FOR-DMD – FOR YOU!

Newsletter 3 – 6th September 2013

A MESSAGE FROM KATIE BUSHBY

Many of you will have been aware that I have been out of action since the end of May. In the words of my consultant I had an "abdominal catastrophe" (actually a caecal volvulus) which required emergency hemicolectomy. My recovery has been slow but steady and I am returning to work now. I was fortunately home when this happened so was treated in my own hospital where the NHS did a great job.

The other people who have done a great job are those who have had to fill in for my various roles while I have been off. Michela Guglieri especially has been working tirelessly on FOR DMD, but extra work has fallen on all of the members of the co-ordination group. I am also very grateful for the work put in by my colleague Hanns Lochmuller, especially in facilitating the activation of the German and Italian sites.

It is quite exciting to come back to work and see the majority of the sites now active and screening and recruitment under way in all five countries! The US and the UK seem to be neck and neck in numbers of children recruited but with Canada really doing consistently well at the site level. We will be hoping for lots of activity in all sites over the coming months. I look forward to catching up with many of you at the MSG in Oxford!

Katie Bushby, FOR-DMD Chief Investigator

KEEPING IN TOUCH

Don't forget to visit our web-site http://for-dmd.org and to let us know what you think of it; there's a link there for making contact with the study team.

Between 4th April and 31st August 2013, we have had a total of 1395 page visits, with 435 unique visitors from 79 different countries.

We are now on Twitter! Follow us @FOR_DMD

SITE ACTIVATION

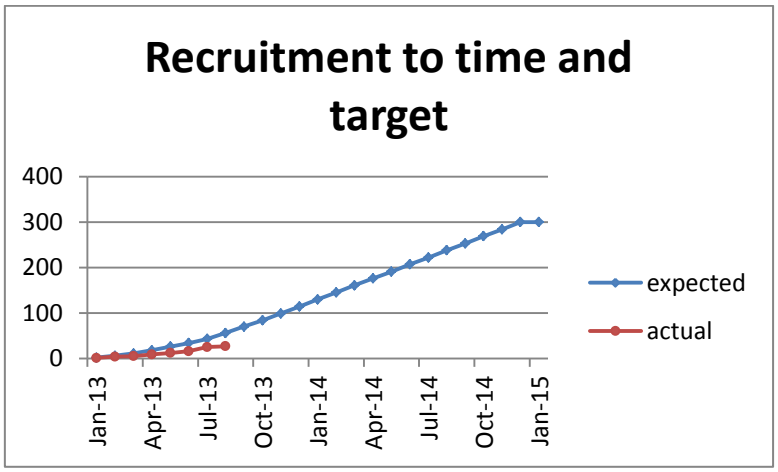
The summer months have seen a flurry of site activations. Since our last newsletter on 8th April, thirteen more sites have been activated: two in the US, one in Canada, six in the UK and four in Germany. Final ethical and regulatory approvals were obtained in Italy and all six sites in that country are now open to recruitment. This brings the number of active sites to 35. A further seven sites are going through the processes necessary for activation, and we hope that these will open to recruitment between early September and mid December 2013.

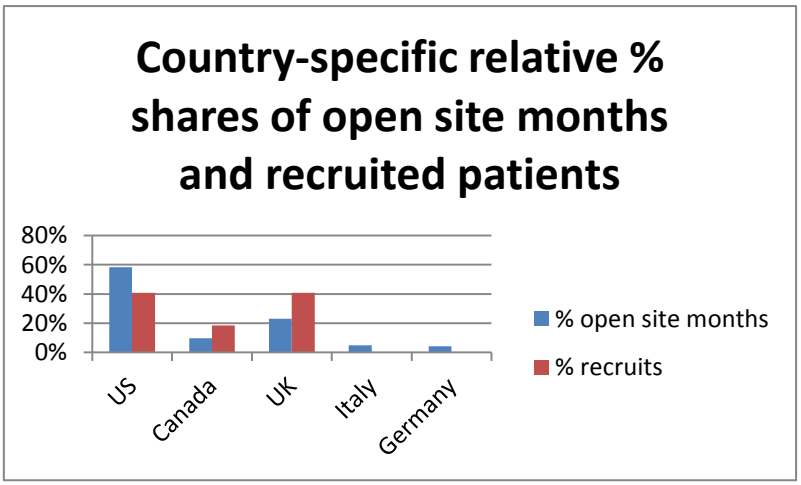
PATIENT IDENTIFICATION AND RECRUITMENT

Based on projected activation dates and assuming that recruitment terminates on 2nd January 2015 (24 months from the date on which our first site opened), we anticipate having a total of 816 site months of recruitment (site A recruiting for 24 months = 24 site months, as does the combination of site B recruiting for 13 months and site C recruiting for 11 months).

With 27 patients randomised to 31st August, we have recruited 48% of the number expected (56) by this time, based on the number of open sites and the dates on which they were activated. UK and Canadian sites have recruited more patients than expected to date. The support of the NIHR Medicines for Children Research Network in the UK has been a valuable asset in this respect.

