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 2 - May 2014

Dear Investigators and DEEP-2 Study Participants,
the first two centres started enrollment... who will be the next one?

First patients enrolled!

Enrollment has begun at the Naples centre involving 8 patients, male and female, aged from 3 to 10 years. The Palermo (Cervello) centre has enrolled his first 3 year-old patient, after the concomitant DEEP-1 results communication.

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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Informative booklets and Consent forms available in six languages on the DEEP website.

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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, Sassari, Cosenza. We are currently completing the authorization status in the other Italian and non-Italian centres. The FerriScan Set up was completed for 10 centres (Athens, Bari, Cairo, Cosenza, Naples, Nicosia, Padua, Palermo Cervello, Tirane, Tunis). The MRI T2 Setup was completed for the Athens, Bari, Padua, Palermo Cervello and Tirane centres.

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 / V
02	Cairo	Egypt	Prof. Amal El-Beshlawy				V /
03	Athens	Greece	Prof. Antonis Kattamis				V / V
04	Tirane	Albania	Dr. Manika Kreka	OK EC 30/04/2014			V / V
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 EC 12/12/2013	V / V
09	Bari	Italy	Dr. Giovanni Carlo Del Vecchio	OK EC 28/11/2012	N. 307 21/03/2013	OK EC 25/03/2014	V / V
10	Palermo (Civico)	Italy	Dr. Liana Cuccia	OK EC 29/10/2012	N. 000022 03/01/2013	OK EC 06/03/2014	
11	Cosenza	Italy	Dr. Mariagrazia Bisconte	OK EC 16/10/2012	N. 620 27/05/2013	OK EC 25/02/2014	V /
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 EC 25/03/2014	
15	Cagliari	Italy	Dr. Raffaella Origa				
16	Florence	Italy	Dr. Tommaso Casini	OK EC 12/11/2013		OK EC 08/04/2014	
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	1	1
Cairo	125		
Athens	12		
Tirane	10		
Nicosia	8		
Naples	18	8	8
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**	**9**	**9**

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, Cairo and Tirane were completed. The Site Initiation Visits (SIVs) were conducted in Palermo (Cervello and Civico), Naples, Modena and Sassari centres. Naples and Palermo Cervello centres have started to enroll their first patients. The first Monitoring Visit (MOV) was held at the Naples and Palermo Cervello centre.

Centre	PSQV	SIV	MOV 1
Palermo (Cervello)	10/09/2013	20/11/2013	15/05/2014
Cairo	10/02/2014		
Athens	19/03/2014		
Tirane	07/05/2014		
Nicosia	05/05/2014		
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	09/04/2014	
Cosenza	11/11/2013		
Lentini	25/09/2013		
Modena	08/10/2013	07/02/2014	
Sassari	23/09/2013	15/05/2014	
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

What do I do If a blood sample is lost?

Next time the patient will come back to the hospital, e.g. for a transfusion, I will repeat the missed analysis I need. I will then register the results only in the medical chart.

How do I define "contraindication" to DFO for a patient naïve to the chelation therapy, in order to include him/her in the study?

A contraindication to DFO, in addition to the medical contraindication listed in the Ferriprox SmPC, can be also based on the inability of the patient to achieve adequate adherence to parental treatment regimen. The reason for contraindication must be recorded in the medical chart.

Can I include patients under combined chelation therapy in the study?

As detailed in the study protocol, only patients that are in monotherapy just before their inclusion in the study can be enrolled.

If an adverse event occurs during the treatment period, what should I do regarding the study treatment?

DFP and DFX can be scaled down for the safety reasons detailed in Table 4 of the study protocol.

In the protocol statement "All tests on hepatitis serology will be carried out on the same sample as collected for blood haematology/biochemistry", what do I mean with "the same sample"?

The blood sample for hepatitis serology will be collected during the same withdrawal for Haematology/Biochemistry, but in a different test tube in order to avoid any additional needle puncture.

How do I dispense deferiprone between two consecutive visits?

The amount of Deferiprone to be dispensed at each visit/dispensation day must always cover the exact number of days expected between one visit/dispensation day and the following. The actual day of both visits/dispensation day must always be included during the calculation of the total volume to be dispensed. At each visit/dispensation day, all the drug received in the previous visit must be returned by the patient. I can then dispense new DFP bottles, keeping into account again the three daily doses of both the visit/dispensation-days. It is important to remember that, for the evaluation of patient's compliance in terms of discrepancies between the actual remaining volume and the expected volume to be returned, the drug volumes consumed during the visit/dispensation-days will not be included in the calculation.

For those patients entering the trial with very high levels of ferritin, should I increase the dose of the drug if ferritin values remain stably high but do not increase further than the 20% margin as specified in the study protocol?

The observation period must be of 3 months. If, after this period, the ferritin values remain stably high, therapy can proceed with a dose increase, as detailed in Section 6.3 "Dose adjustments" of the study protocol.

See all DEEP-2 FAQ's on the DEEP website.