# FOR-DMD – FOR YOU!

**Newsletter 5 – 7th April 2014**

SITE ACTIVATION

Four more sites have been added since our last newsletter in November 2013. Hauner's Children's Hospital, Munich (Germany) joined us on 22nd January 2014; Children's Hospital of Eastern Ontario, Ottawa and British Columbia Children's Hospital, Vancouver (both Canada) joined us on 14th March 2014; University of North Carolina, Chapel Hill (US) joined us on 20th March 2014. We extend a warm welcome to colleagues at those sites. Four further sites are still going through the processes necessary for activation, and we hope that these will open to recruitment by May 2014. Unfortunately, two sites have had to withdraw from the study: SUNY Downstate (US) and University of Giessen both left us on 14th January 2014.
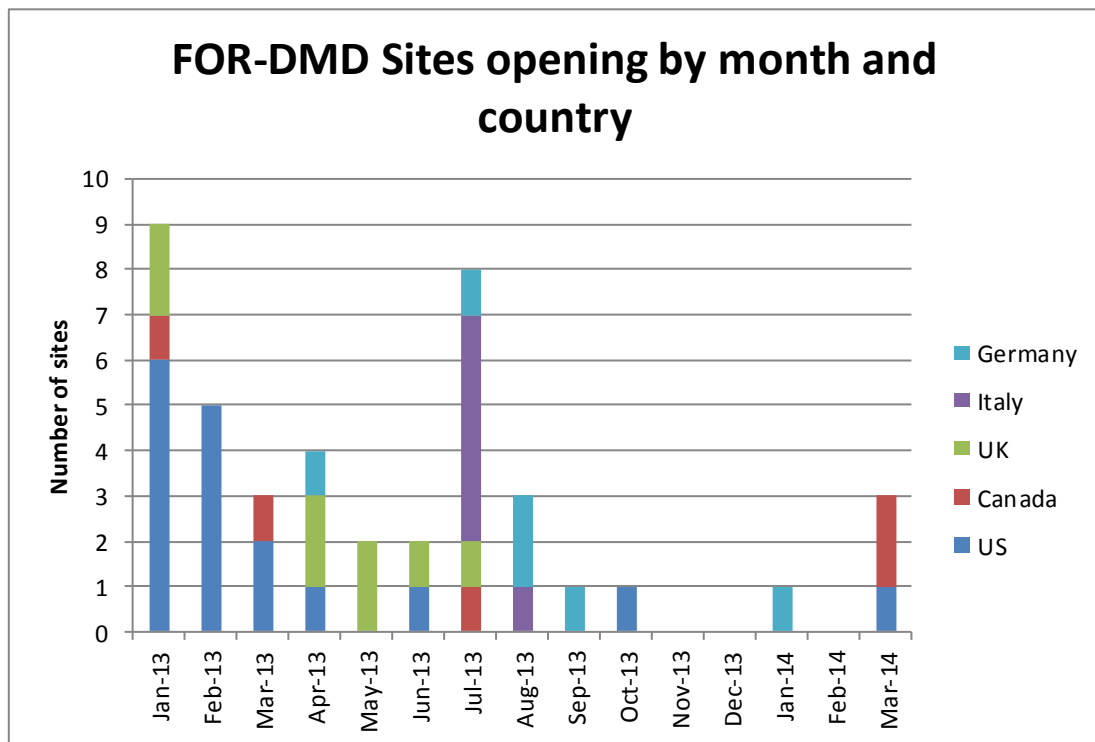
PRE-SCREENING AND SCREENING FAILURES

