Impact of individualized physical training on fatigue in multiple sclerosis patients treated with Fingolimod (Gilenya®): design of a phase IV study (PACE)

PACE
PHYSICAL ACTIVITY IN GILENYA TREATED MS PATIENTS

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INTRODUCTION

- Fingolimod (FTY720; Gilenya™, Novartis Pharma AG), a sphingosine 1-phosphate receptor modulator,[1,2] is approved for the treatment of relapsing multiple sclerosis (MS) at a once-daily oral dose of 0.5 mg.
- Fatigue is one of the most common and disabling symptoms of multiple sclerosis and it is reported by up to 80% of all MS patients [3]. Up to 40% of patients with MS report fatigue as the most disabling problem, severely affecting daily activities and thus reducing quality of life [4].
- A recent pilot study (ms-int@kt) compared the impact of an an internet-based at home physical training protocol (e-Training) with a control group. The study enrolled 126 MS patients in two centres (University of Erlangen and Caritas Hospital Bad Mergentheim) and showed positive effects on several outcomes such muscle strength, lung function and physical activity [5].
- The improvement of fatigue by training is not shown consistently in the literature. Therefore the effect of an individualized e-training combining endurance and strength training on fatigue is investigated in this study in a large population of fingolimod treated MS patients.

METHODS

Patients:

- Patients who are eligible for inclusion in the study are aged 18–65 years and have a diagnosis of RRMS (according to the 2010 revised McDonald criteria [6]), an Expanded Disability Status Scale (EDSS) score of 0–3.5 and provided written informed consent.
- Patients are required to fulfil the EU label of fingolimod and are treated for at least 1 month prior baseline with fingolimod. A fatigue cut off score of ≥ 14 assessed by Modified Fatigue Impact Scale (mFIS) needs to be reached for inclusion.
- Patients with cardiac risk factors or with any disability, clinical impairment or orthopaedic disease that might interfere with physical training are excluded from this study.

Design:

- PACE (**P**hysical **AC**tivity in Gilenya treated MS pati**E**nts; ClinicalTrials.gov identifier NCT01490840) is a prospective, 6-month, randomized, controlled, parallel-group study in approximately 226 patients with RRMS treated with fingolimod plus structured e-training versus no training with delayed onset in waiting list control group starting after core phase (see figure 1)
- Patients who meet all study requirements will have a baseline visit (V1a) at the central training centre at the University in Erlangen to assess muscular and aerobic capacities by a dynamometer and spiroergometry.
- At the baseline visit (V2) at the study centre patients are randomized 1:1 to study groups receiving either a structured e-training intervention or no physical intervention. Patients assigned to the training group will visit an exercise introductory day (V2a) at the study centre hosted by a sports therapist to provide information (exercise basics, disease-specific exercise information, motivation) and practical experience. Patients start their individual training thereafter.
- Patients assigned to the waiting group are not supposed to change their training behavior and will have an identical introductory day after V6 and start their training thereafter.
- All patients will be contacted periodically by phone by the investigator to collect data on concomitant medication and adverse events and have a visit every 3 months. After 6 months (V6a) the core phase for the training group and the waiting phase for the waiting group are completed and all patients will undergo a physical assessment at the central training centre at the University of Erlangen.

E-Training

- The e-training intervention employs a web-based application to administer an adaptive and individualized exercise protocol with the emphasis on endurance and strength training but also containing additional balance and core stability exercises.
- All exercises can be easily performed at home without the need of expensive devices. Strength training exercises are performed against own body weight or with training aids like elastic rubber bands or gymballs. All exercises are home-based.
- For each muscle group, a set of exercises of increasing difficulty allows for individual and progressive training adaptation. Therapists can choose from an exercise database of approximately 150 different strength exercises with different graduation. Exercise sheets are provided to the patients visualizing and describing the respective exercise (see figure 2).
- Concerning endurance training, patients receive recommendations on exercise duration, intensity (heart rate) and frequency for (nordic) walking, running, swimming and cycling. Recommendations are deduced from performance diagnostics (spiroergometry).
- The individual training schedule is comprised of strength exercises twice a week for 30-45 minutes and endurance training once a week for 20-60 minutes.
- The participants document each training session thoroughly via the web-based application (duration, type of exercises, number of repetitions and sets, perceived exertion). In order to keep track of their accomplished and upcoming training sessions, patients use an electronic training diary which can be supervised by the sports therapist who adapts the training according to the individual physical limitations and the training progression (see figure 3).
- Additionally, subjects receive specific behavioural support to increase exercise adherence (action planning etc.)

