

PRECISIONSM
ONCOLOGY

↻ Has retwitteado



Tori Tomalia @lil_lytnin · 20h



I recently passed 5 yr mark w
widely metastatic NSCLC.

Extensive spread thru both lungs,
bones, liver, brain. Today I take pills
1x/day to control the disease. I
can't even begin to explain what a
game changer targeted medicine
and researchers behind it have
been to me. [#LCSM](#)

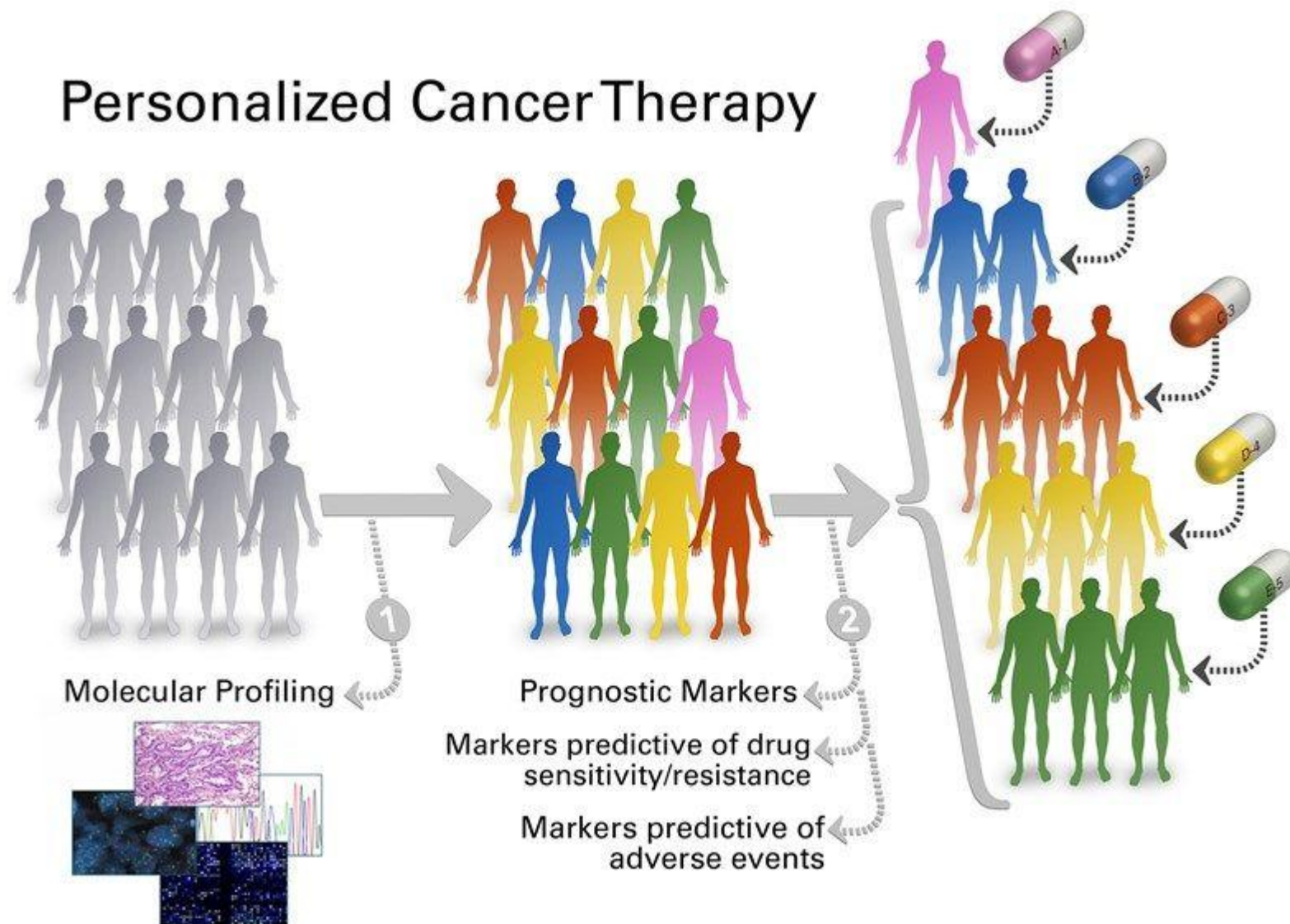


**Sally Davis
2017**

**Directora Médica
Servicio Nacional de Salud
(NHS), Inglaterra**

**A todo paciente de Cancer
se le debería ensayar el
perfil tumoral de su ADN
para acelerar diagnóstico y
salvar más vidas**

Personalized Cancer Therapy



Biomarkers are helping personalize cancer care...



**Different People's Tumours Have
Different Biomarkers**

Biomarkers commonly found in
non-small cell lung cancer



Questions that can be answered by cancer biomarkers

Prognostic

Is it likely to develop this cancer?

Is it likely to be an aggressive form?

Diagnostic

What type of cancer is it?

Predictive

Is this the optimal drug for my cancer?

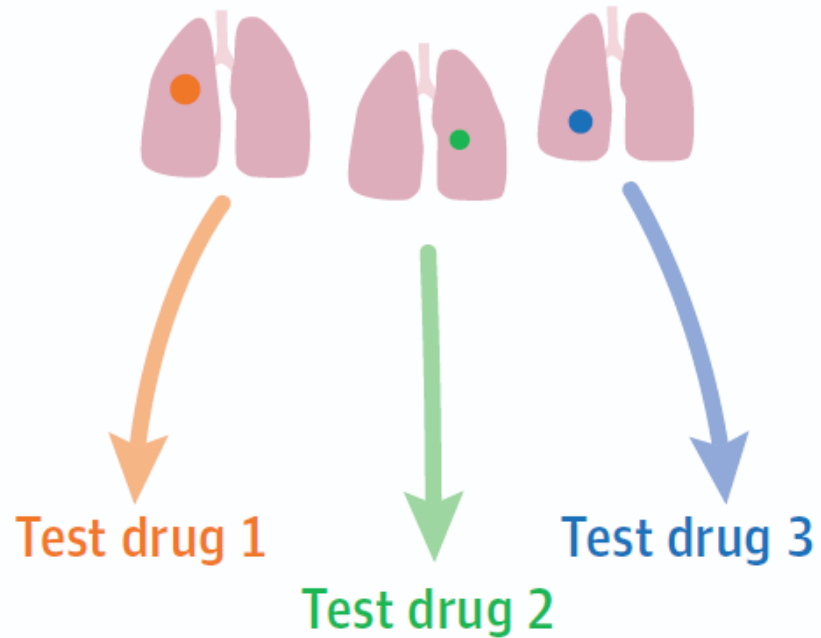
Will the cancer return?

Novel precision medicine trial designs

Umbrella trial

1 type of cancer

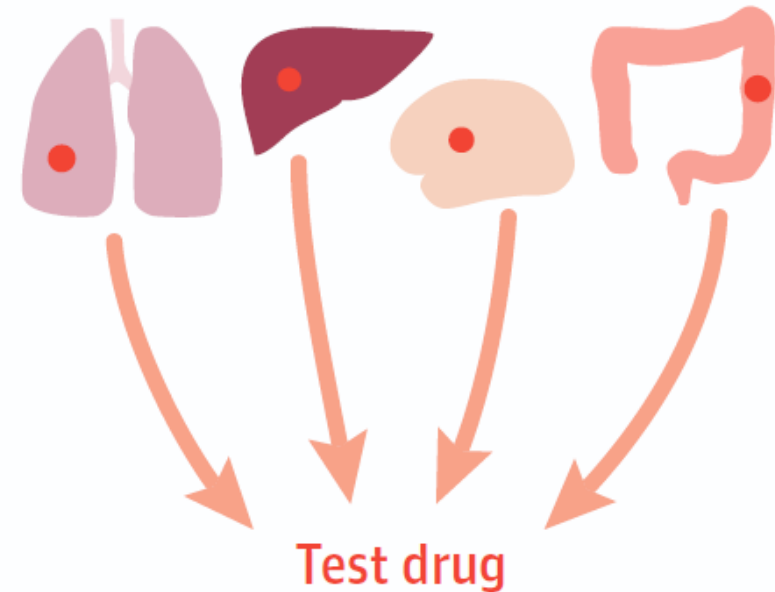
Different genetic mutations (●●●)



