A Phase II Trial of TRC102 (methoxyamine HCl) in Combination with Temozolomide in Patients with Relapsed Colorectal Carcinoma

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Background
The basic excision repair (BER) pathway has been shown to play a major role in promoting resistance to both alkylating agents and antimetabolites. The agent TRC102 acts through a novel mechanism to inhibit BER and has shown chemopotentiation in murine models of human cancer, suggesting that TRC102 may enhance the activity of alkylating and antimetabolite chemotherapy in patients (1). Published studies indicate that TRC102 has the ability to interrupt the process of BER by binding to apurinic/apyrimidinic (AP) sites produced during the initial step of BER (2, 3). These AP sites are not substrates for apurinic/apyrimidinic endonuclease (APE), which performs an essential step in BER.

Phase II Objectives

Primary Objective:
To explore the response rate of the combination of TRC102 and TMZ in patients with CRC, NSCLC, and granulosa cell ovarian cancer

Secondary Objective:
To explore the response rate of the combination of TRC102 and TMZ in patients with CRC, NSCLC, and granulosa cell ovarian cancer

Exploratory Objectives:
- Investigate tumor genomic and transcriptomic alterations potentially associated with sensitivity and/or the development of resistance to TRC102 and TMZ
- Determine the effects of the study treatment on the level of intratumoral γH2AX in circulating tumor cells (CTCs) and tumor and correlate the γH2AX response in tumor and CTCs

CRC Cohort Schema and Trial Design

Main eligibility criteria:
- Histopathologically confirmed colorectal adenocarcinoma that has progressed after at least two lines of therapy
- ECOG ≤ 2
- Normal organ function

Main exclusion criteria:
- MH1-Graded CRC not previously treated with immunotherapy
- Symptomatic CNS disease or carcinomatous meningitis
- Pregnant or nursing women
- Unstable medical illness
- HIV+ on protease inhibitors
- Unstable medical illness
- Pregnant or nursing women
- Symptomatic CNS

Cohort design phase II trial of this combination is currently underway based on objective responses documented during the phase I portion of the study in patients with CRC, non-small cell lung cancer, and granulosa cell ovarian cancer.

Common adverse events

- Adverse event (grade 3/4) Frequency
- Grade 3
- Grade 4

Cohort Results

- Patient characteristics
- Common adverse events

References

Acknowledgements
https://ncicancer.gov