

FOR-DMD – FOR YOU!



Newsletter 4 –1st November 2013

FOCUS ON RECRUITMENT

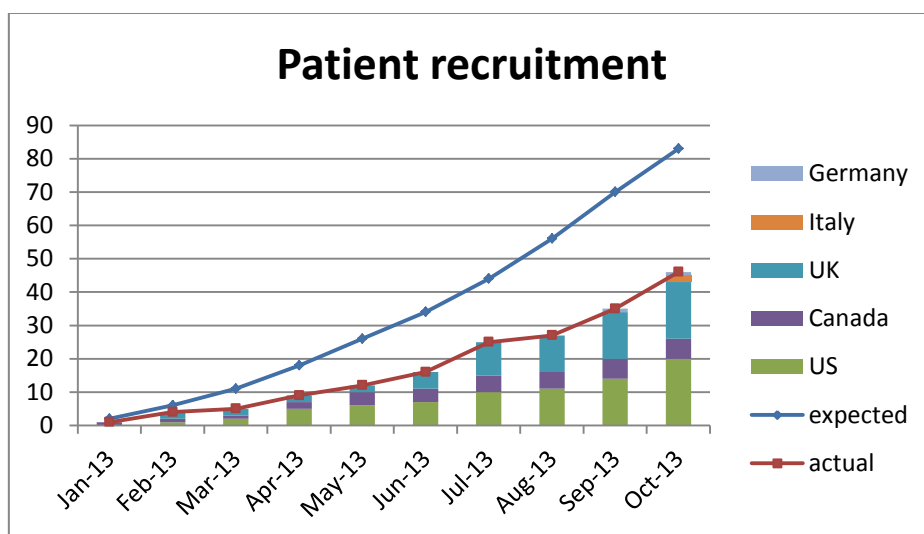
SITE ACTIVATION

Three more sites have been added since our last newsletter on 6th September, bringing the total number of active sites to 38. University of Giessen (Germany) joined us on 25th September, Utah (US) joined on 10th October, and Oxford (UK) on 31st October – 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 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 812 site months of recruitment.

With 46 patients randomised to 31st October, we are unfortunately somewhat behind our recruitment target at this time, with 55% of the number (83) expected to be randomised by now, based on the number of open sites and the dates on which they were activated. **To reach our target of 300 patients randomised by 2nd January 2015, we need all sites to be randomising an average of 5 patients per year from now on.**









































To ensure that we reach our target, we are exploring the opening of additional sites in the US, Canada and Italy and participant identification centres in the UK and Ireland.

		Months open	Identified	In screening	Screened	Screen failures	Screen failure %	Days since last screen started
	Royal Hospital for Sick Kids, Glasgow	6.05	<u>10</u>	4	6	3	50%	42
	Birmingham Heartlands	6.77	8	2	6	4	67%	10
	Alberta Children's Hospital	9.57	8	1	7	4	57%	46
	University of Rochester	9.53	7	3	4	1	25%	18
	University California Los Angeles	<u>9.93</u>	5	0	5	0	0%	32
	Dresden University	2.86	4	1	3	3	100%	11
	Leeds Teaching Hospital	6.51	4	2	2	0	0%	42
	Nemours Children's Hospital	8.55	4	1	3	2	67%	121
	Alder Hey (Liverpool)	9.07	4	0	4	0	0%	49
	Newcastle University	9.63	4	0	4	0	0%	130
	University of Messina	3.52	3	3	0			4
	Neuromuscular Centre Turin	3.52	3	0	3	1	33%	29
	Royal Manchester Children's Hospital	5.36	3	2	1	1	100%	8
	London Health Sciences Centre	7.89	3	0	3	0	0%	182
	University California Davis	8.75	3	1	2	0	0%	<u>2</u>
	Lurie Children's Hospital of Chicago	9.04	3	0	3	1	33%	71
	Great Ormond Street Hospital	4.21	2	0	2	0	0%	14
	University Medical Center, Freiburg	6.12	2	0	2	1	50%	46
	Nationwide Children's Hospital (Ohio)	6.77	2	1	1	0	0%	72
	Kansas University Medical Center	7.73	2	1	1	0	0%	78
	Boston Children's Hospital	8.32	2	1	1	0	0%	78
	University of New Mexico	8.65	2	1	1	0	0%	14
	Penn State Hershey Medical Center	9.04	2	0	2	0	0%	169
	IRCCS Medea	3.09	1	1	0			3
	Neurological Institute Milan	3.48	1	1	0			44
	Kennedy Krieger Institute	8.58	1	0	1	0	0%	238
	SUNY Downstate Medical Center	7.13	1					
	Oxford	0.03	<u>0</u>					
	Utah	0.72	<u>0</u>					
	University of Giessen	1.22	<u>0</u>					
	University of Padova	2.17	<u>0</u>					
	Goettingen University	2.40	<u>0</u>					
	Essen University	3.06	<u>0</u>					
	University of Manitoba	3.32	<u>0</u>					
	University Hospital Wales (Cardiff)	3.32	<u>0</u>					
	Second University of Naples	3.48	<u>0</u>					
	University of Minnesota	4.73	<u>0</u>					
	Vanderbilt Children's Hospital	9.44	<u>0</u>					
	TOTAL	223.56	94	26	39	10		

