

# AN EVALUATION OF FACIT-FATIGUE IN PATIENTS WITH LOCALLY ADVANCED OR METASTATIC BREAST CANCER RECEIVING TREATMENT WITH TAXANE-BASED CHEMOTHERAPY

Alessandra Fabi<sup>1</sup>, Steven Hager<sup>2</sup>, Laura Lourdes<sup>3</sup>, Chiara Gandini<sup>4</sup>, Elizabeth M. Gavioli<sup>5</sup>, Renuka Wakade<sup>5</sup>, Enrico Minnella<sup>5</sup>, Marcello Allegretti<sup>5</sup>, Rebecca Pedersini<sup>6</sup>

1. Precision Medicine in Breast Cancer, Fondazione Policlinico Universitario A. Gemelli, IRCCS – Rome (Italy), 2. California Cancer Associates for Research and Excellence – California (USA), 3. Cancer Specialists of North Florida - Florida (USA), 4. Fondazione IRCCS Policlinico San Matteo- Pavia (Italy), 5. Dompé Farmaceutici SpA - Milan (Italy), 6. ASST Spedali Civili - Brescia (Italy)

## CONCLUSIONS

- In patients with locally advanced or metastatic breast cancer starting treatment with taxane-based CT, a MCID of 2.4 points represented relevant changes in fatigue as measured with the FACIT-Fatigue Scale.
- Most patients indicated that all FACIT-Fatigue items were relevant, and the most important items to them were: “I have energy,” “I am able to do my usual activity,” and “I have to limit my social activity because I am tired.” They indicated that a change of 1 category for each item would be a meaningful change to them.
- Limitations of this study include the risk of bias due to its noninterventive prospective design, patient lost to follow-up, and international comparability and validity of FACIT-Fatigue after translated.
- The validation of FACIT-Fatigue should be utilized for future clinical trials and clinical practice to aid in the diagnosis of CRF, and to identify effective therapeutic options.

## BACKGROUND

- Cancer-related fatigue (CRF) is a persistent and debilitating state of physical, emotional, and/or mental exhaustion that is unrelated to activity level and interferes with usual functioning.<sup>1</sup>
- CRF occurs in nearly all patients with breast cancer. The peak of CRF is typically during treatment with over 87% of patients with breast cancer who receive taxane-based chemotherapy reporting experiencing CRF.<sup>2</sup>
- Multiple factors can lead to the development of CRF, including an overactive inflammatory response.<sup>3</sup> Dysregulated signaling at the IL-8–CXCR1/CXCR2 axis has been associated with inflammatory diseases.<sup>4,5</sup>
- Additionally, taxane-based chemotherapy is the standard treatment for metastatic breast cancer; however, paclitaxel can lead to an increase in IL-8 in patients with breast cancer, potentially worsening fatigue symptoms.<sup>6</sup>
- Poor outcomes including lower quality of life, disruption of normal daily activities, and chemotherapy interruptions and dose delays have been associated with CRF.<sup>3,7-10</sup>
- Fatigue is a subjective symptom and must be assessed through patient questionnaires, such as numerical rating scales of symptom intensity or the FACIT-Fatigue (Functional Assessment of Chronic Illness Therapy Fatigue) survey; however, its validation in this specific population remains lacking<sup>1,11,12</sup>

## RESULTS

Parameter	Participants (N=62)
Age, mean (SD)	55.5 (12.2)
Gender, n (%)	62 (100.0)
Ethnicity, Hispanic, n (%)	7 (11.3)
BMI (kg/m <sup>2</sup> ), mean (SD)	25.7 (5.2)
Months since BC diagnosis, Mean (SD)	43.2 (86.4)
BC stage at baseline, n (%)	
0	1 (1.8)
I	2 (3.5)
II	12 (21.1)
III	20 (35.1)
IV	22 (38.6)
Taxane-based CT regimen, n (%)	
Single agent	35 (57.4)
In combination	26 (42.6)
Line of treatment, n (%)	
First	42 (68.9)
Second	3 (4.9)
Third	6 (9.8)
Fourth	6 (9.8)
Fifth or greater	4 (6.6)
Performance status (ECOG), n (%)	
0	49 (79.0)
1	11 (17.7)
2	2 (3.2)

BMI, body mass index; CT, chemotherapy; ECOG, Eastern Cooperative Oncology Group; SD, standard deviation.

