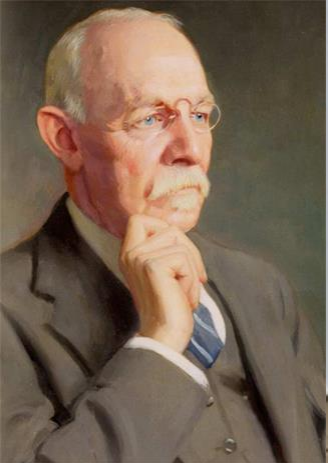


# Hitos Oncológicos

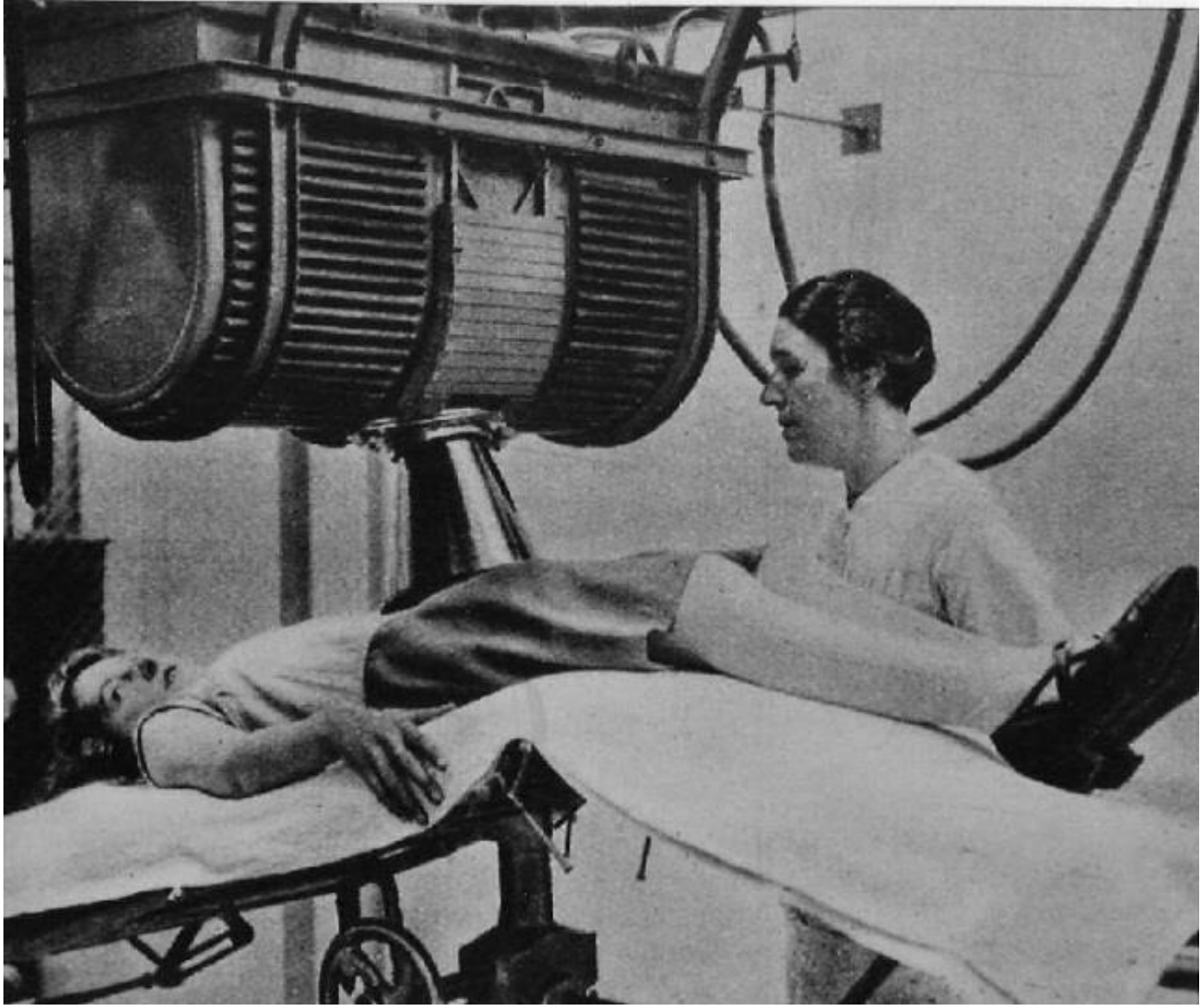
## El nuevo paradigma



David López Sánchez  
Unidad Oncología Médica  
27 de Febrero de 2015



REGULATIONS for the THEATRE  
Approved by the Board of the National Association of Actors and Actresses  
The Board of the Actors and Actresses of the Theatre  
The National Association of Actors and Actresses  
The National Association of Actors and Actresses  
The National Association of Actors and Actresses



# Tratamientos sistémicos

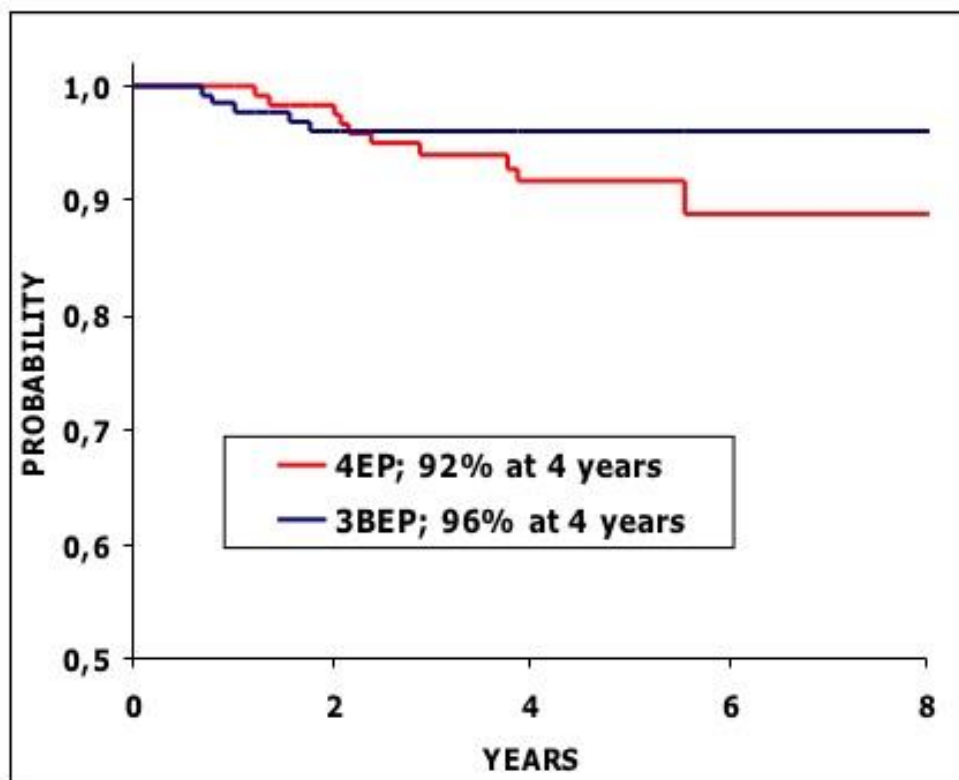


# Tumores germinales



# GETUG T93 trial: 3 BEP vs 4 EP

Overall Survival



**BEP:**  
**5 deaths**

**EP:**  
**12 deaths**

**Logrank**  
**p=0.14**

**Median follow-up = 51 months**

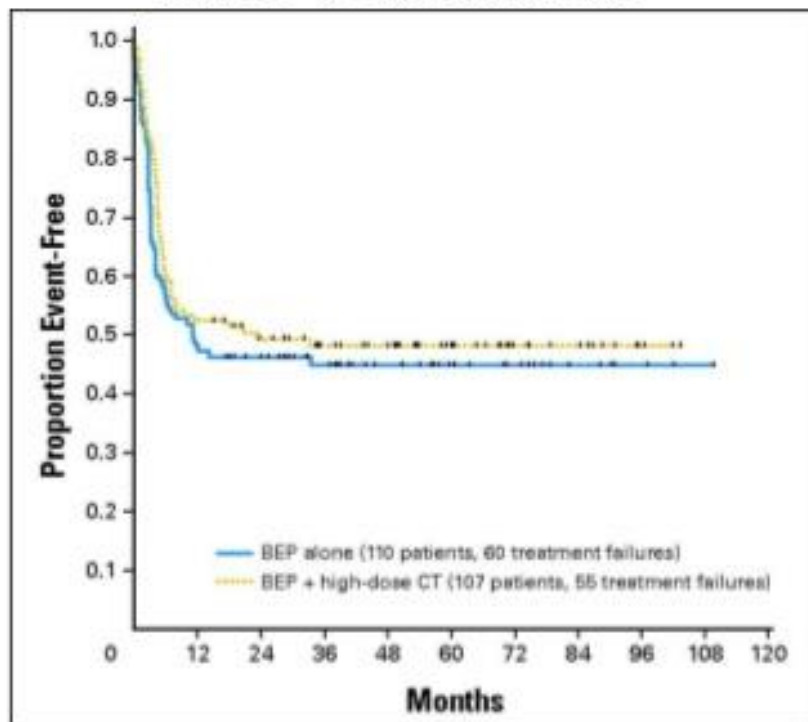
Culine et al., Ann Oncol 2007

# Phase III intergroup US trial

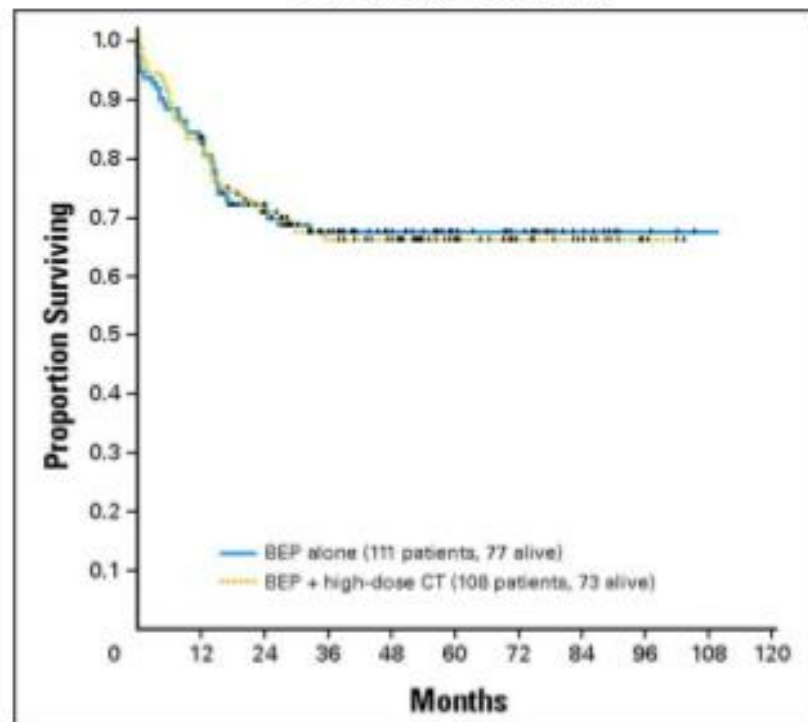
Intermediate/poor risk pts  
 n= 219



Time to treatment failure



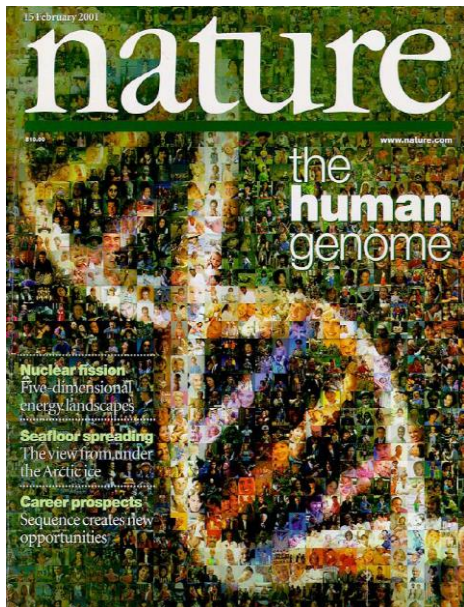
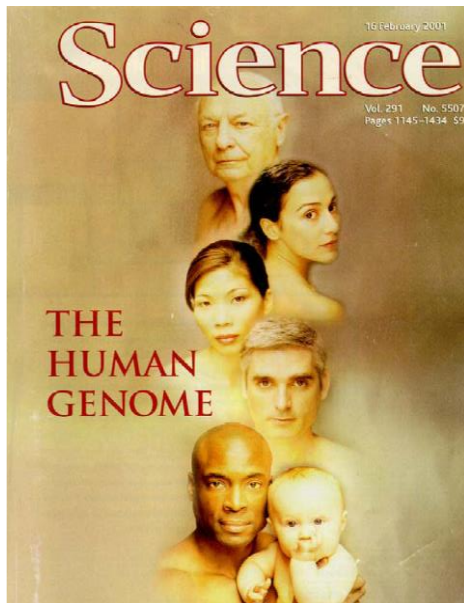
Overall survival



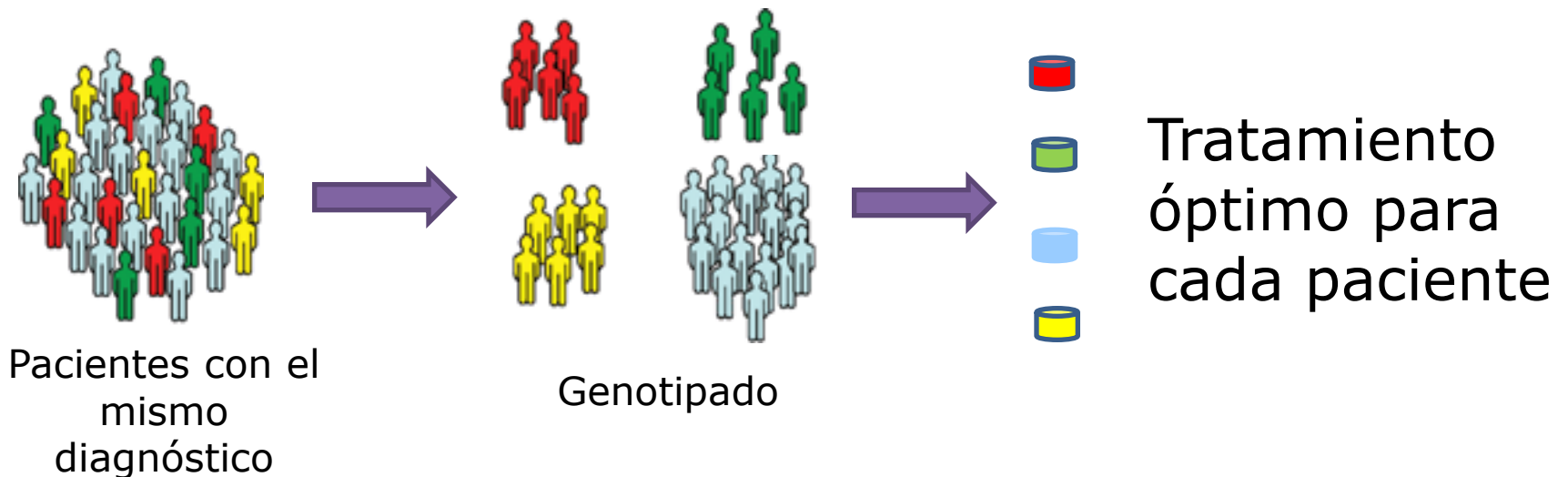
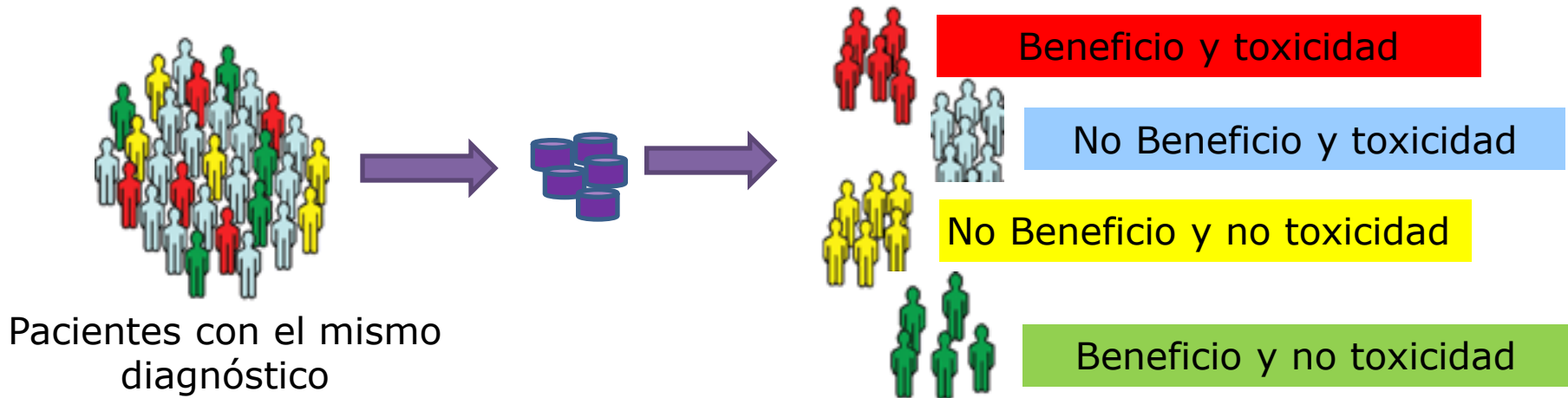




