VIEW ASCO 2020 SCIENTIFIC ABSTRACT

TARGETED TREATMENT OF BILE DUCT CANCER: RESPONSE TO TREATMENT AND SIDE EFFECT MANAGEMENT IN PATIENTS TREATED WITH FUTIBATINIB

Date: May 2020

Clinical study number: NCT02052778

Abstract title: FOENIX-CCA2: A phase 2, open-label, multicenter study of futibatinib in patients with intrahepatic cholangiocarcinoma (iCCA) harboring *FGFR2* gene fusions or other rearrangements

Summary of results from an ongoing clinical trial

These are interim results from a phase 2 trial that has completed patient enrollment.

Results presented in this summary are from a phase 2 clinical trial studying the safety and efficacy of futibatinib in patients with bile duct cancer (iCCA)

This summary contains information from a scientific presentation given at ASCO 2020; the scientific abstract of this study contains preliminary data, which were updated for the presentation. The abstract can be accessed here: https://meetinglibrary.asco.org/record/186878/abstract

Futibatinib is currently being investigated in a phase 3 clinical study in patients with iCCA who have already received chemotherapy with gemcitabine/cisplatin; futibatinib is not yet approved for use outside of clinical studies

Researchers and physicians should review the results of several studies and reports to gain an understanding of the mechanism, safety, and efficacy of medications

Medical terms

Before reading further, please review the following medical information and terms used in this summary:

Clinical trials (or clinical studies): Investigations to explore new and potential treatments in consenting patients with a specific disease or condition to learn if the treatment is both effective and safe for use in the general population.

Fibroblast growth factor receptor 2 (*FGFR2*): Fibroblast growth factor receptors are on the surface of cells and, when triggered, send signals to start important processes such as cell growth.

Hyperphosphatemia: An electrolyte disorder in which there is an elevated level of phosphate in the blood. Most people have no symptoms, but some develop calcium deposits in the soft tissue. There may also be low calcium levels, which can result in muscle spasms.

Intrahepatic cholangiocarcinoma (iCCA): A rare cancer that develops in the bile ducts inside the liver.

Locally advanced/metastatic cancer: When cancer cells have spread outside the tissue where they first start to grow, either to nearby tissue (locally advanced) or to more distant areas in the body (metastatic cancer).

Mutation: A permanent change in the DNA of an individual; in cancer, mutations can cause the normal signals that regulate cell growth to either turn off or be overactive.

Response rate: The percentage of patients in the study whose tumor has decreased in size; patients whose tumors cannot be detected anymore have had a complete response, and those whose tumors have shrunk in size by 30% or more have had a partial response.

Tolerability: Relates to whether a patient has side effects from taking a medication and how severe the effects may be. It is not uncommon for patients to have side effects from a medication, and they can often be regulated by lowering the medication dose (**dose reduction**) or taking a brief break from the medication (**dose interruption**).

Bile duct cancer (iCCA) and futibatinib

- Patients with iCCA often have mutations in the *FGFR* gene that cause FGFR to send more growth signals than normal
- Futibatinib is an oral medication being investigated as a possible treatment for iCCA; it interacts with FGFR to stop/lessen the overactive signals that occur when the *FGFR* gene is mutated and the receptor is overactive

Futibatinib clinical trial design

Patients

- With advanced/metastatic iCCA
- Who were previously treated with chemotherapy
- With a fusion or rearrangement of the *FGFR2* gene
- Who completed a consent form

Treatment[1]

- 20 mg of futibatinib once a day
- Cycles were 21 days, repeated continuously with no breaks in treatment

Goals of study

- Response rate*
- How long a response lasts
- Tolerability/safety

*The proportion of patients who responded to the treatment.

Enrollment is closed to new patients, but this study is ongoing, and current patients are continuing to take futibatinib until one of the following occurs:

- their disease progresses,
- they cannot tolerate the drug, or
- they choose to withdraw from the study

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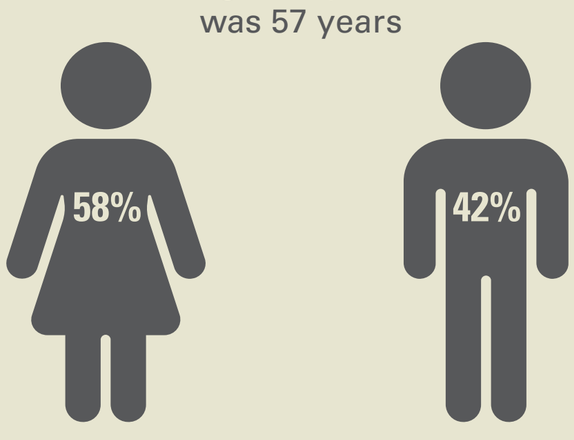
Participating patients

