

TYPE OF CANCER: Metastatic Cancer
TYPE OF TRIAL: Phase I
TRIAL SPONSOR: Nevada Cancer Institute

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STUDY SUMMARY

Inhibition of DNA Methylation by 1-hr Infusion of 5-aza-2'-deoxycytidine (Decitabine) x 10 Days (M-F) with Escalating Doses of SC Pegylated (PEG) Interferon-alfa 2B: A Phase I Study with Molecular Correlates

TREATMENT OVERVIEW

- Patients will receive decitabine 3.7 mg/m²/day i.v. over 1 hour daily in 10 doses over 2 weeks elapsed time (Monday-Friday) every 28 days
- In addition, some patients will receive a fixed dose of PEG-Intron weekly by subcutaneous injection in 28-day cycles

PRE-TREATMENT ASSESSMENTS

- Medical history
- Physical Exam
- Weight
- Performance status
- Toxicity notation
- Hematology
- Serum Chemistry
- Amylase
- Thyroid stimulating hormone
- Pregnancy test if applicable
- Disease assessment by CT or MRI
- Molecular correlates

ENTRANCE CRITERIA FOR PARTICIPATION IN TRIAL

Patient selection criteria:

Inclusion Criteria

1. Patient must have a biopsy proven cancer, which is metastatic or unresectable, for which (in the opinion of the investigator), no curative or more effective treatment exists.
2. Patients must have biopsy accessible tumor and must indicate willingness to undergo biopsies of tumor and normal skin on days 1, 15 and 29.
3. Patient must have measurable disease by RECIST criteria by scans performed within 28 days of study enrollment.

4. Patient may not have untreated brain metastasis. Patients with previously treated brain metastasis must no longer be receiving steroid therapy for the treatment of their brain metastasis.
5. Patient must have a Zubrod performance status of 0 - 2.
6. Prior surgery, radiotherapy or chemotherapy is allowed. The patient must not have received chemotherapy, radiotherapy, surgery, biologic therapy or any other investigational drug for any reason within 28 days prior to registration. Concomitant treatment with other anti-cancer agents or radiotherapy, including investigational agents during the course of study treatment is not allowed.
7. Patients with extensive pelvic irradiation or prolonged nucleoside analogue pretreatment are excluded due to increased risk for hematologic toxicity.
8. Patient must have adequate liver function as defined by a serum bilirubin ≤ 1.5 x the institutional upper limit of normal (IULN), SGOT or SGPT ≤ 2.5 x the institutional upper limit of normal (or ≤ 5 x the institutional upper limit of normal if hepatic metastases is present) obtained within 14 days prior to registration.
9. Patient must have an adequate renal function as defined by a serum creatinine ≤ 1.5 x the institutional upper limit of normal, as well as a calculated or measured creatinine clearance (CrCl) ≥ 50 ml/min.
10. Patient must have an ANC $> 1,500/\mu\text{l}$, platelet count $> 100,000/\mu\text{l}$ and hemoglobin > 9 gm/dl (this may be achieved by transfusion if needed) obtained within 14 days prior to registration.
11. All patients must be informed of the investigational nature of this study and must provide written acknowledgement of informed consent in accordance with institutional and federal guidelines.
12. Both men and women of all races and ethnic groups are eligible for this trial.
13. Patients must be ≥ 18 years of age.

Exclusion Criteria

1. Class 3/4 cardiac problems as defined by the New York Heart Association Criteria (e.g., congestive heart failure, myocardial infarction within 2 months of study).
2. Severe and/or uncontrolled concurrent medical disease (e.g., uncontrolled diabetes, uncontrolled chronic renal or liver disease, or active uncontrolled infection, e.g., HIV).
3. Patient must not be pregnant or nursing mothers because PEG-Intron or decitabine may be harmful to the developing fetus and newborn. Women/men of reproductive potential must agree to use an effective contraceptive method. Women of reproductive potential must have a negative serum pregnancy test within 7 days prior to registration. Postmenopausal women must be amenorrheic for at least 12 months to be considered of nonchildbearing potential. Male and female patients of reproductive potential must agree to employ an effective barrier method of birth control throughout the study and for up to 3 months following discontinuation of study drug.
4. Medical or psychological conditions that, in the opinion of the investigator, make the patient unable to tolerate or complete the treatment, or to grant reliable informed consent are not eligible for this study.

5. No other prior malignancy is allowed except for the following: adequately treated basal cell or squamous cell skin cancer, in situ cervical cancer, adequately treated Stage I, II, or III cancer from which the patient is currently in complete remission, or any other cancer from which the patient has been disease-free for 5 years.