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VIRTUAL CONFERENCE

Animal Models of Liquid Biopsy in Hepatocellular Carcinoma Reveal Clone-dependent Release of Circulating Tumor DNA

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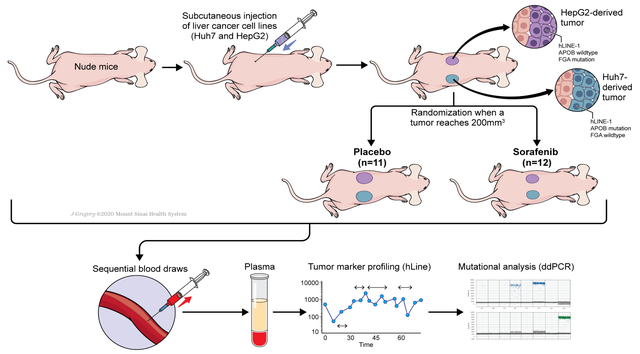
INTRODUCTION

- Liquid biopsy has emerged as a promising tool in cancer management.
- However, studies exploring liquid biopsy in basic research are scarce., particulary in hepatocellular carcinoma (HCC)
- How circulating tumor DNA (ctDNA) is released into blood remains unclear.

AIMS

- **To use ctDNA as a surrogate of tumor progression.**
- **To trace cancer clonal composition.**

DESIGN

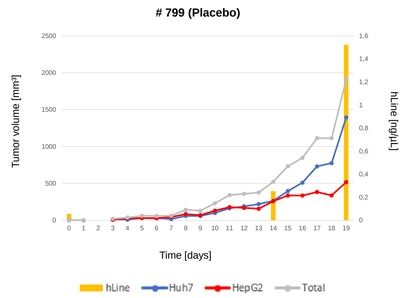


METHOD

- Female athymic nude mice were subcutanesouly xenografted with HCC cell lines (Huh7 and HepG2), in each flank.
- When tumors reached 200 mm³, mice were randomized to either receive placebo (n=11) or sorafenib (n=12).
- Blood samples were sequentially collected in each animal. DNA was extracted from plasma and submitted to real-time PCR (qPCR) and digital droplet PCR (ddPCR).
- The human long interspersed nuclear element-1 (hLINE-1), a human specific DNA product, was quantified by qPCR in 7 mice.
- DdPCR was performed to detect selected mutations specific to each of the cell lines injected (*APOB* for Huh7 and *FGA* for HepG2) in 22 mice.

RESULTS

Tumor marker profiling (hLINE-1)

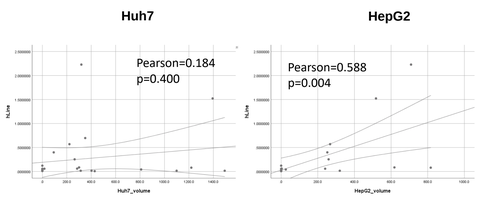


- 7 mice
- 23 plasma samples

⇒ ctDNA correlated with tumor progression

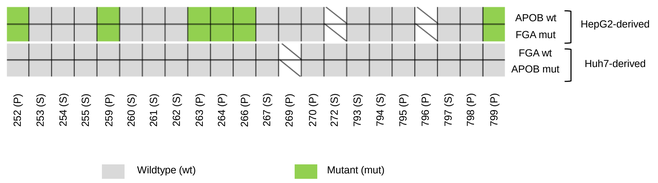
⇒ ctDNA recapitulates clinical events
- Response to therapy
- Tumor ulcers

Only in mice with HepG2 tumors



hLINE-1 showed a stronger correlation with tumor progression and events related to HepG2, compared to Huh7.

Mutational analysis (ddPCR)



Detection of mutations in plasma:

- Derived from HepG2 (FGA mutations) => **6/20**
- Derived from Huh7 (APOB mutations) => **0/21**

p=0.031

Higher detection rate of mutations deriving from HepG2, compared to Huh7

CONCLUSIONS

- **Modelizing liquid biopsy in xenografts is feasible and insightful.**
- **The yield of DNA released from tumors varied between different cancer cell clones.**
- **These results stress the need to nuance our interpretation of ctDNA analyses.**

CONTACT INFORMATION

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