103
patients enrolled

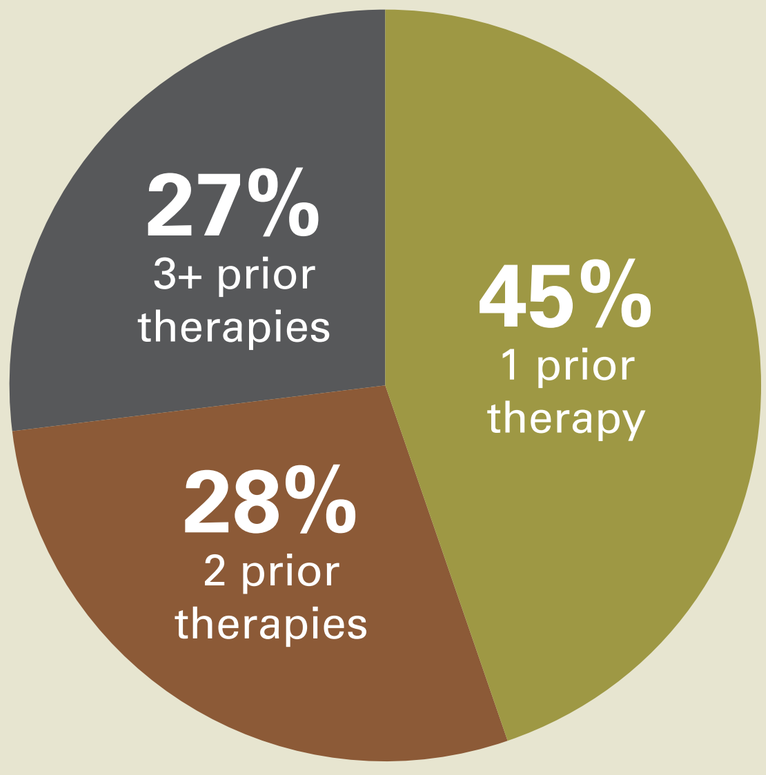
This early report includes information for **67 patients** who had data collected for at least *6 months* from their first dose of futibatinib

Age midpoint was 57 years



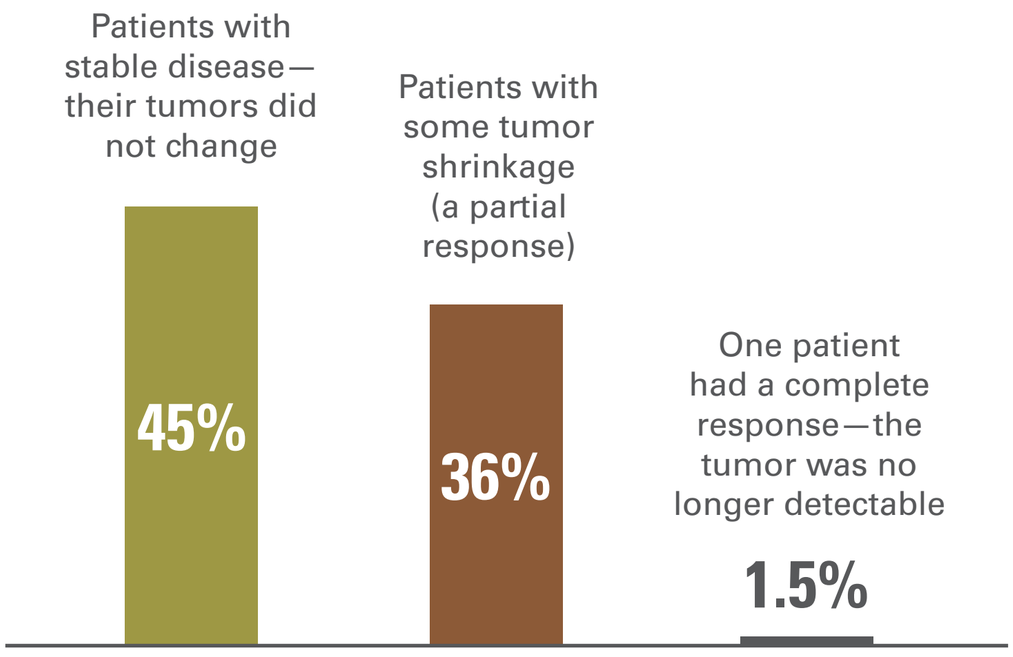
Note: Data for the remaining 36 patients are expected to be available in 2021.

All 67 patients had previously received chemotherapy



Response to futibatinib

The overall response rate across 67 patients was 37.3%.



Of patients who responded to treatment, half…

…responded within **2.5 months** of the first dose

…had a response lasting at least **8.3 months**

Safety of futibatinib

- Some patients experienced mild side effects, presenting symptoms that have been observed with other drugs that block FGFR activity[2]
- Overall, hyperphosphatemia, diarrhea, and dry mouth were the most common side effects reported
  - One of the growth factors that binds FGFR (fibroblast growth factor 23) helps regulate absorption of phosphate by the body[3]
  - Because of the role FGFR plays in regulating phosphate, patients who take an FGFR inhibitor may experience increased phosphate levels in their blood
- Information on how hyperphosphatemia can be managed by adjusting futibatinib doses and other medications is forthcoming

Percentage of patients with side effects related to treatment

Side effects	Low grade	High grade
Hyperphosphatemia	54%	27%
Diarrhea	37%	0%
Dry mouth	33%	0%

Note: The top 3 side effects related to treatment are shown. *Low grade* or *high grade* refers to how severe a treatment side effect is: low = grade 1 or 2, high = grade 3.

Side effects related to treatment were managed by adjusting futibatinib dosing

51%
of patients had a dose reduced

55%
of patients had a dose delayed

1.5%
of patients (1 patient) completely stopped treatment

Key takeaways

- Early data from this study suggest that
  - iCCA tumors with *FGFR2* fusions and other rearrangements respond to treatment with futibatinib, and
  - using futibatinib is safe for patients whose iCCA has progressed after previously receiving chemotherapy

Clinical study sponsor

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Further information
https://meetinglibrary.asco.org/record/186878/abstract
FOENIX-CCA2: https://clinicaltrials.gov/ct2/show/NCT02052778

1. NIH US National Library of Medicine. A study of TAS-120 in patients with advanced solid tumors. https://clinicaltrials.gov/ct2/show/NCT02052778
2. Chae YK, et al. *Oncotarget*. 2017;8:16052-16074. 3. Erben RG. *Front Endocrinol*. 2018;9:267.