# Efficacy and Safety of Modafinil versus Dexamethasone in Cancer-related Fatigue: A Prospective, Randomized Controlled Study

Uttiya Deb, Sandip Mukhopadhyay, Sanatan Banerjee, Supreeti Biswas
Department of Pharmacology & Radiation Oncology
Burdwan Medical College & Hospital, Burdwan, India

# Background

- Cancer-related fatigue(CRF) described as “a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning.”
- CRF occurs in > 60% cancer patients; > 80% receiving cancer treatment
- **Dexamethasone :** corticosteroid; anti-inflammatory property; shown improvement in CRF
- **Modafinil:** Psychostimulant; dopamine & nor adrenaline reuptake inhibitor; ↑ alertness, combats fatigue
- Paucity of data on head-to-head comparison between these two drugs in CRF

# Objective

- Primary objective:

  To compare the **efficacy** of **modafinil** & **dexamethasone** in control of cancer-related fatigue using FACIT-F scale

- Secondary objectives:

  a) To note the **incidence of adverse drug reaction(ADR)** of the study drugs in the utilized dose & causality assessment using WHO-UMC scale

  b) To assess **change in quality of life** with these two interventions

# Methodology

- **Study design**: Prospective, randomized controlled study

- **Study population**: Patients with histologically proven malignancy who received atleast 3 cycles of chemotherapy or completed a course of curative or palliative radiotherapy attending Radiation oncology outpatient department.

