The NCCN Oncology Research Program (ORP) strives to improve the quality of life for patients and reduce cancer-related deaths by advancing cancer therapies through research. Since the program's establishment in 1999, the NCCN ORP has brought millions of dollars in research grants to investigators at NCCN Member Institutions. Research grants are provided to NCCN through collaborations with pharmaceutical and biotechnology companies; these grants are in turn used to support scientifically meritorious cancer research efforts.

NCCN ORP studies typically explore new avenues of clinical investigation and seek answers to important cancer-related questions. All studies are approved and funded through a scientific peer-review process and are overseen by the ORP.

This feature highlights an NCCN study funded through the grant mechanism.

doi: 10.6004/jnccn.2019.0056

For more information on specific trials, including patient selection criteria, use the contact information listed with each study.

For more information on the NCCN ORP, including a complete detailing of the clinical studies currently underway at NCCN Member Institutions, go to www.NCCN.org/clinical_trials/clinicians.asp.

Phase II Trial of Trifluridine/Tipiracil in Combination With Irinotecan in Biliary Tract Cancers

Principal Investigator: Amit Mahipal, MBBS, MPH

Condition: Biliary Tract Cancer

Institution: Mayo Clinic Cancer Center

This is a single-arm, phase II trial to assess the efficacy of trifluridine/tipiracil in combination with irinotecan in advanced, refractory biliary tract cancers using a 2-stage design. In the first stage, 15 patients will be enrolled. If ≥ 2 patients are progression-free and alive at 16 weeks, an additional 10 patients will be enrolled. If ≤ 5 of 25 evaluable patients remain progression-free at 16 weeks, then the regimen will be considered ineffective. The total sample size of this study is 28 to account for 3 possible nonevaluable subjects. Patients will receive trifluridine/tipiracil at a dose of 25 mg/m² on days 1 through 5 and irinotecan, 180 mg/m² on day 1 of each 14-day cycle. Patients will receive treatment until disease progression or development of unacceptable toxicities. Patients will undergo restaging scans every 4 cycles, and will be monitored for adverse events from initiation of study drug administration to 28 days after the last dose. Blood samples will be collected for determination of cell-free DNA (cfDNA) and circulating tumor cells (CTCs) at baseline, after 4 cycles, and at disease progression. Tumor biopsy specimens will be collected before treatment initiation to develop patient-derived tumor organoid (PDO).

Primary Objective:

- Determine efficacy of trifluridine/tipiracil + irinotecan in patients with refractory biliary tract cancers based on progression-free survival (PFS) at 16 weeks

Secondary Objectives:

- Assess safety and tolerability of trifluridine/tipiracil + irinotecan in patients with refractory biliary tract cancers through adverse event monitoring
- Explore efficacy of trifluridine/tipiracil + irinotecan in patients with refractory biliary tract cancers based on overall response rates (ORRs), disease control rates (DCRs), and overall survival (OS)

Exploratory Objectives:

Correlative Research

- Determine whether the number of CTCs or level of cfDNA at baseline is prognostic or predictive to the response to therapy
- Determine whether changes in CTCs or cfDNA correlate with efficacy endpoints
- Determine whether drug response from a parallel ex vivo trial using PDO correlates with clinical response to trifluridine/tipiracil + irinotecan
- Evaluate role of thymidine kinase 1 (TK1) in predicting the clinical benefit of trifluridine/tipiracil + irinotecan and discover potential mechanisms of resistance using PDO and pretreatment biopsy specimen

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Exploratory Research

- Evaluate PFS, safety and tolerability, ORR, DCR, and OS in patients who received prior treatment with 5-FU independently from the entire population

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ClinicalTrials.gov Identifier: NCT04072445

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