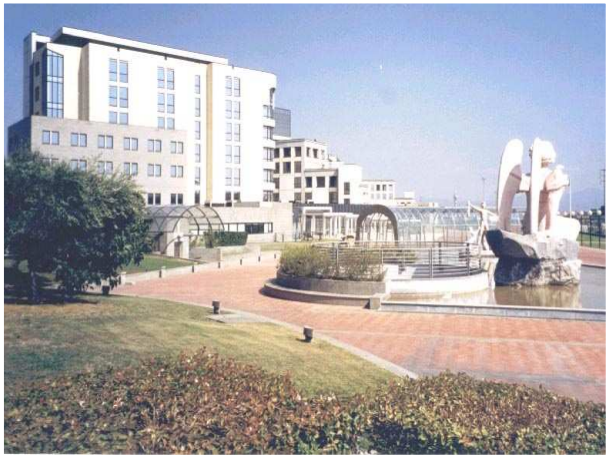
FARMACI INNOVATIVI

Qualità Efficacia Appropriatezza

Garanzia dell'Universalità delle Cure sul Territorio Nazionale

Farmaci e Dintorni, Spesa o Risparmio per il S.S.N.?

Farmaci innovativi mirati: efficaci ma costosi per il S.S.N.



Prof. Francesco Cognetti

Direttore,

Dipartimento di Oncologia Medica

IRE - Istituto Nazionale Tumori Regina Elena, Roma

Roma, CAMERA DEI DEPUTATI, 5 Giugno 2009

'Outline' della presentazione

- I progressi in oncologia:
  - A livello internazionale
  - A livello nazionale
- Perché tali successi?
- Gli scenari 'futuribili' in relazione al costo dei nuovi farmaci
- Il ruolo della ricerca

L'industria del farmaco, la salute del Paese

30 anni di crescita e innovazione in Italia

FARMINDUSTRIA

Riduzione del tasso di mortalità standardizzata in Italia dal 1978

Tutte le cause	**-38%**
Malattie apparato circolatorio	-52%
Patologie tumorali	-9%
Malattie apparato respiratorio	-46%
Malattie apparato digerente	-52%
Altre patologie	-24%

nota: numero di morti per 100 mila abitanti, tasso standardizzato

Successi in Oncologia

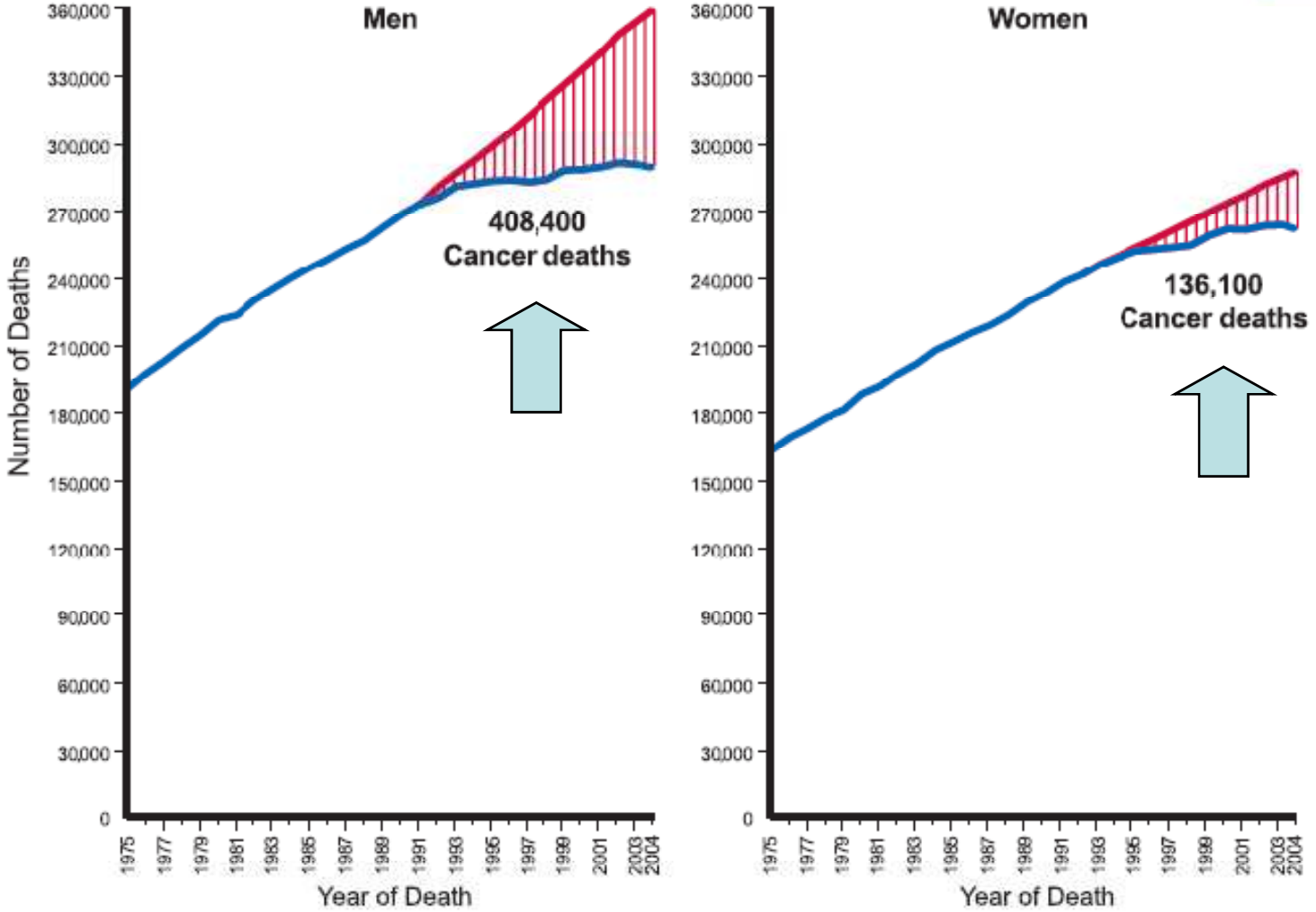
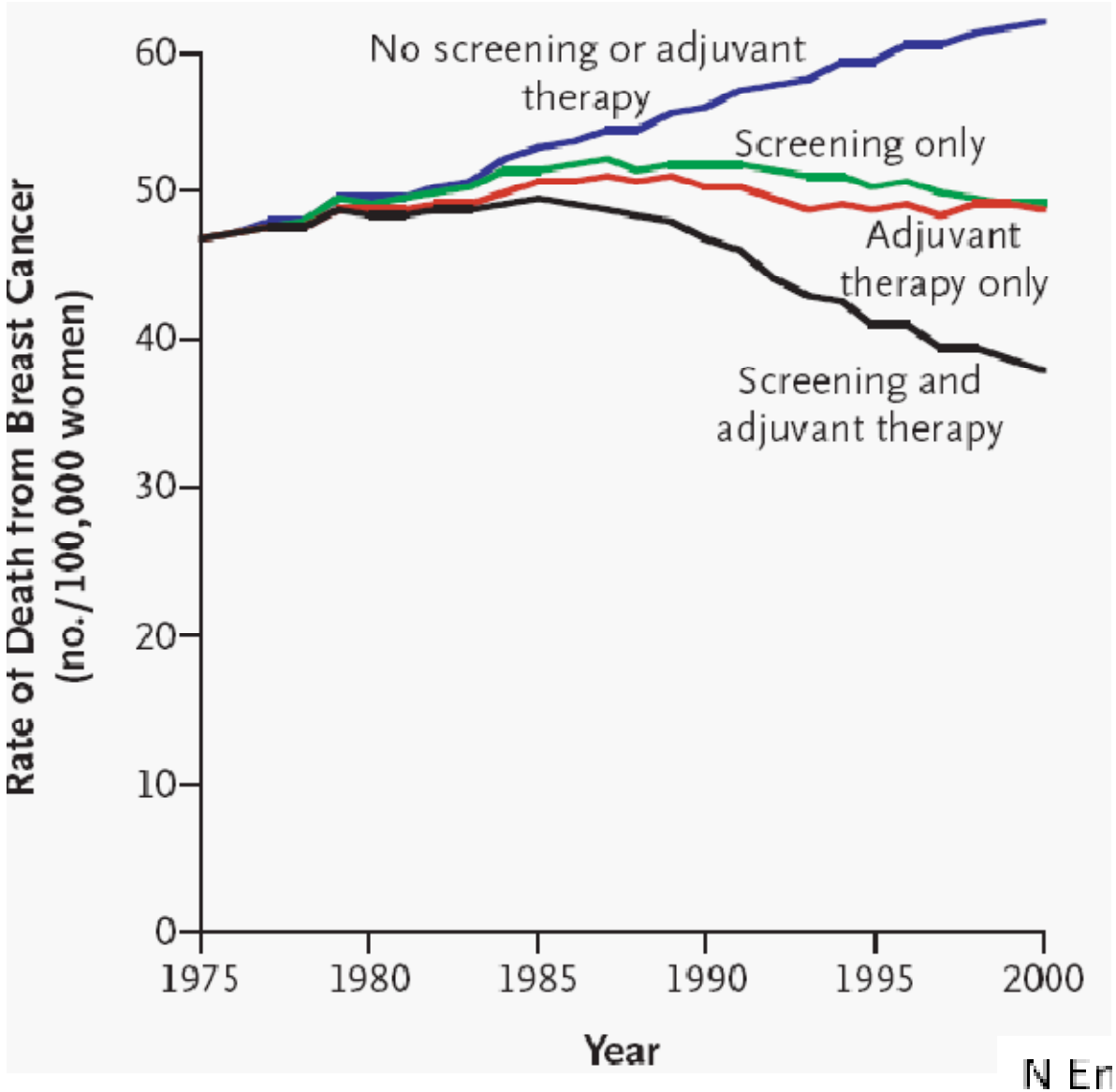


FIGURE 7 Total Number of Cancer Deaths Avoided from 1991 to 2004 in Men and 1992 to 2004 in Women.

CA Cancer J Clin 2008;58:71–96

Effect of Screening and Adjuvant Therapy on Mortality from Breast Cancer



13%
18%

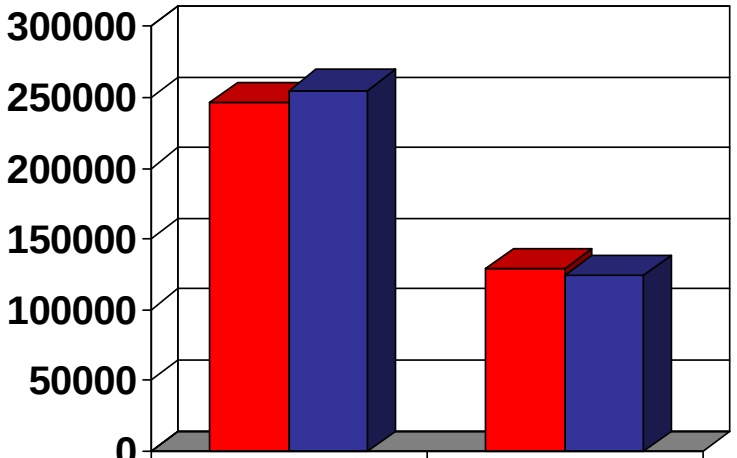
12%
15%

25%
30%

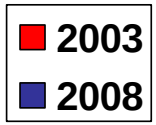
!

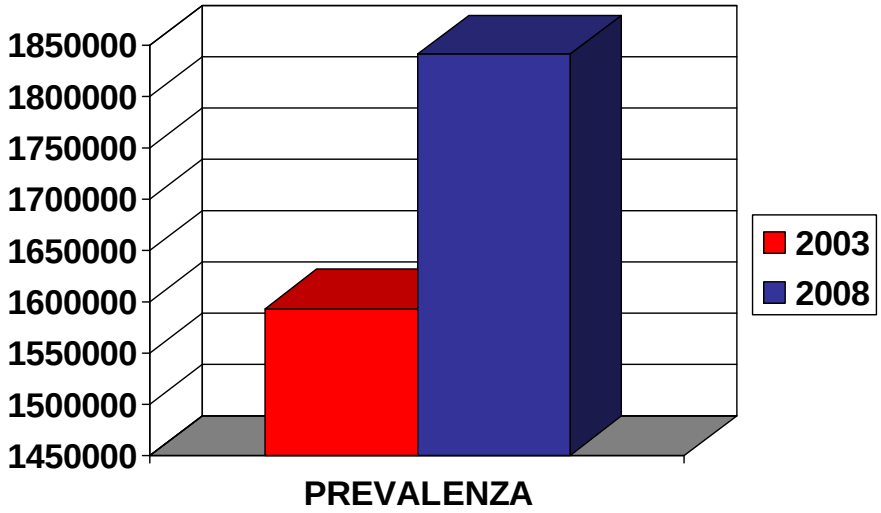
N Engl J Med 2005;353:1784-92.