OBJECTIVES

- The primary objective is to evaluate the effect of individualized physical e-training vs. no training on fatigue in fingolimod-treated MS patients assessed by mFIS fatigue scale.
- In addition, the effect of exercise on aerobic capacity and muscular strength (isometric and dynamic knee flexion/extension, trunk flexion/extension) will be assessed.
- Improvement of quality of life will be measured using the Hamburg Quality of Life Questionnaire in Multiple Sclerosis (HAQUAMS) [7] and effects on depression will be assessed by Beck Depression Inventory (BDI-II).

CONCLUSION

This study will provide first-time data on the efficacy of an individualized e-training on fatigue in a large cohort of fingolimod-treated MS patients. The e-training protocol is a very suitable and promising form of intervention, especially in MS patients. It offers a custom-built training schedule containing easy to access, home-based exercises, and thus takes account for the diversity of symptoms of multiple sclerosis and facilitates long-term commitment to exercise.

References

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Disclosures

K.Schuh, M.Meergans are Novartis employees
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Figure 1: Study Design

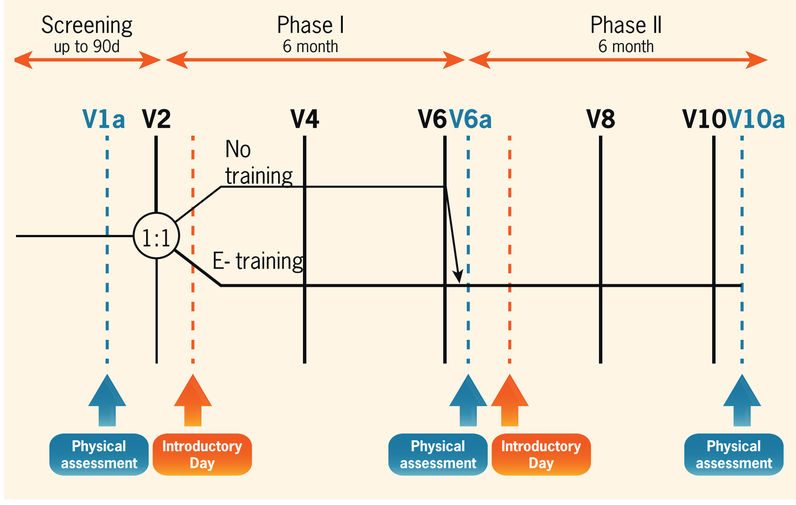


Figure 2: Exercise Sheet Example: Description and pictures explaining the exercise

Exercise description

Starting position

- Stable stance
- Knee slightly bent
- Feet pointing slightly outwards
- Abs put under tension
- Upper body straight

Movement description

- Movement initiation: pelvis down and backwards
- Knees bent
- Upper body is kept straight

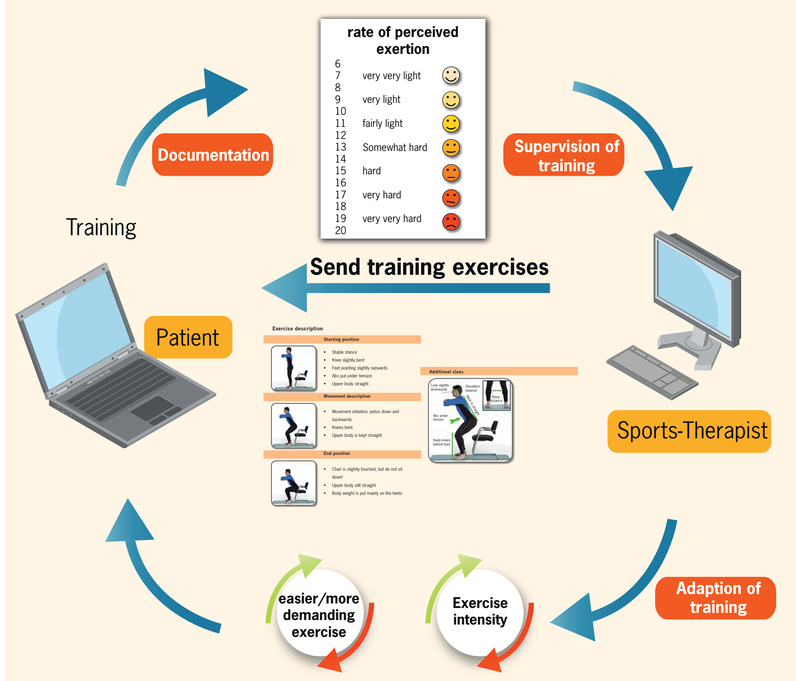
End position

- Chair is slightly touched, but do not sit down!
- Upper body still straight
- Body weight is put mainly on the heels

Additional clues

Have an enjoyable and successful workout!

Figure 3: Interaction and individual adaption of training between patient and sport therapist



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