P24-2 Protocol

AN OPEN-LABEL, MULTICENTER STUDY OF PARTICIPANTS WITH METASTATIC CASTRATE-RESISTANT PROSTATE CANCER AND HIGH-RISK GENETIC ALTERATIONS PREVIOUSLY TREATED WITH PROVENGE AND WITH A SINGLE INFUSION RETREATMENT WITH SIPULEUCEL-T

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1.5. Study Design and Duration

A schematic of the study design is presented in Figure 1.

The timing of the study visits and follow-up is presented in Table 2.

1.5.1. Study Population and Sample Size

This is an open-label, multicenter phase 1 study of participants with high-risk genetic alterations and metastatic castrate-resistant prostate cancer (mCRPC) previously treated with Provenge (sipuleucel-T) who will receive a single infusion retreatment with sipuleucel-T and will enroll up to approximately 10 participants.

1.5.2. Eligibility Criteria

Potential participants are men aged ≥18 years with a diagnosis of mCRPC, prior treatment with Provenge (sipuleucel-T), and high-risk genetic alteration.

1.5.2.1. Inclusion Criteria

1. Men aged ≥18 years
2. Confirmed diagnosis of mCRPC
3. Prior treatment with on-label Provenge completed within the last 10 years (Provenge, 2017)
4. Identification of 1 or more high risk genetic alterations, including but not limited to:
   - Genetic alterations in *TP53*
   - Genetic alterations in *PTEN*
   - Deleterious *BRCA1/2* mutations
   - Mismatch repair deficiency (dMMR)
   - Microsatellite instability high (MSI-H)
5. Written informed consent prior to the initiation of study procedures

6. ECOG PS 0-2
7. Estimated life expectancy ≥12 months

1.5.2.2. Exclusion Criteria

1. Prostate cancer diagnosis of local or castration-sensitive disease
2. Has not previously received on-label Provenge
3. Lack of high-risk genetic alterations
4. Need systemic chronic immunosuppressive therapy, including antitumor necrosis factor alpha monoclonal antibodies, glucocorticoids, systemic steroids, blood products, GM-CSF or granulocyte colony-stimulating factor (G-CSF), or experimental and investigational therapies (see Section 6.6)
5. Uncontrolled, concurrent illness including, but not limited to the following: ongoing or active infection (bacterial, viral, or fungal), or psychiatric illness that would limit compliance with study requirements, as well as any condition that would preclude a participant from completing a single infusion retreatment with sipuleucel-T.
6. On experimental or investigational therapy
7. Significant cardiac disease, such as recent (within 6 months prior to first dose of the study drug) myocardial infarction or acute coronary syndromes (including unstable angina pectoris), congestive heart failure (New York Heart Association class III or IV), uncontrolled hypertension, uncontrolled cardiac arrhythmias, severe aortic stenosis.
8. A baseline QT interval as corrected by Fridericia's formula (QTcF) >470 msec, a complete left bundle branch block (defined as a QRS interval ≥120 msec in left bundle branch block form) or an incomplete left bundle branch block
9. History of thromboembolic or cerebrovascular events, including transient ischemic attacks, cerebrovascular accidents, deep vein thrombosis, or pulmonary emboli within 3 months prior to first dose of the study drug.