To 8th April, there have been a total of 41 pre-screening (i.e. before informed consent) and 28 screen (i.e. after informed consent) failures. Expressed as a percentage of all those consented, the overall screen failure rate is 25%, with country specific rates of 20% for the UK, 25% for the US and Germany, 36% for Italy and 46% for Canada. Reasons for pre-screening and screening failures (to 8th April 2014) are shown below.
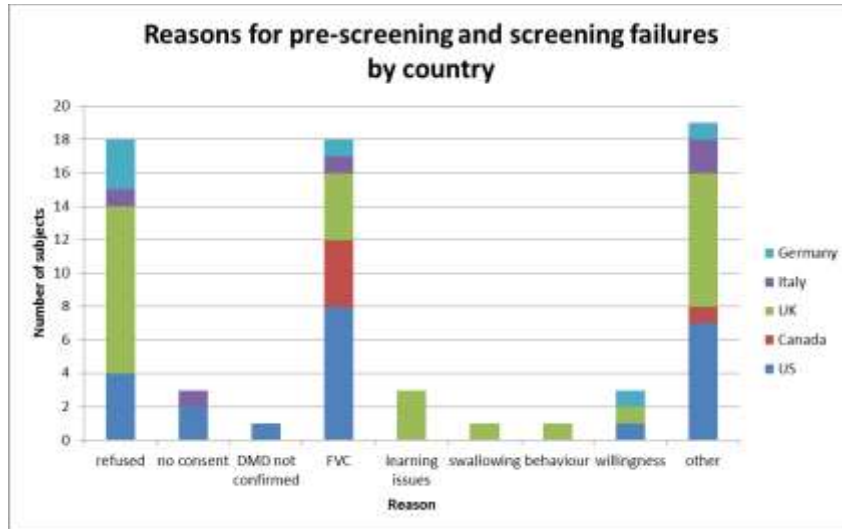
Queries from one site suggest that site staff may be experiencing some confusion regarding completion of screening logs. There is a paper log (CRF00) that tracks pre-screening and screening information. It's available in the document sharing area of EXPeRT under the CRFs folder. On this paper log there are multiple lines to allow sites to keep a continuous running log of all their pre-screens and screens. Since EXPeRT is designed to enter data at the subject level, each line on the paper log becomes just one line of data under the appropriate subject number.

 CRF00 tracks the date the site first became aware of the subject, how they found out about the boy, whether or not the boy will be formally screened (i.e. consented and have study procedures performed on them), and if the boy is not eligible why not, and whether or not they can be re-screened. Those details should be recorded on CRF00 for any boy considered for entry in the study. If the boy is to be formally screened, then informed consent must be obtained and documented on CRF01. The results of any screening procedures done are then recorded on the appropriate CRFs and summarized on CRF01. If all eligibility criteria are met the boy can then be randomized. If not then CRF01 documents the reason why they failed.

 So let's say the site has a 5th boy who they considered for the study (i.e. the boy met the basic criteria of age range, steroid naïve and presumed DMD) but who they didn't screen because of language issues. In these circumstances, they would create a line on the paper CRF00 log for S05 (5th boy pre-screened or screened) and enter the appropriate information, with Screened=N. They would then create a subject ID in EXPeRT for S05. A screening visit would be created, including CRF00 (but just one line of data), where they would enter the info from the paper log. In this case, they should enter 'N' for 'screened' and 'N' for 'eligible to re-screen', since presumably the language issue is a permanent one. We don't have a specific reason code for language, so one could enter 'O' for 'Other', but we would actually recommend entering 'E' for 'not eligible' to allow that 'Language issues' can then be entered in the text field. We would also recommend that site staff specify the exact language issues, such as 'family only speaks xxxxxxx' so that we see what other languages are appearing. If there are enough of a given language we could conceivably add a translation for it.

Please do take care to follow these instructions. It is important that we document pre-screen failures, so if you have any problems with the above please let us know.

PATIENT IDENTIFICATION AND RANDOMISATION

With 85 patients randomised by 8th April, we still remain behind our recruitment target at this time, with only 57% of the number (148) expected to be randomised by now, based on the number of open sites and the dates on which they were activated.

On a more positive note, one site randomised their first patient in November 2013, three sites randomised their first patient in each of December 2013 and January 2014, and two sites randomised their first patient in March 2014. We have had 5 patients randomised since the beginning of April, which is very encouraging.

As of 8th April, we also have 8 patients under review (i.e. in pre-screening) and 6 patients undergoing screening. We're really grateful to all sites for their ongoing efforts in patient identification, screening and randomisation – please keep up the good work!

