I SIMPOSIO NACIONAL de ONCOLOGÍA de PRECISIÓN

Vigo, del **28** de **febrero** al **1** de **marzo** de **2019**

Nuevos tumores listos para biopsia líquida

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idis

oncomet oncología médica traslacional

Consultant or Advisory Role: Pfizer, Boehringer, Novartis, Roche, Astra Zeneca, MSD, Sanofi

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Speaking: Novartis, Astra Zeneca, Bristol, Jansen, Pfizer

Grant support: No

I SIMP

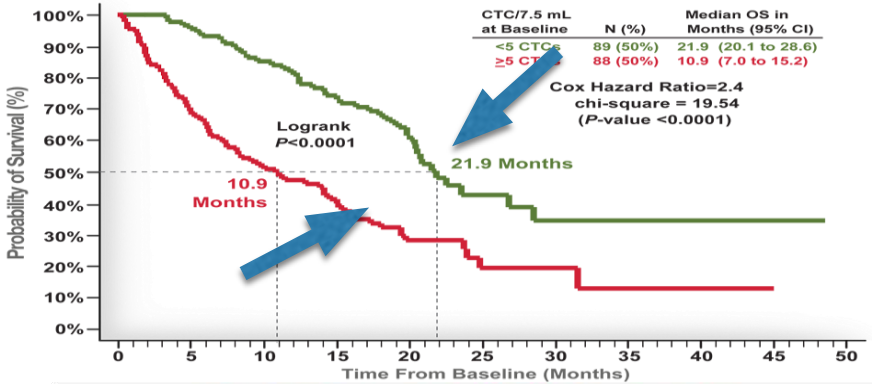
Vigo, del 28

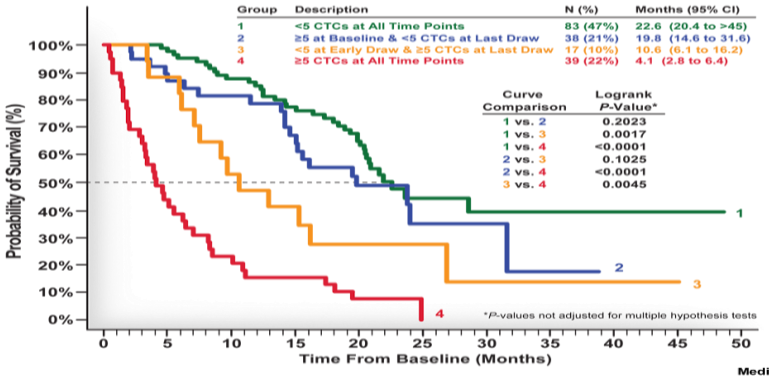
FARO DE VIGO

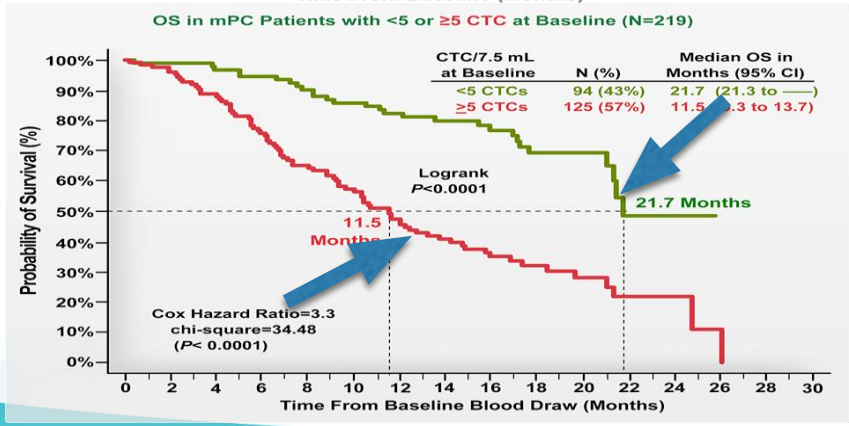
Noticias de Vigo

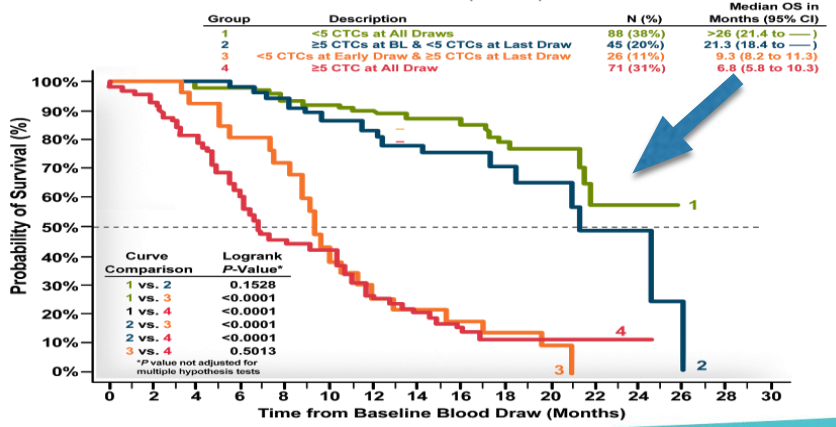
Sergio Vázquez: "Hemos pasado de la bomba atómica a atacar justo aquello que hace crecer el tumor"

El I Simposio Nacional de Oncología de Precisión reúne por primera vez a clínicos, investigadores y gestores para agilizar nuevos tratamientos









Hayes Clin Cancer Res 2006; De Bono Clin Cancer Res 2008

FDA Approved Companion Diagnostics	Therapeutic Products				
	Afatinib	Gefitinib	Erlotinib	Osimertinib	Dacomitinib
Therascreen EGFR RGQ PCR Kit	X	X	-	-	X
Cobas EGFR Mutation Test V2	-	X	X	X	-
Oncomine Dx Target Test	-	X	-	-	-
FoundationOne CDx	X	X	X	-	-

Circulating Tumor DNA Analysis in Patients With Cancer: American Society of Clinical Oncology and College of American Pathologists Joint Review

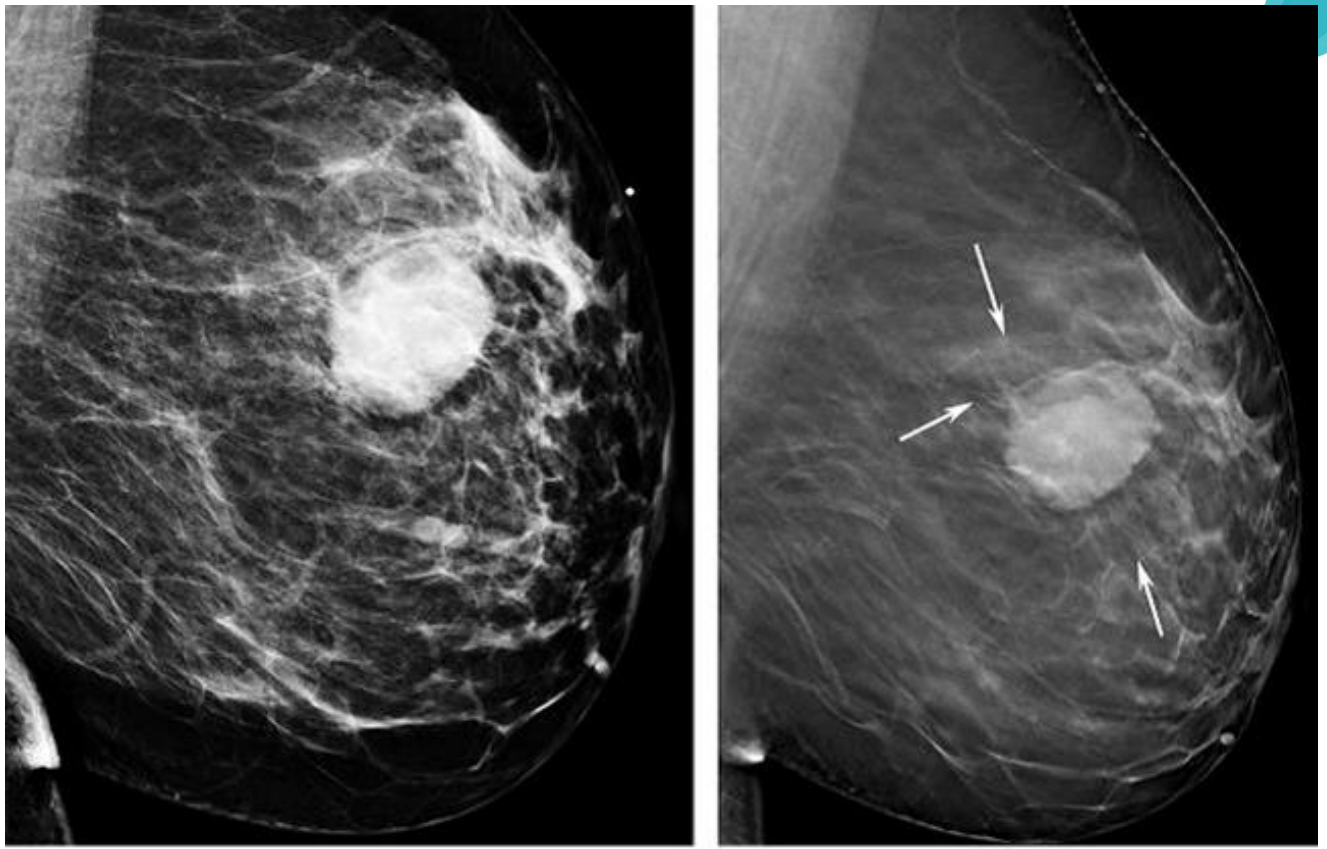
Jason D. Merker, Geoffrey R. Oxnard, Carolyn Compton, Maximilian Diehn, Patricia Hurley, Alexander J. Lazar,

Table 3. Comparison of ctDNA Versus Tumor Tissue Testing

Consideration	ctDNA Assay	Tissue Assay
Logistics	Easy to draw	Invasive, more challenging to obtain
	Variable venipuncture risks	Variable biopsy risks
	Easy serial testing	Serial testing more difficult
Biology	Cannot directly correlate ctDNA results with histology or cellular phenotype	Can correlate with histology and cellular phenotype
	More likely to represent whole tumor, but differential tumor cell turnover may bias representation	Represents one small tumor region
Pre-analytical	Easier to standardize across sites	More difficult to standardize across sites
	Requires special processing and handling unless using cell-stabilization tubes	Uses existing, validated tissue processing and handling approaches
	Limited data on confounding patient-related factors	
Clinical utility	Limited evidence for treatment selection in advanced cancer	Substantial evidence for treatment selection in multiple malignancies for early and advanced cancers
	No evidence for other potential indications	

Abbreviation: ctDNA, circulating tumor DNA.

