DEFERIPRONE EVALUATION IN PAEDIATRICS

The research leading to these results has received funding from the European Union (FP7) under Grant Agreement n° 261483

DEEP-2 STUDY NEWSLETTER
ISSUE 1 - March 2014

Dear Investigators and DEEP-2 Study Participants,
WELCOME to the first newsletter of the DEEP-2 study

What is DEEP-2

DEEP-2 is a multicentre, randomized, open label, controlled trial aimed at comparing the efficacy of deferiprone versus deferasirox in pediatric patients. The aim of the study is to demonstrate the non-inferiority of deferiprone versus deferasirox in reducing serum ferritin levels and cardiac iron overload.

Additional objectives include the evaluation of deferiprone efficacy in reducing hepatic iron concentration, the assessment of deferiprone safety, and the compliance to treatment.

Study outline

Run-in period			Treatment and observation period				End of study
Screening		*Washout*	*Baseline*				*Follow-up*
Days -28 to -8	Day -7	Days -6 to -1	Day 0	Month 1	Month 2	Months 3-12	Month 13
V1	**V2**		**V3**	**V4**	**V5**	**V6 to V15**	**V16**

Study contacts

Trial Leader
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Trial Management Team
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Authorization Status and MRI Facilities Activation

We successfully received the study approval for the centres located in Palermo (Cervello and Civico), Bari, Modena, Naples, Florence, Catania, Padua. We are currently completing the authorization status in the other Italian and non-Italian centres. The FerriScan Set up was completed for 6 centres (Palermo Cervello, Athens, Nicosia, Naples,Tunis, Padua).

CODE	TOWN	COUNTRY	PRINCIPAL INVESTIGATOR	ETHICS APPROVAL	COMPETENT AUTHORITY APPROVAL	LAST AMENDMENT APPROVED	FERRISCAN/ MRI T2 SETUP
01	Palermo (Cervello)	Italy	Prof. Aurelio Maggio	OK EC 02/08/2012	N. 517 29/11/2012	OK EC 06/03/2014	V /
02	Cairo	Egypt	Prof. Amal El-Beshlawy				
03	Athens	Greece	Prof. Antonis Kattamis				V /
04	Tirane	Albania	Dr. Manika Kreka				
05	Nicosia	Cyprus	Dr Soteroula Christou				V /
06	Naples	Italy	Dr. Aldo Filosa	OK EC 24/01/2013	N. 144 22/02/2013	OK EC 11/09/2013	V /
07	Tunis	Tunisia	Prof. Bejaoui Mohamed	OK EC 07/11/2013			V /
08	Padua	Italy	Dr. Maria Caterina Putti	OK EC 15/04/2013	10/01/2014	OK EC12/12/2013	V /
09	Bari	Italy	Dr. Giovanni Carlo Del Vecchio	OK EC 28/11/2012	N. 307 21/03/2013	OK EC 16/10/2013	
10	Palermo (Civico)	Italy	Dr. Liana Cuccia	OK EC 29/10/2012	N. 000022 03/01/2013	OK EC 20/11/2013	
11	Cosenza	Italy	Dr. Mariagrazia Bisconte	OK EC 16/10/2012	N. 620 27/05/2013		
12	Lentini	Italy	Dr. Francesca Commendatore	OK EC 19/07/2013	N. 845 11/10/2013		
13	Modena	Italy	Dr. Giovanni Palazzi	OK EC 09/04/2013	N. 14013 18/06/2013	OK EC 29/08/2013	
14	Sassari	Italy	Dr. Carlo Cosmi	OK EC 26/10/2012	N. 153 28/02/2013	OK EC11/03/2014	
15	Cagliari	Italy	Dr. Raffaella Origa				
16	Florence	Italy	Dr. Tommaso Casini	OK EC 12/11/2013		OK EC 12/11/2013	
17	Catania	Italy	Dr. Vincenzo Caruso	OK EC 26/09/2013		OK EC 26/09/2013	
18	London	UK	Dr. Paul Telfer				

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Patient Recruitment

We have a total of 18 recruiting centres: Italy (12), Egypt (1), Greece (1), Albania (1), Cyprus (1), Tunisia (1), UK (1). These centres are expected to enroll 412 subjects into the study, as detailed in the following table:

Town	Subjects Estimated	Subjects Screened	Subjects Enrolled
Palermo (Cervello)	10		
Cairo	125		
Athens	12		
Tirane	10		
Nicosia	8		
Napoli	18	4	4
Tunis	125		
Padua	8		
Bari	14		
Palermo (Civico)	4		
Cosenza	4		
Lentini SR	6		
Modena	3		
Sassari	12		
Cagliari	9		
Florence	4		
Catania	10		
London	30		
Patients No.	**412**		

DEEP-2 is a competitive trial that will terminate when 310 patients will have completed the study. To this purpose, at least 344 patients will be enrolled.

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Monitoring Status

The Pre-study Site Qualification Visits (PSQVs) for all the Italian centres and for Tunis, Nicosia, Athens and Cairo were completed. The Site Initiation Visits (SIVs) were conducted in Palermo (Cervello), Naples and Modena, which are now ready for recruitment. The first Monitoring Visit (MOV) will be held at Naples centre.

Centre	PSQV	SIV	MOV 1
Palermo (Cervello)	10/09/2013	20/11/2013	
Cairo	10/02/2014		
Athens	19/03/2014		
Tirane			
Nicosia	22/10/2013		
Naples	24/10/2013	06/12/2013	16/04/2014
Tunis	05/11/2013		
Padua	10/10/2013		
Bari	17/10/2013		
Palermo (Civico)	10/09/2013		
Cosenza	11/11/2013		
Lentini	25/09/2013		
Modena	08/10/2013	07/02/2014	
Sassari	23/09/2013		
Cagliari	24/09/2013		
Florence	27/11/2013		
Catania	25/09/2013		
London			

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We would like to clarify a few issues raised by some investigators:

FAQ

How long is the washout period?

We consider the day -7 (V2) as the last day of the screening period, while the washout period is 6 days long, from day -6 to day -1 included (Protocol Table 5). Therefore, patients who are non-naive to chelation therapy will suspend their ongoing chelator from day -6 to day -1 (with the last chelator administration no later than 24:00 on day -7). If the last dose of chelator is expected to be administered to the patient after midnight of day -7 then the patient should not take it, in order to comply with the protocol procedure which recommends the drug suspension from from the first minute after midnight.

Should treatment-naïve patients go through the wash-out period?

Chelation-naïve patients are not expected to go through the washout period.

Can the other medications being administered to the patient interfere with study treatment?

If the patient is in treatment, even chronically, with a drug that is not included among the prohibited medications (as described in the Study Procedures Manual, section 12.2) and such medication does not preclude enrollment in the study, this treatment should not be interrupted during the washout period. If the drug is included in the prohibited medications and the treatment needs to be continued by the patient, he/she shall not be included in the study. In the case of an antibiotic treatment, it is advisable to wait until the end of the antibiotic cycle before starting the washout.

Can a patient with high ALT values caused by muscular dystrophy be enrolled in the DEEP-2 study?

No, because the study treatment may further alter ALT values.

When will the clinical site receive the PK kit?

Close to the time of sampling for PK, i.e.V15.

When will the V3 screenshot appear in the e-CRF?

After V2 validation. V2 will appear after the validation of the “Informed consent and assent form” in V1.

Is it possible to prefill the Exjade labels?

Not before the patient’s randomization.

How many label logs for DFP and DFX should be used?

One label per visit per patient.