DEFERIPRONE EVALUATION IN PAEDIATRICS

SEVENTH FRAMEWORK PROGRAMME

DEEP Project presentation 03/03/2014 – Caltanissetta

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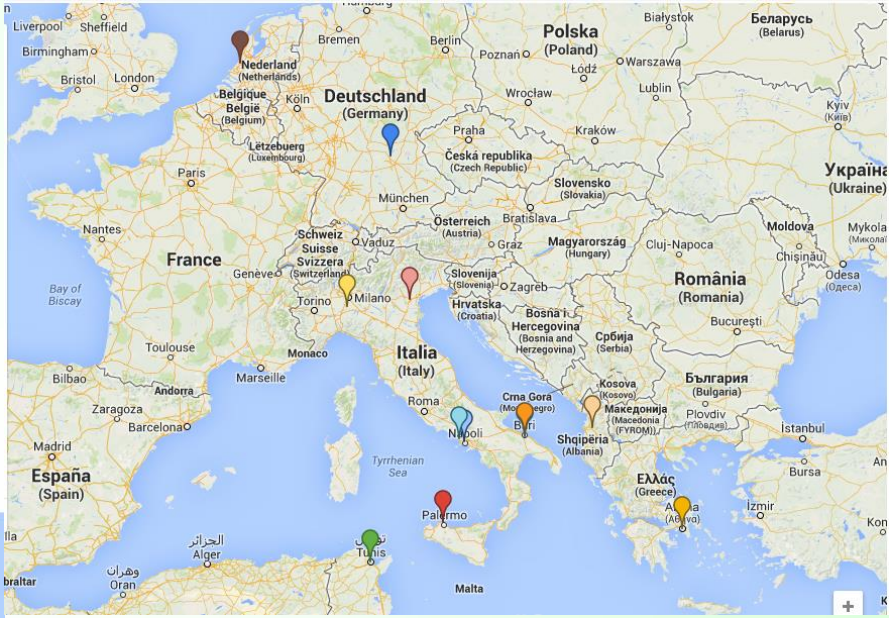
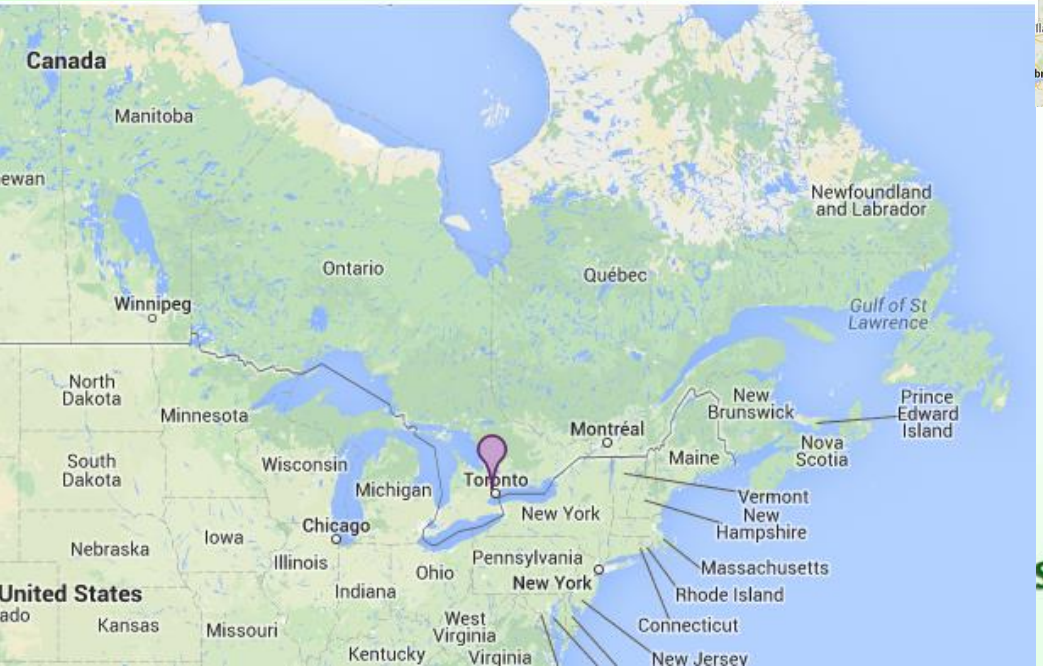
DEEP

Project

- **DEEP** is a multinational reserch project aimed to perform pharmacokinetics, efficacy and safey studies with deferiprone in children

- It is funded by the European Commission within the 7° Framework Program





Consortium

Composed of **16** Partners, from Italy, Greece, Cyprus, Egypt, Germany, The Netherlands, Tunisia, Albania and Canada

