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Somatic Mutation Analysis in Clinical Tumour Samples to Select Patients for Experimental Therapies

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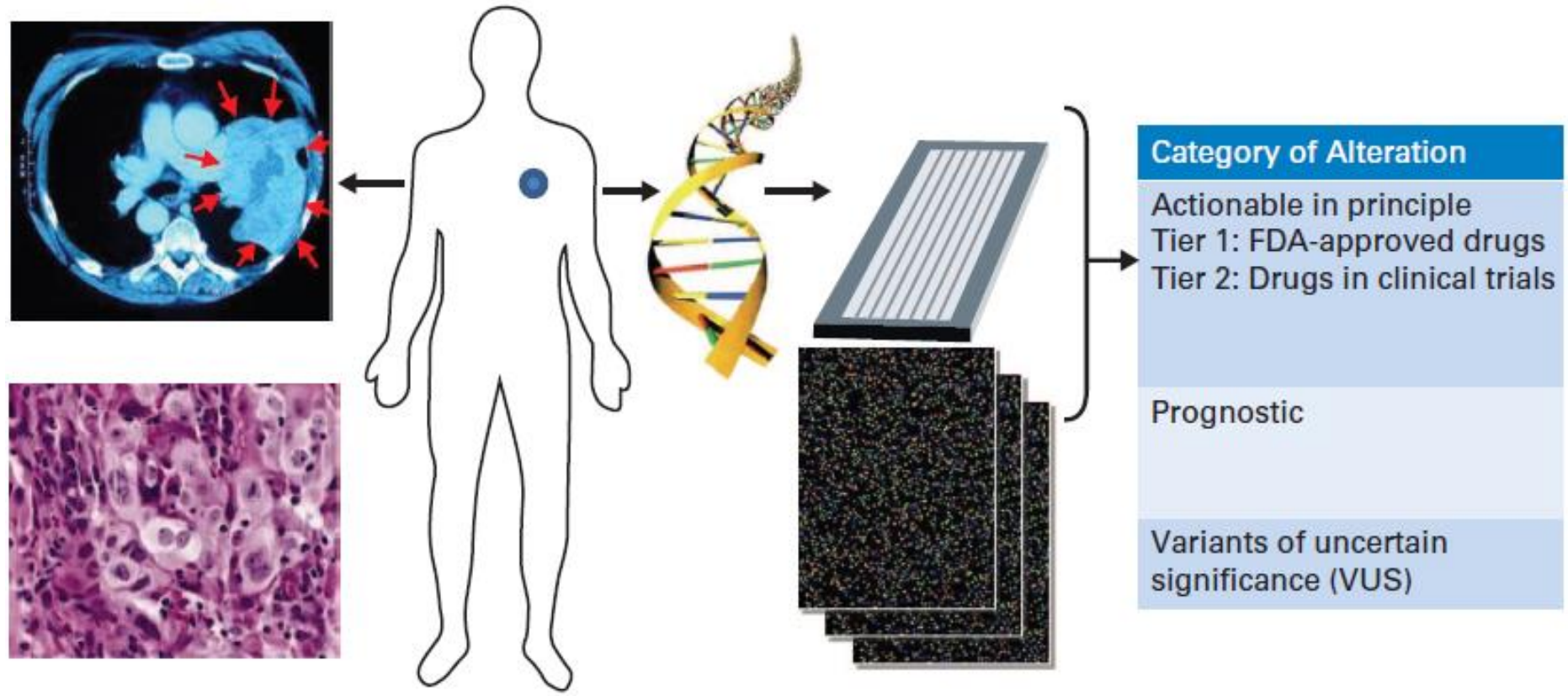
Disclosures

