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Consent to Participate in a Research Study

Effects of physical therapy and Dalfampridine on functional mobility and lower extremity strength in non ambulatory subjects with MS

You are being asked to participate in a research study. The purpose of this document is to provide you with information to consider in deciding whether you would like to participate. Your consent should be made on your understanding of the nature and risks of the medication being offered, the exercise testing and training procedures. Please ask questions if there is anything you do not understand. Your participation is voluntary and will have no effect on the quality of your medical care if you choose not to participate. Your signature at the end of this consent form will indicate that the Principal Investigator, or her associates, has answered all of your questions and that you voluntarily consent to participate in this study.

1. INVESTIGATORS CONDUCTING THE STUDY

Who will be conducting the study?

The investigators for the study are:

Susan Bennett, PT, DPT, Ed.D. Clinical Associate Professor, Rehabilitation Science
515 Kimball Tower, University at Buffalo, Buffalo, NY 14214
Phone: 829-6719, E-mail: sbennett@buffalo.edu

Bianca Weinstock-Guttman, MD. Associate Professor of Neurology, University at Buffalo
100 High Street, Buffalo NY 14203
Phone: 716-859-7051, Email: bguttman@thejni.org

2. SOURCE OF SUPPORT

Who is sponsoring the research study?

The sponsor for this study is Acorda Therapeutics

3. SITE OF THE RESEARCH STUDY

Where will the study be conducted?

The study will be conducted in the Wellness Center at DeGraff Memorial Hospital.

4. PURPOSE OF THE RESEARCH STUDY

What is the purpose of the research?

The purposes of this study is to assess the change in standing tolerance, transfers, repeated sit to stand, arm and leg strength and cognitive processing for non-ambulatory individuals with MS between subjects on Dalfampridine who receive physical therapy and those who participate in physical therapy and receive a

placebo. We will also be looking at how receiving physical therapy alone affects standing tolerance, transfers, repeated sit to stand, arm and leg strength.

5. ELIGIBILITY

Who is being asked to participate in this research study?

You are being asked to participate because you have been diagnosed with MS and have moderate disability.

Inclusion criteria:

- Have a definite diagnosis of MS made by a neurologist
- You are at least 20 years old
- You can not walk with or without an assistive device for more than 16 feet.

Exclusion criteria:

- Had a relapse or active disease within the last 30 days
- Subject with a history of seizures or renal function disease
- Have limited range of motion, neuropathic pain, or poor strength in your legs
- You are pregnant
- Inability to give consent

If you have any of the exclusion criteria or do not meet all of the inclusion criteria, you will not be allowed to participate in the study.

6. PROCEDURES

What procedures will be performed for research purposes?

If you decide to take part in this research study after you have received a thorough explanation, you will then sign the informed consent and HIPAA authorization. Upon completion of those two documents you will be asked to come to DeGraff Hospital for a total of 30 visits over a 21 week period. Transportation, if needed, will be free of charge. At the initial visit you will undergo the following procedures (that are not part of your standard medical care) a physical therapy evaluation that will include assessing the muscle strength of your legs, range of motion, and tests for spasticity and balance. At the conclusion of the physical therapy examination you will be asked to complete the follow questionnaires and tests (A) Respond to a questionnaire describing your health history, symptoms associated with MS, and current medications (B) respond to a questionnaire that describes your overall quality of life (C) A spasm frequency scale (D) two tests of your cognition and ability to recall information. After completing these questionnaires you will be seated in the waiting room to rest for 15 minutes. Following the rest period you will then complete the following physical therapy tests to assess your functional mobility and cognition with mandatory rest periods between specific tests: (1) Strength testing of the arms and legs (2) Standing as long as you can for 2 trials (3) a cognitive test looking at shapes (4) Transfer onto a low mat table with assistance if needed (5) Maintain sitting posture on the low mat table for 2 minutes (6) then transfer back into your wheelchair (7) a cognitive test looking at symbols and lastly (8) you will be asked to repeatedly stand up from sitting 5 times for two trials. You will then be asked to return 2 weeks later to undergo all testing except the physical therapy examination. Prior to your return visit for testing you will be randomly assigned to Group 1 (the experimental group) or Group 2 (the control group). You will NOT know your assignment. Group 1 will receive Dalfampradine 2 times a day while Group 2 will receive a placebo pill 2 times a day. After the two

