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History of Changes for Study: NCT00729664

Phase 1 Open Label Study of MDX-1105 in Subjects With Solid Tumors

Latest version (submitted September 3, 2015) on ClinicalTrials.gov

- A study version is represented by a row in the table.
- Select two study versions to compare. One each from columns A and B.
- Choose either the "Merged" or "Side-by-Side" comparison format to specify how the two study versions are to be displayed. The Side-by-Side format only applies to the Protocol section of the study.
- Click "Compare" to do the comparison and show the differences.
- Select a version's Submitted Date link to see a rendering of the study for that version.
- The yellow A/B choices in the table indicate the study versions currently compared below. A yellow table row indicates the study version currently being viewed.
- Hover over the "Recruitment Status" to see how the study's recruitment status changed.
- Study edits or deletions are displayed in ~~red~~.
- Study additions are displayed in green.

Study Record Versions

Version	A	B	Submitted Date	Changes
1	◉	◉	August 4, 2008	None (earliest Version on record)
2	○	○	April 17, 2009	Recruitment Status, Contacts/Locations, Study Status, Arms and Interventions, Outcome Measures, Study Description, Eligibility and Oversight
3	○	○	June 18, 2009	Study Status and Sponsor/Collaborators
4	○	○	June 24, 2009	Contacts/Locations, Arms and Interventions, Study Design, Study Identification, Study Description, Study Status, Eligibility, Outcome Measures and Conditions
5	○	○	July 22, 2009	Contacts/Locations, Study Status, Conditions and Study Identification
6	○	○	July 31, 2009	Contacts/Locations and Study Status
7	○	○	October 27, 2009	Contacts/Locations, Arms and Interventions, Study Status, Eligibility, Study Design, Conditions and Study Description
8	○	○	January 22, 2010	Study Status and Contacts/Locations
9	○	○	March 12, 2010	Sponsor/Collaborators, Contacts/Locations, Study Status and Study Identification
10	○	○	March 29, 2010	Study Status and Study Identification
11	○	○	April 22, 2010	Study Status
12	○	○	June 24, 2010	Study Status, Eligibility and Study Design
13	○	○	December 2, 2010	Study Status
14	○	○	January 19, 2011	Arms and Interventions, Study Status, Study Identification, Conditions, Eligibility and Study Design
15	○	○	May 24, 2011	Contacts/Locations, Study Status and Study Design
16	○	○	July 25, 2011	Study Status and Eligibility
17	○	○	January 11, 2012	Sponsor/Collaborators, Study Status and Contacts/Locations
18	○	○	January 16, 2012	Study Identification and Study Status
19	○	○	February 2, 2012	Contacts/Locations and Study Status
20	○	○	February 15, 2012	Study Status
21	○	○	March 1, 2012	Study Status
22	○	○	March 14, 2012	Contacts/Locations and Study Status
23	○	○	March 30, 2012	Study Status and Contacts/Locations
24	○	○	April 16, 2012	Study Status
25	○	○	April 30, 2012	Contacts/Locations and Study Status
26	○	○	May 10, 2012	Outcome Measures, Study Status and Study Description
27	○	○	June 18, 2012	Study Status
28	○	○	February 1, 2013	Study Status, Contacts/Locations and References
29	○	○	February 7, 2013	Study Status
30	○	○	February 22, 2013	Study Status

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Version	A	B	Submitted Date	Changes
31	○	○	March 14, 2013	Recruitment Status, Contacts/Locations and Study Status
32	○	○	March 28, 2013	Study Status
33	○	○	May 7, 2014	Study Status
34	○	○	June 25, 2014	Study Status
35	○	○	November 13, 2014	Study Status
36	○	○	November 20, 2014	Study Status
37	○	○	December 5, 2014	Study Status
38	○	○	April 27, 2015	Study Status
39	○	○	May 5, 2015	Study Status
40	○	○	May 19, 2015	Study Status
41	○	○	June 1, 2015	Study Status
42	○	○	September 3, 2015	Recruitment Status, Study Status and Study Design

Compare

Comparison Format: ◉ Merged ○ Side-by-Side

Scroll up to access the controls

Study NCT00729664
Submitted Date: August 4, 2008 (v1)

Study Identification

Unique Protocol ID: MDX 1105-01

Brief Title: Phase 1 Open Label Study of MDX-1105 in Subjects With Solid Tumors

Official Title: A Phase 1, Open-Label, Dose-Escalation, Multidose Study of MDX-1105 Administered Every 14 Days in Subjects With Selected Advanced or Recurrent Solid Tumors