Todos tenemos el mismo número de genes y sin embargo somos completamente distintos

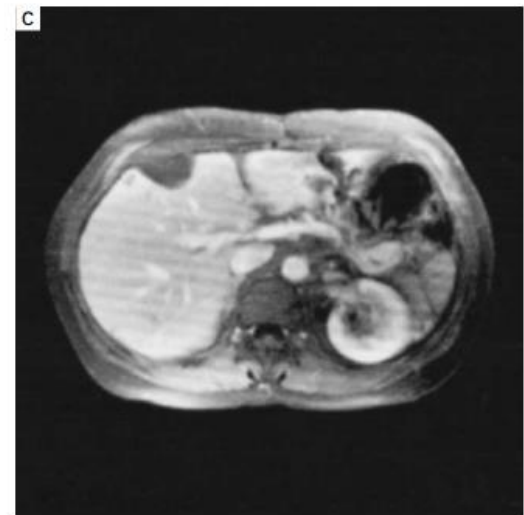
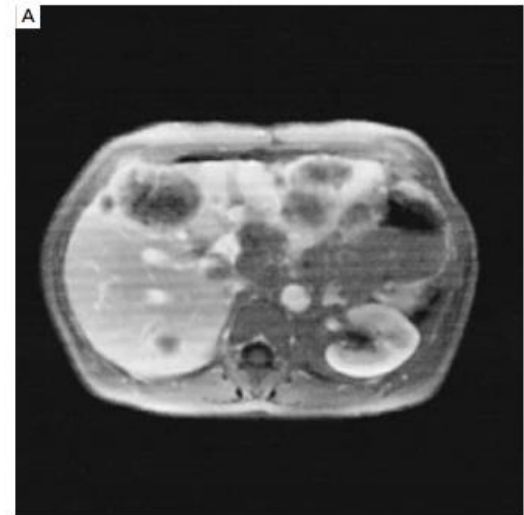
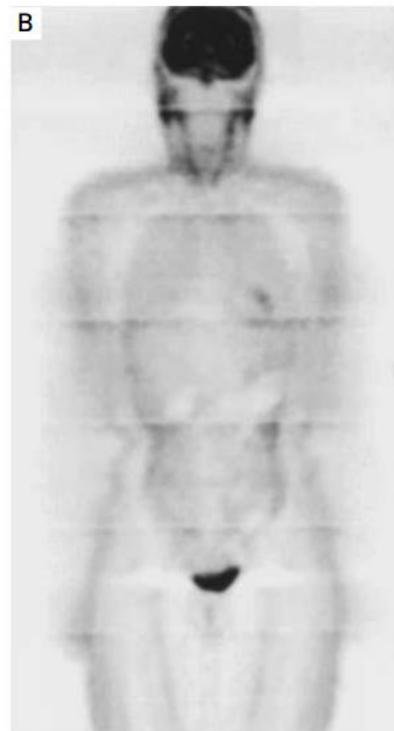


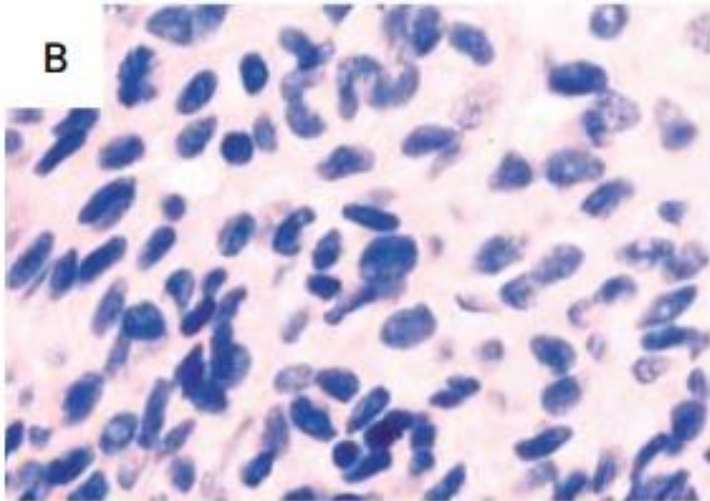
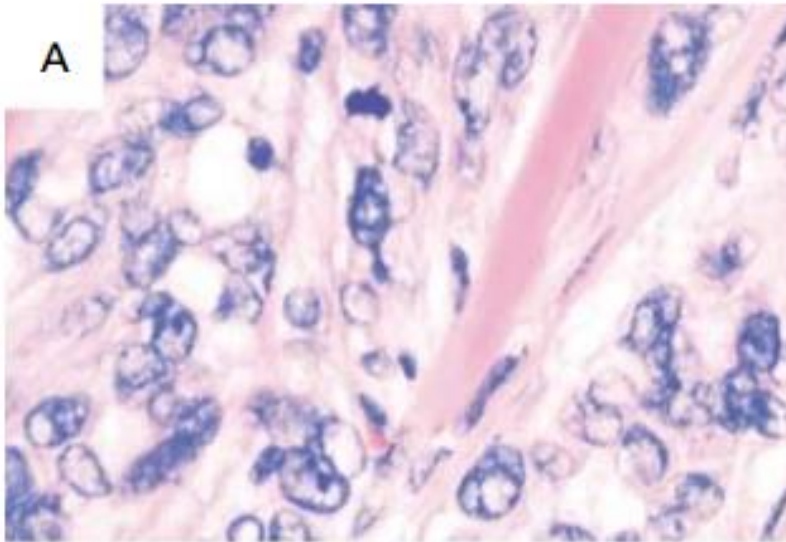
# Medicina personalizada



Brief Report

**EFFECT OF THE TYROSINE  
KINASE INHIBITOR STI571  
IN A PATIENT WITH A METASTATIC  
GASTROINTESTINAL STROMAL TUMOR**





MAY 28, 2001 www.time.com AOL Keyword: TIME

# TIME

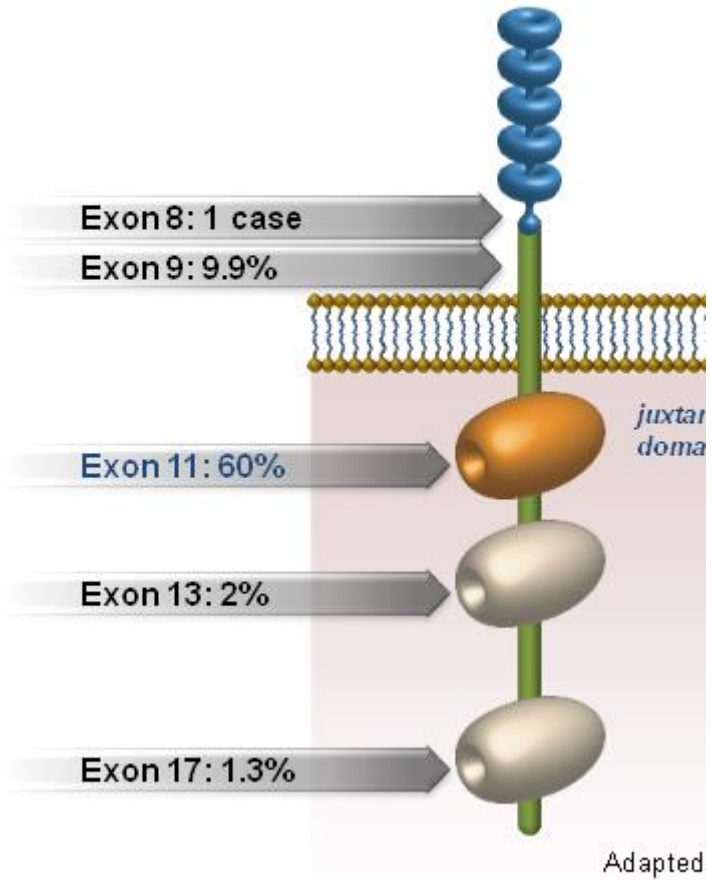
THERE IS NEW **AMMUNITION**  
IN THE WAR AGAINST  
**CANCER.**  
**THESE ARE THE BULLETS.**

Revolutionary new pills like **GLEEVEC** combat cancer by targeting only the diseased cells. Is this the breakthrough we've been waiting for?

