

FAST FACTS

ALLIANCE A221805 - DULOXETINE TO PREVENT OXALIPLATIN-INDUCED CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE II TO PHASE III STUDY

Eligibility Criteria

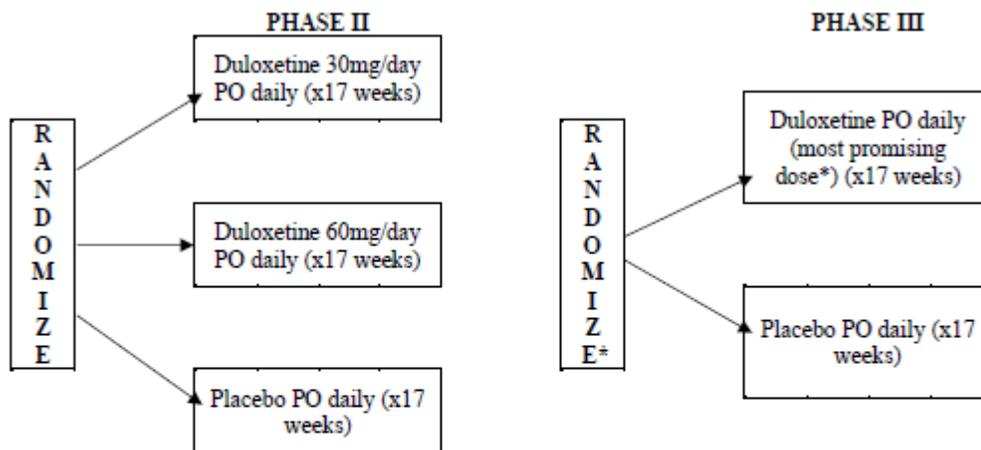
1. **Stage II-III colorectal cancer patients scheduled to receive oxaliplatin via one of the following treatment regimens:**
 - a. **FOLFOX (3-month): 510 mg/m² (total planned maximum cumulative dose) over 12 weeks (6 cycles), in which patients are scheduled to receive oxaliplatin 85 mg/m² every 2 weeks.**
 - b. **FOLFOX (3-month): 510 mg/m² (total planned maximum cumulative dose) over 12 weeks (6 cycles), in which patients are scheduled to receive oxaliplatin 85 mg/m² every 2 weeks.**
 - c. **CAPOX (3-month): 520 mg/m² (total planned maximum cumulative dose) over 12 weeks (4 cycles) in which patients are scheduled to receive oxaliplatin 130 mg/m² every 3 weeks.**
2. **No prior neurotoxic chemotherapy.**
3. **No pre-existing clinical or pre-clinical peripheral neuropathy from any cause.**
4. **Comorbid conditions: Patients with the following comorbid conditions are not eligible:**
 - a. History of seizure disorder
 - b. Narrow-angle glaucoma
 - c. History of suicidal thoughts
 - d. Symptoms of or a history of schizophrenia, bipolar disease, and/or a major depression
 - e. A serious eating disorder such as bulimia or anorexia
 - f. Known diagnosis of ethanol (ETOH) addiction/dependence within the past 10 years
5. **Concomitant medications:**
 - a. **No concomitant use of other adjuvant pharmacologic interventions (e.g., gabapentin, pregabalin, venlafaxine) with known or hypothesized efficacy for peripheral neuropathy. Must be discontinued at least 7 days prior to start of protocol treatment.**
 - b. **No concomitant use of other adjuvant pharmacologic interventions (e.g., gabapentin, pregabalin, venlafaxine) with known or hypothesized efficacy for peripheral neuropathy. Must be discontinued at least 7 days prior to start of protocol treatment.**
 - c. No anticipated or concurrent use of warfarin or heparin products while patients are receiving study drug. No anticipated or concurrent use of any antidepressant or serotonin-altering agent or other potent CYP2D6 inhibitors (e.g. paroxetine, fluoxetine, quinidine) known to interact with duloxetine, due to concern regarding cumulative toxicity and potential drug interactions. Use of an MAOI or other antidepressants must be discontinued at least 14 days prior to start of protocol treatment.
 - d. Chronic concomitant treatment with drugs that are extensively metabolized by CYP2D6 and that have a narrow therapeutic index, including certain antidepressants, phenothiazines, and Type 1C antiarrhythmics should be approached with caution.
 - i. Concomitant administration of duloxetine and thioridazine should be avoided.

- e. Chronic concomitant treatment with strong CYP1A2 inhibitors should be avoided during this trial due to concern regarding cumulative toxicity and potential drug interactions.
6. **Not pregnant and not nursing, because this study involves an investigational agent whose genotoxic, mutagenic and teratogenic effects on the developing fetus and newborn are unknown.**
Therefore, for women of childbearing potential, a negative pregnancy test done ≤ 7 days prior to registration is required.
 7. Age ≥ 25 years. Duloxetine black box warnings indicate an increased risk of suicide in patients < 25 years of age.
 8. ECOG Performance Status 0-2
 9. Language: In order to complete the mandatory patient-completed measure, patients must be able to speak and read English.
 10. Required Initial Laboratory Values:
Calculated Creatinine Clearance > 30 mL/min.
AST / SGOT ≤ 3 x upper limit of normal (ULN).

ePRO-E Eligibility Criteria

1. Must be enrolled in A221805.
2. **Participant must own a smartphone or tablet computer, and have access to Wi-Fi.**

Schema



All patients will receive oxaliplatin on both phases of the trial. Further, for all patients the 17th week of study drug will be a tapering period.

* Additional patients will be recruited to the Phase III trial. The most promising dose of duloxetine will be determined after the initial Phase II, and this dose will be used for Phase III for patients randomized to the duloxetine arm.

Please refer to the full protocol text for a complete description of the eligibility criteria and intervention plan.