This case illustrates that p.C382R is an oncogenic target and should be treated with pemigatinib. Treatment with pemigatinib results in a complete functional remission in FDG-PET/CT.

The following report describes a patient with an intrahepatic cholangiocarcinoma (iCC) and detected FGFR 2

In vivo data suggest that FGFR2 point mutations might also be oncogenic. FGFR2 mutations may cause uncontrolled activation of the FGFR2 signaling pathway independent from ligand binding.

In a patient with a coincidental PTEN loss of function, the p.C382R mutation of the FGFR2 receptor in iCC is sensitive to targeted therapy with pemigatinib and leads to a complete functional remission.

The point mutation p.C382R in the transmembrane domain of FGFR2 is oncogenic and leads to a complete functional remission after treatment with pemigatinib in cholangiocarcinoma

A new promising oncogenic target (p.C382R) for treatment with pemigatinib in patients with cholangiocarcinoma

ABSTRACT

The following report describes a patient with an intrahepatic cholangiocarcinoma (iCC) and detected FGFR 2

FGFR2 mutations may cause uncontrolled activation of the FGFR2 signaling pathway independent from ligand binding.

Pemigatinib is approved for FGFR2 fusion and rearrangements.

In vivo data suggest that FGFR2 point mutations might also be oncogenic.

INTRODUCTION

PRIOR TO PEMIGATINIB

9- month Disease-free survival

3-months after initiation of pemigatinib

5- month follow-up

biopsy of liver lesion

biopsy of blood sample

CONCLUSION

The point mutation p.C382R in the transmembrane domain of FGFR2 is oncogenic and leads to a complete functional remission.

The report supports the importance of the transforming activity and drug sensitivity in vitro assay as described by Nakamura and others in a clinical application.

Multigene sequencing should be performed in every patient with advanced iCC since not only FGFR fusions/rearrangements but other gene alterations may have oncogenic potency and respond to targeted treatment.

REFERENCES


Acknowledgement

louisa.hempel@med.sfu.ac.at

Disclosure: The authors declare no competing interests.

Ethical standards: All procedures performed in studies involving human participants or on human tissue were in accordance with the ethical standards of the institutional and/or national research committee and with the 1975 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from the participant included in the study.

Key findings:

- p.C382R mutation of the FGFR2 receptor in iCC is sensitive to targeted therapy with pemigatinib and leads to a complete functional remission in a patient with a coincidental PTEN loss of function.

- Multigene sequencing should be performed in every patient with advanced iCC since not only FGFR fusions/rearrangements but also other gene alterations may have oncogenic potency and respond to targeted treatment.

- The 76-year-old male was diagnosed with iCCA and liquid samples were taken for a hybrid capture based NGS service platform (FoundationOne CDx, Porsche, Germany) was performed for the tissue biopsies and FoundationOne Liquid CDx for the blood samples.

- After the fifth treatment cycle, progressive disease (PD) was observed.

- Biopsies of the liver lesions as well as a liquid biopsy were taken and a hybrid capture-based NGS service platform (FoundationOne CDx, Porsche, Germany) was performed for the tissue biopsies and FoundationOne Liquid CDx for the blood samples.