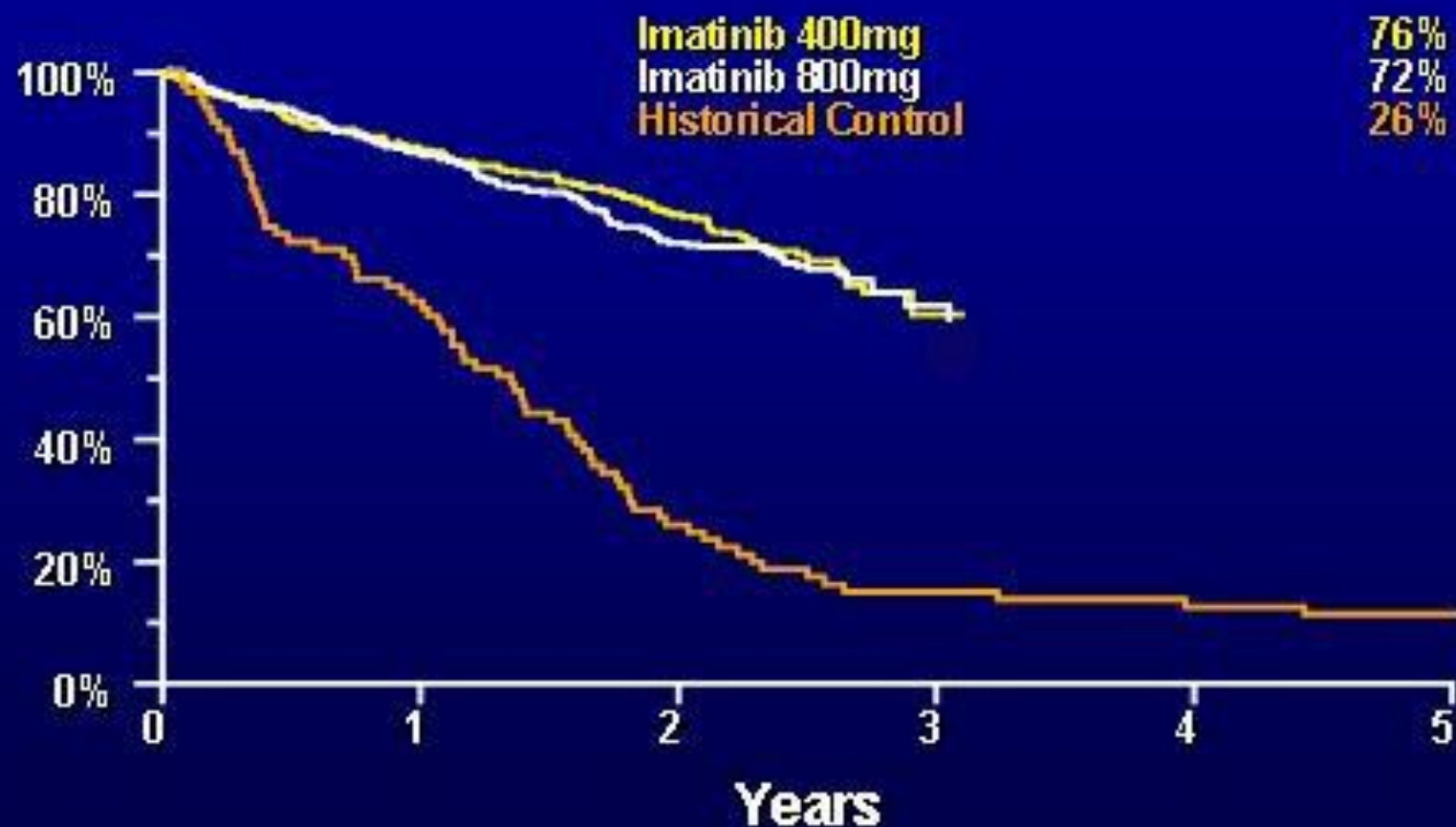


# GIST

## KIT Mutations

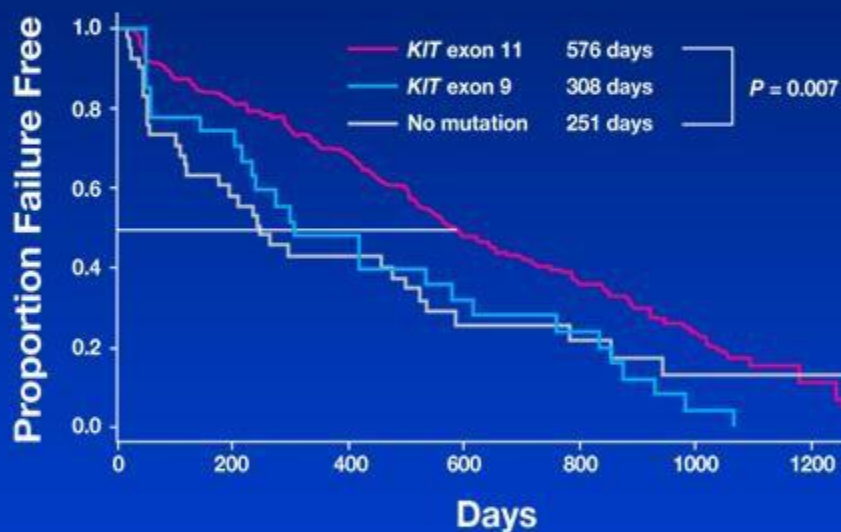


# Imatinib Triples Overall Survival in GIST Patients

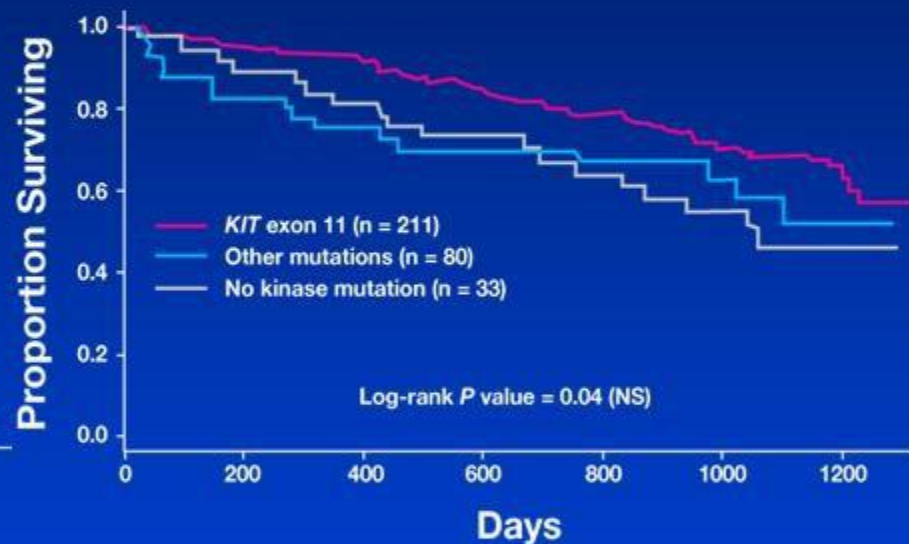


# Phase 3 Intergroup S0033 Study: PFS and OS by Mutational Status

## Progression-Free Survival



## Overall Survival

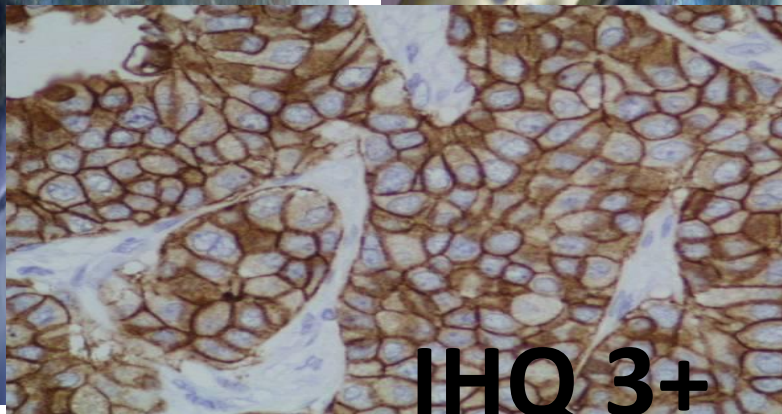
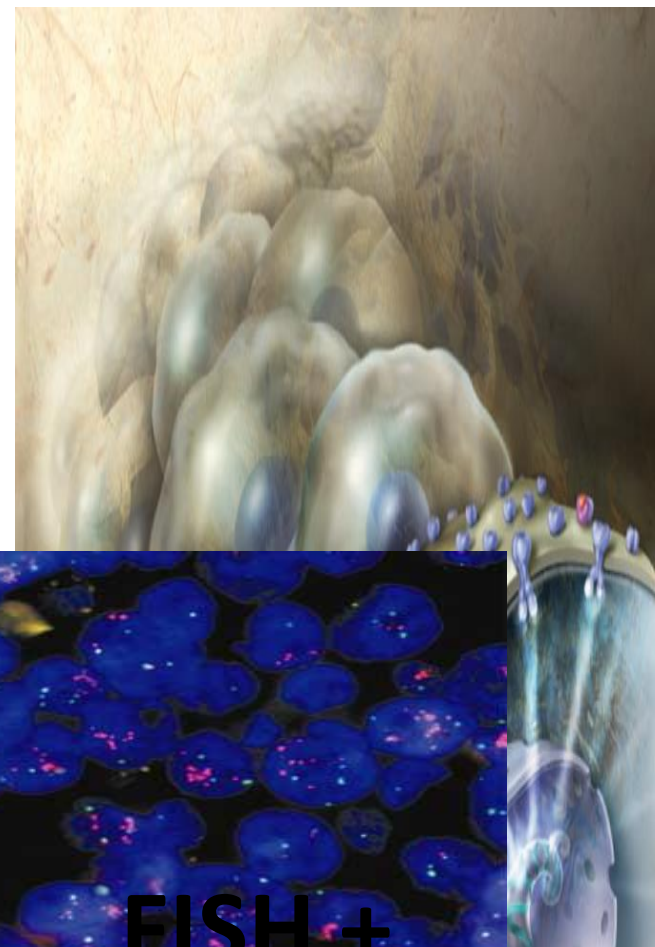
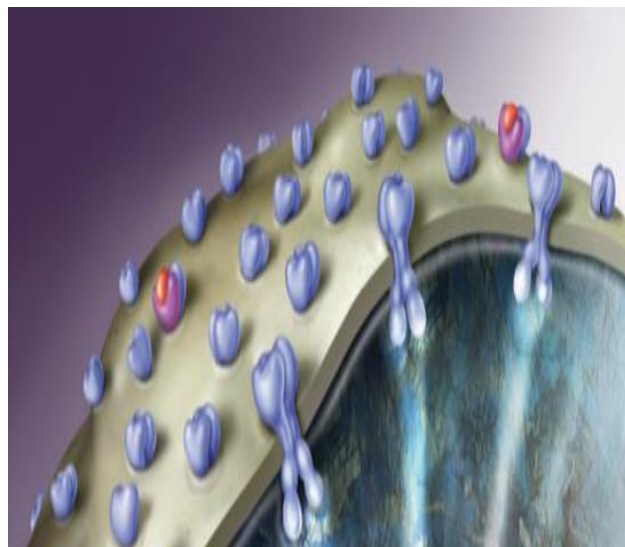
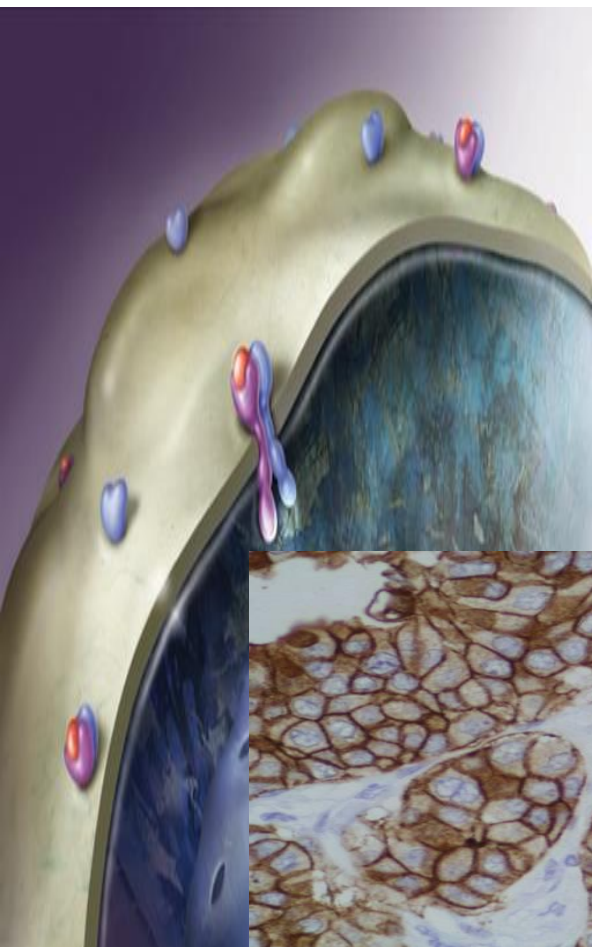




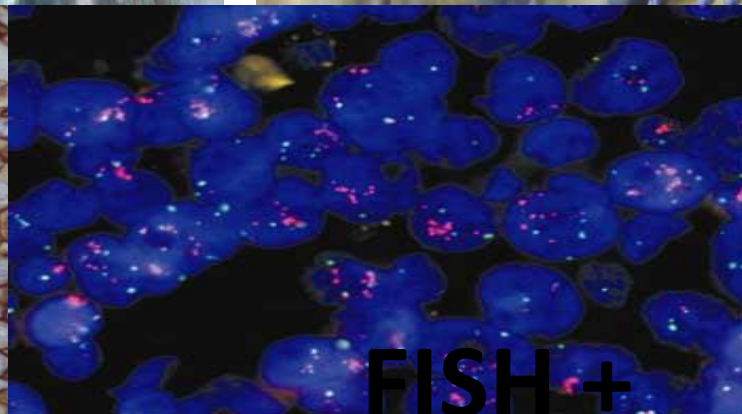
Normal HER2  
expresión

Amplificación de los genes  
HER2 overexpression

Sobreexpresión de HER2  
conduce a la  
proliferación tumoral

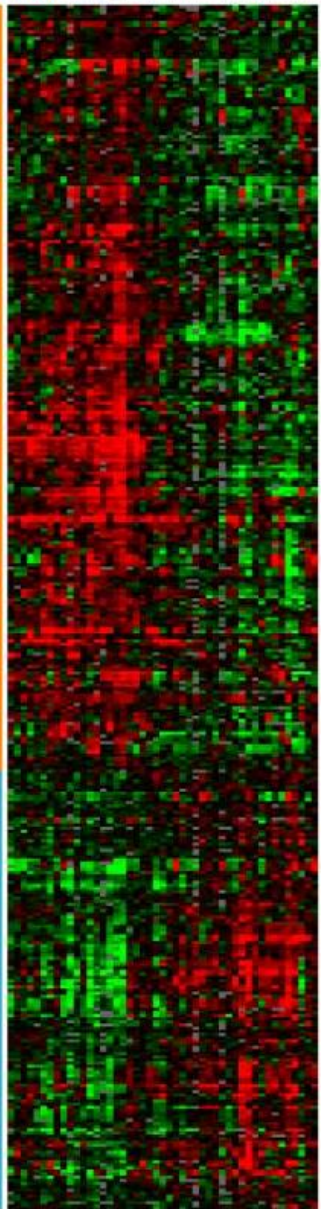


IHQ 3+

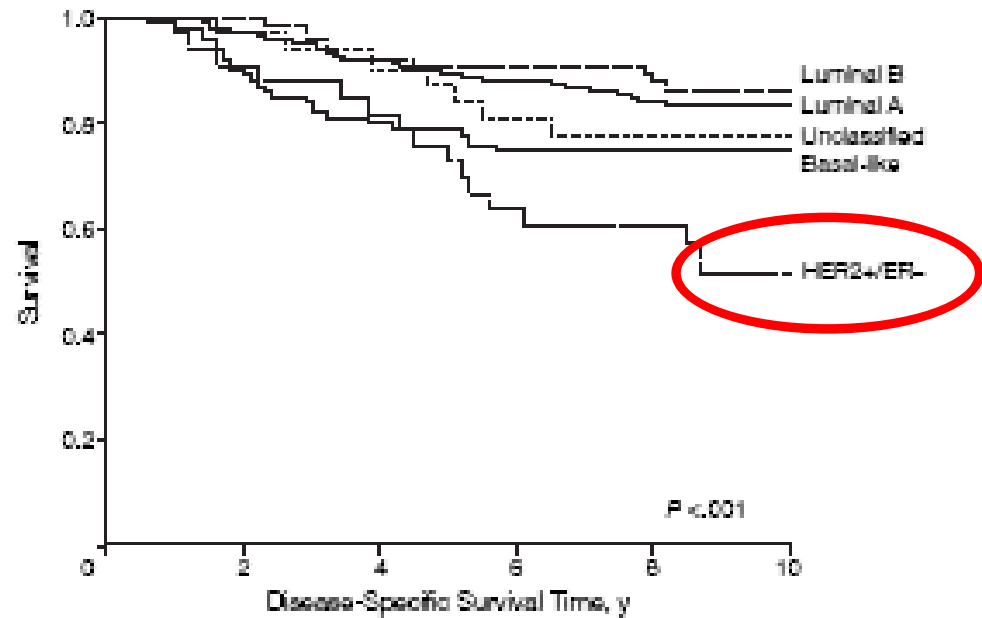


FISH +

# Microarrays de DNA y comportamiento clínico



**Figure 2.** Survival Analysis of the Carolina Breast Cancer Study Cases Grouped Using the Refined Breast Tumor Immunohistochemical Intrinsic Subtypes



No. at Risk

Luminal B	76	67	65	63	17
Luminal A	245	226	213	197	61
Unclassified	30	28	25	23	9
Basal-like	80	78	72	71	25
HER2+ER-	30	27	21	20	7



# The NEW ENGLAND JOURNAL of MEDICINE

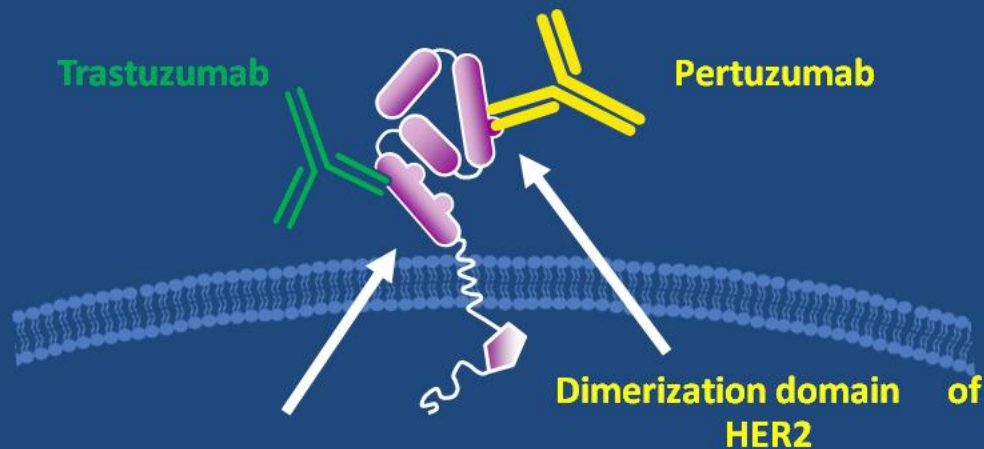
ESTABLISHED IN 1812

JANUARY 12, 2012

VOL. 366 NO. 2

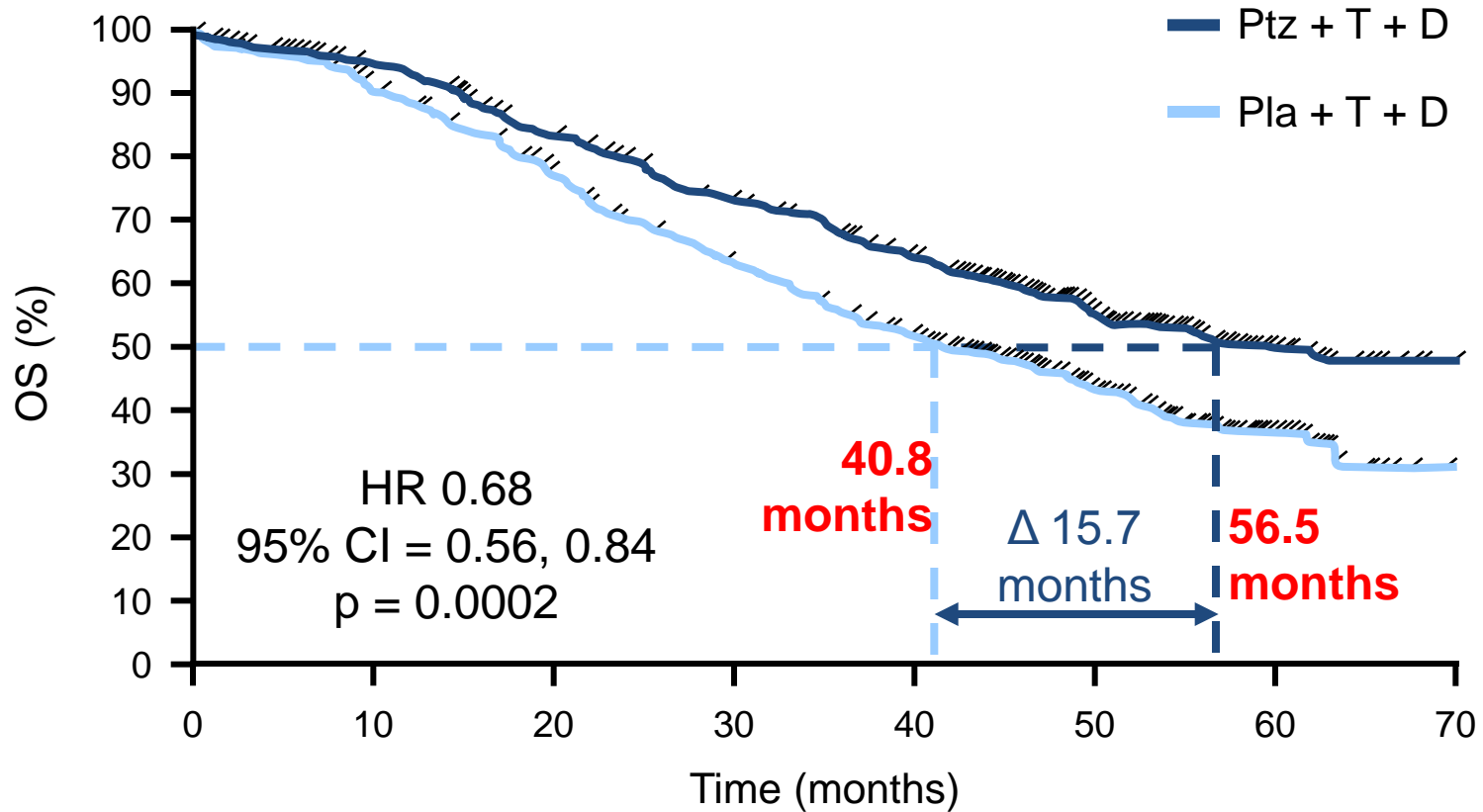
Pertuzumab plus Trastuzumab plus Docetaxel  
for Metastatic Breast Cancer