Secondary IDs:

Study Status

Record Verification: August 2008

Overall Status: Not yet recruiting

Study Start: November 2008

Primary Completion:

Study Completion:

First Submitted: August 4, 2008

First Submitted that Met QC Criteria: August 4, 2008

First Posted: August 7, 2008 [Estimate]

Last Update Submitted that Met QC Criteria: August 4, 2008

Last Update Posted: August 7, 2008 [Estimate]

Sponsor/Collaborators

Sponsor: Medarex

Responsible Party:

Collaborators:

Oversight

U.S. FDA-regulated Drug:

U.S. FDA-regulated Device:

Data Monitoring: No

Study Description

Brief Summary: The primary purpose of this study is to determine the safety of MDX-1105, including the maximum dose that can be tolerated when administered for 14 days in subjects with solid tumors. The study will also evaluate the preliminary effectiveness of the study drug in various types of solid tumors. How MDX-1105 is absorbed,distributed,metabolized and eliminated from the body will also be studied.

Detailed Description: This is a Phase 1 study of a fully human monoclonal IgG4 antibody targeting the Programed Death-Ligand 1 (PD-L1). Up to 40 subjects with measurable advanced or recurrent solid tumors (renal cell carcinoma, non-small cell lung cancer, malignant melanoma, or epithelial ovarian cancer will be enrolled in the study.

An accelerated titration design (ATD) will be utilized for this Phase 1 study. Five dose levels are planned and include: 0.3, 1, 3, 10, and 15 mg/kg/dose. Subjects will be assigned to a dose level in the order of study entry.

The first cohort of 1 subject will receive MDX-1105 0.3 mg/kg/dose administered as an intravenous infusion every 14 days for a total of 3 infusions. Enrollment into the next cohort cannot begin until 2 weeks have elapsed since the last subject's dosing in the previous cohort. One subject will be enrolled in each cohort until 1 subject experiences a greater then or equal Grade 2 drug-related adverse event,whereupon an additional 2 subjects will be enrolled at that dose level. Thereafter, the study will become the traditional 3+3 design with 3 or 6 subjects treated at this dose level and at all subsequent dose levels depending on the incidence of DLT's. If no DLT's occur in a cohort of 3 subjects, a new cohort of 3 subjects will be treated at the next higher dose level. If 1 of 3 subjects in a cohort experiences a DLT, that cohort will be expanded to 6 subjects. If only 1 of the 6 subjects has a DLT, then the next cohort of 3 subjects will be treated at the next higher dose level. If 2 or more DLT's occur within a cohort, then that dose level will be above the MTD (the highest dose where no more than 1 of 6 subjects has experience a DLT), and new subjects will be enrolled at the previous lower (tolerated) dose level until that cohort has 3 or 6 subjects. This lower dose level will be considered the MTD if less then or equal to 1 in 6 subjects has a DLT. Depending on toxicity, an intermediate dose level may be defined by a protocol amendment. A subject who withdraws from the study during cycle 1 for reasons other than a DLT will be replaced.

A total of 16 subjects (6 in the dose-escalation cohort + 10 in the expansion cohort) will be enrolled at the MTD or the highest dose studied if the MTD is not identified. For the expansion cohort, if 3 or more subjects experience a DLT, enrollment will be stopped and the data will be reviewed by the Medarax Medical Monitor before any subject continues in the study.

A DLT is defined as a greater than or equal to Grade 3 drug-related adverse event occurring within the first cycle(42 days) of dosing (excluding tumor flare defined as local pain, irritation, or rash localized at site of known or suspected tumor or a transient Grade 3 infusion adverse event) using National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0. A DLT will be considered related to study drug unless there is a clear, well-documented, alternative explanation for the adverse event.

Delayed DLT's are drug-related adverse events that occur after Cycle 1. delayed DLT's will not be used to determine the MTD for dose escalation. Delayed DLT's will be collected and evaluated by the Investigators and Medarex on an ongoing basis. If 4 or more such delayed DLT's are noted, accrual will be held pending safety analysis and will be restarted only with Investigator and Medarex approval.

