Trial record **1 of 1** for: PH-L19IL2TNF-02/15

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Neoadjuvant L19IL2/L19TNF- Pivotal Study (Pivotal)

This study is currently recruiting participants.

See Contacts and Locations

Verified May 2017 by Philogen S.p.A.

Sponsor:
Philogen S.p.A.

ClinicalTrials.gov Identifier:
NCT02938299

First Posted: October 19, 2016
Last Update Posted: May 31, 2017

Information provided by (Responsible Party):
Philogen S.p.A.

Full Text View | Tabular View | No Study Results Posted | Disclaimer
How to Read a Study Record

Purpose

Phase III, open-label, randomized, controlled multi-center study. In the study, 214 patients will be enrolled and parallel assigned (via randomization system) in a 1:1 fashion to one of two different arms.

Condition	Intervention	Phase
Malignant Melanoma	Drug: L19IL2 + L19TNF Procedure: Surgery	Phase 3

Study Type: Interventional

Study Design: Allocation: Randomized
Intervention Model: Parallel Assignment
Masking: None (Open Label)
Primary Purpose: Treatment

Official Title: A Pivotal Phase III, Open-label, Randomized, Controlled Multi-center Study of the Efficacy of L19IL2/L19TNF Neoadjuvant Intratumoral Treatment Followed by Surgery Versus Surgery Alone in Clinical Stage III B/C Melanoma Patients

Resource links provided by NLM:

MedlinePlus related topics: Melanoma

Genetic and Rare Diseases Information Center resources: Carcinoid Tumor Neuroepithelioma

U.S. FDA Resources

Further study details as provided by Philogen S.p.A.:

Primary Outcome Measures:

- Recurrence-free survival (RFS) rate [Time Frame: 1 year after randomization.]

  Recurrence-free survival (RFS) rate in the L19IL2/L19TNF plus surgery treatment group (Arm 1) versus surgery alone (Arm 2), assessed at 1 year after randomization.

Secondary Outcome Measures:

- Local recurrence-free survival (LRFS) rate [Time Frame: 1year, 2years, 3years after randomization and 1year after surgery]
- Distant metastasis-free survival (DMFS) rate [Time Frame: 1year, 2years, 3years after randomization and 1year after surgery]
- Recurrence-free survival (RFS) rate [Time Frame: 2years, 3years after randomization]
- Overall survival (OS) [Time Frame: 1year, 2years, 3years after randomization]

- Percentage of Participants With On-Study Adverse Events (AEs) and Serious Adverse Events (SAEs) [Time Frame: up to 3 years]
- Percentage of Participants With Worst On-Study Hematological and Chemistry Abnormalities [Time Frame: up to 36 months]
- Clinically Meaningful Changes in Vital Signs and Physical Examinations [Time Frame: up to 36 months]
- Changes in absolute counts and relative percentages of lymphocytic subpopulations over time [Time Frame: (1) At screening, (2) At Day of surgery: from Day 1 to Day 54, (3) After 3 months from surgery: Day 91 to Day 144]

  Immunophenotypic characterization of PBMCs for changes in absolute counts and relative percentages of lymphocytic subpopulations (e.g., Tregs, MDSCs etc.) over time (only for patients recruited in German centers).

- HAFA [Time Frame: (1) At Day 1, (2) At Day 29, (3) After 3 months from surgery: Day 119 to Day 144]

  Assessment of the formation of human anti-fusion protein antibodies (HAFA) against L19IL2 and L19TNF.

Estimated Enrollment:	214
Study Start Date:	July 2016
Estimated Primary Completion Date:	December 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Arm 1: neoadjuvant + surgery Patients in Arm 1 will receive multiple intratumoral administrations into all injectable cutaneous, subcutaneous, and nodal tumors of a mixture of L19IL2 and L19TNF once weekly for up to 4 weeks (or until all injectable tumors have disappeared, or intolerance to study treatment or in the opinion of the investigator immediate surgical resection or any other treatment for melanoma is warranted, whichever occurs first). Newly occurring injectable melanoma lesions within the 4 weeks treatment period will also be treated as described. Surgical resection of all existing metastases will follow within 4 weeks after end of treatment. Surgery will be performed after the safety evaluation carried out at week	Drug: L19IL2 + L19TNF Mixture of L19IL2 and L19TNF once weekly Procedure: Surgery Surgical resection of melanoma tumor lesions