Trastuzumab y Pertuzumab se unen a  
diferentes partes del receptor Her2



# Final OS Analysis

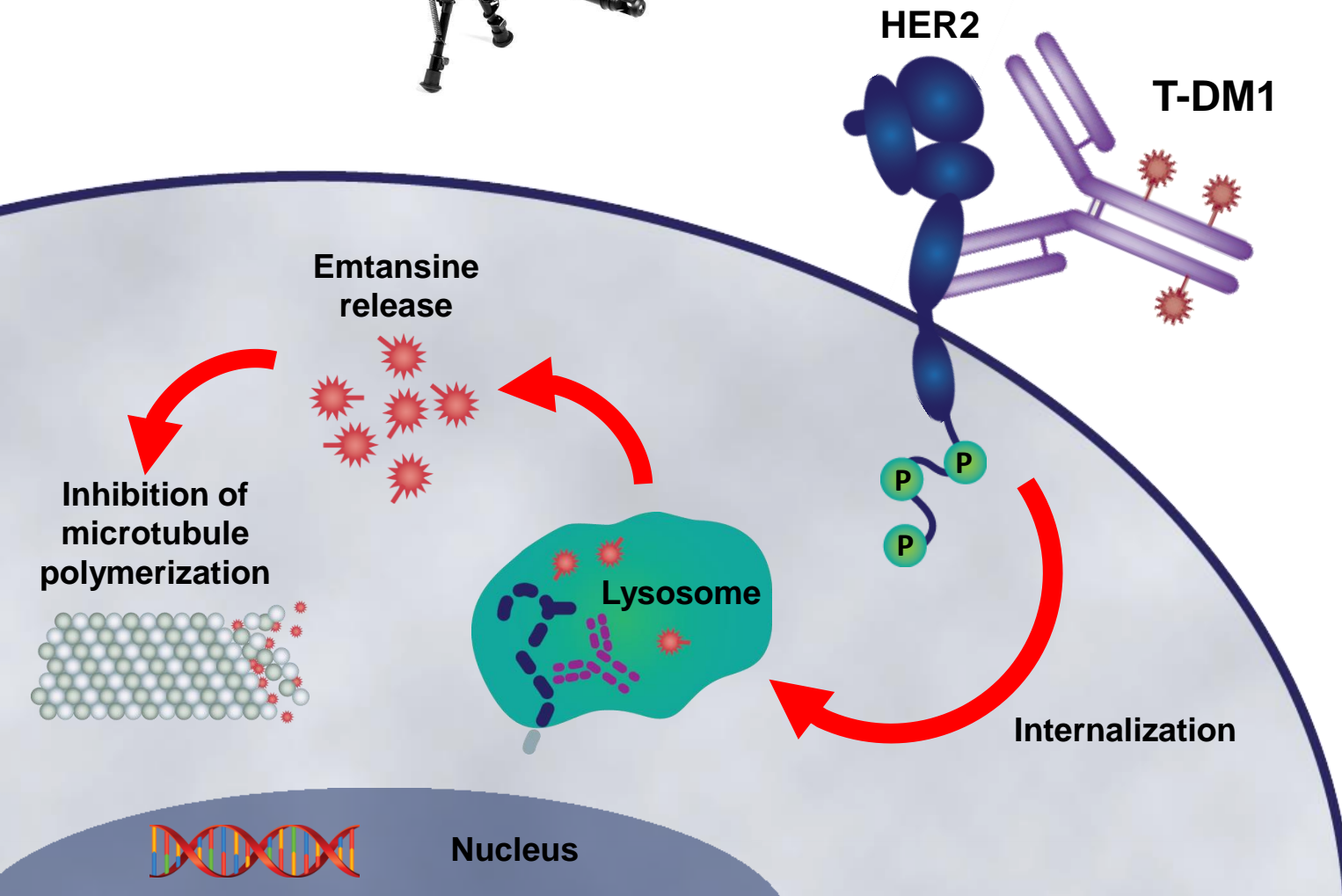
Median follow-up 50 months (range 0–70 months)



n at risk

— Ptz + T + D	402	371	318	268	226	104	28	1
— Pla + T + D	406	350	289	230	179	91	23	0

# DM1: Mechanism of Action



# Podemos analizar cáncer a nivel molecular

1. Patient's tumor

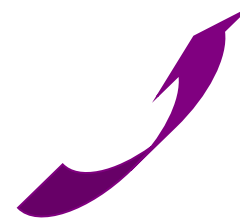
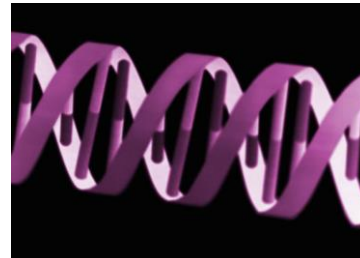


5. Shared Decision Making



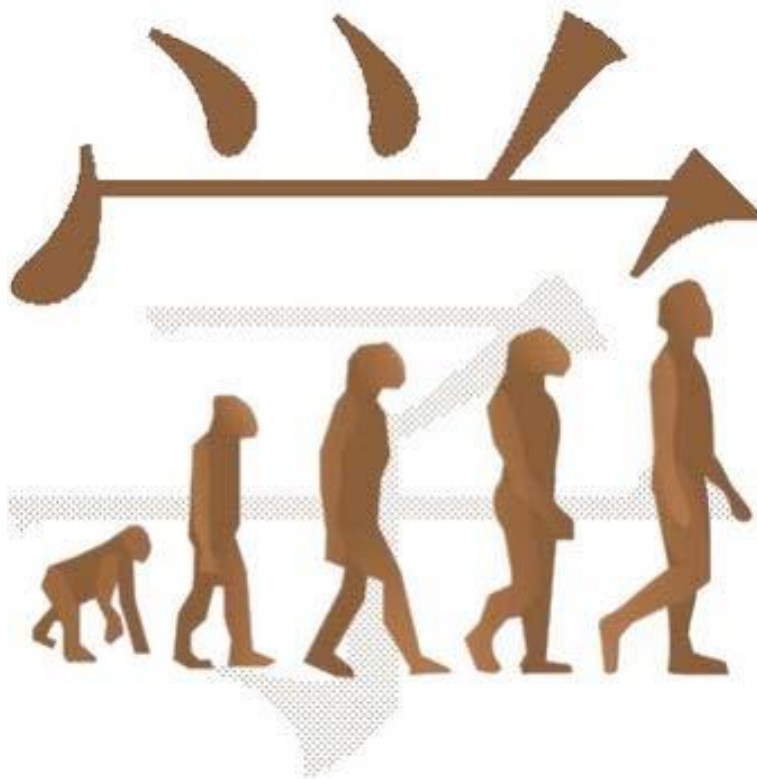
2. Oncotype DX<sup>®</sup> Assay

4. Oncotype DX<sup>®</sup> Report

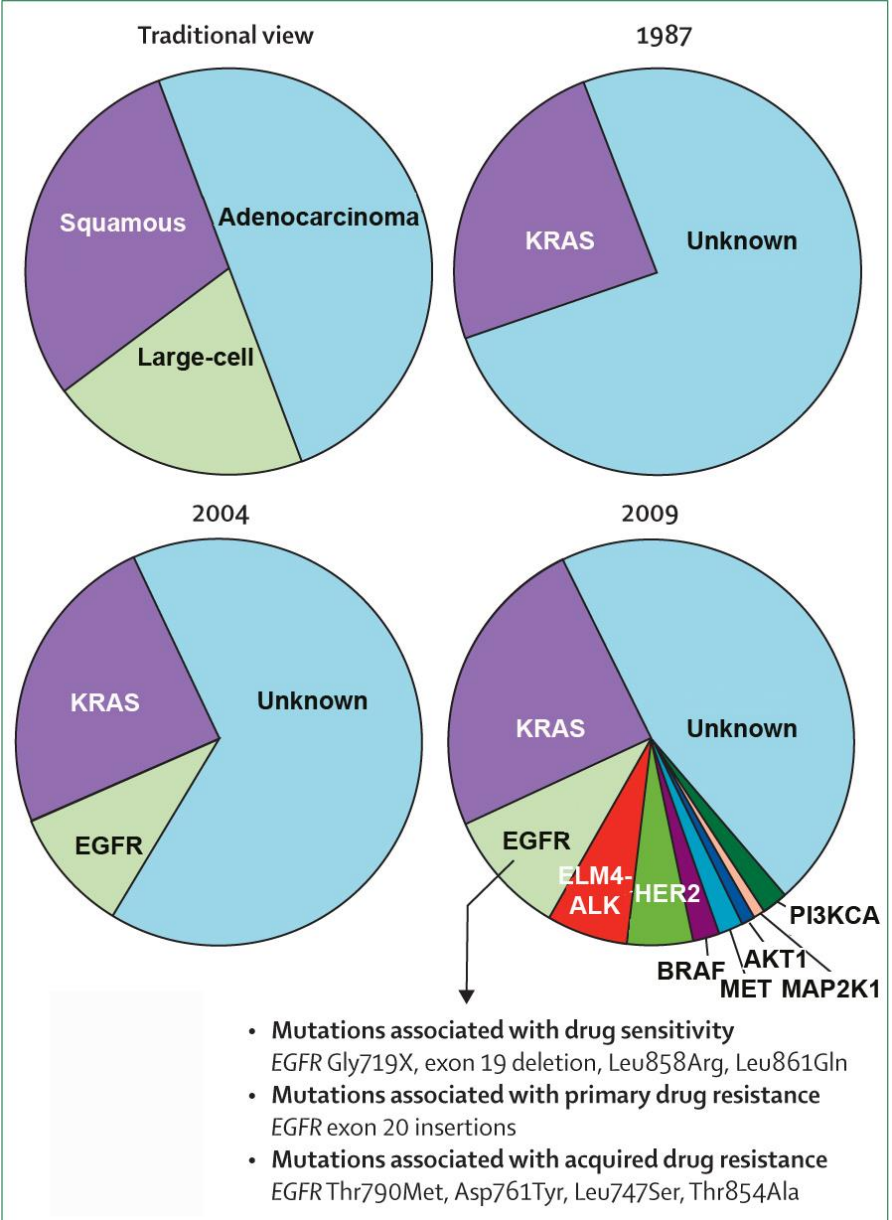


3. Analyze expression of tumor's genes



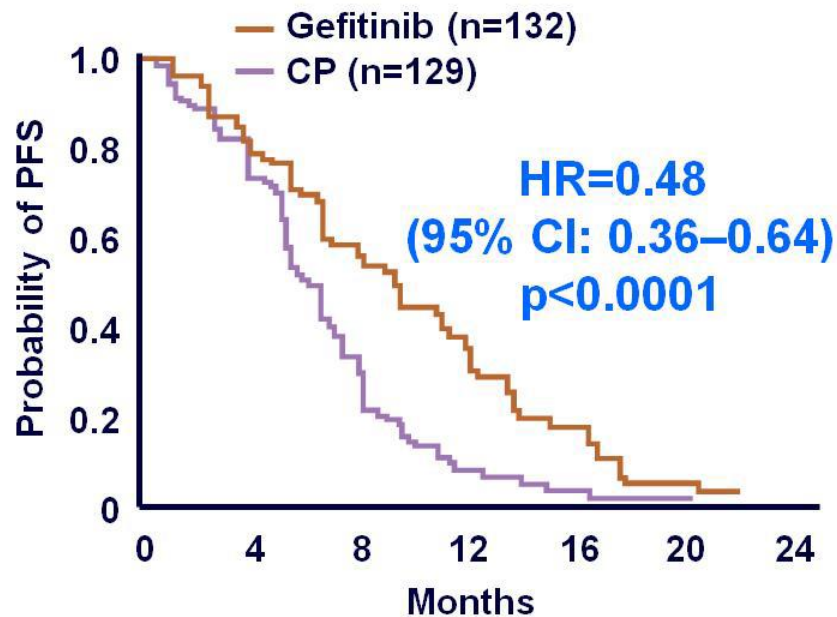


**Importancia de la  
calidad y cantidad  
de muestra**

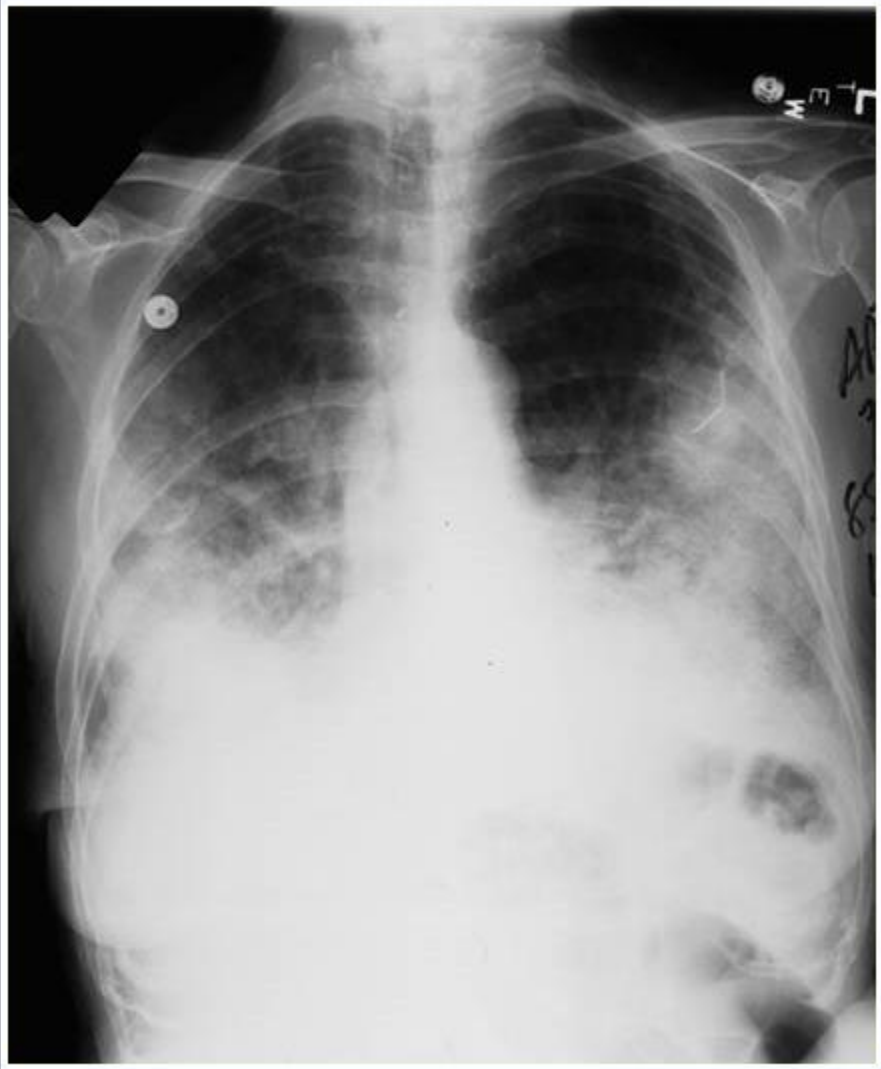


# IPASS results: benefit of gefitinib limited to *EGFR* mutation-positive disease

***EGFR* mutation +  
(60% of tested population)**



- Prognostic and predictive value of *EGFR* mutation status confirmed
- *EGFR* mutation status is required for treatment decisions

