SUPPLEMENTARY APPENDIX

Fatigue in chronic myeloid leukemia patients on tyrosine kinase inhibitor therapy: predictors and the relationship with physical activity

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Supplementary Material

S1 Methods

Part 1: Questionnaire

Fatigue severity: The Checklist Individual Strength, a validated fatigue questionnaire assessing fatigue over the past two weeks, was used to measure fatigue severity (1). A score of 35 or above on the subscale "subjective experience of fatigue" (CIS-fatigue) was considered as severe fatigue. In addition, participants were asked to score quality of life on a 10-point Likert scale ranging from 1 (poor) to 10 (excellent).

General characteristics: Questions about general characteristics included age, gender, height and weight to calculate body mass index (BMI), education level, and marital status. Education level was categorized into three groups: low (below high school), middle (high school), and high (college or higher). For marital status, two groups were created: single and married (including common-law marriage).

Medical history: Both CML-related and non-CML-related medical history were assessed. CML-related medical history included the year of diagnosis, TKI type and dose, duration of TKI treatment, and CML disease control. CML disease control was categorized into major molecular response (MMR; % BCR-ABL transcripts on International Scale ≤ 0.1) and no MMR (% BCR-ABL transcripts on International Scale >0.1). The Charlson Comorbidity Index (CCI) (2) was used to quantify participants' medical comorbidities. Both over-the-counter and prescribed medication known to cause fatigue (i.e. benzodiazepines, opioids, beta-blockers, and metformin) were assessed for prediction analysis.

Lifestyle habits: Potential lifestyle predictors included smoking, daily fluid and caffeine intake, alcohol consumption (beer and wine), and physical activity. Smoking was categorized

into current smoker and non-smokers (including former smokers). Total caffeine intake was calculated from the consumption of coffee, tea, energy drinks, soft drinks, and chocolate according to the caffeine content determined by the Dutch Nutrition Center (3). Physical activity was assessed by the Short Questionnaire to Assess Health-enhancing physical activity (SQUASH) (4). To calculate the amount of physical activity, Metabolic Equivalent of Task (MET) values were derived from the Ainsworth's Compendium of Physical Activities (5). Subsequently, participants were categorized into four groups: inactive (<500 MET minutes/week; based on the minimum level of physical activity recommended by the American College of Sports Medicine and the American Heart Association (6)), moderately active (500-1499 MET minutes/week), vigorously active (1500-2999 MET minutes/week), and very vigorously active (>3000 MET minutes/week).

Part 2: Activity monitor

Physical activity was measured with the activPAL3 micro (PAL Technologies Ltd, Glasgow, UK) (7), which contains an inclinometer to measure limb position (e.g. lying/sitting and standing) and an accelerometer to assess different intensities of activity. The activPAL3 micro was covered with medical adhesive dressing (Tegaderm; 3M, Saint Paul, MN, USA), and attached by trained staff to the anterior right thigh. Participants wore the activity monitor 24 hours per day for 7 consecutive days and were asked to maintain normal daily activities. Subjects were instructed to keep a sleep log on bed- and waking times. In addition, participants were asked to report their employment status and total work time. A modified version of the script of Winkler et al (8) was used to analyse raw activity monitor data. We classified physical activity intensity as either light (MET values < 3) or moderate to vigorous (MET values ≥3) (9). Participants with at least 3 valid week days and 1 valid weekend day were included in the final analysis.

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