Best performing site per country highlighted in red; overall top performer underlined

Sites with no patients identified to date highlighted in bold and underlining

		Months open	Recruits to date	Min target by 2 Jan 2015	% of target achieved	% of time elapsed	BRAG rating	Days since last recruit
	University California Los Angeles	<u>9.93</u>	<u>5</u>	9	56%	41%	green	15
	Alder Hey (Liverpool)	9.07	4	9	47%	39%	green	11
	Newcastle University	9.63	4	9	46%	41%	green	58
	Royal Hospital for Sick Kids, Glasgow	6.05	3	7	40%	30%	green	39
	London Health Sciences Centre	7.89	3	8	37%	36%	green	156
	University of Rochester	9.53	3	9	34%	40%	green	<u>2</u>
	Alberta Children's Hospital	9.57	3	9	34%	40%	green	39
	Neuromuscular Centre Turin	3.52	2	7	31%	20%	green	7
	Great Ormond Street Hospital	4.21	2	7	30%	23%	green	3
	Leeds Teaching Hospital	6.51	2	8	26%	32%	green	123
	Birmingham Heartlands	6.77	2	8	26%	32%	green	59
	University California Davis	8.75	2	8	24%	38%	green	3
	Lurie Children's Hospital of Chicago	9.04	2	9	23%	39%	amber	31
	Penn State Hershey Medical Center	9.04	2	9	23%	39%	amber	134
	University Medical Center, Freiburg	6.12	1	7	13%	30%	amber	45
	Nationwide Children's Hospital (Ohio)	6.77	1	8	13%	32%	amber	108
	Kansas University Medical Center	7.73	1	8	12%	35%	amber	49
	Boston Children's Hospital	8.32	1	8	12%	37%	red	58
	Nemours Children's Hospital	8.55	1	8	12%	38%	red	116
	Kennedy Krieger Institute	8.58	1	8	12%	38%	red	203
	University of New Mexico	8.65	1	8	12%	38%	red	100
	Oxford (opened 31 Oct 2013)	0.03	0	5	0%	0%		
	Utah	0.72	<u>0</u>	5	0%	5%	black	
	University of Giessen	1.22	<u>0</u>	6	0%	8%	black	
	University of Padova	2.17	<u>0</u>	6	0%	13%	black	
	Goettingen University	2.40	<u>0</u>	6	0%	15%	black	
	Dresden University	2.86	<u>0</u>	6	0%	17%	black	
	Essen University	3.06	<u>0</u>	6	0%	18%	black	
	IRCCS Medea	3.09	<u>0</u>	6	0%	18%	black	
	University of Manitoba	3.32	<u>0</u>	6	0%	19%	black	
	University Hospital Wales (Cardiff)	3.32	<u>0</u>	6	0%	19%	black	
	Neurological Institute Milan	3.48	<u>0</u>	6	0%	20%	black	
	Second University of Naples	3.48	<u>0</u>	6	0%	20%	black	
	University of Messina	3.52	<u>0</u>	7	0%	20%	black	
	University of Minnesota	4.73	<u>0</u>	7	0%	25%	black	
	Royal Manchester Children's Hospital	5.36	<u>0</u>	7	0%	28%	black	
	SUNY Downstate Medical Center	7.13	<u>0</u>	8	0%	34%	black	
	Vanderbilt Children's Hospital	9.44	<u>0</u>	9	0%	40%	black	
	TOTAL	223.63	46	300*			green	

Best performing site per country highlighted in red; overall top performer underlined

Sites with no patients identified to date highlighted in bold and underlining

*total includes projected targets for sites yet to open, based on estimated date of opening

BRAG RATING

In the table above, we introduce 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 opening 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 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.