TREND (2003-2008) TUMORI MALIGNI



	INCIDENZA	MORTALITA'
2003	246208	128893
2008	255000	124000





IRE ISTITUTO NAZIONALE TUMORI REGINA ELENA

Five Year Relative Survival Rates for Breast Cancer: 1973 - 2003

	Localized	Regional	Distant
1973	85	53	<10
2003	**98**	**85**	**28**

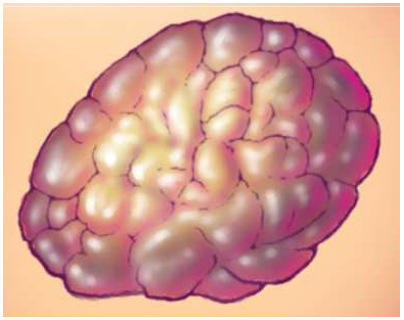
Cancer survivors increased from 3 M to 9 M in the same period

ITALY: breast cancer death risk reduction of 2,9% from 1985 to 1995

CA, Jan 1973 and Jan 2008; Breast Cancer Facts & Figures 2007-8

Targeted Therapy For Cancer





Tumor



Get back to lab!

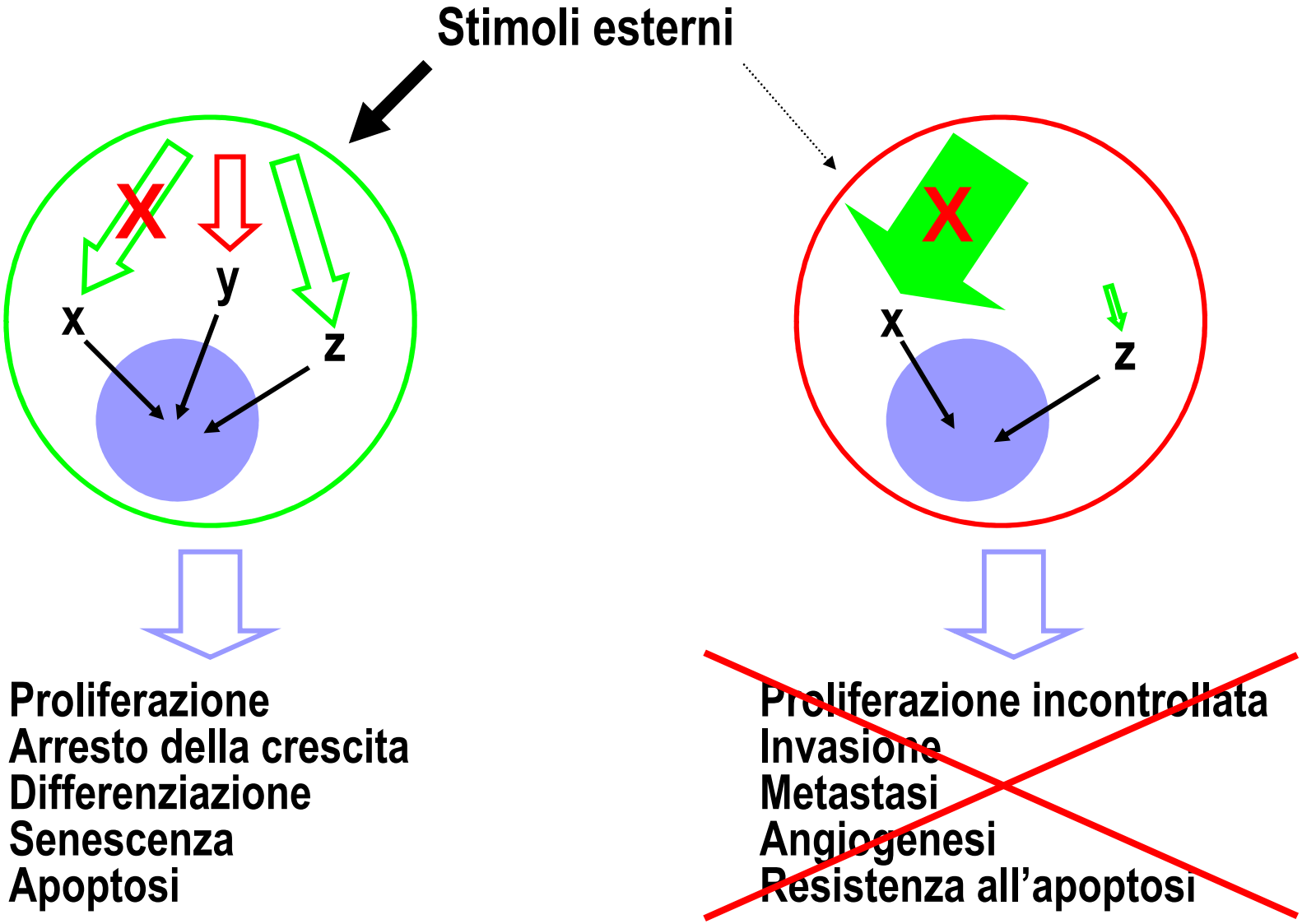




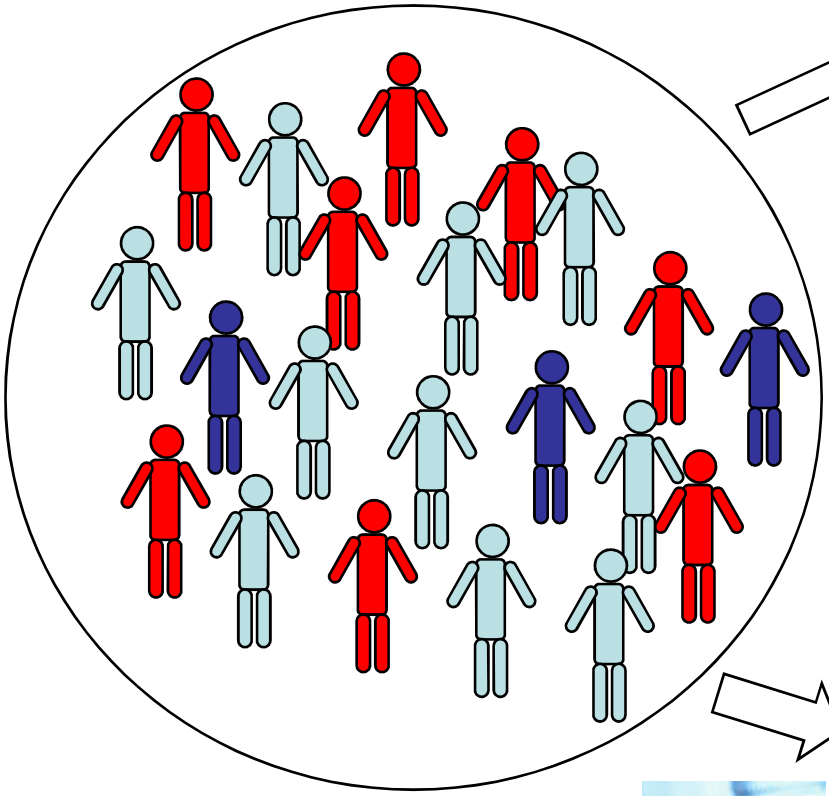
Translational Medicine

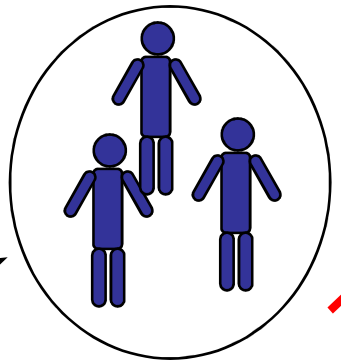
(‘from bench to bedside, and back!)

La Cellula Tumorale *Dipende* da Certi Segnali



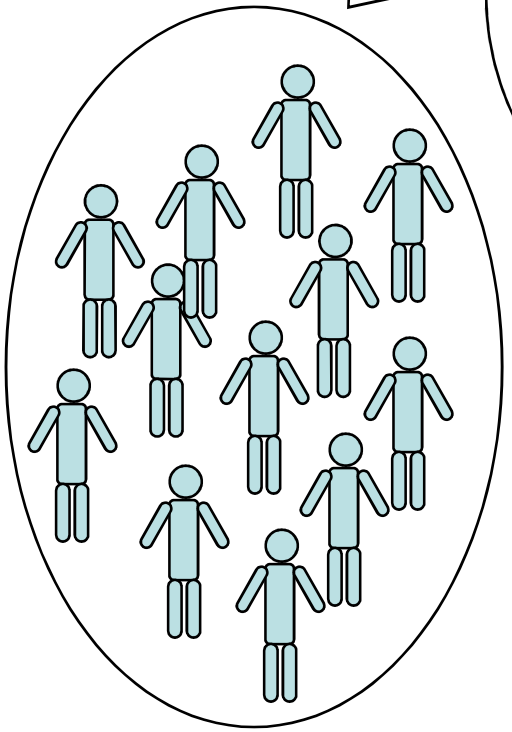
Ieri:
…tanti pazienti, una sola terapia…

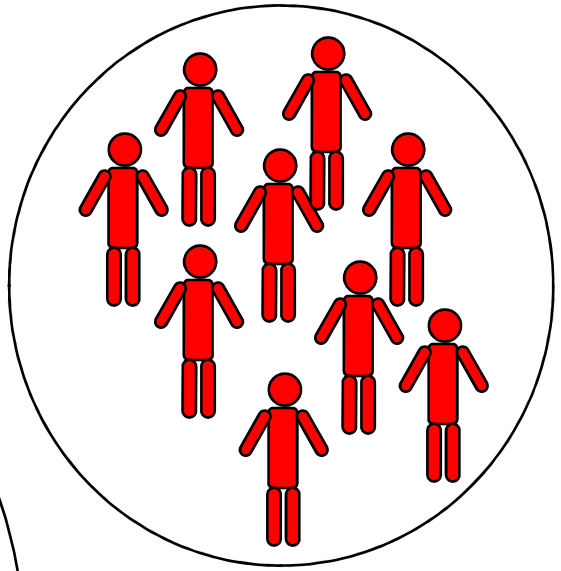










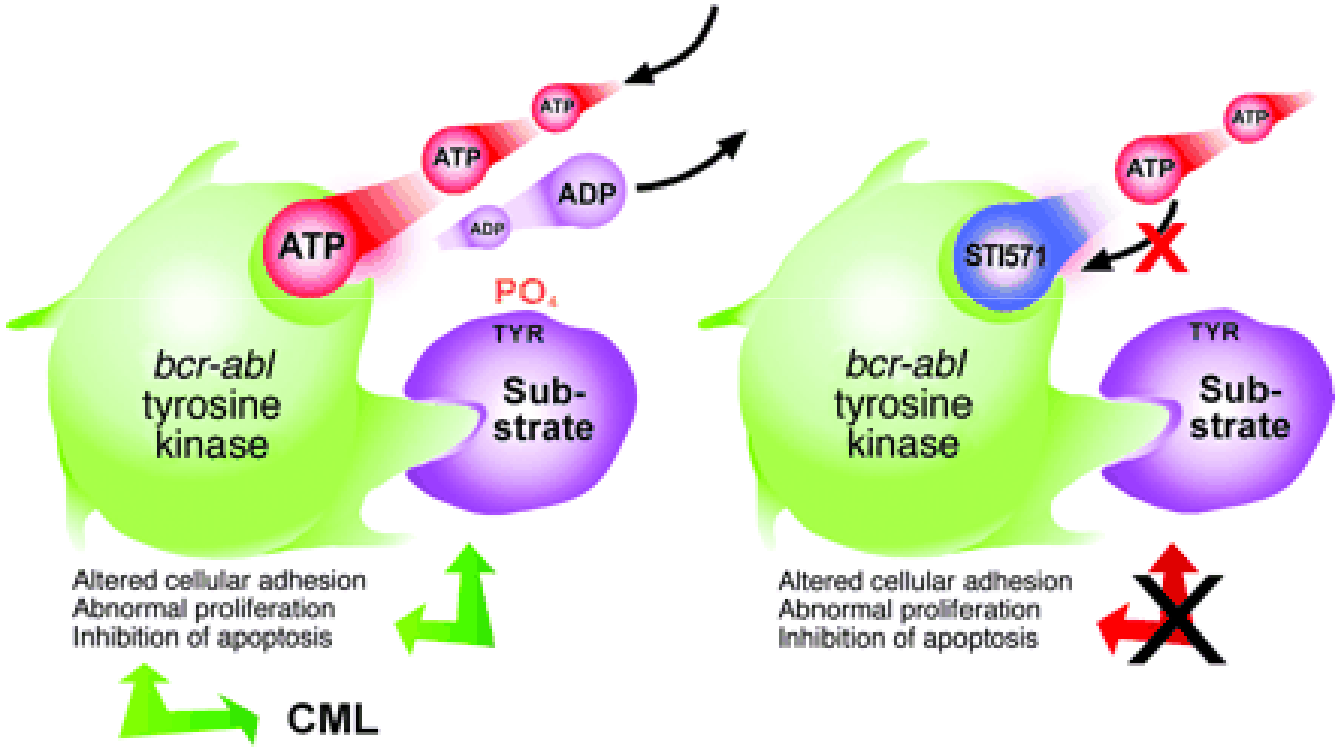




Oggi:
… a ciascuno la sua terapia!

