



IMPROVEMENT OF CANCER RELATED FATIGUE IN PATIENTS RECEIVING PLACEBO IN BLINDED AND OPEN LABELED FASHION IN CANCER-RELATED FATIGUE TREATMENT TRIALS

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BACKGROUND

- Cancer-related fatigue (CRF) is the most common and debilitating symptom in advanced cancer.
- Despite numerous well-designed studies to treat CRF there is currently no established pharmacological therapy for CRF.
- The purpose of this study was to compare the improvement of CRF between cohorts of advanced cancer patients who received placebo as part of CRF clinical trials in a blinded fashion, and patients who received open-label placebo for treatment of CRF in a randomized controlled study.

MATERIALS AND METHODS

- In this study, data of advanced cancer patients from CRF clinical treatment trials (from February 2003 through September 2023) who received placebo in a blinded, and as an open labeled fashion at a tertiary cancer center were reviewed.
- Eligibility criteria:** Presence of CRF of ≥ 4 , on a 0-10 numerical scale during the previous 24 hours in which 0 equals no fatigue, and 10 was worst possible CRF; No clinical evidence of cognitive failure; Sign written informed consent; Patients must be 18 years or older; Hemoglobin of ≥ 8 g/dl within 2 weeks of enrollment. All these studies were completed and published studies.
- We accessed demographic data including age, sex, cancer diagnosis, ethnicity, and performance status at baseline, baseline, day 8 Edmonton Symptom Assessment Scale (ESAS), Functional Assessment of Cancer Therapy - General (FACT-G), and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scores.
- Demographic data, baseline and day 8 with Functional Assessment of FACIT-F and ESAS scores were pooled, and changes in FACIT-F (placebo response), and ESAS from baseline to day 8 in the two cohorts were compared.
- We also examined the association of placebo response with demographics factors, FACT-G, FACT-G sub scales, ESAS symptoms, and ESAS symptom distress scores.

RESULTS

- A total of 362 patients were eligible, out of which, $n = 58$ for blinded placebo and $n = 40$ for open label placebo trials were included in the primary analysis.
- Females were 57%, breast cancer was the most common cancer type (22%). Mean (SD) of FACIT-F score was 29.0 (15).
- We found no significant difference in placebo response in patients receiving placebo either using blinded, and open labeled design in fatigue trials. The change in FACIT-F scores were 6.6 vs 7.9, -1.3 ($P=0.87$), and change in ESAS fatigue scores were -1.9 vs -1.7, -0.27 ($P=0.87$) respectively.
- We found significant association between change in CRF (FACIT-F scores) used to measure placebo response and baseline fatigue ($P=0.0001$), gastrointestinal cancers ($p=0.02$), ESAS- pain ($P=0.04$), ESAS anxiety($p=0.003$), and ESAS - Symptom Distress Score ($P=0.012$).

Table 1: Difference from Baseline in Outcomes in Blinded Placebo and Open Labeled Placebo Fatigue Studies

Outcome	Blinded Placebo (P value) n=58	Open Labeled Placebo (P value) n=40	Differences between Groups (P value) D8-BL
FACIT-Fatigue	6.6 ($p = 0.69$)	7.9 ($p = 4.6 \times 10^{-5}$, $n = 40$)	-1.3 ($p = 0.87$)
ESAS FATIGUE	-1.9 ($p = 0.49$)	-1.7 ($p = 0.0087$, $n = 37$)	-0.27 ($p = 0.87$)
ESAS -SDS	-8.1 ($p = 0.50$)	-14 ($p = 0.0015$)	-6.4 ($p = 0.65$)
ESAS Physical	-5.7 ($p = 0.5$)	-10 ($p = 0.0028$)	-4.4 ($p = 0.66$)
ESAS Emotional	-1.6 ($p = 0.0041$)	-3.2 ($p = 2.2 \times 10^{-6}$)	-1.5 ($p = 0.084$)
ESAS Well-Being	-0.54 ($p = 0.26$)	-2.4 ($p = 3.5 \times 10^{-5}$, $n = 39$)	-1.9 ($p = 0.014$)

CONCLUSIONS

- In this study we found placebo response was not significantly different between patients receiving placebo as part randomized controlled CRF clinical trials in a blinded, or open-label design for treatment of CRF.
- These results suggests that the placebo response plays a similar role in alleviating cancer-related fatigue in both these settings, highlighting the potential benefit of placebo treatments in managing this challenging symptom.
- In this study we also found a significant association between placebo response and baseline fatigue, gastrointestinal cancers, ESAS- pain, anxiety, and ESAS - symptom distress score.
- Further research is essential for understanding the role of placebo in treatment of CRF.

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