Merker JCO 2018

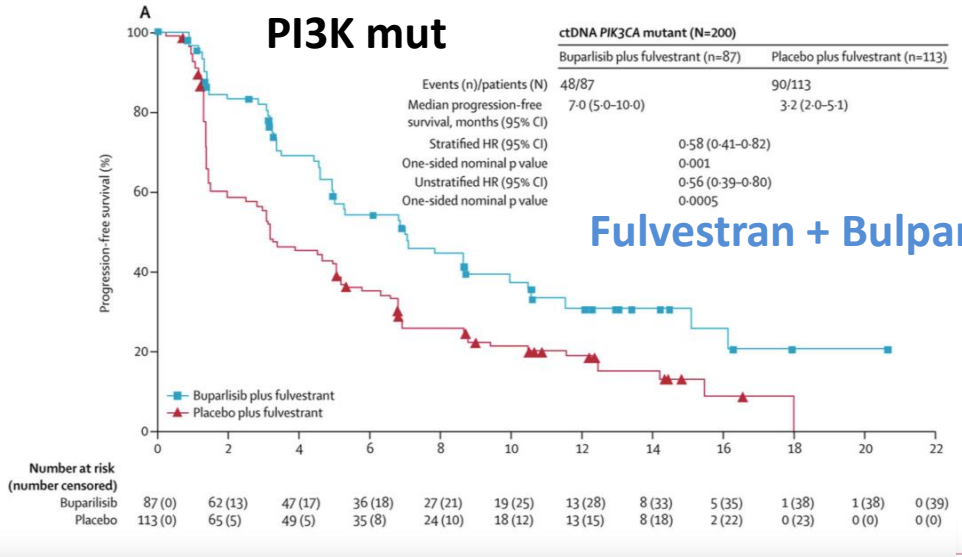


Analyte	Marker	Prognostic/Predictive Value in IBC-Primary Tumour	Successfully Applied in CTCs
DNA	*HER2* amplification	Strong predictive value.	Yes, can be robustly assessed.
	PIK3CA gain-of-function mutation	Prognostic factor linked to good prognosis; not applied in routine clinical practice.	Yes, can be robustly assessed.
	TP53 loss-of-function mutation	Prognostic factor linked to poor prognosis; no predictive value in routine clinical practice.	Yes, can be robustly assessed.
	RB1	Prognostic factor linked to poor prognosis. Predictive value—low *RB1* expression in triple negative/ER-negative breast cancers related to good prognosis in patients treated with chemotherapy.	Yes, can be assessed.
	ESR1 mutations	Prognostic factor linked to poor prognosis, potentially to be applied in clinics as a negative predictive factor (hormone resistance).	Yes, can be robustly assessed.
	Ion AmpliSeq™ Cancer Hotspot Panel v2	Not assessed.	Yes, can be robustly assessed.

Braun Cancers 2019

Estudio BELLE. PI3K mut mejor PFS, no mejor OS

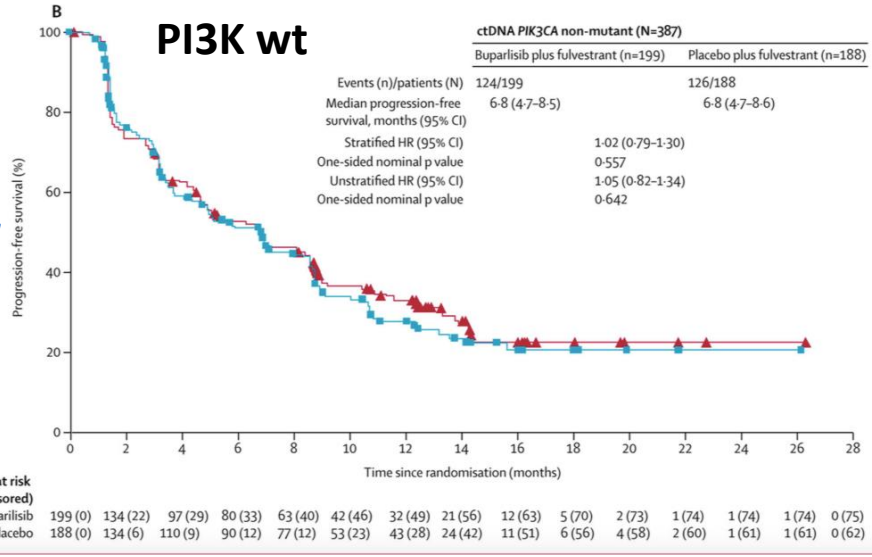
PI3K mut



ctDNA *PIK3CA* mutant (N=200)	Buparlisib plus fulvestrant (n=87)	Placebo plus fulvestrant (n=113)
Events (n)/patients (N)	48/87	90/113
Median progression-free survival, months (95% CI)	7·0 (5·0–10·0)	3·2 (2·0–5·1)
Stratified HR (95% CI)	0·58 (0·41–0·82)	
One-sided nominal p value	0·001	
Unstratified HR (95% CI)	0·56 (0·39–0·80)	
One-sided nominal p value	0·0005	

Fulvestran + Bulparlisiv

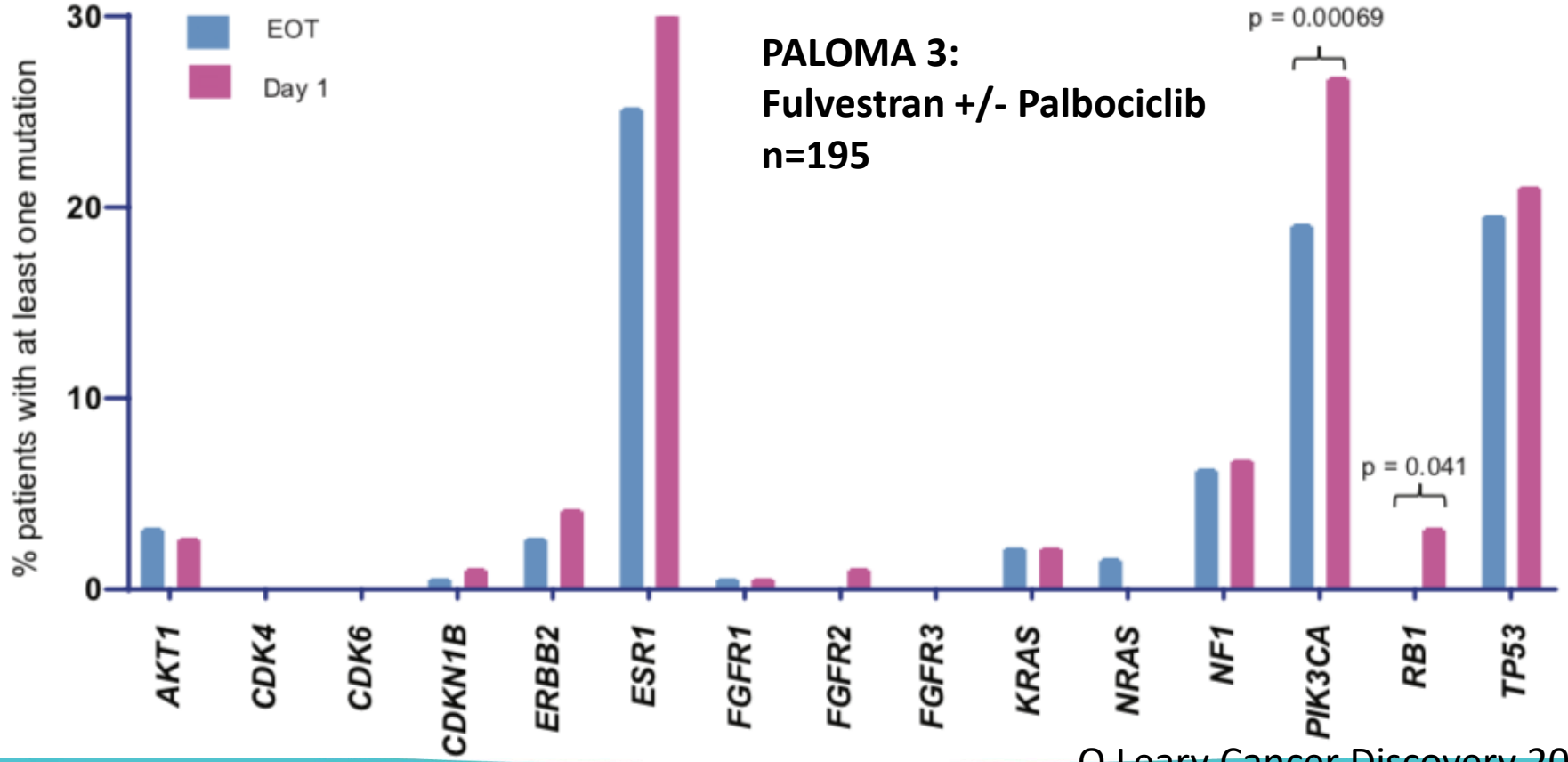
PI3K wt



ctDNA *PIK3CA* non-mutant (N=387)	Buparlisib plus fulvestrant (n=199)	Placebo plus fulvestrant (n=188)
Events (n)/patients (N)	124/199	126/188
Median progression-free survival, months (95% CI)	6·8 (4·7–8·5)	6·8 (4·7–8·6)
Stratified HR (95% CI)	1·02 (0·79–1·30)	
One-sided nominal p value	0·557	
Unstratified HR (95% CI)	1·05 (0·82–1·34)	
One-sided nominal p value	0·642	