Basket trial

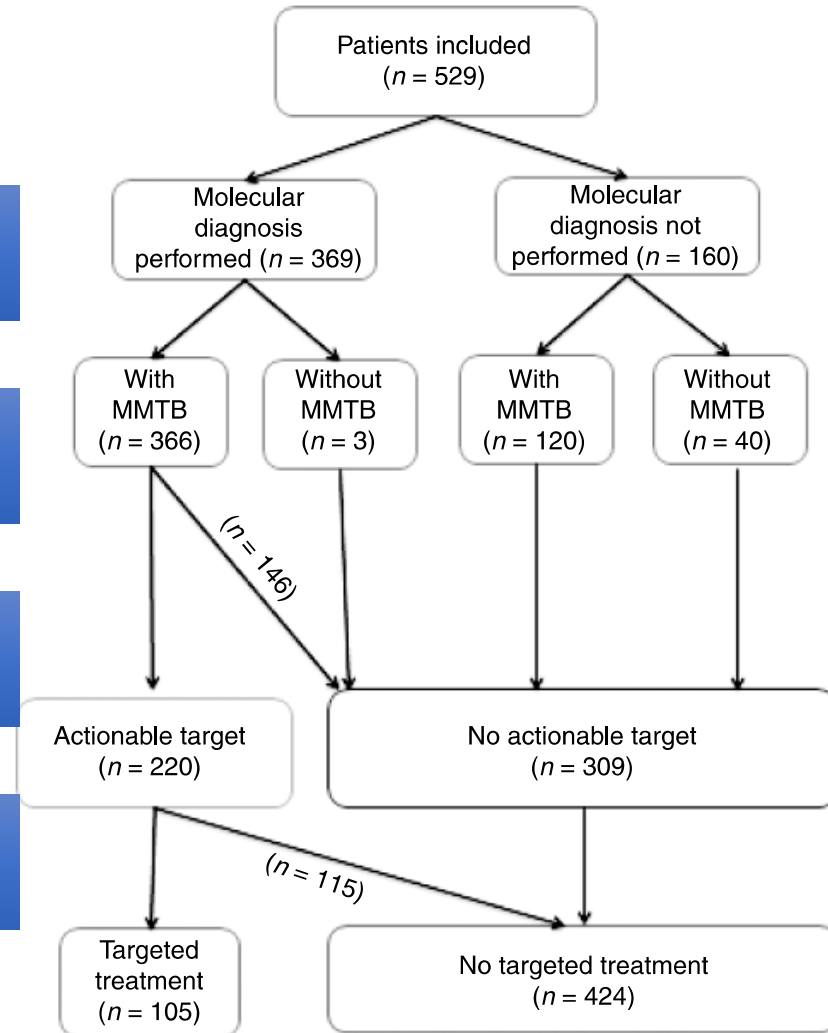
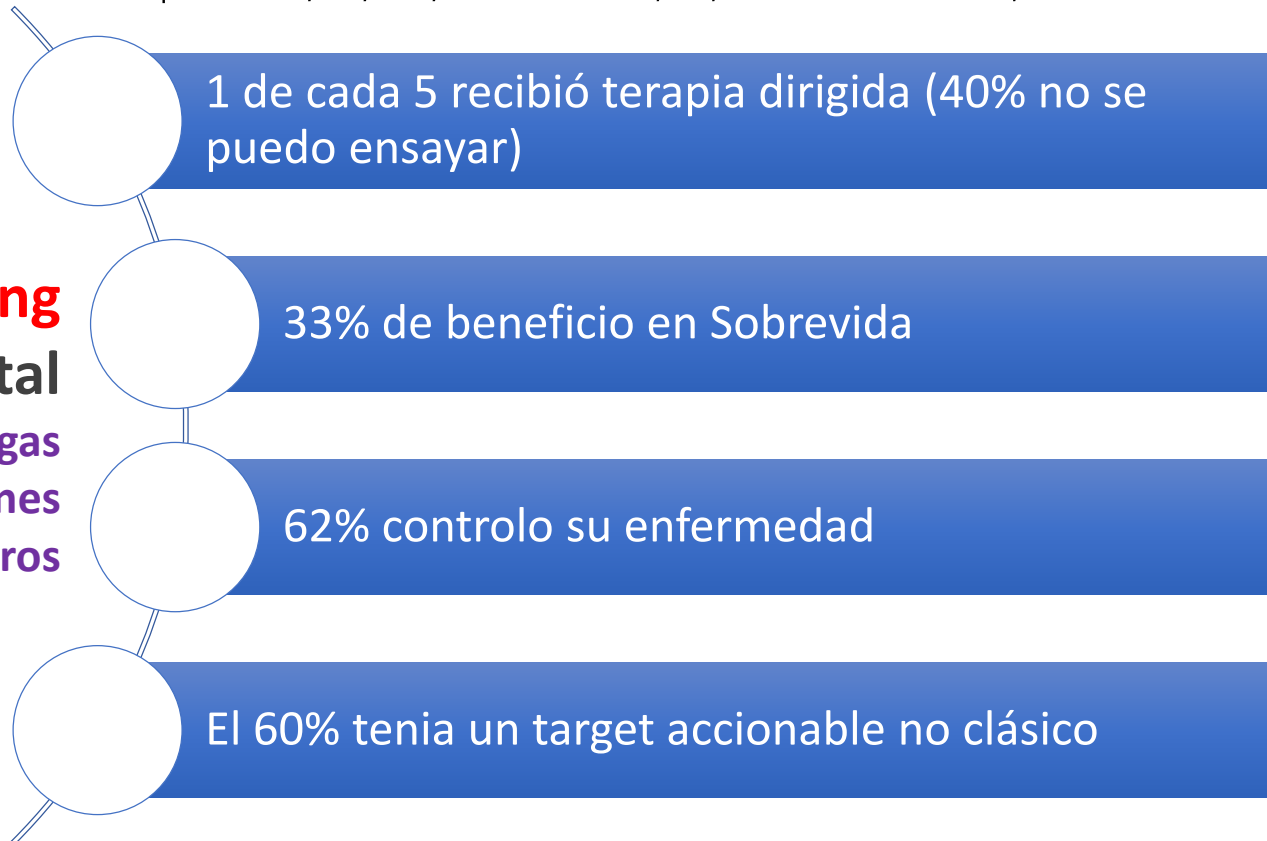
Multiple types of cancer

1 common genetic mutation (●)



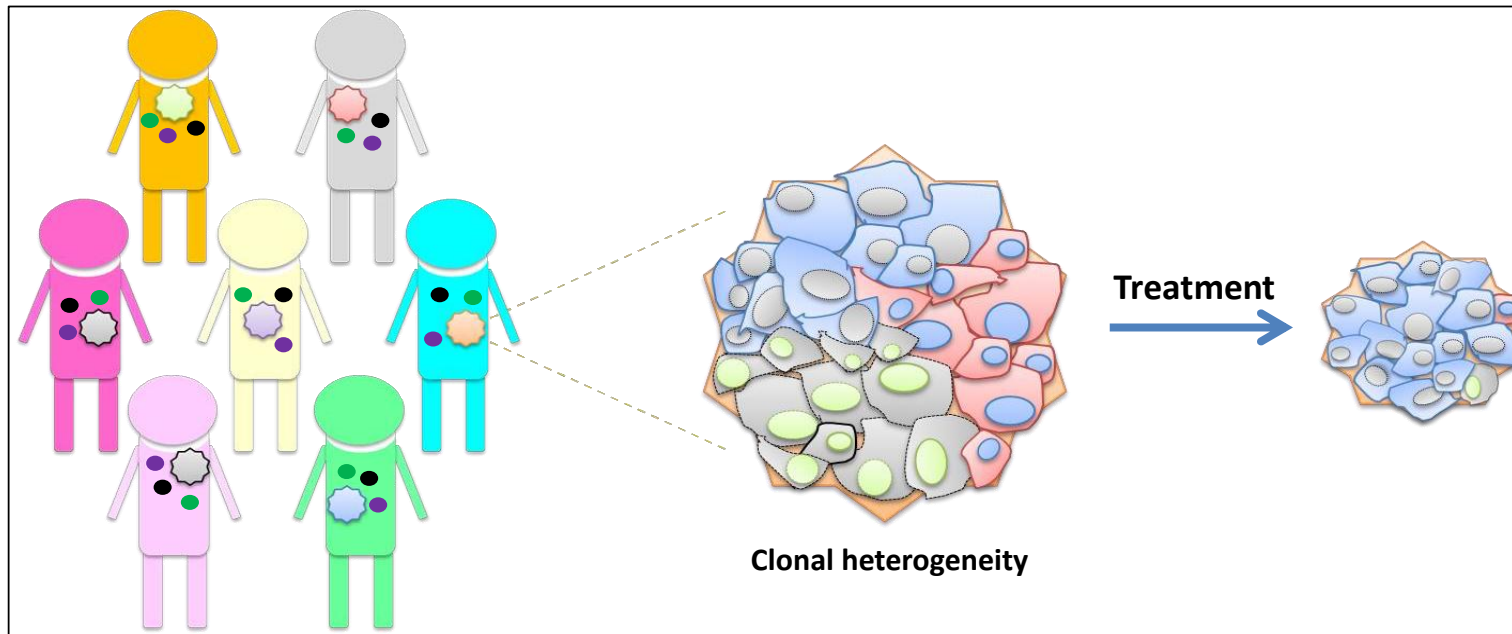
The cost of molecular-guided therapy in oncology: a prospective cost study alongside the MOSCATO trial

Arnaud Pagès, PharmD, MSc¹, Stéphanie Foulon, MD, MSc^{1,2}, Zhaomin Zou, PhD^{1,2},
 Ludovic Lacroix, PharmD, PhD^{3,4,5}, François Lemare, PharmD, PhD^{6,7}, Thierry de Baère, MD^{4,8},
 Christophe Massard, MD, PhD⁹, Jean-Charles Soria, MD, PhD^{4,9} and Julia Bonastre, PhD^{1,2}