SP1 - Cooperation HEALTH-F4-2010-261483

Goals

- to evaluate pharmacokinetics and pharmacodynamics properties of deferiprone in children less than 6 years of age

→ **DEEP1 Paediatric PK Study**

- to evaluate efficacy and safety of deferiprone compared to deferasirox therapy in 1 month to 17 year-old children affected by hereditary hemoglobinopathies

→ **DEEP2 Paediatric Efficacy/Safety Study**

- to provide long term safety data by analysing all events potentially related to deferiprone use (alone or in combination with deferoxamine) in children observed in a time frame of 3 years of clinical practice

→ **DEEP3 Paediatric long term safety Study**

According to a Paediatric Investigational Plan (PIP) approved

DEEP-2 (EudraCT 2012-000353-31)

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

Phase III study, providing efficacy and safety data after one year treatment with DFP and DFX

DEEP2 Study

Population

344 iron chelator-naïve and non naïve paediatric patients of both genders aged between 1 months to less than 18 years, randomized 1:1 to one of two groups (DFP/DFX) to ensure at least 310 evaluable patients, taking into account a possible dropout rate

Duration

13-14 months

Design

multicentre, randomized, open label, active comparator controlled, parallel group trial

Objectives

to assess the non-inferiority of DFP compared to DFX in terms of changes of ferritin levels and heart iron concentration

DEEP-2 sites

Country	Recruitment Sites
Italy	**12** (2 x Palermo, Padova, Bari, Napoli, Cosenza, Lentini, Modena, Sassari, Cagliari, Firenze, Catania)
Egypt	**1** (Cairo)
Greece	**1** (Athens)
Albania	**1** (Tirana)
Cyprus	**1** (Nicosia)
Tunisia	**1** (Tunis)
UK	**1** (London)

Trial design

Pts assessed for eligibility
(n >= 344)

Excluded
- Not meeting inclusion criteria
- Declined to participate
- Other reasons

Pts randomized
(n = 344)

Allocation

Pts allocated to DFP (n = 172)
75-100 mg/kg/day liquid formulation for seven days per week
NEW STRENGHT 80 mg/ml

Pts allocated to DFX (n = 172)
20-40 mg/Kg/day

Follow-up

Drop-out 10%

Drop-out 10%

Analysis

Pts to be analysed (n = 155)

Pts to be analysed (n = 155)

Visit schedule and evaluations

***= Centralized evaluation**

Pharmacokinetic
→ Leiden/Amsterdam Center for Drug Research (LACDR), Leiden, The Netherlands

Liver &Cardiac MRI
→ MRI Centre, Resonance Health Ltd, Perth, Australia

Centralized serum ferritin
→ Ferritin Evaluation Centre, Palermo, Italy

	Run in			Treatment													
	Day				Month												
	Screening -28→-8		washout -6→-1	Baseline Day 0	1	2	3	4	5	6	7	8	9	10	11	12	13 Follow-up
Visit	1	2		3	4	5	6	7	8	9	10	11	12	13	14	15	16
Demographic characteristics	X																
Randomization				X													
Informed consent	X																
Inclusion/exclusion criteria		X															
Pregnancy test	X															X	
Physical examination	X			X	X	X	X	X	X	X	X	X	X	X	X	X	X
Medical history and current medical conditions	X																
Pharmacokinetics*																X	
Vital signs	X			X	X	X	X	X	X	X	X	X	X	X	X	X	X
Liver function history	X																
Heart function history	X																
Liver MRI*				X												X	
Serum Ferritin *	X			X	X	X	X	X	X	X	X	X	X	X	X	X	
ECG	X			X			X			X			X			X	
Cardiac MRI T2*				X						X						X	
Urinalysis	X			X	X	X	X	X	X	X	X	X	X	X	X	X	
Renal function	X			X	X	X	X	X	X	X	X	X	X	X	X	X	
Haemoglobin	X			X	X	X	X	X	X	X	X	X	X	X	X	X	
Neutrophil count	X			X	X	X	X	X	X	X	X	X	X	X	X	X	
Hepatitis serology	X															X	
Haematology/ Biochemistry	X			X	X	X	X	X	X	X	X	X	X	X	X	X	
Ocular and audiometric test				X												X	
Concomitant medications				X	X	X	X	X	X	X	X	X	X	X	X	X	X
Medical events				X													
Adverse events					X	X	X	X	X	X	X	X	X	X	X	X	X
Body height/weight	X			X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pubertal staging				X						X						X	
Compliance					X	X	X	X	X	X	X	X	X	X	X	X	
CHQ questionnaire				X						X						X	
Healthcare Resources					X	X	X	X	X	X	X	X	X	X	X	X	

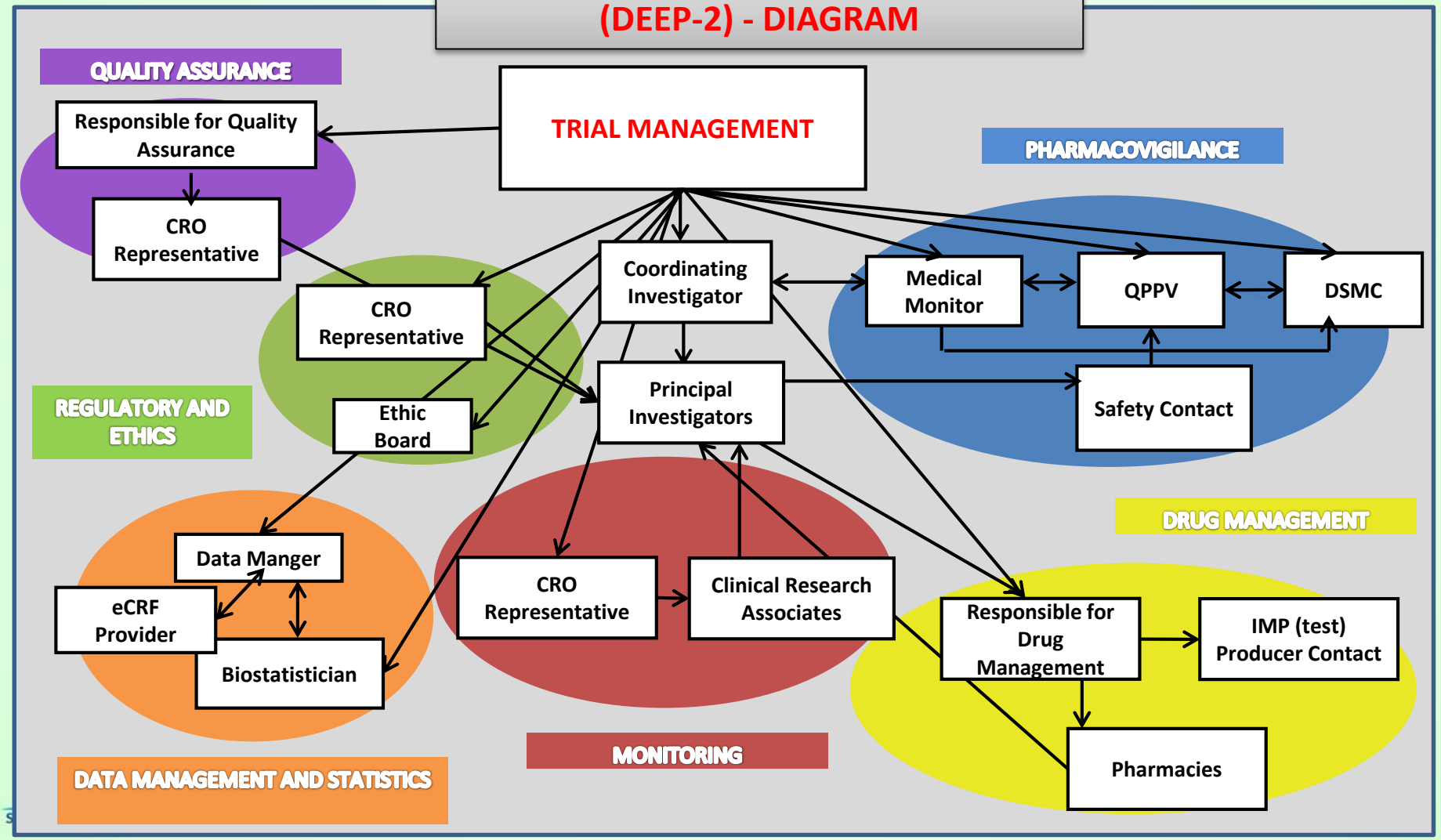
SEVENTH FRAMEWORK PROGRAMME

DEFERIPRONE EVALUATION IN PAED

Scientific Coordinator | Project Manager

Project Scientific Committee

CLINICAL TRIAL STRUCTURE (DEEP-2) - DIAGRAM



Summary

Italy

-**11** centers: EC approval

-**9** centers: EC and CA approval

-**3** already recruiting centers:
- -Palermo Villa Sofia-Cervello
- -Napoli Cardarelli
- -Modena Az. Osp. Universitaria

Tunisia

-**EC** approval
-**CA** approval expected in March 2014

-Expected EC Submission: ➔

Greece	**February 2014**
Cyprus	
Albania	
Egypt	
UK	

-Expected EC/CA Approval: ➔

Greece	**May 2014**
Cyprus	
Albania	
Egypt	
UK	

Goals

- Include all patients within June 2014
- 12 months experimental treatment
- End of trial: June 2015

New strenght will be authorized in the paediatric population