HEalth-Related quality of life-intervention in survivors of Breast and other cancers experiencing cancer-related fatigue using TraditionAL Chinese Medicine: The HERBAL Trial

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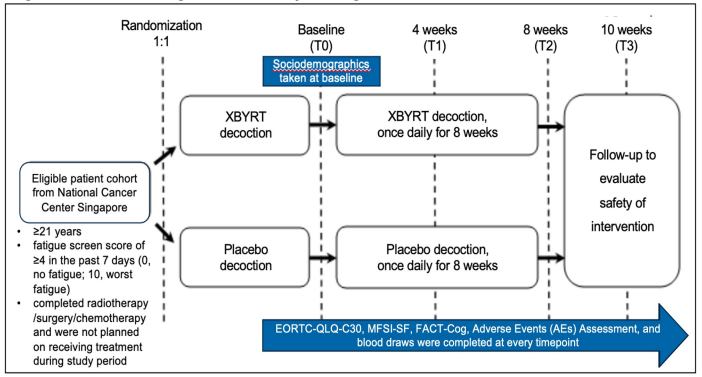
Introduction

- Cancer-related fatigue (CRF) refers to physical, emotional, and/or cognitive tiredness related to the disease or anticancer treatments that can negatively impact quality of life (QOL).
- Pharmacological therapies remain investigational with limited efficacy, integrative therapies such as traditional Chinese medicine (TCM) could be explored for relieving symptoms.
- Thus, we sought to evaluate the efficacy and safety of a TCM decoction modified Xiang Bei Yang Rong Tang (XBYRT) on QOL and CRF, compared to placebo (5% of active intervention) with a pilot, randomized, double-blinded, placebo-controlled trial (ClinicalTrials.gov: NCT04104113)

XBYRT Ingredients: *Radix Astragaliseu Hedysari*, *Radix Codonopsis Pilosulae*, *Rhizoma Atractylodis Macrocephalae*, *Poria*, *Radix Paeoniae Alba*, *Fructus Lycii*, *Frutus Ligustri Lucidi*, *Plantago asiatica*, *Endothelium corneum gigeriae galli*, *Hordeum vulgare L*, *Fructus Alpinia oxyphylla*, *Rhizoma Cyperi*, *Radix Polygalae*, *Bulbus Fritillariae Thunbergii*, *Smilax glabra Roxb*

Methods

Figure 1: Flow diagram of study design



- Primary objective: compare T2 and T3 EORTC-QLQ C30 global health status (GHS) scores between both groups to assess QOL
- Secondary objectives: compare MFSI-SF and FACT-Cog total and subscale scores, plasma BDNF and cytokine levels, at T2 and T3, as well as prevalence of adverse events (AEs), between both groups
- Differences in all outcomes were tested at T2 and T3 using linear regression with or without baseline adjustment.

