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Ilustre Colegio Oficial de Médicos de Madrid. Aula Jiménez Díaz. Madrid

OBSERVATIONAL, MULTICENTER, PROSPECTIVE STUDY TO ASSESS THE IMPACT IN PATIENTS' OUTCOME OF A SYSTEMATIC SCREENING OF ONCOGENIC DRIVERS IN ADVANCED CANCER: THE GETHI XXX-16 STUDY

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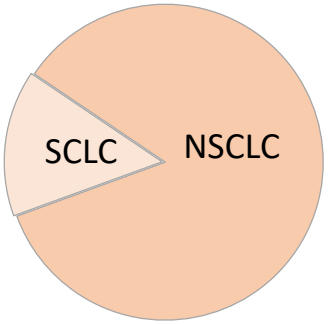
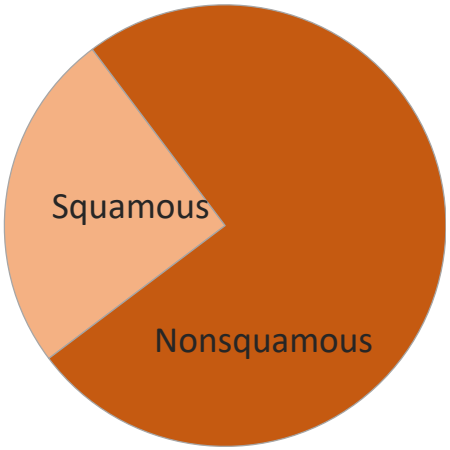
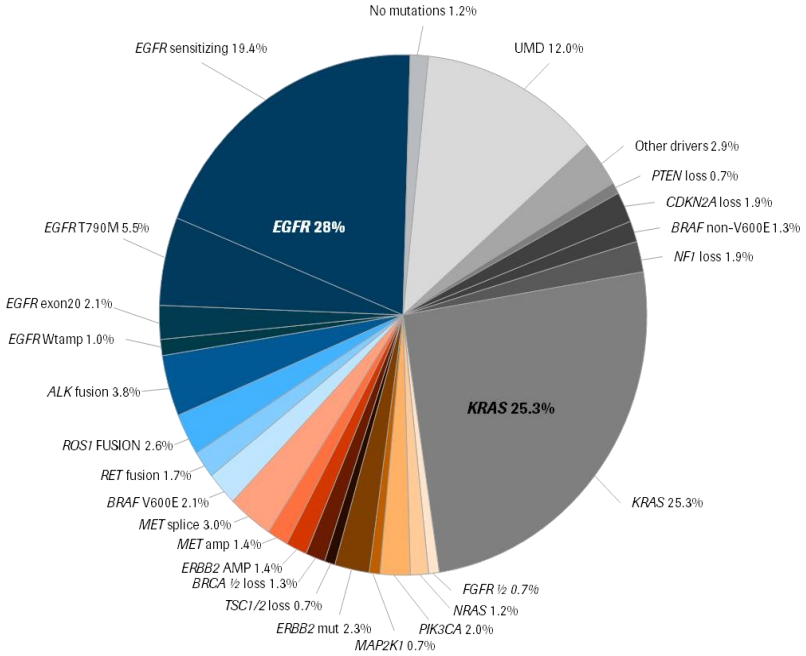
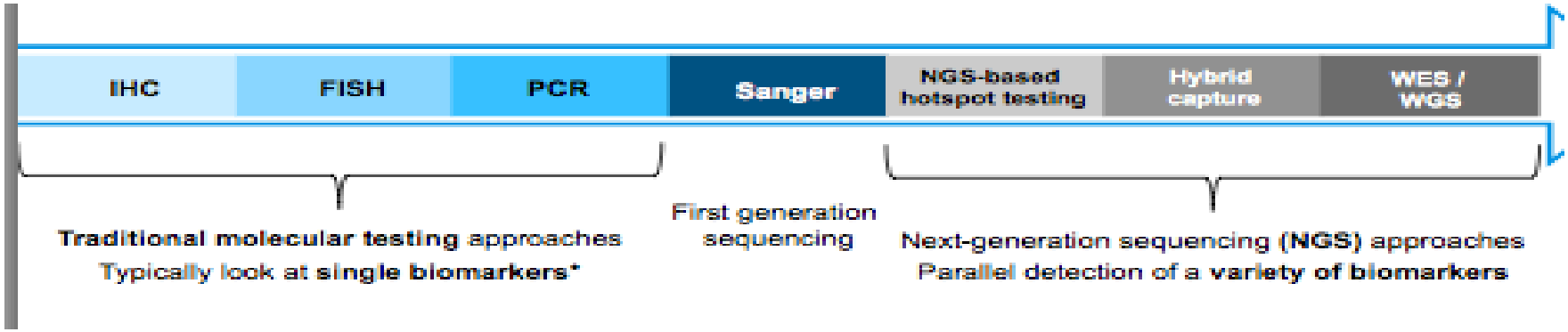






