DEFERIPRONE EVALUATION IN PAEDIATRICS

This project has received funding from the European's Union's Seventh Framework Programme for research, technological development and demonstration under Grant Agreement n° 261483

DEEP-2 STUDY NEWSLETTER
ISSUE 29 - AUGUST/SEPTEMBER 2017

Dear DEEP-2 Investigators,
we are glad to inform you that the Last Patient ended Last Visit!

The TMT is very glad to inform all of you that even the last patient has completed the study, thus performing the last visit (V16) on September 21st, 2017 at the Nicosia site (ID:05).

Next Study Activities

At this phase of the study, between the LVLP and the Close Out Visits, the main aim is addressed to complete all the activities that will lead to the High Data Quality of the Data Base in terms of consistency, completeness and timelessness in order to put the experimental centers in complete safety.

Therefore the actions to be taken are:

- completion of the Data Entry activities;
- resolution of the all queries arisen;
- completion of the Source Data Verification (SDV) on site.

Also the activities carried out by the whole study team, such as the verification of the essential documents described in paragraphs 8.2 e 8.3 of the Good Clinical Practice (GCP), have to be up-to-dated in the Centre File (CF) and Investigator File (IF).

If there are missing documents, that have to be retrieved from the site, the CRA in charge will arrange their collection during the next monitoring visit and/or close out visit.

Frequently Asked Questions (FAQs)

What if the PI or his/her delegate wants to fill in the Drug Management section of the e-CRF, but one or more treatment numbers are missing on the dropdown menu?

PI has to:

- contact the CRA and explain the issue describing in details the missing treatment number/s and the Visit number of the patient;

CRA has to:

- communicate via email to the Data Manager (trial.assistant@cvbf.net) the issue, who will provide with the required support.

Please, refer to the DEEP Website to keep up to date about the Frequent Asked Questions (FAQs) and Alerts & Recommendations concerning the most relevant aspects of the study.
These sections are regularly updated in order to support You and all the Study Team.
You can also find all revised DEEP-2 FAQs in the "*General Information*" section of the e-CRF.

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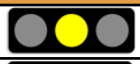
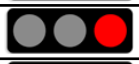
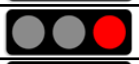
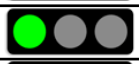
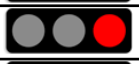
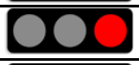
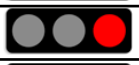
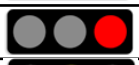
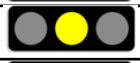
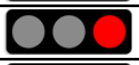
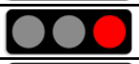
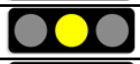
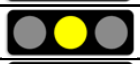
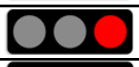
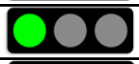
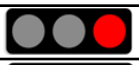
Study Conduct

As the IMP'dispensing procedures are finished, now it's time for the final sprint to continue destroying the IMPs! To this aim, we have updated the table below about the status of the disposal process in each clinical center related to both Deferiprone and Deferasirox.

The legend describes:

- in **green** the centers that successfully ended the disposal of all those IMPs available in place,
- in **yellow** the centers in which the disposal process is on going, as in case of:
  1. partial disposal of the IMPs at the center,
  2. IMPs already withdrawn from the center to be disposed by the Sponsor.
- in **red** the centers that have not performed the disposal yet.

Site ID	Deferiprone Status	Deferasirox Status
ITA/01		
EGY/02		
GRE/03		
ALB/04		
CYP/05		
ITA/06		
TUN/07		
ITA/08		
ITA/09		
ITA/10		N/A
ITA/11		N/A
ITA/12		N/A
ITA/13		N/A
ITA/14		
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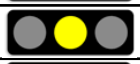
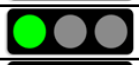
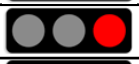
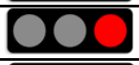
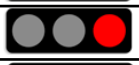
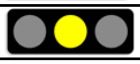
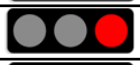
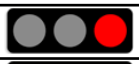
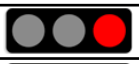
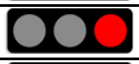
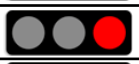
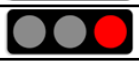
ITA/16		
ITA/17		
UK/18		
UK/19		
UK/20		N/A
EGY/23		
EGY/24		
ALB/31		

As you can see, in these last two months the percentage of the centers that have not begun the disposal yet, has fallen to the 67% for the DFX and to the 43% for the DFP. Your efforts are always precious to turn all in **green** lights and unburden the center with the IMPs to be disposed.