Visit	Number of Patients	FACIT-Fatigue Score		Change From Baseline	
		Mean (SD)	95% CI	Mean (SD)	95% CI
BL	62	39.0 (8.7)	36.8 – 41.2	-	-
1	53	36.2 (9.4)	33.6 – 38.8	-2.4 (6.4)	-4.1 – -0.6
2	54	35.7 (10.4)	32.8 – 38.5	-3.7 (8.1)	-5.9 – -1.5
3	46	32.7 (11.5)	29.3 – 36.2	-5.7 (10.0)	-8.7 – -2.7
4	15	36.5 (13.6)	28.9 – 44.0	-7.1 (11.7)	-13.6 – -0.7
EOS	40	35.9 (10.6)	32.5 – 39.3	-3.6 (10.1)	-6.8 – -0.3

BL, baseline; CI, confidence interval; EOS, end of study; FACIT, Functional Assessment of Chronic Illness Therapy; SD, standard deviation. FACIT-Fatigue scores ranged from 0 (maximum fatigue) to 52 (no fatigue at all).

MCID Method	MCID	Relative Weight
Anchor-based (MCID 1)	2.0	0.4
Distribution-based (MCID 2)	3.4	0.4
Qualitative-based (MCID 3)	0.9	0.2
Final MCID <sup>a</sup>	2.4	-

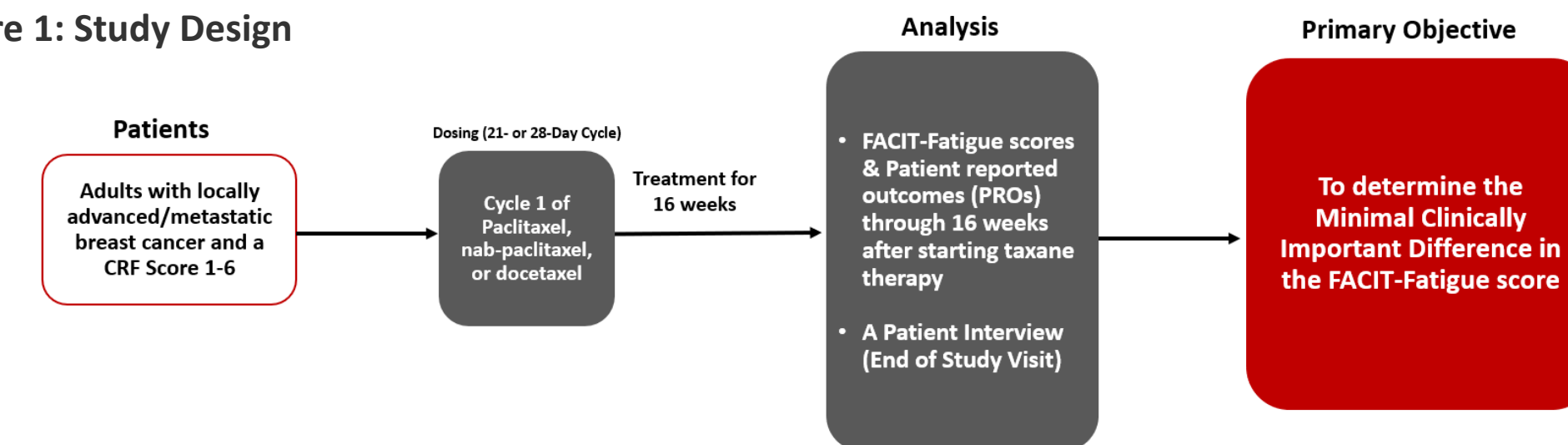
MCID, most clinically important difference. <sup>a</sup>Final MCID was calculated as a weighted mean of the three MCID methods.

**Primary Endpoint:** 62 female patients were included in the USA and Italy, with a mean ± SD age of 55.5±12.2 years, mainly with stage III (35.1%) and IV (38.6%) BC (Table 1). Baseline mean (95% CI) FACIT-Fatigue scores were 39.0 (36.8 – 41.2), and fatigue worsened over time ranging from -2.4 (-4.1 – -0.6) at Visit 1 to -7.1 (-13.6 – -0.7) at Visit 4 (Table 2a). A MCID of 2.4 points represented relevant changes on the FACIT-Fatigue survey; final MCID was calculated as a weighted mean of the anchor-based, distribution-based, and qualitative-based MCID methods (Table 2b).

## STUDY DESIGN

This was a prospective, non-interventional, multinational, study, from October 2021 to August 2023 in adult patients with locally advanced or metastatic breast cancer who had mild-to-moderate CRF and were eligible to receive cycle 1 of taxane-based chemotherapy. Patients were asked to complete the FACIT-Fatigue questionnaire before starting chemotherapy and then every 3-4 weeks, according to the CT regimen, until treatment completion; a subgroup of patients participated in a semi-structured, phone-based cognitive interview to explore fatigue factors deemed important to patients and to what extent an improvement was considered meaningful. The aim of this study was determine the minimum clinically important difference (MCID) in the FACIT-Fatigue scores.

Figure 1: Study Design



	PGI-S	PGI-C	BFI	EQ-5D-VAS	Utility Score	Clinician Rated
n	39	39	39	40	40	16
Correlation coefficient	-0.7314	-0.6359	-0.8753	0.8068	0.7774	-0.2282
P value	<0.001	<0.001	<0.001	<0.001	<0.001	0.3954

BFI, Brief Fatigue Inventory; EOS, end of study; EQ-5D-VAS, EuroQol 5 Dimensions visual analog scale; FACIT, Functional Assessment of Chronic Illness Therapy; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity.

FACIT-Fatigue item	Meaningful change, n (%)		
	1-Category change	2-Category change	3-Category change
1. I feel fatigued	16 (69.6)	4 (17.4)	-
2. I feel weak all over	14 (63.7)	6 (27.3)	-
3. I feel listless	16 (72.7)	5 (22.7)	1 (4.5)
4. I feel tired	15 (71.4)	3 (14.3)	-
5. I have trouble starting things because I am tired	13 (65.0)	3 (15.0)	2 (10.0)
6. I have trouble finishing things because I am tired	15 (75.0)	3 (15.0)	1 (5.0)
7. I have energy	17 (85.0)	2 (10.0)	-
8. I am able to do my usual activity	17 (81.0)	2 (9.5)	-
9. I need to sleep during the day	15 (71.4)	3 (14.2)	1 (4.7)
10. I am too tired to eat	11 (57.1)	8 (38.1)	1 (4.8)
11. I need help doing my usual activities	13 (70.0)	5 (25.0)	1 (5.0)
12. I am frustrated by being too tired to do the things I want to do	14 (70.0)	4 (20.0)	2 (10.0)
13. I have to limit my social activity because I am tired	13 (72.2)	5 (27.8)	-

## Secondary Endpoint:

There was a statistically significant correlation between the coefficients of the FACIT-Fatigue and other questionnaires demonstrating good internal consistency among the FACIT-Fatigue items (Table 3).

**Sub-study:** A total of 23 participants underwent the qualitative interview and most of them confirmed that all FACIT-Fatigue items were relevant to assess fatigue (66.7% to 90.9%). The most important to them were: “I have energy”, “I am able to do my usual activity” and “I have to limit my social activity because I am tired.” Fatigue impacts on work (n=13/19, 68.4%) was the most frequently reported, followed by impacts on social functioning and family relationships (n=12/19, 63.2%), and difficulties with household chores (n=9/19, 47.4%). Most participants indicated that a change of 1-category would be a meaningful change to them (n=16/23 69.6%).

DISCLOSURES: EMG, RW, EM, MA, are Dompé employees

FUNDING: This study was funded by Dompé Farmaceutici SpA

## REFERENCES:

- NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Version 2. 2022.
- Kirca K, Kutluturkan S. *Eur J Breast Health*. 2018;14(3):18-155.
- Bower JE. *Nat Rev Clin Oncol*. 2014;11(10):597-609
- Cohen RA, et al. *J Neuroimmunol*. 2019;334:577001.
- Sorenson M, et al. *Neurosci Med*. 2012;3(1):47-53.
- Pusztai L, et al. *Cytokine*. 2004;25(3):94-102.
- Gupta D, et al. *J Pain Symptom Manage*. 2007;34(1):40-47.
- Bower JE. *Nat Rev Clin Oncol*. 2014;11(10):597-609.
- Curt GA, et al. *Oncologist*. 2000;5(5):353-360.
- Diaz N, et al. *Clin Transl Oncol*. 2008;10(11):753-757..
- Wang XS, et al. *Gynecol Oncol*. 2015;135(3):446-452.
- FACIT.org. FACIT-Fatigue.

## CONTACT INFORMATION:

Elizabeth M. Gavioli, Dompé Farmaceutici SpA; [Elizabeth.gavioli@dompe.com](mailto:Elizabeth.gavioli@dompe.com)