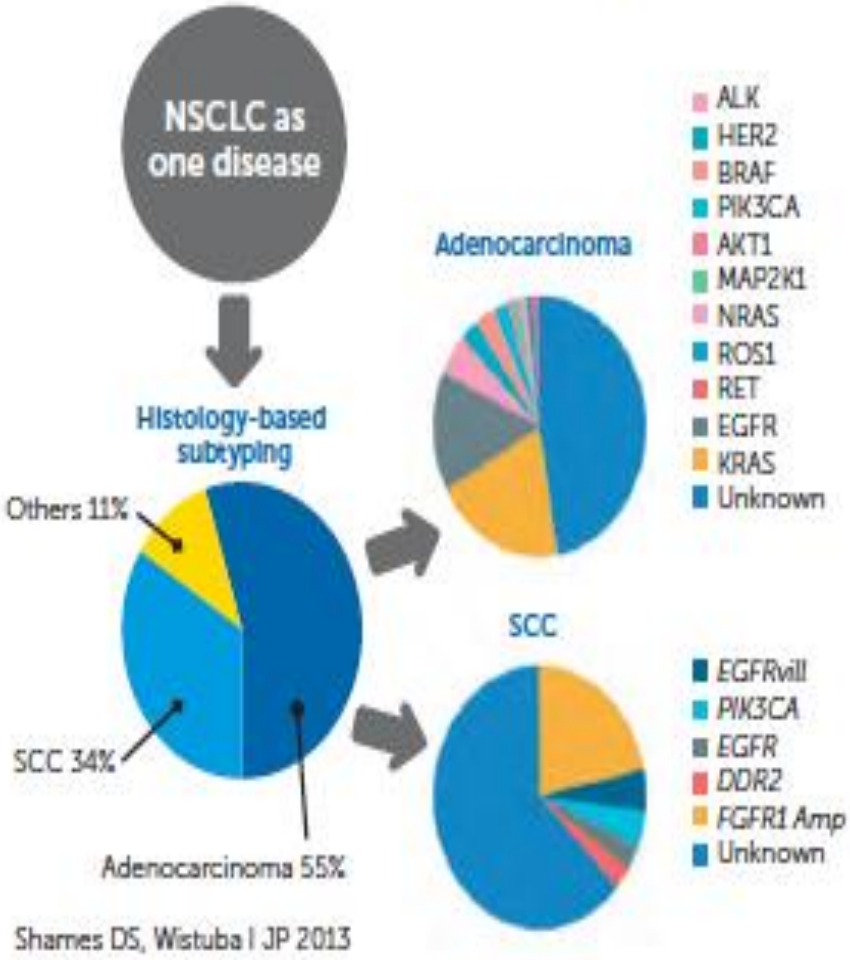


Spectrum of oncogenic drivers associated to 860 patients with lung adenocarcinoma identified by MSK-Impact.

SCLC: small cell lung cancer, NSCLC: non-small cell lung cancer; UMD: no actionable mutation.