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Data Cleaning

After LVLP, data cleaning activities are starting with the aim to ensure that the data included in the final database are comply with the protocol, Good Clinical Practice and applicable regulatory requirements.

Executive process-General remarks

Data cleaning starts with the identification of not consistent data in the e-CRF. It proceeds with the investigation of the reasons and ends only after the resolution of the queries.

Queries include the outliers, missing values, discrepancies or all data not handled in accordance with the protocol.

Who is involved in the data cleaning process?

The Data Manager (DM), the CRAs, the Investigators.

Data cleaning steps

» Step 1: The DM creates queries and transfers them in a "e-query list" to be sent to the CRA (fig. 1)

e-Query list

Study Title	Multicentre, randomised, open label, non-inferiority active-controlled trial to evaluate the efficacy and safety of deferiprone compared to deferasirox in paediatric patients aged from 1 month to less than 18 years affected by transfusion dependent haemoglobinopathies.
Study Code	DEEP-2
EudraCT No.	2012-000353-31
Sponsor	CVBF
PI name	
Centre ID	XX **Last update**

Query generation part						*Query resolution part*	
DCF No. (SiteNo./Prog.No.)	**Query detection date**	**Subject ID**	**Visit**	**Form**	**Query text**	**Query solved (Yes/No)**	**Comment**
SITE XX	21/09/2017	XX01	3	Examination	Body weight value:it differs by more 6 kg from weight values entered in the previous and nexts visits. Please confirmor correct the value.		

figure 1

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In case the queries cannot be solved through the e-CRF, the DM transfers them in a Data Clarification Form (DCF) to be sent (directly or through the CRA) to the site (fig. 2).

The queries are based on Version 4.0 of the DEEP-2 protocol.

» Step 2: the CRA verifies that the queries are generated in accordance with the version of DEEP-2 protocol in force at the time of data entry in the e-CRF; then transfers the queries of the "e-query list" in the e-CRF, while the DCF must be transmitted directly to the Investigator.

» Step 3: the Investigator proceeds to answer queries by checking clinical data. The CRA makes sure the Investigator completes all requests of clarification.

DATA CLARIFICATION FORM

Study Title: _
Multicentre, randomised, open label, non-inferiority active-controlled trial to evaluate the efficacy and safety of deferiprone compared to deferasirox in paediatric patients aged from 1 month to less than 18 years affected by transfusion dependent haemoglobinopathies

Study Code: DEEP-2
Sponsor: CVBF
PI: _____

EudraCT No.: 2012-000353-31

Centre ID: XX

Subject ID: XX01

To be completed by the Data Manager			*To be completed by the Investigator*
Visit	**Form**	**Query**	**Answer/Comment**
3	Laboratory	Totally daily dose: is it possible that it has been reported not in mg/die but in mg/kg for mistake? Please confirm or correct the value. The value reported is 20 mg/die but this value is not consistent with a DFX dosage	

figure 2

Discrepancies not solved

When a discrepancy cannot be solved, justification must be provided by the CRA using a Deviation Form (fig. 3). If a deviation from the protocol occurred several times in the same patient, the CRA can report it in a single deviation form including all visits in which the deviation has occurred.

Tracking process

During the Data Cleaning process the DM maintains tracking of the queries. In case of DFCs, the investigator must complete the DCF, sign and date it and return the DCF back to the Sponsor.

DEFERIPRONE EVALUATION IN PAEDIATRICS

SPONSOR:	Consorzio per Valutazioni Biologiche e Farmacologiche (CVBF)
TRIAL CODE:	DEEP-2
SITE NUMBER:	
REFERRED TO:	**General** ☐ **Patient ID** _____

Deviation(s) discussed with the Investigator to prevent recurrence:

