A TSEC for Symptom Management in Menopausal Women with Multiple Sclerosis
NCT02710214
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SAP: A TSEC for Symptom Management in Menopausal Women with Multiple Sclerosis

Data Cleaning/Testing of Assumptions: Prior to proceeding with the following data analysis plan, we will examine variable distributions for outliers and evaluate whether the necessary assumptions are met for the planned analyses (e.g., normality and homogeneity of variances, as applicable). If outliers are detected or assumptions are violated, I will consult with CTSI statistics regarding appropriate analytic methods and will consider distribution transformations, non-parametric analyses, and/or analyses methods more robust to such violations. All analyses will be performed according to the intention-to-treat principle (primary) then the per-protocol principle.

Power calculation: Given this is a pilot study, we will view the study as a success if the observed mean change in the treatment group is larger by any amount compared to the placebo group ("play the winner" approach). In healthy women treated with estradiol for 8 weeks,(Joffe et al., 2014) VMS decreased by 2.2 daily in the placebo group and 4.5 in the estradiol group and the SD for the change was 3.4. Assuming same differences and SD, we will have 80% power to find the treatment arm mean difference to be larger with our proposed sample size.

Groups:
1. Treatment (Duavee); N=12
2. Placebo; N=12

Timepoints:
1. V1=baseline
2. V2=8 wks, for efficacy
3.

Primary Predictor:
Treatment group

Other Predictors:
4. Age
5. Disease duration
6. DMT

Baseline Comparisons:
1. Characteristics at baseline (compare using t-test):
    i. *Age*
2. Characteristics at baseline (compare using chi-square test):
    i. *Disease type*
    ii. *DMT*
3. Characteristics at baseline (compare using Fisher's exact test):
    i. *Race*
4. Functional measures at baseline (compare using Wilcoxon rank sum test):
    i. *Functional System Scores (vision, brainstem, pyramidal, cerebellar, sensory, bowel and bladder, cerebral, ambulation)*
    ii. *EDSS Total*
    iii. *T25FW*
    iv. *SDMT (raw score)*
    v. *SDMT (z-score)*
    vi. *LNS*
5. Patient reported measures at baseline (compare using Wilcoxon rank sum test):

i. *MSQOL-54 (mental)*
ii. *MSQOL-54 (physical)*
iii. *MSQOL-54 (energy)*
iv. *MSRS Composite*
v. *MSNQ*
vi. *BLCS*
vii. *Hot Flashes (per 24 hours, from 2 wks diaries)*
viii. *HFRDIS*
ix. *ISI*

Outcomes:

2. Menopausal symptoms
    a. Number of daily vasomotor symptoms (VMS) from diary
    (1) Compare groups using GEE for linear regression
    (2) Adjust model in (1) by age
    (3) Adjust model in (1) by disease duration

    b. Sleep quality from sleep diary (PSQI)
    (1) Compare between treatment groups at each time point
    (2) Calculate differences between two time points and compare between treatment groups using Wilcoxon rank sum test

    c. Insomnia severity post treatment with Duavee/placebo (from ISI both numeric and categorical values)
    (1) Compare between treatment groups at each time point. (numeric)
    (2) Compare treatment arms using chi-square test. (categorical)

    d. HFDRIS
    (1) Take average of two measurements and compare averages between treatment groups using t-test.

3. MS symptoms and MS QOL
    a. Change in clinical symptoms:
        i. *Functional System Scores (vision, brainstem, pyramidal, cerebellar, sensory, bowel and bladder, cerebral, ambulation)*
        ii. *EDSS Total Score*
        iii. *T25FW*
    (1) Calculate difference between V1 and V2 measures for each group; compare groups using Wilcoxon rank sum test.

    b. TSEC Cognitive
        i. *SDMT (raw score)*
        ii. *SDMT (z-score)*
        iii. *LNS*
    (1) Calculate difference between V1 and V2 measures for each group; compare groups using Wilcoxon rank sum test. (SDMT raw score and LNS)
    (2) Calculate difference between V1 and V2 measures for each group; compare groups using t- test. (SDMT z-score)

    c. QOL Surveys
        i. *MSQOL-54 (mental)*
        ii. *MSQOL-54 (physical)*

(1) Calculate difference between V1 and V2 measures for each group; compare groups using t-test.

iii. *BLCS*
iv. *MSRS*
v. *MSQOL-54 (mental)*
vi. *MSQOL-54 (physical)*
vii. *MSQOL-54 (energy)*
viii. *MSNQ*
ix. *BLCS*
x.

(1) Calculate difference between pre- and post- measures for each group; compare groups using Wilcoxon rank sum test.

4. Tolerability
    a. Patient side effects: percentage reporting side effects on TSQM
    b. Scores in domains on TSQM (effectiveness, side effects, convenience, and global satisfaction)

(1) Compare two groups using t-test.

    c. Number of missed doses

(1) Compare groups using Wilcoxon rank sum test.

    d. Number of new inflammatory lesions on 8-wk MRI
        i. *New T2 Lesions*
        ii. *New gadolinium enhancing lesions*

(1) Compare groups using Wilcoxon rank sum test.