Tumor Profiling
6% del costo total
 54% drogas
 35% hospitalizaciones
 5% otros

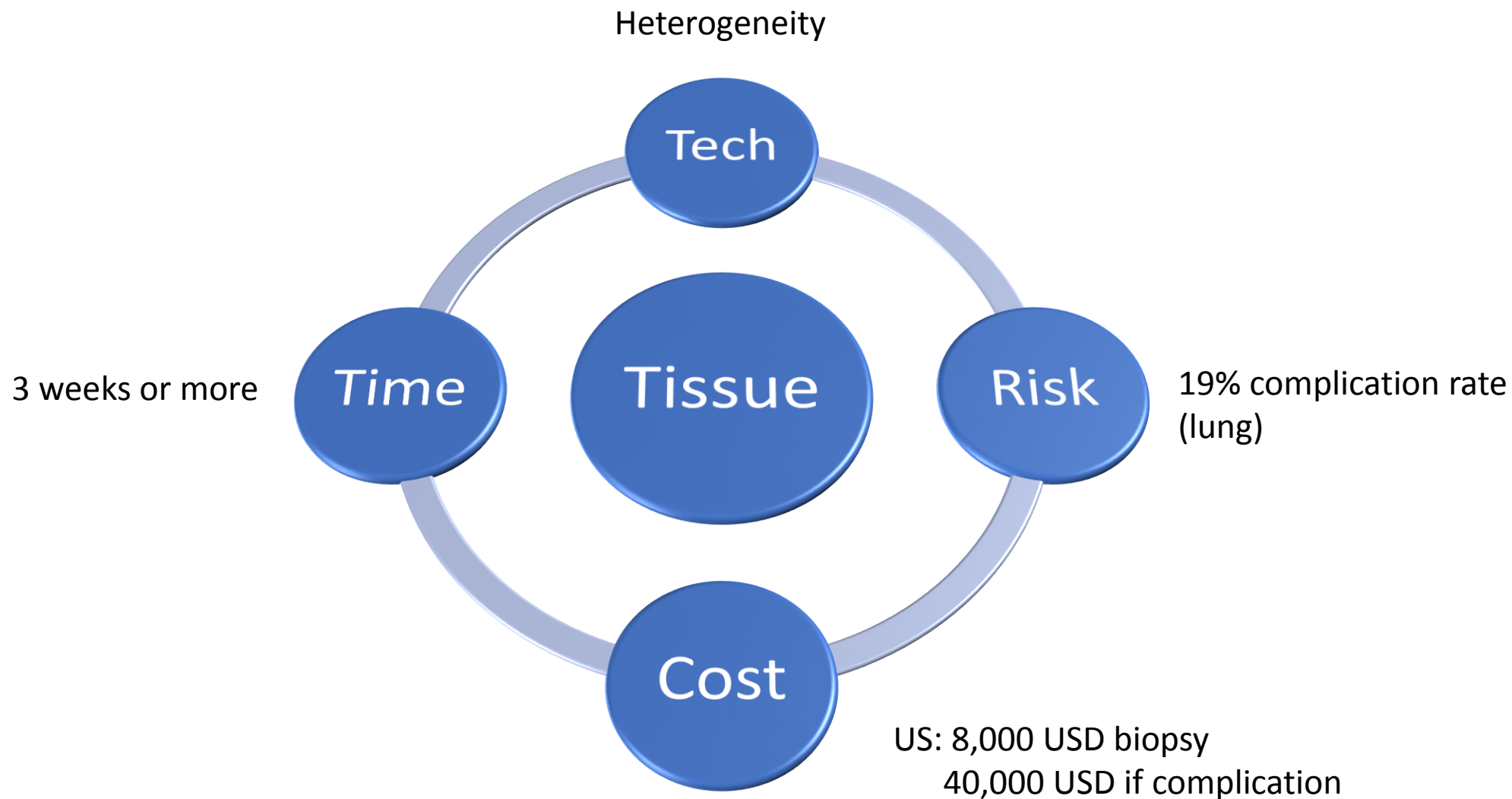
The issue with tissue: heterogeneity

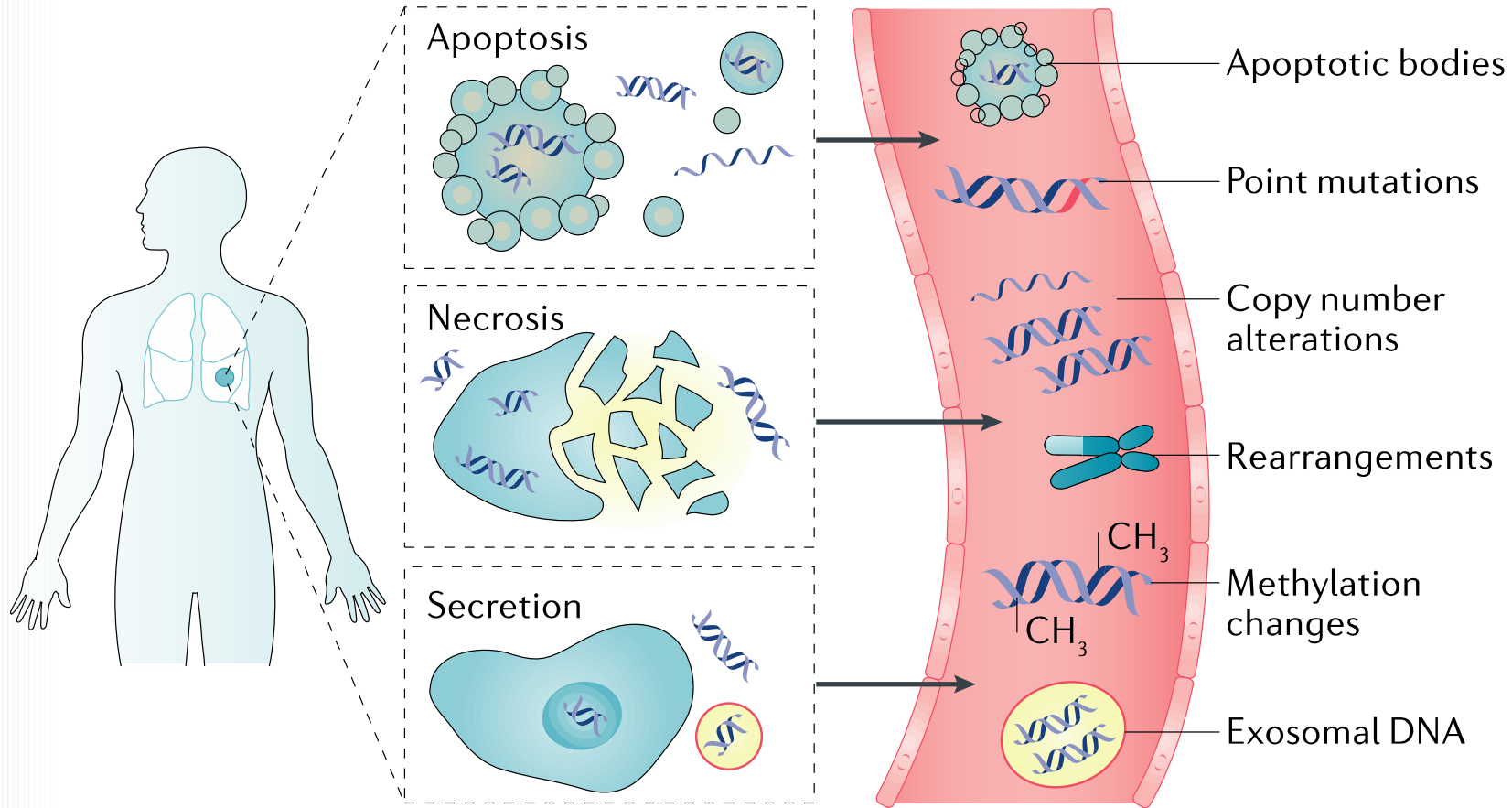


Inter-tumor heterogeneity

Intra-tumor heterogeneity

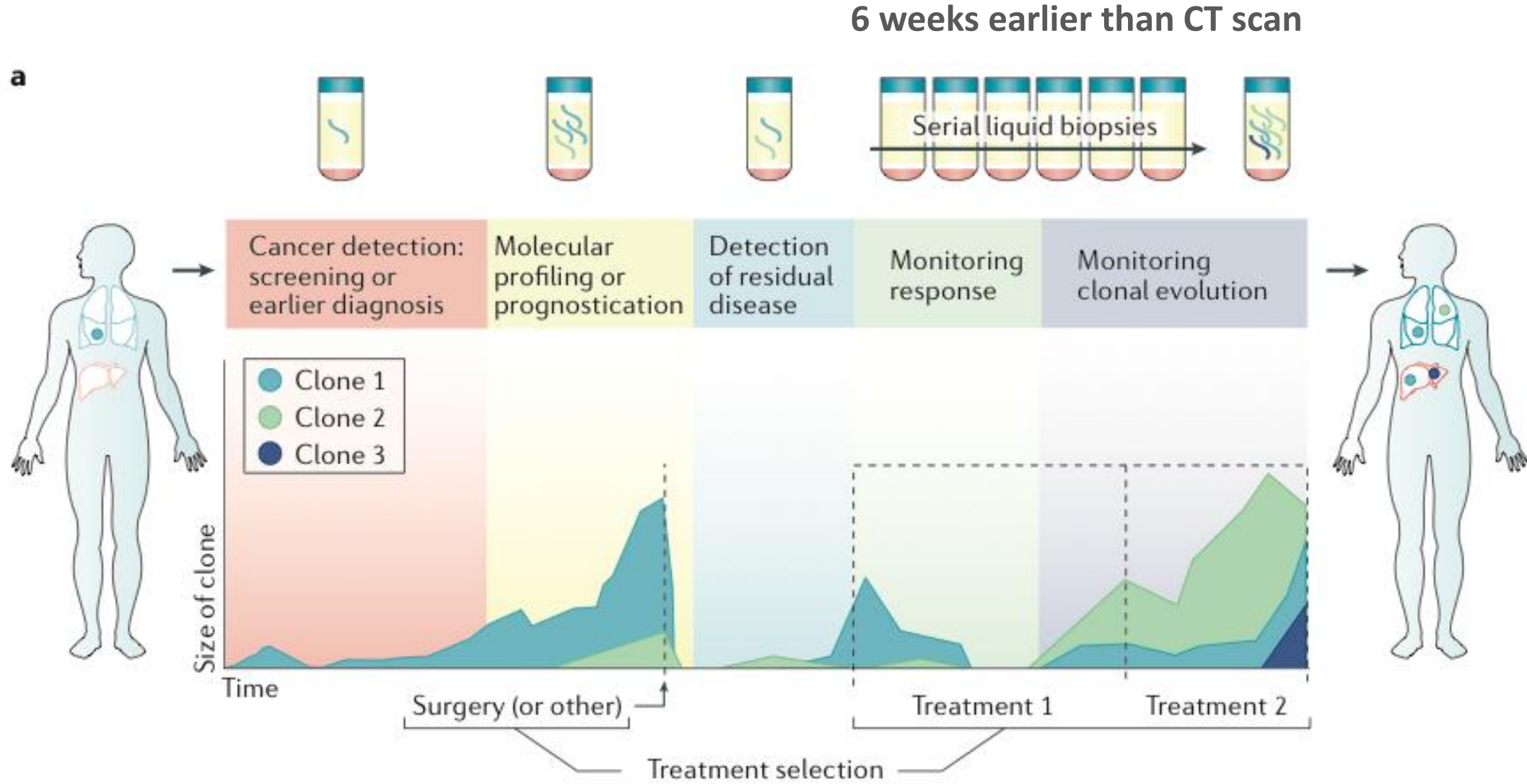
9 biopsias del mismo tumor
Solo compartieron el 39% de las mutaciones

