Contemporary Clinical Trials Communications 11 (2018) 113–119

Contents lists available at ScienceDirect

Contemporary Clinical Trials Communications

journal homepage: www.elsevier.com/locate/conctc

Recruitment & retention program for the NeuroNEXT SMA Biomarker Study: Super Babies for SMA!

Amy Bartlett[a,1], Stephen J. Kolb[a,b,*,1], Allison Kingsley[a], Kathryn J. Swoboda[c,d,e], Sandra P. Reyna[c,d,f], Ai Sakonju[c,d,g], Basil T. Darras[e], Richard Shell[h], Nancy Kuntz[i], Diana Castro[j], Susan T. Iannaccone[j], Julie Parsons[k], Anne M. Connolly[l], Claudia A. Chiriboga[m], Craig McDonald[n], W. Bryan Burnette[o], Klaus Werner[p], Mathula Thangarajh[q], Perry B. Shieh[r], Erika Finanger[s], Christopher S. Coffey[t], Jon W. Yankey[t], Merit E. Cudkowicz[u], Michelle M. McGovern[u], D. Elizabeth McNeil[v,f], W. David Arnold[a,w], John T. Kissel[a], The NeuroNEXT Clinical Trial Network and on behalf of the NN101 SMA Biomarker Investigators

[a] Department of Neurology, The Ohio State University Wexner Medical Center, Columbus, OH, United States
[b] Department of Biological Chemistry & Pharmacology, The Ohio State University Wexner Medical Center, Columbus, OH, United States
[c] Department of Neurology, University of Utah, Salt Lake City, UT, United States
[d] Department of Pediatrics, University of Utah, Salt Lake City, UT, United States
[e] Department of Neurology, Boston Children's Hospital, Boston, MA, United States
[f] Biogen, Boston, MA, United States
[g] SUNY Upstate Medical Center, Syracuse, NY, United States
[h] Nationwide Children's Hospital, Columbus, OH, United States
[i] Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, United States
[j] UT Southwestern Medical Center, Dallas, TX, United States
[k] Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, CO, United States
[l] Washington University School of Medicine in St. Louis, St. Louis, MO, United States
[m] Department of Neurology, Columbia College of Physicians and Surgeons, New York, NY, United States
[n] University of California - Davis, Davis, CA, United States
[o] Vanderbilt University, Nashville, TN, United States
[p] Duke University Medical Center, Durham, NC, United States
[q] Children's National Medical Center, Washington, DC, United States
[r] University of California - Los Angeles, Los Angeles, CA, United States
[s] Dorenbecher Children's Hospital, Portland, OR, United States
[t] Department of Biostatistics, NeuroNEXT Data Coordinating Center, University of Iowa, Iowa City, IA, United States
[u] Department of Neurology, NeuroNEXT Clinical Coordinating Center, Massachusetts General Hospital, Boston, MA, United States
[v] National Institute of Neurological Disorders and Stroke, Bethesda, MD, United States
[w] Department of Physical Medical and Rehabilitation, The Ohio State University Wexner Medical Center, Columbus, OH, United States

ARTICLE INFO

Keywords:
Social media
Altruism
Spinal muscle atrophy
Healthy controls
Network

ABSTRACT

Background/Aims: Recruitment and retention of research participants are challenging and critical components of successful clinical trials and natural history studies. Infants with spinal muscular atrophy (SMA) have been a particularly challenging population to study due to their fragile and complex medical issues, poor prognosis and, until 2016, a lack of effective therapies. Recruitment of healthy infants into clinical trials and natural history studies is also challenging and sometimes assumed to not be feasible.

Methods: In 2011, our group initiated a two-year, longitudinal natural history study of infants with SMA and healthy infant controls to provide data to assist in the analysis and interpretation of planned clinical trials in infants with SMA. The recruitment goal was to enroll 27 infants less than 6 months of age with SMA and 27 age-matched healthy infants within the two-year enrollment period. A detailed recruitment and retention plan was

* Corresponding author. Department of Neurology, Wexner Medical Center at The Ohio State University, Rightmire Hall, Rm 226A, 1060 Carmack Road, Columbus, OH, 43210, United States.
E-mail address: Stephen.Kolb@osumc.edu (S.J. Kolb).
[1] Authors contributed equally to this work.

https://doi.org/10.1016/j.conctc.2018.07.002
Received 8 February 2018; Received in revised form 26 June 2018; Accepted 12 July 2018

developed for this purpose. In addition, a survey was administered to participant families to understand the determinants of participation in the study.

Results: All healthy infants were recruited within the study's first year and 26 SMA infants were recruited within the two-year recruitment period. Thirty-eight participant families responded to the recruitment determinants survey. Nearly half of respondents (18/38, 48%) reported that they first heard of the study from their physician or neurologist. The most common reason to decide to enroll their infant (22/38, 58%) and to remain in the study (28/38, 74%) was their understanding of the importance of the study. Thematic recruitment tools such as a study brochure, video on social media, and presentations at advocacy meetings were reported to positively influence the decision to enroll.