1. Bode, A. M., and Dong, Z., (2018) *npj Precision Onc* 2:1; 2. Jordan EJ *et al.* (2017) *Cancer Discov.* 2017; 7: 596-609.

Evolución diagnóstica del CPNM. Subtipos moleculares



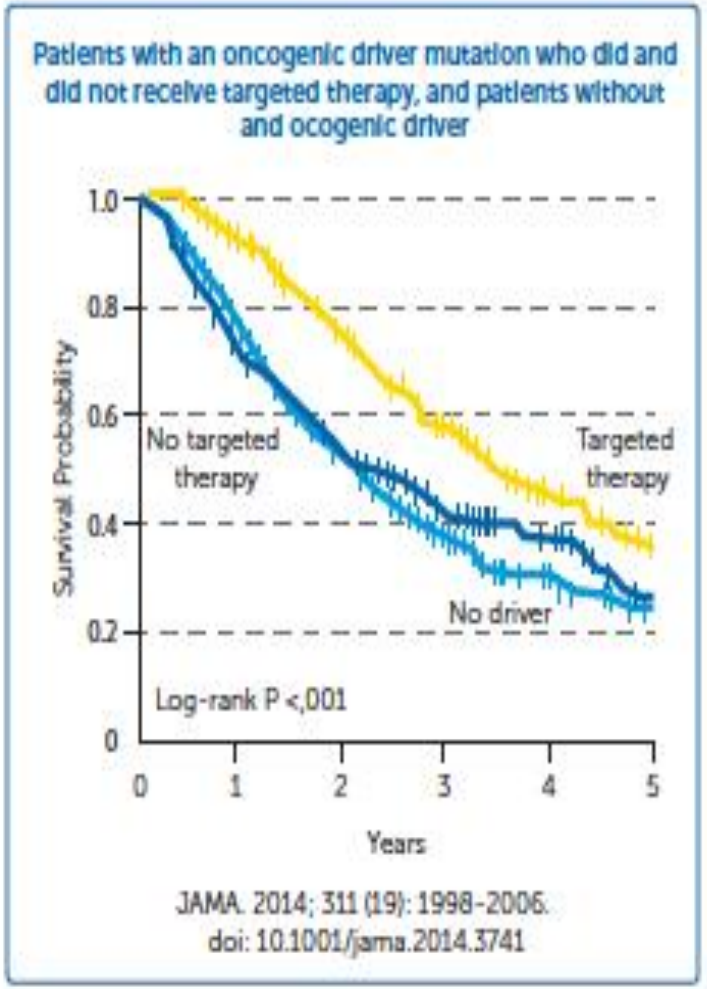


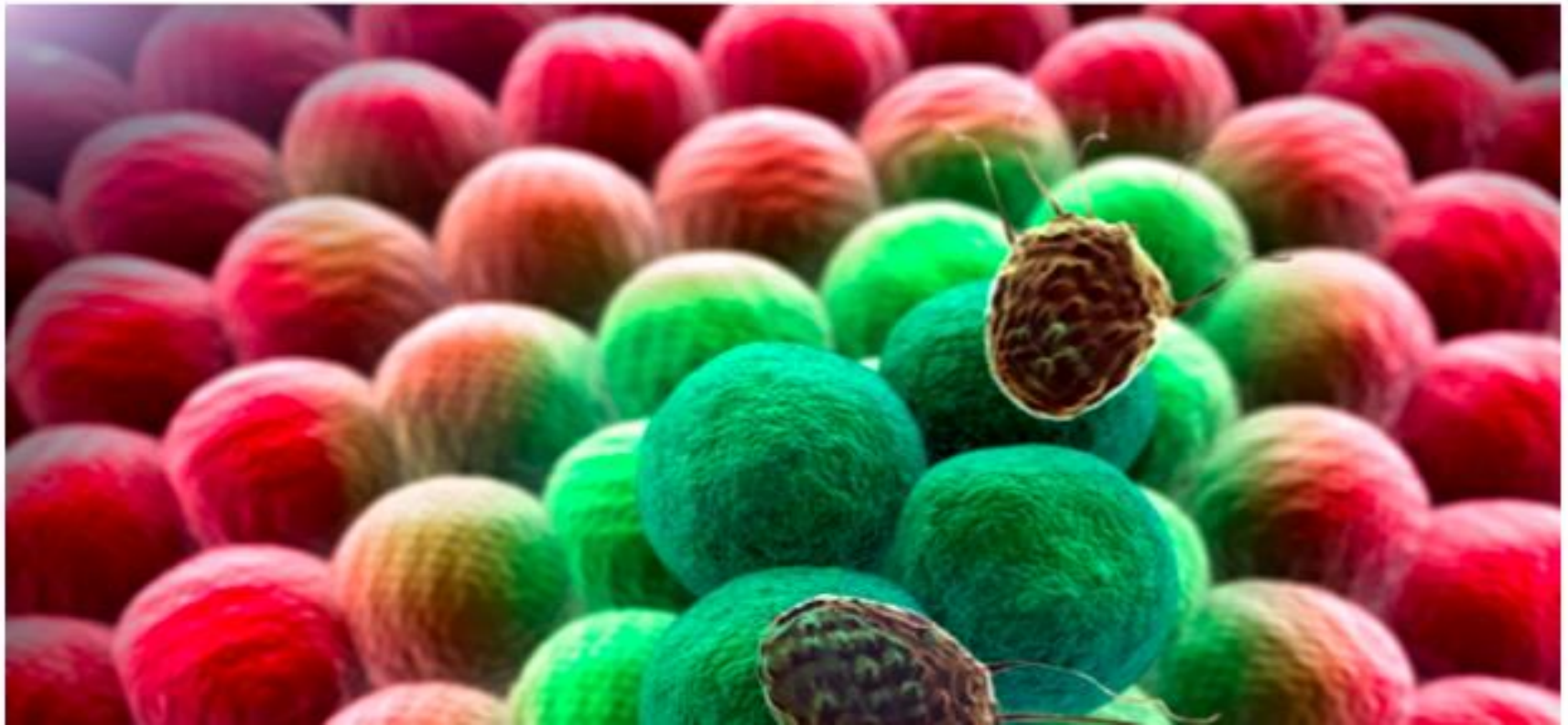
Figura 7. Subtipos histológicos y moleculares. Estudio con anti-EFGR con participación Grupo Español de C. Pulmón.

Tumores en los que la anotación molecular no está tan desarrollada

EE.UU.: La FDA aprueba el primer tratamiento para cualquier cáncer con un rasgo genético específico

El tratamiento es válido con independencia de cuál sea el órgano afectado.

La Food and Drug Administration (o FDA, el organismo que regula los fármacos en Estados Unidos) emitió ayer una nota de prensa en que anunciaba la "aprobación acelerada" del medicamento.



BACKGROUND

- Identification of “agnostic” genetic drivers in cancer is forseen as a major step forward in precision medicine.

- We aimed to analyze the real impact on patients management of the implementation of a systematic screening of genetic alterations in centers of the Spanish Group for Rare Cancer (GETHI)

METHODS

- Observational, prospective and multicenter study to molecularly characterize any adult patient with advanced cáncer.

- Clinical data regarding treatment administered and outcome, were collected from patiens identifies as harboring drugable alterations.

Analysis steps:

1)TrkA-C, ROS1 and ALK proteins IHC

2)RT-PCR validation

3)NGS predesigned pannel (Archer Fusion Plex)

