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A Randomized, Double-Blind Placebo Controlled Study of Armodafinil (Nuvigil®) To Reduce Cancer-Related Fatigue in Patients with High Grade Glioma

PI

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Goals of Study

Primary outcome:

- To determine preliminary efficacy of two doses (150mg and 250mg) of armodafinil in treating severe fatigue compared to placebo for a follow-up definitive phase III trial in patients with high grade glioma

Secondary outcome:

- To evaluate the tolerability of armodafinil in this patient population
- To assess the effect of armodafinil on cognitive function in patients with high grade glioma
- To assess the impact of armodafinil on global quality of life and other fatigue endpoints, such as usual fatigue and activity interference, in this patient population with high grade glioma
- Explore the correlation between the BFI and PROMIS measures as well as the relationship of fatigue and cognitive difficulties

Eligibility Criteria

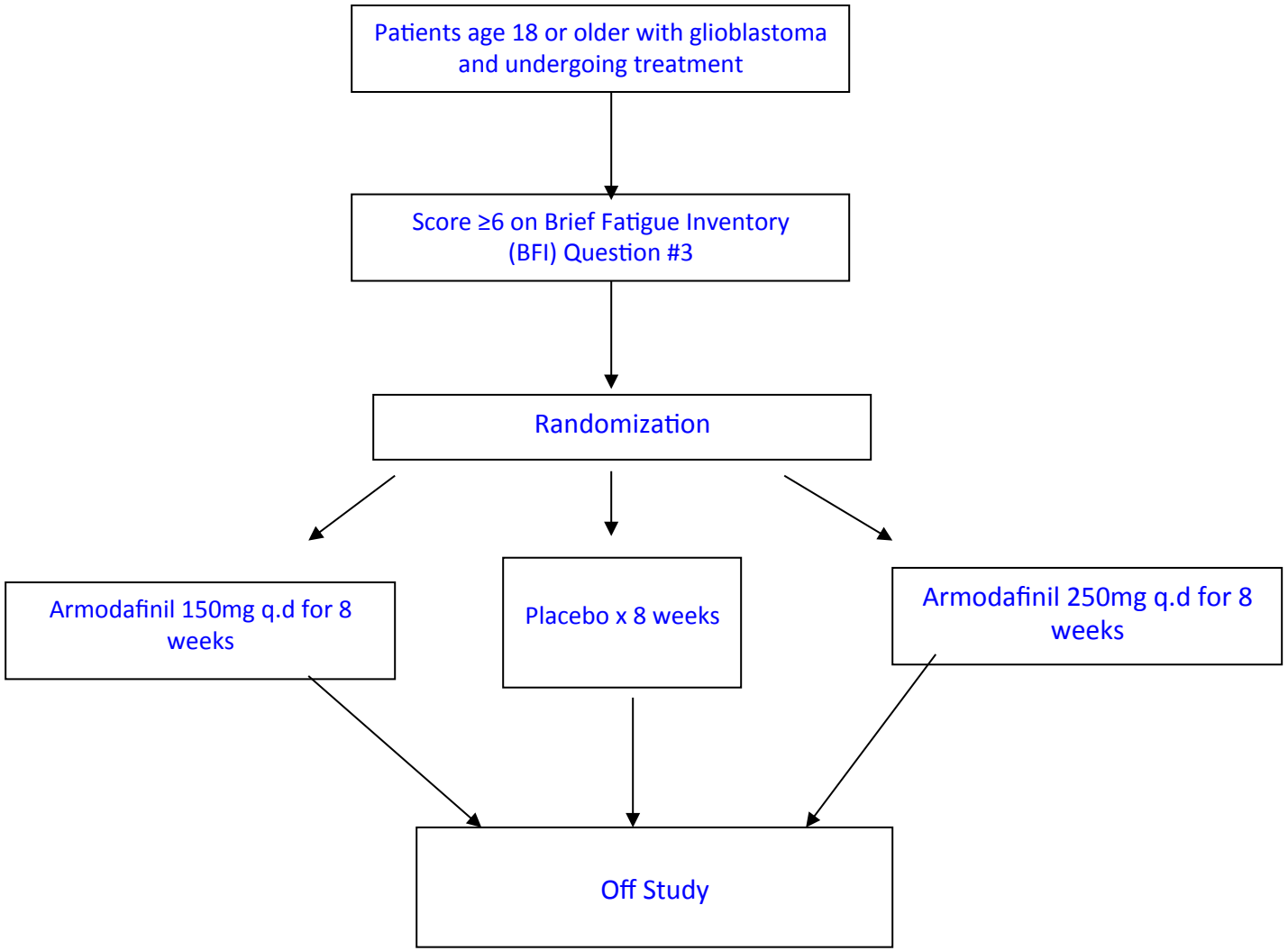
Inclusion Criteria

- Patients age 18 or older with GBM (and subtypes), AO, and AA who are clinically stable and have completed radiation therapy > 4 weeks prior to enrollment. Clinical stability will be defined as a stable or improved KPS compared to the prior month.
- ECOG Performance status of 1, 2, or 3
- Patients will be identified by self report of fatigue and then screened for eligibility based on the Brief Fatigue Inventory. Those that meet the cutoff of ≥6 points on the worst fatigue question of the BFI will qualify for treatment and randomized to the armodafinil or placebo arm.
- All patients will have undergone surgery (gross total or subtotal resection) or biopsy and will have been treated with concurrent radiation therapy and chemotherapy as standard of care for glioblastoma.

Exclusion criteria

- Patients who have received radiation therapy < 4 weeks prior to enrollment
- Serious medical or psychiatric illness that would prevent informed consent, completion of protocol therapy, or completion of the questionnaires
- History of hypersensitivity to other psychostimulants
