CCF IRB CC396 NOVA 1507

Full Title
An open-label, multicenter, Phase II study to evaluate the activity of Patupilone (EPO906), in the treatment of recurrent or progressive brain metastases in patients with NSCLC

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Objectives
Primary Objective:
Tumor response as assessed by radiologic techniques and/or physical examination based on Response Evaluation Criteria in Solid Tumors

Secondary Objectives:
- Time to progression of the brain metastases
- Pharmacokinetics (PK) of patupilone in blood

Eligibility
Inclusion
1. World Health Organization (WHO) performance status of 0, 1 or 2 (corresponding to Karnofsky performance status of 50 or better)
2. Patients with radiologically proven (by gadolinium-enhanced [Gd-] magnetic resonance imaging [MRI]) parenchymal brain metastases from histologically confirmed non-small cell lung cancer (the primary disease may be quiescent). Gd-MRI must be performed within 2 weeks of study entry.
3. Patients should have at least one bidimensionally measurable intracranial lesion of a minimum of 2 cm as defined by Gd-MRI. If the patient has had previous radiation to the marker lesion(s), there must be evidence of residual disease > 2 cm or the lesion must have demonstrated progression since the radiation.
4. Those patients progressing on radiotherapy must have a 25% increase in the size of the previously radiated intracranial lesion based on the Neuro-Oncology Criteria of Tumor Response for Central Nervous System (CNS) Tumors or appearance of new lesions.
5. Patients must be controlled on medication and neurologically stable: stable on steroids and anticonvulsants for at least 2 weeks prior to obtaining the baseline Gd-MRI of the brain, and/or at least 2 weeks prior to beginning study treatment.
6. Female patients must have a negative serum pregnancy test at screening. (Not applicable to patients with bilateral oophorectomy and/or hysterectomy or to those patients who are postmenopausal.)
7. All patients of reproductive potential must agree to use an effective method of contraception during the study and for three months following termination of treatment.
8. Written informed consent must be obtained.
Exclusions

1. Clinical evidence of leptomeningeal disease
2. Patients with extracranial disease in more than 3 organ sites including the primary tumor.
3. Patients who have received any investigational compound within the past 28 days or who are planning to receive other investigational drugs while participating in the study
4. Prior administration of epothilone(s)
5. Patients with peripheral neuropathy > grade 1
6. Patients with unresolved diarrhea within the last 7 days before treatment.
7. Patients receiving known diarrheogenic agents must stop treatment with these agents prior to enrollment in the study.
8. Radiotherapy < 3 weeks prior to study entry
9. Prior intracranial surgery < 3 weeks prior to study entry; patient must have recovered from surgery prior to study entry.
10. Chemotherapy < 3 weeks prior to study entry; < 6 weeks from prior nitrosoureas.
11. Severe cardiac insufficiency (New York Heart Association [NYHA] III or IV), with uncontrolled and/or unstable cardiac or coronary artery disease
12. Radiotherapy not permitted while on study. Exception: palliative radiotherapy of metastasis in extremities is allowed, but such lesions cannot be used as target or non-target lesions.
13. Patients receiving hematopoietic growth factors except for erythropoietin
14. Patients taking Coumadin® or other agents containing warfarin, with the exception of low dose Coumadin® (1 mg or less daily) administered prophylactically for maintenance of indwelling lines or ports