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GUSTAVE ROUSSY
CANCER CAMPUS GRAND PARIS

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LIQUID BIOPSIES FOR MONITORING BRAF^{V600E} MUTATION IN ADVANCED BRAF^{V600E} NON-SMALL CELL LUNG CANCER (NSCLC)

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DISCLOSURES

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- ***No personal financial disclosures***

BACKGROUND

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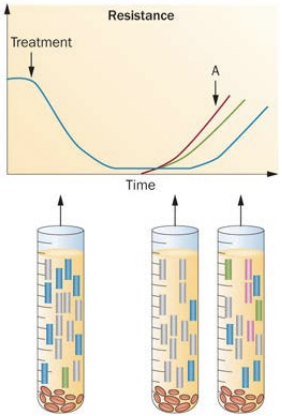
- ***Liquid biopsy (ctDNA)*** is a useful tool for monitoring EGFR mutations in blood (T790M) in NSCLC patients
- BRAF mutation ≈ **2% of advanced NSCLC** patients, mainly at V600E within exon 15 of the kinase domain
- **Dabrafenib + trametinib** have been approved by the FDA and EMA for the treatment of advanced BRAF^{V600+} NSCLC
- **BRAF^{V600+} *ct*DNA monitoring** for assessing the response to targeted therapy has still not been studied
- **Objective**: Clinical relevance of BRAF^{V600E} *ct*DNA for *monitoring* the response to BRAF+/-MEK in advanced BRAF^{V600E+} NSCLC patients
  Exploratory: study of *associated mutations* at radiological progression



Remon Ann Oncol 2017
Crowley Nature Review Clin Oncol 2013
Planchard Lancet 2016

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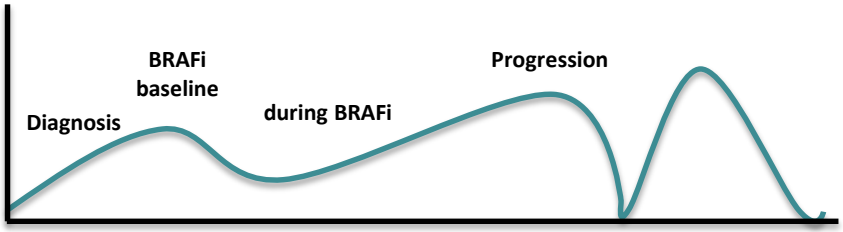
METHODS

- **Prospective cohort** of advanced BRAF^{V600E+} NSCLC patients treated with BRAFi +/- MEKi in Gustave Roussy from Mars 2013
- Blood samples were longitudinally collected from June 2016 until today *(ongoing)*
- At **different timepoints***:



- ***Molecular analysis*** was performed using the **Inivata InVision platform** (enhanced tagged-amplicon next-generation sequencing (eTAM-Seq)

RESULTS

Baseline characteristic	N=15 (%)
Sex, female	9 (60%)
Age, median (years, range)	63 (35-81)
Smoking	
Non smoker	11 (73%)
Smoker	4 (27%)
Histology	
Adenocarcinoma	15 (100%)
Stage at diagnosis	
IIIB	1 (7%)
IV	14 (93%)
Metastasis sites at diagnosis	
Bone	6 (40%)
Pleural	6 (40%)
Lung	4 (27%)
Targeted therapy	
Line of therapy	2 (1-4)
BRAF inhibitor	1 (7%)
BRAF + MEK inhibitor	14 (93%)
Best response rate	
Complete/partial response	9 (61%)
Stable disease	4 (27%)
Progressive disease	1 (7%)

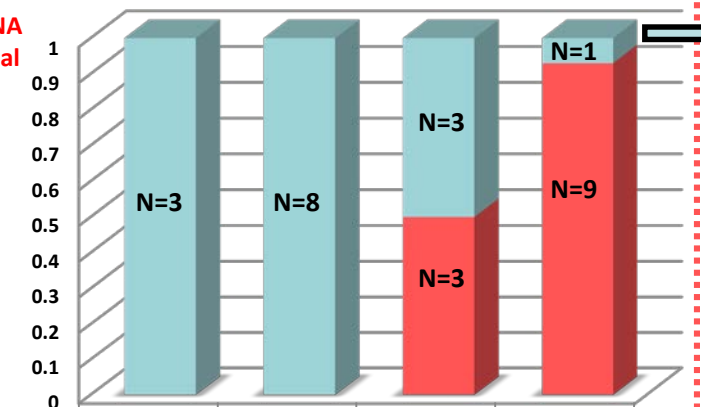
- ✓ The median PFS was **19.5 months** [95% CI 4- not reached (NR)]
- ✓ The median OS was **NR**. Median follow-up 33 months [95% CI 9-49]