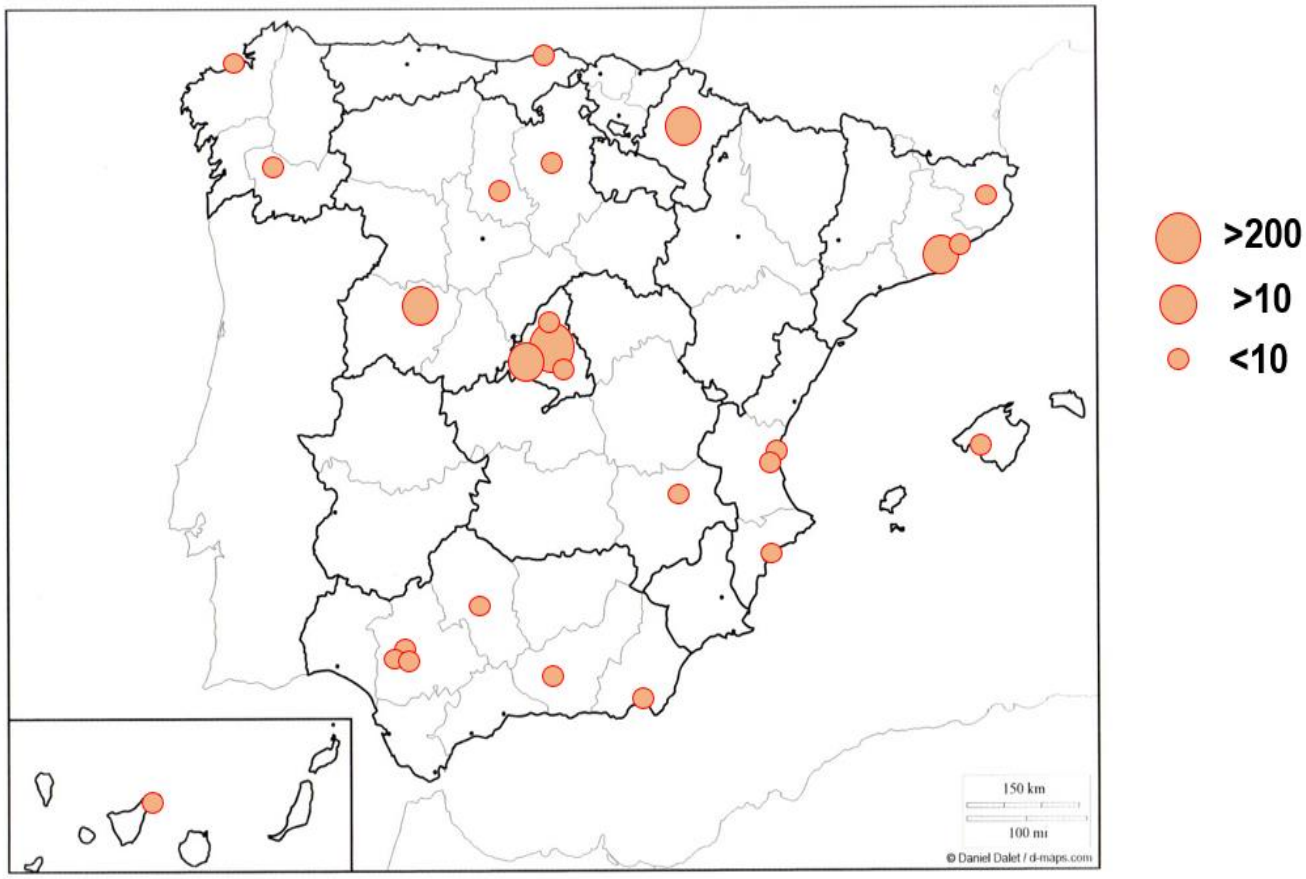
4)Extended molecular report to propose therapeutic options according to the molecular findings described

Genes analyzed in Archer Fusion Plex Solid Tumor Panel

AKT3	ARHGAP26	ALK	AXL	BRD3	PRKCA
BRAF	BRD4	EGFR	ERG	ESR1	ROS1
ETV1	ETV4	ETV5	ETV6	EWSR1	TFEB
FGFR1	FGFR2	FGFR3	FGR	INSR	PRKCB
MAML2	MAST1	MAST2	MET	MSMB	RSPO2
MUSK	MYB	NOTCH1	NOTCH2	NRG1	THADA
NTRK1	NTRK2	NTRK3	NUMBL	NUTM1	RAF1
PDGFRA	PDGFRB	PIK3CA	PKN1	PPARG	RSPO3
TMPRSS2	TFE3	TERT	RELA	RET	

