



GIORNATA
MONDIALE
SUL TUMORE
OVARICO



**Prima Giornata Mondiale
sul
Tumore Ovarico
8 maggio 2013**



GIORNATA
MONDIALE
SUL TUMORE
OVARICO



ACTO
ONLUS
ALLEANZA CONTRO
IL TUMORE OVARICO

8 MAGGIO 2013

Unisciti a noi



WORLD
OVARIAN
CANCER
DAY

May 8, 2013

ovariancancerday.org

Tweet with the hashtag #WorldOvarianCancerDay on
[Twitter](https://twitter.com/WorldOvarianCancerDay)

Facebook.com/
WorldOvarianCancerDay

Share this graphic
to help spread
awareness.

Aggiornamenti sulla ricerca clinica

Nicoletta Colombo

Universita' Milano Bicocca

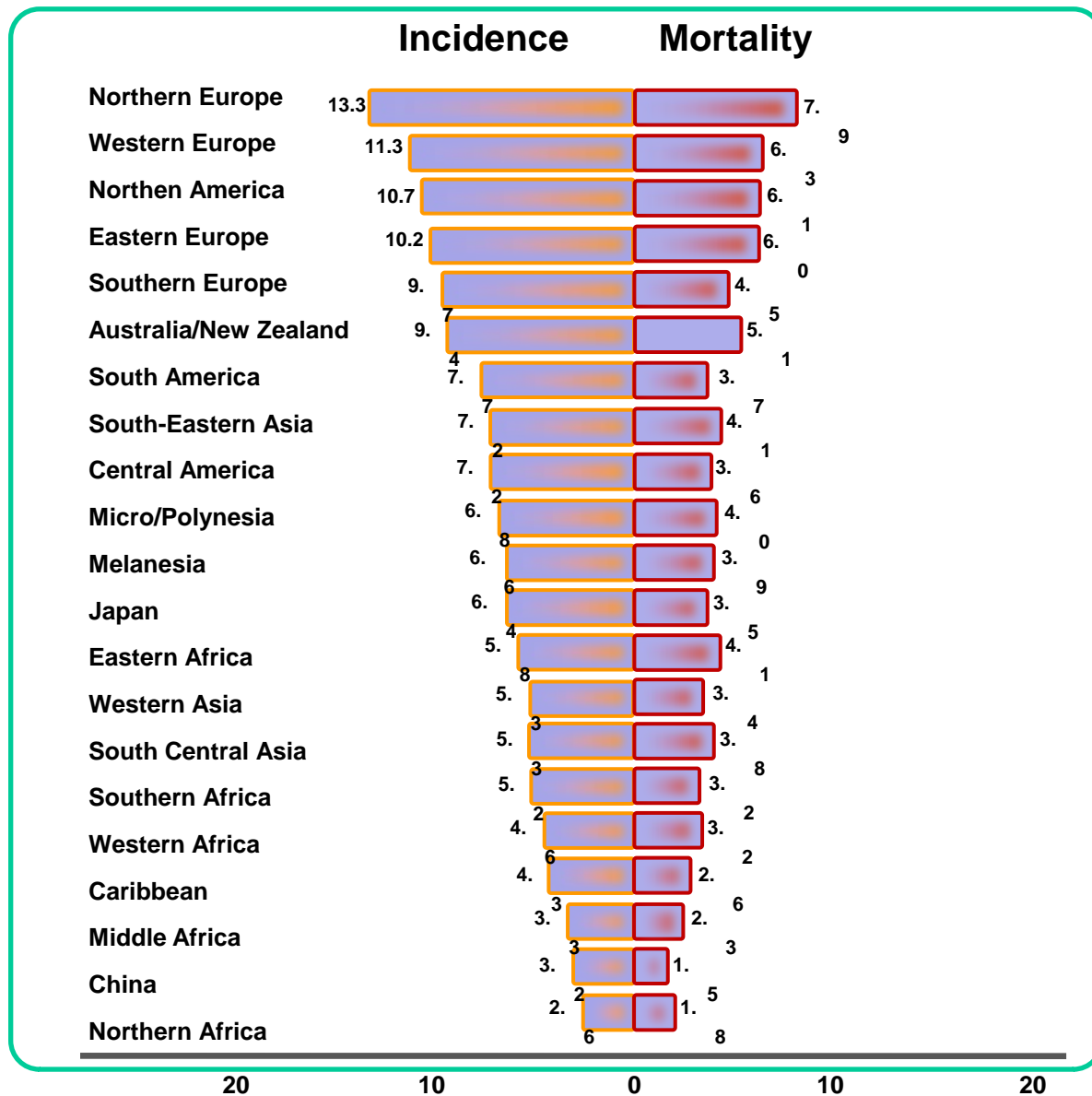
Istituto Europeo Oncologia

Milano



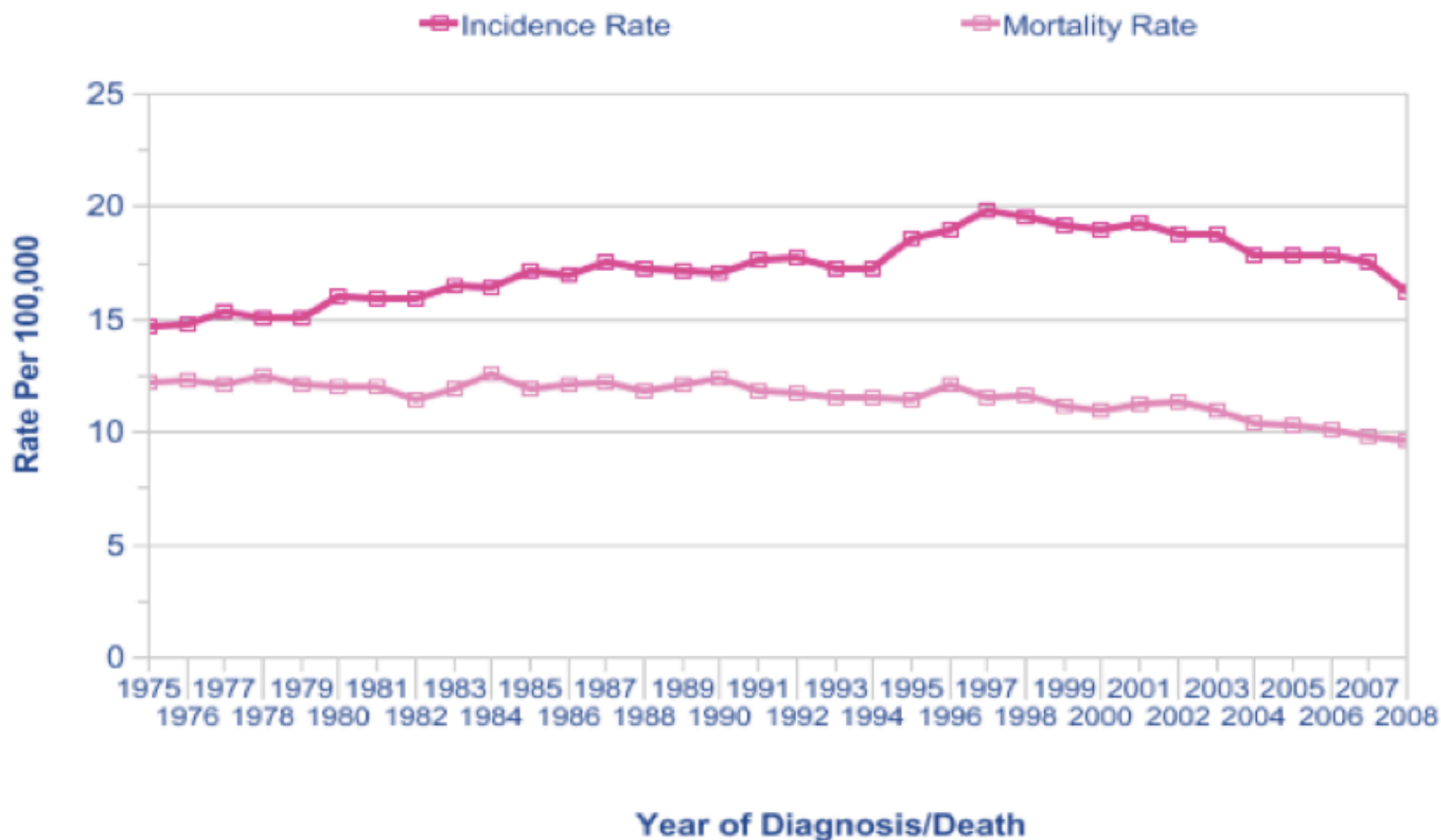
Incidenza e mortalità per carcinoma ovarico

(Tassi standardizzati per età/100.000)



- **204.000 casi/anno**
(4,0% dei tumori nelle donne)
- **125.000 decessi/anno**
(4,2% dei decessi per cancro nelle donne)

