Orphalan | Innovation for Orphan Diseases

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International Wilson's Disease Patient Registry
Newsletter: ORPH-131-005

Introductory Message from Orphalan

From left to right: Tim Jenkins, Naseem Amin, Frank Verheggen, Benedicte Deloux, Betsie Faber, Maureen Richardson, Carla Bennett

Dear Investigators and Site Staff,

We welcome you to the study and hope you all enjoy reading the first edition of our iWilson disease (iWD) registry Newsletter. We plan to circulate these on a quarterly basis to share information on study status, to highlight our study successes whilst also providing helpful hints and tips to help the study run smoothly.

Here at Orphalan we are truly excited to be opening this registry across Europe and beyond (we may have news on this in issue #2!). The registry will be a unique dataset to help healthcare professionals better understand Wilson's disease (WD) through collection of contemporary data on the natural history of Wilson's Disease. From this we anticipate patient benefit from the identification of unmet needs and analysis of data through scientific publications.

Whilst we are still in the early phases of the study, we are already able to celebrate some important milestones because of all your collective efforts – a huge thank you for your commitment to the iWD registry and many congratulations on these achievements:

- 13 sites open in 5 countries (2 sites in France to go live before the summer
- Over 150 subjects enrolled from 13 sites !!

Our scientific advisory board will be convening in April to review data entered into the eCRF from the first 50 subjects enrolled and we will summarise their findings and recommendations in our next newsletter.

Finally, in this issue, we would like to introduce you all to one of our star recruiters, Professor Marina Berenguer, located at La Fe University and Polytechnic Hospital, Valencia with some interesting facts we obtained from a quickfire Q&A!

Once again, many congratulations to you all for a successful launch of the iWD registry and your continued support with ongoing enrolment.

With Warm Regards,

Omar Kamlin MD
Senior Medical Director, Orphalan SA

Key Announcements

Study Updates/ Important Reminders

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iWilson Registry now open in 5 countries (Poland, Spain, Germany, Belgium and UK). Pending activation of French sites.

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Enrollment

161 patients have now been enrolled.

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Timelines

First Annual Report planned for Autumn 2023.

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Top Recruiting Sites

1. Prof. Czlonkowska (Warsaw Poland)
2. Prof. Berenguer (Le Fe, Spain)
3. Prof. Hartmann (Dusseldorf)

Country	Site; Activation date (FPI)	Site Name	Total
Belgium	3201; October 2022	University Hospital Leuven	10
France	3301; TBD 2023	Hospital Woman Mother Child	-
	3302; TBD 2023	Hospital Foundation Adolphe De Rothschild	-
Spain	3401; January 2023	Hospital Virgen del Rocio	8
	3402; October 2022	La Fe University and Polytechnic Hospital	25
	3403; August 2022	University Hospital Clínic de Barcelona	12
	3404; March 2023	University Hospital GC Dr Negrín	3
UK	4401; January 2022	Leeds Teaching Hospitals	6
	4402; December 2022	Royal Free Hospital London	11
Poland	4801; July 2022	Institute of Psychiatry and Neurology	33
	4802; June 2022	The Children's Memorial Health Institute	3
Germany	4901; December 2022	University Clinic Duesseldorf	19
	4902; September 2022	Charite Medical University Berlin	16
	4903; December 2022	University Clinic Leipzig	3
	4904; September 2022	Hannover Medical School (MHH)	12
		Total	**161**

Helpful Tips and Reminders

Please contact your local Ergomed CRA for General Queries & Support

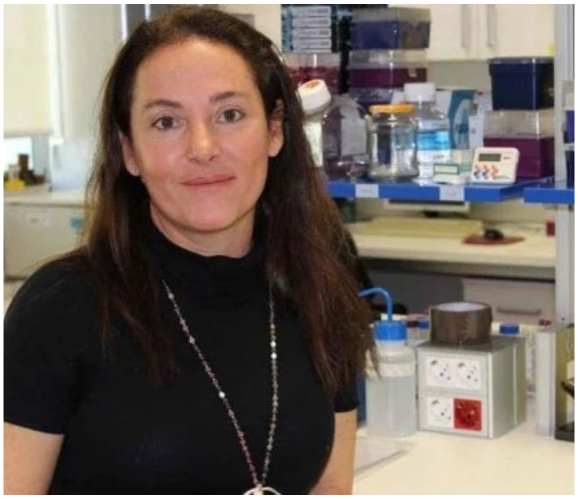
A- Friendly reminder for data entry and query resolution timeline:

- A new patient should be created in eCRF, within 5 business days of signing Informed Consent
- Baseline and follow-up visit data should be entered in eCRF within 10 business days of the visit/assessment; completion of laboratory data/ missing fields are expected to be completed within 3 months of the clinic visit

B- Reminder on Monitoring expectation:
Qu. How frequently will the data be reviewed by Monitor?
An. At the start, i.e., during Enrolment Period: First onsite visit should take place within two months of FPFV or once 3 patients have been enrolled (whichever occurs first). Subsequent onsite visits should occur at intervals of every 5 to 10 patients enrolled. The duration of the visit will be either 1 day (if 1-9 patients enrolled) or 2 days (if 10 or more patients enrolled) since the previous on-site visit.

C- Reminder of data collection frequency:
Qu. How frequently should collected data be entered into the eCRF?
An. At Baseline (inclusive of Screening Data) and from each follow up visit assuming standard of care is 1-2 visits per year. Any extra or additional visits should be summarised and entered at the following SOC visit (6 or 12 months after the previously entered visit). For a given 12 month period no more than 2 visits should be entered into the CRF.

Spotlight on Professor Marina Berenguer located at La Fe University and Polytechnic Hospital, Valencia, Spain.



Dr Marina Berenguer studied in the French school in Valencia, and then went to the Medical School in Valencia. Her father was a gastro-hepatologist and he was passionate about his job, particularly when the liver transplant unit opened in 1990 and this inspired her to specialize in hepatology. She provides clinical care for approximately 50 patients with Wilson’s disease and has so far recruited 25 onto the iWilson Registry.

Marina informs us that her WD clinics typically run twice a year for stable patients with additional visits as needed for unstable patients (i.e. those starting therapy, recently diagnosed, or who develop complications). Her clinics are multidisciplinary with a specialized Nurse and neurologist. They have a transition program for paediatric patients transferring into the adult clinics and they have strong links with geneticists specializing in rare diseases.

Quick Fire Questions:

What do your patients feel the value of participating in the registry? WD patients do everything for their "community". They all understand that it is not a common disease and want to help in any way they can. They are very committed patients, despite the fact that compliance with therapy is not always optimal.

Approximately how far does the patient who lives furthest away have to travel to the WD clinic? Most are relatively close, but a few have to travel 2-3 hours. We try to do as many phone visits as possible.

How are you and your team finding the interactions with your Ergomed CRA? How did you first monitoring visit go? Fine. They didn’t miss one single detail.

How has you/your team found entering data into the eCRF/EDC? Are there are specific pain-points that you are experiencing that you feel could be improved?
It is a very detailed registry, and there are too many items to be entered. Quite often WD are referred from other centres, and we don´t have data on their first lab results. When this is the case, it is very difficult to fill in the registry. And this is a very common issue with rare diseases. Patients quite often move from place to place until they are seen by a Specialist in the specific rare disease, and the results from the tests performed in the first health care places are not always available.

If you had it your way and hospital budget was not an issue, what would you change and why?
I would make sure that patients would always be seen by psychologists and/or psychiatrists and would make sure that all the copper related techniques were available in our center. Currently that is not the case. Intrahepatic copper quantitation and exchangeable copper are sent away to an external laboratory.

What do you see is the value of a WD registry? As for all rare diseases, a registry is the only way to obtain information on general features, trends, outcome measures, and then based on these we can come up with specific studies and hypotheses.

And finally - Where would you recommend tourists visit in Valencia? I would recommend them to visit the central market, the Plaza de la virgen, la plaza redonda, la Lonja de la Seda ...all situated downtown. Then I would recommend them to bike the "river". It is now a huge garden that surrounds the whole city, and many activities take place there. Finally, I would recommend having lunch in the Cabanyal (o Las Arenas), a beach promenade that is full of good restaurants to have lunch.

Interview conducted by Carmen García, Orphalan Medical Affairs Spain on 15 Feb 2023