Tumor response will be evaluated using Response Evaluation Criteria in Solid Tumors (RECIST) with modifications. End of cycle tumor response assessments for all subjects will occur within Days 38 to 42. Subjects with initial progressive disease (PD) based on sum of the longest diameter (SLD) or development of new lesions at the end of a cycle, but with otherwise stable or improved performance and clinical status, will continue to be treated with study drug for 1 additional cycle. At the next scheduled imaging evaluation, if there is further increase in the SLD, or development of additional new lesions, then PD has been confirmed and the subject will stop treatment and complete the off-treatment procedures. If the SLD remains the same or decreased and no additional new lesions develop and the subject is otherwise stable or improved in performance and clinical status, then PD has not been confirmed and the subject will continue to be treated with study drug for 1 additional cycle until the next scheduled imaging evaluation.

In the absence of confirmed disease progression, subjects who discontinue MDX-1105 treatment should continue in the study until at least 70 days following the last dose of MDX-1105 or the next scheduled visit has been performed which is even longer.. Subjects who discontinue MDX-1105 because of a treatment-related adverse event will remain in the study and continue to be followed until 70 days following the last dose of MDX-1105 or until stabilization or resolution of the event, whichever is longer. Subjects who discontinue MDX-1105 administration due to an adverse event and who have a demonstrated complete response(CR) partial response(PR) or stable disease(SD) will remain in the study and be followed every 3 months for up to to 6 months until relapse, confirmed disease progression, or initiation of new therapy, whichever occurs first.

Subjects who achieve a confirmed CR will not receive further cycles of MDX-1105 and will be followed every 3 months for 6 months until relapse, initiation of a new therapy, or a total of 6 months follow-up, whichever occurs first. Subjects with a response of PR/SD will continue to receive MDX-1105 treatment until achievement of a confirmed CR, confirmed disease progression, development of a greater than or equal to Grade 3 CTCAE, or intolerability to therapy. If a subject is eligible to receive additional cycles, the first dose of the next cycle should be given 14 days after the last dose of the prior treatment cycle but should be given no later than 21 days. No subject will be permitted dose escalations or de-escalations. The maximum duration of study drug treatment for a subject is 2 years. Those subjects who continue to receive clinical benefit after 2 years of therapy(subjects with CR, PR, or SD) will be followed every3 months from the last day they received study drug for 6 months until relapse, confirmed disease progression, initiation of a new therapy, or a total of 6 months follow-up, whichever occurs first. The maximum total study participation duration for a subject is 2.5 years.

Conditions

Conditions: Renal Cell Carcinoma
Non-Small Cell Lung Cancer
Malignant Melanoma
Epithelial Ovarian Cancer

Keywords:

Study Design

Study Type: Interventional
Primary Purpose: Other
Study Phase: Phase 1
Interventional Study Model: Parallel Assignment
Number of Arms: 1
Masking: None (Open Label)
Enrollment: 40 [Anticipated]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1 5 cohorts (0.3,1,3,10,and 15mg/kg/dose)	Biological: MDX-1105 MDX-1105 i.v.infusion, 5 cohorts,0.3,1,3,10,15mg/kg/dose every 14 days for a total of 3 infusions

Outcome Measures

Primary Outcome Measures:

1. To determine the safety, maximum tolerated dose(MTD and dose-limiting toxicity(DLT)of MDX-1105
   [Time Frame: MDX-1105 administered as an infusion every 14 days for a total of 3 infusions]

Secondary Outcome Measures:

1. Evaluate preliminary efficacy in solid tumors on the basis of objective responses
   [Time Frame: Days 1, 15 and 29]

Eligibility

Minimum Age: 18 Years
Maximum Age:
Sex: All
Gender Based:
Accepts Healthy Volunteers: No

Criteria: Inclusion Criteria:

1. Adults at least 18 years of age
2. Life expectancy greater than or equal to 12 weeks
3. ECOG performance status of 0 or 1
4. Criteria specific to each tumor type:

   RCC: Subjects must have a histologically confirmed diagnosis of renal cell carcinoma(clear cell component)with advanced or recurrent disease that is not amenable to cure by surgery or other means, and must have failed at least 1 previous systemic therapy, including, but not limited to, treatment with sunitinib, temsirolimus, sorafenib, interleukin-2 and or chemotherapy.

   NSCLC: Subjects must have refractory or recurrent histologically or cytologically confirmed advanced NSCLC. The malignancy must be deemed unresectable, and subjects must have failed at least 1 prior systemic taxane-based therapy.