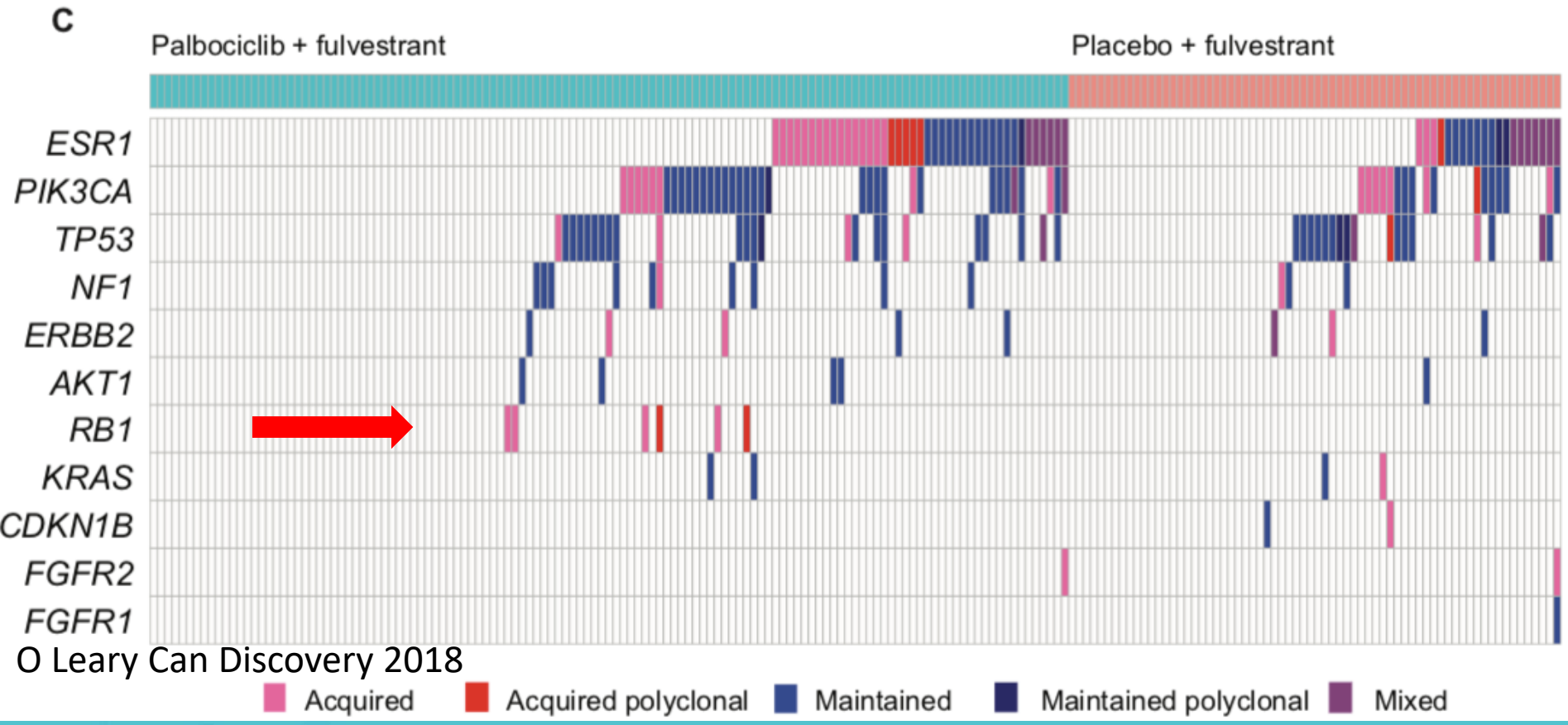
Baselga, Lancet Oncol 2017

A



PALOMA 3:
Fulvestran +/- Palbociclib
n=195

O Leary Cancer Discovery 2018



O Leary Can Discovery 2018

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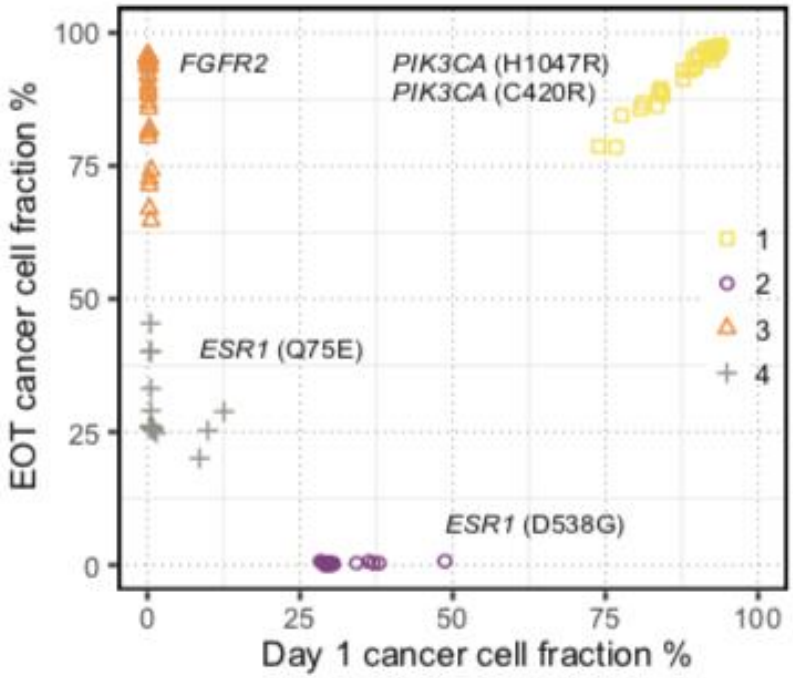

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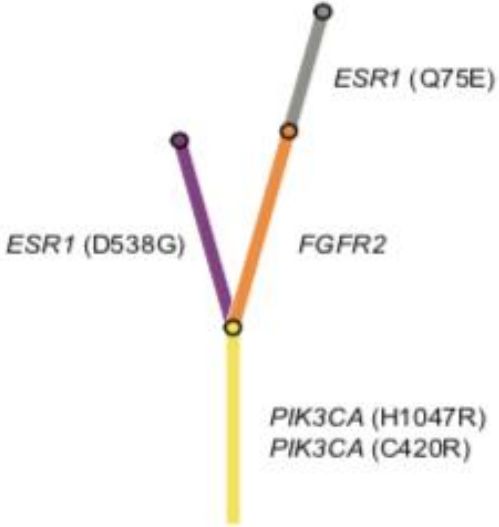
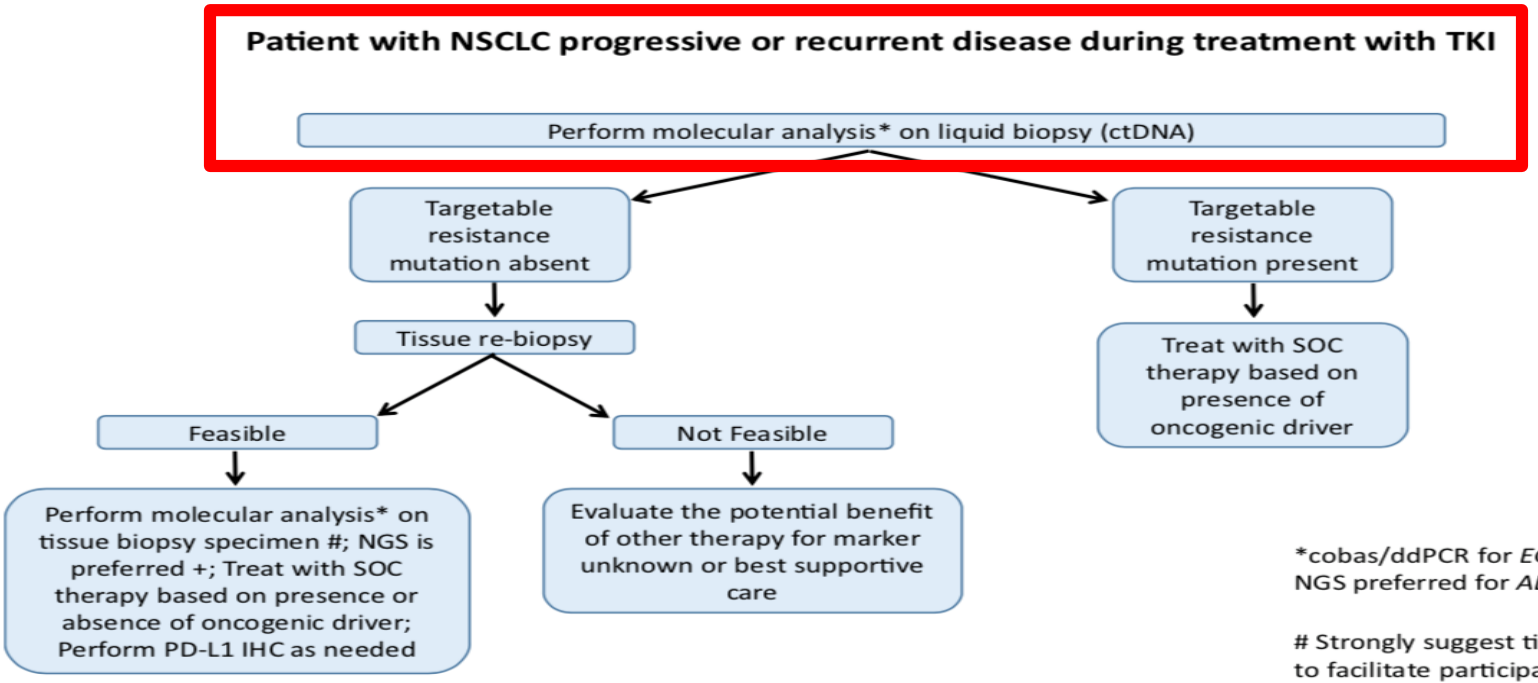


O Leary Cancer Discovery 2018

Liquid biopsy for advanced Non-Small Cell Lung Cancer (NSCLC): A Statement Paper from the IASLC



*cobas/ddPCR for *EGFR* mutation
NGS preferred for *ALK* and *ROS1*

Strongly suggest tissue sparing to facilitate participation in clinical trials

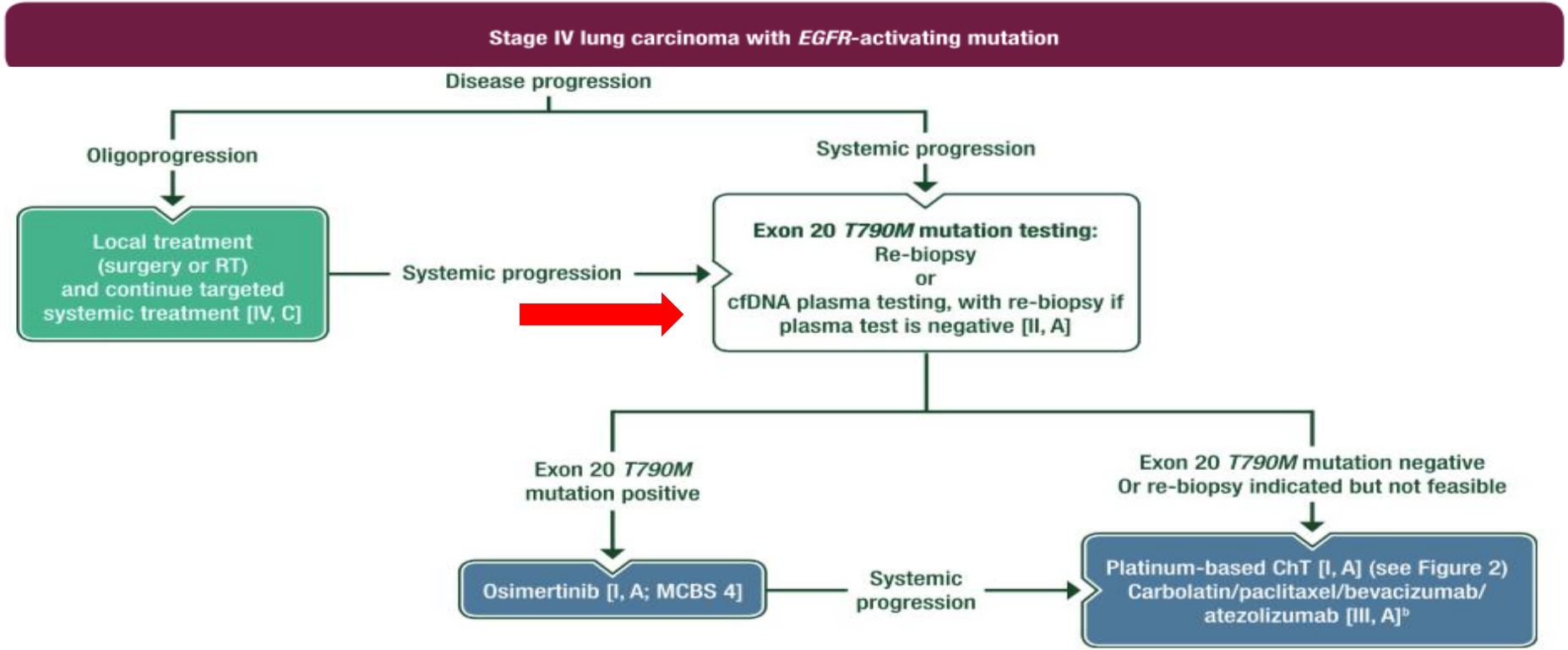
+ While NGS is preferred, based on availability, other validated assays are acceptable