- **Study duration**: 19 months; February 2018-August 2019

- **Sample size** =80
- Serial enrolment

- **Study funding:** Indian Council of Medical Research, New Delhi

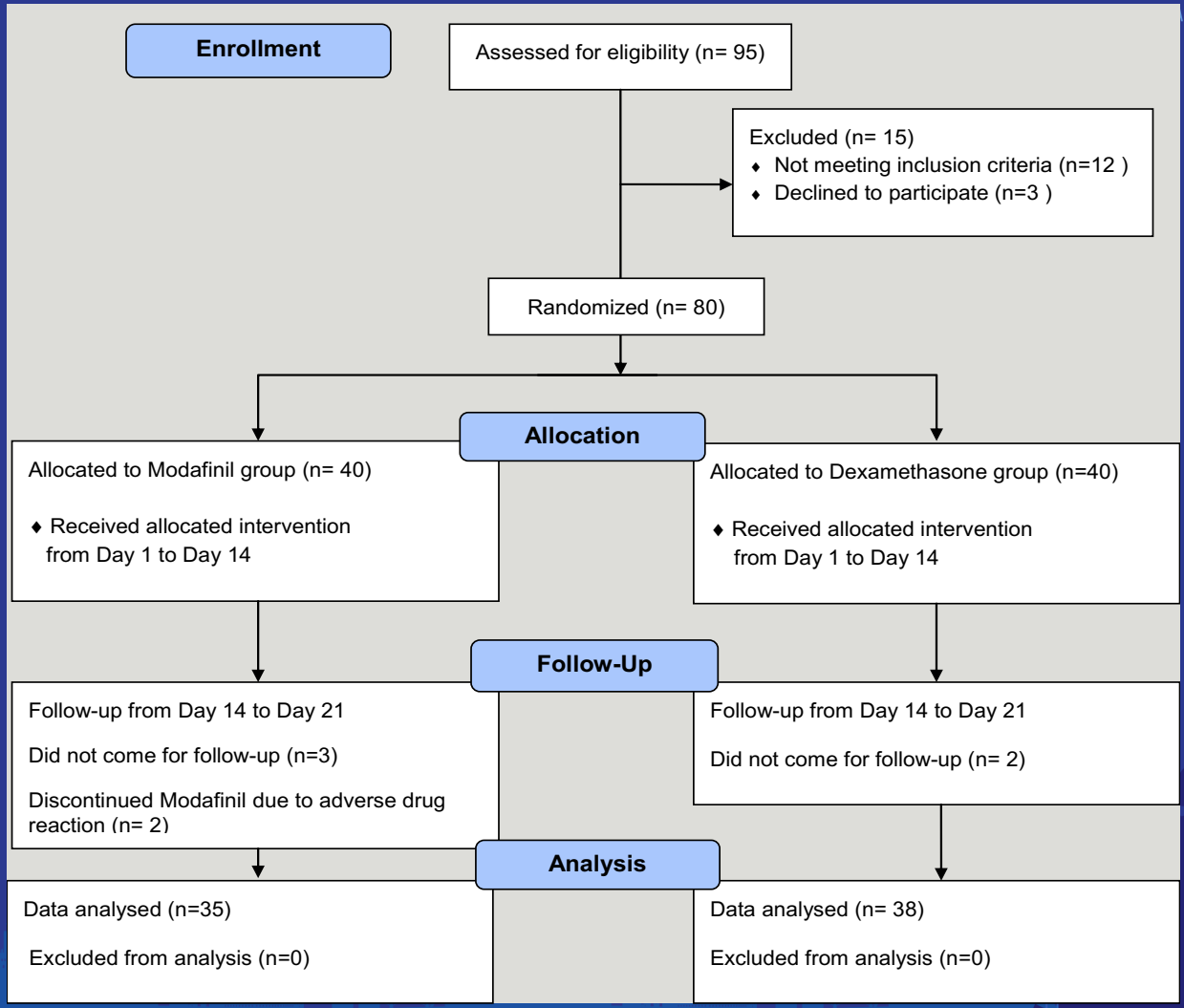
## ...contd. Methodology

- **Key inclusion criteria**:
  - Cancer patients (age 18-70 years),either gender with fatigue severity score ≥ 5 on a 0-to-10 NRS
  - Edmonton Symptom Assessment Scale (ESAS ; scale of 0 to 10)
  - Presence of ≥ 3 symptoms during previous 24 hours with average intensity of ≥ 4 on
  - Eastern Cooperative Oncology Group(ECOG) Performance status: 0 to 2

- **Key exclusion criteria**:
  - History of previous intake of modafinil or any psychostimulant such as amphetamine, methylphenidate or a monoamine oxidase inhibitor or tricyclic antidepressant or clonidine, on a regular basis within past 30 days
  - Any history of clinically significant cardiac, respiratory, renal and hepatic disorder
  - Presence of glaucoma, severe headache, seizure disorder, narcolepsy

Enrolled patients randomized to **dexamethasone group** & **modafinil group** (received Dexamethasone 4 mg once daily and Modafinil 100 mg once daily x 14 days respectively.
- Follow up after 2 weeks

# CONSORT diagram summarizing the flow of patients in the study



# Results

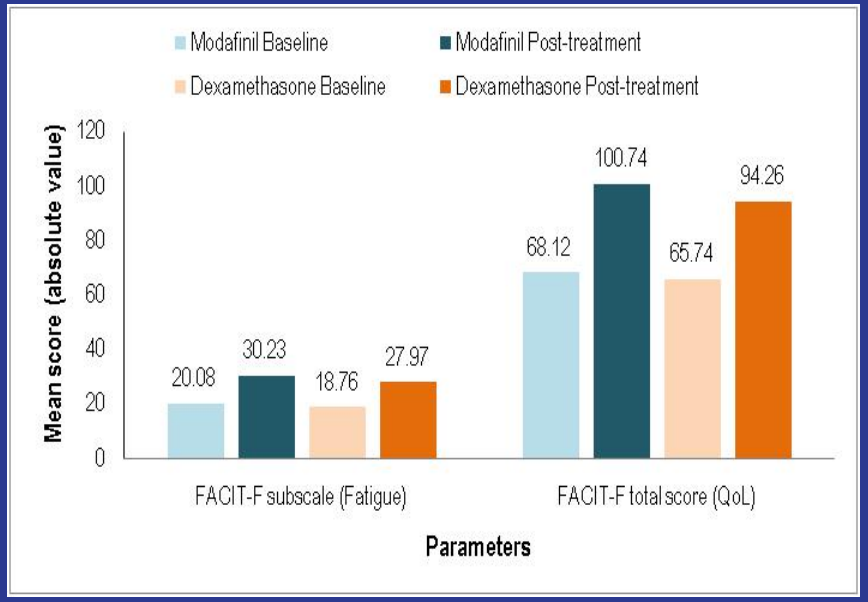



Figure: Comparison of Fatigue & quality of life(QoL) scores among modafinil & dexamethasone groups

