PLEASE NOTE: *This study has been imported from ClinicalTrials.gov without additional data checks.*

Trial Description

Title

A Phase 2, Randomized, Double-blind Study Comparing Tremelimumab to Placebo in Second- or Third-line Treatment of Subjects With Unresectable Pleural or Peritoneal Malignant Mesothelioma

Trial Acronym

Tremelimumab

URL of the trial

[---]*

Brief Summary in Lay Language

This is a Phase 2, randomized, double-blind, parallel-group study. Subjects with unresectable pleural or peritoneal malignant mesothelioma will be randomized in a 2:1 ratio to receive either tremelimumab or placebo. Approximately 180 subjects will be enrolled at study centers in multiple countries. The study consists of a screening period, a treatment period, and a 90-day follow-up period.

Brief Summary in Scientific Language

This is a Phase 2, randomized, double-blind, parallel-group study. Subjects with unresectable pleural or peritoneal malignant mesothelioma will be randomized in a 2:1 ratio to receive either tremelimumab or placebo.

Randomization will be stratified by EORTC status (low-risk vs high-risk), line of therapy (second vs third), and anatomical site (pleural vs peritoneal). This study plans to use the EORTC to stratify subjects into high or low risk groups in order to ensure balanced randomization to the different treatment groups. For subjects in whom pemetrexed was contraindicated or not tolerated or not an approved therapy (eg, peritoneal mesothelioma), prior therapy with a first-line platinum-based regimen is required. Approximately 180 subjects will be enrolled at study centers in multiple countries.

The study consists of a screening period, a treatment period, and a 90-day follow-up period.

Organizational Data

- DRKS-ID: **DRKS00005210**
- Date of Registration in DRKS: **2013/08/16**
- Date of Registration in Partner Registry or other Primary Registry: **2013/04/22**
- Investigator Sponsored/Initiated Trial (IST/IIT): **no**
- Ethics Approval/Approval of the Ethics Committee: **[---]***
- (leading) Ethics Committee Nr.: **[---]***

Secondary IDs

- Primary Registry-ID: **NCT01843374 (ClinicalTrials.gov)**
- Sponsor-ID: **D4880C00003 (MedImmune LLC)**

Health condition or Problem studied

- Free text: **Unresectable Pleural or Peritoneal Malignant Mesothelioma**
- ICD10: **C45.0 - Mesothelioma of pleura**
- ICD10: **C45.1 - Mesothelioma of peritoneum**

Interventions/Observational Groups

- Arm 1: **Drug: Tremelimumab**
- Arm 2: **Drug: Placebo**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **patient/subject, caregiver, investigator/therapist, assessor**
- Control: **Placebo**
- Purpose: **Treatment**

Study Type: **Interventional**

Study Type Non-Interventional: **[---]***

Allocation: **Randomized controlled trial**

Blinding: **[---]***

Who is blinded: **patient/subject, caregiver, investigator/therapist, assessor**

Control: **Placebo**

Purpose: **Treatment**

- Assignment: **Parallel**
- Phase: **II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

- Overall survival (OS) time by treatment arm; time frame: Time from randomization until death due to any cause, assessed up to 3 years.; The primary analysis of OS will be performed after a number of deaths have occurred among the approximately 180 participants randomized. For participants who are alive at the time of the primary analysis or lost to follow-up, OS will be censored on the last date when participants are known to be alive.

Secondary Outcome

- Durable disease control rate by treatment arm; time frame: Time from randomization to disease progression or death, whichever occurs first, assessed up to 3 years.; Durable DCR is defined as the proportion of participants with best response of complete response (CR), partial response (PR), or stable disease (SD) of ≥ 6 months duration
- Length of progression-free survival by treatment arm; time frame: Time from randomization to disease progression or death, whichever occurs first, assessed up to 3 years.; Progression-free survival will be measured from randomization to the first documentation of disease progression or death due to any cause, whichever occurs first.
- Overall response rate by treatment arm; time frame: Time from randomization to disease progression or death, whichever occurs first, assessed up to 3 years.; Overall response rate is defined as the proportion of participants with confirmed CR or PR.
- Duration of response by treatment arm; time frame: Time from randomization to disease progression or death, whichever occurs first, assessed up to 3 years.; Duration of response will be defined as the duration from the first documentation of objective response (CR or PR) to the first documented disease progression.
- Number of participants reporting any adverse event; time frame: Day 1- 90 days post dose; Any untoward medical occurrence in a patient or clinical investigation participants administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment.
- Number of participants with changes in patient-reported outcomes; time frame: Time from randomization to disease progression or death, whichever occurs first, assessed up to 3 years.; Patient-reported outcomes as measured by the LCSS-