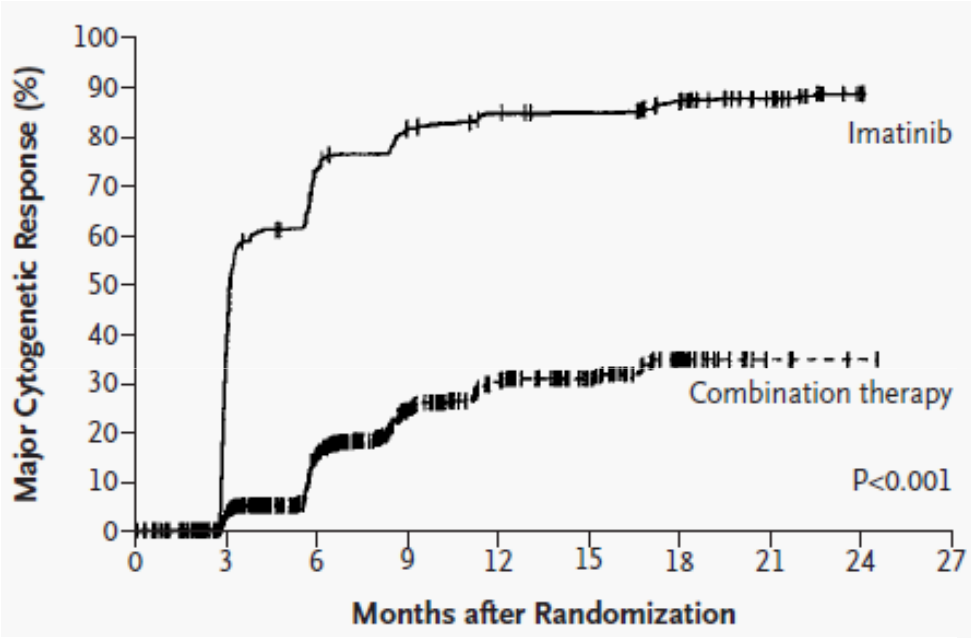
La Nuova Frontiera: Le Terapie “Targeted”

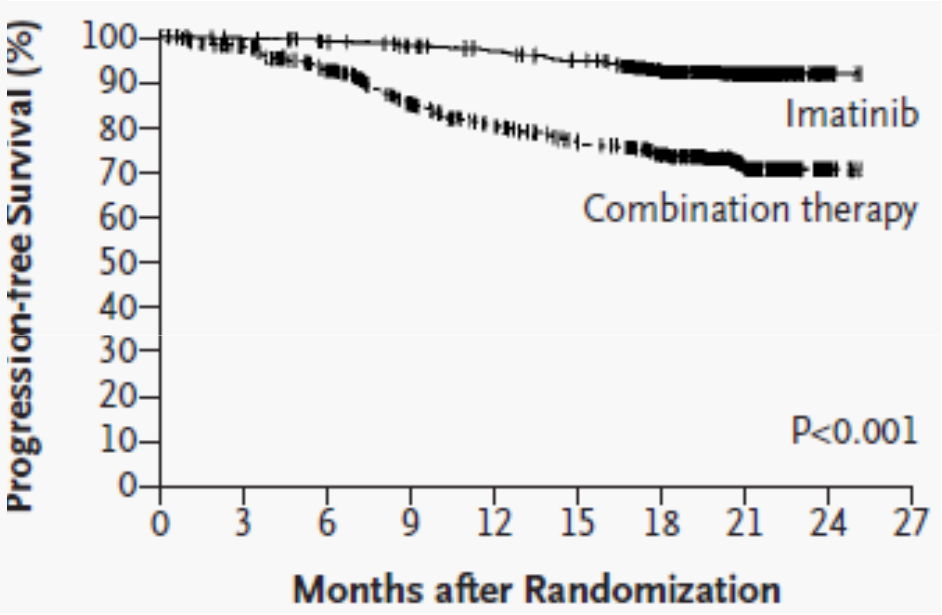






Imatinib Compared with Interferon and Low-Dose Cytarabine for Newly Diagnosed Chronic-Phase Chronic Myeloid Leukemia

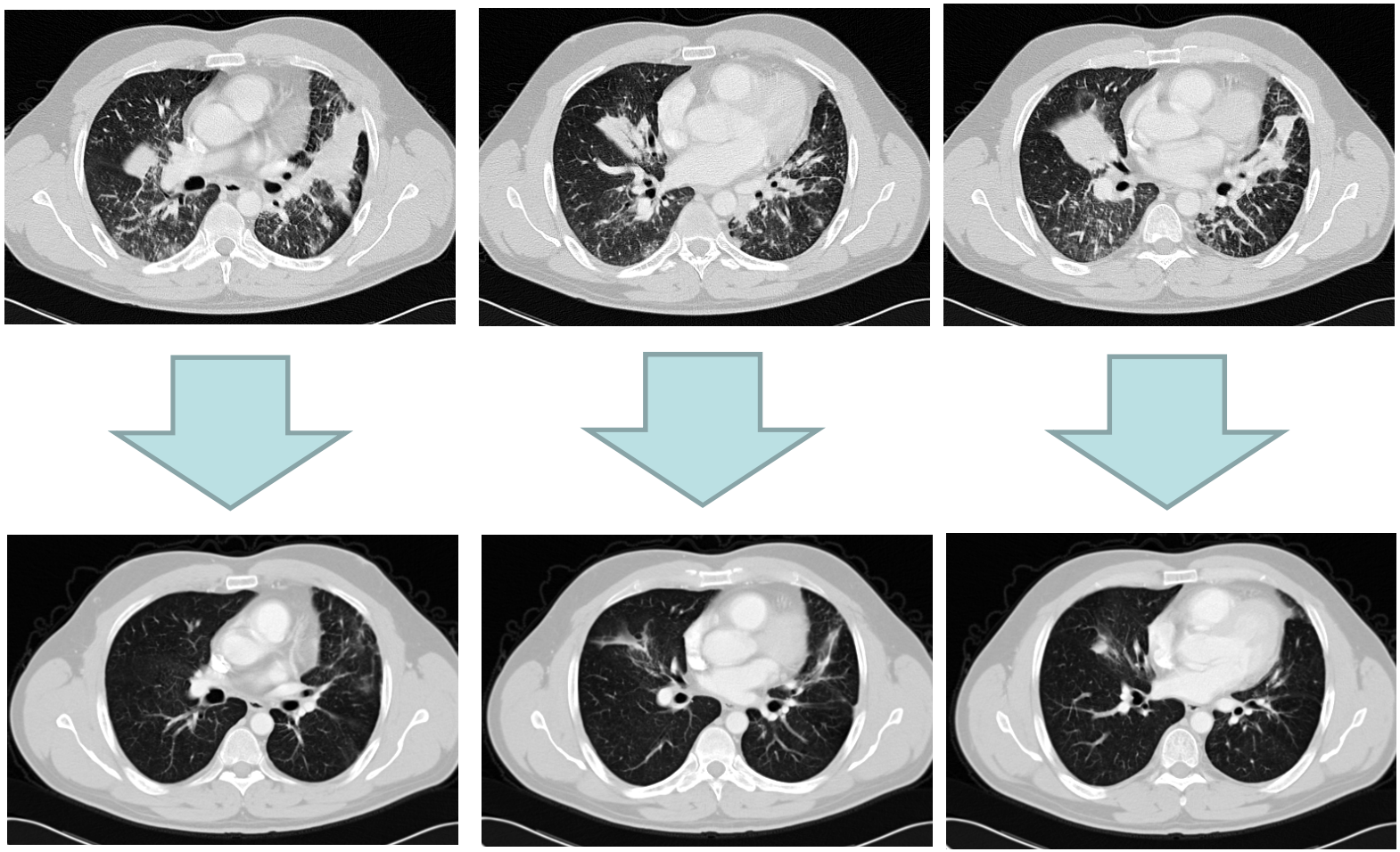




CONCLUSIONS

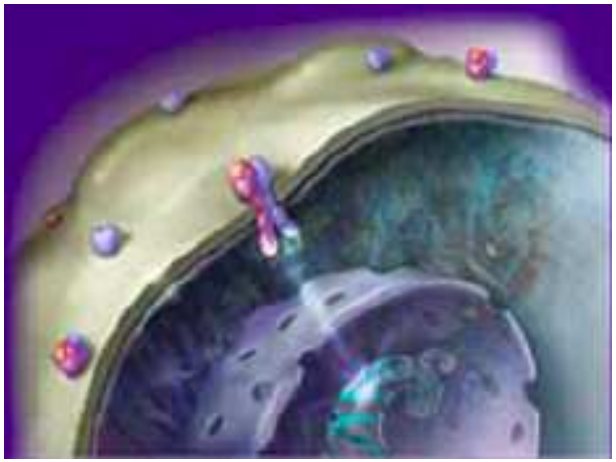
In terms of hematologic and cytogenetic responses, tolerability, and the likelihood of progression to accelerated-phase or blast-crisis CML, imatinib was superior to interferon alfa plus low-dose cytarabine as first-line therapy in newly diagnosed chronic-phase CML.

…Si, ma quanto funzionano?



