MBP-426 is a novel liposome-encapsulated oxaliplatin, in combination with 5-FU/leucovorin (LV) – Phase I/II results of a Phase I/II study in gastro-esophageal adenocarcinoma, with pharmacokinetics

N. N. Senzer, K. Matsuno, N. Yamagata, T. Fujisawa, E. Wasserman, S. Sutherland, S. Sharma, A. Pan* 1. MOOCD, Osaka, TX; 2. metabolism Co., Ltd, Tokyo, Japan; 3. A Pharma, San Antonio, TX; 4. A Pharma, Laiesine Bullier, France; 5. Homerun Cancer Institute, Salt Lake City, UT; 6. N.D Antenho Cancer Center, Houston, TX

Abstract #C01

MBP-426 is a liposomal drug product in which the drug component is oxaliplatin, in combination with 5-FU/LV as the de Gramont regimen. MBP-426 was designed to improve the safety and tolerability of oxaliplatin, with an acceptable range of the principal toxicity to oxaliplatin, neutropenia, and peripheral neuropathy, and to allow for the dosing of predetermined doses in a phase Ib/II trial in combination with 5-FU/LV.

Study Design (continued)

• Phase Ib/II, open-label, non-randomized, single arm study of MBP-426 in combination with 5-FU/LV (de Gramont schedule) administered every 21 days.

• MBP-426 is infused as an iv bolus with an initial dose of 226 mg/m2, escalated to 301 mg/m2 and 400 mg/m2.

• The transferrin-conjugated liposomal formulation MBP-426 was administered as a 2-hr iv infusion. Over 46 hours.

• The co-administration of 5-FU and LV did not appear to alter the pharmacokinetics of oxaliplatin, indicating that the pharmacokinetic of oxaliplatin is independent of 5-FU/LV.

• All recommended dose level 170 mg/m2 on 5-FU/leucovorin (grade 3)/non hematological adverse events were observed, while one out of six patients had grade 3 thrombocytopenia.

• Peripheral neurotoxicity has been reported with this new oxaliplatin formulation, which is not a common toxic effect of conventional oxaliplatin treatment.

Study Objectives

Primary Objective

To determine the RD of MBP-426 in combination with 5-FU/LV (de Gramont schedule) administered every 21 days.

Secondary Objective

To characterize the safety profile

To characterize the pharmacokinetic profile

To evaluate the antitumor activity of MBP-426 in combination with 5-FU/LV (de Gramont schedule).

To characterize the safety profile of the combination therapy

Eligibility Criteria

Inclusion criteria

- Adequate organ and system function defined by the following parameters:
  - Hematologic: Absolute neutrophil count of ≥ 1500/mm3, platelet count of ≥ 100 x109/L, and an adequate peripheral blood smear; hemoglobin of ≥ 12gm/dL in females or ≥ 13gm/dL in males.
  - Hepatic: Total bilirubin ≤ 1.5 x upper limit of normal (ULN) or ≤ 2.5 x ULN if direct bilirubin is ≥ 1.5 x ULN; alkaline phosphatase (ALP) ≤ 3 x ULN; aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 3 x ULN.
  - Renal: Serum creatinine ≤ 1.5 x ULN.
  - History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.
  - Adequate organ and system function defined by the following parameters:

- Adequate organ and system function defined by the following parameters:
  - Hematologic: Absolute neutrophil count of ≥ 1500/mm3, platelet count of ≥ 100 x109/L, and an adequate peripheral blood smear; hemoglobin of ≥ 12gm/dL in females or ≥ 13gm/dL in males.
  - Hepatic: Total bilirubin ≤ 1.5 x upper limit of normal (ULN) or ≤ 2.5 x ULN if direct bilirubin is ≥ 1.5 x ULN; alkaline phosphatase (ALP) ≤ 3 x ULN; aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 3 x ULN.
  - Renal: Serum creatinine ≤ 1.5 x ULN.

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.

- Adequate organ and system function defined by the following parameters:

- History of allergy to any of the treatment components (oxaliplatin, 5-FU, folinic acid, MTX, LV).

- Measurable disease as defined by RECIST.