The first two graphs below show recruitment to end March 2014; the third displays performance against target to 8th April.
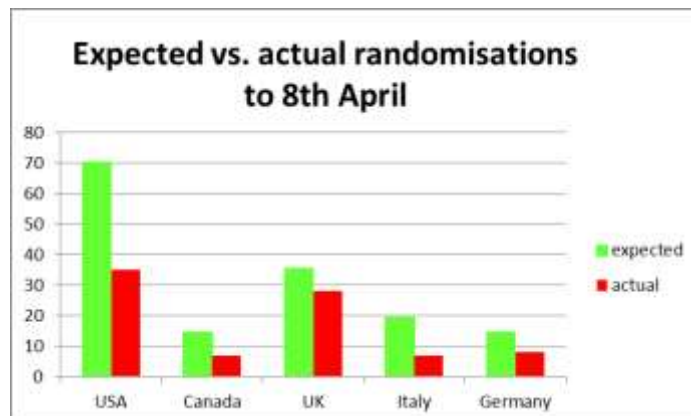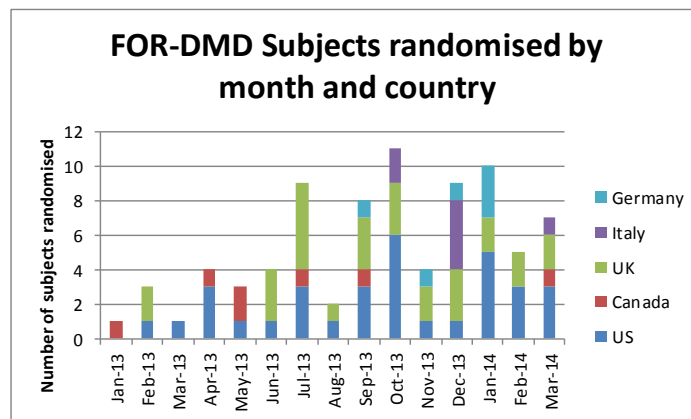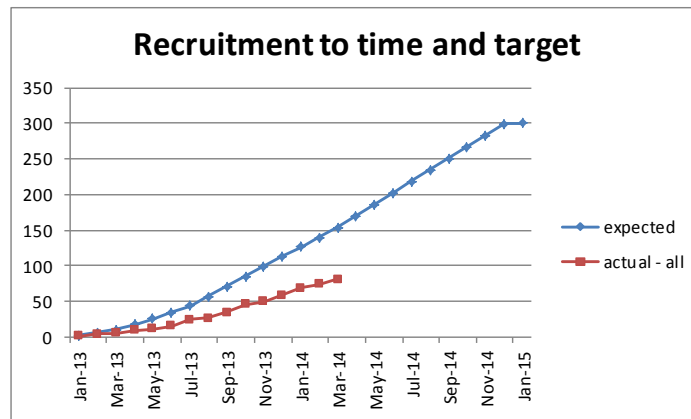
BRAG RATING

In the last newsletter, we introduced the concept of BRAG (Black-Red-Amber-Green) rating of recruitment to time and target. This is based on two parameters for each site: the number of months from that site being activated to the current closing date of 2nd January 2015, and the number of patients randomised. Each site has a minimum target of patients to be recruited, with a higher target for those sites opening earlier.

We express: the number of months the site has been open to date as a % of the total number of months from its opening to 2nd January 2015 (i.e. % time elapsed); the number of patients recruited to date at that site as a % of the site's minimum target (i.e. % of patients recruited vs. target). We then compare these two percentages to come up with the BRAG rating.

- If **no** patients have been randomised to date, the site gets a Black rating.
- If % of patients recruited vs. target lags behind % of time elapsed by more than 25%, the site gets a Red rating.
- If % of patients recruited vs. target lags behind % of time elapsed by between 15% and 25%, the site gets an Amber rating.
- If % of patients recruited vs. target lags behind % of time elapsed less than 15%, or % of patients recruited vs. target is ahead of % of time elapsed the site gets a Green rating.