RESULTS

Figure 1: Hospitals involved in the study. 341 samples collected from 26 National Hospitals (36 MDs) distributed all over the country



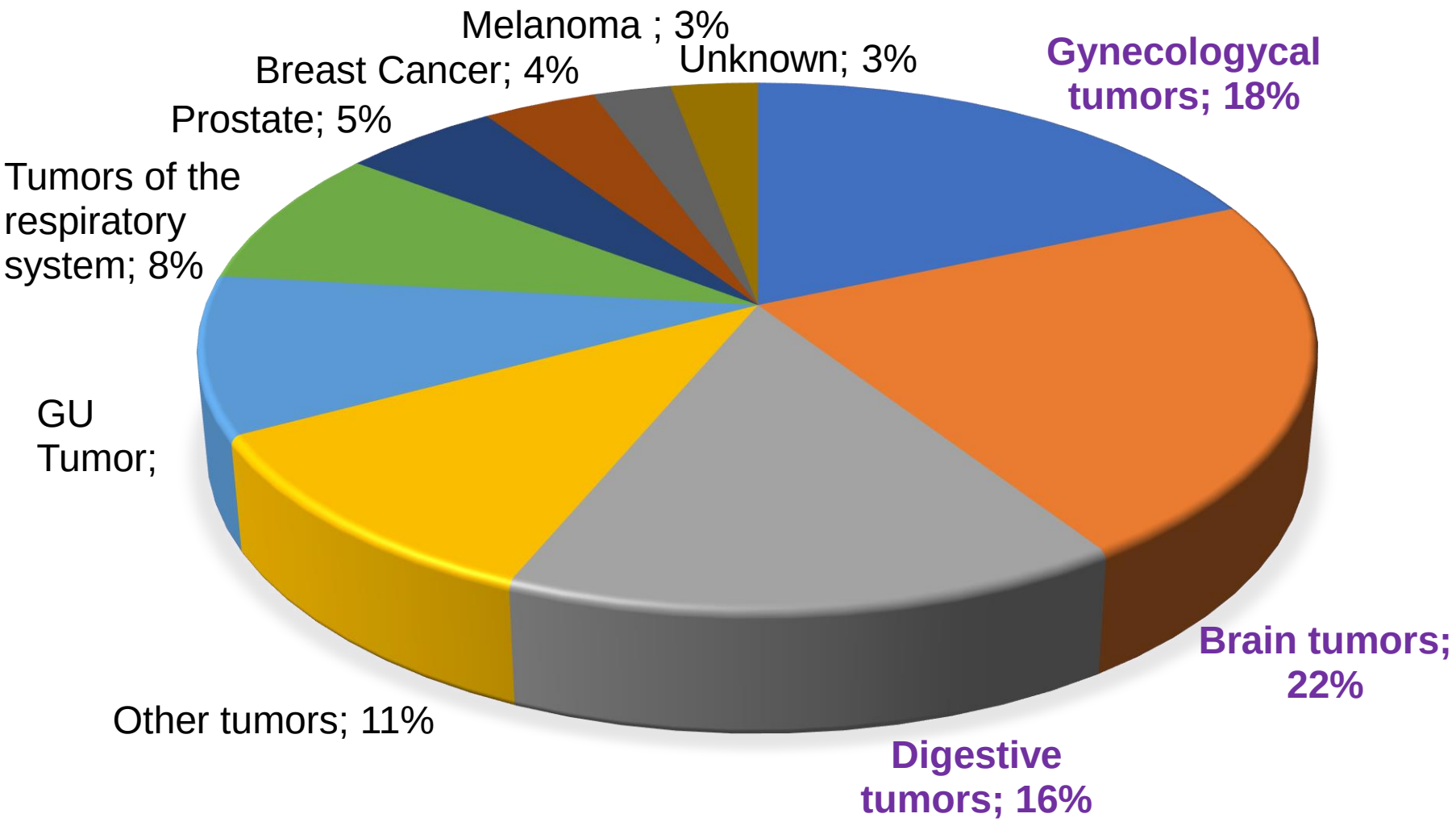

Melanoma ; 3%
Unknown; 3%
Breast Cancer; 4%
Gynecologycal tumors; 18%
Prostate; 5%
Tumors of the respiratory system; 8%
GU Tumor;
Brain tumors; 22%
Other tumors; 11%
Digestive tumors; 16%

