FOR-DMD – FOR YOU!

Newsletter 7 – 18th September 2015

Apologies for the long gap since the last newsletter. We have been awaiting some important decisions to be ratified by our Steering Group and our Data Safety and Monitoring Board, which we can now report below. We will now be resuming more regular newsletters and will be introducing e-blasts to keep all sites updated on progress and plans.

RECRUITMENT TARGET REDUCED – NEW TARGET 225 PATIENTS: HELP THE STUDY FULLY ENROL SOON!

Based on analysis of accumulating FOR-DMD trial by our trial biostatistician Dr Mike McDermott (blinded to treatment group), the correlations between the three components of the composite primary outcome measure have been found to be quite small and lower than originally anticipated. This results in a higher power and allows us to achieve the goals of the study with fewer boys: **a revised sample size of 225 boys rather than 300** as originally planned. This reduction in sample size has been approved by the Data Safety and Monitoring Board. **Recruitment and randomization will now continue to 31 August 2016 or until 225 boys have been randomised, whichever is the earlier**. Current randomizations stand at 156, so we are at 69% of our target with just over 11 months to go. If each site managed to recruit another two patients in the coming months, we can make that target! Please make every effort to continue to recruit boys to the study. Ongoing recruitment will be on a competitive basis, with no upper limit for any site and it would be fantastic if we could finish recruitment before our target date. If you require an amendment to your site sub-agreement to allow for this altered target, please contact Kim Hart (Kim_Hart@URMC.Rochester.edu).

UPCOMING PROTOCOL AMENDMENTS

To assist in reaching our revised targets, we are currently preparing to implement two major amendments to protocol which will broaden study eligibility criteria; these changes have been agreed by the Data Safety and Monitoring Board.

The first will allow enrolment of boys aged **3 years and over**, subject to these boys fitting all other study eligibility criteria and being able to comply with study procedures.

The second will allow boys who wish to enrol in Sarepta's current and future exon skipping trial(s) to **also remain in FOR-DMD**. This provision for co-enrolmentis thanks to an agreement on sharing data. In respect of future Sarepta studies, within the last month, the U.S. Food and Drug Administration (FDA) has accepted their New Drug Application (NDA) for eteplirsen to treat DMD and has granted this drug priority review. The date for a decision on the application by FDA is 26 February 2016. The arrangements for co-enrolment in Sarepta trials and FOR-DMD will also apply to this study once it commences.

We have also clarified that boys prescribed **Ataluren/ Translarna** as part of routine care are allowed to stay in FOR-DMD.

The FOR-DMD trial coordination team are currently seeking approvals from regulatory authorities, IRBs and RECs for these protocol amendments and will notify you when these come through. In the meantime, the current protocol and eligibility criteria should be followed. If you have any queries regarding these amendments, please contact Michela Guglieri (Michela.Guglieri@newcastle.ac.uk).

SAREPTA AND MARATHON TO SUPPORT FOR-DMD

Because of delays in study start-up and recruitment, we will need to obtain additional drug supplied and to support sites for longer than expected. We are pleased to report that both Sarepta and Marathon have agreedd to help support the study, in recognition of its importance. We expect other pharma companies working on DMD may also help.

SITE CHANGES

Since our last newsletter, we have added new sites in Cambridge, UK and Washington DC, USA and are in the process of opening a site in Pisa, Italy. The following sites have withdrawn from the study: Kennedy Krieger Institute (USA); Cardiff (UK); IRCCS Eugenio Medea (Italy); Hauner's Children's Hospital, Munich (Germany).

SPAIN TO JOIN FOR-DMD

We are delighted to announce that we expect to open FOR-DMD in Spain in late 2015/early 2016. Four Spanish sites – Barcelona, Seville, Madrid and Valencia – have expressed interest in taking part. We are currently going through the process of obtaining regulatory and ethical approval for the study from the Spanish authorities.

NEW BUDGET YEAR

We are now in a new year of the trial (1 July 2015 – 30 June 2016). Sub-agreement modifications to reflect the budget period and new account number should have been received by all sites' Sponsored Programs/R&D Department by end of August 2015. Please check that your site has received its modified sub-agreement and inform Kim Hart (Kim_Hart@URMC.Rochester.edu) if it has not arrived. Payments to sites on a quarterly basis will continue, while the sub-agreements are under modification. If you have any queries regarding payment, please contact Kim.