For example, UCLA opened on 3 January 2013. Therefore it has been open for 9.93 months out of a total of 24 months (3 January 2013 to 2 January 2015), so 41% (9.93/24) of its total number of months are elapsed. UCLA's 'share' of the total target of 300 patients is given by multiplying 300 by this site's share of the total number of site months (24/812), giving a minimum target of 9. To date, UCLA has recruited 5 patients, so its % recruitment to target is $5/9 = 56\%$. The difference between % elapsed time and % recruitment to target is $56\% - 41\% = 15\%$, leading to a Green rating.

PERFORMANCE HIGHLIGHTS



University of Rochester (Dr Ciafaloni and colleagues) are the best US performer in terms of patients identified, and hold the current record for the shortest interval from screening to randomisation (2 days). UCLA (Dr Shieh and colleagues) was the first FOR DMD site to open, and is our overall top recruiter to date, with five patients randomised, ahead of target at this time. Elsewhere in this newsletter, the UCLA team share their hints on patient recruitment.



Alberta Children's Hospital (Dr Mah and colleagues) lead the way in Canada for patients identified (eight) and screened (seven).



Alberta and London Ontario (Dr Campbell and colleagues) have both randomised three patients, with London edging slightly ahead when % recruitment to target is compared to % elapsed time.

Royal Hospital for Sick Children Glasgow (Dr Horrocks and colleagues) is our overall best performing site for patient identification, with ten children identified, six of whom have been screened.

Alder Hey (Dr Spinty and colleagues) and Newcastle (Professor Straub and colleague) share top spot for recruitment in the UK, with four patients each randomised; in both sites the % of recruits to target exceeds the % of time elapsed.



Our Italian sites only opened to recruitment in July and August, so the focus to date has primarily been on patient identification and screening. University of Messina (Dr Vita and colleagues) and Neuromuscular Center Turin (Dr Mongini and colleagues) have both identified three patients.

Neuromuscular Center Turin has gone on to randomise two patients, twice as many as expected of them at this time.



The majority of our German sites also only opened to recruitment from July onwards, so have also been focusing on patient identification and recruitment. Dresden University (Dr von der Hagen and colleagues) leads the way in Germany for patients identified, with four identified and three screened.

University Medical Center, Freiburg (Dr Kirschner and colleagues) has randomised one patient.

HINTS FOR RECRUITMENT

Dr Perry Shieh and colleagues from UCLA, our top recruiting site, share their experiences and hints for successful recruitment. Dr Shieh says:-

"When I identify potential subjects at the clinic, I ask my coordinator, Angel Hu, to give the family an overview of the study. My coordinator provides a copy of the Informed Consent Form to the family and encourages them to study it carefully so that they can be better informed about the trial. After a week or two, my coordinator will reach out to the family via phone call to see how the family feels about participating in the trial. We emphasize that it is really unclear which of the three arms of the study is best for the child and thus it is important to do the study. Many families are naturally a little overwhelmed about the study's agenda, but we also emphasize that the study is mostly collecting data that is otherwise standard of care. For example, one family showed initial interest and wanted to discuss about the ICF with their own neurologist a month later. After a month, my coordinator reached out to the family again to listen to their thoughts about the trial, and the family's interest about enrolling in the FOR-DMD trial solidifies afterwards. With professionalism and approachability, our site was able to resolve these families' concerns, thus, successfully enrolling the boys in the trial.

We encountered some problems with subjects being able to swallow the tablets. One particular subject was fearful and unfamiliar with pills, so he was resistant. With patience and encouragement from a number of our team members, including our MDA representative at our neuromuscular clinic, the subject finally conquered his fear of pills and passed screening procedures."