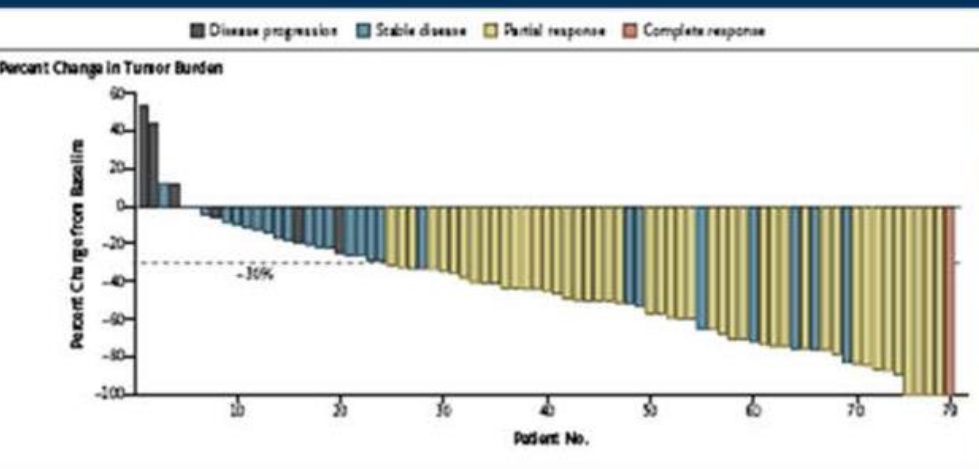


# The NEW ENGLAND JOURNAL of MEDICINE

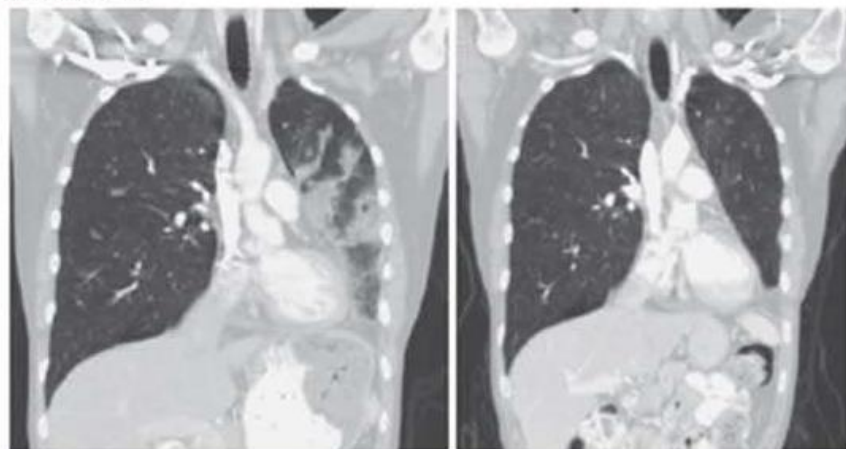
ESTABLISHED IN 1812

OCTOBER 28, 2010

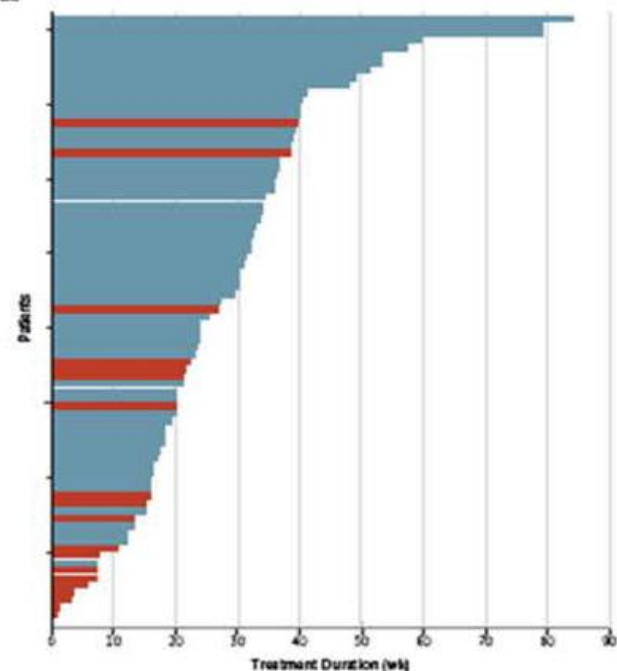
VOL. 363 NO. 18



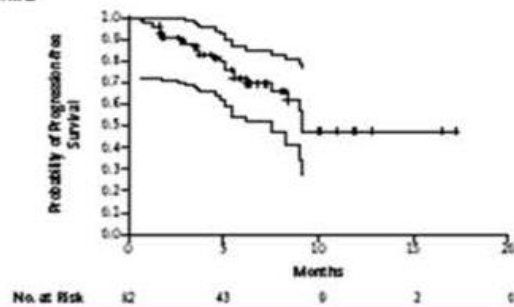
CT before and after Crizotinib



A Duration of Treatment



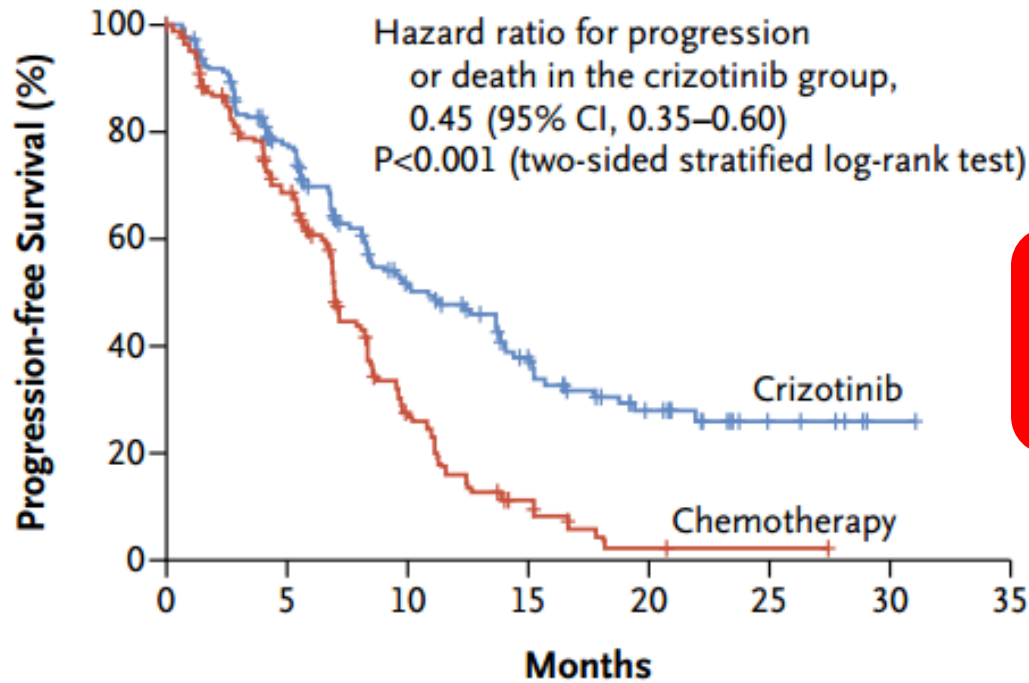
B Progression-free Survival



ORIGINAL ARTICLE

# First-Line Crizotinib versus Chemotherapy in ALK-Positive Lung Cancer

## A Progression-free Survival



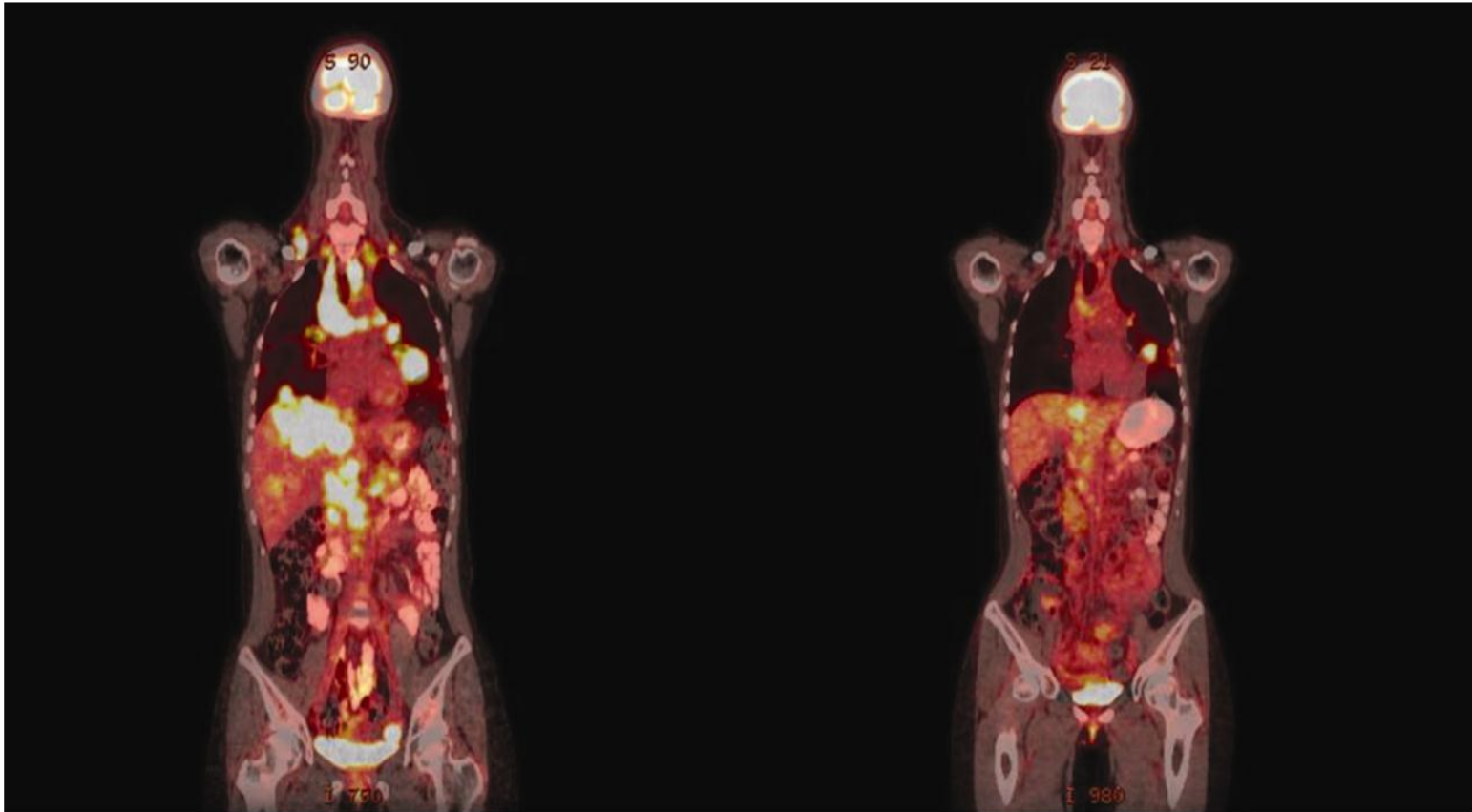
¡¡calidad de vida!!

No. at Risk

Crizotinib	172	120	65	38	19	7	1	0
Chemotherapy	171	105	36	12	2	1	0	0

# Crizotinib produce respuestas rápidas

- Example of a patient with a large tumour burden, showing marked response at 14 days



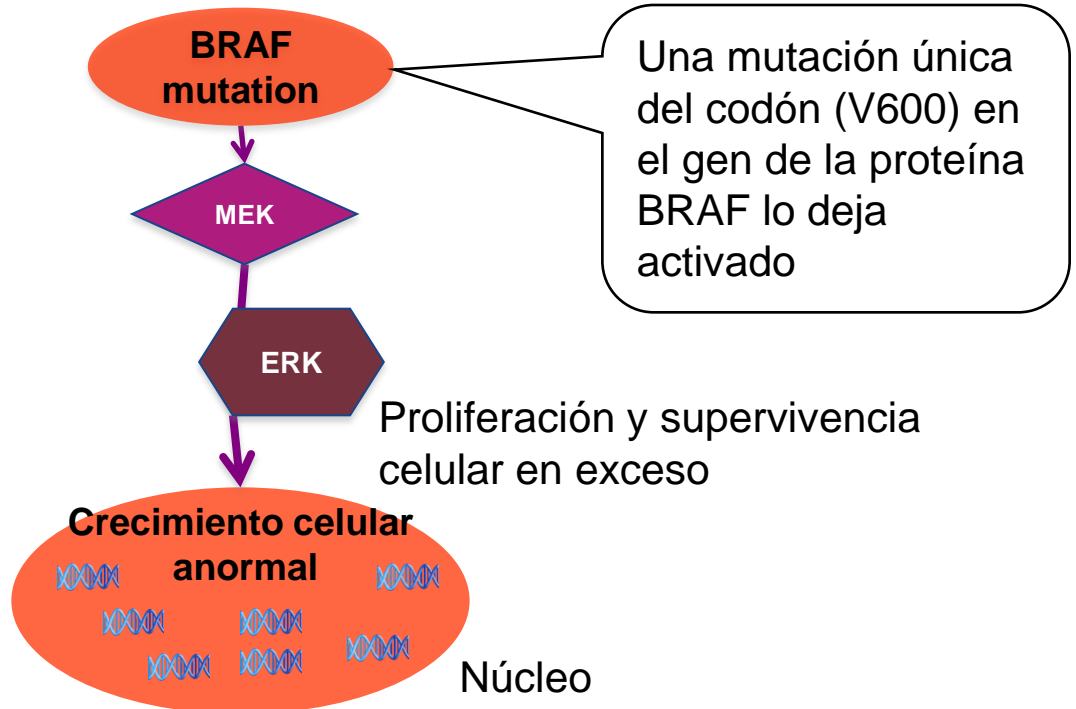
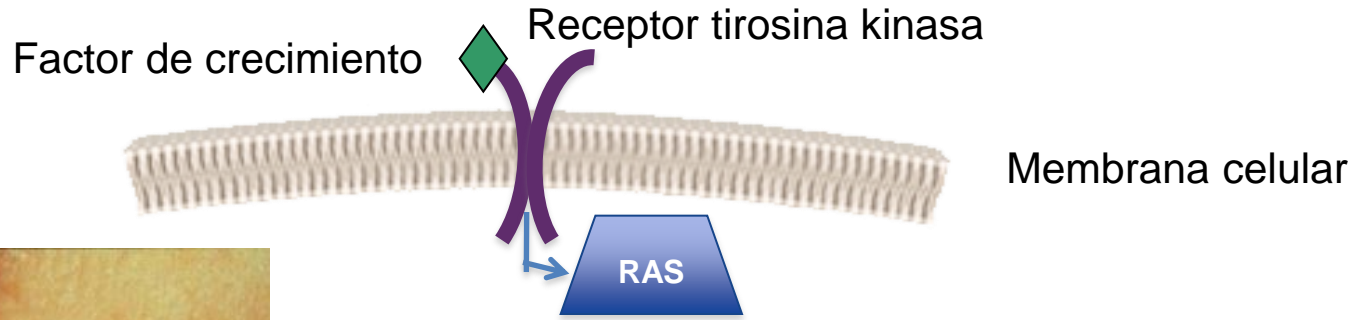