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initial baseline measurements are completed you will be scheduled for your physical therapy appointments. The physical therapy program will be 45 minute sessions 2 times a week for 12 weeks at the Wellness Center at DeGraff Memorial Hospital. The physical therapy intervention will consist of manual stretching, cycling on a reclined stationary bike, tall kneel and quadruped core activities, seated balance activities, bridging exercise, repeated sit to stand, and standing squats in parallel bars. The prescribed home exercise program will be performed 3x/week and will consist of self stretching, wheelchair pushups, bridging, short arc quads and resistive band exercise for trunk and upper extremity strengthening. You will be retested on all initial testing minus the physical therapy evaluation at 9 weeks, 15 weeks, 18 weeks and 21 weeks of the study. If you do NOT receive Dalfampradine during the study, you will be given the drug after the study conclusion for 12 weeks free of charge.

7. RISKS

What are the possible risks, side effects, and discomforts of this research study?

Dalfampradine is a FDA approved drug for the MS population however, it does have side – effects, most common being urinary tract infection, insomnia, dizziness, headache, nausea, weakness, burning, tingling, itching, constipation, indigestion, pain in throat. The most serious side effect is a chance of seizure. You will be instructed in dosing related to the medication (how to take it, how often, and what to do if you miss a dose). In addition, you will be monitored closely by the physical therapist providing your treatment. If you have any side effects you should report them to your neurologist and to the principal investigator of this study [Dr. Susan Bennett]. Also, the physical therapy treatment and testing may cause some minor muscle soreness and fatigue. You will be asked to wear a gait belt and will be monitored continuously by a physical therapist during all testing and treatment. Appropriate rest and recovery time will be provided.

8. BENEFITS

What are the possible benefits from taking part in this research study?

You will receive 12 weeks of physical therapy treatment as part of this study. Physical therapy has been shown to improve strength, functional mobility and quality of life in Multiple Sclerosis.

9. ALTERNATIVE TREATMENT

What treatments or procedures are available if I decide not to participate in this research study?

If you participate or do not participate in this study, we will not alter your medical care or other medication.

10. NEW FINDINGS

Will I be told of any new information or new risks that may be found during the course of the study?

You will be notified of any significant new developments that may cause you to change your mind about participating in the research study.

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11. COST ASSOCIATED WITH THE RESEARCH STUDY

Will my insurance provider or I be charged for any costs of any procedures performed as part of this research study?

There are no costs to you or your insurance provider associated with this study.

12. REIMBURSEMENT FOR MEDICAL TREATMENT

Who will pay if I am injured as a result of taking part in this research study?

Routinely, the University at Buffalo, State University of New York, its agents, or its employees do not compensate for or provide free medical care for human subjects/participants in the event that any injury results from participation in a human research project. In the unlikely event that you become ill or injured as a direct result of participating in this study, you may receive medical care, but it will not be free of charge even if the injury is a direct result of your participation.

13. COMPENSATION FOR SUBJECT PARTICIPATION

Will I be paid for participating in this study?

You will not be paid for your participation in this study.

14. CONFIDENTIALITY

Who will know about my participation in this research study?

Information related to you will be treated in strict confidence to the extent provided by law. Your identity will be coded and will not be associated with any published results. Your code number and identity will be kept in a secured file of the Principal Investigator. In order to monitor this research study, representatives from the Health Sciences Institutional Review Board, and other federal agencies such as the ORHP (Office of Human Research Protection) may inspect the research records which may reveal your identity.

Any disclosure of results required by the FDA (Food and Drug Administration) may reveal your identity. There are, however, limited circumstances that would allow the FDA to require such disclosure. Any disclosure of results to pharmaceutical companies may reveal your identity. However, your records containing your name will not be removed from the Principal Investigator's office nor will any copies of these records with your name be made. Any records or data sent to pharmaceutical companies will have your identity protected by subject code and will not contain your name.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by US Law. This website will not include information that can identify you. At most the website will include a summary of the results. You can search this website at any time.

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15. AUTHORIZATION for the Use and Disclosure of Identifiable Health Information for Research Purposes

The following information is provided to you as part of the Health Insurance Portability and Accountability Act (HIPAA), requiring that additional safeguards be put into place to protect the privacy and security of an individual's health information, including persons enrolled as research subjects.