- History of steroid psychosis
- History of or who are taking medications for attention deficit hyperactivity disorder, severe anxiety disorder, schizophrenia, or substance abuse by patient record and/or self report.
- Patients who have required an increase in their corticosteroid dose or in the preceding month before enrollment
- Patients who are currently using any other pharmacologic agents or nonpharmacologic interventions to specifically treat fatigue including psychostimulants, antidepressants, acupuncture, etc. will be excluded. Note: Antidepressants used to treat items other than fatigue (such as hot flashes or depression) are allowed if the patient has been on a stable dose for ≥ 1 month and plans to continue for the duration of the trial. Erythropoietin agents to treat anemia are allowed. Exercise is allowed.
- Patients anticipating surgery, those with hypothyroidism (TSH>5), profound anemia (hemoglobin level of <10), and profound depression
- Active or a history of Tourrette's syndrome or tic disorder
- History of or active glaucoma
- Patients who are pregnant or breast feeding
- History of intractable epilepsy, or uncontrolled seizure disorder

Schema


Patients age 18 or older with glioblastoma and undergoing treatment
Score ≥6 on Brief Fatigue Inventory (BFI) Question #3
Randomization
Armodafinil 150mg q.d for 8 weeks
Placebo x 8 weeks
Armodafinil 250mg q.d for 8 weeks
Off Study

Test Schedule	Active-Monitoring Phase						
	≤28 days prior to registration	Baseline (Prior to taking study agent)	Week 1	Week 2	Week 3	Week 4	Week 8
General neurological exam, weight, performance status	X						
Pregnancy test	X[1]						
Performance status						X[4]	X[4]
Neurocognitive testing (Appendix VII)		X[3]				X[3,5]	X[3,5]
Adverse Event Assessment		X				X	X
Patient Questionnaire Booklet • Brief Fatigue Inventory (BFI) • PROMIS • PRO-CTCAE (for fatigue and cognition items) • Linear Analogue Self-Assessment (LASA) • FACT-Cog • Godin Leisure Time Exercise Questionnaire (GLTEQ) (Appendices III-VI, XIII, XIV)		X[2]	X[2]	X[2]	X[2]	X[2,5]	X[2,5]
Nurse/CRA Phone Contact (Appendix XII)						X	X

Current status

- 190 approved sites
- 121 patients enrolled as of 2/29/16