

TYPE OF CANCER: Advanced Solid Tumors
TYPE OF TRIAL: Phase I/II
TRIAL SPONSOR: CanBas

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STUDY SUMMARY

Phase I/II study of a triplet combination of CBP501, pemetrexed and cisplatin in patients with advanced solid tumors and in chemotherapy-naïve patients with **malignant pleural mesothelioma**

TREATMENT OVERVIEW

This is an open-label, multicenter, international Phase I - II study of CBP501, pemetrexed and cisplatin administered as consecutive IV infusions according to a once-every-3-weeks schedule. The multicenter study will be conducted in the USA for the phase I part of the study and internationally for the phase II part of the study. Phase I part will be evaluated in a patient population with advanced solid tumors. The phase I part of the study is a dose-finding study of escalating doses of CBP501 combined with full-dose cisplatin and pemetrexed in patients with histologically confirmed solid malignancy that is metastatic or unresectable and for which standard curative or palliative measures do not exist or are no longer effective.

PRETREATMENT ASSESMENT

- Informed consent
- Inclusion/exclusion criteria
- Demographics/ Medical history
- Physical Examination
- Vital signs (height, weight, ECOG)
- Disease Assessment [modified RECIST for MPM]
- LVEF (echocardiography or MUGA scan)
- Cardiac risk factors
- Pulmonary function (FEV1, FVC, and SVC) (Only phase II part)
- EKG/ECG
- Chest X-ray
- FDG-PET (only phase II)
- Hematology
- Serum Biochemistry
- Serum mesothelin measurement (only phase II)
- Pregnancy test

- Concomitant medications

ENTRANCE CRITERIA FOR PARTICIPATION IN TRIAL

Inclusion Criteria

1. Signed informed consent obtained prior to initiation of any study specific Procedures
2.
 - Phase I: Histologically confirmed solid malignancy that is metastatic or unresectable and for which standard curative or palliative measures do not exist or are no longer effective or would otherwise be eligible for cisplatin and pemetrexed as first-line therapy
 - Phase II: Histologically or cytologically confirmed diagnosis of malignant pleural mesothelioma (MPM), not amenable for radical resection, who has not received previous chemotherapy or other systemic treatment
3. Measurable disease according to the modified Response Evaluation Criteria in Solid Tumors (RECIST, see below)
4. Male or female patients aged at least 18 years
5. ECOG Performance Status (PS): 0-2
6. Previous anticancer treatment must be discontinued at least 3 weeks prior to first dose of study treatment (6 weeks for mitomycin C; 6 weeks for anti-androgen therapy if discontinued prior to treatment initiation, with the exception of 8 weeks for bicalutamide)
7. Life expectancy > 3 months
8. Adequate organ function, including the following:
 - Bone marrow: white blood cell count $\geq 4 \times 10^9/L$
 - Absolute neutrophil count (ANC) $\geq 1.5 \times 10^9/L$,
 - Platelet count $\geq 100 \times 10^9/L$,
 - Hemoglobin ≥ 10 g/dL
 - Hepatic: Bilirubin ≤ 1.5 x the upper limit of normal (ULN),
 - Aspartate transaminases (AST/SGOT) and alanine transaminases (ALT/SGPT)
 - ≤ 2.5 x ULN (or ≤ 5 x ULN if liver metastases are present)
 - INR ≤ 1.5 x ULN
 - Renal: Serum creatinine ≤ 1.5 mg/dL or creatinine clearance ≥ 60 mL/min (calculated according to the Cockcroft and Gault formula)

9. Female patients of child-bearing potential must have a negative pregnancy test and be using at least one form of contraception as approved by the Investigator for 4 weeks prior to the study and 4 months after the last dose of study drug. For the purposes of this study, childbearing potential is defined as: "All female patients unless they are postmenopausal for at least one year or are surgically sterile"

10. Male patients must use a form of barrier contraception approved by the investigator during the study and for 4 months after the last dose of study drug

11. Ability to cooperate with the treatment and follow-up

Exclusion Criteria

1. Radiation therapy to more than 30% of the bone marrow prior to entry into the study

2. Phase II only: Mesothelioma originating outside the pleura (e.g. peritoneum)

3. Absence of measurable lesions

4. The patient has an ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, symptomatic or poorly controlled cardiac arrhythmia, uncontrolled thrombotic or hemorrhagic disorder, or any other serious uncontrolled medical disorders in the opinion of the investigator.

5. Any previous history of another malignancy within 5 years of study entry (other than cured basal cell carcinoma of the skin or cured in-situ carcinoma of the cervix)

6. Presence of any significant central nervous system or psychiatric disorder(s) that would hamper the patient's compliance

7. Evidence of peripheral neuropathy > grade 1 according to NCI-CTCAE Version 3

8. Treatment with any other investigational agent, or participation in another clinical trial within 28 days prior to study entry

9. Pregnant or breast-feeding patients or any patient with childbearing potential not using adequate contraception

10. Known HIV, HBV, HCV infection

11. Presence of CNS metastases