PEMIGATINIB BENEFIT IN A HIGH BURDEN CHOLANGIOCARCINOMA WITH A RARE FGFR2 SINGLE-NUCLEOTIDE VARIANT

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IPO COIMBRA

AMMF THE CHOLANGIOCARCINOMA CHARITY

INTRODUCTION

FIGHT-202 trial showed **40% disease control (DCR) for patients with FGFR2 mutant cholangiocarcinoma treated with pemigatinib** (1). FGFR2 Y375C is a likely pathogenic rare single-nucleotide variant (SNV), that, to our knowledge, has not been included in any clinical trials of FGFR2 inhibitors. We hereby present a case of an intrahepatic cholangiocarcinoma (iCCA) harbouring a **somatic FGFR2 Y375C variant treated with pemigatinib**.

- Female
- 37 years-old
- ECOG PS 0

- **No previous medical history**
- **No daily medications**
- **Smoker: 18 pack-year**

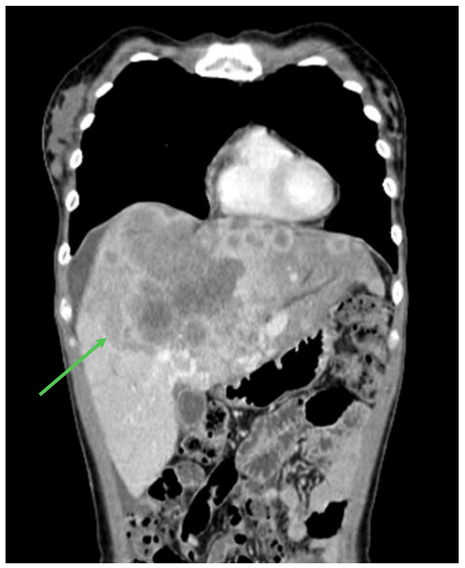

Image 1: CT-scan showing an enormous 18,5 cm in diameter iCCA (green arrow), at diagnosis.

DIAGNOSIS

- **iCCA** (liver biopsy)
- **cT4N1M1 - Stage IV** (AJCC 8th edition)
- **FoundationOne®CDx**
  - **FGFR2 Y375C (SNV)**
  - **Microsatellite stable**
- Multidisciplinary team meeting: Systemic oncological treatment

1st LINE: gemcitabine/cisplatin/Durvalumab

Gemcitabine 1250 mg/m^2 D1 + D8
Cisplatin 25 mg/m^2 D1 + D8
iv, each 21 days
+ Durvalumab 150 mg iv, each 4 weeks

Alopecia grade 1◊
Nausea grade 1◊
Hypomagnesemia grade 1◊
Vasculitis Grade 3◊, after 6 cycles, treated with prednisolone 1mg/Kg (response after 3 days)

2nd LINE: pemigatinib

Molecular tumour board discussion:

- Likely pathogenic variant of FGRF2
- Pemigatinib *off lable*, 13,5 mg id, *per os*, 2 weeks on/ 1 week off

Alopecia grade 1◊
Abdominal pain grade 1◊
Constipation grade 2◊
Recurrent hyperphosphatemia grade 2◊ leading to a first level **dose reduction according to RCM to 9 mg id**

DURING TREATMENT

ECOG PS 0
On treatment during 10 months with clinical benefit;

Under best supportive care for two months;
Died April 2024
Overall survival of 20 motnhs

Set 2022 | Mar 2023 | Apr 2023 | Jun 2023 | Sept 2023 | Feb 2024 | Apr 2024

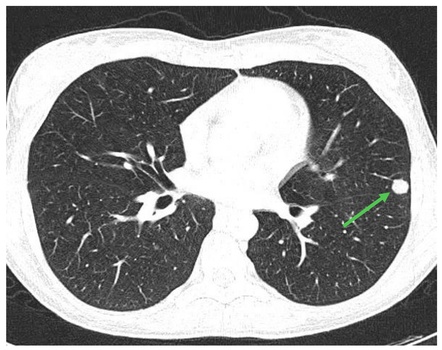

Image 2: CT-scan showing pulmonary metastasis (green arrow).

DISEASE PROGRESSION*

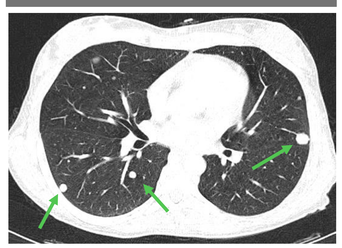

Image 3: CT-scan showing multiple lung metastasis (green arrows)

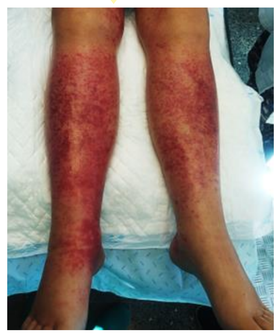

Image 4: biopsy confirmed lower limb vasculitis secondary to durvalumab.

Symptomatic pleural effusion treated with pleurodesis.

Cholangitis treated with iv antibiotics and stenting with ERCP (endoscopic cholangiopancreatography)

DISEASE PROGRESSION*

ECOG PS 1
Increased bilirrubine grade 3◊
Unfit for oncological treatment
Stopped Pemigatinib
Referred for best supportive care only

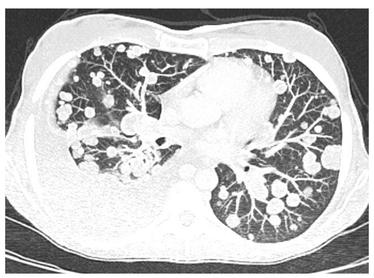

*Image 5: CT-scan showing, at progression, a typical sign of **cannonball metastasis** in the lung.*

DISCUSSION

The basket trial FIGHT-207 showed that, **in different tumors with FGFR1-3 actionable SNVs, it was possible to achieve up to 56.3% DCR and 3.7 months of median progression free survival (PFS)** (2). Our real-world case shows **even greater efficacy in extending PFS**, but also the **high tolerability and clinical benefit** of second line targeted FGFR2 treatment in high burden iCCAs with a rare actionable mutation, rather than gene fusions or rearrangements. On the other hand, it raises the question of whether the sudden radiological and clinical progression of the disease could be related to the mechanisms of resistance to FGFR2 inhibitors.

References: 1 Abou-Alfa GK, Sahai V, Hollebecque A, et al. Pemigatinib for previously treated, locally advanced or metastatic cholangiocarcinoma: a multicentre, open-label, phase 2 study. Lancet Oncol. 2020 May;21(5):671-684. doi: 10.1016/S1470-2045(20)30109-1.

2 - Rodón J, et al. AACR Annual Meeting 2023; April 14-19, 2023; Orlando, FL. Abstract CT016.

Note: The patient signed an informed consent for the presentation of the case and all images displayed.

*** All image response evaluated with RECIST criteria version 1.1.**
◊ All toxicity graded according to CTCAE v.5