NB: inibitori TKI, NSCLC

Trastuzumab: Storia Di Un Successo…



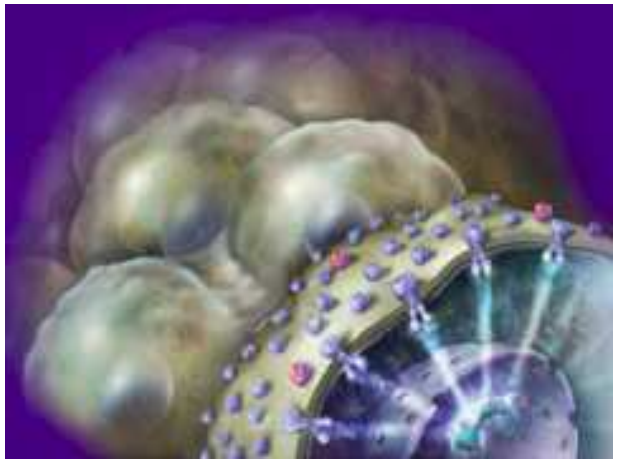
HER-2 Normale

1



HER-2 iperespresso

2



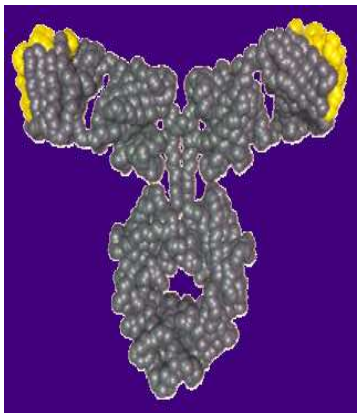
Proliferazione incontrollata

3

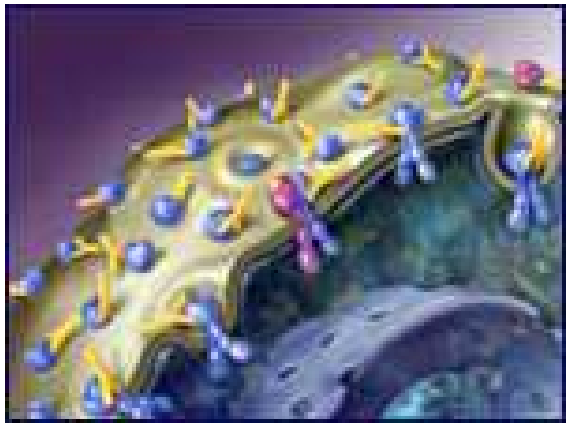


HER-2 iperespresso

4



5

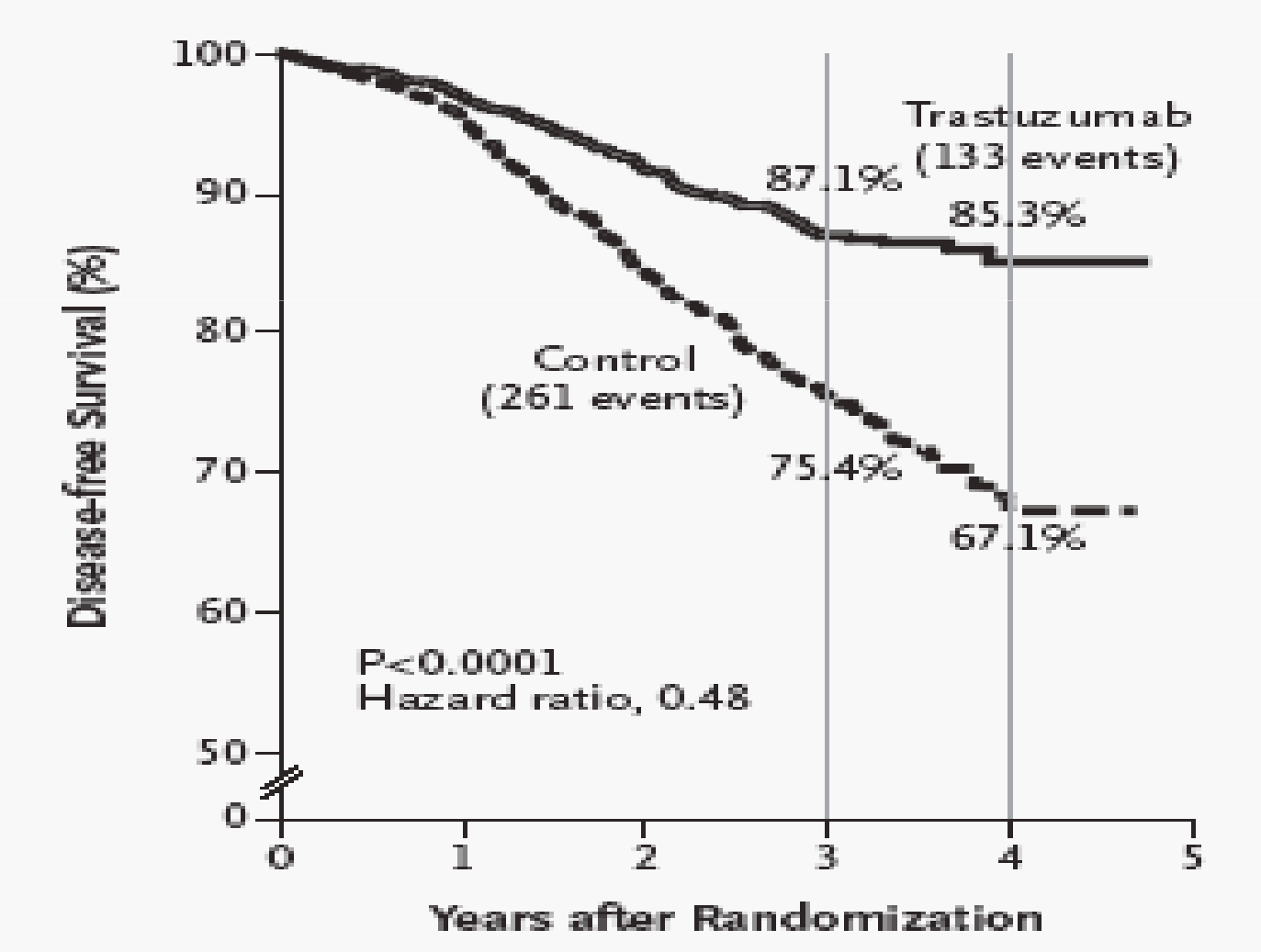


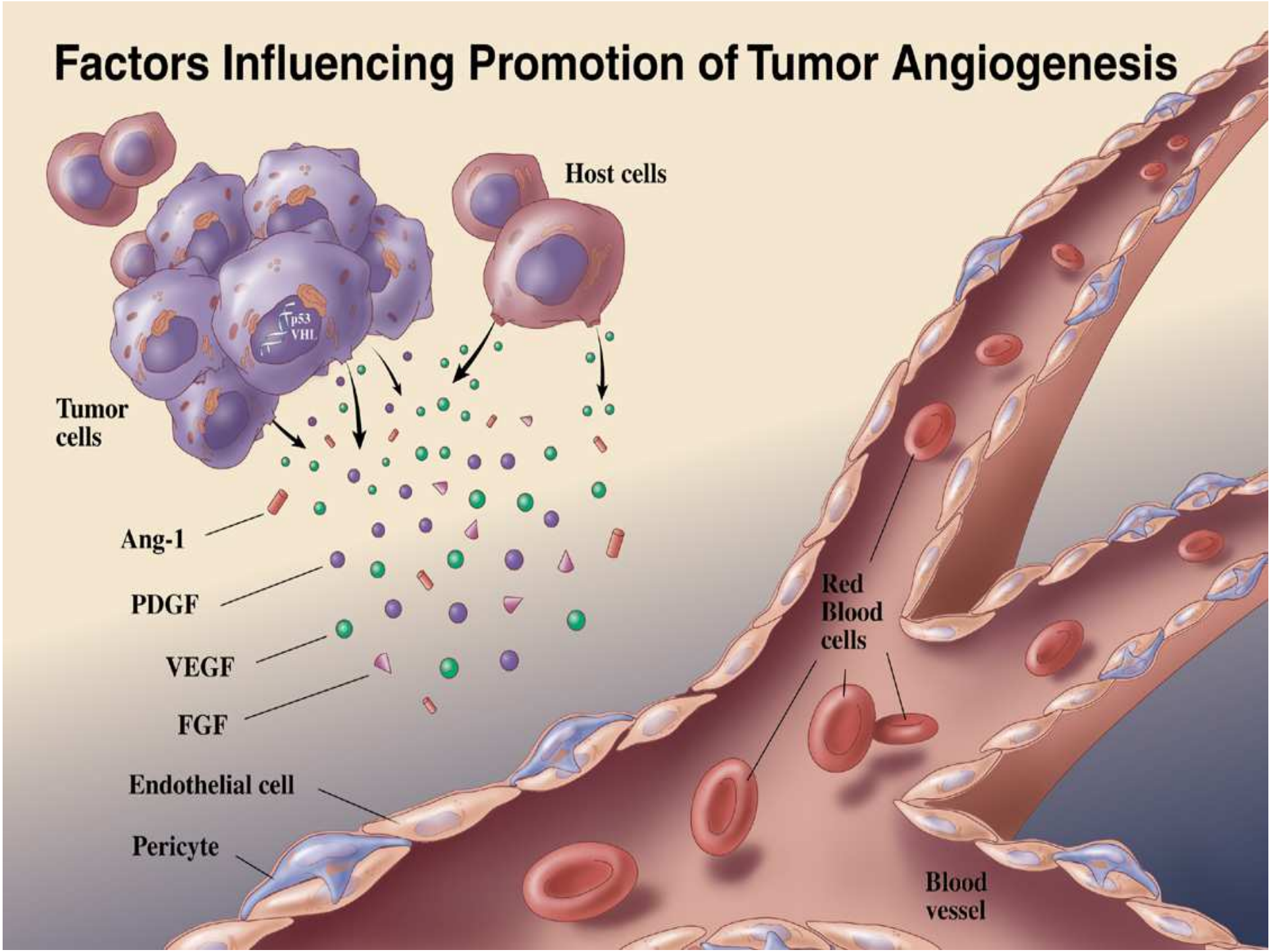
Trastuzumab blocca HER-2

6

…e se guardiamo le ‘Curve’..

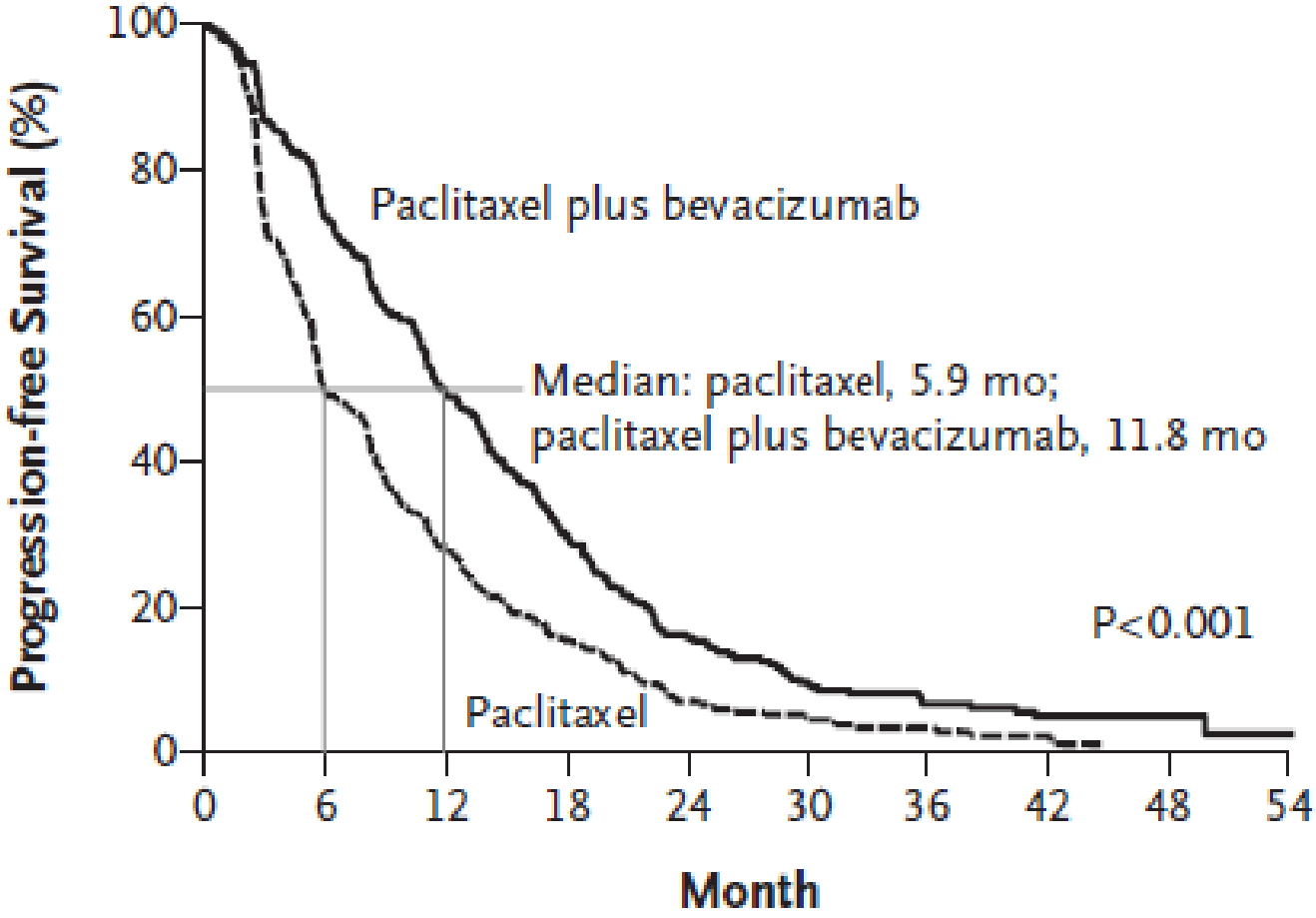
Trastuzumab adiuvante




Factors Influencing Promotion of Tumor Angiogenesis
Host cells
Tp53
VHL
Tumor cells
Ang-1
PDGF
VEGF
FGF
Endothelial cell
Pericyte
Red Blood cells
Blood vessel