Results

Figure 2: Subject CONSORT diagram

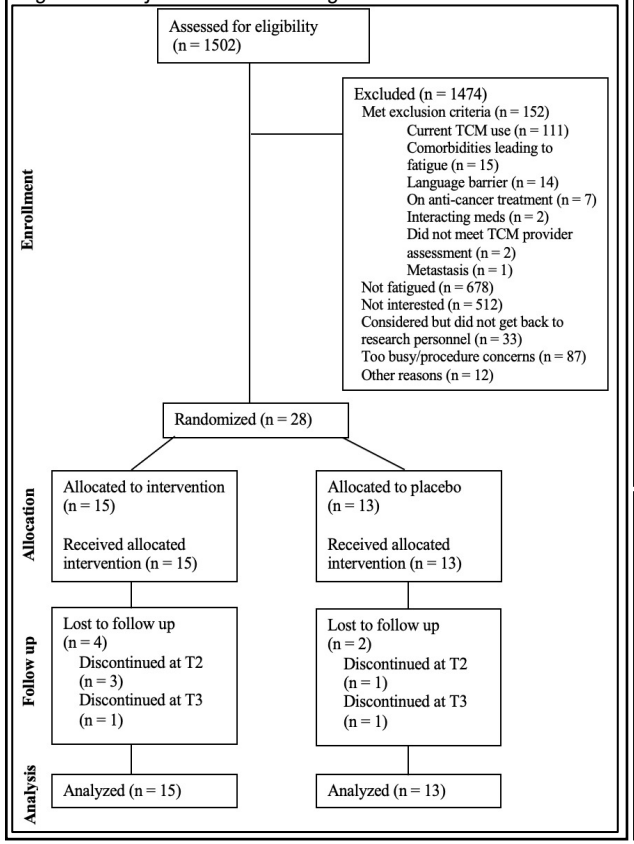


Table 1: Subject baseline characteristics

Variables	XBYRT (n = 15)	Placebo (n = 13)
Age, mean (SD)	58.5 (6.3)	65.0 (13.4)
Female, n (%)	15 (100.0)	12 (92.3)
Chinese, n (%)	14 (93.3)	8 (61.5)
Type of cancer, n (%)		
Breast	13 (86.7)	8 (61.5)
Other[a]	2 (13.3)	5 (38.5)
Cancer stage, n (%)		
I	3 (20.0)	4 (30.8)
II	9 (60.0)	6 (46.2)
III	3 (20.0)	3 (23.1)

[a]Other cancer types: lymphoma, endometrial, pancreatic, ovarian, lung, and uterine

Safety Outcomes

Table 2: Most frequently observed AEs (Grade ≥2) from T1-T3

Adverse Events	XBYRT (n = 15)	Placebo (n = 13)
Dry mouth, n (%)	3 (20.0)	3 (23.1)
Constipation, n (%)	3 (20.00)	2 (15.4)
Insomnia, n (%)	4 (26.7)	4 (30.8)
Headache, n (%)	2 (13.3)	3 (23.1)
Flushing, n (%)	3 (20.0)	1 (7.7)

Primary Outcome

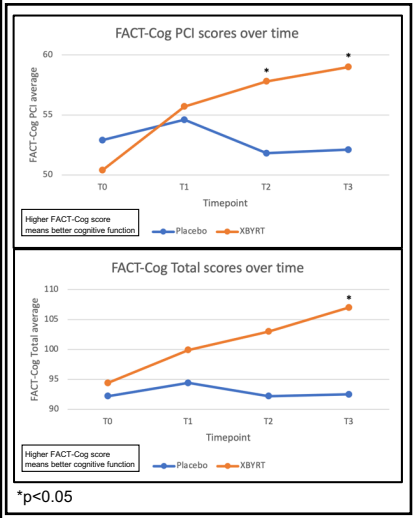
No significant differences in GHS scores were found between the XBYRT and Placebo groups

Secondary Outcomes – **without** baseline adjustment

- XBYRT arm had better MFSI emotional fatigue symptoms at T3 (P=0.045)
- XBYRT also had higher BDNF levels at T2 (P=0.047) and T3 (P=0.029) without baseline adjustment

Secondary Outcomes – **with** baseline adjustment

Figure 3. Outcomes with statistical significance with baseline adjustment



*p<0.05

- After adjusting for baseline, XBYRT had better FACT-Cog perceived cognitive impairment (PCI) at T2 (P=0.011) and T3 (P=0.017), and better total FACT-Cog score at T3 (P=0.028).
- The other secondary outcomes had no significant differences with baseline adjustments between both groups

Discussion & Conclusion

- This randomized controlled pilot trial found XBYRT to be a potentially safe integrative therapy that produced encouraging improvements in cognitive and fatigue symptoms, although there was a lack of a significant relationship between the intervention and GHS
- Clinical outcomes consistent with therapeutic intent for individual ingredients of XBYRT, such as *Radix Astragaliseu Hedysari* and *Rhizoma Atractylodis* which are known to improve fatigue, and *Radix Polygalae* which is known to improve cognitive function
- Limitation of small sample size due to patient ineligibility, concerns with TCM use, and recruitment barriers because of Covid-19
- Larger, multi-centered trials are necessary future steps to generate more robust evidence for XBYRT as an appropriate intervention to manage and improve symptoms in cancer patients and survivors

Acknowledgements

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Reference

Yap NY, et al. Trials. 2020 Nov 4;21(1):909.