Figure 2: Epidemiology and tumor types. 41 different histologies were collected

TYPE OF TUMOR (number of cases)

OVARY	52	RECTUM/SIGMA ADENOCARC	6	LYMPHOMA/LEUKEMIA/MYELOMA	3
GLIOBLASTOMA	45	GLIOMA	6	TESTIS	2
LUNG	27	OLOGODENDROGLIOMA	6	BRAIN	2
PROSTATE	18	SALIVARY GLAND	6	MEDULOBLASTOMA	2
RENAL	17	GATRIC CANCER	6	NEUROBLASTOMA	2
BREAST	13	CHOLANGIOCARCINOMA	6	PHARYNX	2
BLADDER	13	THYME	6	GALLBLADDER	2
COLON	10	MESOTELIOMA	5	LARYNX	2
UNKOWN ORIGIN	9	SARCOMA	5	VAGINA	1
MELANOMA	8	BONE	4	PENIS	1
PANCREATIC CANCER	7	CERVIX	3	PARAGANGLIOMA	1
ENDOMETRIUM	7	LIVER	3	ESOPHAGUS	1
ASTROCITOMA	7	THYROID CANCER	3	AMYGDALA ADENOCARC	1
HEAD AND NECK	1	PITUITATY GLAND	1	PARATID GLAND TUMOR	1

