingly the case in all trials these days and we appreciate everybody's efforts to get the necessary contracts signed.

3. It has taken time in some centres to get the necessary internal organisation in place.

As a consequence, UK and Germany sites in particular are still awaiting (7 sites in total). Similarly, some sites have been changed and/or added lately to the study, requiring new submissions in both Italy and France (3 sites in total). However, sites within both countries will be opened in the coming month and should be active soon. The Warsaw site as well as Trousseau Hospital have been initiated this Month. All sites should be initiated by the end of March.

Enrolment

The planned enrolment period is **ending on the 31st of July, 2011**. The duration of the treatment being 2 years, you will easily understand that we have to strive to meet the July 31st deadline for obvious practical reasons. The challenge is important for the sites initiated recently or to be initiated soon. These sites have searched their databases and identified patients who can be screened. Thanks to all the sites that are actively involved in this trial. We are having a good start.



Sites		Patients	
		Screened	Enrolled
01	**Leuven**	6	6
14	**Rome**	7	4
07	**Bron**	5	4
06	**Lille**	2	1
05	**Garches**	1	1
02	**Ghent**	2	
20	**Utrecht**	2	
08	**Marseille**	2	
	TOTAL	**27**	**16**

Frequently Asked Questions and General Comments

Procedure for ECG transmission: "ECG on-line reading Form" is no longer required for ECG identification by Cardiabase. Instead, the ECG labels, which contain all the information for patient and visit identification, will be used. It is then very important to properly report the exact information needed; Visit #, Date, Subject ID, Date of Birth, Hour and Gender.

Priority Order for samples collection: The numerous blood tests required at each visit can present a difficulty in drawing a sufficient volume to perform all the tests. Indeed, we've designated the following priority list of tests to be performed:

- PK sample
- Haemostasis
- Biochemistry
- Haematology
- Glucose
- Genotyping
- Biobank

Then, blood samples should be drawn according to this list. If necessary, Genotyping and Biobank blood samples of screening visit can be drawn on randomization visit, as no other blood samples have to be collected at that visit.

Haemostasis: Haemostasis test have to be done locally for each visit (except V0 visit, where no blood tests are required). A Note to File will be written in order to clearly specify this point and to avoid any confusion.

Pharmacokinetic samples: PK samples from the first enrolled patients will be analysed for the first Data Monitoring Committee which is due mid of March. Three sites are concerned so far and will be informed to send the stored samples by the end of February, beginning of March (1 vial per patient) for PK trough analysis; 01-Leuven, 07-Bron and 14-Roma.

Fasting status: for blood sampling, laboratory request form requires the fasting status of the patients. If a patient was on an empty stomach for at least 6 hours, you should tick "Yes" on the lab request form. Otherwise, the "No" box should be ticked.

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Sites List

Country	Site Number	City
BELGIUM	01	Leuven
	02	Ghent
FRANCE	03	Trousseau
	04	Montpellier
	05	Garches
	06	Lille
	07	Bron
	08	Marseille
GER	09	Freiburg
	10	München
	11	München
	12	Essen

Country	Site Number	City
ITALY	14	Roma
	15	Roma
	16	Messina
	17	Milano
	18	Milano
	19	Genova
NLD	20	Utrecht
PLD	21	Warsaw
UK	22	Newcastle
	23	London
	24	Birmingham