

DISCERN: A Randomized Pilot Study Comparing Dual Versus Single Immune Checkpoint Blockade Plus Chemotherapy in PD-L1 Negative Advanced NSCLC



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INTRODUCTION

Immune checkpoint inhibitors (ICIs) have improved outcomes in metastatic non-small cell lung cancer (NSCLC) but benefit in tumors lacking PD-L1 expression remains limited. Dual checkpoint blockade may enhance antitumor immunity by overcoming an immunologically “cold” tumor microenvironment.

Circulating tumor DNA (ctDNA) is a non-invasive biomarker capable of detecting molecular responses to therapy prior to radiologic changes.

METHODS

The DISCERN study is a single-center, randomized, open-label pilot trial comparing dual immune checkpoint blockade (nivolumab + ipilimumab) plus chemotherapy (Arm A) versus single ICI (pembrolizumab) plus chemotherapy (Arm B) in patients with PD-L1-negative, stage IV NSCLC. The study plans to enroll 24 patients, with ctDNA positivity required at baseline. ctDNA response is evaluated at Cycle 3 Day 1 using Guardant Infinity NGS platform.

The primary endpoint is ctDNA response. Secondary endpoints include RECIST-based response rates, progression-free survival (PFS), and overall survival (OS).

DISCUSSION

The DISCERN study is a randomized, two-arm, phase II pilot trial evaluating molecular responses by ctDNA in patients receiving dual vs. single ICI-based chemoimmunotherapy. The trial targets a highly underserved patient population – PD-L1-negative, advanced NSCLC, which is characterized by comparatively poor response to standard immunotherapy.

DISCERN incorporates only standard-of-care regimens, ensuring external validity. All participants receive four cycles of platinum-doublet chemotherapy along with their assigned ICI regimen. The choice of chemotherapy backbone is histology-driven (carboplatin-pemetrexed or carboplatin-paclitaxel). Maintenance therapy will continue per standard guidelines.

Conclusion

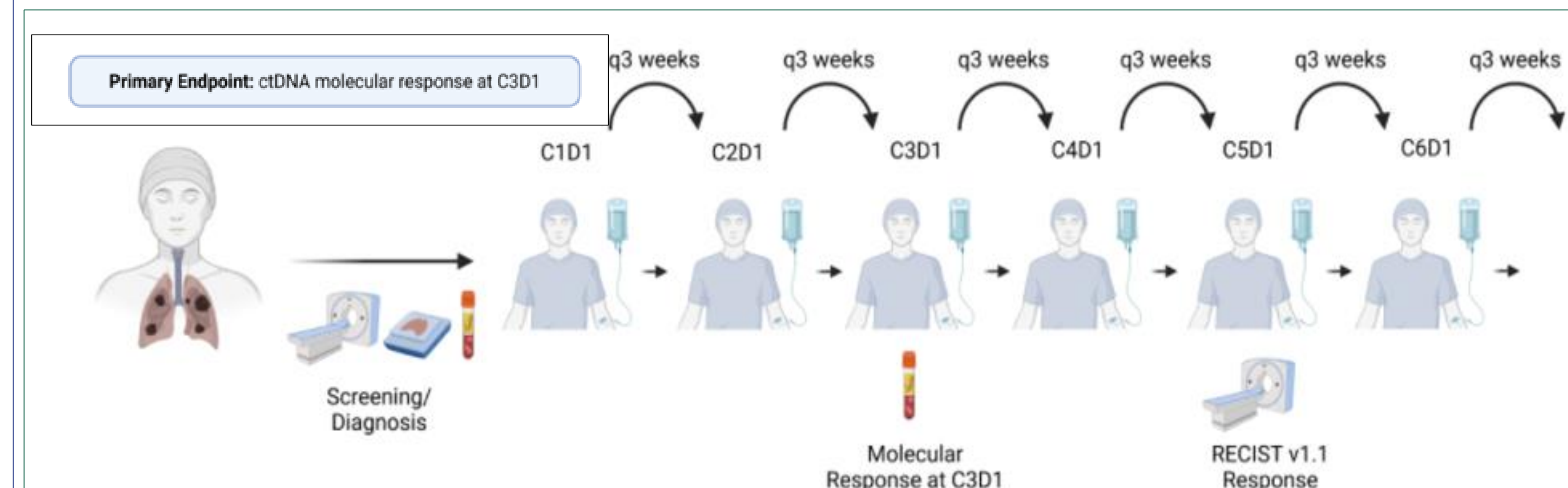
DISCERN will provide novel insight into the comparative impact of dual versus single ICI regimens in PD-L1-negative NSCLC

It will also shed a light on the role of ctDNA clearance as an early marker of treatment efficacy in this subset of NSCLC.

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Design

Molecular Response plan



Study Schema