With the end of the summer holidays, we hope that screening and recruitment rates will pick up from September onwards. To achieve our target of 300 patients randomised by 2nd January 2015, **sites now need to be recruiting an average of 5 boys per year**.





SITE PERFORMANCE 'LEAGUE TABLE'

		Months open	Identified	In screening	Screen failures	Recruits
	Royal Hospital for Sick Children, Glasgow	4.04	7	3	2	2
	Birmingham Heartlands	4.77	7	3	3	1
	Alberta Children's Hospital	7.56	6	1	3	2
	Nemours Children's Hospital	6.54	4	1	2	1
	University of Rochester	7.53	4	2	1	1
	London Health Sciences Centre	5.88	3	0	0	3
	Lurie Children's Hospital of Chicago	7.04	3	1	1	1
	Alder Hey (Liverpool)	7.07	3	0	0	3
	Newcastle University	7.63	3	0	0	3
	University Medical Center, Freiburg	4.11	2	2	0	0
	Leeds Teaching Hospital	4.50	2	0	0	2
	Nationwide Children's Hospital (Ohio)	4.77	2	1	0	1
	Boston Children's Hospital	6.31	2	2	0	0
	University California Davis	6.74	2	1	0	1
	Penn State Hershey Medical Center	7.04	2	0	0	2
	University California Los Angeles	7.92	2	0	0	2
	Kansas University Medical Center	5.72	1	1	0	0
	Kennedy Krieger Institute	6.58	1	0	0	1
	University of New Mexico	6.64	1	0	0	1
	University of Padova	0.16	0	0	0	0
	Goettingen University	0.39	0	0	0	0
	Dresden University	0.85	0	0	0	0
	Essen University	1.05	0	0	0	0
	IRCCS Medea	1.08	0	0	0	0
	University of Manitoba	1.32	0	0	0	0
	University Hospital Wales (Cardiff)	1.32	0	0	0	0
	Neurological Institute Foundation Milan	1.48	0	0	0	0
	Second University of Naples	1.48	0	0	0	0
	University of Messina	1.51	0	0	0	0
	Neuromuscular Centre Turin	1.51	0	0	0	0
	Great Ormond Street Hospital	2.20	0	0	0	0
	University of Minnesota	2.73	0	0	0	0
	Royal Manchester Children's Hospital	3.35	0	0	0	0
	SUNY Downstate Medical Center	5.13	0	0	0	0
	Vanderbilt Children's Hospital	7.43	0	0	0	0
	TOTAL	151.38	57	18	12	27

'Best performing site(s)' in each country highlighted in red; overall 'best performing site(s)' highlighted by yellow shading. It is recognised that, due to summer holidays, those sites which opened in the last two months have had limited opportunity to screen and randomise; therefore Italy excluded from rating of screening performance, and Germany and Italy excluded from rating of randomisation performance.

Our top recruiting sites are: London Health Sciences Centre (Canada); Newcastle upon Tyne (UK); Alder Hey (UK), all with 3 boys randomised to date. Congratulations to the teams at these sites.

HINTS FOR RECRUITMENT

Two of our top recruiting sites, Newcastle upon Tyne and Alder Hey (both in the UK) have shared with us their experience of site opening, screening and recruitment. Their ideas may be of help to other newly opened sites and those currently experiencing problems.

The Newcastle team gave us the following "Top Tips":

- Make sure that you know the protocol inside out; this will save you a lot of time in the long run. Check the FOR-DMD newsletter and website regularly, especially the Frequently Asked Questions (FAQs) section. This has lots of useful information on specific questions, eg "What do I do if the patient has recently had a DEXA scan?"
- We looked at all DMD boys in our care and made a shortlist of those who fit the eligibility (inclusion and exclusion) criteria for the study. We approached these boys in several ways. We either discussed the study in clinics or we telephoned the boys' parent(s) or guardian(s) at home. We followed this up by sending the Patient Information Sheet in the post, and telephoning again a few weeks later to discuss the study again.

Colleagues at Alder Hey told us the following:

"I found that the meeting that we held prior to the first screening to identify all the tests and paperwork that needed to be done on that day really helped. We marked who had to do what with a colour coding system, so that on the day, when there is so much to do, each person could clearly and quickly identify what was their responsibility.

Potential participants are identified by the Principal Investigator and Clinical Evaluator, and offered an individual appointment to discuss the implications and commitments of the study. We have known about the possibility of the trial for some time so this has already been mentioned to our patients at general clinics. All likely research is discussed openly with parents who may wish to join in, or just be kept informed of what is happening generally with research relevant to their child.

The first screening visit was challenging and the logistics of getting all the required tests done without exhausting the child and family took a lot of working out. It is quite an onerous day for the families, and they need to be prepared. We then sat down and decided how best to rearrange the timings, and the second screening was much smoother as a result. Hopefully the third should be relatively straightforward!"