La resurrección de Lázaro , Claravaggio 1609

# BRAF mutada

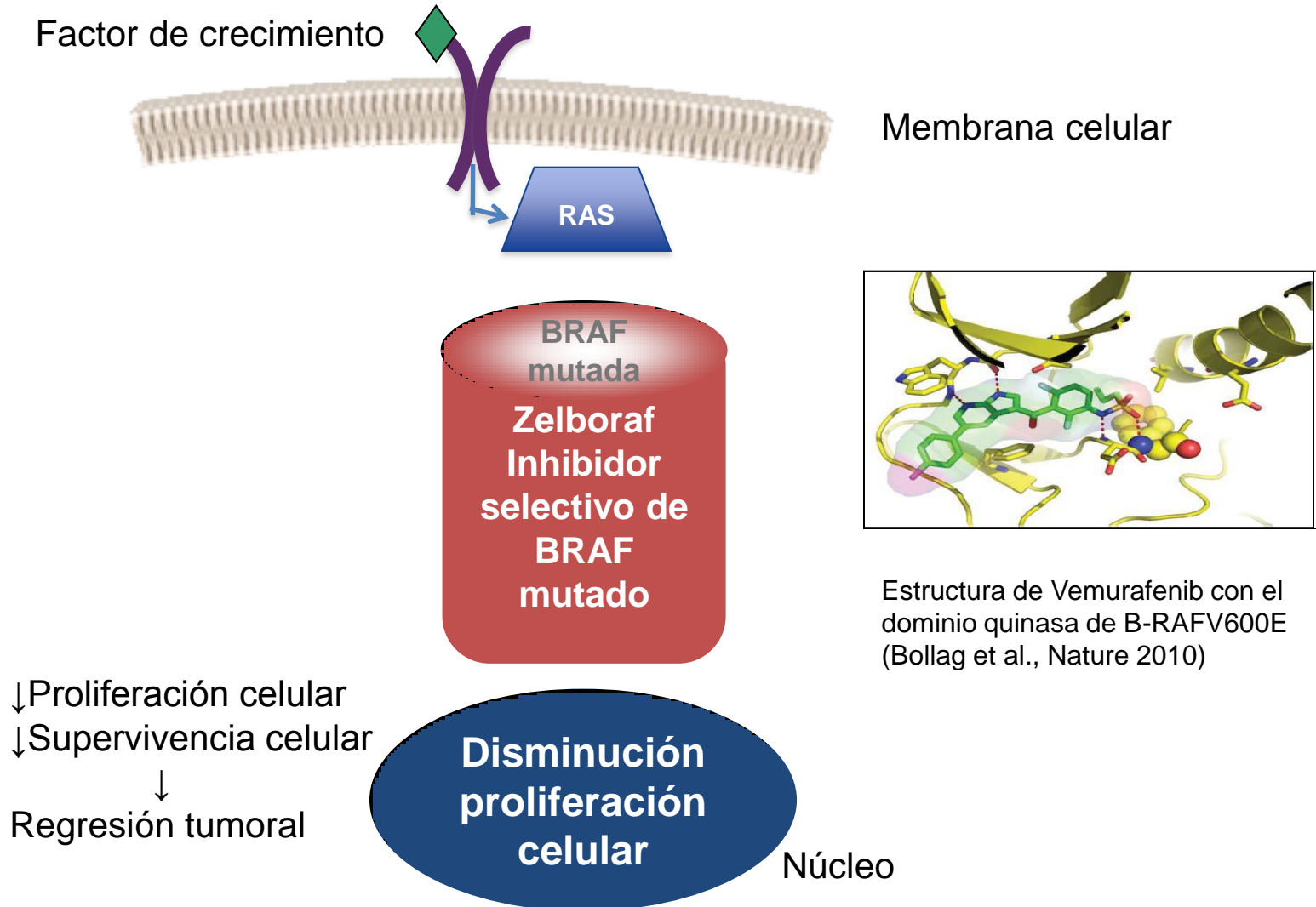


Aproximadamente el 40% de los melanomas presentan mutación BRAF V600



# BRAF mutada. Papel de Zelboraf

## Inhibidor oncogénico de BRAF



# SUCCESS AND FAILURE

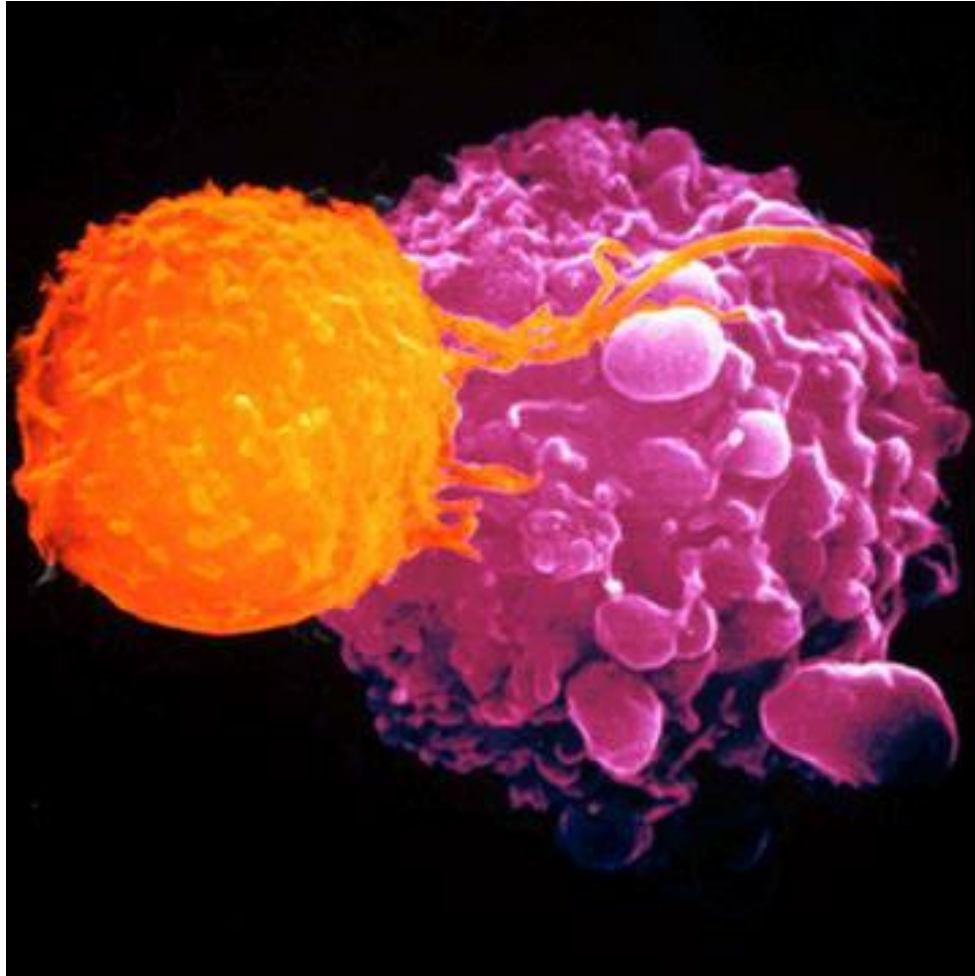
**A**



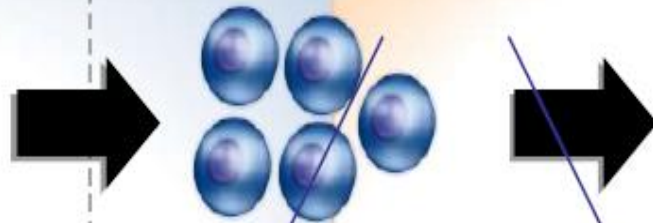
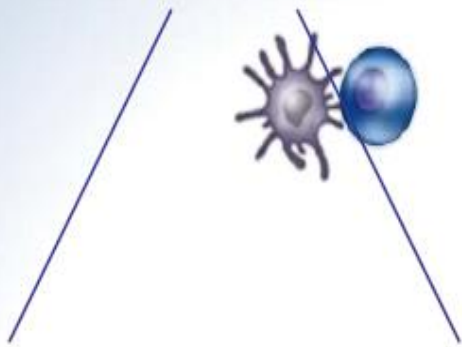
**B**



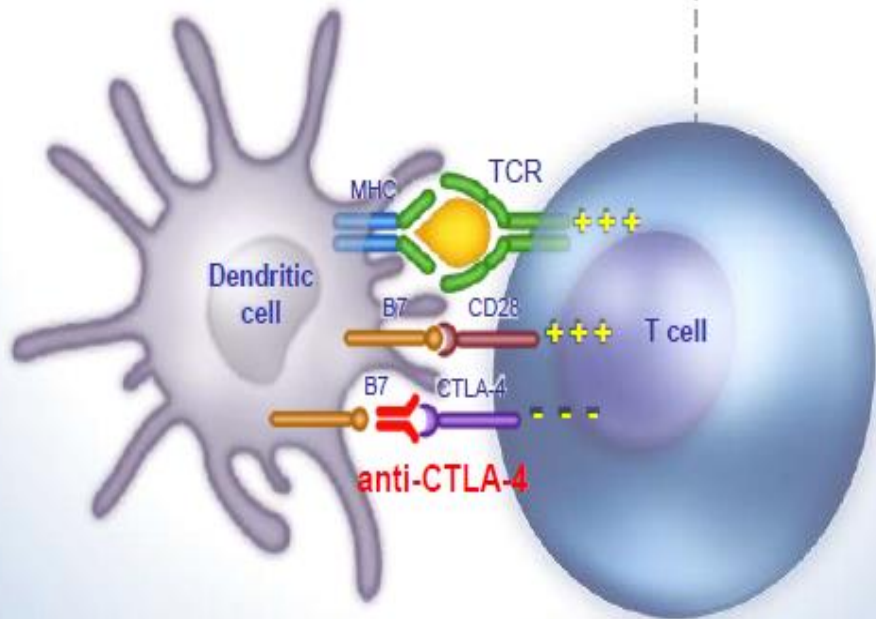
# Inmunoterapia



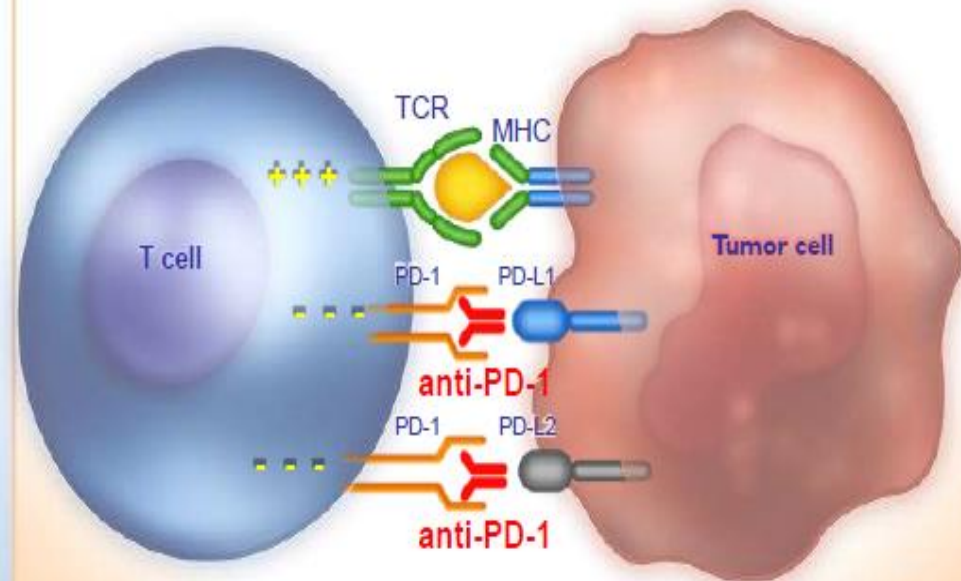
# Tumor Microenvironment



**Activation**  
(cytokines, lysis, proliferation,  
migration to tumor)

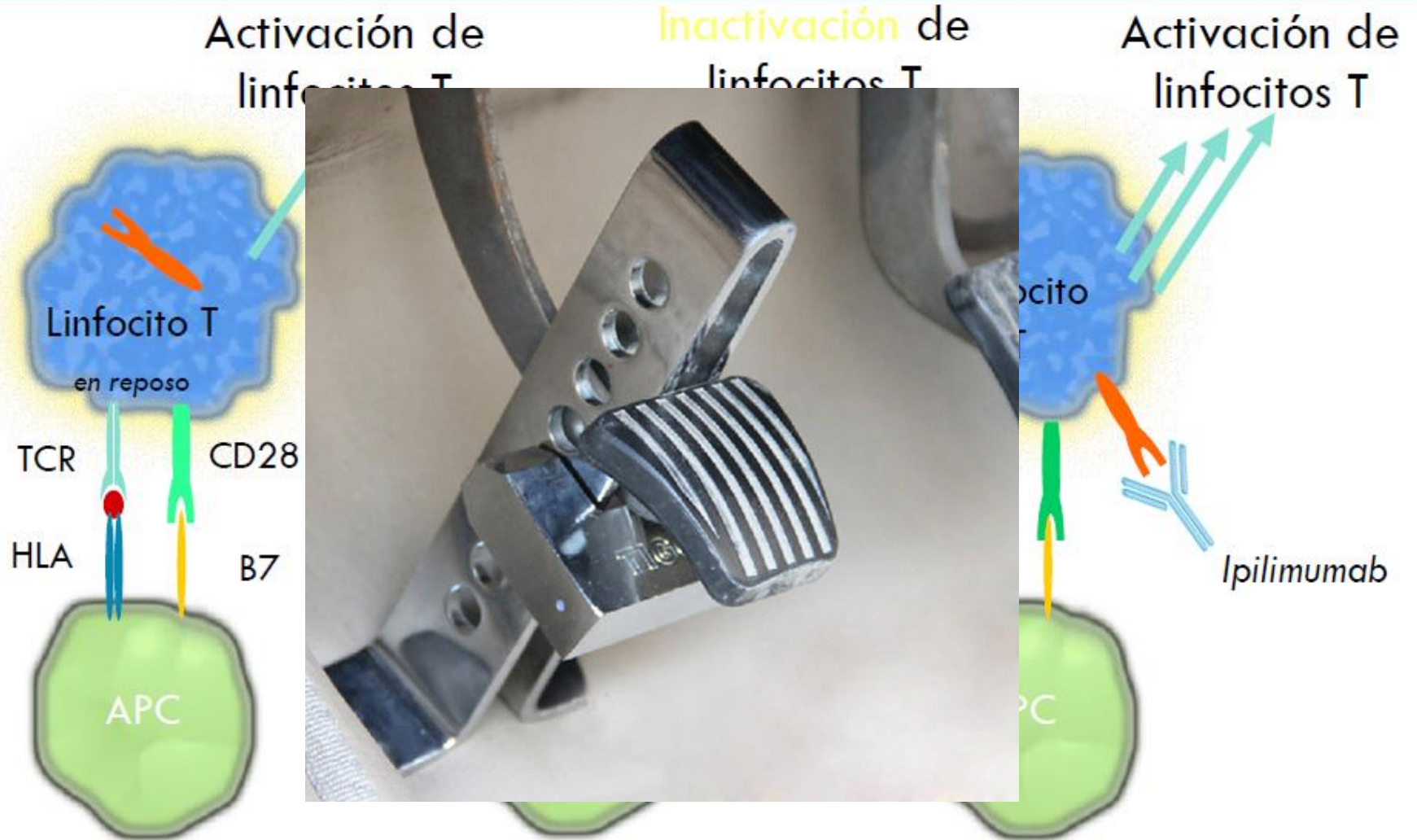


**CTLA-4 Blockade (ipilimumab)**



**PD-1 Blockade (nivolumab)**

# Ipilimumab: mecanismo de acción





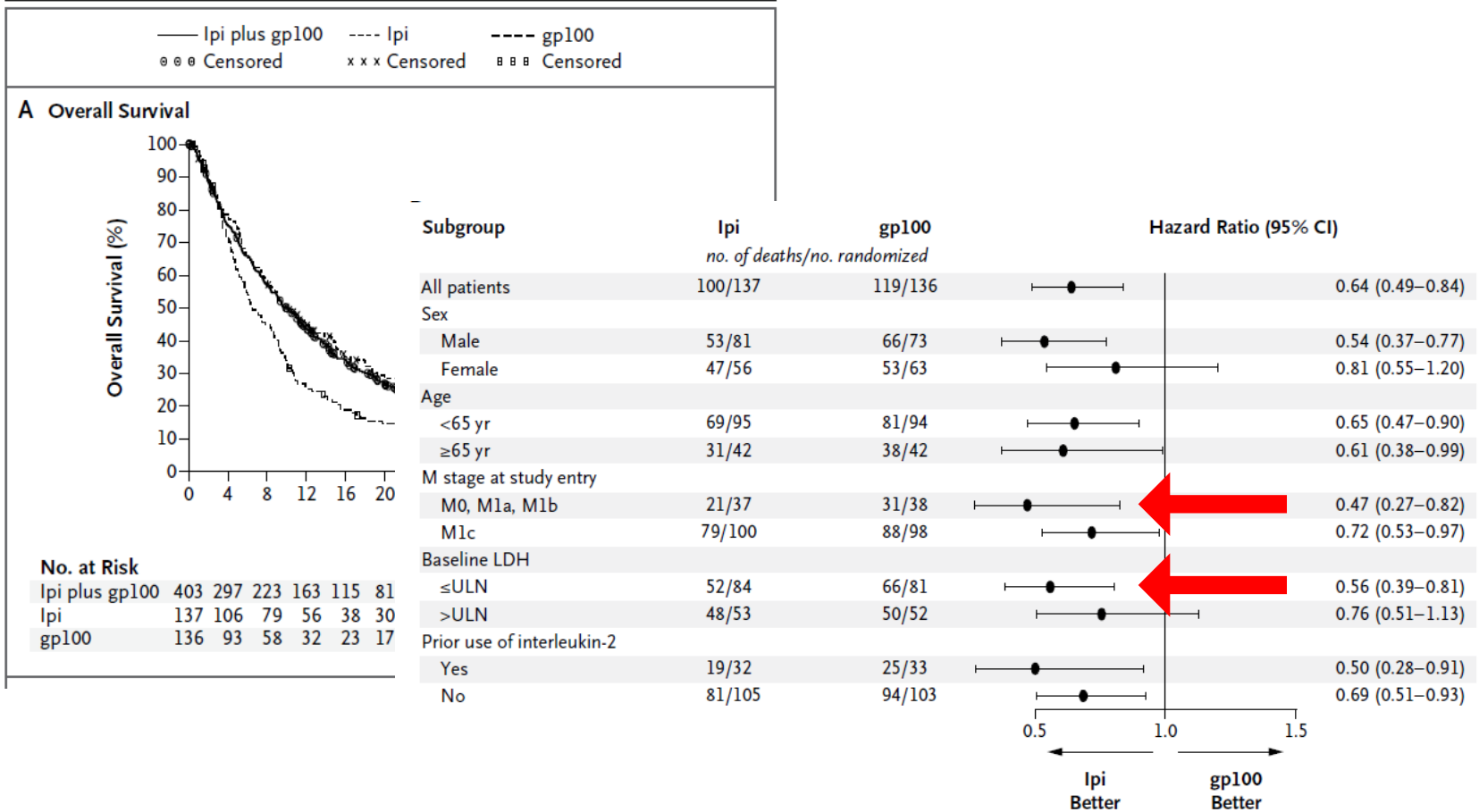
# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