RAISING A MUG TO SUCCESS

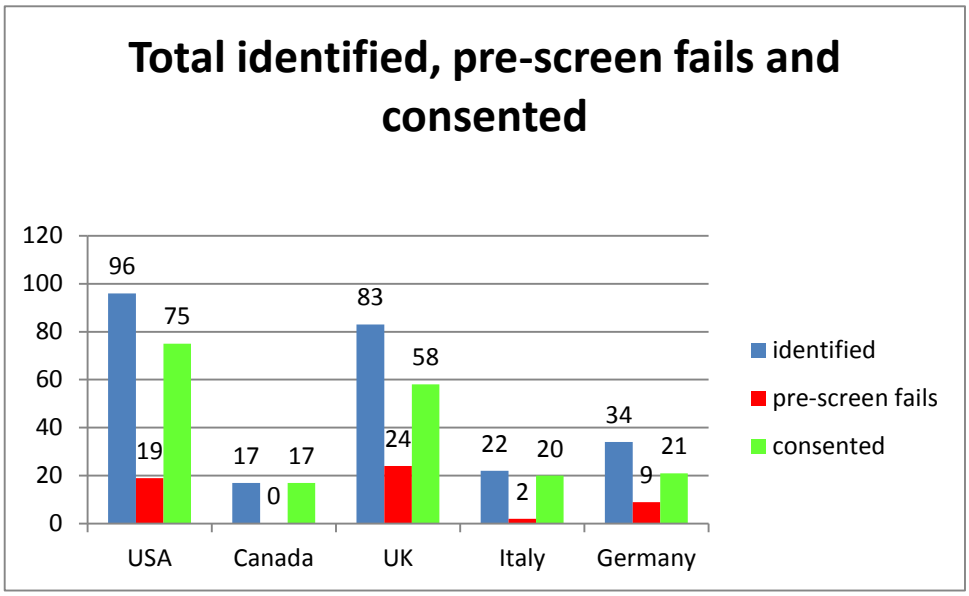
Since our last newsletter, the following sites have won sets of mugs: 110th randomization – Boston (Dr Kang and colleagues); 120th randomization – Essen (Dr Schara and colleagues); 130th randomization - Alder Hey (Dr Spinty and colleagues); 140th randomization – New Mexico (Dr Morrison and colleagues); 150th randomization – Freiburg (Dr Kirschner and colleagues). Ohio (Dr Flanigan and colleagues) also received a set of mugs for excellent effort. Will your site be next?

PERFORMANCE HIGHLIGHTS

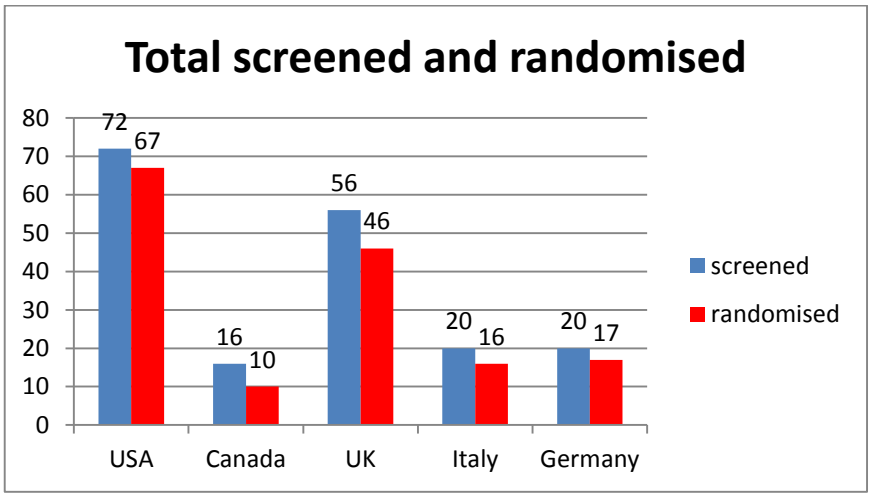
We salute our top 11 recruiting sites, who between them have randomized 86 patients. Congratulations also to Alberta Children's Hospital, Calgary, our top recruiting site in Canada, and Dresden and Essen Universities, joint top recruiting sites in Germany; each of these sites has randomized 5 patients.

Site	Country	Randomized Patients
University California Los Angeles		10
Newcastle University		9
Lurie Children's Hospital of Chicago		8
Royal Hospital for Sick Kids, Glasgow		8
Leeds Teaching Hospital		8
University of Rochester		8
Alder Hey (Liverpool)		7
Birmingham Heartlands		7
Neurological Institute Milan		7
Nationwide Children's Hospital (Ohio)		7
Utah		7

OVERALL SITE PERFORMANCE



As of 18th September 2015, a total of 252[1] patients have been identified, with 7 currently in pre-screening. There have been 54 pre-screen failures. A total of 191 patients have been consented, 7 of whom are currently going through screening.



Also as of 18th September 2015, a total of 184 patients have been screened post-consent, with 28 screen failures, an overall screen failure rate of 15%. A total of 156 patients have been randomised. According to the revised target of 225, we should have randomised 158 patients by now. Going forward, to hit our target of 225 boys by 31st August 2016, we need all sites to be recruiting and randomising at an average rate of 2 patients per site per year.

Eight boys have terminated participation in the study; a further four have withdrawn from study drug but are continuing in the FOR-DMD trial for purposes of data collection. Within the last few weeks, the first four boys enrolled have reached their 30-month follow-up. Two boys have moved sites for follow-up, in one case following closure of the site at which they were originally recruited and on the other following family re-location.

[1] Numbers identified and pre-screen fails include withdrawn sites

FOR-DMD IN THE SOCIAL MEDIA

Remember that we have our own Twitter account! Follow us @FOR_DMD. If you are a member of the Twitterati, please re-tweet our messages.

Please also visit our website – www.for-dmd.org