The graph below shows the number of open sites in each country currently rated as Black, Red, Amber and Green.   As of 8th April, overall, of the 39 open sites, 9 (23%) are Black rated, 12 (31%) are Red rated, 8 (21%) are Amber rated and 10 (26%) are Green rated. Ideally, we would like to see all sites Green rated and to have zero Black rated sites.   Several of the currently Black rated sites have only opened to recruitment recently, and we therefore look forward to them 'changing colour' very soon!
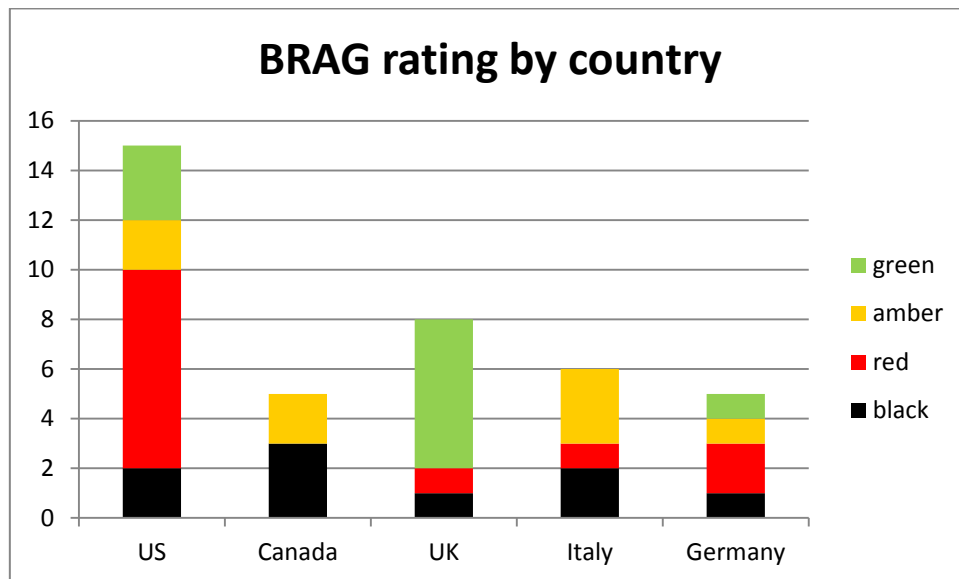
DSMB REPORT

The FOR DMD Data Monitoring and Safety Board (DSMB) met by teleconference on 10th February 2014. As no safety concerns were identified, it was agreed that the study should continue as planned. The DSMB recognised that the study remained important and complimented the investigators on getting it up and running and for addressing practical problems such as pill swallowing and performance of pulmonary function tests.

However, significant concerns were raised about the slow patient accrual rate; at the time of the meeting 71 subjects (less than 25% of the overall target of 300 subjects to be recruited by January 2015) had been randomised. Outreach to the patient population and to health care providers was recommended, and the investigators were advised to continue to put poorly performing sites on probation.

We are especially counting on the newly opened sites, and those in Germany and Italy that have recently started to screen patients to help accelerate the rate of recruitment.

Concerns were also expressed that only two Black and nine Hispanic subjects had been enrolled by the time of the DSMB meeting. This was of concern because rates of adverse events may differ by racial/ethnic background.

Please help us to address the DSMB's concerns by increasing efforts to identify and randomise patients, and to reach out to minority communities. Please let us know of any language barriers, inadequate publicity to certain populations or other barriers hindering accrual, especially among minority populations.

LET'S RAISE A MUG TO SUCCESS

Following the DSMB's exhortation to us to "encourage friendly competition among the sites with respect to recruitment", we have introduce a prize for the sites that randomise every 10th patient (i.e. the 80th, 90th, 100th etc) These lucky sites will receive a set of three coffee mugs – one for each of the study team – bearing the FOR DMD logo. Congratulations go to Dr Iain Horrocks and colleagues at Yorkhill Children's Hospital, Glasgow who become the first recipients of this prize, for randomising the 80th patient on 31st March 2014. **Will your site be the next one to earn a set of mugs?**

RESOURCES TO SUPPORT RECRUITMENT

The MDA are hosting a YouTube video webinar entitled: "FOR-DMD: Finding the optimal steroid regimen for Duchenne muscular dystrophy". This webinar gives parents of children with Duchenne and their advocates an opportunity to hear from Dr Robert Griggs, Co-CI for FOR DMD. Ms Jamie Roberts from the NINDS Office of Clinical Research at NIH also presents. Please view the webinar at https://www.youtube.com/watch?v=k1Z-OL3mjGk and share this link with families who may be interested.

We have also produced a video to use with families (once ethical approval has been granted). For the time being, site staff may view this video at   http://vimeo.com/album/2796835. The site is password protected, and the password is FORDMD. Please note that UNDER NO CIRCUMSTANCES should this video be shared with any families, potential or existing subjects until we upload it to YouTube and send formal notification to sites. This notification will follow the granting of ethics committee approval, which we expect any day now.

CONGRATULATIONS TO KATIE BUSHBY

The Expertscape organisation, which employs an expert ranking algorithm to quantify biomedical expertise, has recognised Professor Katie Bushby, Co-CI for FOR DMD, as the world's top medical specialist in Duchenne muscular dystrophy research and treatment.

Katie was also the recipient of an honorary doctorate from the University of Southern Denmark at Odense, in recognition of her work on diagnosis and treatment in muscular dystrophy. A fellow recipient at the same ceremony was Count Jacques Rogge, former President of the International Olympics Committee.