5 and, if indicated, may be carried out on the same day of the safety evaluation.	
Active Comparator: Arm 2: surgery alone Patients in Arm 2 will receive directly surgical resection of melanoma tumor lesions within 4 weeks after randomization.	Procedure: Surgery Surgical resection of melanoma tumor lesions

Detailed Description:

Phase III, open-label, randomized, controlled multi-center study. In the study, 214 patients will be enrolled and parallel assigned (via randomization system) in a 1:1 fashion to one of two different arms:

ARM 1:

Patients in Arm 1 will receive multiple intratumoral administrations into all injectable cutaneous, subcutaneous, and nodal tumors of a mixture of L19IL2 and L19TNF once weekly for up to 4 weeks (or until all injectable tumors have disappeared, or intolerance to study treatment or in the opinion of the investigator immediate surgical resection or any other treatment for melanoma is warranted, whichever occurs first). The whole volume of L19IL2/L19TNF will be equally distributed among all injectable lesions.

Newly occurring injectable melanoma lesions within the 4 weeks treatment period will also be treated as described. For the new lesions the treatment period will not be extended beyond the pre-defined 4 week- treatment period with a clock start at the time of the first intralesional L19IL2/L19TNF injection. Surgical resection of all existing metastases will follow within 4 weeks after end of treatment. Surgery will be performed after the safety evaluation carried out at week 5 and, if indicated, may be carried out on the same day of the safety evaluation.

ARM 2:

Patients in Arm 2 will receive directly surgical resection of melanoma tumor lesions within 4 weeks after randomization.

Eligibility

Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the

study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years and older (Adult, Senior)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

1. Diagnosis of malignant melanoma of the skin in clinical stage III B and III C, eligible for complete surgical resection.
2. Eligible subjects must have measurable disease and must be candidate for intralesional therapy with at least one injectable cutaneous, subcutaneous, or nodal melanoma lesion (≥ 10 mm in longest diameter) or with multiple injectable lesions that in aggregate have a longest diameter of ≥ 10 mm.
3. Males or females, age ≥ 18 years
4. ECOG Performance Status/WHO Performance Status ≤ 1
5. Life expectancy of at least 24 months (see paragraph 6.3.1)
6. Absolute neutrophil count > 1.5 x 109/L
7. Hemoglobin > 9.0 g/dL
8. Platelets > 100 x 109/L
9. Total bilirubin ≤ 30 µmol/L (or ≤ 2.0 mg/dl)
10. ALT and AST ≤ 2.5 x the upper limit of normal (ULN)
11. Serum creatinine < 1.5 x ULN
12. LDH serum level ≤ 1.0 x ULN
13. Documented negative test for HIV, HBV and HCV. For HBV serology, the determination of HBsAg, anti-HBsAg Ab and anti-HBcAg Ab is required. In patients with serology documenting previous exposure to HBV (e.g. anti-HBs Ab with no history of vaccination and/or anti-HBc Ab) negative serum HBV-DNA is also required.
14. All acute toxic effects (excluding alopecia) of any prior therapy must have resolved to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) (v4.03) Grade ≤ 1 unless otherwise specified above
15. All female subjects must have negative pregnancy test results at the screening. Women of childbearing potential (WOCBP) must be using, from the screening to three months following the last study drug administration, highly effective contraception methods, as defined by the "Recommendations for contraception and pregnancy testing in clinical

trials" issued by the Head of Medicine Agencies' Clinical Trial Facilitation Group and which include, for instance, progesterone-only or combined (estrogen- and progesterone-containing) hormonal contraception associated with inhibition of ovulation, intrauterine devices, intrauterine hormone-releasing systems, bilateral tubal occlusion, vasectomized partner or sexual abstinence. Pregnancy test will be repeated at the end of treatment visit.

16. Male patients with WOCBP partners must agree to use simultaneously two acceptable methods of contraception (i.e. spermicidal gel plus condom) from the screening to three months following the last study drug administration.
17. Evidence of a personally signed and dated informed consent document indicating that the subject has been informed of all pertinent aspects of the study.
18. Willingness and ability to comply with the scheduled visits, treatment plan, laboratory tests and other study procedures.

