VIRTUAL 2020 ESMO congress

Personalized circulating tumor DNA assay for the detection of minimal residual disease in patients with oligometastatic CRC undergoing resection of metastases

Fotios Loupakis, MD, PhD

Medical Oncology Unit 1

Istituto Oncologico Veneto – IRCCS

Padova - ITALY

AFFILIATIONS and DISCLOSURE INFORMATION

Complete Author Affiliations:

Fotios Loupakis[1], Madiha Derouazi[2], Sabina Murgioni[1], Mario Domenico Rizzato[3], Shruti Sharma[4], Derrick Renner[4], Svetlana Shchegrova[4], Himanshu Sethi[4], Bernhard Zimmermann[4], Alexey Aleshin[4], Marta Schirripa[1], Giada Munari[5], Angelo Paolo Dei Tos[5], Sara Lonardi[1], Matteo Fassan[5]

[1]Medical Oncology Unit 1 Veneto Institute of Oncology IOV - IRCCS; [2]Boehringer Ingelheim, Geneva, Switzerland; [3] Medical Oncology 1, Veneto Institute of Oncology IOV-IRCCS, Padua, Italy, Department of Surgery, Oncology and Gastroenterology, University of Padua, Padua, Italy[4]Natera Inc., San Carlos, US; [5]Unit of Surgical Pathology, Department of Medicine (DIMED), University of Padua, Italy, University of Padua, Italy

Disclosures:

- Dr Loupakis: Consulting or Advisory Role Company: Amgen; Astellas; Roche, Bayer, Amal
- Dr Fassan: Consulting or Advisory Role Company Astellas, Diaceutics, Tesaro Research Funding: Astellas and QED Therapeutics
- Dr Lonardi: Consulting or Advisory Role Company: Amgen; Merck Serono; Lilly; Speakers' Bureau: Roche; Lilly; Bristol-Myers Squibb; Servier; Merck Serono; Research Funding: Amgen; Merck Serono
- DR, SS, HS, BZ and AA are full time employees of Natera Inc. with stock/options to own stock in the company. AA is an advisor with Mission Bio and Notable Labs

BACKGROUND/RATIONALE

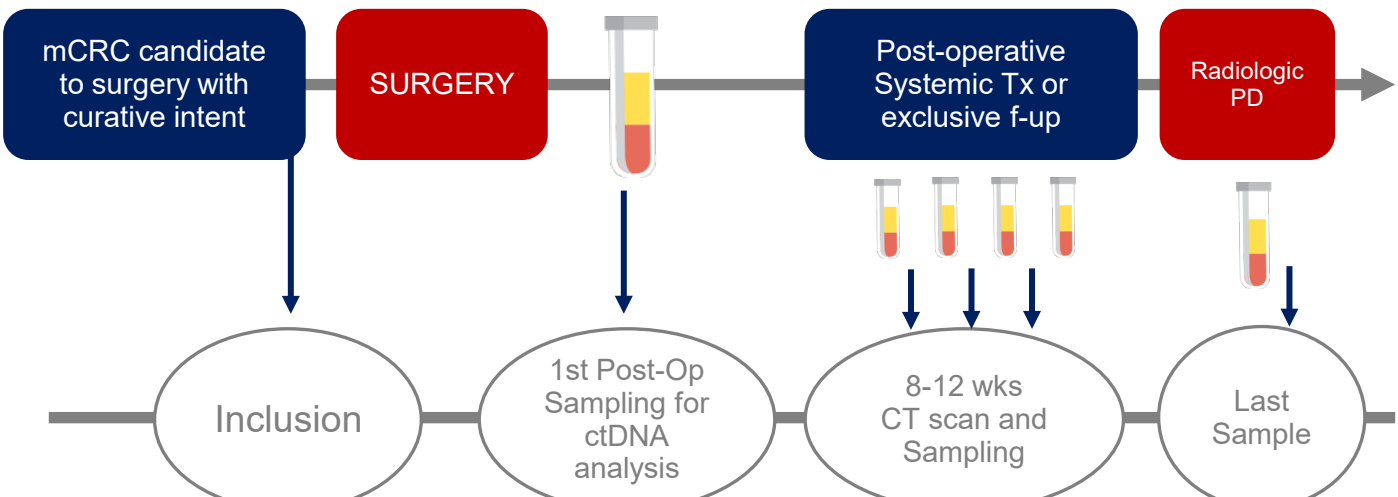
- Surgical resection of mets for CRC pts is feasible and indicated in approximately 30% of cases and is potentially curative in less than 25% of them.

- Preliminary evidence suggest that detection of ctDNA after resection of metastes has strong prognostic impact

- However, currently available tests are mainly limited by relatively low sensitivity and limited clinical data

- Signatera™ ctDNA (bespoke, mPCR NGS) assay was recently demonstrated to be a powerful tumor-informed tool for ctDNA detection

