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PARIS 2022 ESMO congress

ctDNA ANALYSIS AS A PROGNOSTIC FACTOR FOR EARLY-STAGE AND OLIGOMETASTATIC PATIENTS TREATED WITH RADIOTHERAPY

IMOMA INSTITUTO DE MEDICINA ONCOLÓGICA Y MOLECULAR DE ASTURIAS

Guadalupe A. Cifuentes[1]*, Adrián Santiago[1], Lucía Méndez Blanco[2], María Fueyo[2], Esther López Martínez[2], Raquel Soria[2], Irene Martín López[1], Noelia S. Durán[1], Rebeca Álvarez[1], Claudia G. Lago[1], Andrea Otero[3], Marta Diñeiro[1], Raquel Capín[1], Juan Cadiñanos[1] y Rubén Cabanillas[3,4].

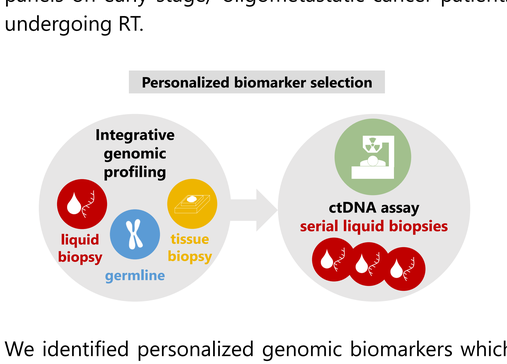
[1]Laboratory of Molecular Medicine, Instituto de Medicina Oncológica y Molecular de Asturias (IMOMA), Oviedo, Asturias, Spain; [2]Radiation Oncology, Instituto de Medicina Oncológica y Molecular de Asturias (IMOMA), Oviedo, Asturias, Spain; [3]Precision Medicine department, Instituto de Medicina Oncológica y Molecular de Asturias (IMOMA), Oviedo, Asturias, Spain; [4]Cabanillas Precision Consulting (CPC), Zurich, Switzerland; *presenting author guadalupe.alvarez@imoma.es

BACKGROUND

High precision radiotherapy (RT) techniques, such as stereotactic body radiotherapy (SBRT), are increasingly used in the management of non-resectable early-stage lung cancer and also in oligometastatic disease, usually with curative intent. However, there is a need for personalized prognosis biomarkers to stratify patients, adapt treatments and assess treatment performance. Although, nowadays, more than 50% of cancer patients require RT, genomics has not yet been integrated into the clinical practice of Radiation Oncology.

PATIENTS AND METHODS

Patient cohort



We performed germline, tissue- and liquid-biopsy NGS panels on early-stage/ oligometastatic cancer patients undergoing RT.

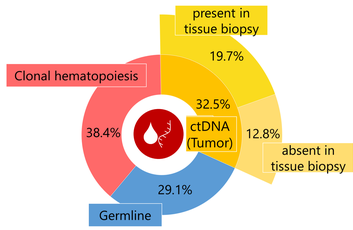
Personalized biomarker selection

We identified personalized genomic biomarkers which were then monitored in circulating tumor DNA (ctDNA) from serial liquid biopsies collected during RT and follow-up. ctDNA signal was compared to patient clinical response, assessed according to RECIST criteria.

RESULTS

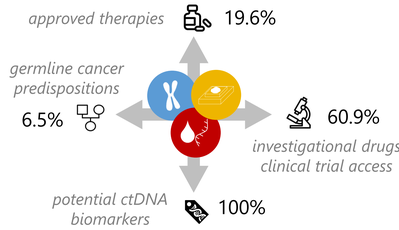
- The integration of the different genomic tests enabled to determine the real origin of the variants identified, essential for successful biomarker selection. Considering all the patients, ~1/3 of the DNA variants identified by the **liquid biopsy panel** were **real tumor variants** (32.5%).

Real origin of liquid biopsy variants



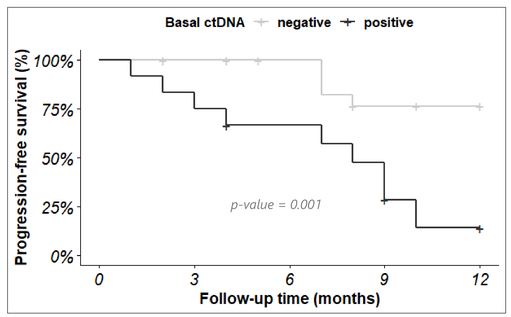
- The integrative approach revealed DNA variants associated to different categories of **clinical actionability** in most patients.

Clinical utility of integrative genomic profiling



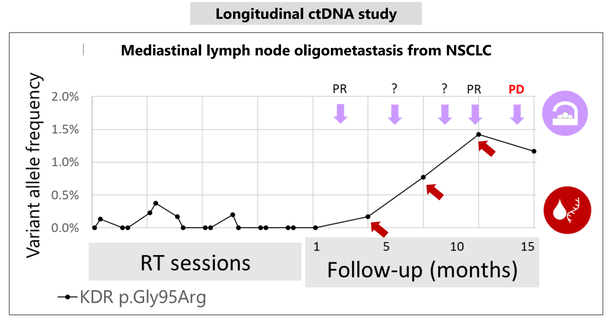
- The **basal ctDNA** signal (pre-treatment) showed significant association with progression-free survival after RT.

ctDNA as a prognostic factor



- Longitudinal ctDNA analysis served as a follow-up biomarker. Considering ctDNA-shedding patients with full clinical follow-up, **ctDNA signal showed concordance with the clinical status** of 81.5% of the patients (N=27). **ctDNA signal anticipated** diagnostic imaging test in **disease progression detection** in 33.3% of the patients who relapsed (N=12).

Longitudinal ctDNA study



PR: partial response on CT scan
PD: progressive disease on CT scan
?: inconclusive imaging

CONCLUSIONS

In patients with early stage or oligometastatic disease treated with RT, integrative genomic profiling showed a wide range of benefits. In this cohort, ctDNA detection during the treatment and the follow-up has the potential to assess prognosis and to identify the patients who may benefit from further therapeutic interventions. Liquid biopsy stands as a useful tool for follow-up after RT when diagnostic imaging test can be ambiguous due to post-RT tissue modifications.

Study supported by
FUNDACIÓN MARÍA CRISTINA MASAVEU PETERSON
Roche