Exclusion Criteria:

1. Uveal melanoma and mucosal melanoma
2. Evidence of distant metastases at screening
3. Previous or concurrent cancer that is distinct in primary site or histology from the cancer being evaluated in this study except cervical carcinoma in situ, treated basal cell carcinoma, superficial bladder tumors (Ta, Tis & T1), second primary melanoma in situ or any cancer curatively treated ≥ 5 years prior to study entry
4. Presence of active infections (e.g. requiring antimicrobial therapy) or other severe concurrent disease, which, in the opinion of the investigator, would place the patient at undue risk or interfere with the study.
5. History within the last year of acute or subacute coronary syndromes including myocardial infarction, unstable or severe stable angina pectoris.
6. Inadequately controlled cardiac arrhythmias including atrial fibrillation
7. Heart insufficiency (> Grade II, New York Heart Association (NYHA) criteria)
8. LVEF ≤ 50% and/or abnormalities observed during baseline ECG and Echocardiogram investigations that are considered as clinically significant by the investigator.
9. Uncontrolled hypertension
10. Ischemic peripheral vascular disease (Grade IIb-IV)
11. Severe diabetic retinopathy
12. Active autoimmune disease
13. History of organ allograft or stem cell transplantation
14. Recovery from major trauma including surgery within 4 weeks prior to enrollment.
15. Known history of allergy to IL2, TNF, or other human proteins/peptides/antibodies or any other constituent of the product.

16. Breast feeding female
17. Anti-tumor therapy (except small surgery) within 4 weeks before enrollment
18. Previous in vivo exposure to monoclonal antibodies for biological therapy in the 6 weeks before enrollment
19. Planned administration of growth factors or immunomodulatory agents within 7 days before enrollment
20. Patient requires or is taking corticosteroids or other immunosuppressant drugs on a long-term basis. Limited use of corticosteroids to treat or prevent acute hypersensitivity reactions is not considered an exclusion criterion.
21. Any conditions that in the opinion of the investigator could hamper compliance with the study protocol.

Contacts and Locations

Information from the National Library of Medicine NIH NLM

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT02938299***

Contacts

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Locations

Germany

Charité Campus Mitte (CCM) **Recru**
Berlin, Germany, D-10117
Contact: Felix Kiecker, MD

Universitätsklinikum Carl Gustav Carus an der Technischen Universität Dresden **Recru**
Dresden, Germany, D-01307
Contact: Friedegund Meier, MD

Klinik für Dermatologie, Medizinische Fakultät Universitätsklinikum Essen **Recru**

Essen, Germany, 45122
Contact: Dirk Schadendorf, MD

Hauttumorzentrum Hannover (HTZH) **Recru**
Hannover, Germany, D-30625
Contact: Ralf Gutzmer, MD

Heidelberg University Hospital **Recru**
Heidelberg, Germany, D-69120
Contact: Jessica C. Hassel, MD

Kiel University Hospital **Recru**
Kiel, Germany, D-24105
Contact: Katharina C. Kähler, MD

Leipzig University Hospital **Recru**
Leipzig, Germany, D-04103
Contact: Ian Simon, MD

Tübingen University Hospital **Recru**
Tübingen, Germany, D-72076
Contact: Benjamin Weide, MD 0049 7071 2986880 benjamin.weide@med.uni-tuebingen.de

Italy

IRCCS A.O.U. San Martino - IST **Recru**
Genova, Italy, 16132
Contact: Paola Queirolo, MD

Fondazione IRCCS Istituto Nazionale dei Tumori **Recru**
Milan, Italy, 20133
Contact: Mario Santinami, MD

Istituto Oncologico Veneto, IRCCS **Recru**
Padova, Italy, 35128
Contact: Carlo Riccardo Rossi, MD

Poland

Centrum Onkologii-Instytut im. Marii Skłodowskiej-Curie Warszawa **Recru**
Warsaw, Poland, 02-781
Contact: Piotr Rutkowski, MD

Sponsors and Collaborators

Philogen S.p.A.

Investigators

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Principal Investigator:	Mario Santinami, MD	Istituto Nazionale Tumori Milano

More Information

Responsible Party:	Philogen S.p.A.
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Additional relevant MeSH terms:

Melanoma	Neoplasms by Histologic Type
Neuroendocrine Tumors	Neoplasms
Neuroectodermal Tumors	Neoplasms, Nerve Tissue
Neoplasms, Germ Cell and Embryonal	Nevi and Melanomas