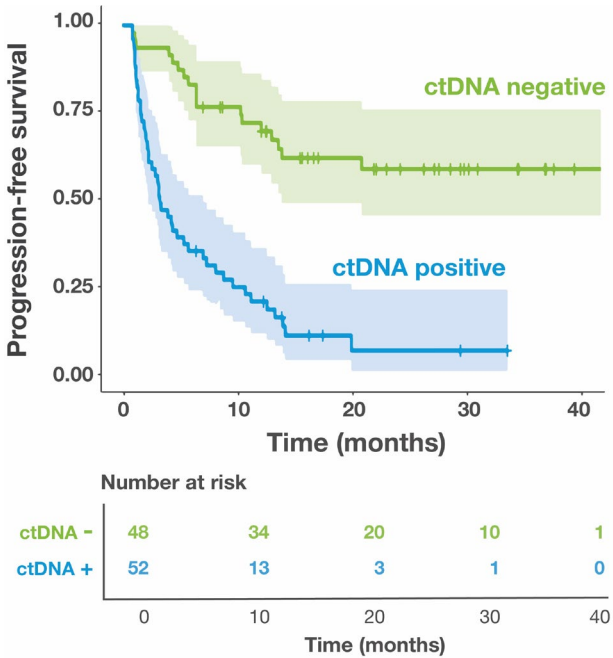
STUDY DESIGN



RESULTS - 1 (descriptive)

- A total of 113 patients were enrolled;
- Of which 100 (88.5%) were eligible for ctDNA analyses on post-op samples;
- Median age at diagnosis of met disease = 60 years, synchronous metastases presentation = 51%, Site of metastasis: Liver= 58%, Lung= 21%, Peritoneum=14%, Others= 7%.
- The patients were followed-up for a median of 8.7 (0.9-42.2) months at the time of the present analysis

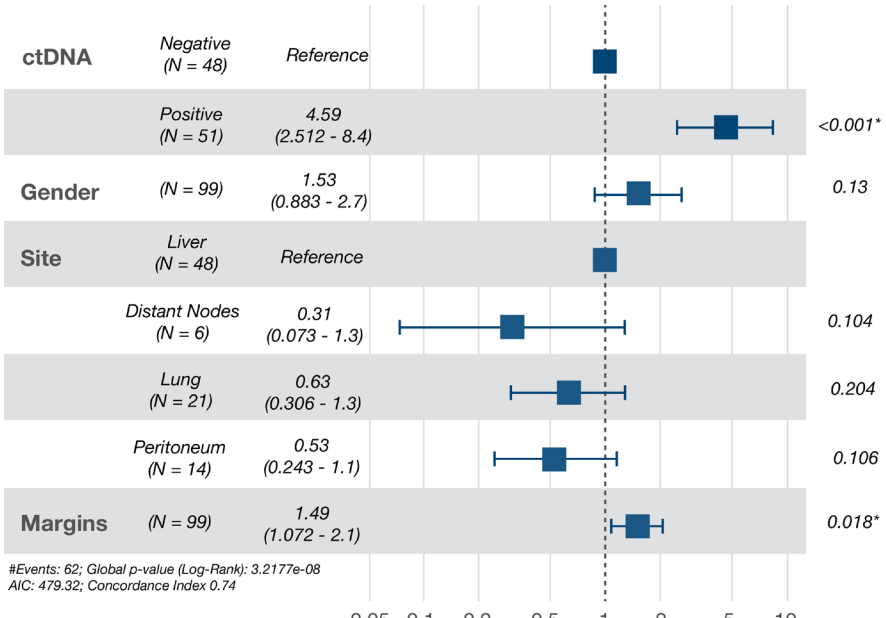
RESULTS - 2 (Primary endpoint: PFS acording to post-op ctDNA status)



HR:4.6; 95% CI: 2.6-8.1;

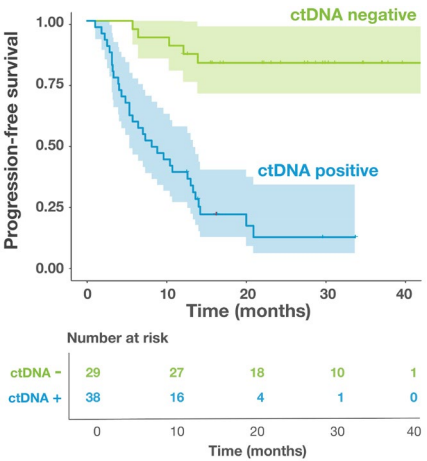
P<0.001

RESULTS - 3 (PFS, multivariate analysis)



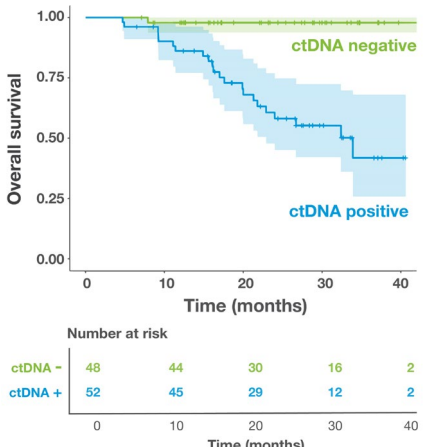
RESULTS - 4 (exploratory)

Progression-Free Survival (Serial)



HR: 10; 95% CI, 3.8-26; P<0.001***

Overall Survival (Serial)



HR: 22; 95% CI: 3.0-166.0; P=0.002

Conclusions

- Signatera, a personalized and tumor-informed ctDNA assay can detect residual disease in patients with oligometastatic CRC treated with curative intent.
- Primary EP was met. ctDNA positive status at the post-surgical timepoint was associated with worse PFS.
- The multivariate analysis showed ctDNA to be most significant marker associated with PFS (HR: 4.6, 95% CI: 2.5-8.4; $p<0.001$).
- Furthermore, MRD negativity was associated with exceptional outcomes with an OS of 98% with 40 months of follow-up.
- Taken together, these results suggest the possible future clinical utility to guide prognostic evaluation, follow-up planning and adjuvant treatment study design and decision making in this setting.