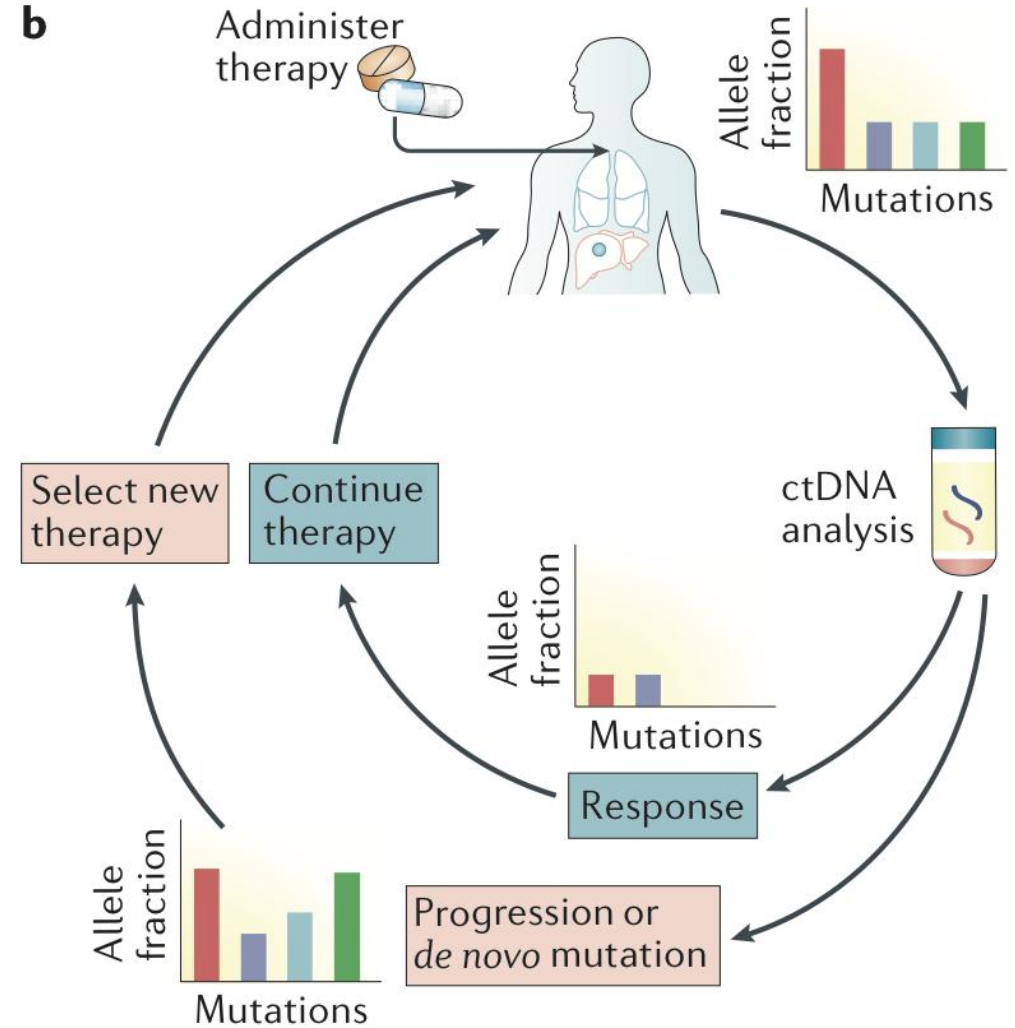
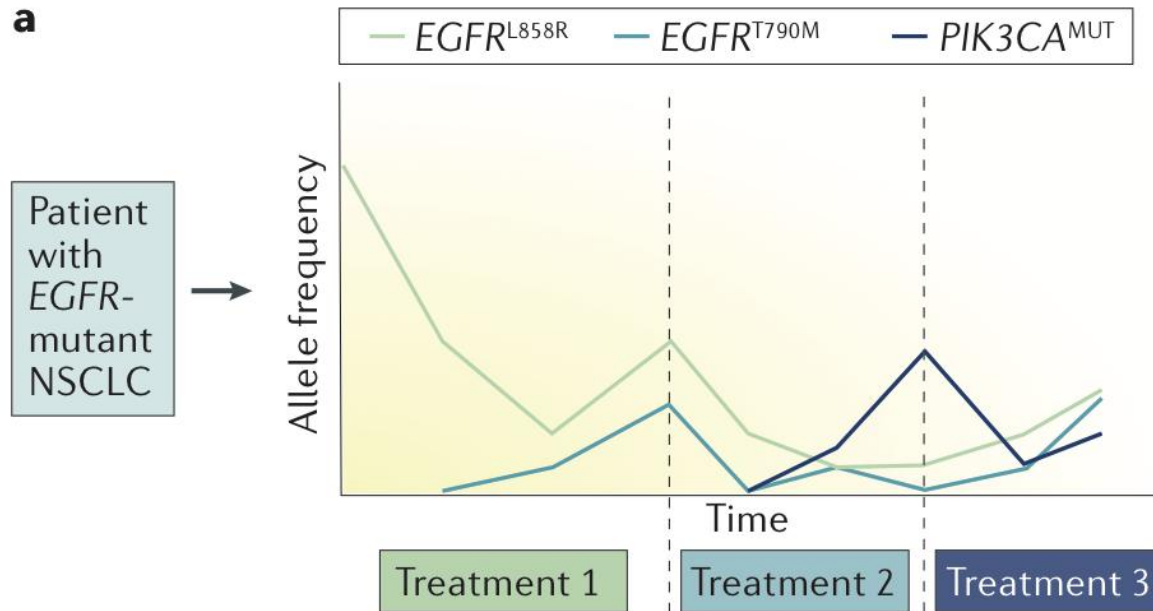


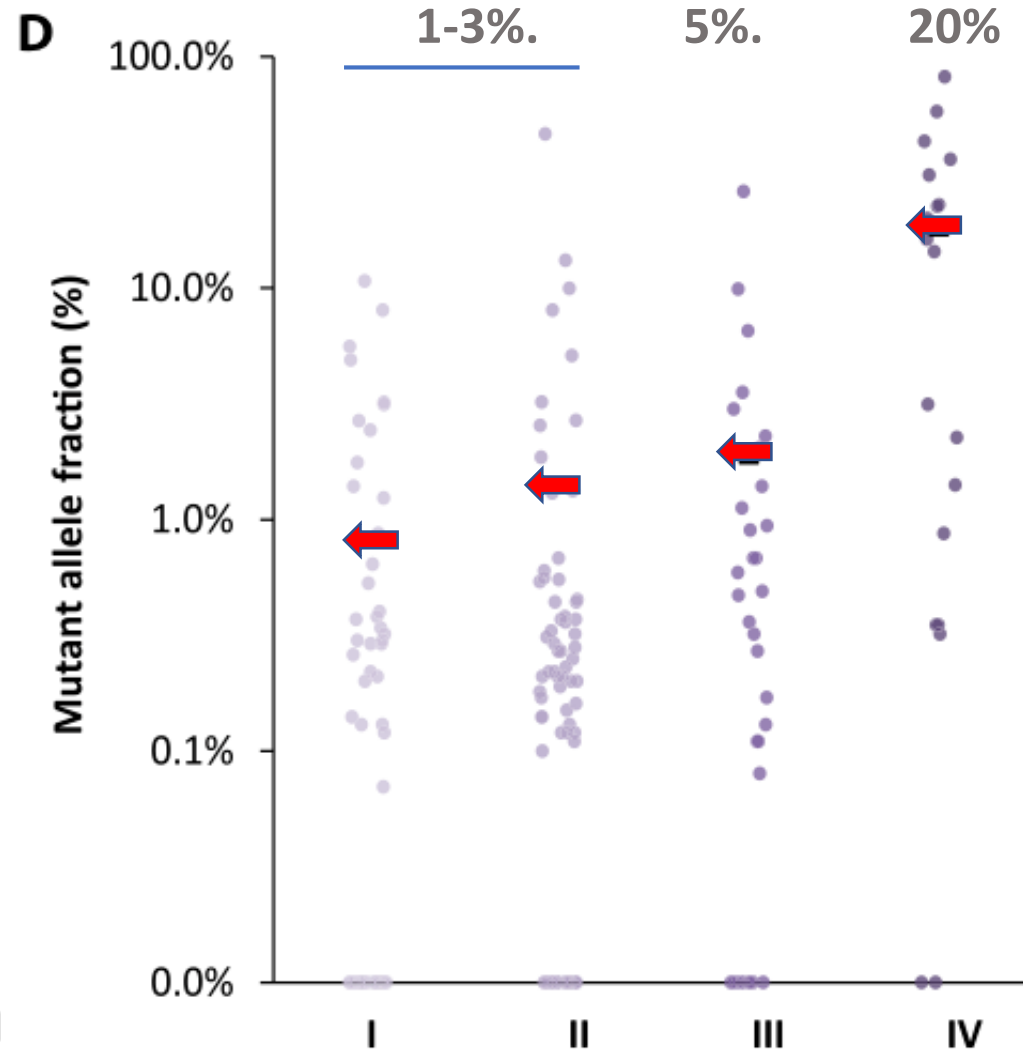
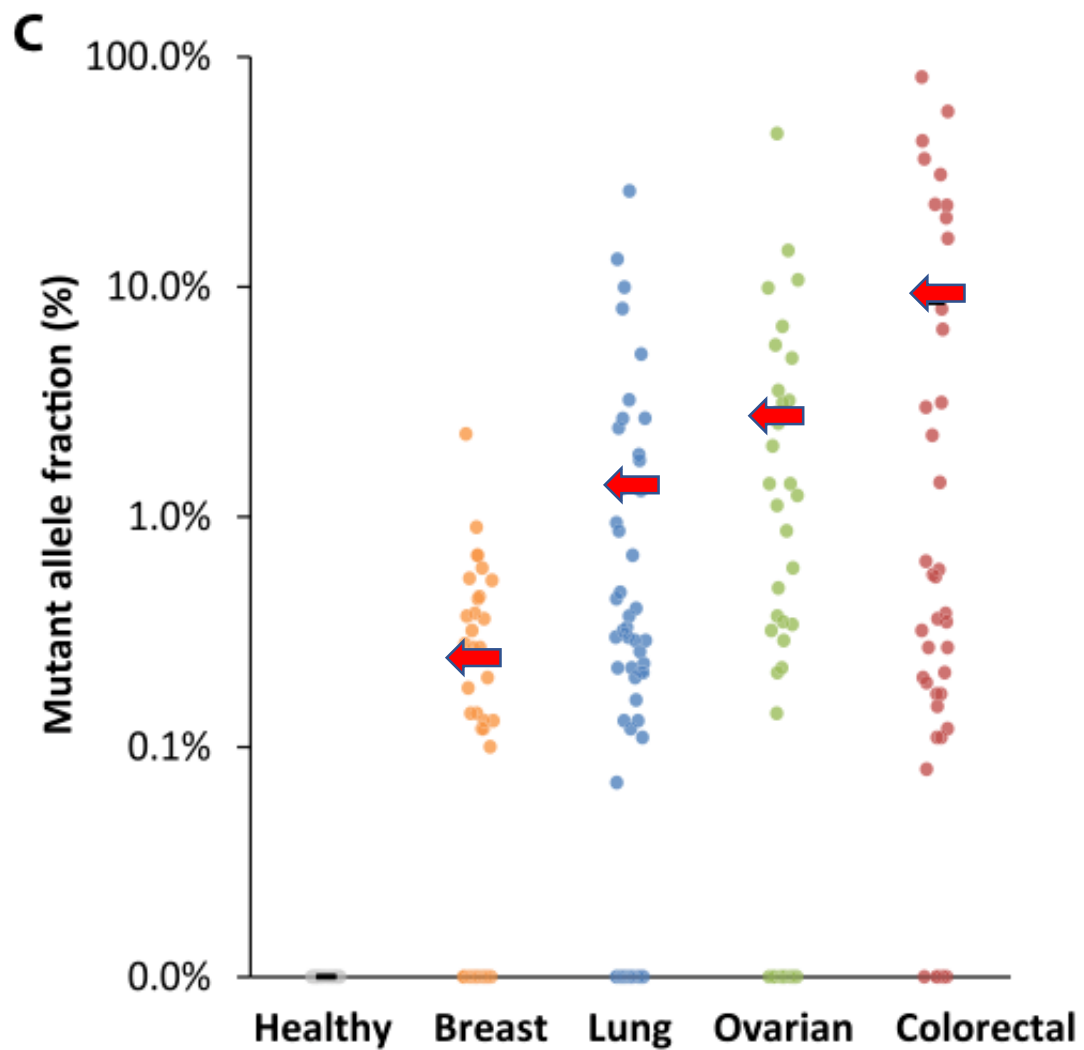


ctDNA vida media:
16 min a 2.5hs
Real-time Snapshot

- Diagnóstico
- Pronóstico
- Predicción







BREAST CANCER IN WOMEN: KNOW THE SUBTYPE

It's important for guiding treatment and predicting survival.