	Yes	No	If yes comment:
Protocol	☐	☐	_____
ICH-GCP	☐	☐	_____

figure 3

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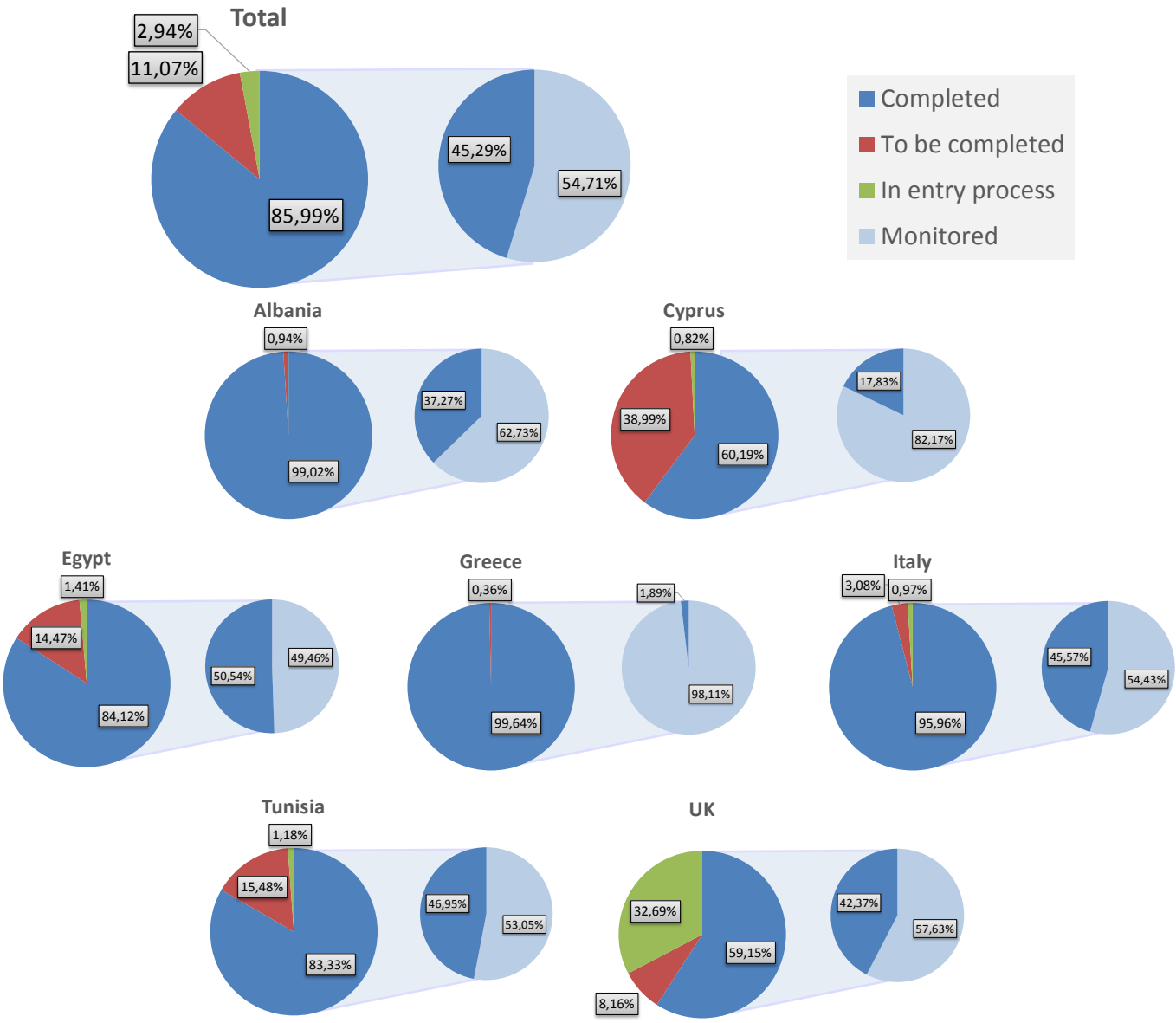
e-CRF Form Review Status at different centres

The Trial Management Team wishes to remind Investigators **to correctly complete and validate all data in the e-CRF sections** to allow the CRAs appointed to each study center to perform the check during the monitoring visits.



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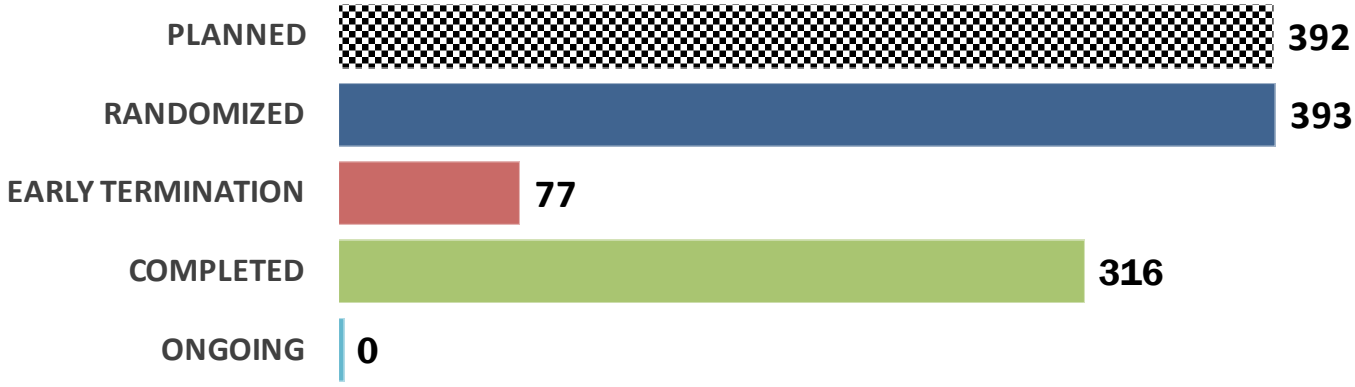
Patients' Status