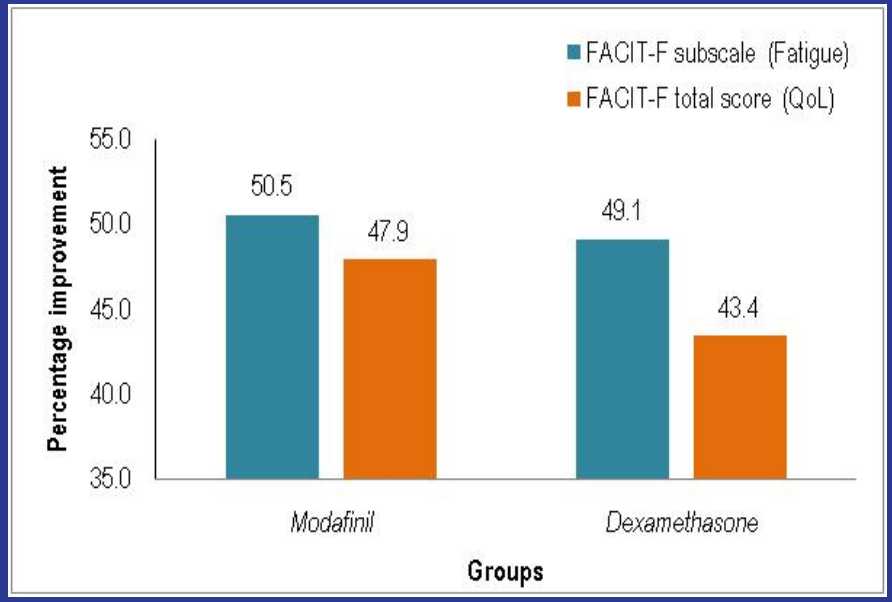



Figure: Comparison of percentage improvement of Fatigue & quality of life(QoL) among modafinil & dexamethasone groups

# ...contd. Results

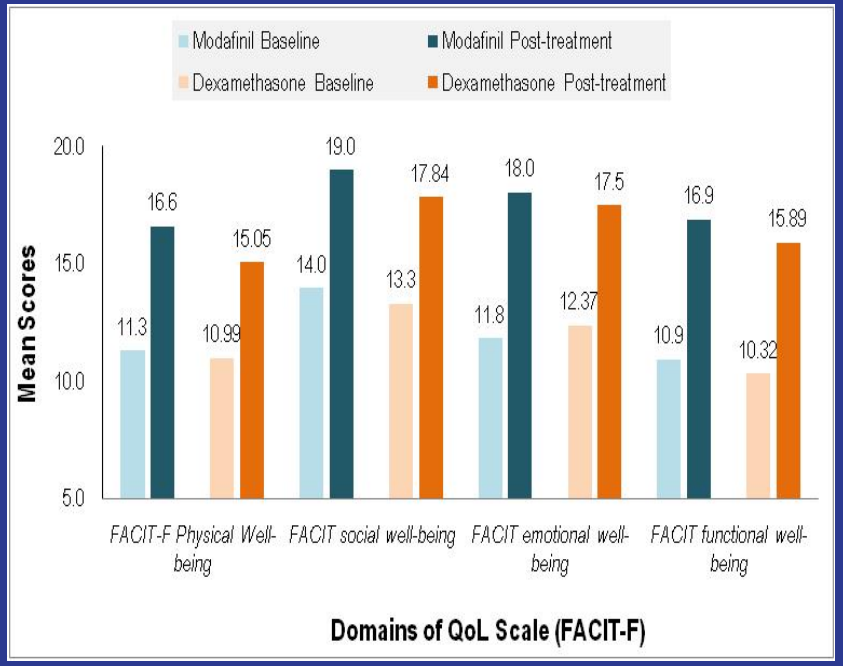



Figure : Comparison of the domains of the quality of life (QoL) scale among modafinil & dexamethasone groups