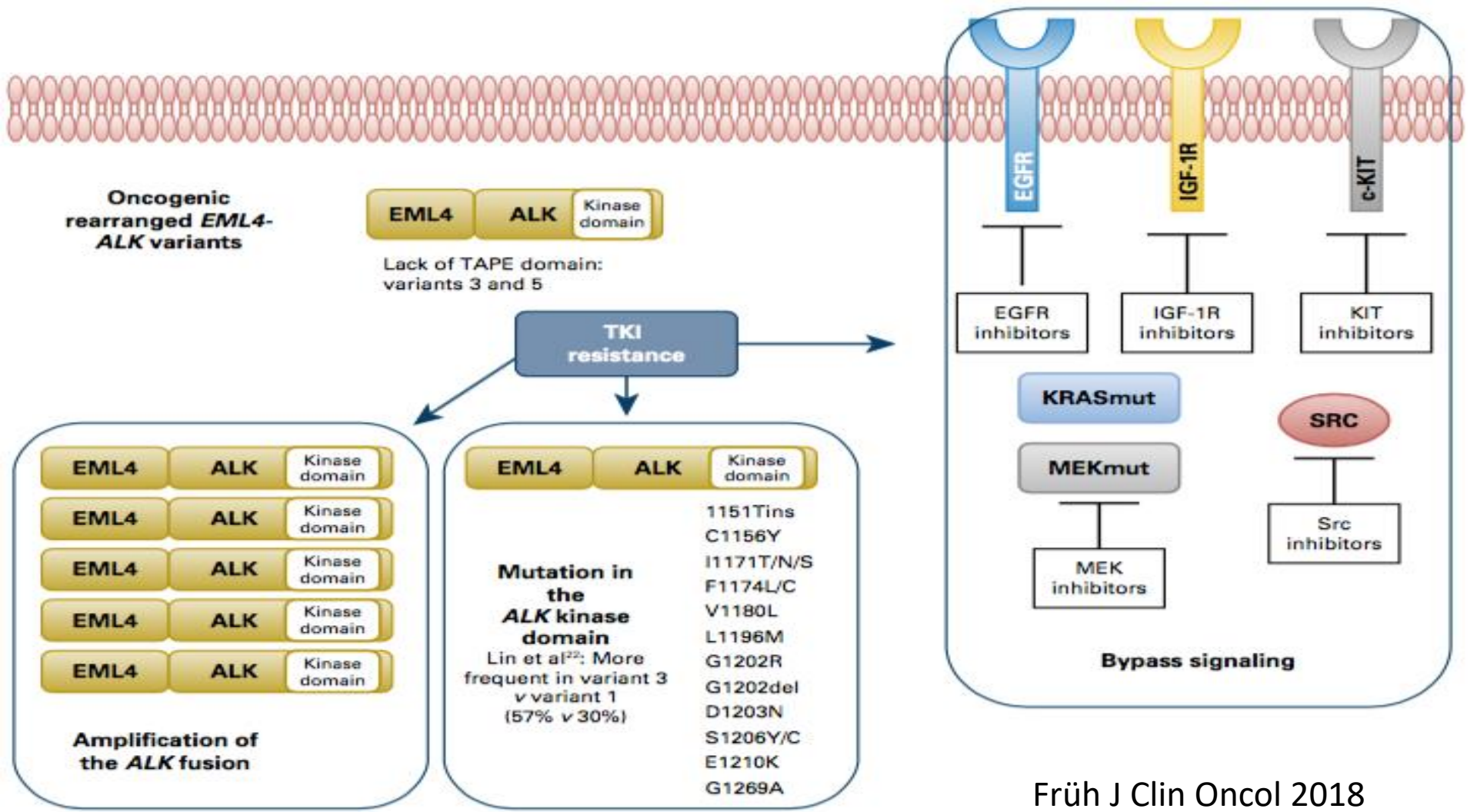
Rolfo et al, Journal of Thoracic Oncology, Vol.13 No 9:1248-1268

Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

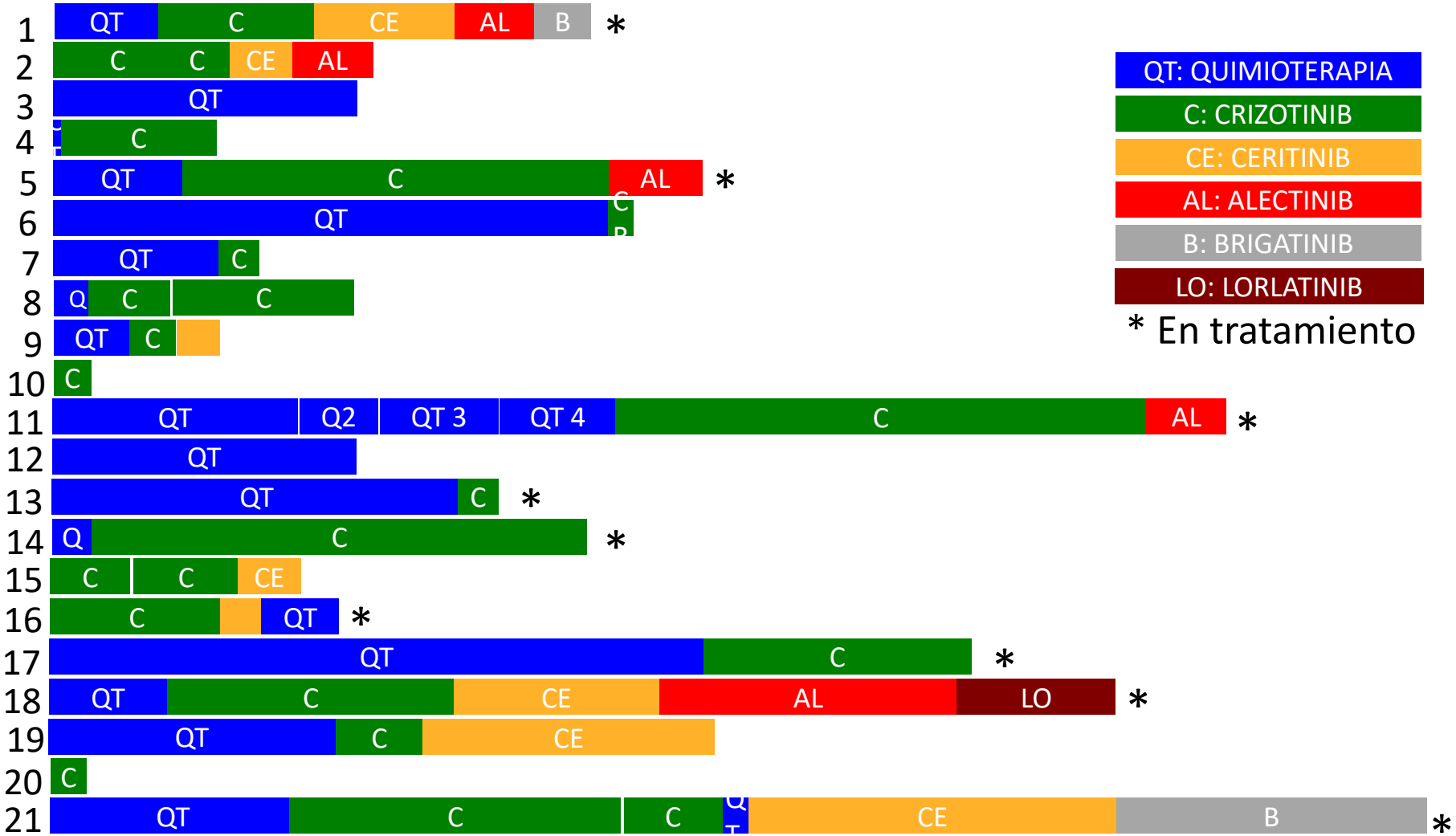
Ann Oncol 29 (supp 4): iv192-1v237, 2018

D. Planchard[1], S. Popat[2], K. Kerr[3], S. Novello[4], E. F. Smit[5], C. Faivre-Finn[6], T. S. Mok[7], M. Reck[8], P. E. Van Schil[9], M. D. Hellmann[10] & S. Peters[11], on behalf of the ESMO Guidelines Committee*