Paclitaxel plus Bevacizumab versus Paclitaxel Alone for Metastatic Breast Cancer

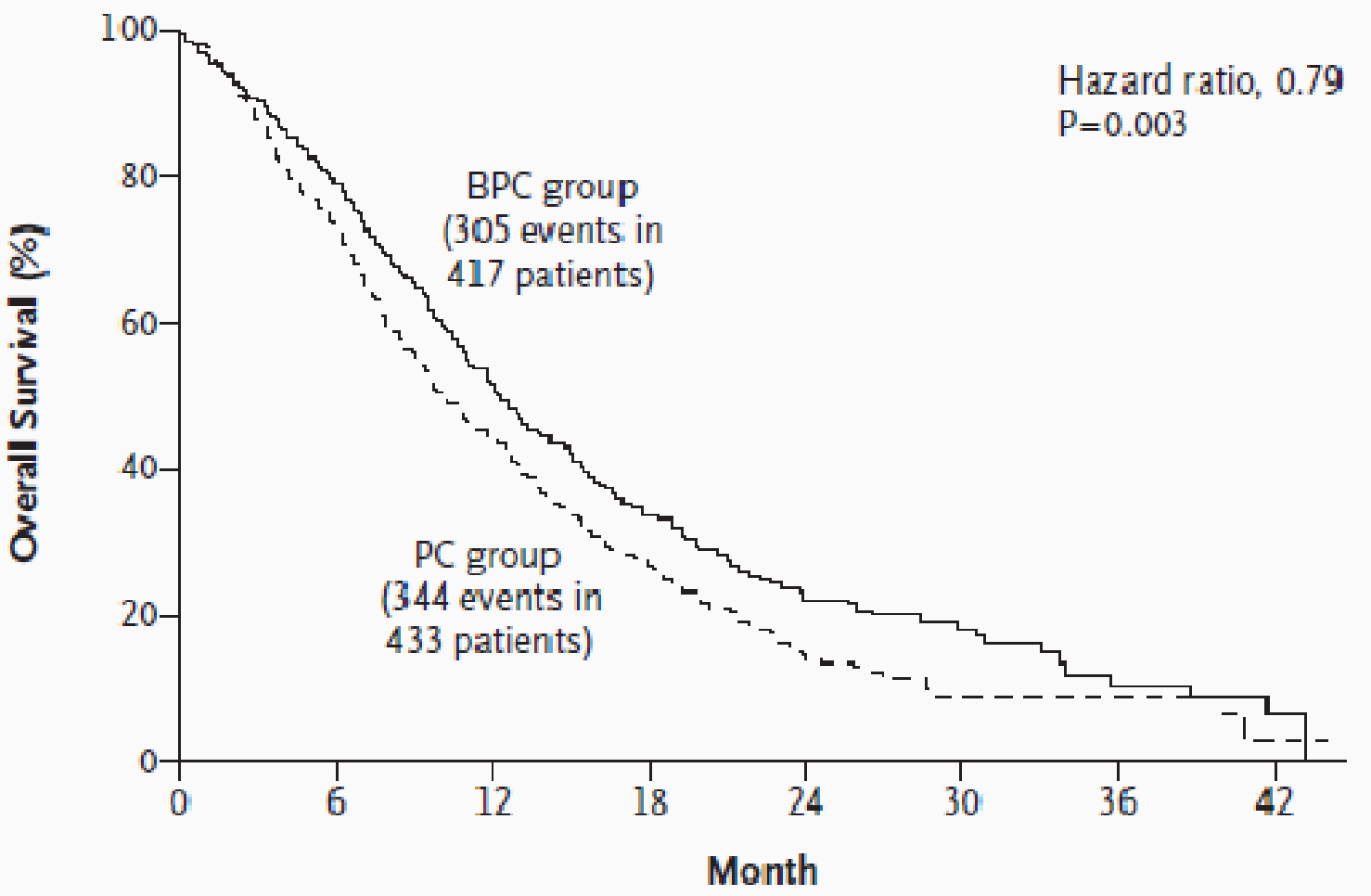
Kathy Miller, M.D., Molin Wang, Ph.D., Julie Gralow, M.D., Maura Dickler, M.D., Melody Cobleigh, M.D., Edith A. Perez, M.D., Tamara Shenkier, M.D., David Cella, Ph.D., and Nancy E. Davidson, M.D.



N Engl J Med 2007;357:2666-76.

Paclitaxel–Carboplatin Alone or with Bevacizumab for Non–Small-Cell Lung Cancer

Alan Sandler, M.D., Robert Gray, Ph.D., Michael C. Perry, M.D., Julie Brahmer, M.D., Joan H. Schiller, M.D., Afshin Dowlati, M.D., Rogerio Lilenbaum, M.D., and David H. Johnson, M.D.



N Engl J Med 2006;355:2542-50.

Carcinoma del rene:
..'*a change of season – PART 1*'....
MRCC Treatment Options

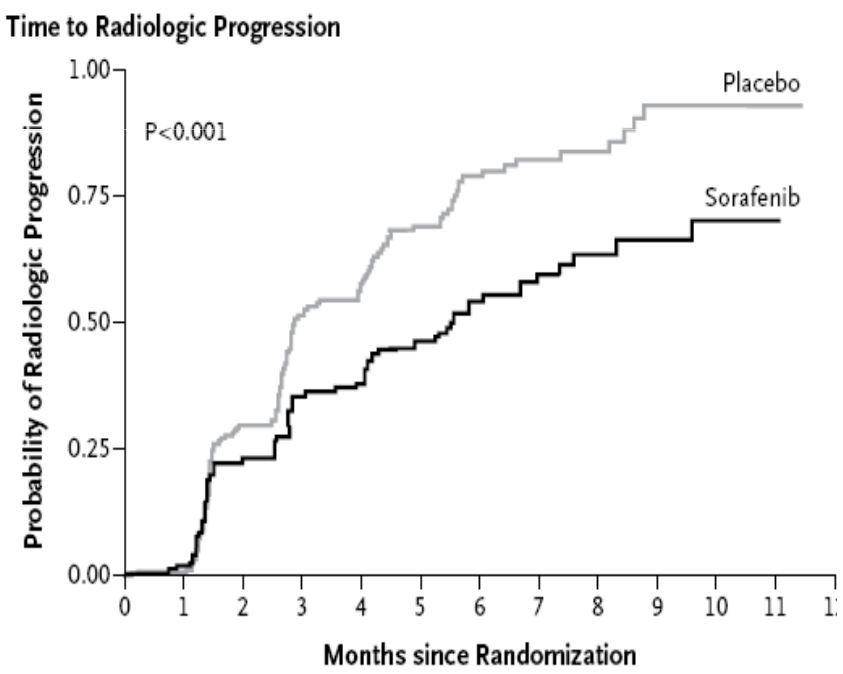
	1st Line	2nd Line
Good Prognosis	**Beva+IFN** **Sunitinib** **HD IL-2**	**Sorafenib** **Temsirolimus/ Everolimus** **Sorafenib**
Intermediate Prognosis	**Beva+IFN** **Sunitinib**	**Temsirolimus/ Everolimus**
Poor Prognosis	**Temsirolimus**	**New Drug**

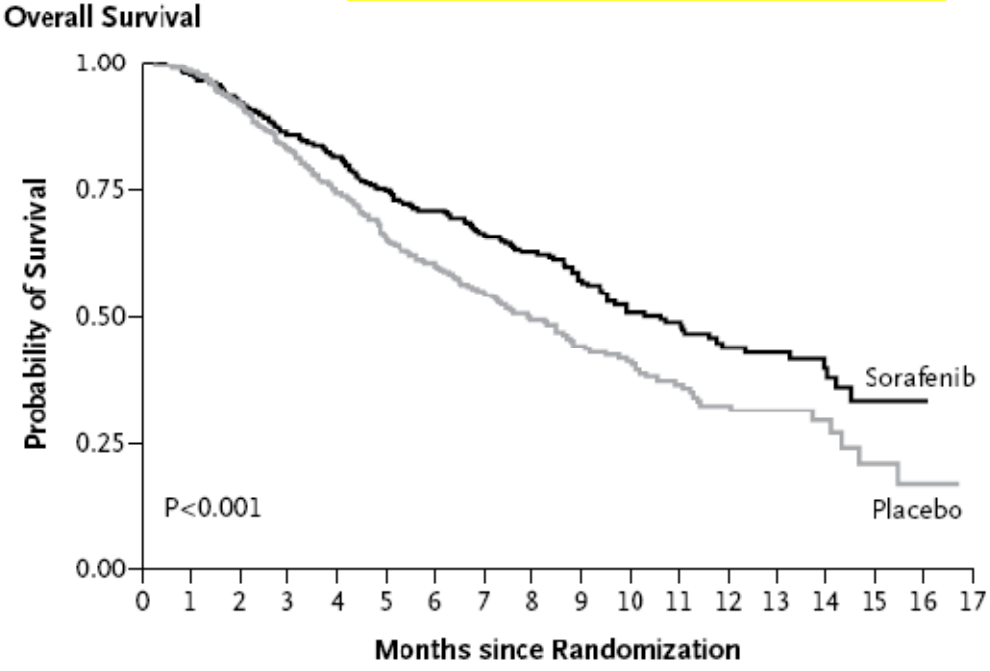
www.thelancet.com Vol 372 August 9, 2008

Epatocarcinoma:
..'*a change of season – PART 2*'....

Sorafenib in Advanced Hepatocellular Carcinoma

Phase III SHARP Trial





N ENGL J MED 359;4 WWW.NEJM.ORG JULY 24, 2008

Quali scenari si prospettano?

Cost of Adjuvant Chemotherapy

• CMF (PO) x 6	• U$ 1,152
• CMF (IV) x 6	• U$ 391
• AC x 4	• U$ 828
• FAC x 6	• U$ 1,087
• CAF x 6	• U$ 1,304
• AC x 4 → Pac x 4	• U$ 7,374
• FAC x 4 → Pac x 4	• U$ 7,271
• DocAC x 6	• U$ 12,885

Mod. By Hortobagyi, Rome 2008

Cost of Adjuvant Chemotherapy II

• Dose-dense AC x 4 → Pac x 4 (65 kg)	• U$ 20,121
• Dose-dense AC x 4 → Pac x 4 (85 kg)	• U$ 27,681
• Dose-dense A x 4 → P x 4 → C x 4 (65 kg)	• U$ 26,495
• Dose-dense A x 4 → P x 4 → C x 4 (85 kg)	• U$ 37,835

Mod. By Hortobagyi, Rome 2008

Cost of Adjuvant Endocrine Therapy

• Surgical oophorectomy	U$ 10,000
• Tamoxifen x 5 years	U$ 7,843
• Toremifene	U$ 7,050
• Anastrozole, letrozole, or exemestane x 5 years	U$ 14,000
• Tamoxifen x 2 years + AI x 3 years	U$ 11,540
• Tamoxifen x 5 years + Letrozole x 5 years	U$ 21.820
• Goserelin x 2 years	U$ 11,180
• Goserelin x 3 years	U$ 16,920
• Goserelin x 2 years + Tamoxifen x 5 years	U$ 19,023
• Goserelin x 3 years + Anastrozole x 5 years	U$ 30,983

Mod. By Hortobagyi, Rome 2008

Cost of Adjuvant Targeted Therapies

• Trastuzumab x 1 year	U$ 44,000
• Trastuzumab x 12 weeks	U$ 11,000
• Trastuzumab x 2 years	U$ 88,000
• Bevacizumab x 1 year	U$ 100,000
• Trastuzumab + Bevacizumab x 1 year	U$ 144,000
• Lapatinib x 1 year	???
• Lapatinib x 6 months	???

