Efficacy of Daromun Neoadjuvant Intratumoral Treatment in Clinical Stage IIIB/C/D Melanoma Patients

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

1. Histologically or cytologically confirmed diagnosis of clinical stage IIIB, IIIC, and IIID (AJCC 8th edition) locoregional melanoma that is eligible for complete surgical resection of all metastases (surgically resectable). 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. Prior anti-tumor treatment for the primary melanoma lesion, including surgery and approved adjuvant treatments (e.g., radiotherapy, immune checkpoint inhibitors, BRAF/MEK inhibitors, etc.) is allowed. Before enrollment in the study, a wash-out period of 6 weeks is required and toxicities from prior treatments should be resumed to Grade ≤1. 4. Males or females, age ≥ 18 years. 5. ECOG Performance Status/WHO Performance Status ≤ 1. 6. Life expectancy of \> 24 months. 7. Absolute neutrophil count \> 1.5 x 109/L. 8. Hemoglobin \> 9.0 g/dL. 9. Platelets \> 100 x 109/L. 10. Total bilirubin ≤ 30 µmol/L (or ≤ 2.0 mg/dl). 11. ALT and AST ≤ 2.5 x the upper limit of normal (ULN). 12. Serum creatinine \< 1.5 x ULN. 13. LDH serum level ≤ 1.5 x ULN. 14. Documented negative test for HIV, HBV and HCV. For HBV serology, the determination of HBsAg and anti-HBcAg Ab is required. In patients with serology documenting previous exposure to HBV (i.e. positive anti-HBsAg with not vaccination and/or positive anti-HBcAg Ab), negative serum HBV-DNA is also required. 15. 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. 16. All women of childbearing potential (WOCBP) must have negative pregnancy test results at the screening. WOCBP must be using, from the screening to three months following the last study drug administration, highly effective contraception methods. WOCBP and effective contraception methods are 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 safety visit (only WOCBP and only for patients in Arm 1). 17. 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. 18. Evidence of a personally signed and dated informed consent document indicating that the subject has been informed of all pertinent aspects of the study. 19. Willingness and ability to comply with the scheduled visits, treatment plan, laboratory tests and other study procedures. Exclusion Criteria 1. Uveal melanoma or 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, curatively 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 requiring or taking corticosteroids or other immunosuppressant drugs on a long-term basis will be evaluated case by case with the Sponsor for inclusion/exclusion in the study. Limited use of corticosteroids to treat or prevent acute hypersensitivity reactions is not considered an exclusion criteria. 21. Any conditions that in the opinion of the investigator could hamper compliance with the study protocol. 22. Previous enrolment and randomization in the same study.

Conditions & Interventions

Interventions:
DRUG: Daromun, PROCEDURE: Surgery, DRUG: Adjuvant therapy
Conditions:
Melanoma Stage IIIB, Melanoma Stage IIIC, Melanoma Stage IIID
Keywords:
Melanoma Stage IIIB, Melanoma Stage IIIC, Melanoma Stage IIID

More Information

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