HR+/HER2- aka "Luminal A"

73% of all breast cancer cases

- Best prognosis
- Most common subtype for every race, age, and poverty level



HR-/HER2- aka "Triple Negative"

13% of all breast cancer cases

- Worst prognosis
- Non-Hispanic blacks have highest rate of this subtype at every age and poverty level



HR+/HER2+ aka "Luminal B"

10% of all breast cancer cases

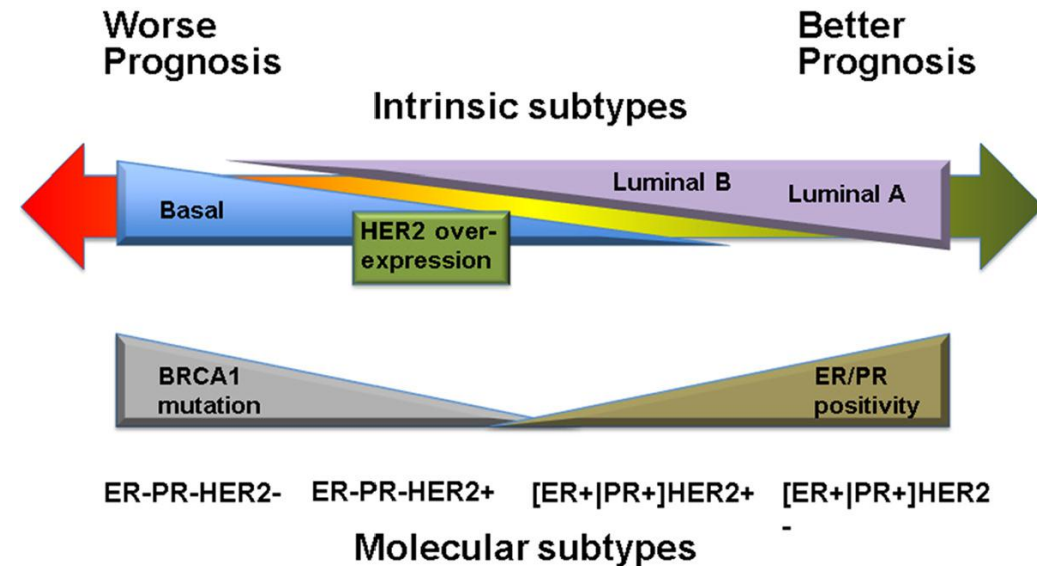
- Little geographic variation by state

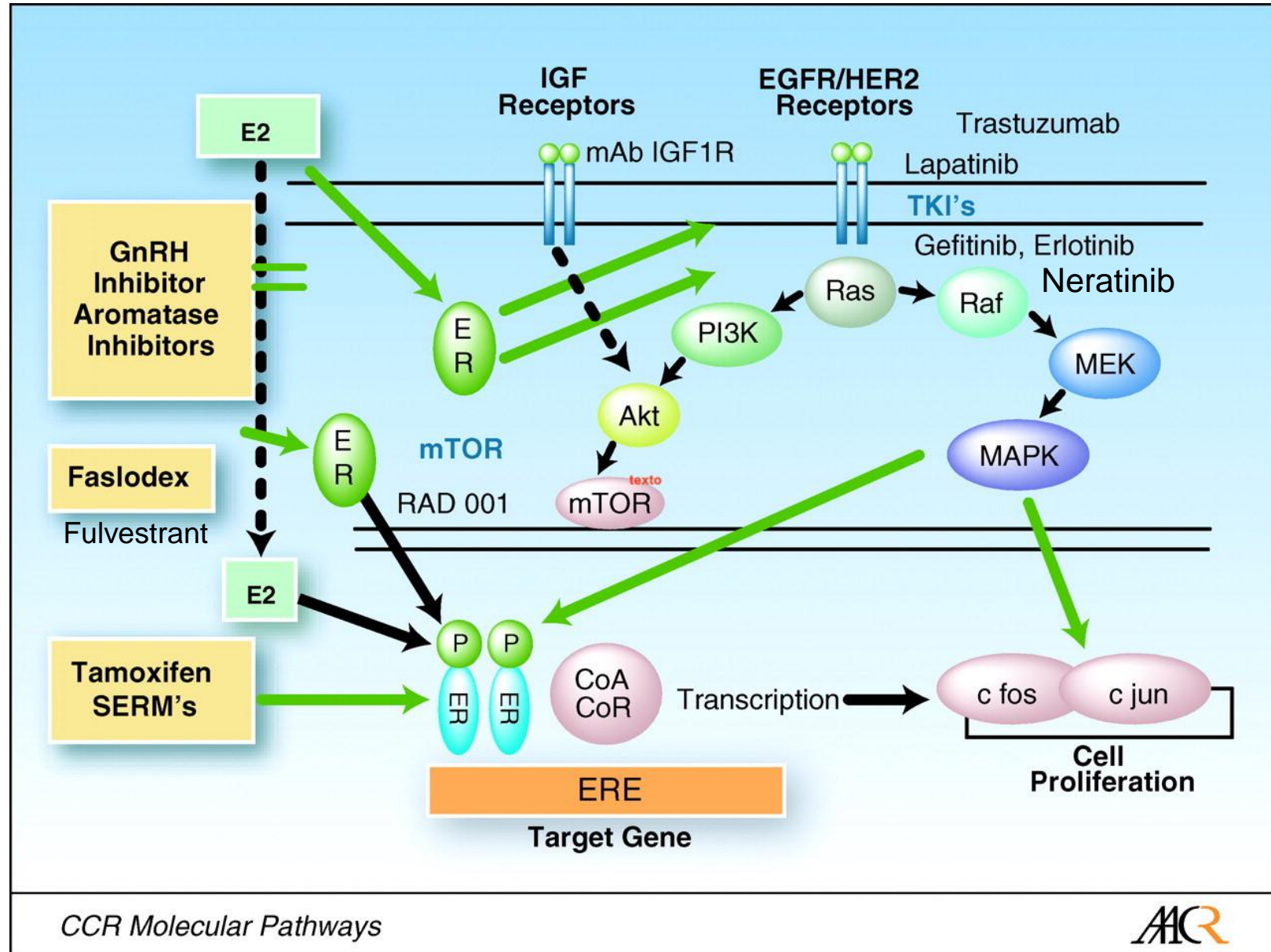


HR-/HER2+ aka "HER2-enriched"

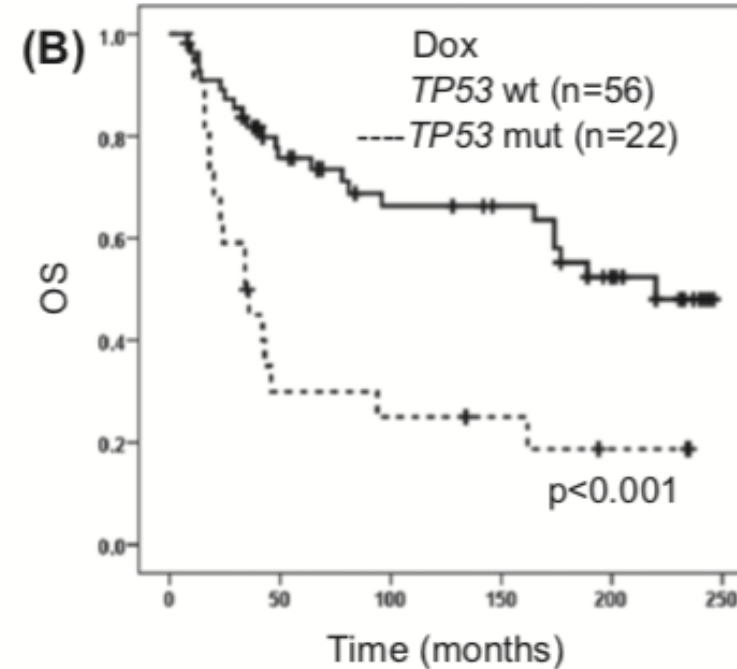
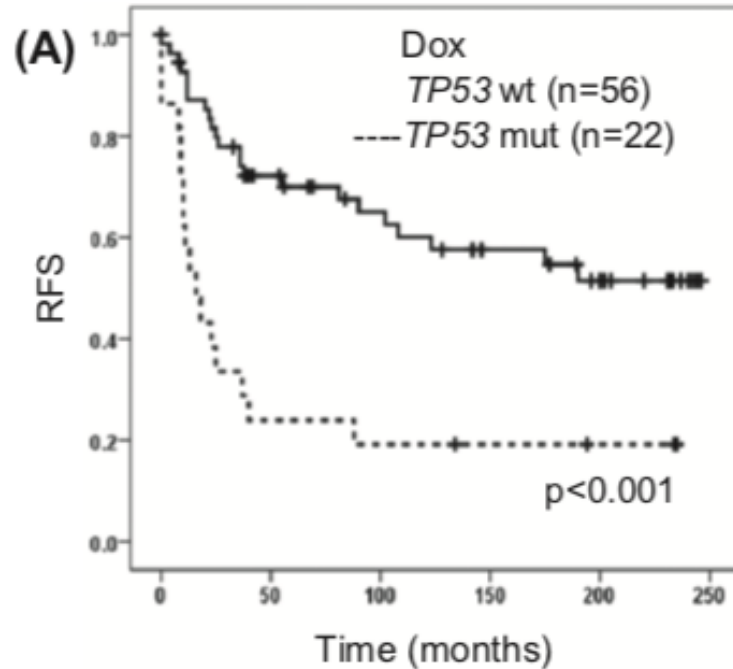
5% of all breast cancer cases

- Lowest rates for all races and ethnicities





TP53 status es pronóstico de sobrevida en pacientes con cáncer de mama avanzado



- ✓ TP53 *mut* aparece en todos los subtipos de MBC
- ✓ TP53 *mut* es pronóstico en HR+ con PIK3CA *mut*
- ✓ TP53 *mut* es peor pronóstico de OS en HR+

2014 TP53 status predicts long-term survival in locally advanced breast cancer after primary chemotherapy

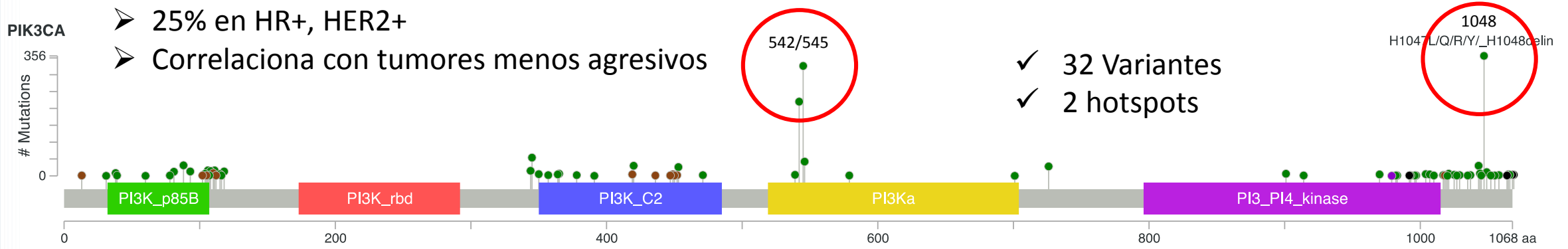
Hans P. Eikesdal, Stian Knappskog, Turid Aas & Per E. Lønning

2018 ORIGINAL REPORTS
Survival Outcomes by TP53 Mutation Status in Metastatic Breast Cancer

Funda Meric-Bernstam, Xiaofeng Zheng, Maryam Shariati, Senthil Damodaran, Chetna Wathoo, Lauren Brusco...

