

TYPE OF CANCER: Advanced Non-Small Cell Lung Cancer
TYPE OF TRIAL: Phase II
TRIAL SPONSOR: CanBas

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STUDY SUMMARY

Phase II study of a triplet combination of CBP501, pemetrexed and cisplatin as first line treatment in patients with locally advanced (stage IIIB with malignant pleural effusion or pericardial effusion) or metastatic (stage IV) non-squamous non small cell lung cancer (NSCLC)

TREATMENT OVERVIEW

- Patients will be randomized to receive either CBP501, pemetrexed, and cisplatin or pemetrexed and cisplatin
- CBP501 (Arm A only), pemetrexed and cisplatin will be administered on the same day (Day 1), every 3 weeks for a maximum of six cycles. A cycle is considered to be 3 weeks (21 days).
- Patients will receive a maximum of six cycles of study treatment unless any of the following are observed earlier:
 - disease progression
 - unacceptable toxicity
 - withdrawal of consent
 - serious protocol violation
 - treatment delay > 2 weeks (except in the case of potential or perceived patient benefit)
- Following treatment discontinuation, patients will be followed every 8 weeks until disease progression or initiation of further systemic anticancer therapy, and then every 6 months until death.

PRE-TREATMENT ASSESSMENTS

- Informed consent.
- Compliance with inclusion and exclusion criteria.
- Patient demography.
- Medical history: complete history of previous, present and concomitant conditions and treatment.
- Pregnancy test, if applicable.
- Physical examination: a complete physical examination, including height, weight and BSA (within 1 week of treatment).
- Vital signs: blood pressure, body temperature, heart rate, respiration rate (within 1 week of treatment).

- ECOG Performance Status (within 1 week of treatment).
- Chest X-ray.
- 12-lead ECG.
- LVEF by echocardiography or MUGA scan.
- CT scan of chest and abdomen (within 21 days of the first planned dose); the same method used at entry is to be used for disease assessment throughout the study. Tumoral assessment is to be conducted according to RECIST criteria.
- Bone scan.
- Brain CT scan.
- Hematology: hemoglobin, differential white blood cell count, platelet count and INR.
- Biochemistry: ALT/SGPT, AST/SGOT, LDH, alkaline phosphatase, total serum bilirubin, sodium, potassium, calcium, magnesium, urea, albumin and, creatinine; including creatinine clearance (calculated using the Cockcroft formula).
- Where available, tumor samples will be assessed for biomarkers assessment.
- Concomitant medication.

ENTRANCE CRITERIA FOR PARTICIPATION IN TRIAL

INCLUSION CRITERIA

1. Signed informed consent obtained prior to initiation of any study-specific procedures
2. Histologically or cytologically confirmed diagnosis of non-squamous non small cell lung cancer (NSCLC), not amenable for radical resection, stage IIIB with pleural or pericardial effusion or stage IV, who has not received previous chemotherapy or other systemic treatment
3. At least one unidimensionally measurable lesion according to the Response Evaluation Criteria in Solid Tumors (RECIST)
4. Male or female patients aged at least 18 years
5. ECOG Performance Status (PS): 0-1
6. Life expectancy > 3 months
7. Prior local radiotherapy is allowed if it was completed ≥ 3 weeks prior to the first dose of the study medication
8. Concomitant palliative radiotherapy to an existing bone lesion for pain control is allowed
9. Prior surgery is allowed if it is performed at least 4 weeks prior to the first dose of study medication and patient should be fully recovered
10. Adequate organ function, including the following:
 - Bone marrow: white blood cell (WBC) 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 ≥ 9 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, albumin ≥ 3.0 g/dL

- Renal: Serum creatinine \leq 1.5 mg/dL or creatinine clearance \geq 45 mL/min (calculated according to the Cockcroft and Gault formula)
11. 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”
 12. 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
 13. 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. Histology of pure bronchioloalveolar carcinoma or neuroendocrine features in the tumor sample
3. Previous treatment with chemotherapy, new biological therapies (small molecules, antibodies), immunotherapy
4. Absence of measurable lesions
5. 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
6. 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)
7. Presence of any significant central nervous system (CNS) or psychiatric disorder(s) that would hamper the patient’s compliance
8. Evidence of peripheral neuropathy > grade 1 according to NCI-CTCAE Version 3
9. Treatment with any other investigational agent, or participation in another clinical trial within 28 days prior to study entry
10. Pregnant or breast-feeding patients or any patient with childbearing potential not using adequate contraception
11. Known HIV, HBV, HCV infection
12. Presence of symptomatic brain metastasis. Patients with brain metastases must: Have stable neurologic status following local therapy (surgery or radiation) for at least 2 weeks after completion of the definitive therapy. Be without neurologic dysfunction that would confound the evaluation of neurologic and other AEs
13. Inability or unwillingness to take folic acid, vitamin B12 or corticosteroids
14. Inability to interrupt aspirin or other nonsteroidal anti-inflammatory agents, other than aspirin dose \leq 1.3 grams per day, for a 5-day period (8-day period for long-acting agents, such piroxicam)
15. Significant weight loss (\geq 10% body weight during preceding 6 weeks)
16. Presence of clinically significant (by physical exam) third space fluid collections, e.g., ascites or pleural effusions that cannot be controlled by drainage or other procedures prior to study entry