   MEL: Subjects must have a histologically confirmed diagnosis of melanoma with advanced disease(previously treated, therapy-refractory or recurrent Stage III (unresectable) or Stage IV); disease no longer controlled by surgery, chemotherapy, or radiotherapy; and disease refractory to or relapsed after standard therapy(may include high-dose interleukin-2). All melanomas regardless of primary site of disease will be allowed.

   epOC: Subjects must have a histologically confirmed diagnosis of epithelial ovarian cancer with advanced or recurrent disease that is not amendable to cure by surgery or other means and must have failed at least 1 prior systemic platinum-based therapy.

5. Must have measurable disease with at least 1 unidimensional measurable lesion per RECIST with modifications
6. May have been treated with up to 3 previous systemic therapies for advanced/recurrent disease or have become intolerant to a systemic therapy
7. Prior treated brain metastases must be without MRI evidence of progression for at least 8 weeks and off steroids for at least 4 weeks before study drug administration to be eligible
8. May have been treated with radiation therapy(TR) provided there are measurable lesions outside the field of RT
9. Prior systemic RT completed at least 4 weeks before study administration. Prior focal radiotherapy completed at least 2 weeks before study drug administration. No radiopharmaceuticals (strontium, samarium) within 8 weeks before study drug administration
10. At least 28 days since the last chemotherapy, immunotherapy, biological or investigational therapy, radiation, or at least 2 weeks from approved tyrosine kinase inhibitor therapy before the first dosing of MDX-1105 and have recovered from any toxicity associated with such treatment
11. Systemic or topical corticosteroids must be discontinued at least 4 weeks before study drug administration
12. Prior major treatment-related surgery completed at least 4 weeks before study drug administration.
13. Screening laboratory values must meet the following criteria:

    WBC greater then or equal to 3000/uL Neutrophils greater then or equal to 1500/uL Platelets greater then or equal to 100,000/uL Hemoglobin greater then or equal to 9.0g/dL Creatinine less then or equal to 2mg/dL AST less then or equal to 2.5 X ULN ALT less then or equal to 2.5 X ULN Bilirubin less then 1.5 mg/dL

14. Women must meet 1 of the following criteria: post-menopausal for at least 24 consecutive months; surgically incapable of bearing children or utilizing a reliable form of contraception. Women of child bearing potential must agree to use a reliable form of contraceptive during the study Treatment Period and for at least 70 days following the last dose of study drug; and
15. Men must agree to the use of male contraception during the study treatment and for at least 180 days after the last dose of study drug. -

Exclusion Criteria:

1. History of severe hypersensitivity reactions to other monoclonal antibodies
2. Prior therapy with an anti-PD-1, anti-PD-L1, or anti-CTLA-4 antibody
3. Any other malignancy, excluding basal or squamous cell carcinoma of the skin, cervical carcinoma in situ, or localized prostate cancer, from which the subject has not been disease-free for at least 5 years
4. Active infection requiring i.v. systemic therapy within 28 days prior to the first dose of MDX-1105
5. Evidence of bleeding diathesis or coagulopathy
6. Any active autoimmune disease or a documented history of autoimmune disease, or history of syndrome that required systemic steroids or immunosuppressive medications, except for subjects with vitiligo
7. Recent history of attenuated viral vaccination within 30 days prior to the first dose of study drug
8. Known current drug or alcohol abuse
9. Apparent active or latent tuberculosis infection as indicated by any of the following: PPD recently converted to positive; chest x-ray with evidence of infections infiltrate; recent unexplained changes in fever/chill patterns
10. Underlying medical conditions that, in the Principal Investigator's opinion, will make the administration of study drug hazardous or obscure the interpretation of toxicity determination or adverse events
11. Concurrent medical condition requiring the use of immunosuppressive medications, or systemic or topical corticosteroids. Inhaled or intranasal corticosteroids(with minimal systemic absorption may be continued if the subject is on a stable dose). Non-absorbed intra-articular steroid injections will be permitted
12. Use of other investigational drugs within 30 days before study administration
13. Psychiatric illness or social situation that would preclude study compliance; or
14. Pregnant or nursing. -

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Contacts/Locations

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Study Officials: Henry C Pitot, MD
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Locations: **United States, Minnesota**

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Contact: Principal Investigator: Henry C Pitot, MD

IPDSharing

Plan to Share IPD:

References

Links:

Available IPD/Information:

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