Protocol Title: A Phase 3 Randomized Placebo Controlled Clinical Trial of Donepezil in Chemotherapy Exposed Breast Cancer Survivors with Cognitive Impairment

Target Population: Breast Cancer with Cognitive Impairment / Memory Impairment 1-5 Years after Chemotherapy

Summary: This study is to compare the safety and effects of Donepezil (Aricept) or if it decreases memory loss after receiving chemotherapy for breast cancer. A randomized, placebo controlled, double-blind, parallel group Phase 3 design will be used to assess the effect of 24 Weeks of Donepezil on cognitive function (memory) in breast cancer survivors who report having cognitive dysfunction and demonstrate memory impairment 1-5 Year post chemotherapy. Patients who meet the eligibility criteria will be stratified by age (<50, 50-59, 60-69, ≥70) and randomized to Donepezil or placebo with equal probability.

Key Inclusion Criteria:
- Women ≥18 years old with history of Invasive Breast Cancer
- Completed ≥ 4 cycles of adjuvant.neo-adjuvant cytotoxic chemotherapy between 1-5 Years prior to registration
- Receiving ongoing hormonal therapy for breast cancer must be on the same hormonal agent for at least 3 Months prior to study registration and plan to continue for the duration of the study (9 Months)
- Use of psychotropic medications is permitted if dose is stable over previous 12 Weeks
- Self-reported cognitive problem plus a measured memory deficit
  - Score <7 on single trial of Eligibility Pre-screen HVLT-R Form C
- Prior treatment with > 4 Cycles of adjuvant.neo-adjuvant cytotoxic chemotherapy
- ECOG performance status 0-2

Key Exclusion Criteria:
- Evidence or suspected recurrent or metastatic disease
  - Prior brain irradiation is not allowed
- May not currently be taking Ketoconazole or Quinidine
- History of dementia, Alzheimer's disease, multi-infarct dementia or CVA (history of TIA is allowed)
- Current use of Donepezil, Galantamine, Rivastigmine, Tacrine, Memantine, Methylphenidate, Dextroamphetamine, or any other specific cognition enhancing drugs are not allowed
- History of allergic reactions attributed to compounds of similar chemical or biologic composition to Donepezil
  - Hypersensitivity to Donepezil
- Uncontrolled intercurrent illness
- Traumatic brain injury, multiple sclerosis, acute severe fatigue, chronic fatigue syndrome or fibromyalgia
- Psychiatric illness/social situations that would limit compliance with study requirements including but not limited to a history of schizophrenia, psychosis or substance abuse
- Untreated current severe depression
- Pregnant women are excluded from this study
- It is unknown whether Donepezil is excreted in breast milk, for this reason women who are currently breast-feeding are not eligible for this study

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For additional information: https://clinicaltrials.gov/ct2/show/NCT02822573