AUGUST 19, 2010

VOL. 363 NO. 8

## Improved Survival with Ipilimumab in Patients with Metastatic Melanoma



# Judah Folkman



- La angiogénesis es necesaria para el crecimiento de los tumores sólidos.
- “Without angiogenesis , tumor would be unable to grow beyond 1mm in size”

# TERAPIA ANTIANGIOGENICA

Con fármaco

Sin fármaco

Inicio

Retirada

CAMBIOS VASCULARES



Antiangiogénesis



Normalización vascular



Inhibición tumoral



Rápida revascularización



Desorganización vascular

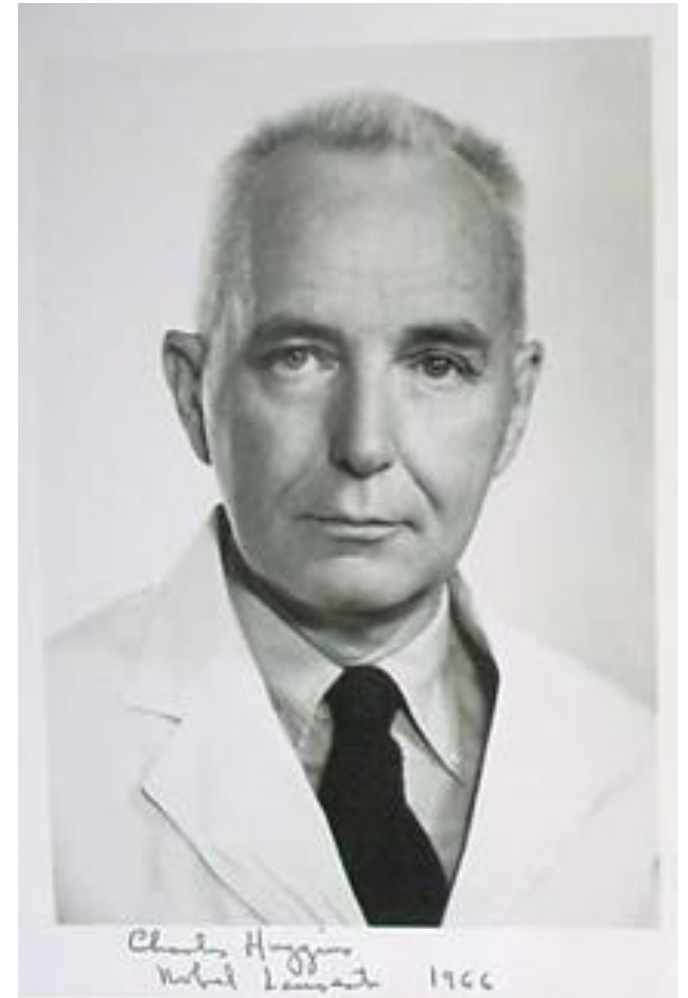


Crecimiento tumoral acelerado



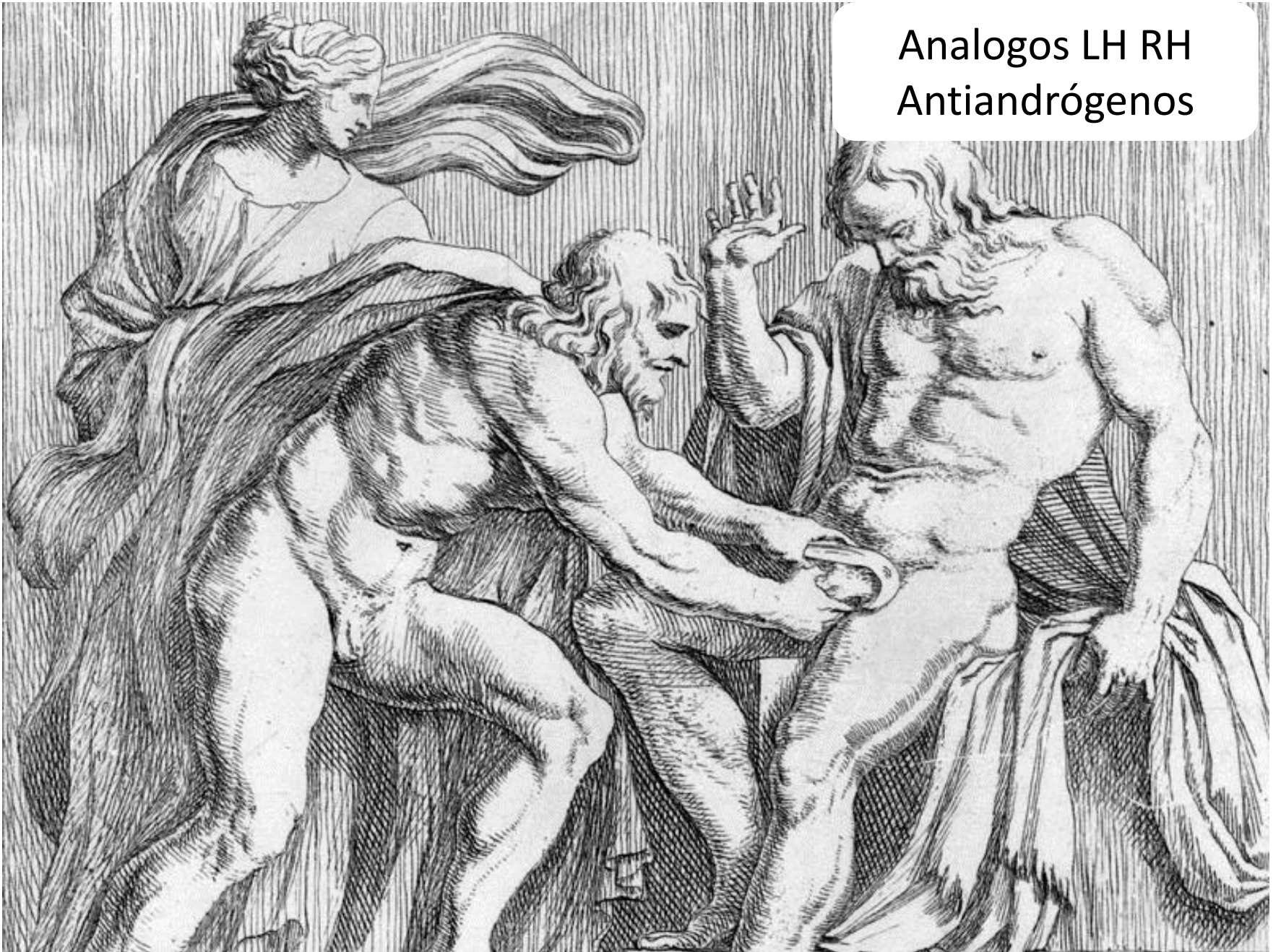
Orquiectomía en el cáncer de próstata

El cáncer puede ser tratado con fármacos



**Charles Brenton Huggins ( 1901 –1997)**  
Premio Nobel de Medicina en 1966

Análogos LH RH  
Antiandrógenos



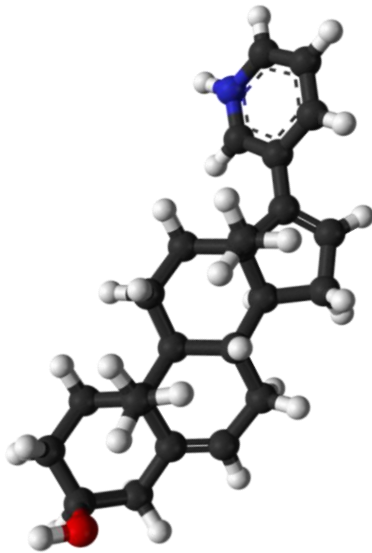
# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

MAY 26, 2011

VOL. 364 NO. 21

## Abiraterone and Increased Survival in Metastatic Prostate Cancer



- **Primer inhibidor oral e irreversible** de CYP17 (P450c17)
  - 17 $\alpha$  –hydroxylase ( $IC_{50}$  = 4 nM)
  - C17,20-lyase ( $IC_{50}$  = 2.9 nM)
- **Supresión de andrógenos** a nivel sérico y de las células prostáticas a **niveles indetectables**

# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

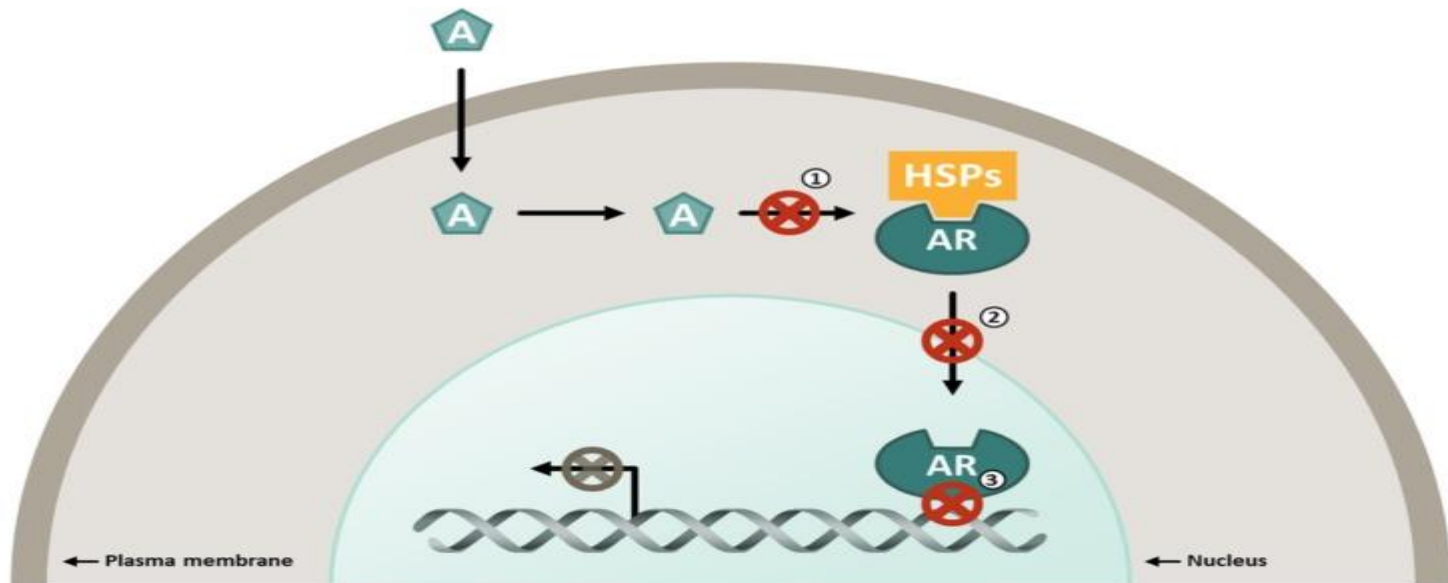
SEPTEMBER 27, 2012

VOL. 367 NO. 13

## Increased Survival with Enzalutamide in Prostate Cancer after Chemotherapy

Howard I. Scher, M.D., Karim Fizazi, M.D., Ph.D., Fred Saad, M.D., Mary-Ellen Taplin, M.D., Cora N. Sternberg, M.D.,

1. Inhibits binding of androgens (A) to androgen receptors (ARs)
2. Inhibits nuclear translocation of ARs
3. Inhibits AR-mediated DNA binding



# The NEW ENGLAND JOURNAL of MEDICINE

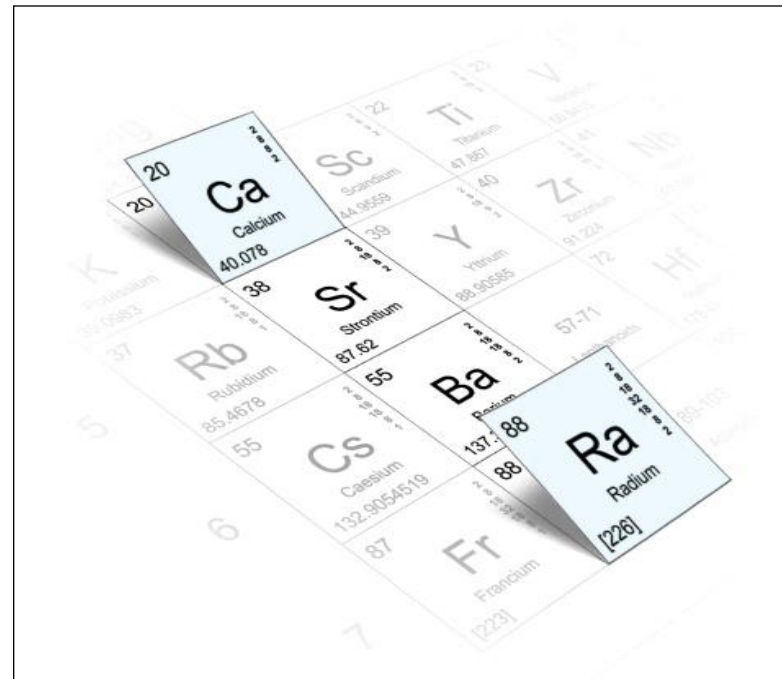
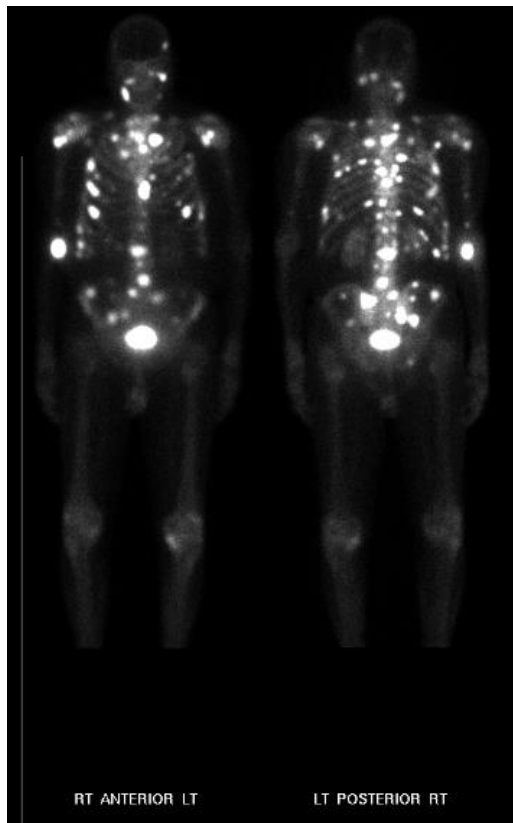
ESTABLISHED IN 1812

