SUPPLEMENTARY INFORMATION

Eligibility criteria

Inclusion criteria

- Signed written, informed consent form before any study-related procedure is undertaken that is not part of the standard patient management.
- Male or female patients ≥18 years of age.
- Histologically or cytologically proven advanced or metastatic solid malignancies for which no effective standard therapy exists or has failed, or patients who are intolerant to established therapy known to provide clinical benefit for their condition.
- Eastern Cooperative Oncology Group performance status of 0 or 1 at Screening.
- Patients who have been treated previously with a checkpoint inhibitor may enroll.
- Adequate hematologic function as defined below:
    a) Absolute neutrophil count ≥1500/mm^3 or ≥1.5 × 10^9/L
    b) Platelet count ≥100,000/mm^3 or ≥100 × 10^9/L
    c) Hemoglobin ≥9 g/dL.

- Adequate hepatic function, defined by a total bilirubin level ≤1.5 × upper limit of normal (ULN), an aspartate aminotransferase (AST) level ≤2.5 × ULN, and an alanine aminotransferase (ALT) level ≤2.5 × ULN.

    a) Patients with documented Gilbert's syndrome are allowed if total bilirubin >1.5 × ULN but <3 × ULN

    b) Patients with tumor involvement in their liver: AST <3.0 × ULN, ALT < 3.0 × ULN, with normal bilirubin ≤1.5 × ULN and international normalized ratio <1.5.

- Adequate renal function, defined by an estimated glomerular filtration rate >50 mL/min.

- Male participants must agree to use and to have their female partners use a highly effective contraception method (i.e., with a failure rate of <1% per year) for 30 days before the first dose of study treatment (as appropriate), during the treatment period, and for at least 60 days after the last dose of study treatment of M4112, and must refrain from donating sperm during this period.

- A female participant is eligible to participate if she is not pregnant, not breastfeeding, and at least one of the following conditions applies:

    a) Not a woman of childbearing potential (WOCBP)

    OR

    b) A WOCBP who agrees to use a highly effective contraception method (i.e., with a failure rate of <1% per year) for 30 days before the first dose of study treatment (as appropriate), during the treatment period,

and for at least 60 days after the last dose of study treatment of M4112. Since the effect of the potential of M4112 to induce or inhibit cytochrome P450 3A4 (CYP3A4) is unknown at this time, WOCBP that are currently using hormonal contraception that is a substrate for CYP3A4 should also use double barrier contraception.

- WOCBP must have a negative plasma pregnancy test at the Screening Visit and a negative urine pregnancy test on day 1 before enrollment and dosing.

Exclusion Criteria

- Persisting toxicity related to prior therapy grade >1 National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03; however, sensory neuropathy grade ≤2 is acceptable and alopecia is acceptable.
- Prior organ transplantation, including allogeneic stem-cell transplantation.
- All patients with known brain metastases, except those meeting the following criteria:
    a) Brain metastases that have been treated locally and are clinically stable for at least 4 weeks prior to the start of treatment
    b) No ongoing neurologic symptoms that are related to the brain localization of the disease (sequelae that are a consequence of the treatment of the brain metastases are acceptable).
    c) Patients must be either off steroids or on a stable or decreasing dose of <10 mg daily prednisone (or equivalent).

- Concurrent treatment with a nonpermitted drug/intervention:

  a) Strong inhibitors or inducers of CYP3A4, and drugs with a narrow therapeutic index that are predominantly metabolized by CYP3A4, should be discontinued 7 days prior to treatment and avoided during treatment

  b) Drugs known to have a high risk of prolonging QT interval as per label

  c) Drugs that are known to increase gastric pH should be stopped at least 1 week before the start of study treatment

  d) Anticancer treatment (e.g., cytoreductive therapy, radiotherapy, immune therapy, cytokine therapy, monoclonal antibody therapy, targeted small molecule therapy) or any investigational drug within 4 weeks prior to the start of study treatment, or not recovered from adverse events related to such therapies, with the following exceptions:

     i. Palliative bone-directed radiotherapy is permitted (concurrently or within pretreatment period)

     ii. Hormonal therapies acting on the hypothalamic–pituitary–gonadal axis are permitted (i.e., luteinizing hormone–releasing hormone agonist/antagonists). No other hormonal anticancer therapy is permitted.