N= 35 samples longitudinally collected from 15 patients:
46% positive $BRAF^{V600E}$ *ct*DNA in all the timepoints

n= 7, at baseline
n=28, during therapy

$BRAF^{V600E}$ *ct*DNA and radiological response

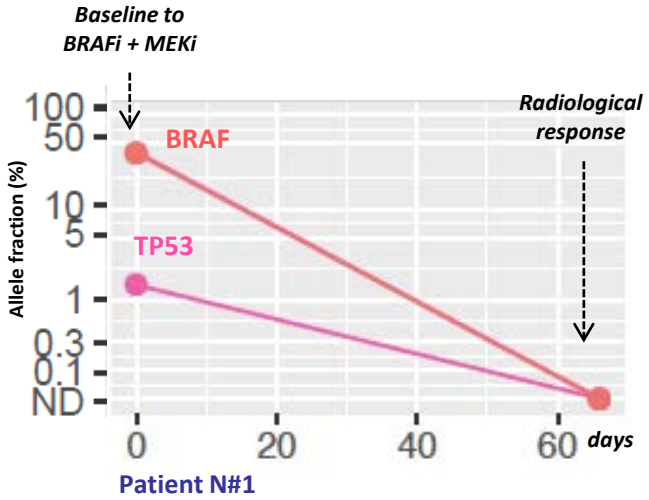
	Positive *BRAF* ctDNA
Baseline to BRAFi *N=7*	**100%**



Nodal oligoPD *after >24months of BRAFi*

Mezquita L et al, WCLC 2017

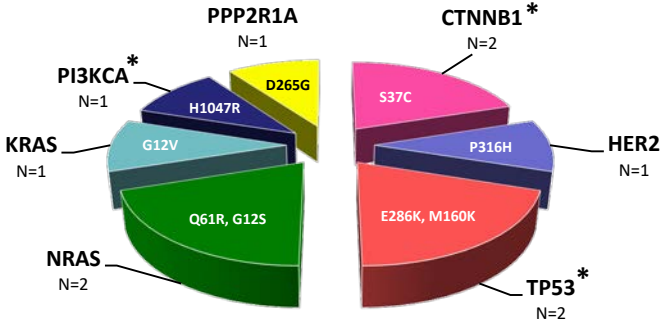
Associated mutations at progression



In **50% of patients** (5/10) were found other mutations on plasma **at progressive disease**

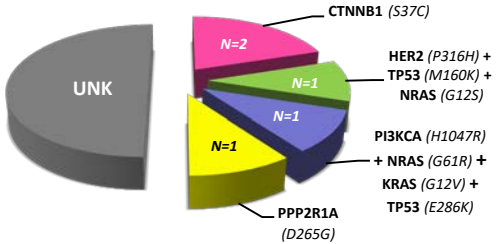
Concurrent mutations detected on plasma at PD

N= 10 mutations



N= 5 Patients

Complex patterns of mutations



TAKE HOME MESSAGES

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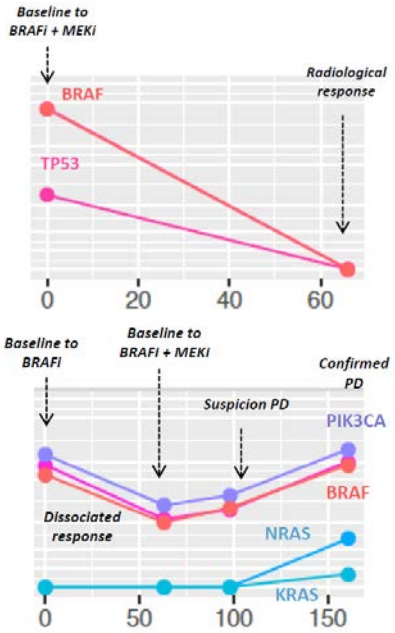
- **Liquid biopsy** *(NGS)* **is feasible and useful in clinical practice**

  - o BRAF^{V600E} *ct*DNA was correlated with the radiological response
  - o For dynamic assessment of the disease
  - o For detection of concurrent or secondary mutation

- This trial **is still ongoing** for validating the liquid biopsy for monitoring the response with a higher number of patients



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