Früh J Clin Oncol 2018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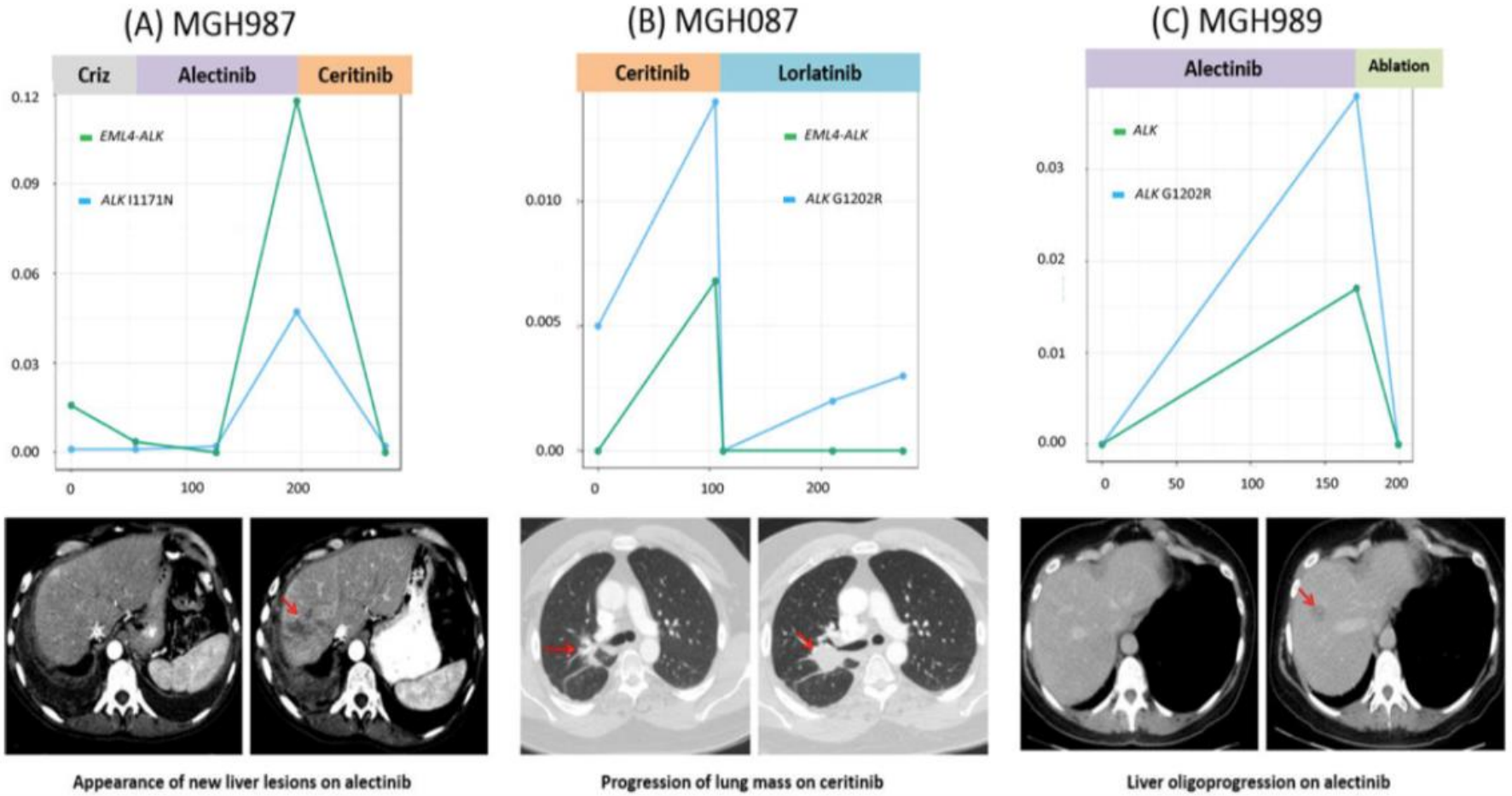
QT: QUIMIOTERAPIA
C: CRIZOTINIB
CE: CERITINIB
AL: ALECTINIB
B: BRIGATINIB
LO: LORLATINIB
* En tratamiento



Dagogo JCO Precision Oncology 2018

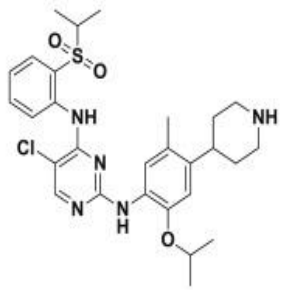
Cellular ALK phosphorylation mean IC_{50} (nmol/L)

Mutation status	Crizotinib	Ceritinib	Alectinib	Brigatinib	Lorlatinib
Parental Ba/F3	763.9	885.7	890.1	2774.0	11293.8
EML4–ALK V1	38.6	4.9	11.4	10.7	2.3
EML4–ALK C1156Y	61.9	5.3	11.6	4.5	4.6
EML4–ALK I1171N	130.1	8.2	397.7	26.1	49.0
EML4–ALK I1171S	94.1	3.8	177.0	17.8	30.4
EML4–ALK I1171T	51.4	1.7	33.6[a]	6.1	11.5
EML4–ALK F1174C	115.0	38.0[a]	27.0	18.0	8.0
EML4–ALK L1196M	339.0	9.3	117.6	26.5	34.0
EML4–ALK L1198F	0.4	196.2	42.3	13.9	14.8
EML4–ALK G1202R	381.6	124.4	706.6	129.5	49.9
EML4–ALK G1202del	58.4	50.1	58.8	95.8	5.2
EML4–ALK D1203N	116.3	35.3	27.9	34.6	11.1
EML4–ALK E1210K	42.8	5.8	31.6	24.0	1.7
EML4–ALK G1269A	117.0	0.4	25.0	ND	10.0
EML4–ALK D1203N+F1174C	338.8	237.8	75.1	123.4	69.8
EML4–ALK D1203N+E1210K	153.0	97.8	82.8	136.0	26.6

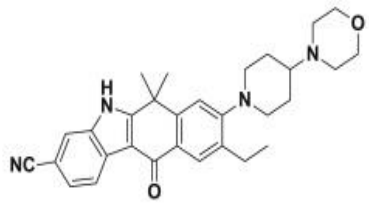
$IC_{50} \leq 50$ nmol/L

$IC_{50} > 50 < 200$ nmol/L

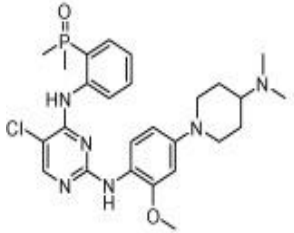
$IC_{50} \geq 200$ nmol/L



Ceritinib

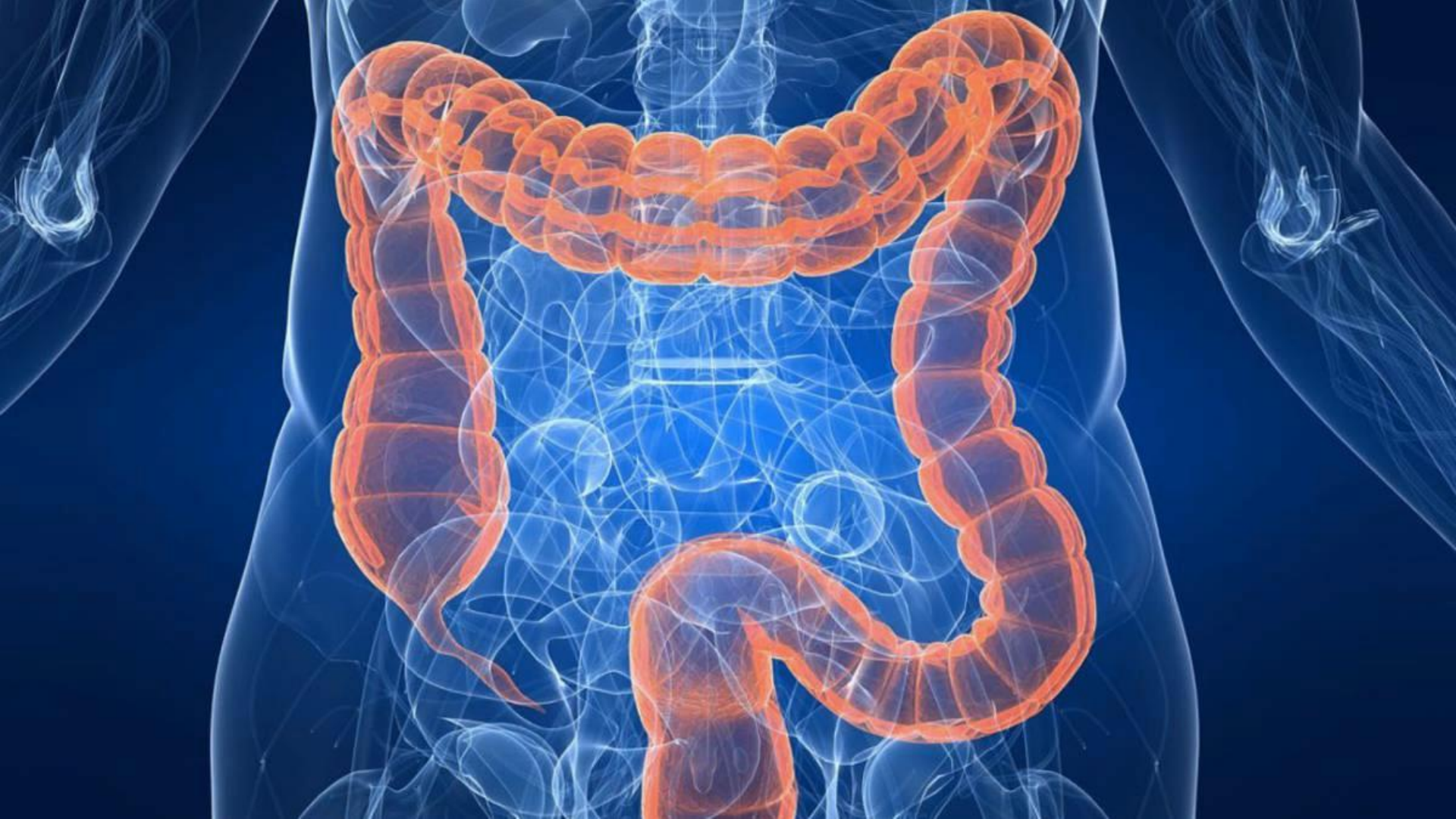


Alectinib



Brigatinib

Gainor *Cancer Discov* 2016



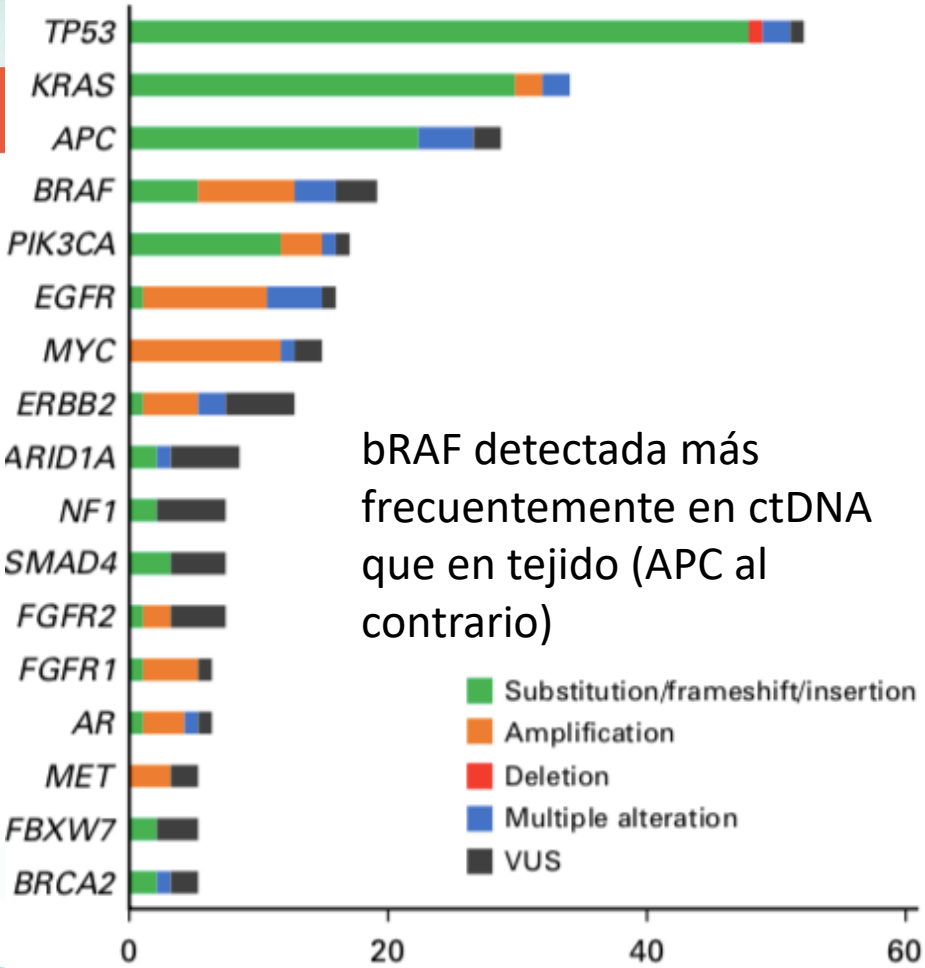
original report

Genomic Assessment of Blood-Derived Circulating Tumor DNA in Patients With Colorectal Cancers: Correlation With Tissue Sequencing, Therapeutic Response, and Survival

Purpose Genomic alterations in blood-derived circulating tumor DNA (ctDNA) from patients with colorectal cancers were correlated with clinical outcomes.