MDA FUNDING FOR PATIENT VISITS IN US AND CANADA

The Rochester Team submitted a grant application to MDA requesting funds for subject travel support in the United States and Canada. The grant has been fully reviewed by MDA and has been recommended for funding. We expect to provide further information in the next FOR-DMD newsletter.

UPDATES, HINTS AND FAQS

What are the allowed visit windows?
The allowable windows are ± 14 days for visits at months 3 and 6 (T3 and T6) and ± 30 days for all subsequent (6 monthly) visits. For phone calls the window is (+/- 7 days) during the first 6 months following the baseline visit, then (+/- 14 days) for subsequent calls. All visit dates and windows are calculated from the ACTUAL baseline visit date (not the target baseline visit date on CRF01).

Do screening procedures need to be repeated if the boy had them recently performed as part of his standard of care?
This should be discussed with the Chief Medical Monitor (Dr Michela Guglieri) on a case by case basis. Procedures will not usually need to be repeated if they have been performed within 90 days of baseline. Please note that if a procedure was performed as part of the subject's standard care, the PI should confirm that the procedure was performed under the same criteria required by the study protocol and that all requested parameters have been collected and reported, in order to complete the appropriate eCRF.

Should the "musculoskeletal" section of the physical examination be completed as normal (since it is normal for DMD) or as abnormal (since it is abnormal for someone without DMD?)
If a subject shows signs of DMD as expected for a boy of his age with this condition, the musculoskeletal section of the physical examination should be completed as "abnormal" - comment: DMD – non clinically significant .

Will families be provided with a diary to document Adverse Events, concomitant medications and any other / problems?
No. Although we appreciate that this would be very useful, diaries are not provided as part of the FOR DMD study.

Can the eye check be performed by a subject local optician or do the boys need to be seen by a specialist at the hospital?
The eye check can be performed by any qualified eye care practitioners and is not required to be carried out by an Ophthalmologist at the hospital. However, the person performing the test must be aware of the study requirements and the specific clinical question as reported in eCRF 26. A written assessment report is required as source data.

BIOBANK and BONE DMD
Have sites been provided with Tubes and vials for Biobanking?
No. Sites should use their own tubes and vials for Biobanking samples. Please contact us if you have any issues with this. Sites have been provided with vials for BONE DMD urine and blood samples only.

Should Biobanking and BONE DMD samples be sent centrally right after collection?
No. Biobank and BONE DMD samples only need to be sent centally once a year. Sites will be contacted by us when shipment is due with details for shipment arrangement. Cost for shipments will be covered by FOR DMD. Please note, Biobank and BONE DMD samples will be delivered to two different centres (in two different countries) and therefore samples cannot be packed together!

EXPeRT

The paper CRF that I am using appears as the same version but in a different format to that on EXPeRT.
Check that you are using the correct document and version number. Sometimes documents appear in an unusual order in the document list (unfortunately, we can't control the order of documents within the folders), so check that you have scrolled down to the document that you need. We are continuously testing the system so hopefully we will reduce the confusion around CRFs and you'll have fewer PDFs to print out. We've also fixed a few other typos in some other forms so we'll be updating all the PDF packets soon. Since minor changes may continue to happen we recommend that each time you have a visit coming up you check the document area of EXPeRT to make sure you have the most recent version of the packet you need.

Study drug ordering – follow up visits.
The field 'dosage held constant despite weight increase' is only intended to be used for study drug dosage adjustments, specifically for keeping the same weight band even though the weight gain would normally have put the subject in a higher band. The field should therefore be entered as 'No' unless the PI decides to maintain the same dose due to a side effect. If a subject increases in weight from the previous visit, but does not move into the next weight band, the field should be entered as 'No' and the system will automatically order the correct dose.

Screening log and screening eCRF
On the screening log, sites should record all subjects who have been considered for the study, regardless of whether or not they agree to take part, complete or fail screening, or are recruited to the study. The screening log helps us to monitor screening and recruitment rates and reasons for failure.
If a subject fails screening before consenting (e.g. refuses to attend the screening visit) only the screening log should be completed - no eCRF needs to be filled in. eCRFs need to be completed only for subjects who have provided signed consent.

Study drug destruction
Destruction of study medication (returned at each visit from subjects) can be performed at site or can be arranged via the clinical trials supply company at the site cost.
If returned study drug is destroyed at site, the study drug can be destroyed only after reconciliation at the second return of the supply (and if the counts are in agreement). If destruction is being performed at site, sites will need to provide the Sponsor with a certificate of destruction (as per GCP requirements).

PedsQL questionnaires:
eCRFs 63 and 64 (PedsQL Core and Neuromuscular module) do not perfectly match with the paper questionnaires. In the Parent Report for Young Children, parents have a choice of five possible answers. In the Young Child Report, children have a choice of three possible answers. For the Young Child report, you can enter the proper numeric code even though the description may not match exactly.
Since all age group versions with the exception of Toddler (2-4 years) require the collection of 2 different PedsQLs per visit (one for the child and one for a parent) you will need to create multiple records for eCRF63 and eCRF64.

A full list of FAQs and detailed responses may be found at http://for-dmd.org/faqs/

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