Site ID	PI	Planned	Randomized	Early termination	Completed	Ongoing
ITA/01	Maggio	10	11	0	11	0
EGY/02	El-Beshlawy	130	133	39	94	0
GRE/03	Kattamis	12	11	3	8	0
ALB/04	Kreka	20	27	2	25	0
CYP/05	Christou	12	8	7	1	0
ITA/06	Filosa	14	14	4	10	0
TUN/07	Bejaoui	30	56	2	54	0
ITA/08	Putti	9	9	1	8	0
ITA/09	Del Vecchio	12	6	0	6	0
ITA/10	Cuccia	4	3	3	0	0
ITA/11	Bisconte	4	1	0	1	0
ITA/12	Commendatore	6	1	0	1	0
ITA/14	Cosmi	5	5	1	4	0
ITA/15	Origa	7	5	2	3	0
ITA/16	Casini	4	3	0	3	0
ITA/17	Caruso	6	2	0	2	0
UK/18	Telfer	20	19	1	18	0
UK/19	Hemmaway	5	4	0	4	0
UK/20	Harewood	5	0	0	0	0
EGY/23	Metwally Sherief	40	40	3	37	0
EGY/24	Hassab	25	23	9	14	0
ALB/31	Zaka	12	12	0	12	0
TOTAL		**392**	**393**	**77**	**316**	**0**

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Study Contacts

Please find below all DEEP-2 contacts that are glad to support you for any information that you may need:

Trial Leader:

Donato Bonifazi - **pmdeep2@cvbf.net**

Trial Coordinating Investigator:

Aurelio Maggio - md.amaggio@gmail.com

Trial Management Team:

- Clinical Research Coordinator: **Gabriele Morselli** - gmorselli@cvbf.net
- Clinical Research Specialist: **Giuseppe Lassandro** - giuseppelassandro@deep-project.net
- Data Manager: **Paola Gandini** - trial.assistant@cvbf.net
- Drug and Technical Operations Manager: **Bianca Tempesta** - btempesta@cvbf.net
- Administrative Manager: **Marina Montanaro** - mmontanaro@cvbf.net

Regulatory Submission Manager and Clinical Trial Archivist:

Elisa Cattani - ecattani@cvbf.net

Pharmacovigilance:

- Safety Contact: **Cristina Manfredi** - pharmacovigilance@deep-project.net
- Qualified Person for Pharmacovigilance: **Mariagrazia Felisi** - mariagraziafelisi@cvbf.net
- Medical Monitor: **Maria Marsella** - mariamarsella@deep-project.net

Ferritin Evalutation Centers:

- **Cristina Passarello** - c.passarello@campuscutino.it

  AORC Villa Sofia - Cervello, U.O.C. di Ematologia delle Malattie Rare del Sangue e degli Organi Emopoietici - Via Trabucco, 180 - 90146 Palermo, Italy

  Ph.: +39 091 680 2770

- **George S. Gorgy** - gsgorgy@gmail.com

  Egyptian Company For Biological Sciences (ECBS), 4 Kassem street, off Dokki street, Dokki, Giza, Egypt

  Ph.: +2 02 33377593 - 333 84 684

  Fax: +2 33377578 - 333 84 679

MRI Centre:

- Resonance Health LTD - Help Desk - support@ferriscan.com

  Postal Address: PO Box 1135 Nedlands, Western Australia, 6909 Australia

  Courier Address: 278 Stirling Highway, Claremont, Western Australia, 6010 Australia

  Ph.: +61 08 9285 300

We would inform you that the new fax number for DEEP-2 pharmacovigilance is: +39 080 9909321