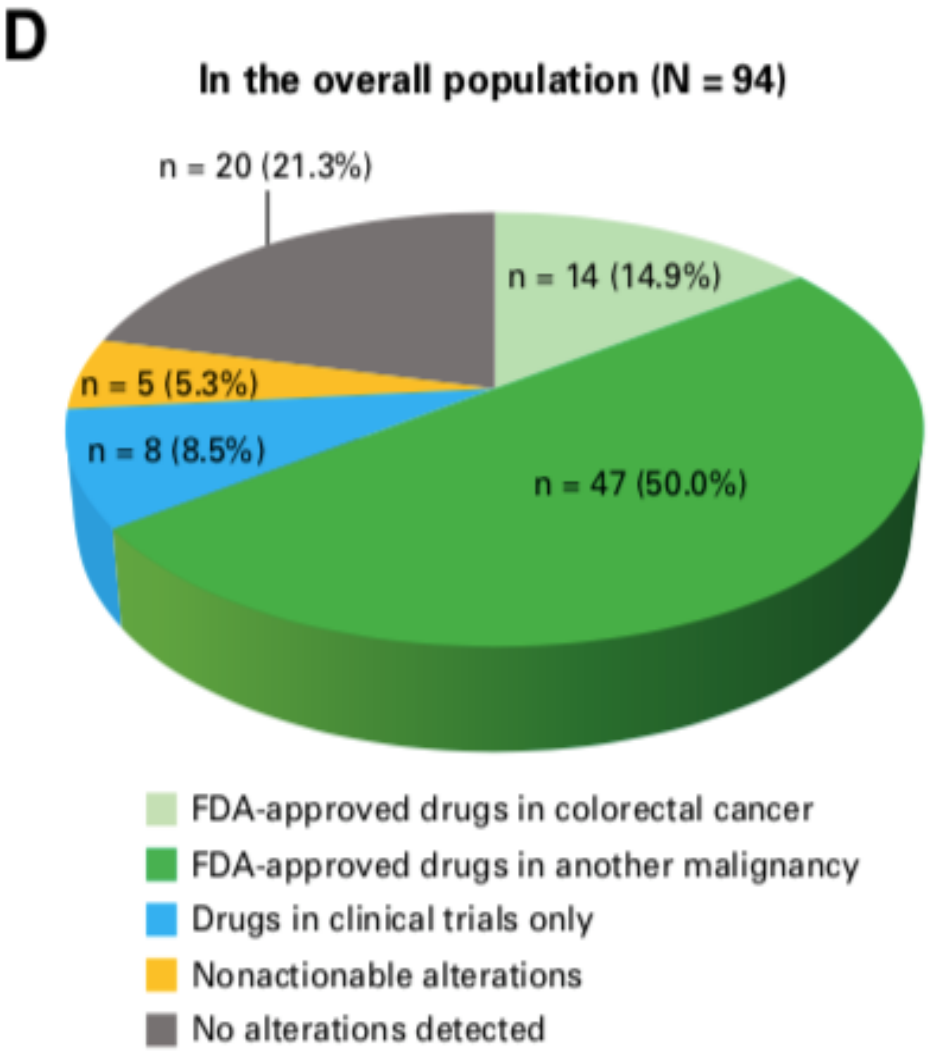
Patients and Methods Next-generation sequencing of ctDNA (54- to 73-gene panel) was performed in 94 patients with colorectal cancer.

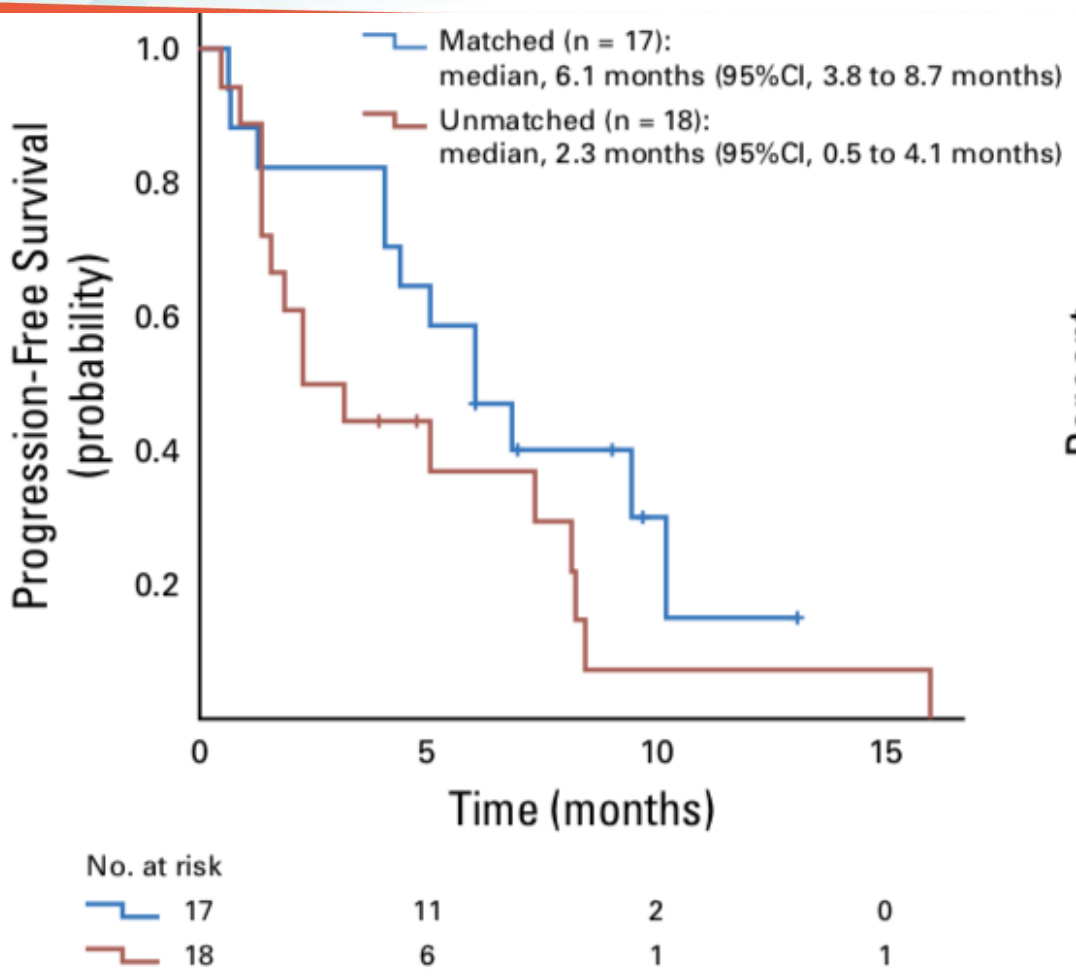
Kato JCO P Onc 2019

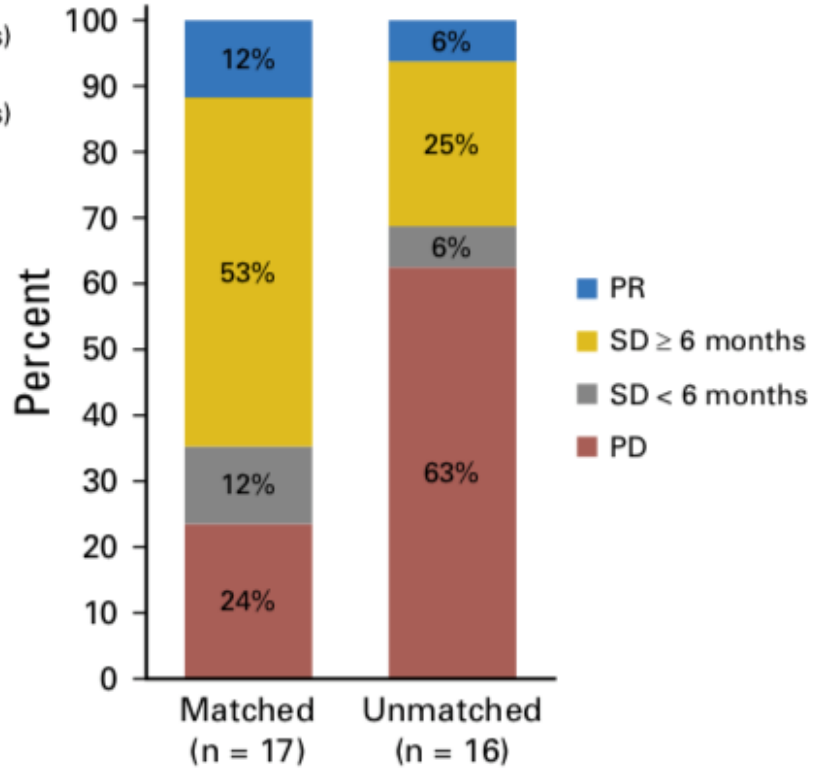


bRAF detectada más frecuentemente en ctDNA que en tejido (APC al contrario)