JULY 18, 2013

VOL. 369 NO. 3

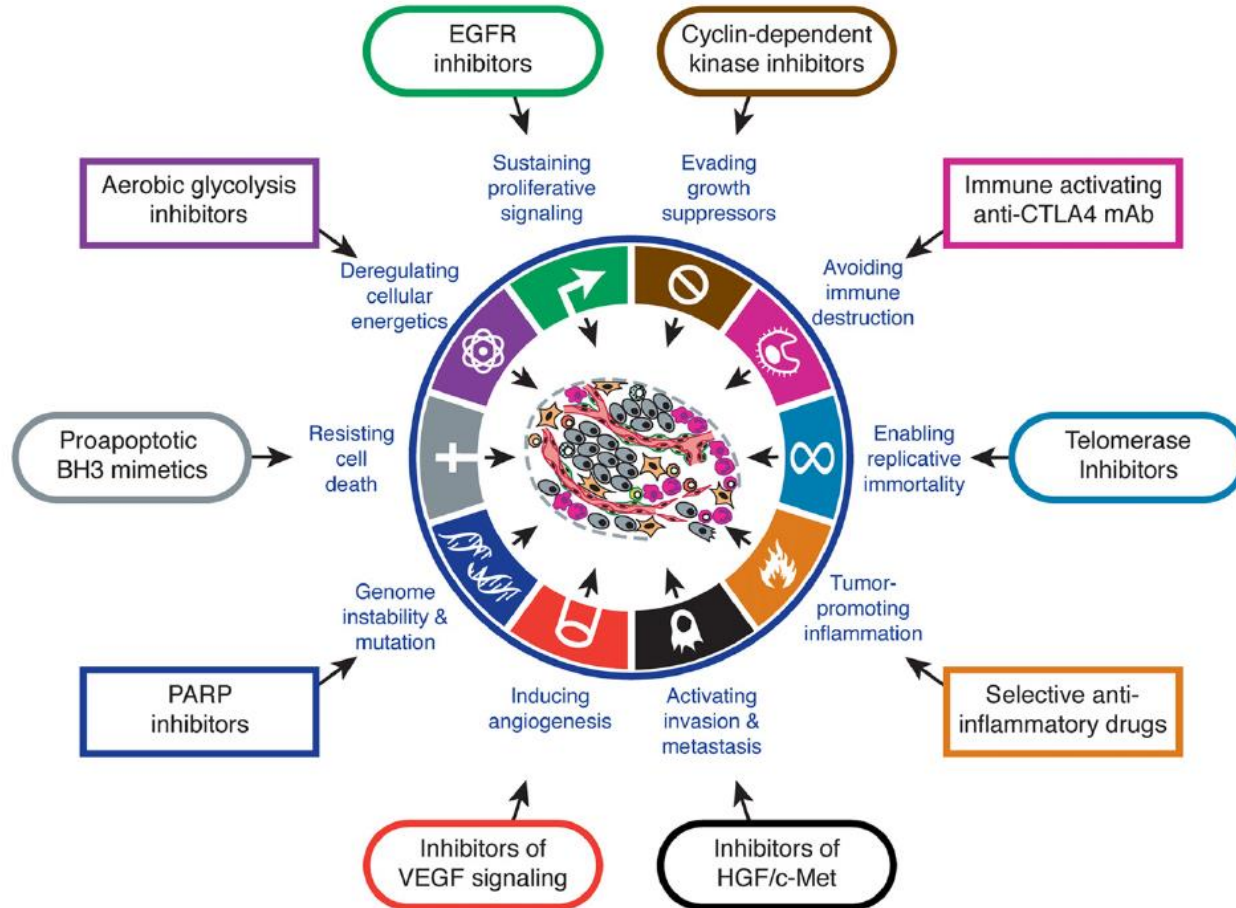
## Alpha Emitter Radium-223 and Survival in Metastatic Prostate Cancer

C. Parker, S. Nilsson, D. Heinrich, S.I. Helle, J.M. O'Sullivan, S.D. Fosså, A. Chodacki, P. Wiechno, J. Logue, M. Seke,

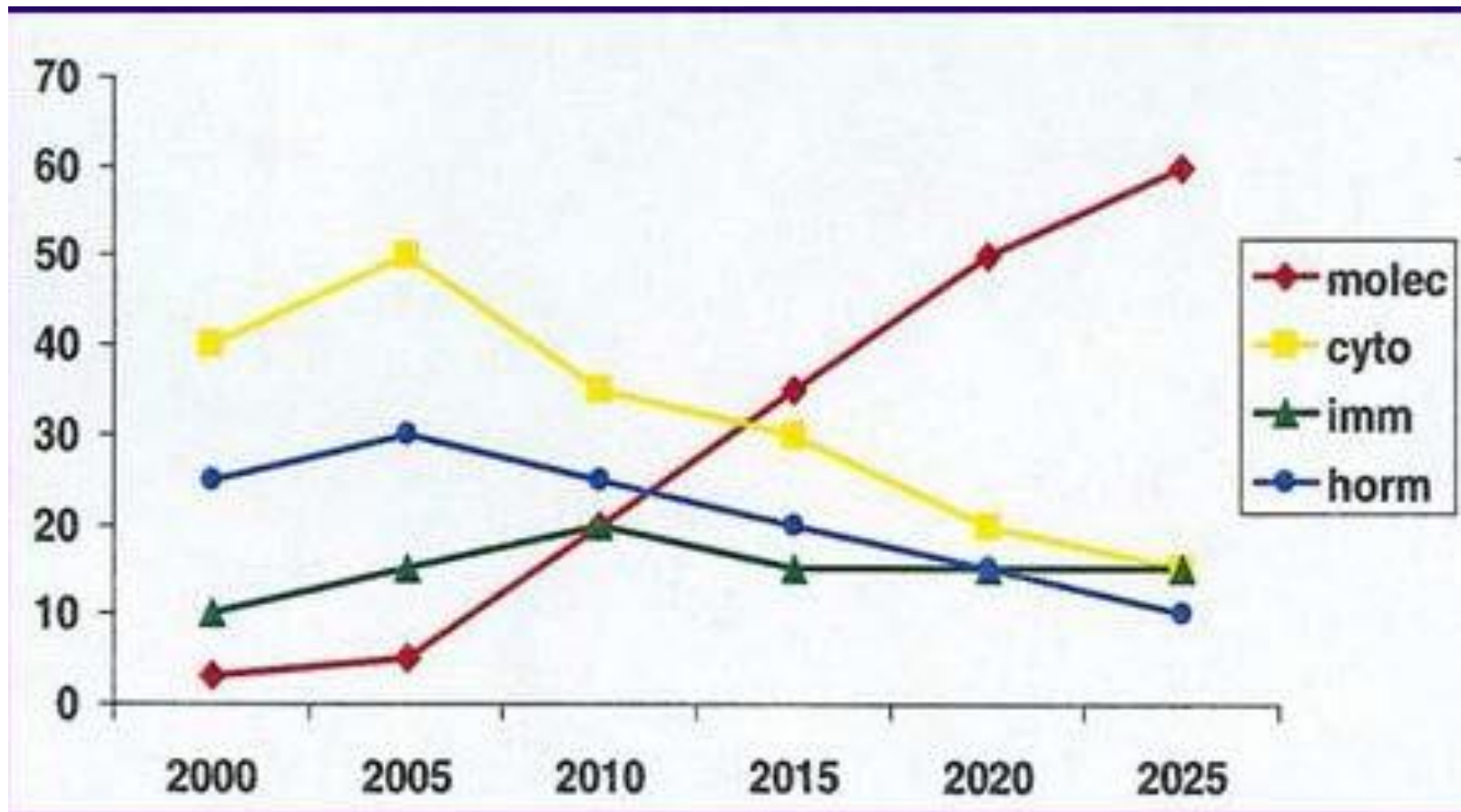


# Hallmarks of Cancer: The Next Generation

Douglas Hanahan<sup>1,2,\*</sup> and Robert A. Weinberg<sup>3,\*</sup>



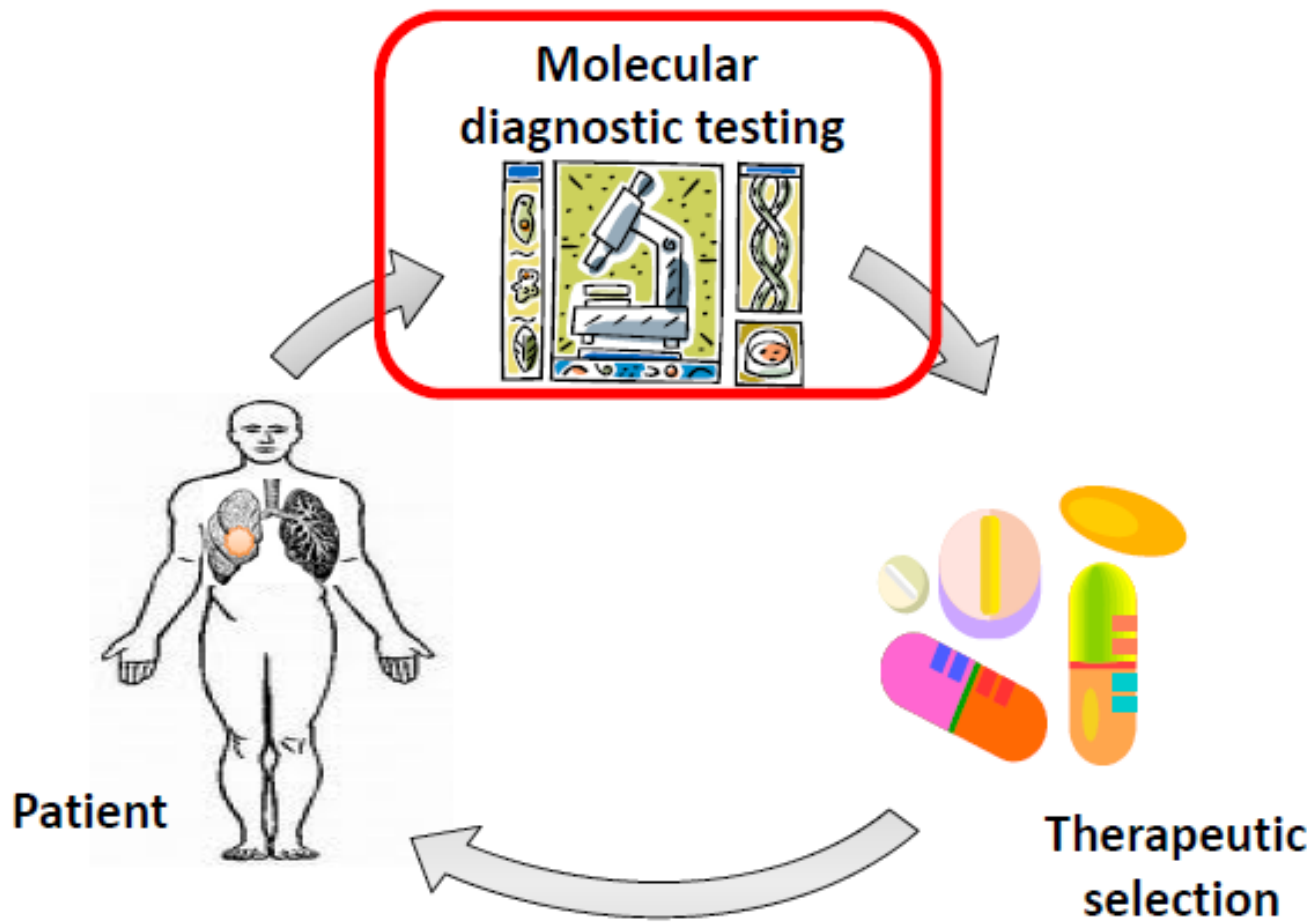
# Desarrollo de Fármacos Antitumorales 2000-2025



# El cambio



# Personalized Cancer Medicine



**El futuro  
no va a ser  
así...**



**HENRY POOLE & Co.**  
15 SAVILE ROW, LONDON

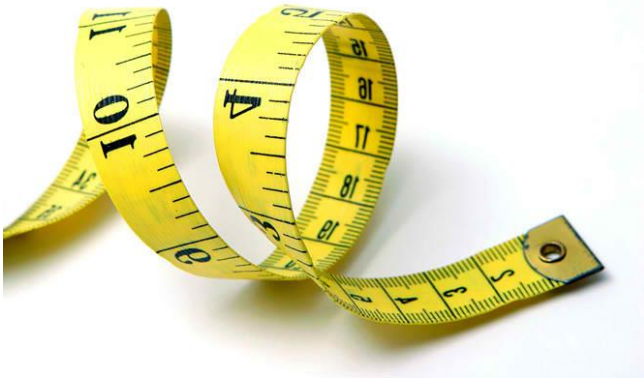
### Bespoke Tailoring

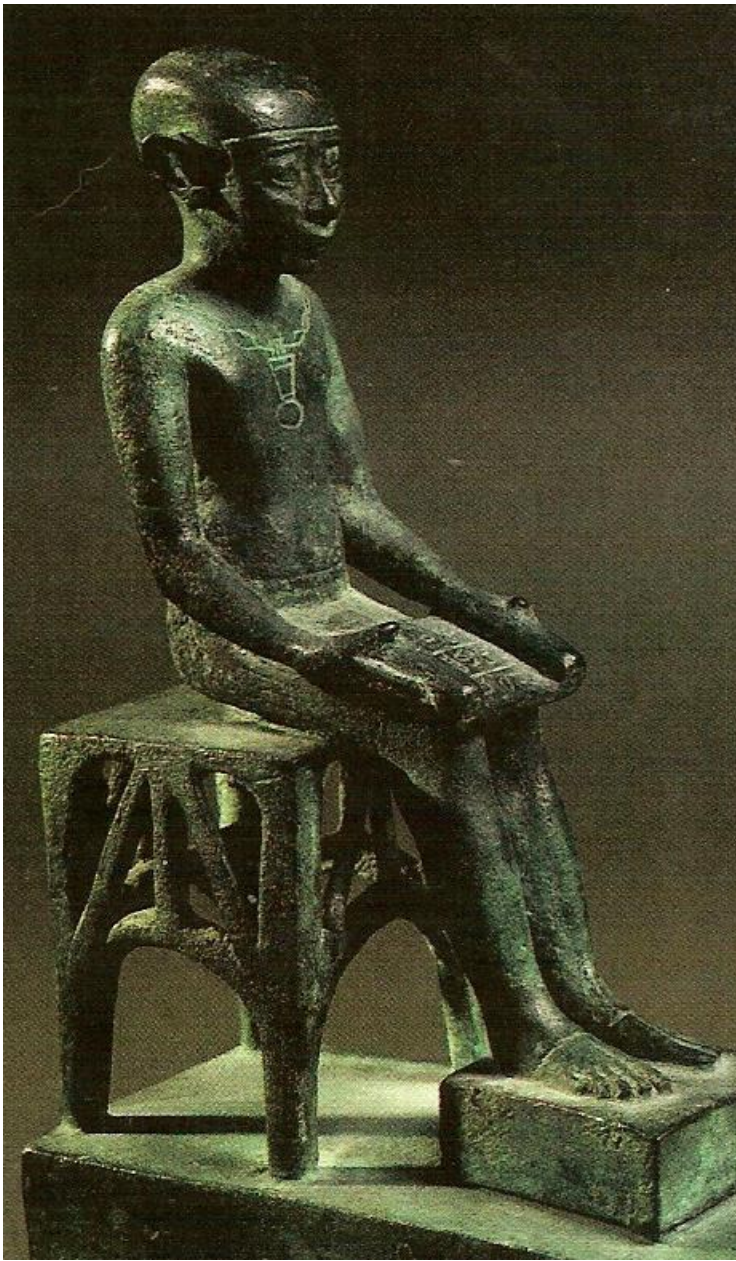
The definition of the word bespoke comes from bespoken giving the characteristic of choice.

This in tailoring terms means to design clothing from a blank canvas, the client adding his own individual choice of styling to those of the skilled cutter.

The cutter will work in tangent with the client's waistcoat maker, coatmaker and trousers maker adjusting the pattern at the various stages of making thus creating the perfect paper pattern.

**Pero será/es así...**





Imhotep escriba, Baja época, 664-332 AJC

