Prolonged clinical benefit with futibatinib in a patient with *FGFR2* fusion-positive intrahepatic cholangiocarcinoma previously treated with an ATP-competitive FGFR inhibitor: case report

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Background

Several FGFR inhibitors (FGFRi) have demonstrated activity in FGFR2 fusion-positive advanced unresectable cholangiocarcinoma.

Futibatinib, an oral irreversible pan-FGFRi, demonstrated the ability to overcome some of the resistance mechanisms limiting ATP-competitive FGFRi's (1).

Here, we present a case of prolonged disease stabilisation with futibatinib following progression on an ATP-competitive FGFRi.

Case presentation

A 50-year-old female was diagnosed in 2015 with an intrahepatic cholangiocarcinoma (iCCA), underwent liver resection (pT3N0).

She relapsed with pulmonary metastases in 2019, and then received chemotherapy: 1st line 6 months(m) gemcitabine/cisplatin followed by 2nd line FOLFOX (6m) upon progression. An end of treatment CT showed disease progression.

Next-generation sequencing on resection tissue identified an *FGFR2-PAWR* fusion which allowed the patient to enter a clinical trial with an ATP-competitive FGFRi in July 2020. During 16 months of treatment serial CTs showed stable disease despite a steady rise in CA 19-9. Side effects were grade(G) 1 xerostomia, G1 hyperphosphataemia and G1 transaminitis.

The patient had multifocal disease progression in December 2021, and accessed futibatinib through an open access program.

She remains on treatment after 15 months, CT evaluations demonstrate minor response to treatment and overall stable disease. CA19-9 decreased after the first treatment cycle from 805U/ml to 370U/ml with a nadir of 219U/ml. Patient remains clinically well, with maintained quality of life and ECOG performance status 0. Treatment-related adverse events are G1-2 hypercalcaemia and G1 hyperphosphataemia.

Results

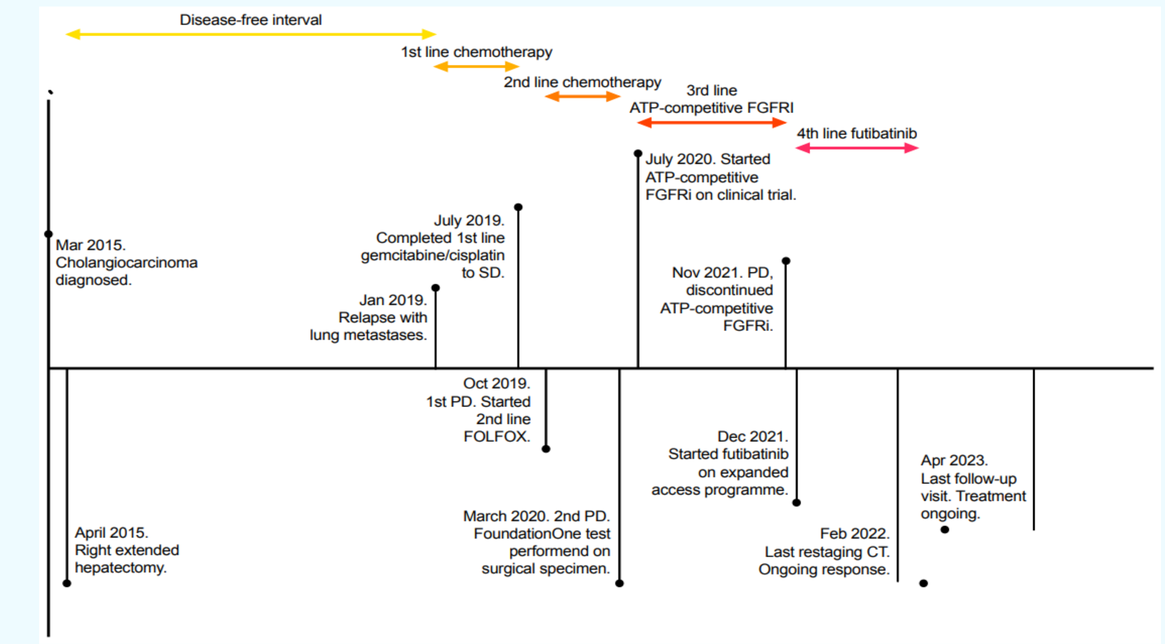

Figure 1. Timeline of events. SD, stable disease, PD, progression of disease, CT, computed tomography .

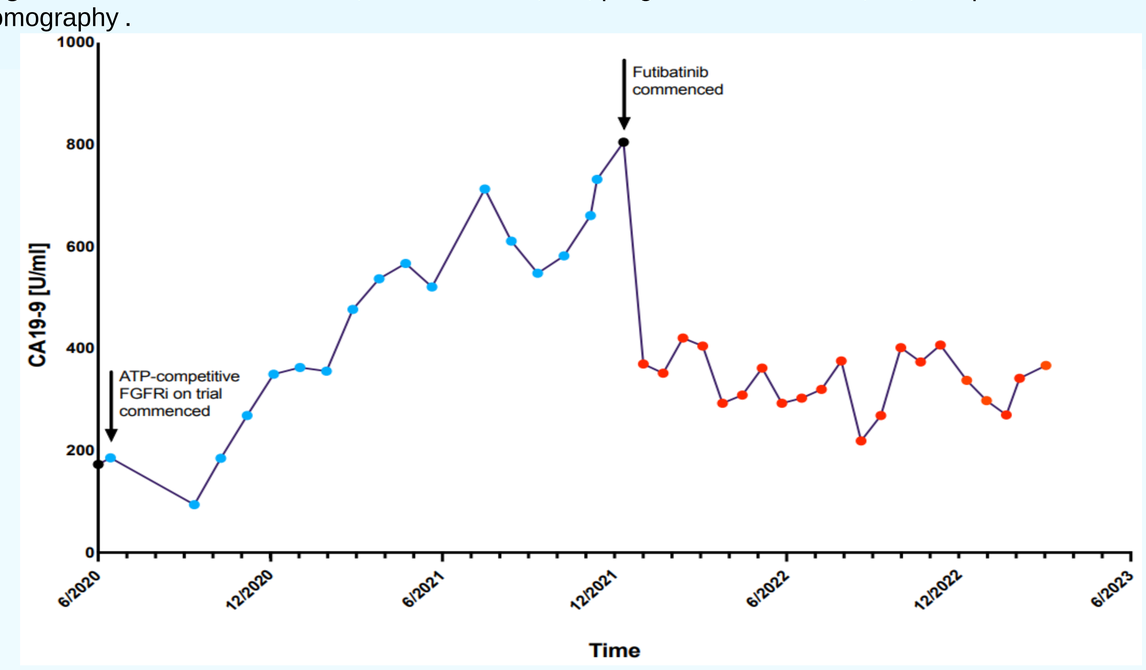

Figure 2. Graph representing CA19-9 levels during treatment with ATP-competitive FGFRi and futibatinib.

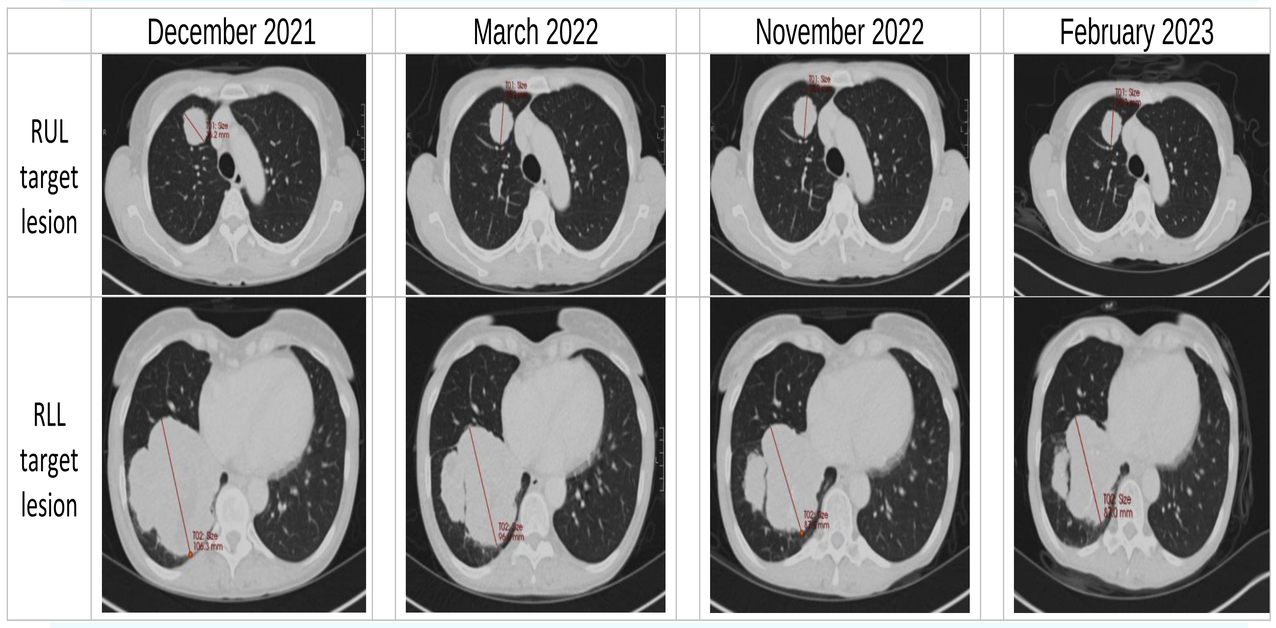

Figure 3. Serial CT imaging of the chest. Images in the top line refer to the right upper lobe (RUL) target lesion and the bottom line shows the right lower lobe (RLL) target lesion. The time points are baseline prior to starting futibatinib, at the first response evaluation time point (3 months after commencing futibatinib), 11 months and the most recent response evaluation scan at 14 months.

Discussion

This case illustrates that patients with FGFR2 fusion-positive iCCA can derive long lasting clinical benefit from FGFRi and irreversible FGFRi's like futibatinib can be highly effective even after progression on a previous ATP-competitive FGFRi.

The duration of associated disease control and treatment tolerability far exceed those offered by third-line chemotherapy and are potentially transformative for this patient subgroup.

References

1. Goyal L, et al. TAS-120 overcomes resistance to atp-competitive FGFR inhibitors in patients with FGFR2 fusion–positive intrahepatic cholangiocarcinoma. Cancer Discov. 2019 1;9:1064–79.

Acknowledgements

Conflicts of Interest

No conflicts of interest to declare.

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