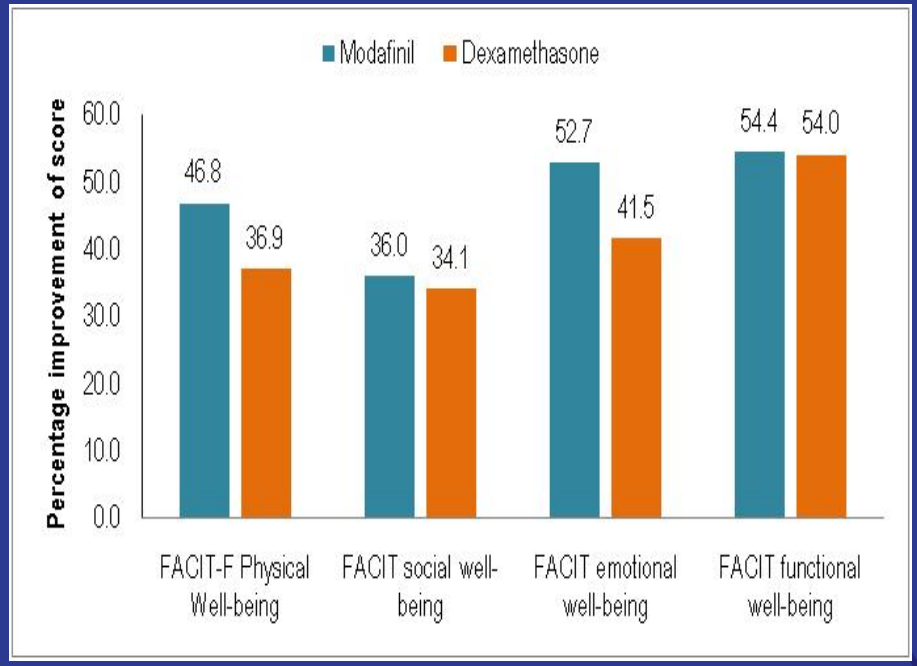



Figure: Comparison of Percentage improvement of domains of quality of life (QoL) scale among modafinil & dexamethasone groups

# Adverse events & causality analysis (WHO-UMC Scale)

## ...contd. Results

| Name of the adverse event | Drug | Number of events n(%) | Causality* |
|---|---|---|---|
| Depression | Modafinil | 3(7.5) | Probable -1<br>Possible -2<br>Unlikely -0 |
| Dizziness | Modafinil | 4(10) | Probable -3<br>Possible -1<br>Unlikely -0 |
| Headache | Modafinil | 3(7.5) | Probable -1<br>Possible -1<br>Unlikely -0 |
| Pain | Modafinil | 1(2.5) | Probable -0<br>Possible -1<br>Unlikely -0 |
| Cough | Dexamethasone | 2(5) | Probable -0<br>Possible -2<br>Unlikely -0 |
| Depression | Dexamethasone | 2(5) | Probable -0<br>Possible -1<br>Unlikely -0 |
| Insomnia | Dexamethasone | 2(5) | Probable -1<br>Possible -1<br>Unlikely -0 |
| Nausea | Dexamethasone | 1(2.5) | Probable -0<br>Possible -1<br>Unlikely -0 |
| Pain | Dexamethasone | 1(2.5) | Probable -0<br>Possible -1<br>Unlikely -0 |

# Discussion

- Improvements with modafinil- marginally more with dexamethasone
  – could not reach a statistically significant difference with the present sample size.

- **Strengths of the study**
  - Randomization to avoid bias
  - Use of validated scales to measure primary and secondary outcomes
  - A relatively homogenous population enrolling moderate to severe CRF patients.

- **Limitations of the study**
  - Small sample size
  - Not blinding the clinician and the patients
  - Relatively short follow up

# Conclusion

- Both modafinil and dexamethasone can improve moderate to severe CRF with similar efficacy
- Modafinil may be better in improvement of some aspects of quality of life in comparison to dexamethasone
- Future double blinded studies on larger population and for a longer duration is recommended before generalization of the study findings in regular patient care