PIK3CA mut – La dinámica temprana en plasma (día 15 vs día 1, CRD15) predice el resultado de Palbociclib + Fulvestrant

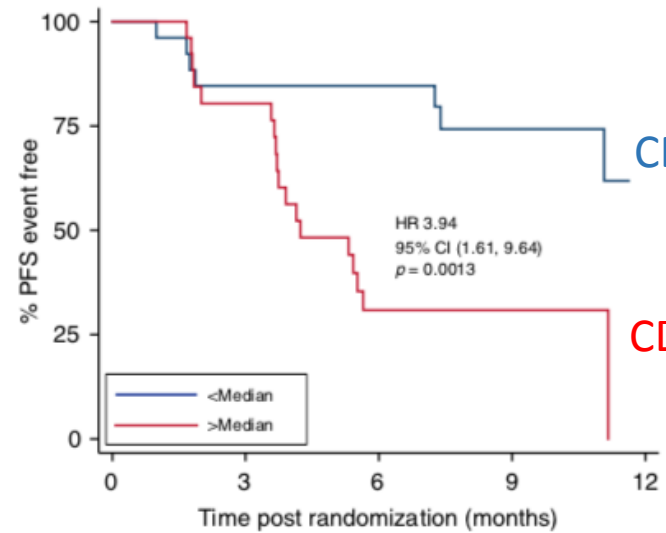
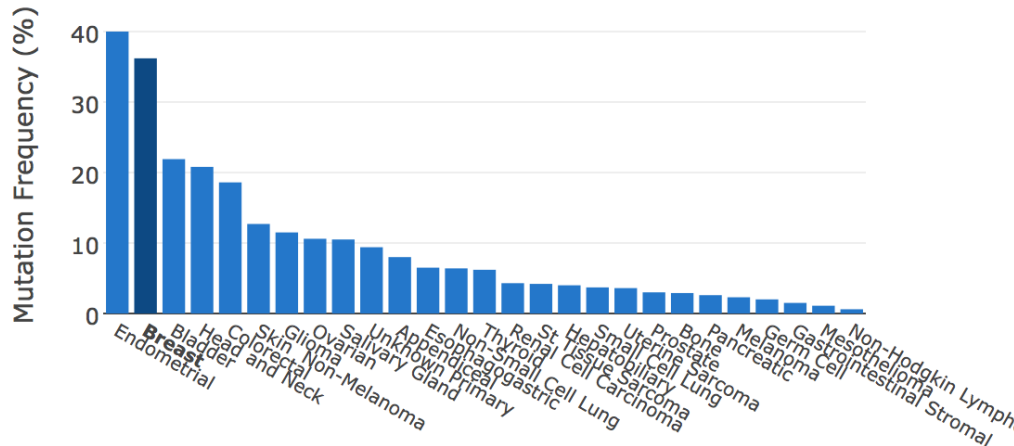
- 31% en HR+, HER2-
- 25% en HR+, HER2+
- Correlaciona con tumores menos agresivos



Hotspots

- ✓ 32 Variantes
- ✓ 2 hotspots

Cancer Types with PIK3CA Mutations



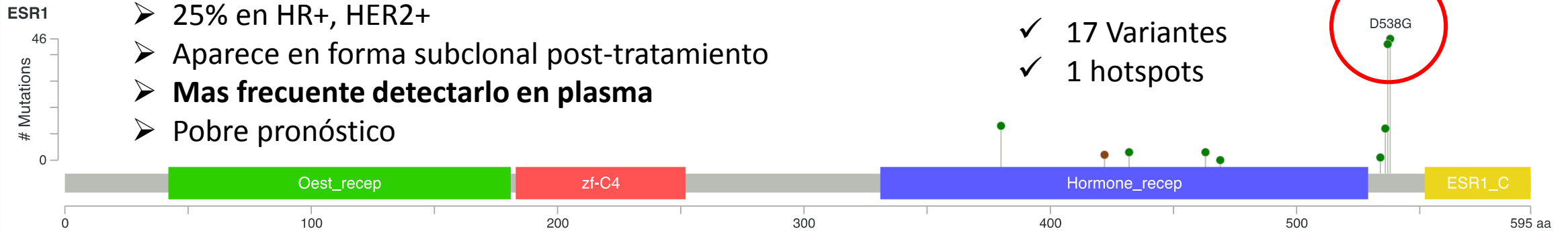
CDR15 bajo
Mut copies PIK3CA
day 15 to day 1
In plasma
CDR15 alto

ESR1 mut predice más débilmente **Palbociclib+Fulvestrant** pero su persistencia en plasma asocia a falta respuesta a **Tamoxifen** y resistencia a **inhibidor Aromatasa (Aromasin)**

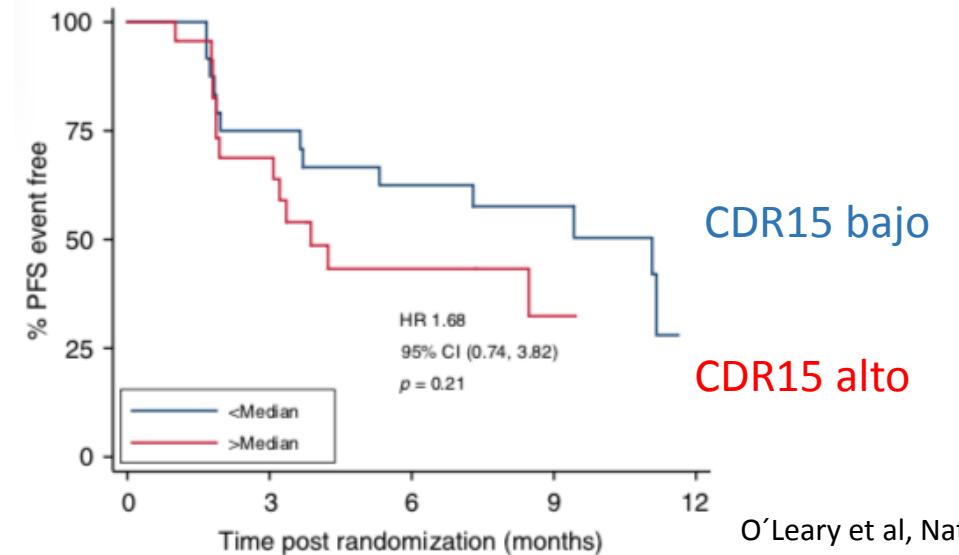
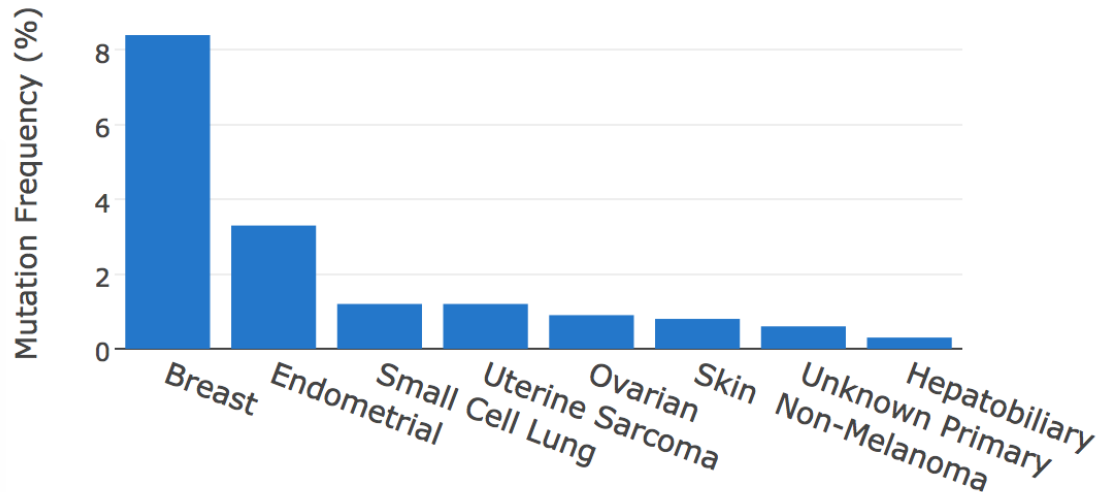
- 34% en HR+, HER2-
- 25% en HR+, HER2+
- Aparece en forma subclonal post-tratamiento
- **Más frecuente detectarlo en plasma**
- Pobre pronóstico

Hotspots

- ✓ 17 Variantes
- ✓ 1 hotspots

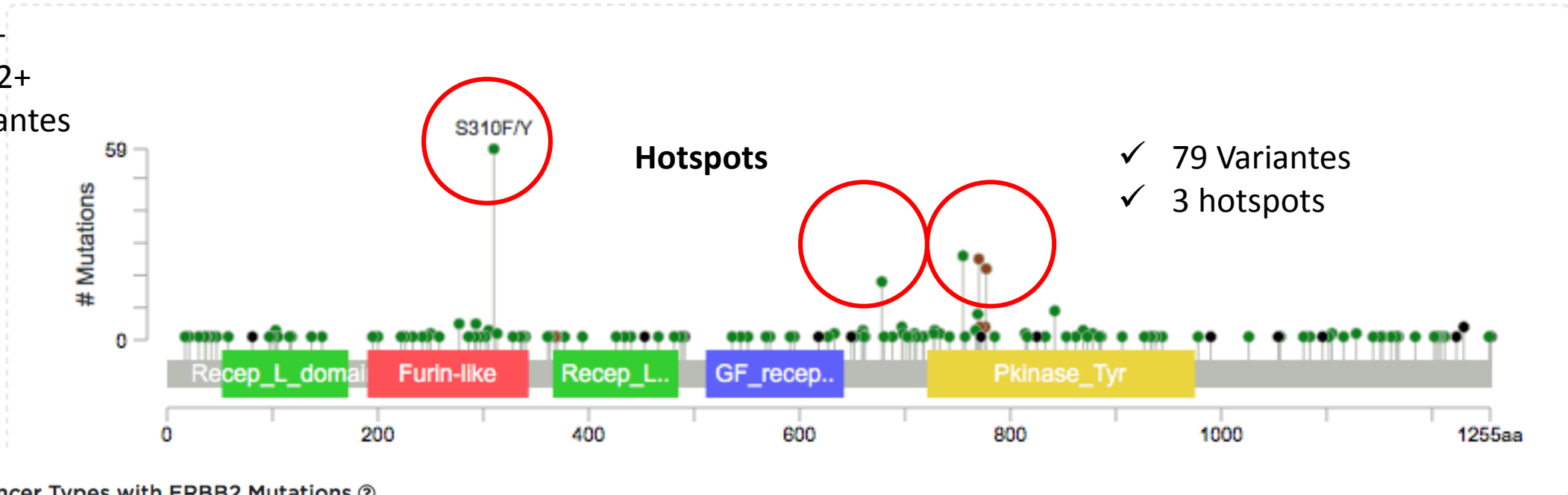


Cancer Types with ESR1 Mutations ?