MEDICINES FOR CHILDREN RESEARCH NETWORK SUPPORT FOR UK SITES

UK sites are reminded that they can access support from the local Medicines for Children Research Network. Contact details are as follows:-

Site name	Name	Email	Phone
Newcastle University	Vicky Stevenson	vicky.stevenson@NUTH.NHS.UK	0191 282 1682
Alder Hey (Liverpool)	Ed Staunton	edward.staunton@alderhey.nhs.uk	0151 252 5570
Birmingham Heartlands	Gemma Slinn	Gemma.slinn@bch.nhs.uk	0121 333 8734
	Claire Callens	Claire.callens@bch.nhs.uk	
Oxford Children's Hospital	Becky Beckley	rebecca.beckley@paediatrics.ox.ac.uk	01865 234332
Great Ormond Street Hospital	Erika Lansdell	Erika.Lansdell@gosh.nhs.uk	020 7829 7991
Leeds Teaching Hospital	Heather Rostrum	Heather.Rostron@cmft.nhs.uk	0161 701 6947
Royal Hospital for Sick Children, Glasgow	Pam Dicks (ScotMCN)	p.dicks@abdn.ac.uk	01224 438474
Royal Manchester Children's Hospital	Carol Beane	carol.beane@cmft.nhs.uk	0161 701 6947
	Donna Danziger (Nurse)	Donna.danziger@cmft.nhs.uk	
University Hospital Wales (Cardiff)	Rhian Thomas (CYPRN)	ThomasR66@cardiff.ac.uk	029 2074 3326
	Anwen Howells (NISCHR)	HowellsAS@cardiff.ac.uk	029 2019 6802

MDA FUNDING FOR PATIENT VISITS IN US AND CANADA

We are happy to report that MDA has agreed to provide travel support for US and Canadian subjects in the FOR-DMD trial **for whom participation would otherwise pose a considerable financial burden** (and possibly prevent participation altogether). We received the Notice of Award yesterday and Kim Hart at University of Rochester is currently setting up subagreements with each US and Canadian site to allow for reimbursement. Sites should be receiving the subagreement for signature this week (to your Sponsored Programs Department).

A few things to keep in mind:

The amount of the award is quite modest, so we are NOT able to reimburse every subject/family. This option should be reserved for those coming from a considerable distance (i.e., have to fly/stay overnight in hotel) or those families who express concern over the travel expense involved. Funds cannot be provided to the family up-front, unless you are willing to do so from a petty-cash account or some other mechanism at your site. Kim will need to receive all travel receipts (with identifying information such as name, credit card number, etc., blacked out) and your University/Hospital will be reimbursed within 2-3 weeks. Note that we **cannot issue reimbursement checks directly to the subject's family** as this would be a breach of confidentiality (Kim would need to know the name, address, SS# of the individual in order to pay them directly).

Please encourage families to arrange modest travel arrangements (we will not reimburse for flying first-class, staying in top line hotel, etc.). Typically, if a family must stay overnight when coming from a distance, the site has some sort of financial arrangement with a local hotel.

Should you have any questions, please feel free to contact Kim (Kim_Hart@URMC.Rochester.edu). Kim will let both the PI and the coordinator know as soon as the sub-agreement is in place at your particular institution, so that travel reimbursement may be offered to families, if needed.

Please submit an amendment to your IRB to address this change – that subjects may be reimbursed (in some instances) for travel. We will not be able to reimburse your site for subject travel until 1) the subcontract described above has been signed by your site, and 2) Kim has a copy of your IRB-approved, amended consent form. Please revise your consent document(s), as follows:

Under the section headed **“What are the costs to participate...”**, please **delete** the sentences that say “You will have to pay for your travel to and from the clinic” (or whatever verbiage might be used in your site-specific consent addressing this issue) and “Neither you nor your child will receive payment or reimbursement of expenses for taking part in this study.”

Please **insert the following text**:

“Neither you nor your child will receive payment for participating in this study. If you must travel a significant distance to the study center for visits (for example, more than 200 miles) and this would present a financial hardship for you, limited funds are available to reimburse your travel expenses (airfare, hotel, etc.). These funds have been provided by a grant from the United States Muscular Dystrophy Association. If you think you may require reimbursement of travel expenses, please discuss with the Principal Investigator/Study Coordinator.”

Please submit this amendment to your IRB ASAP and, once approved, provide me with the amendment approval notice and revised IRB-approved consent document(s).