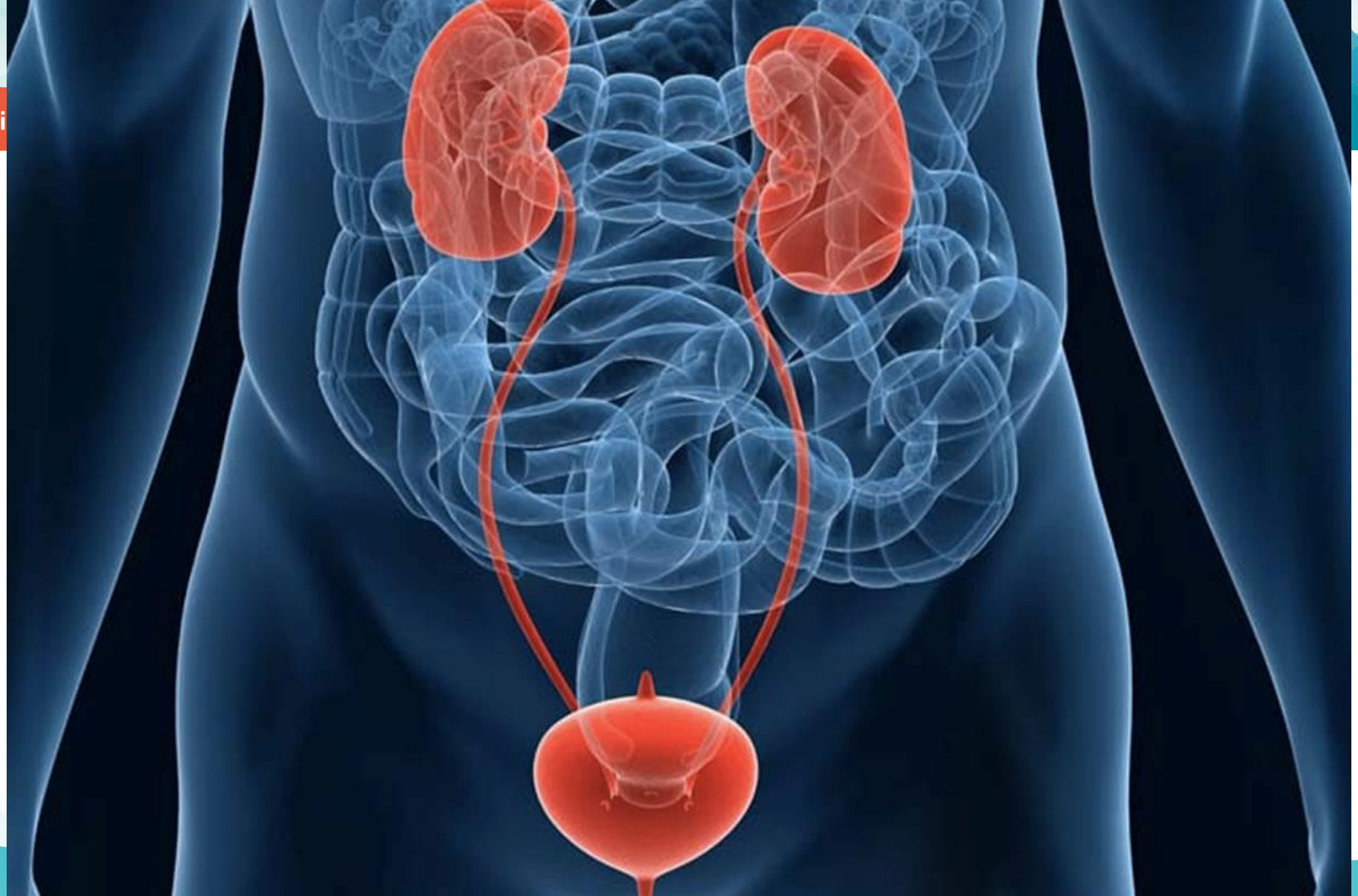
Kato JCO P Onc 2019

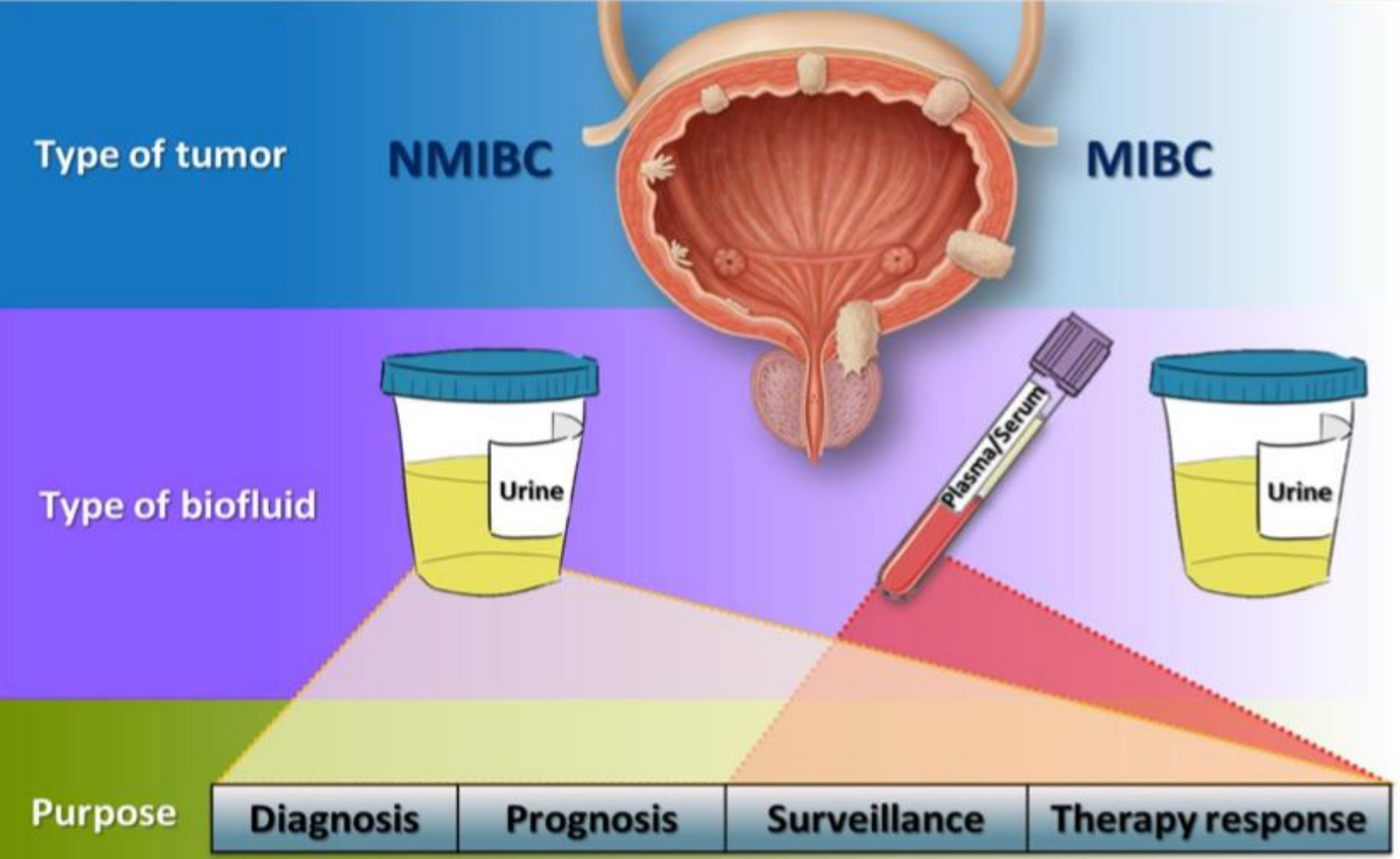






Kato JCO Precision Onc 2019





Lodewijk Int J Mol Science 2018

Cost-effectiveness of SelectMDx for prostate cancer in four European countries: a comparative modeling study

PROSTATE CANCER GENE 3

	France	Germany	Italy	Spain
PCa detection				
Probability PCa	47%	49%	37%	33%
Probability significant PCa	49%	64%	45%	58%
Probability insignificant PCa	51%	36%	55%	42%
Treatment distribution significant PCa				
RP	58%	67%	56%	34%
RT (extRT; BT)	15%	18%	19%	41% (36%; 5%)
ADT	24%	10%	19%	21%
WW	4%	5%	6%	4%

Govers Prostate Prostatics Dis 2019

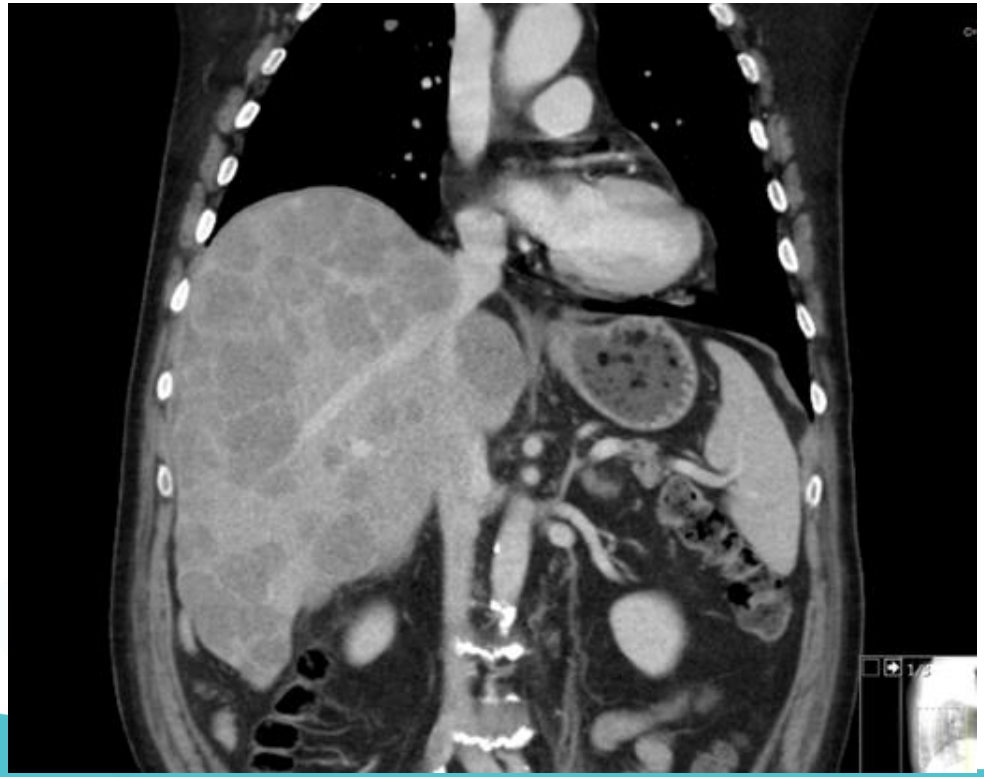
Cost-effectiveness of SelectMDx for prostate cancer in four European countries: a comparative modeling study