  e) Major surgery (as deemed by the Investigator) for any reason, except diagnostic biopsy, within 4 weeks of the study treatment and/or if the

patient has not fully recovered from the surgery within 4 weeks of the study treatment.

f) Patients receiving immunosuppressive agents (such as steroids), for any reason, should be tapered off these drugs before start of study treatment, with the following exceptions:

i. Patients with adrenal insufficiency may continue corticosteroids at physiologic replacement dose, equivalent to <10 mg prednisone daily

ii. Administration of steroids through a route known to result in a minimal systemic exposure (topical, intranasal, intro-ocular, or inhalation)

iii. Previous or ongoing administration of systemic steroids for the management of an acute allergic phenomenon is acceptable as long as it is anticipated that the administration of steroids will be completed in 14 days, or that the dose after 14 days will be equivalent to ≤10 mg prednisone daily.

g) Warfarin or other vitamin K antagonists.

- Current significant cardiac conduction abnormalities, including corrected QT interval (QTc) prolongation of >450 ms or impaired cardiovascular function, ventricular tachycardia, hypokalemia, or a history of paroxysmal atrial fibrillation, serious cardiac arrhythmia, and family history of sudden death or long QT syndrome.

- A history of cardiovascular/cerebrovascular disease as follows: cerebral vascular accident/stroke (<6 months prior to enrollment), myocardial infarction (<6 months prior to enrollment), and unstable angina or congestive heart failure (New York Heart Association Classification Class ≥II).

- Active autoimmune disease that might deteriorate when receiving an immunostimulatory agent:

    a) Patients with diabetes type I, vitiligo, psoriasis, hypo- or hyperthyroid disease not requiring immunosuppressive treatment are eligible

    b) Autoimmune diseases: e.g., inflammatory bowel diseases, interstitial lung disease or pulmonary fibrosis.

- Pneumonitis and history of pneumonitis.

- A history of difficulty of swallowing, gastric or small bowel surgery with history of malabsorption, or other chronic gastrointestinal disease or conditions that may hamper compliance and/or absorption of M4112.

- Any psychiatric condition that would prohibit the understanding or rendering of Informed Consent or interfere with compliance to study requirements and procedures in the opinion of Investigator and/or Sponsor.

- Known current alcohol and drug abuse as determined by the Investigator.

- Hepatocellular carcinoma.

- Legal incapacity or limited legal capacity if no consent by legal representative.

- Significant acute or chronic infections requiring systemic therapy including, among others:

    a) History of testing positive for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome

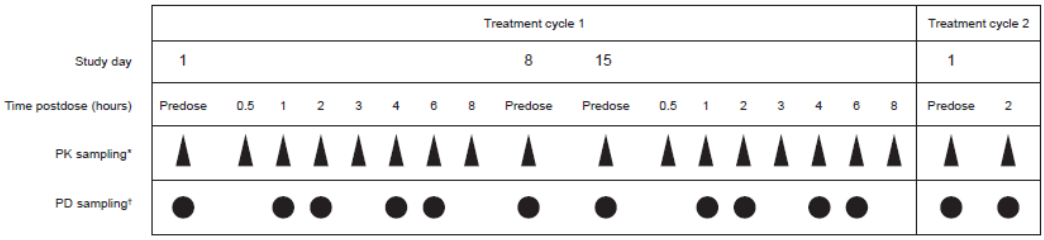
    b) Hepatitis B virus (HBV) or hepatitis C virus (HCV) infection (defined as HBV surface antigen positive and HBV core antibody positive with reflex to positive HBV DNA, or HBV core antibody positive alone with reflex to positive HBV DNA, or positive HCV antibody with reflex to positive HCV RNA). Patients with a history of infection must have polymerase chain reaction documentation that infection has cleared

    c) Active tuberculosis (history of exposure or history of positive tuberculosis test with presence of clinical symptoms, physical, or radiographic findings).

- Known hypersensitivity to the investigation medicinal products or to one or more of the excipients of M4112.

- Administration of a live vaccine within 28 days prior to study entry.

Supplementary figure 1 Schedule of pharmacokinetic and pharmacodynamic assessments in cycle 1 and day 1 of cycle 2



*PK sampling also included an optional metabolite analysis.

†Plasma samples were also taken at screening and on day 1 of cycle 3, day 1 of cycle 5 and at the end of treatment.