Mod. By Hortobagyi, Rome 2008

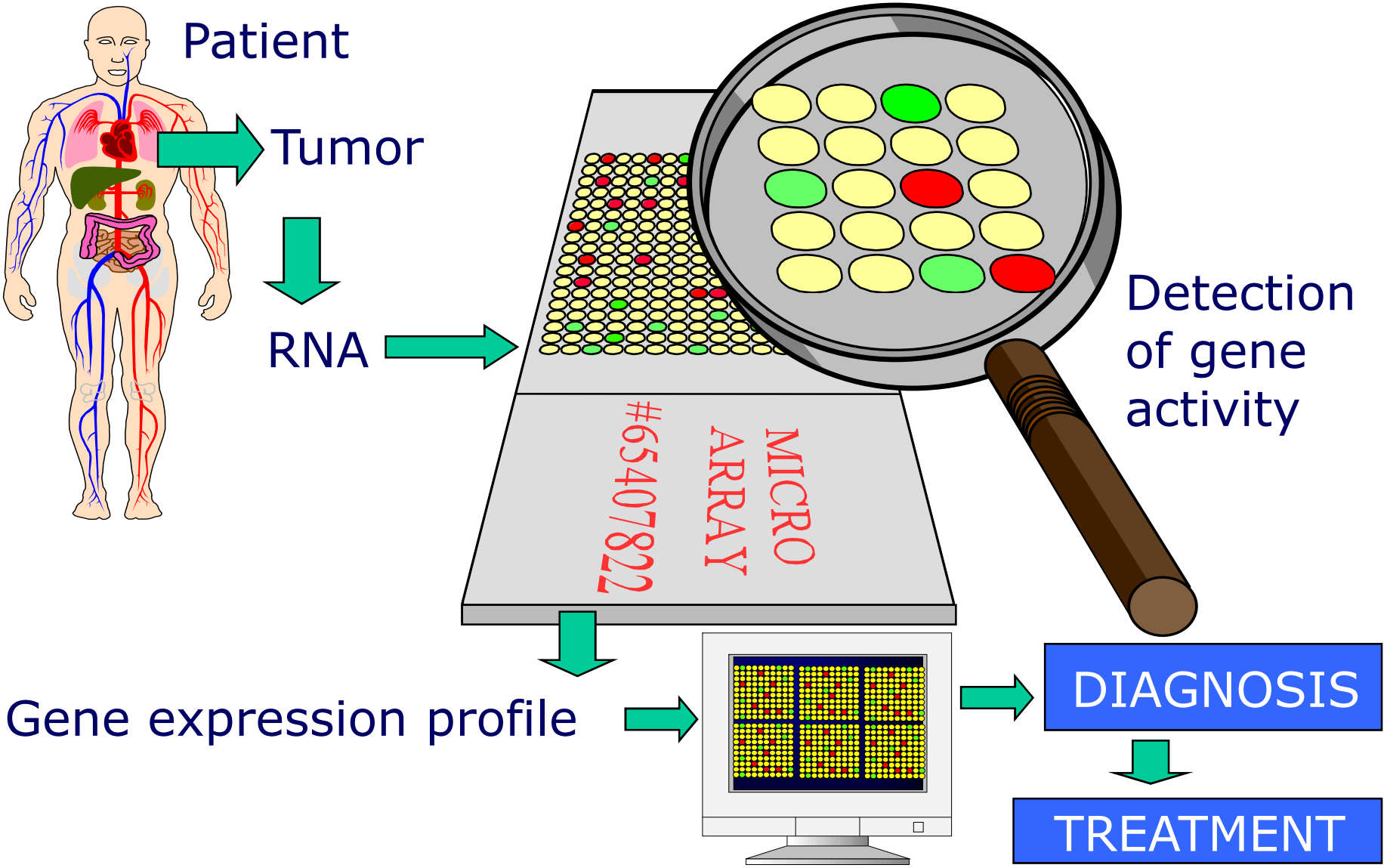
Adjuvant Systemic Therapies: Possible Cost Scenarios

- 62-year-old, ER+, PR+, HER2-, stage II:
  - TACx6 + AI x 5 yrs: **$ 26,885**
- 55-year-old, ER/PR-, HER2+, Stage II:
  - DD AC+pac, trastuzumab x 1 year: **$ 71,681**
- 35-year-old, ER/PR+, HER2+, Stage II:
  - DD AC+pac, trastuzumab x 1 year + Goserelin x 3 years + Anastrozole x 5 years: **$ 102,664**
- 35-year-old, ER/PR+, HER2+, Stage II (in 2012):
  - DD AC+pac, trastuzumab + bevacizumab x 1 year + Goserelin x 3 years + Anastrozole x 5 years: **$ 202,664**

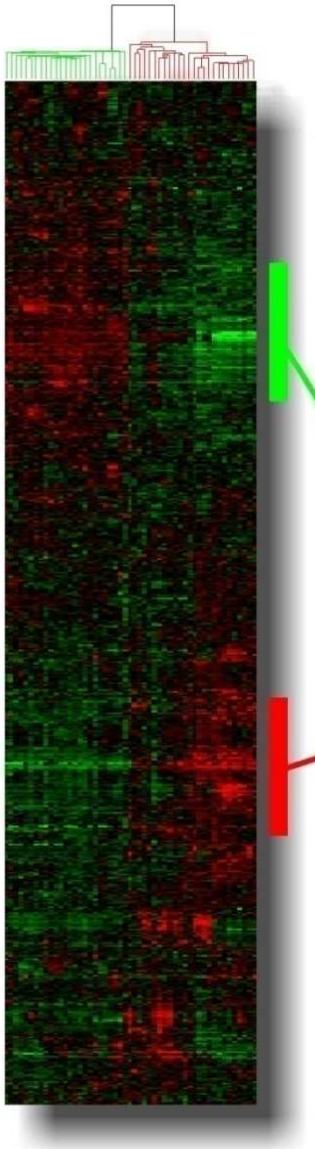
Mod. By Hortobagyi, Rome 2008

……e i costi della [nuova] diagnostica?

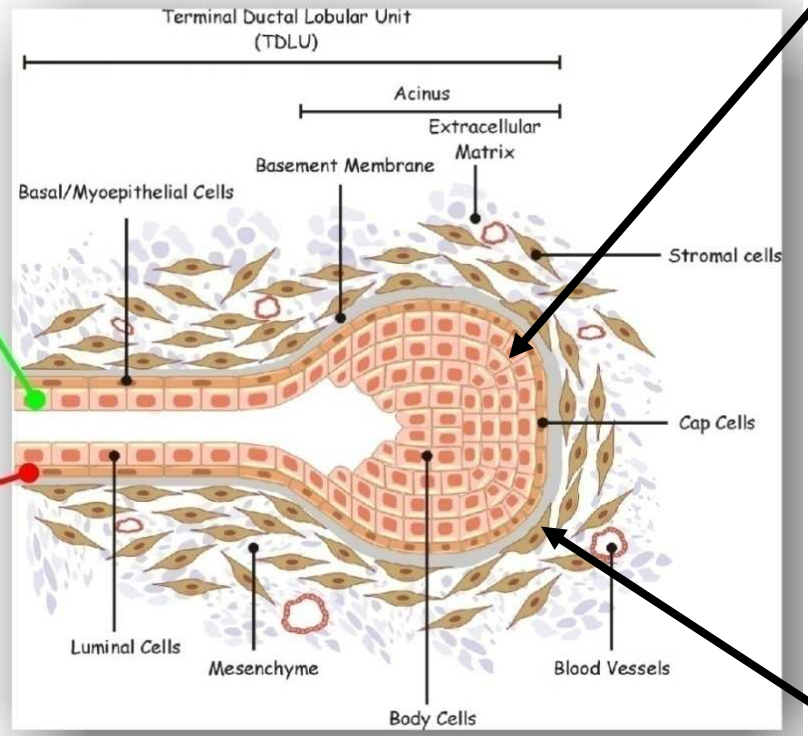
The Future is Becoming Reality!

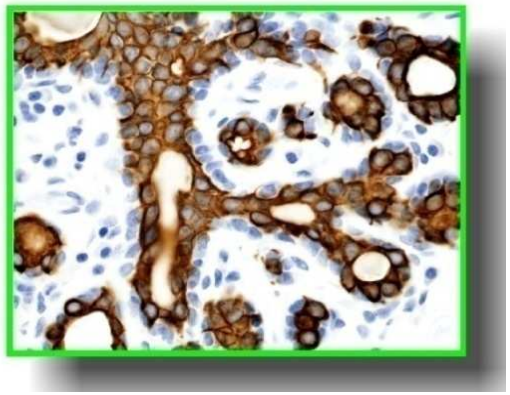


PERSONALIZED MOLECULAR MEDICINE BREAST CANCER

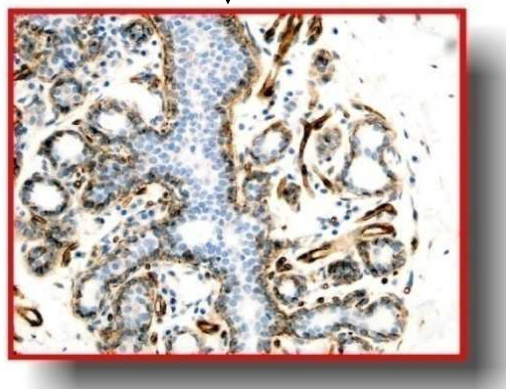


LUMINAL
Hormonal Manipulation





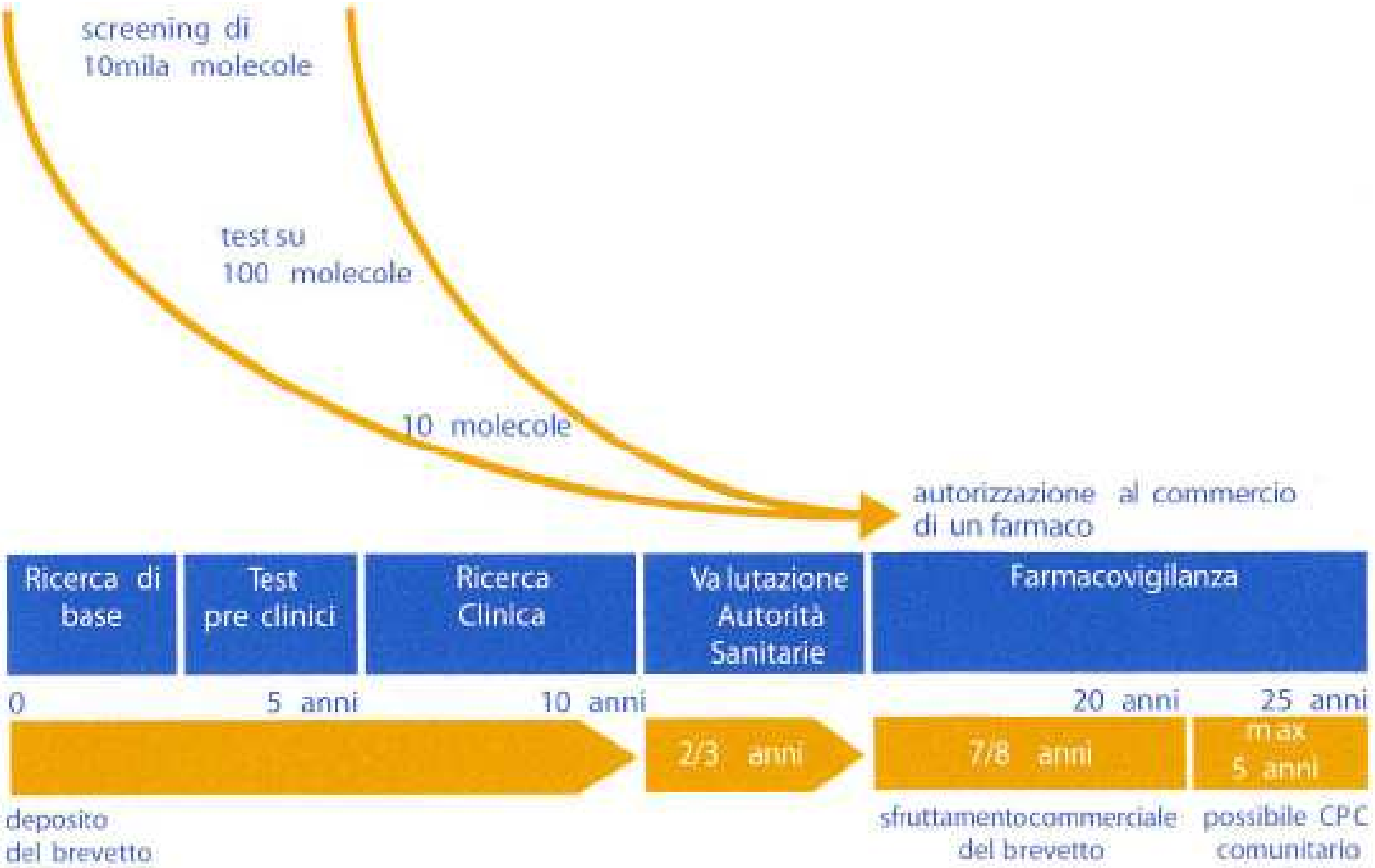
HER2
Trastuzumab
Lapatinib



BASAL
Chemotherapy

Perché costano tanto?