- Nothing to disclose

Introduction

GENOMICS DRIVEN CANCER MEDICINE

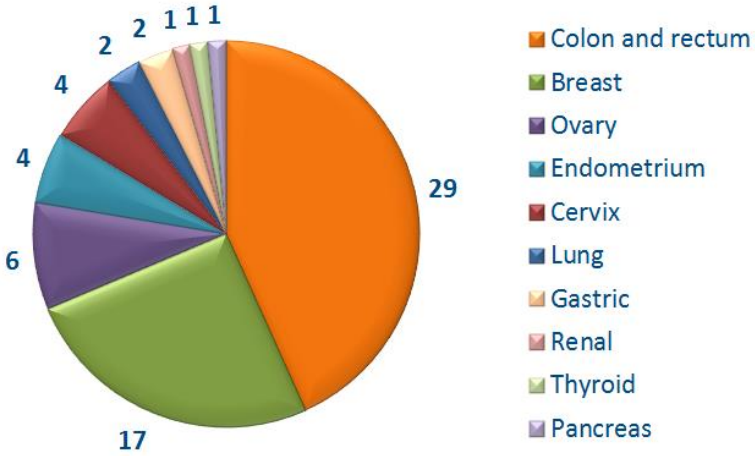


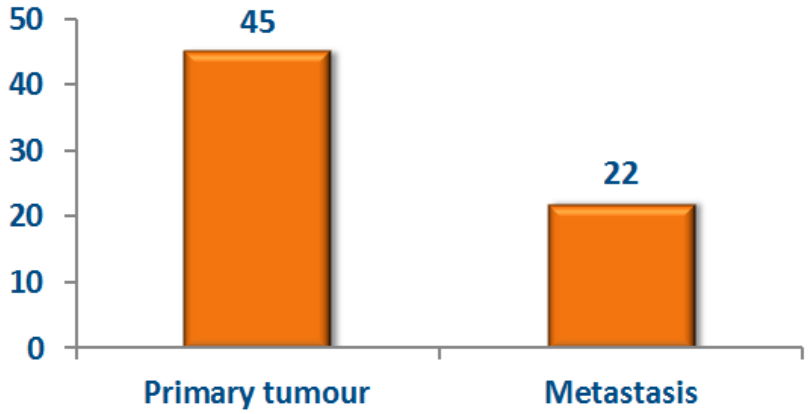
Garraway LA, Verwey J, Ballman K. J Clin Oncol 2013

Subjects and Methods

SUBJECTS

- 67 formalin-fixed paraffin embedded samples from different solid tumours were included in the study
- 45 samples were from primary tumours whereas 22 samples were from metastasis





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Sequenom MassArray technology

OncoCarta ™ PANEL v1.0

238 somatic mutations in 19 common oncogenes
24 multiplexes – 187 assays

CLIA-VALL D'HEBRON CUSTOMIZED PANEL

86 mutations in 14 common oncogenes
9 multiplexes
5 additional genes (GNAS/GNAQ/IDH1/IDH2/MET)
Repeated recurrent mutations and some new ones in 8 genes (AKT1/AKT2/BRAF/EGFR/KRAS/NRAS/PI3KCA/RET)

Gene	No. Mutations	Gene	No. Mutations
ABL1	14	JAK2	1
AKT1	7	KIT	27
AKT2	2	MET	5
BRAF	24	HRAS	6
CDK	2	KRAS	12
EGFR	43	NRAS	8
ERBB2	7	PDGFR	11
FGFR1	2	PIK3CA	13
FGFR3	5	RET	6
FLT3	2		

Different hotspots in these oncogenes are checked such as:

- *BRAF* V600F
- *EGFR* exon 19-20 indels, T790M, L858R
- *KRAS* G12, G13
- *NRAS* G12, G13 and Q61
- …

