PRECISION for medicine

PRECISION epiontisid℠

CASE STUDY

Exploring Biomarkers to Predict the Response to Immunotherapy-Based Combination Treatment in Hepatocellular Carcinoma Using Epiontis ID™

Situation

Immunotherapy-based combinations have revolutionized the treatment of a wide range of cancers. Specifically, the addition of immune checkpoint inhibitors to the treatment regimen is considered promising; however, only subgroups of patients generally experience outcome improvements, responses are not consistent, and in some cases, hyperprogression has been observed following treatment.

In this phase 2 study, investigators in Germany sought to determine the safety and efficacy of transarterial chemoembolization (TACE, a localized chemotherapy) combined with nivolumab, a checkpoint inhibitor, in intermediate stage hepatocellular carcinoma (HCC), and to explore biomarkers from peripheral blood via immunophenotyping with the potential to be predictive of clinical response.

Standardized immune phenotyping with precise and repeatable results is a prerequisite for reliable prediction of clinical response in patient populations.

Challenges

In a clinical study, discovering biomarkers using commonly employed immunophenotyping methods such as flow cytometry can prove challenging due to difficulties in standardization since reagent batches and processes vary in different hospitals and laboratories. This lack of standardization hinders reliable monitoring of biomarker signatures in peripheral blood in a site-independent manner.

Epiontis ID™ is a DNA-based epigenetic immunophenotyping technology that is fully standardized, automated, accredited under ISO 17025, and

does not require any sample processing at the site beyond freezing of peripheral blood. These technical advantages suggest that Epiontis ID may be a promising tool for evaluating predictive biomarkers in patients at the pretreatment stage.

Solution

Epiontis ID was used to characterize immune cells in the peripheral blood prior to treatment in 39 of the 59 patients with HCC enrolled in the study. Patients received up to 2 TACE treatments followed by nivolumab (240 mg every other week), which was continued until progression for a maximum treatment duration of 2 years. Three different immune cell types were quantified to identify potential biomarkers or signatures for response prediction:

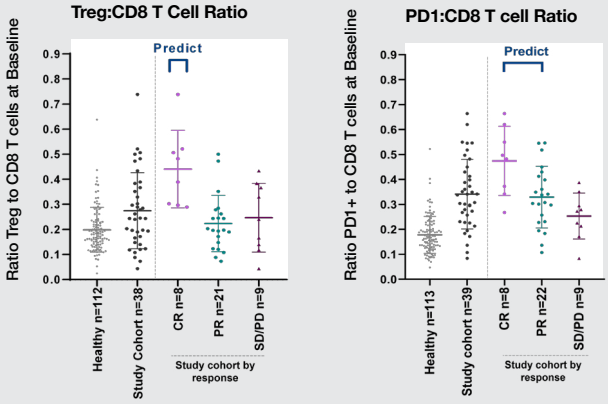
- CD8 T cells, which are involved in the anti-tumor immune response
- Regulatory T cells (Tregs), which play a key role in immune suppression
- Programmed death receptor-1 (PD-1)-positive cells, which characterize immune cells that have been suppressed or exhausted

These immune cell counts were compared to counts observed in healthy donors and evaluated for their potential to predict clinical responses.

Results

Immunophenotyping via Epiontis ID produced data that demonstrated that the Treg:CD8 T cell and PD-1-positive:CD8 T cell ratios are potential biomarkers for clinical response prediction. Patients with high ratios of these marker combinations experienced a significantly increased frequency of complete or partial responses to treatment, while those with low ratios responded less favorably.

Figure 1. Correlations of immune cell ratios with clinical responses



CR: complete response; PR; partial respoonse; SD/PD: stable diseaase/progressive disease

Based on these findings, pretreatment Treg:CD8 T cell and PD-1-positive:CD8 T cell ratios warrant further investigation as biomarkers for predicting clinical responses in patients treated with checkpoint inhibitors.

For more information on how Epiontis ID can be an ideal solution for immune monitoring in research and in clinical trials, please visit epiontis.com, or to learn more about all of Precision for Medicine's therapeutic development solutions, visit precisionformedicine.com.

PRECISION epiontisid℠

PRECISION for medicine