Conclusions: A proactive, thematic and inclusive recruitment and retention plan that effectively communicates the rationale of a clinical study and partners with patients, advocacy groups and the local communities can effectively recruit participants in vulnerable populations. Recommendations for the proactive integration of recruitment and retention plans into clinical trial protocol development are provided.

1. Introduction

Recruitment into clinical trials, particularly in vulnerable patient populations (ie: economically disadvantaged, racial and ethnic minorities, children, the elderly, prisoners and those with terminal illness) is a challenge that affects the cost and timeliness of delivering those potential therapies [1]. An analysis of studies registered in 2011 within the National Library of Medicine clinical trial registry demonstrated that 19% of the clinical trials closed or terminated due to failure to meet accrual goals [2].

Lack of awareness regarding to the availability of clinical trials is one factor for low enrollment [3]. This is often due to a lower priority placed on research by clinicians who are focused on clinical management [4,5]. There is also the belief by some practitioners that families will be overburdened by being asked to participate in research, despite evidence to the contrary [6]. On the other hand, altruism is a major factor for research participation reported by research participants [7]. Healthy volunteers and people enrolled in observational studies more generally state the benefits to enrollment are intangible and include feelings of enhanced self worth and knowing that “one has done a good deed” so long as the trial is not too overwhelming [8,9].

Spinal muscular atrophy (SMA) is a progressive, genetic motor neuron disease that affects 1 in 6000–10,000 births and is the leading genetic killer of infants [10]. SMA is characterized by progressive muscular weakness and in the most common and severe form (type 1), infants do not achieve sitting or higher level motor skills, and respiratory insufficiency and death often occur within the first two years of life [10,11]. This population presents clear challenges for recruitment; infants suffering from a terminal illness with, at the time of our study, no effective therapy. Recruitment in past SMA natural history studies was variably successful in meeting recruitment goals for children older than 6 months and when done retrospectively [12–14]. However, even in a therapeutic trial, enrollment for infantile-onset SMA has been slow due to many patients being too weak to travel, or not interested if the trial includes a placebo arm [14].

The NeuroNEXT SMA Infant Biomarker Study was a prospective, longitudinal natural history study of infants with infantile-onset SMA begun in 2012 [15,16]. Between December 14, 2012 and September 10, 2014, 26 SMA and 27 healthy infants were enrolled marking a successful and on-time recruitment into the study (Fig. 1) [15]. The last study visit occurred in August, 2015. Twenty-three healthy infants (85.2%) completed the study. Two healthy infants (7.4%) discontinued because parents moved from a study site, and two were lost to follow up. Seven SMA infants (26.9%) completed the study. There were 12 deaths (46.2%) in the SMA cohort, and 7 infants (26.9%) withdrew from the study prior to the 24-month visit [16]. The success of the study has contributed to the interpretation of clinical trials in this population and to the approval of the first FDA-approved medication for SMA and promises to contribute to numerous clinical trials involving the study of motor function in infants [17–19].

Here, we report the details of the SMA Infant Biomarker Study recruitment and retention plan. In addition, we report the results of a questionnaire sent to participant families to determine factors that influenced recruitment and retention. Finally, we provide recommendations for the proactive integration of recruitment and retention plans into clinical trial protocol development.

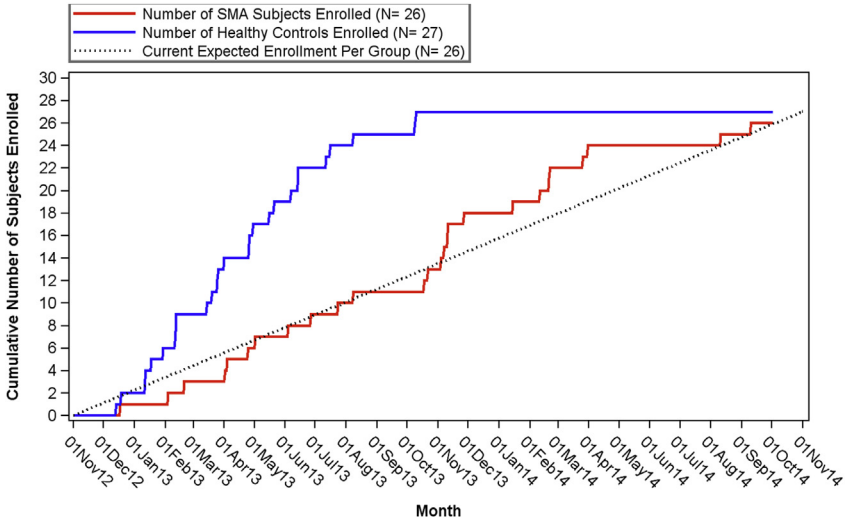

Fig. 1. Cumulative enrollment of the NeuroNEXT SMA Infant Biomarker Study Enrollment of 27 healthy control infants (blue line) and 26 infants with SMA (red line) exceeded expected 2-year enrollment estimate (dotted black line). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)