Meso (for disease-related symptoms and health-related QoL), EQ-5D-3L (for health status), and BPI-sf (for pain) will be summarized descriptively; the change from baseline for total score and individual domain scores by treatment arm at each time point will be explored.
- Number of participants reporting any serious adverse event; time frame: Day 1 to 90 days post dose
- Number of participants with anti-drug antibodies; time frame: Week 5; The immunogenicity titer will be reported for samples confirmed positive for the presence of anti tremelimumab antibodies.
- Tremelimumab blood concentration; time frame: Week 5; Tremelimumab concentration data and summary statistics will be tabulated.

Countries of recruitment

- US **United States**
- AU **Australia**
- CA **Canada**

Locations of Recruitment

Recruitment

- Planned/Actual: **[---]***
- (Anticipated or Actual) Date of First Enrollment: **2013/05/31**
- Target Sample Size: **180**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **International**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

Inclusion criteria:

- Histologically and/or cytologically confirmed pleural or peritoneal malignant mesothelioma. Disease not amenable to curative surgery;

- Age 18 and over at the time of consent;

- ECOG Performance status 0-1;

- Previous receipt of 1-2 prior systemic chemotherapies that included first-line pemetrexed (or anti-folate)-based regimen in combination with platinum agent;

- Recovered from all toxicities associated with prior treatment;

- Measurable disease;

- Adequate bone marrow, hepatic, and renal function;

- Negative screening test results for human immunodeficiency virus (HIV), hepatitis A, B and C;

- Written informed consent and any locally required authorization (eg, HIPAA in the USA, EU Data Privacy Directive authorization in the EU) obtained from the subject/legal representative prior to performing any protocol-related procedures, including screening evaluations;

- Females of childbearing potential who are sexually active with a nonsterilized male partner must use a highly effective method of contraception for 28 days prior to the first dose of investigational product, and must agree to continue using such precautions for 6 months after the final dose of investigational product;

- Nonsterilized males who are sexually active with a female partner of childbearing potential must use a highly effective method of contraception from Day 1 through 90 post last dose.

Exclusion criteria

Exclusion criteria:

- Received any prior monoclonal antibody against CTLA-4, programmed cell death 1 (PD1) or programmed cell death 1 ligand 1 (PD-L1);

- History of chronic inflammatory or autoimmune disease;

- Active, untreated central nervous system (CNS) metastasis;

- History of other malignancy unless the subject has been disease-free for at least 3 years. Non-invasive cancer history (such as carcinoma in situ [CIS] that has been

resected) is allowed;

- Pregnant or breast feeding at time of consent;

- Any condition that would prohibit the understanding or rendering of information and consent and compliance with the requirements of this protocol;

- Active or history of diverticulitis. Note that diverticulosis is permitted;

- Active or history of inflammatory bowel disease (eg, colitis, Crohn's), irritable bowel disease, celiac disease or other serious gastrointestinal chronic conditions associated with diarrhea. Active or history of systemic lupus erythematosis or Wegener's granulomatosis;

- History of sarcoidosis syndrome;

- Currently receiving systemic corticosteroids or other immunosuppressive medications;

- Subjects should not be vaccinated with live attenuated vaccines within one month prior to starting tremelimumab treatment;

- The last dose of prior chemotherapy or radiation therapy (with the exception of palliative radiotherapy) was received less than 2 weeks prior to randomization;

- Any condition that, in the opinion of the investigator, would interfere with evaluation of the investigational product or interpretation of subject safety or study results;

- Concurrent enrollment in another clinical study or receipt of an investigational product within the last 4 weeks (participation in the survival follow-up period of a study is not an exclusion criterion);

- Employees of the study site directly involved with the conduct of the study, or immediate family members of any such individuals.

Addresses

■ **Primary Sponsor**

MedImmune LLC

Primary Sponsor

MedImmune LLC

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
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URL: **[---]***

Sources of Monetary or Material Support

- **[---]***

Bitte wenden Sie sich an den Sponsor / Please refer to primary sponsor

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

The parameters in ClinicalTrials.gov and DRKS are not identical. Therefore the data import from ClinicalTrials.gov required adjustments. For full details please see the DRKS FAQs.

- Translation on version: 304

- Last processed date by ClinicalTrials.gov: 2013/10/20

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*