Ovarian Cancer Incidence and Mortality Great Britain 1975-2008



Incidence and mortality gap fairly constant



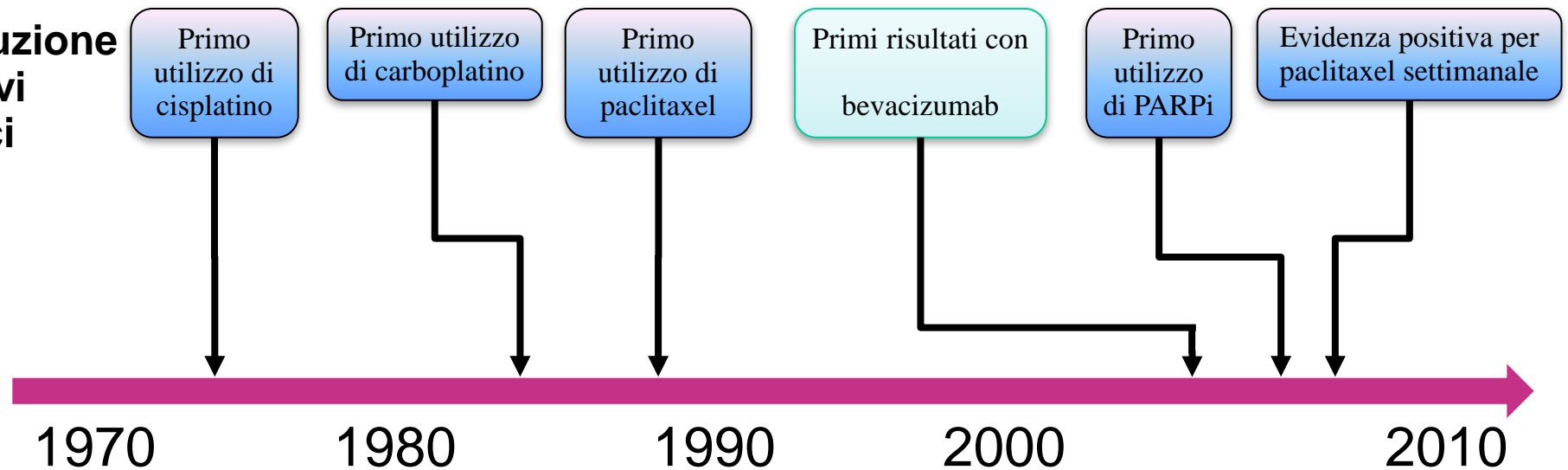
Progressi nella terapia del carcinoma ovarico

evoluzione degli ultimi 40 anni

Sopravvivenza
a 5 anni

15% → 30% → 40% → 50%?

Introduzione
di nuovi
farmaci



Ere della terapia per il cancro

1. Terapia sistemica non specifica



Passato

2. Terapia mirata



Presente

3. L'era della genomica

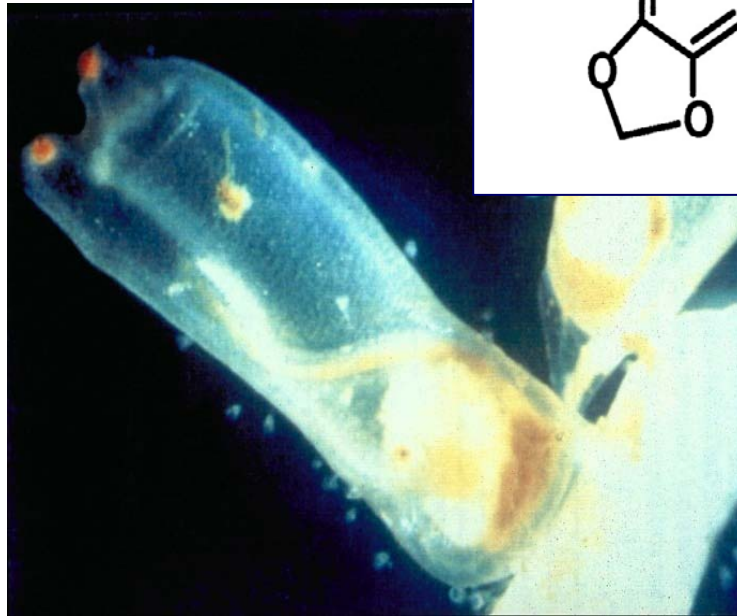
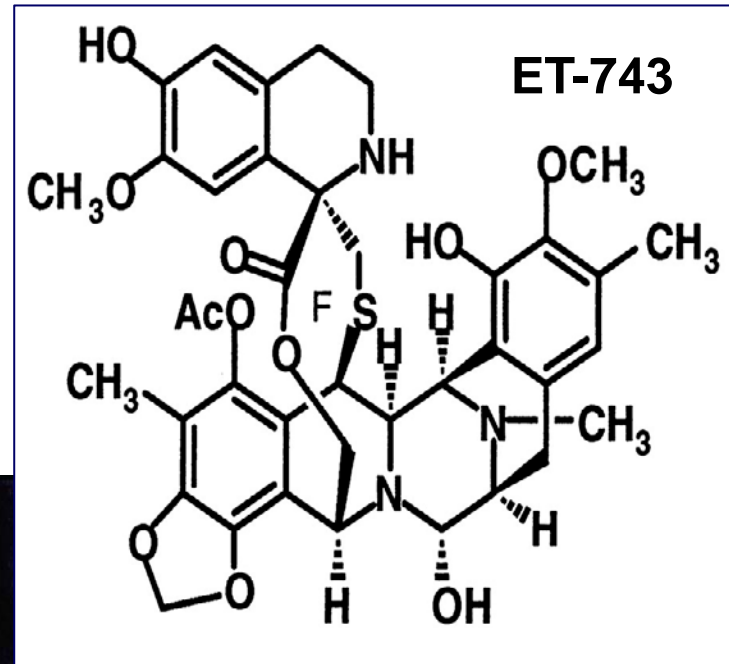


Futuro

Strategie utilizzate per migliorare carboplatino/paclitaxel negli ultimi 15 anni

- Sostituzione di paclitaxel con un altro farmaco
 - SCOTROC, MITO-2
- Aggiunta di un terzo farmaco .
 - 6 GCIG trials...≈ 11000 pazienti
- