Characterization of Two Novel Oncogenic FGFR2 Fusions Sensitive to the FGFR Selective Inhibitor Debio 1347 in Cholangiocarcinoma
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Abstract #689

Identification of FGFR2-VCL and FGFR2-CCDC147, two novel FGFR2 fusions in cholangiocarcinoma patients

The two novel FGFR2 fusions with different fusion partners were identified in two lung samples from cholangiocarcinoma patients.

Results

Debio 1347 significantly inhibited tumor growth, whereas an insignificant effect was observed on body weight.

Conclusions

We report for the first time the discovery of two novel FGFR2 fusions in intrahepatic cholangiocarcinoma patient samples. The two novel FGFR2-VCL and FGFR2-CCDC147 both contain an intact FGFR2 tyrosine kinase domain found in a gate partner encoding at least one oligosaccharide domain, suggesting a mechanism of ligand-independent constitutive kinase activation.

Both fusions display oncogenic activities which were introduced into Rat 2 cells in vitro culture. Cell proliferation assays and were tumorigenic in vivo when implanted subcutaneously in NOD/SCID nude mice.

The selective FGFR inhibitor Debio 1347 significantly reduced cell proliferation in vitro and tumor growth in vivo.

Altogether, these results suggest that cholangiocarcinoma patients harboring these novel fusions could benefit from targeted FGFR inhibitors such as Debio 1347.

Related Presentations

- FGFR2-VCL and FGFR2-CCDC147 fusion expressing tumors are sensitive to FGFR selective inhibitor Debio 1347 in vivo

Acknowledgements

We thank Nicolas Sibilia and Yohann Nabatou of ChemoPharma for their helpful discussions.

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