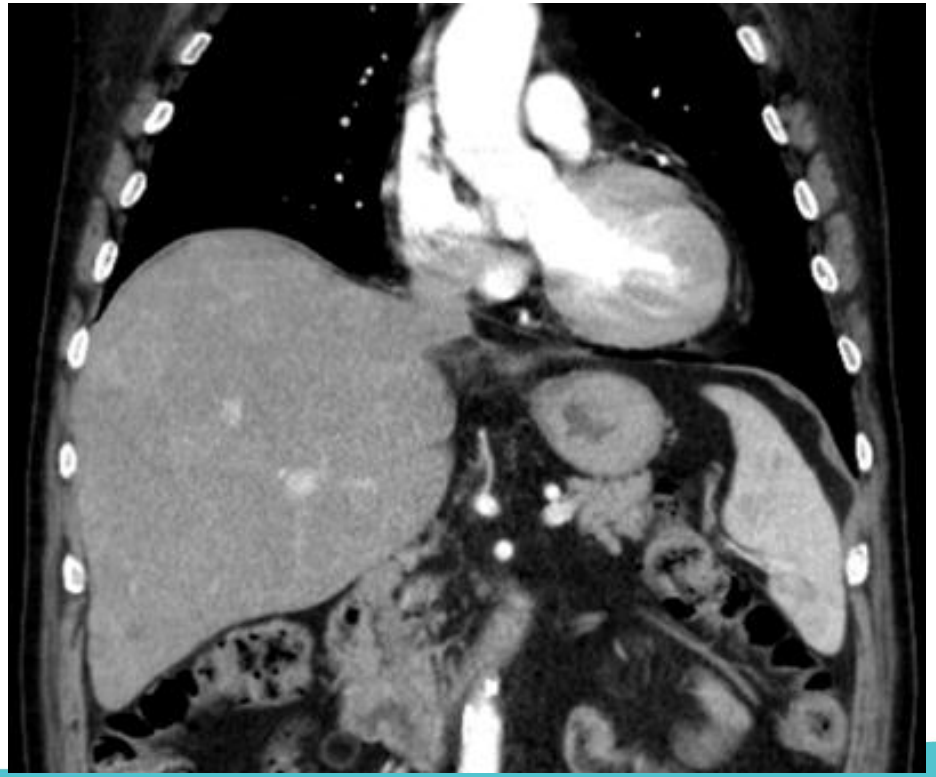
Costs associated with diagnosis				
TRUS-Bx	€887	€559	€400	€166
SelectMDx	€270	€270	€270	€270
Costs associated with treatment				
RP	€14,401[a]	€7243	€10,000	€7197
RT (extRT; BT)	€18,414[a]	€4727	€7030	(€2773; €5413)
ADT (yearly)	€14,775[a]	€1777	€2000	€1521
AS (yearly)	€8222[a]	€95	€208	€208

Govers Prostate Prostatics Dis 2019

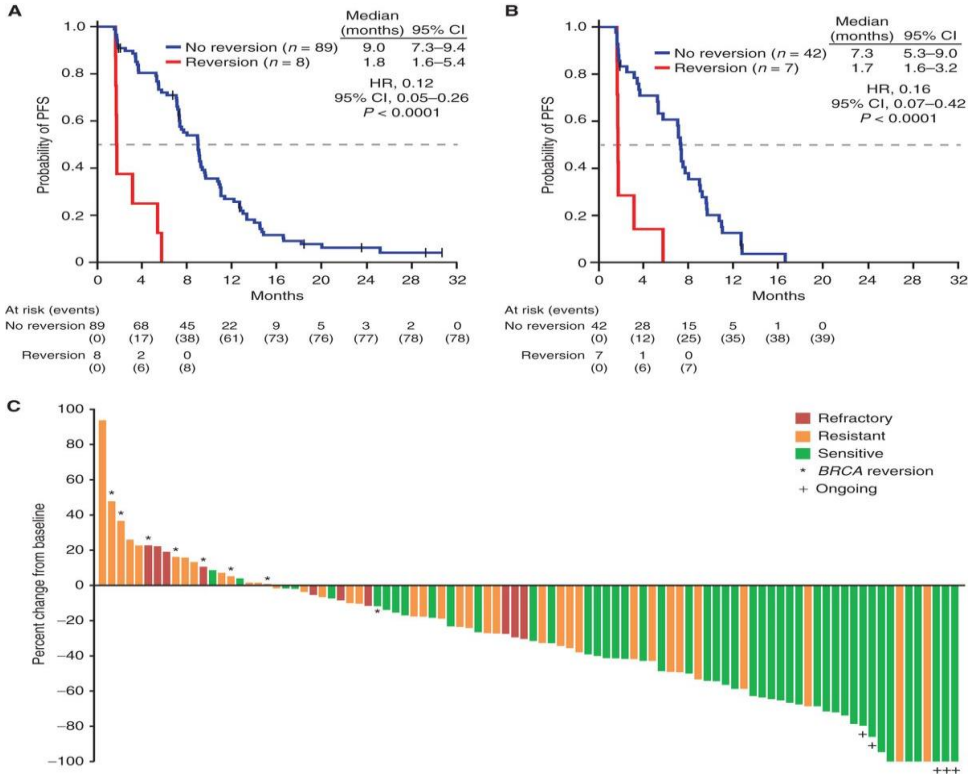
Genomic Analysis of Three Metastatic Prostate Cancer Patients with Exceptional Responses to Carboplatin Indicating Different Types of DNA Repair Deficiency

Zafeiris Zafeiriou [a,b], Diletta Bianchini [a], Robert Chandler [a], Pasquale Rescigno [a,c], Wei Yuan [a],



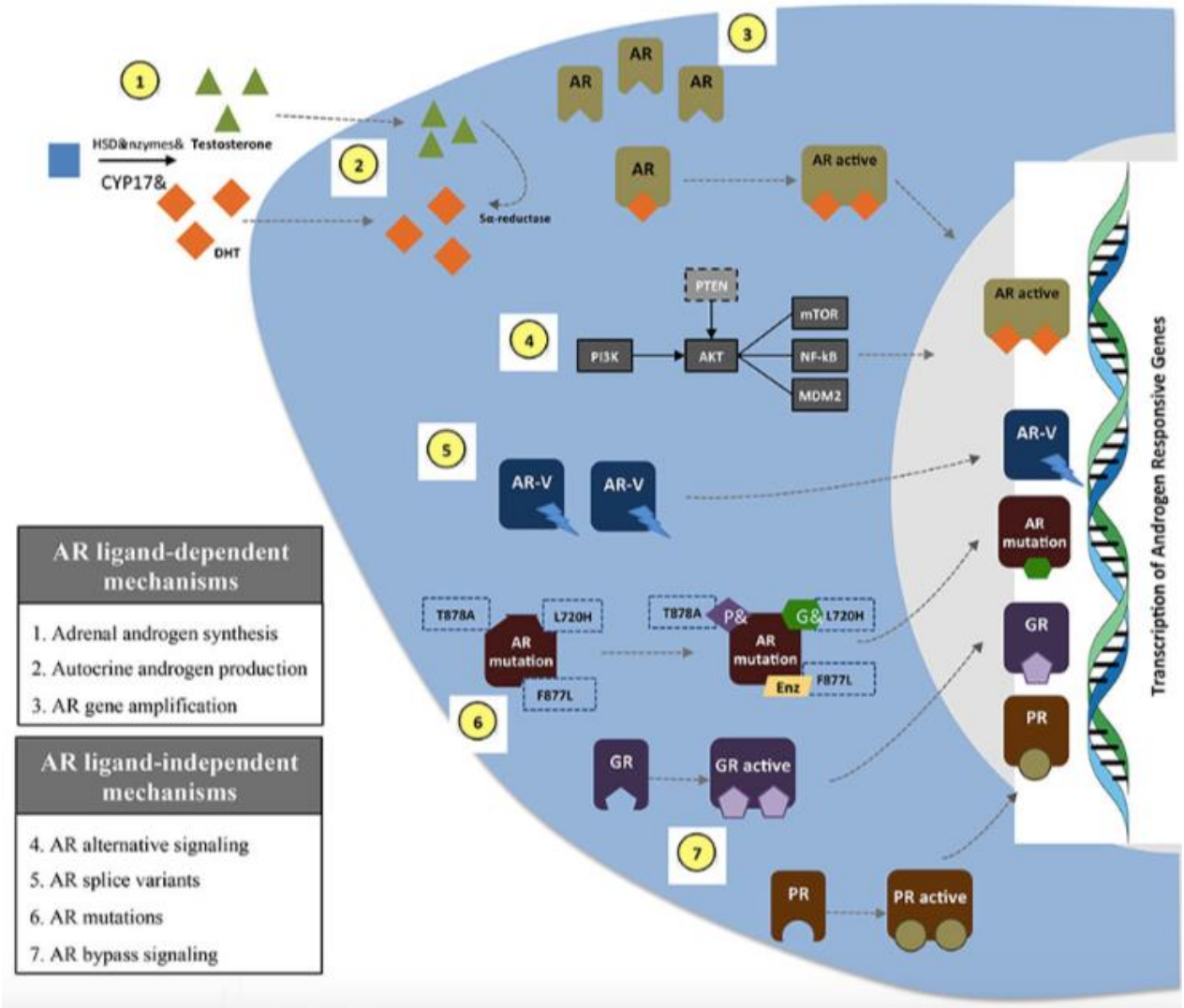


Patients without BRCA reversion mutations detected in pretreatment cfDNA have significantly longer rucaparib PFS in (A) all BRCA-mutant cases and (B) platinum-resistant or platinum-refractory BRCA-mutant



Kevin K. Lin et al. Cancer Discov 2019;9:210-219

AACR American Association for Cancer Research
CANCER DISCOVERY


1
HSD&nzymes&
Testosterone
CYP17&
DHT
2
5α-reductase
3
AR
AR
AR
AR
AR active
4
PTEN
PI3K
AKT
mTOR
NF-kB
MDM2
AR active
5
AR-V
AR-V
AR-V
6
T878A
L720H
AR mutation
F877L
T878A
P&
G&
L720H
AR mutation
Enz
F877L
AR mutation
GR
PR
7
GR
GR active
PR
PR active
Transcription of Androgen Responsive Genes
AR ligand-dependent mechanisms
1. Adrenal androgen synthesis
2. Autocrine androgen production
3. AR gene amplification
AR ligand-independent mechanisms
4. AR alternative signaling
5. AR splice variants
6. AR mutations
7. AR bypass signaling


EN VENTA
673 201 466
PROPIEDAD KINV
mismo precio que el Local de al lado,
DOBLE DE METROS
EN VENTA
676 282 715
PROPIEDAD de OTIMANSA S.L.

¿Nuevos tumores listos para biopsia líquida?

- BL debe ser fácil: tenemos poco tiempo
- Debe ser entendible: solo somos clínicos
- Debe ayudar a la toma de decisiones
- Debe añadir información útil para los pacientes
- Debe guiar el tratamiento: es nuestra misión como médicos

luis.leon.mateos@sergas.es