1. **What individually identifiable health information will be collected about you as part of this research study?**
   Data that will be collected during the study include your name, address, telephone number, and date of birth. Information from your health records that may be obtained is type of MS, date of diagnosis, current medications and dosages, and your Expanded Disability Status Scale (EDSS) score.

2. **Who will provide or collect this information?**

   - Dr. Susan Bennett (Principal Investigator) or her designee
   - Research team member in the Wellness Center at DeGraff
   - Your neurologist (or staff)

3. **With whom will the research team share this information?**

   Your health information may be shared with others outside of the research group for purposes directly related to the conduct of the research study or as required by law, including but not limited to:
   - The clinical staff at your neurologist's office not involved in this research study who may become involved in your care if it is potentially relevant to your treatment.

   Your information may also be shared with individuals responsible for general oversight and compliance of research activities. Examples of this include UB's Privacy and Security Officers or other internal oversight staff, Safety Monitoring Boards, an Institutional Review Board, and accrediting bodies, or with certain government oversight agencies that have authority over the research, including the Office of Human Research Protections. Your information may also be shared with other entities as permitted or required by law. All reasonable efforts will be used to protect the confidentiality of your individually identifiable health information that may be shared with others as described above.

   All reasonable efforts will be used to protect the confidentiality of your protected health information. There is the potential for individually identifiable information and the associated health information obtained with this authorization to be re-disclosed by the recipient(s). After such a disclosure, the information may no longer be protected by the terms of this authorization against further re-disclosure.

4. **How long will this information be kept by the research group?**

   This authorization has no expiration date. The researchers may continue to rely on this authorization to obtain and use protected health information about you unless you revoke this authorization in writing.

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5. **What are your rights after signing this authorization?**

You have the right to revoke this authorization at any time. If you withdraw your authorization, no additional efforts to collect individually identifiable health information about you will be made. You should know, however, that protected health information acquired using this authorization prior to its withdrawal may continue to be used to the extent that the investigators have already relied on your permission to conduct the research. If you choose to withdraw this authorization, you must do so in writing to the following individual:

Dr. Susan Bennett
Dept. of Rehabilitation Science
515 Kimball Tower
University at Buffalo
3435 Main St.
Buffalo, NY 14214

If you withdraw your authorization, we will forward that request to the institutions we have shared it with in order to collect your individually identifiable health information. You may also withdraw this authorization directly with those institutions by writing to your neurologist's Privacy Officer at their particular location.

6. **What will happen if you decide not to sign this authorization?**

Refusing to sign this authorization will not affect the present or future care you receive at this institution and will not cause any penalty or loss of benefits to which you are otherwise entitled. If you decide not to sign this authorization, you will not be able to participate in the research study.

16. FREEDOM TO WITHDRAW

Is my participation in this study voluntary?

Your participation in this study is voluntary and you may stop your participation at any time without prejudice and without affecting future health care.

17. REMOVAL FROM STUDY

Can I be removed from the study without my consent?

It is possible that you may be removed from the research study by the researchers, if for example, you are unable to perform the testing protocols safely, you have a relapse and/or new disease activity, or you are restricted to your home and unable to participate in the physical therapy treatment. If you have an exacerbation or relapse lasting less than 1 week, you may continue in the study. In the event that a relapse lasts for more than 1 week, you will be removed from the study.

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VOLUNTARY CONSENT

All of the above has been explained to me and all of my current questions have been answered. I am encouraged to ask questions about any aspects of this research study before signing this document. If, in the future, I have questions, concerns, or complaints about the research, I should contact:

Name: Susan E Bennett Title: Principal Investigator Phone Number: 716-690-2051

If I have any questions, concerns, or complaints about my rights as a research subject or want to speak to someone who is not associated with the research, I should contact the staff at the Office of the Health Sciences Institutional Review Board, University at Buffalo: (716) 829-2752.

By signing this form I do not waive any of my legal rights.
By signing this form, I voluntarily agree to participate in this research study.

Name of Subject (print)	Signature of Subject	Date

I certify that the nature and purpose, the potential benefits and possible risks associated with participation in this research study have been explained to the above individual and that any questions about this information have been answered. A copy of this consent will be given to the subject.

(Print) Name of **Person Obtaining Consent** (PI or Designee)	Signature of Person Obtaining Consent (PI or Designee)	Date

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