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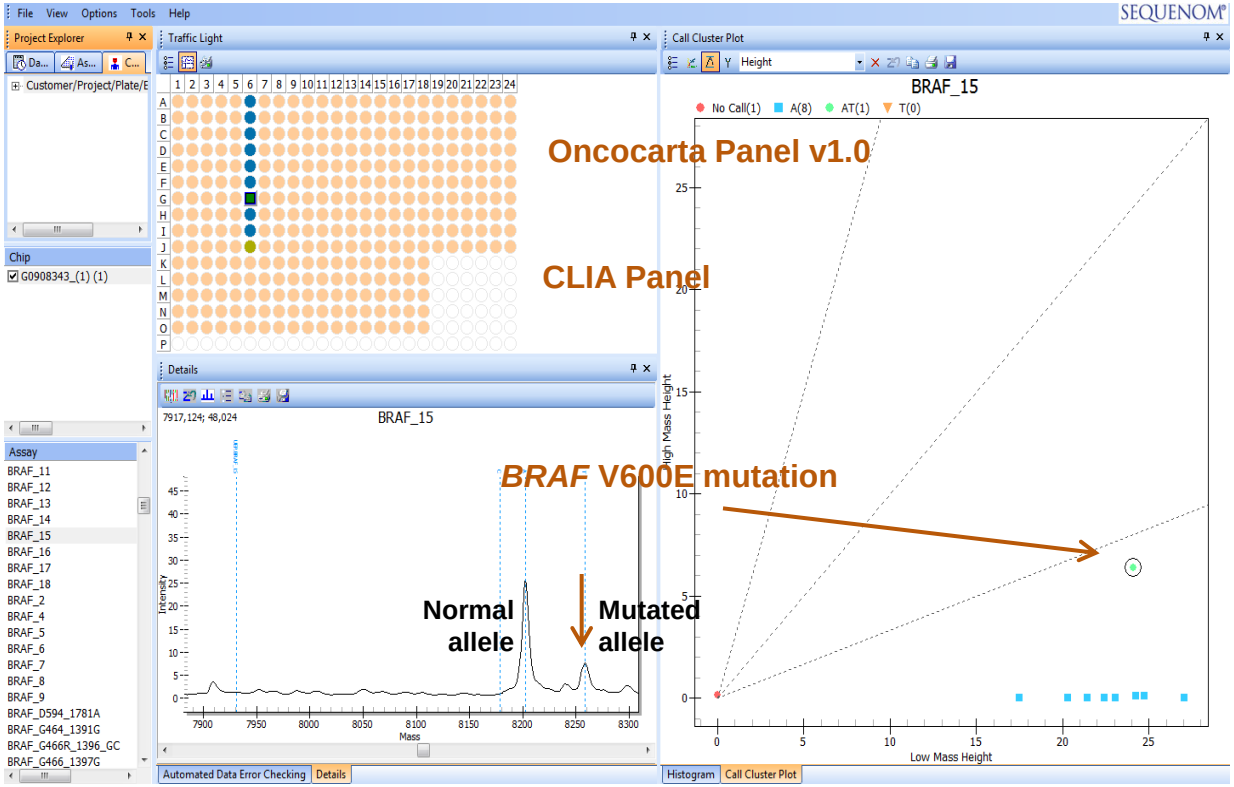
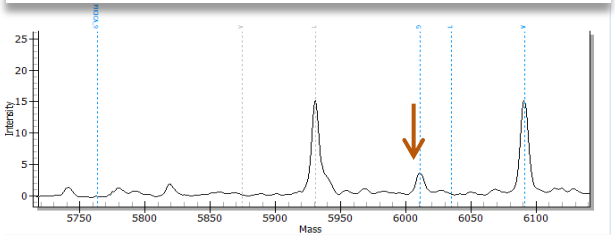


Oncocarta Panel v1.0

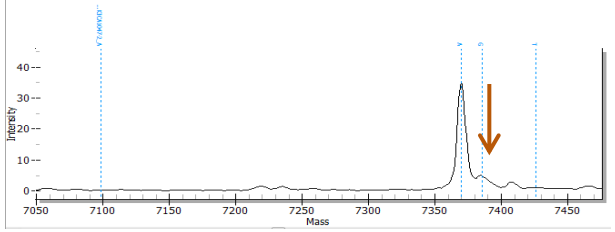
CLIA Panel

BRAF V600E mutation

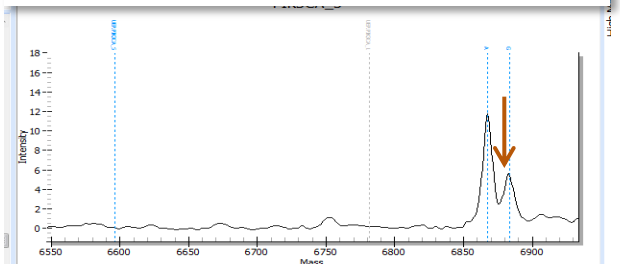
ONCOCARTA *PIK3CA* H1047R 19,5%



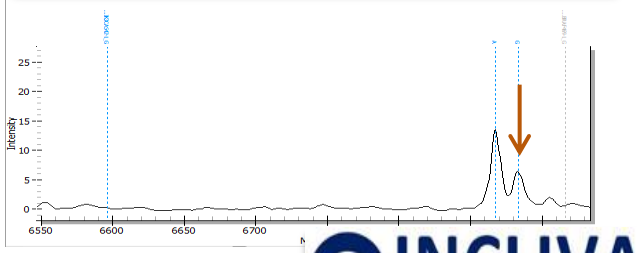
CLIA *PIK3CA* H1047R 12,2%



ONCOCARTA *PIK3CA* E542K 32,0%



CLIA *PIK3CA* E542K 32,7%



Mutations have to be validated on independent chemistries

Frequency of mutation >10%

We used NGS to genotype clinical samples

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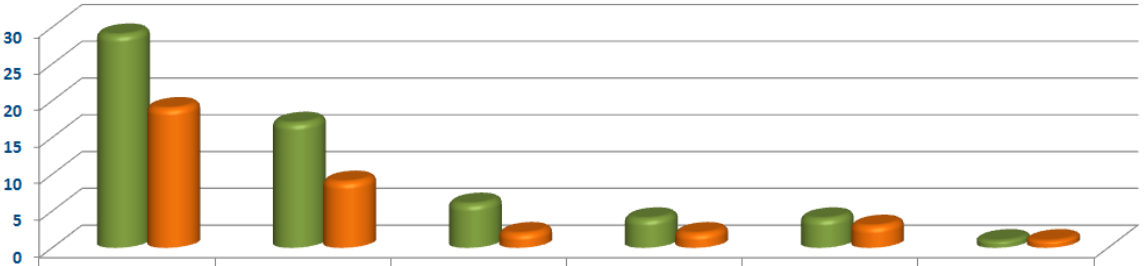
Results

- **36 samples harbour at least one mutation**
- **14 samples with co-ocurrence**

NUMBER OF MUTATIONS FOUND ACROSS DIFFERENT SOLID TUMOURS



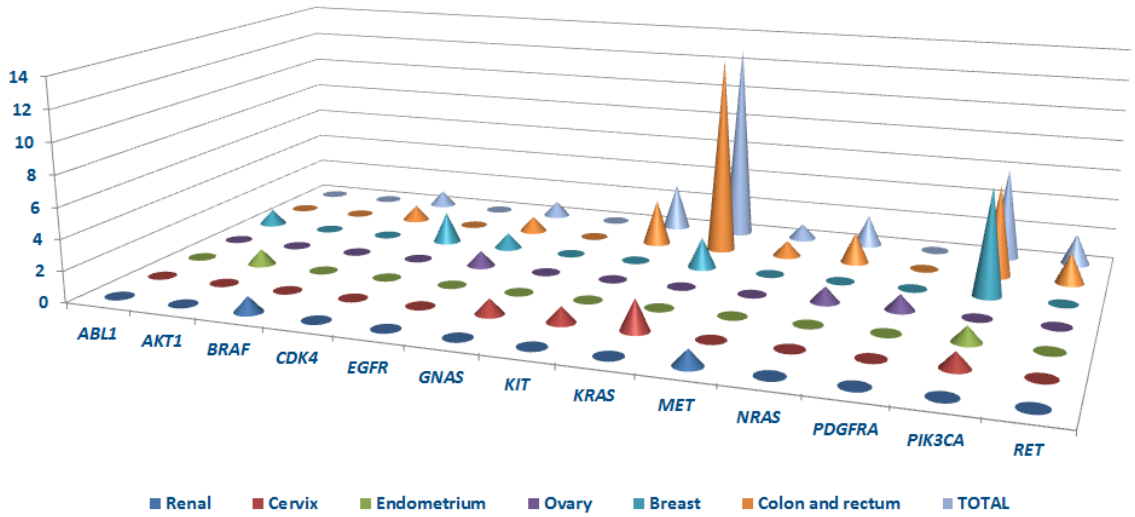
	Colon and rectum	Breast	Ovary	Endometrium	Cervix	Renal
Number of samples studied	29	17	6	4	4	1
Number of samples with mutations	19	9	2	2	3	1

TYPE OF MUTATIONS

Gene	Mutation	Frequency
PIK3CA		15
	C420R	2
	E542K	5
	E545K	1
	H1047R	4
	G1049R	2
	M1043I	1
KRAS		17
	G12D	11
	G12S	1
	Q61R	2
	A146V	2
	G13D	1
KIT		4
	D52N	3
	E839K	1
NRAS		3
	G12S	1
	G13D	1
	Q61R	1
EGFR		3
	P772_H773insV	2
	D770_N771>AGG	1

Gene	Mutation	Frequency
BRAF		2
	L597S	1
	V600E	1
RET		2
	C634W	1
	C634Y	1
CDK4		2
	R24C	1
	R24H	1
MET		2
	R970C	2
GNAS		1
	R201H	1
ABL1		1
	Y253H	1
AKT1		1
	E17DEL	1
PDGFRA		1
	D1071N	1
TOTAL		54

MUTATIONS DISTRIBUTION ACROSS DIFFERENT GENES AND TUMOURS



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Conclusions

- We have characterized the molecular profile of 266 somatic mutations in 24 known cancer genes in a serie of 67 different solid tumours
- 29 different mutations were found
- 53,7% of the samples harbour at least one mutation, mainly localized in the *PIK3CA* and *KRAS* genes
- Results are in accordance with NGS data
- This technology is a rapid method that allows the detection of actionable somatic mutations for selecting patients for personalized therapies

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