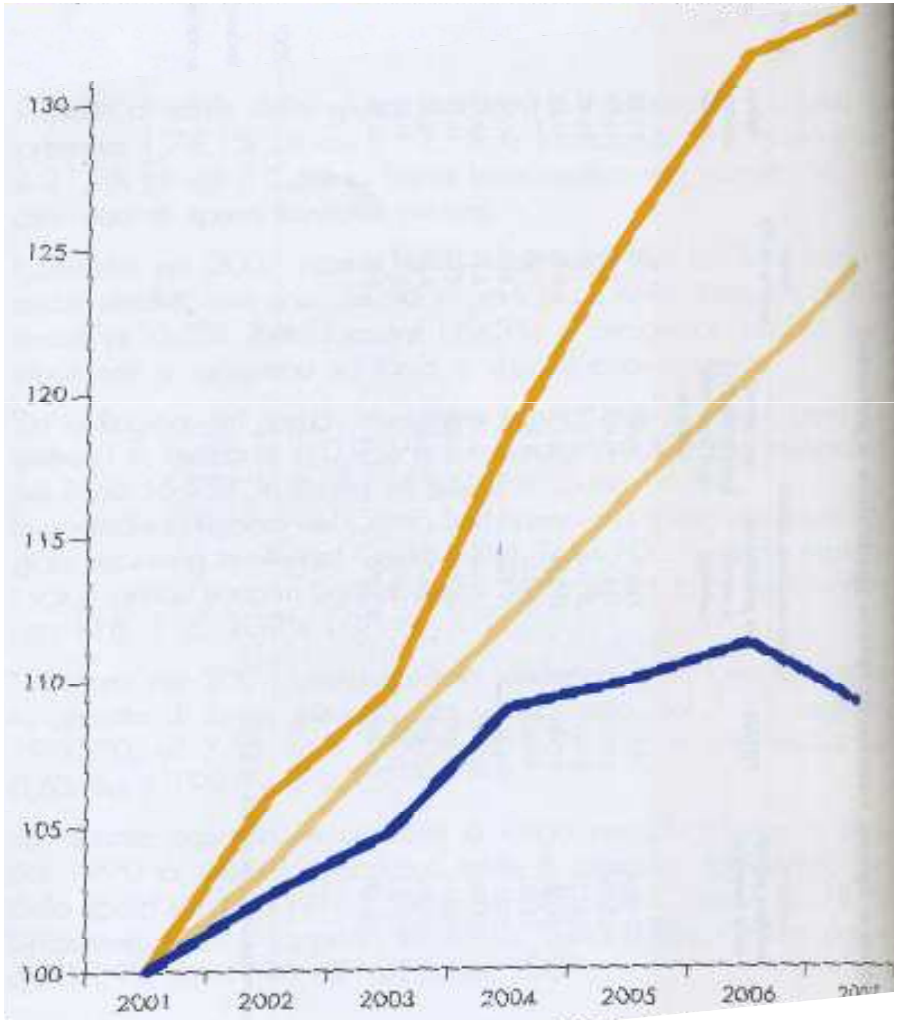
Il percorso per la nascita di un nuovo farmaco



Fonte: Efpia

FARMINDUSTRIA

Evoluzione temporale di spesa farmaceutica e sanitaria totale



Spesa sanitaria totale

Spesa farmaceutica totale

FARMINDUSTRIA

In Italia popolazione tra le più anziane d'Europa, ma spesa farmaceutica pubblica inferiore

Farmaceutica convenzionata (anno 2008)

	spesa pro-capite Indice: Italia=100	in % sul PIL
Francia	169,0	1,04
Germania	173,0	1,08
Regno Unito	112,0	0,71
Spagna	134,0	1,05
Media Paesi	140,0	0,93
ITALIA	100,0	0,72

Fonte: Istat, Associazioni estere

In Italia prezzi dei farmaci con prescrizione inferiori rispetto agli altri paesi UE

Prezzi a ricavo industria dei medicinali con prescrizione

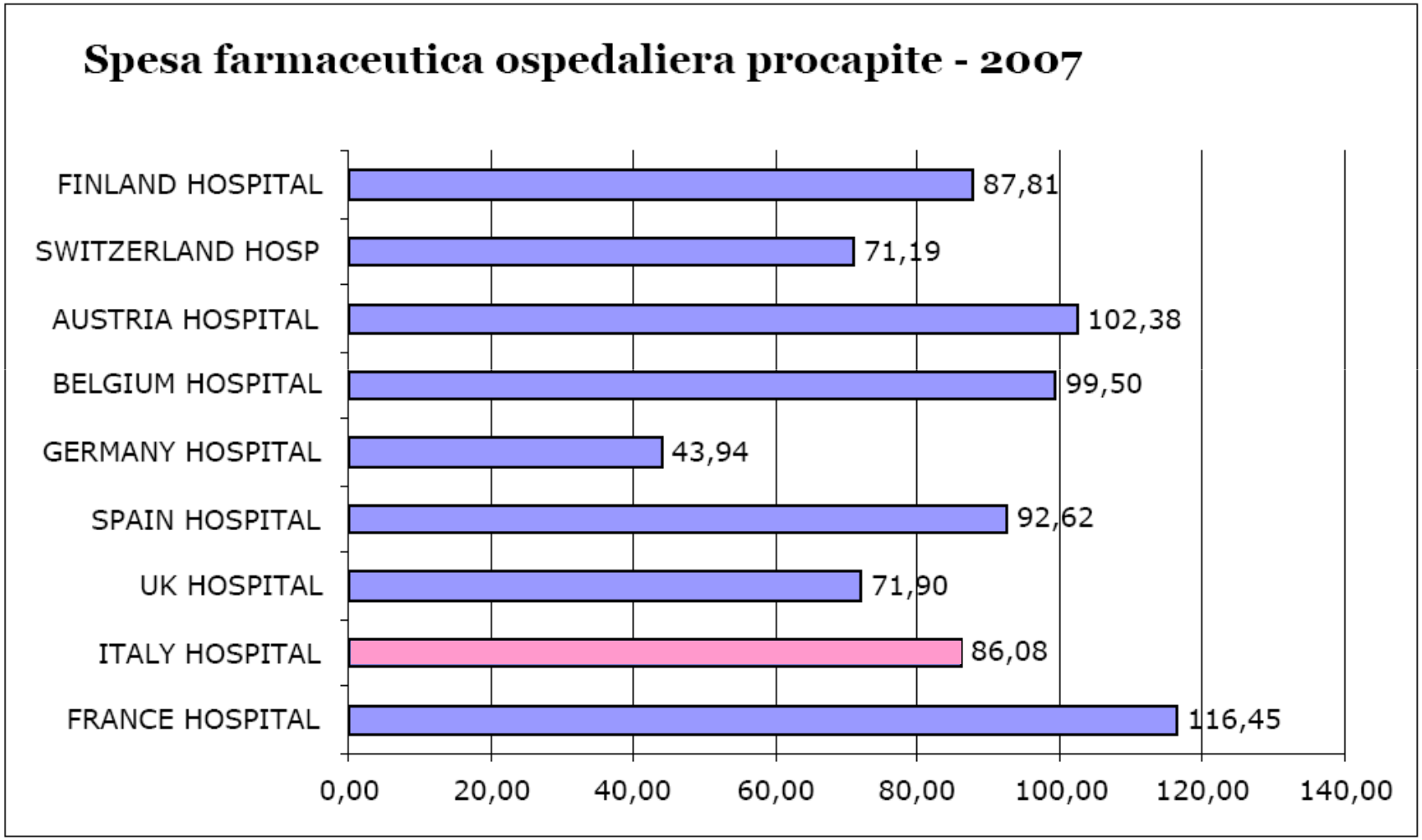
Primi 300 principi attivi a valore, su prodotti lanciati dopo il 1990
Indice di Laspeyres, Italia=100



Italia ~20% in media inferiore agli altri Paesi Ue

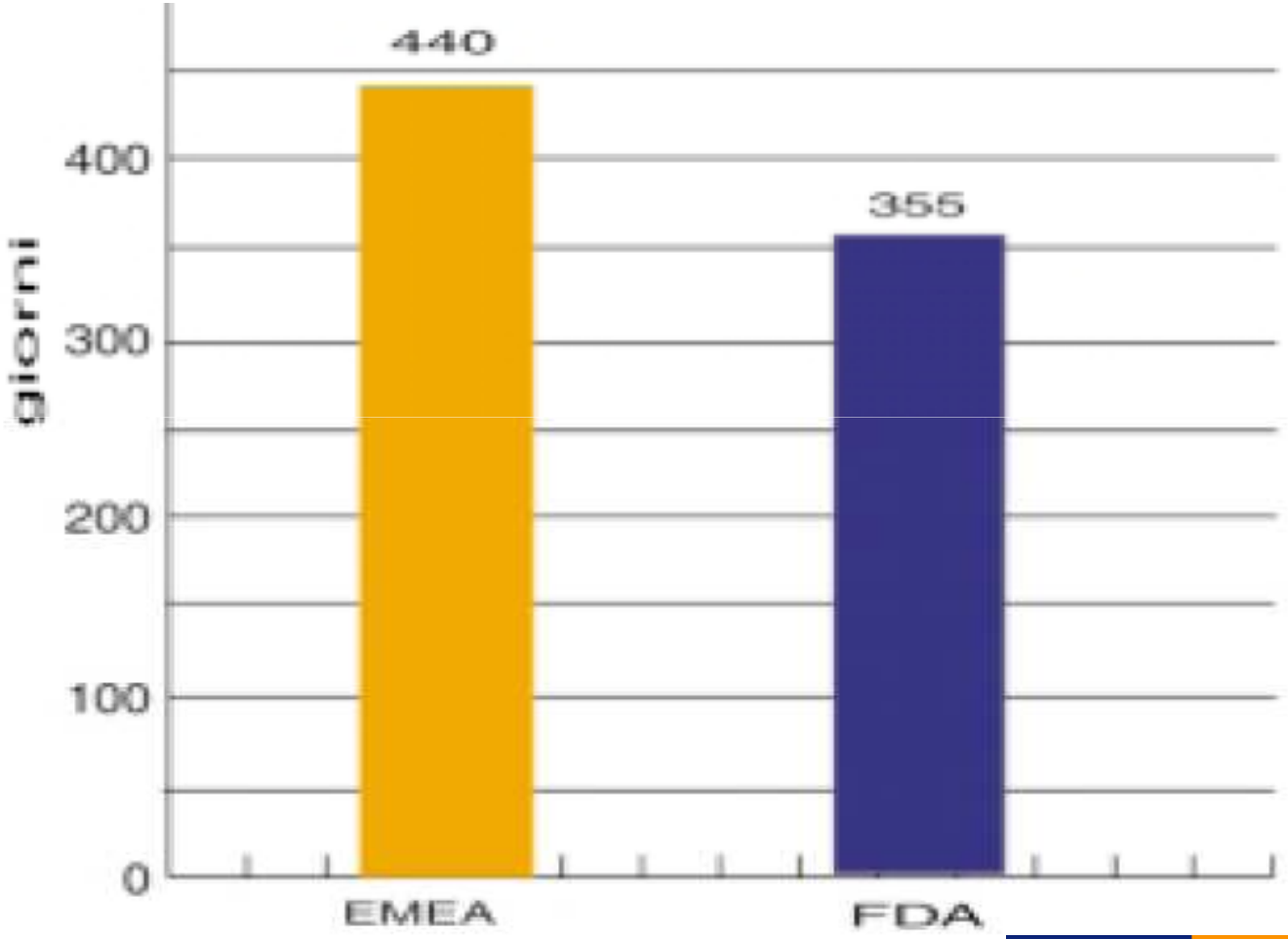
Fonte: Cergas: Bocconi (2007)

In Italia spesa farmaceutica ospedaliera pubblica pro-capite tra le più basse d'Europa



