Introduction

- Colorectal cancer (CRC) is one of the most common cancers with 200,000 U.S. cases per year.
- Adenocarcinoma is the most common type of CRC, making up 95 percent of all CRC cases.
- Checkpoint inhibitors used for CRC have shown efficacy for a specific subset of patients.
- MC38 is one of the robust preclinical tumor models in immuno-oncology due to its characteristics as an immunologically warm tumor and response to some immunotherapies.
- To identify underlying factors that influence differences in treatment response, the tumor microenvironment (TME) of the MC38 model was analyzed following the treatment with anti-programmed cell death protein 1 (PD-1) and anti-cytotoxic T lymphocyte associated protein 4 (CTLA-4).
- Labcorp In Vitro Preclinical Oncology uses molecular signatures within the TME in preclinical models to help inform both test agent mechanism and combination strategies.
- MC38 syngeneic colon tumor model is used as an example of how phenotypic signatures can be leveraged for early identification of predictive biomarkers and for rational design of combination therapies with checkpoint inhibitors to improve patient outcome.

Methods

- MC38-NCl.TD1 cells were implanted subcutaneously into the axilla of female C57BL/6J mice. The dosing was • test agent mechanism and combination strategies.
- Identification of predictive biomarkers and for rational design of combination therapies with checkpoint inhibitors to establish disease is minimally responsive to checkpoint
- In Vitro Preclinical Oncology uses molecular signatures within the TME in preclinical models to help inform both test agent mechanism and combination strategies.
- MC38 syngeneic colon tumor model is used as an example of how phenotypic signatures can be leveraged for early identification of predictive biomarkers and for rational design of combination therapies with checkpoint inhibitors to improve patient outcome.

Results

- Colon cancer (CRC) is one of the most common cancers with 200,000 U.S. cases per year. Adenocarcinoma is the most common type of CRC, making up 95 percent of all CRC cases. Checkpoint inhibitors used for CRC have shown efficacy for a specific subset of patients.
- MC38 is one of the robust preclinical tumor models in immuno-oncology due to its characteristics as an immunologically warm tumor and response to some immunotherapies.
- To identify underlying factors that influence differences in treatment response, the tumor microenvironment (TME) of the MC38 model was analyzed following the treatment with anti-programmed cell death protein 1 (PD-1) and anti-cytotoxic T lymphocyte associated protein 4 (CTLA-4).
- Labcorp In Vitro Preclinical Oncology uses molecular signatures within the TME in preclinical models to help inform both test agent mechanism and combination strategies.
- MC38 syngeneic colon tumor model is used as an example of how phenotypic signatures can be leveraged for early identification of predictive biomarkers and for rational design of combination therapies with checkpoint inhibitors to improve patient outcome.

Conclusions

- The MC38 colon tumor model is minimally responsive to anti-PD-1 therapy and refractory to anti-CTLA-4 treatment under the conditions tested.
- Flow cytometry revealed immunological changes in the MC38 TME following anti-PD-1, but anti-CTLA-4 response was mostly static.
- Changes in gene expression demonstrated by nCounter® complement an immune activation phenotype with anti-PD-1 therapy despite minimal efficacy. This observation can allow for potential synergetic efficacy in combination with immuno-oncology drug candidates.
- The importance of using multiple modalities is essential for an in-depth understanding of the TME.