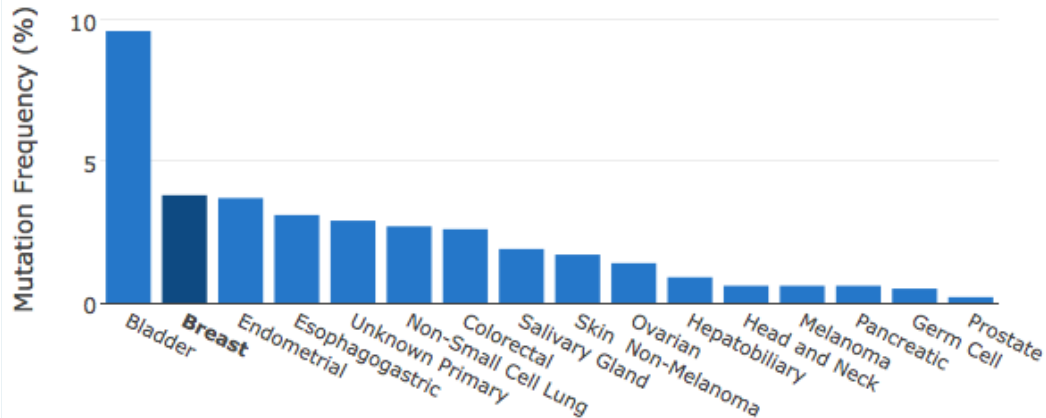


ERBB2 mut predice resistencia a Trastuzumab y sensibilidad a Neratinib

- 3% en HR+, HER2-
- 36% en HR+, HER2+
- Mutaciones activantes



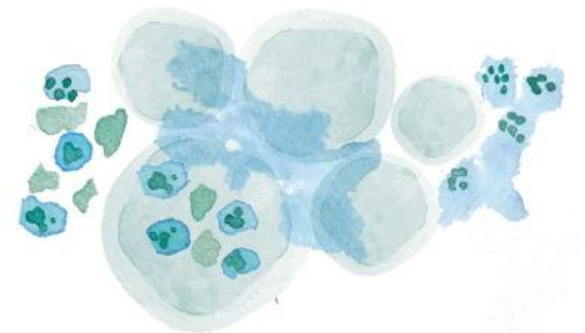
Cancer Types with ERBB2 Mutations ?



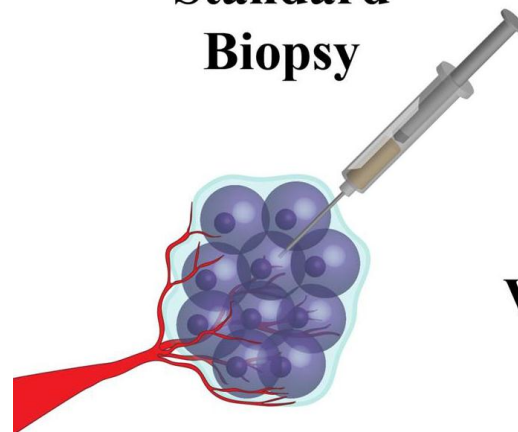


oncoSens

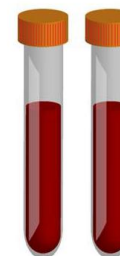
HÉRITAS BIOPSIA LÍQUIDA



**Standard
Biopsy**



**Liquid
Biopsy**



VS.

3 Pacientes/Tumor



Estadio IV

- ✓ Breast
- ✓ NSCLC
- ✓ CRC

T0

T0



Estadio IV
✓ Breast
✓ NSCLC
✓ CRC



Tratamiento
3 MESES

T1

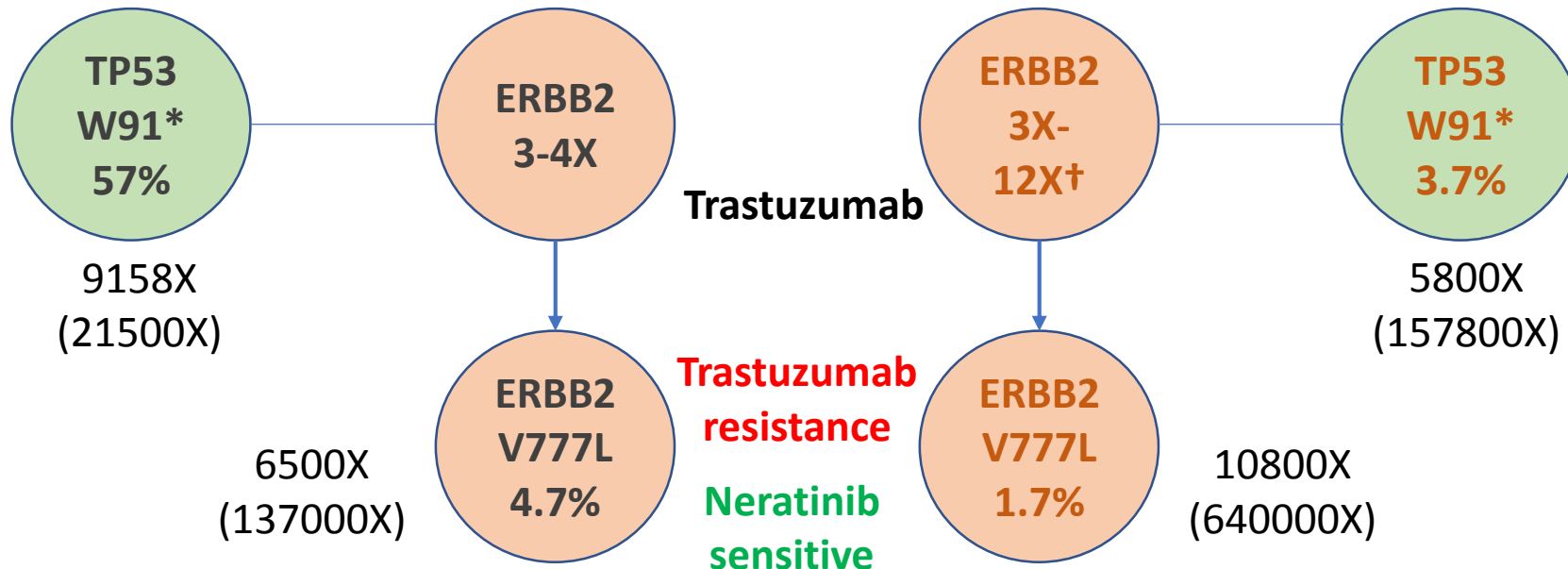
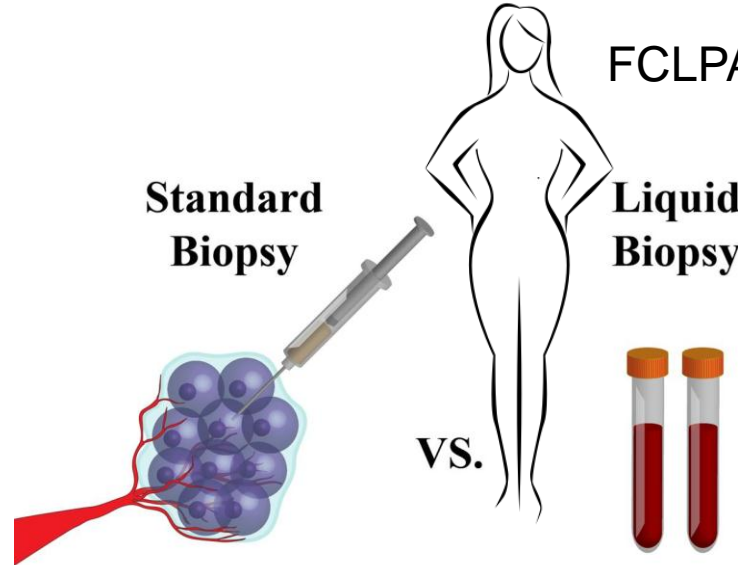


Evolución ctDNA
Monitoreo

Tipo de tumor	Gen	Region target
mama	AKT1	E17K
colon, pulmón	BRAF	EXON 11,12,7,15,16
pulmón	EGFR	Focal amplification, exon 12 (partial), 18, 19, 20, 21 (partial)-insertions, deletions and indels G719/A/C/S, L858R, L861Q, S7681, T790M
mama, pulmón	ERBB2	full CDS
colon, pulmón	KRAS	exon 2 (partial), 3 (partial), 4 - codons 12,13,19,59,61,117,146
colon, pulmón	MET	EXON 19
colon	NRAS	exon 2 (partial) 3 (partial) 4 - codons 12,13,59,61,117,146
pulmón, mama	PIK3CA	full CDS
pulmón	RET	exon 16 - M918T
pulmón, colon	TP53	full CDS
pulmón	ALK	hotspots (exons 5,8,15,18,19,20,22,23,24,25,29)
pulmón	CTNNB1	hotspots (exon 3)
mama	ERBB3	hotspots (exons 2,3,7,8,9,12,23,27)
mama	ESR1	hotspots (exons 2,5,9) intron 7
pulmón, colon	RAF1	hotspots (exon 7)

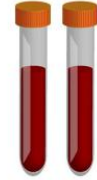
FCLPA 04071977

Patient Zero
 40 years, Dx 2015
 Stage IV
 Invasive Breast Cancer (Her+)
 Lung metastases

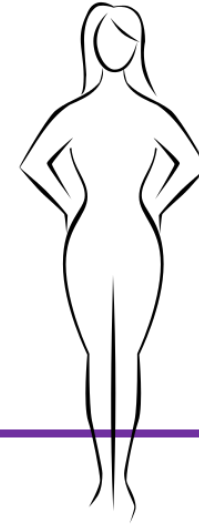


- Poor prognostic outcome
- BRCA1-related?
- Benefits: high-dose of Chemo (epirubicin)