Fonte dati: elaborazioni Farmindustria su dati IMS

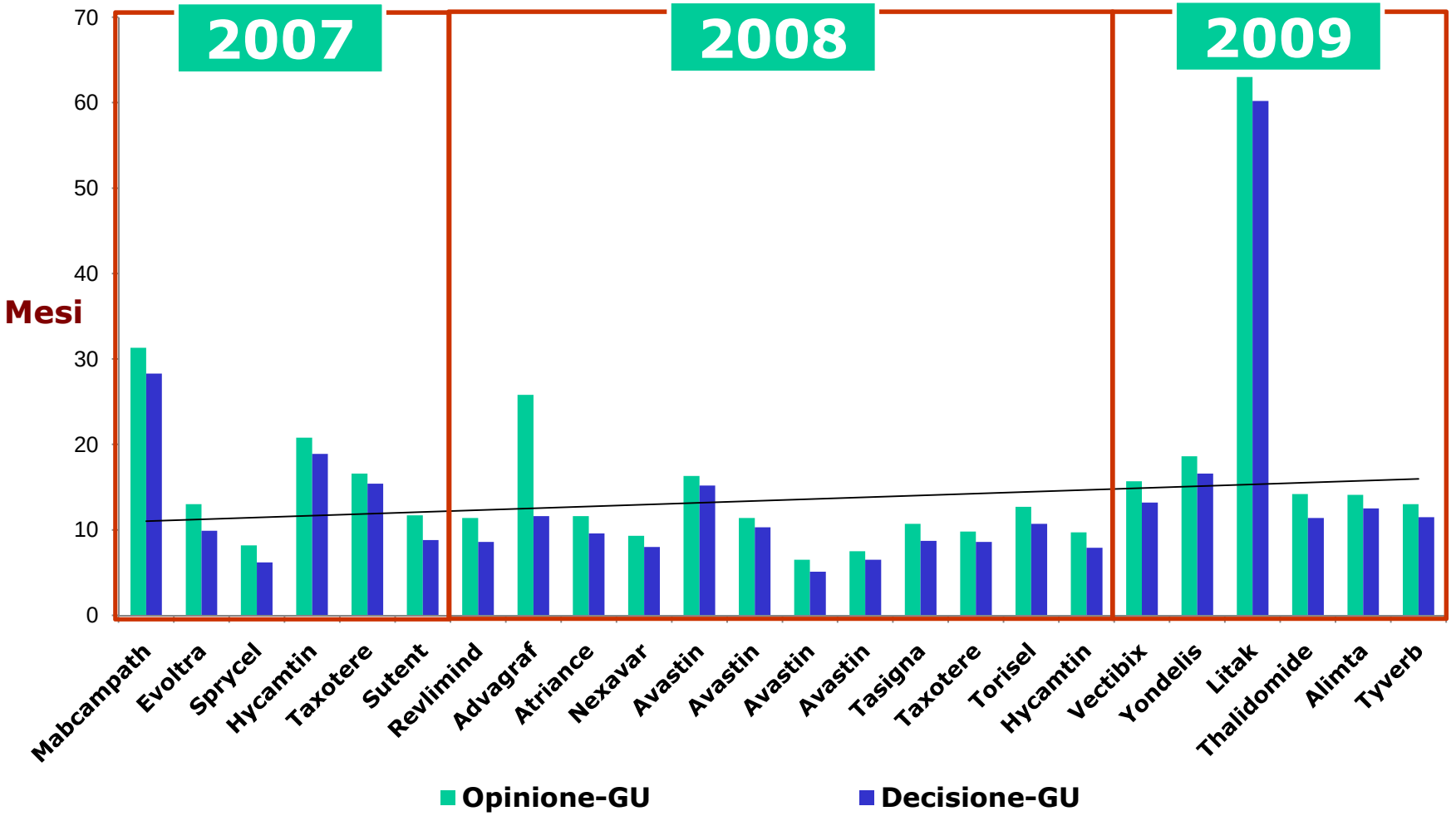
Tempi medi per l’approvazione della registrazione negli USA e in EUROPA



Campione: 15 prodotti registrati in Europa e negli Stati Uniti dal 1997

FARMINDUSTRIA

‘Time-delay’ (mesi) tra Opinion/Decision e G.U.*



*a questi vanno aggiunti i tempi di approvazione degli enti regolatori locali (es. Regioni)

Prevenzione e sprechi

SANITÀ, UNA SFIDA LIBERALE PER IL PAESE

12-MAG-2009

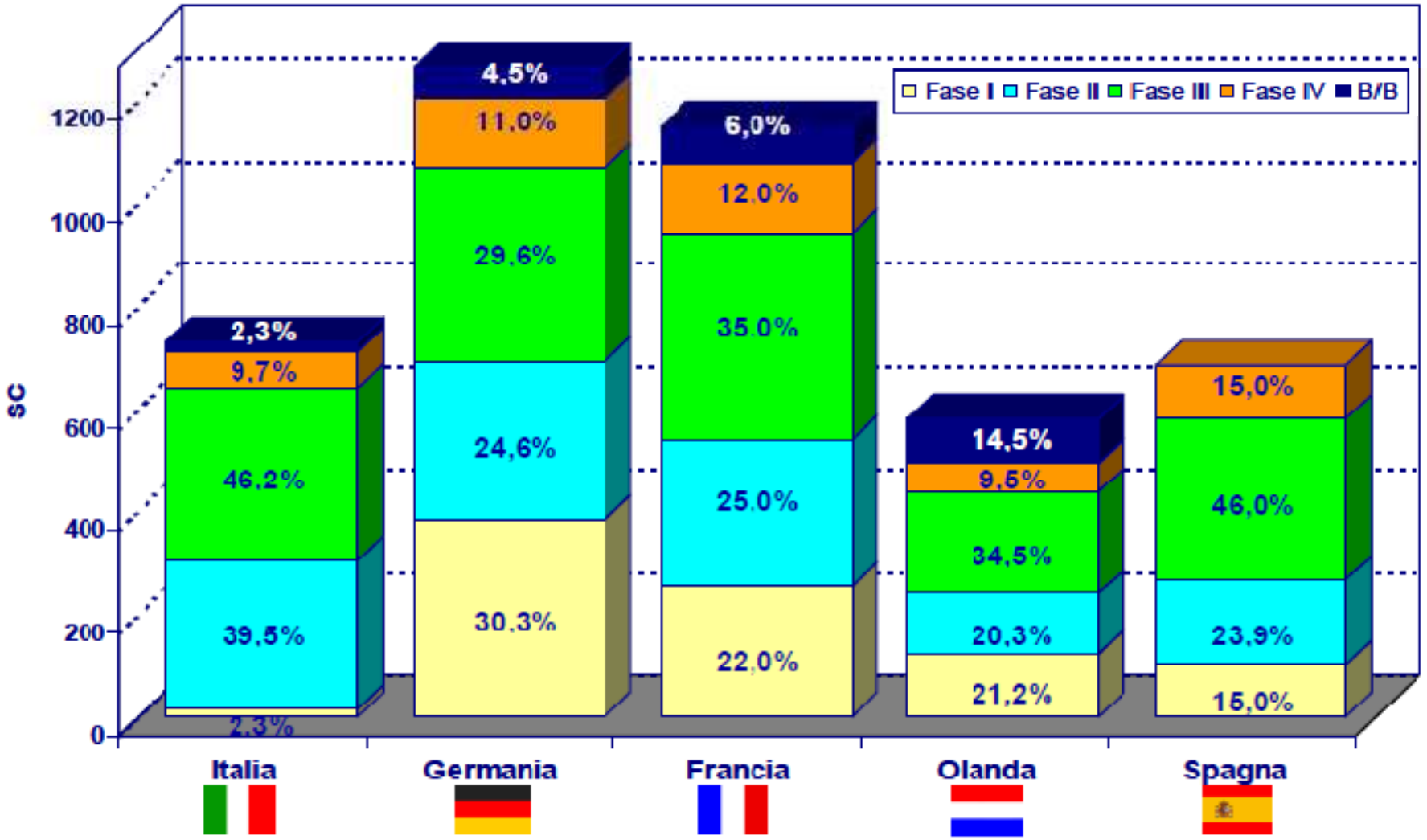
Il Messaggero

Preoccupazione: SOSTENIBILITA'

- Soluzione alternativa al ricorso alle assicurazioni:
  - **Investimento in campagne di prevenzione [!?!?!]**
  - **Fornire solo trattamenti che hanno una base scientifica [!?!?!]**
    - Es.: Spesa farmaceutica ospedaliera determinata per il 40% da farmaci antitumorali con **attività marginale [!?!?!]**

Silvio Garattini

"Documento Programmatico" per la ricerca clinica di Fase I.



Confronto tra diversi Paesi europei nella distribuzione delle SC per fase (anno 2006)

Conclusioni - 1

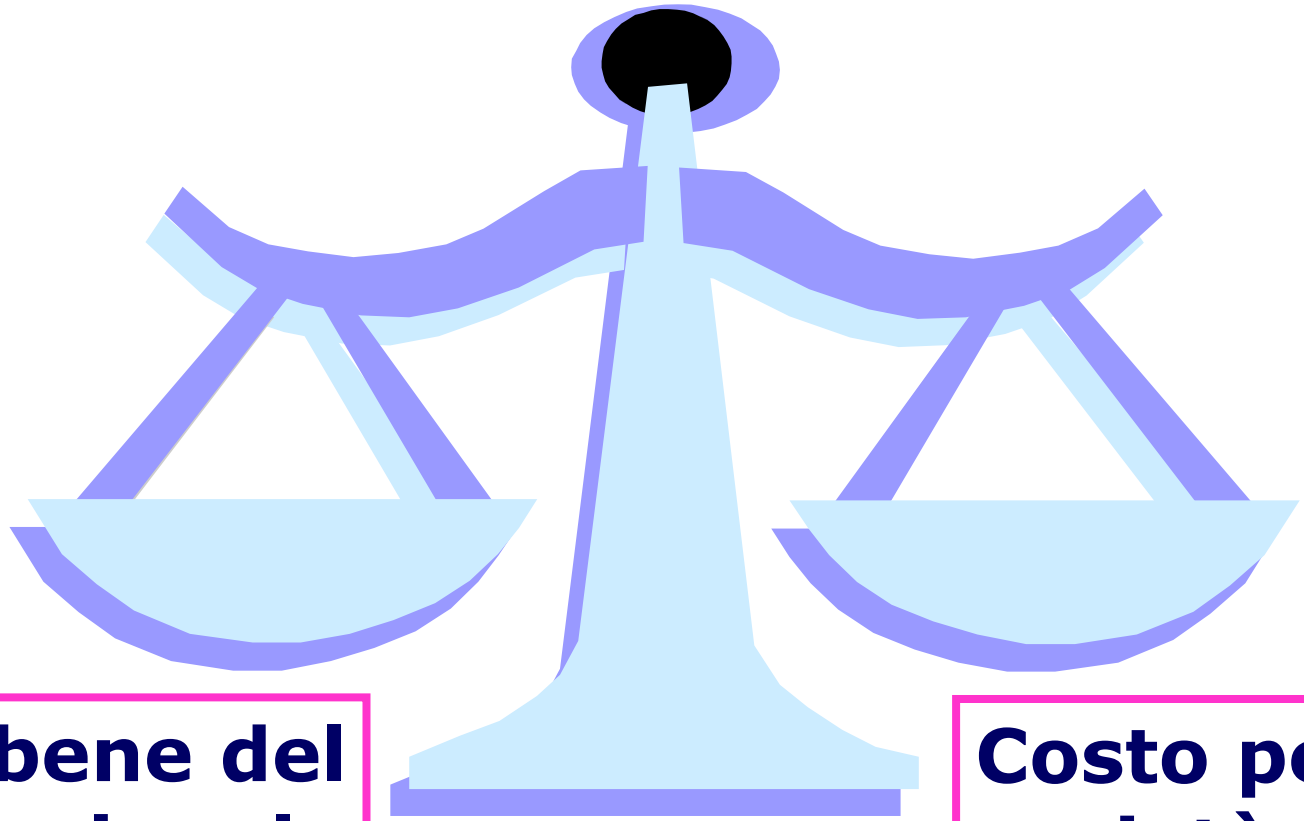
- L’innovazione scientifica ha consentito di mettere a punto nuove tecniche in grado di indentificare target molecolari specifici per determinati pathways di crescita tumorali
- Il tradizionale approccio su dati clinico-patologici si sta trasformando in una visione molecolare del tumore.
- Sulla base di queste acquisizioni, nuovi farmaci non chemioterapici, specificamente diretti contro specifici bersagli molecolari sono stati prodotti, producendo sinora inimmaginabili progressi per i pazienti.

Conclusioni - 2

- A causa dell'imponente processo di R&D alle spalle, il costo di questi nuovi farmaci incide significativamente sulla spesa sanitaria
- Esistono strumenti (attivi e in sviluppo) di contenimento della spesa che possono contribuire a contenere i costi globali
- E' prioritario inserire il contenimento della spesa sanitaria in relazione alle nuove acquisizioni farmaceutiche nelle future programmazioni sanitarie nazionali

La medicina per la Comunità

'Equilibrium' tra:



Il bene del singolo individuo

Costo per la società