Figure 2: Epidemiology and tumor types. 41 different histologies were collected

AGE

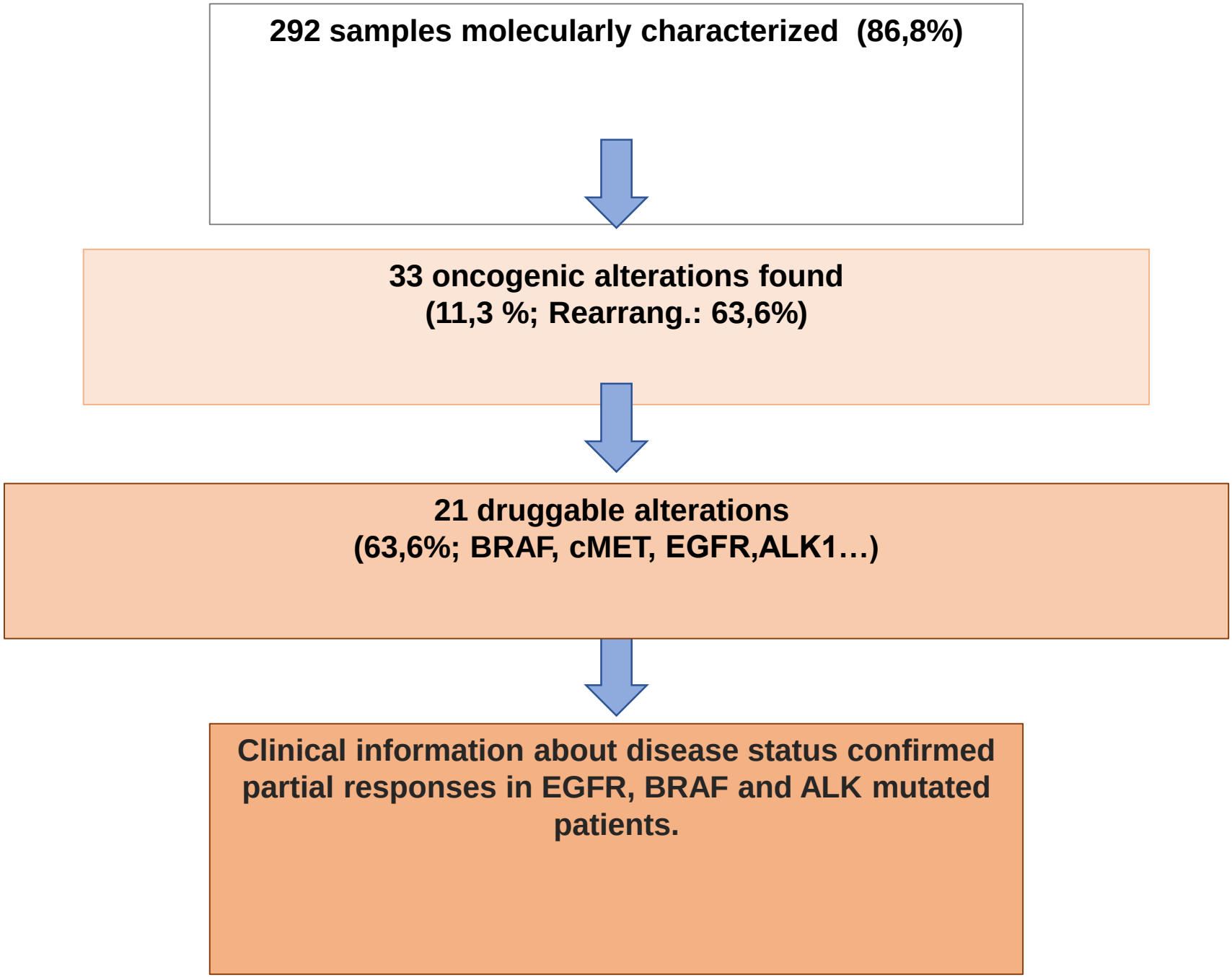
<18	1%
19-40	11%
41-65	56%
>65	33%

GENDER

FEMALE	52%
MALE	48%

TISSUE SAMPLE

PRIMARY TUMOR	82%
METASTATIC TUMOR	18%


292 samples molecularly characterized (86,8%)
33 oncogenic alterations found
(11,3 %; Rearrang.: 63,6%)
21 druggable alterations
(63,6%; BRAF, cMET, EGFR,ALK1…)
Clinical information about disease status confirmed partial responses in EGFR, BRAF and ALK mutated patients.

TUMOR	MOLECULAR FINDINGS
Breast cancer	ESR1 c.1613A>G; p.D538G
	ESR1-NFAT5 fusion
Cholangiocarcinoma	BRAF c.1397G>T; p.G466V
	FGFR2-RBM20 fusion
	HOOK1-**RET** fusion
Collecting duct carc.	MET p.T992I
Estesioneuroblastoma	TFE3-ABCA7 fusion
Ewing Sarcoma	EWSR1-**ERG** fusión
Gastric cancer	CLDN18-ARHGAP26 fusión
Glioblastoma	EGFR pA289V (3)
	EGFR pG598V (2)
	EGFR deletion exon 2-7
	BRAF deletion
	CAPZA2-**MET** fusion
	SRPK2-**MET** fusion
HG Glial tumor	PTPRZ1-**MET** fusion
Lung carcinoma	MET exon 14 deletion
	CD74-**ROS1** fusion
	EML4-**ALK** fusion
Oligodendroglioma	SYN2-PPARG fusion
	FGFR3-TACC3 fusion
Prostate	TMPRSS2-**ERG** fusion (5)
	UNC5D-**NRG1** fusion
	SND1-**BRAF** fusion
Rectum adenoc.	TMPRSS2-ANKRD36 fusion

*, Number of patients harbouring indicated in brackets;

** Oncogenic drivers labelled in bold

CONCLUSIONS

Though only few cases harboring druggable alterations got specific treatment, 50% achieved a meaningful benefit. A wide access to molecular screening and targeted drugs could improve the outcome of cancer patients