Liquid Biopsy



T0



FCLPA 04071977

Patient Zero

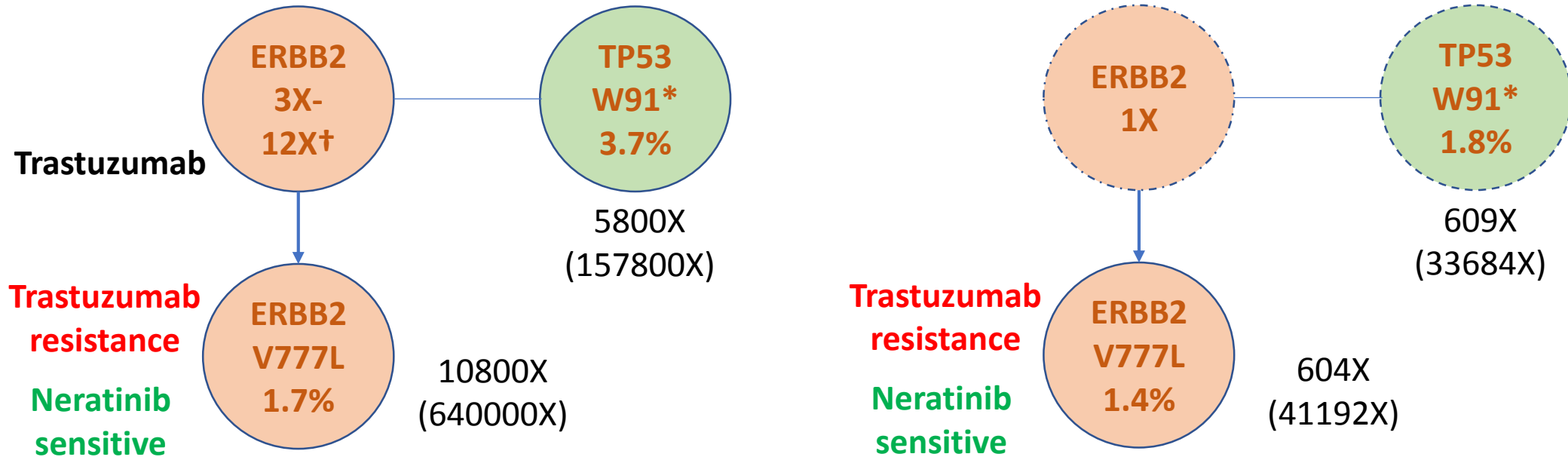
40 years, Dx 2015

Stage IV

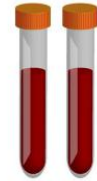
Invasive Breast Cancer (Her+)

Lung metastases

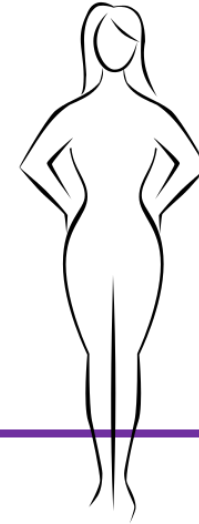
T1



Liquid
Biopsy



T0



FCLPA 04071977

Patient Zero

40 years, Dx 2015

Stage IV

Invasive Breast Cancer (Her+)

Lung metastases

T1

6/2017:

progresión de enfermedad (imágenes y marcador) **CA 15-3: 30**
Comienza Vinorelbine y Trastuzumab.

9/2017:

Progresión de enfermedad, aumento carga tumoral
25%.(a predominio pulmonar)
Sin respuesta a Trastuzumab

10/2017 :

Biopsia Guiada por TAC (T0)

01/2018

progresión de enfermedad a nivel
pulmonar y ganglionar mediastinal.
CA 15-3: 81

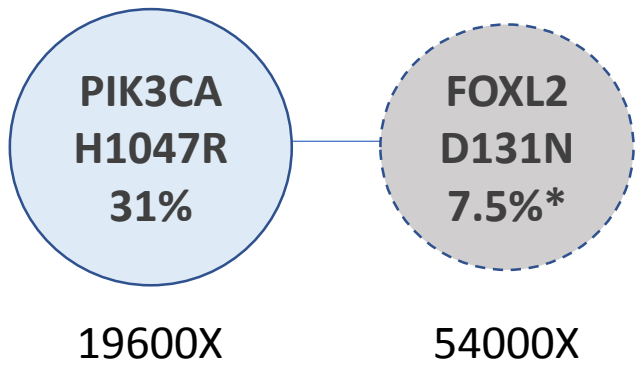
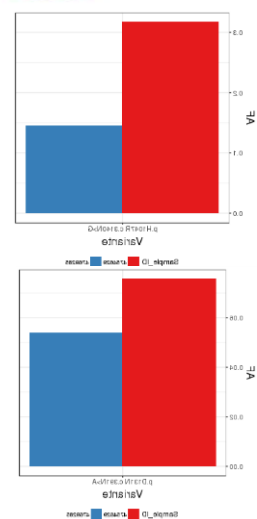
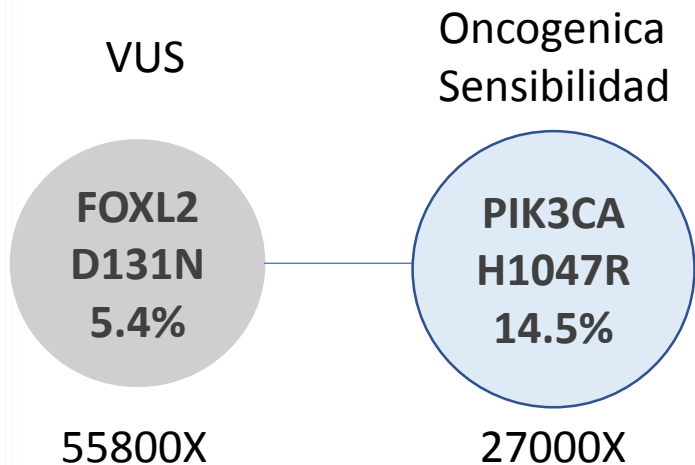
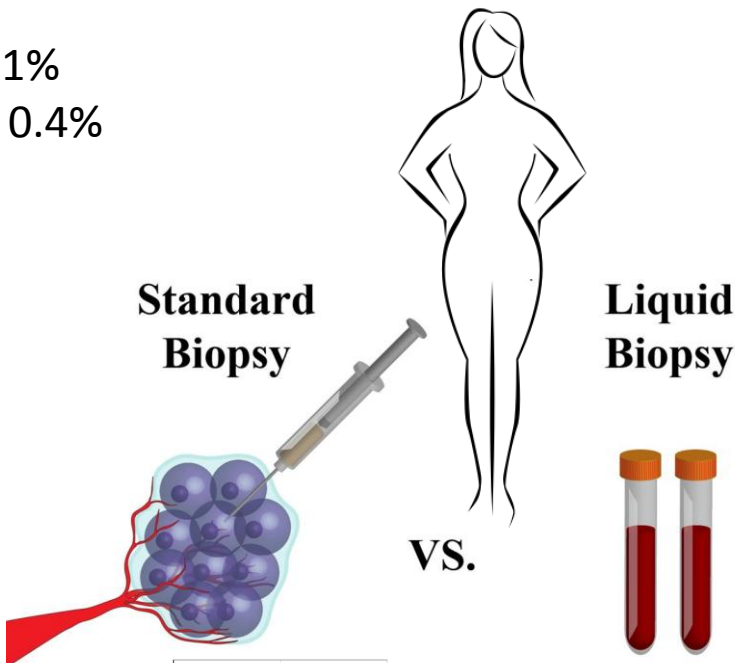
Inició paclitaxel semanal.



Tissue cut-off : 1%
 Plasma cut-off: 0.4%

FPAPE 16111976

Age: 41 years
 Dx: 2011 Breast cancer
 T0: 10/2017
 Stage IV
 Invasive Breast cancer
 Liver, Bone metastases



NO relevant Variants found in:

- AKT1
- ERBB2

55800X

27000X

19600X

54000X



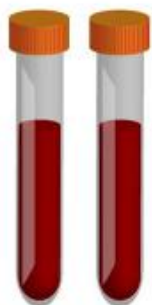
Tissue cut-off : 1%
Plasma cut-off: 0.4%



FPAPE 16111976

Age: 41 years
Dx: 2011 Breast cancer
T0: 10/2017
Stage IV
Invasive Breast cancer
Liver, Bone metastases

Liquid Biopsy



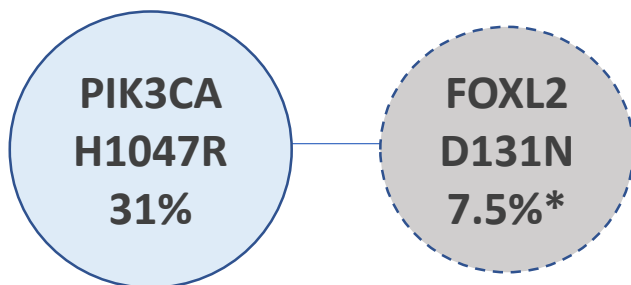
T0

7.11 ng/ul

3 meses

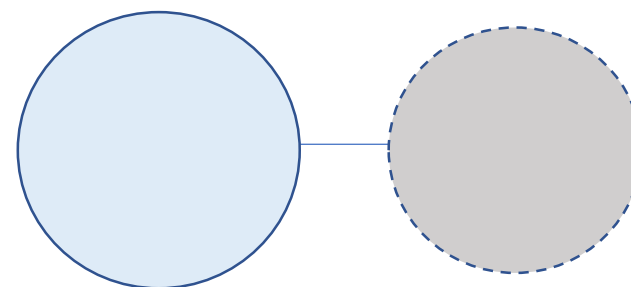
T1

1.46 ng/ul



19600X

54000X



Clínica???
Interpretación?
Interacción analista-oncólogo

FPAPE 16111976

Age: 41 years

Dx: 2011 Breast cancer, HR+, Her2-

T0: 10/2017

Stage IV

Invasive Breast cancer

Liver, Bone metastases



T0

T1

5/2017:

Inicia fulvestrant y zometa + Palbociclib x3C,
10/17,
con progresión hepática y ósea.

10/2017: (T0)

Bx hepática metástasis de carcinoma
mamario. RE 90%, RP 10%, Her2 negativo
(por FISH), Ki67 20%.

CA 15-3: 236

12/2017

Nueva línea con_Paclitaxel 90 mg/m² DT 135 mg
día 1, 8 y 15 + bevacizumab 10 mg/kg DT 500 mg
día 1 y 15 cada 28 días.

02/2018 Control Post C3

- TC TAP: - **Disminución** de tamaño de las
lesiones de aspecto secundario a nivel del hígado,
lesiones óseas estables + beneficio clínico.

CA 15-3: 128.8



@HeritasArg

