DEVELOPING CONCEPT

Phase II feasibility study of donepezil for prevention of chemotherapy-associated cognitive dysfunction in older adults

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Chemo-Associated Cognitive Dysfunction (CACD)

- Objective changes in cognitive function are detected post chemotherapy[1]
  - Most consistently in domains of executive function, verbal ability, visuospatial ability
  - Largest effects are seen proximate to treatment
- Limitations to current knowledge base
  - Most studies are observational
  - Most have focused on breast cancer (little information on gender or other tumor types)
  - Older patients are highest risk yet routinely understudied
  - Few studies have investigated prevention

1. Hodgson et al, Cancer treatment reviews 2013; Jim et al. JCO 2012

Study Design

Adults ≥ 50 years with stage 1-3 colon or breast cancer and planned adjuvant chemotherapy

Stratification factors

1) **Cancer type**
2) **Age > 60 yrs**

Baseline (pre-chemo) testing
Neurocognitive/mood/QOL

Randomization

Placebo (x 6 months)

Donepezil (x 6 months)

3 month assessment

6 month (final) assessment

Donepezil Dose

5 mg/d x 6 wk +
10 mg/d x 18 wk

Outcomes

1^0 : Feasibility
2^0 : Change in neurocognitive measures, PRO (fatigue, mood, QOL)

Eligibility Criteria

Inclusion:

- Adults ≥ 50 years with stages 1-3 breast or colon cancer diagnosed within 4 months of enrollment
- Planned adjuvant chemotherapy within 4 weeks
- Karnofsky ≥60
- ≥ 3 weeks from surgical resection

Exclusion:

- Prior chemotherapy or brain XRT
- Use of acetyl cholinesterase inhibitor
- Medical contraindications:
  - sick sinus syndrome, bradycardia (<60bpm), seizure disorder, O2 dependent COPD/asthma

Study Status

- Concept being finalized
- Expected submission to NCI – 12/2013
- Projected N = 40
- Projected duration = 2 yr.

Goal: demonstrate feasibility and obtain estimates of variability and effect size to support a phase 3 study

Questions or Comments?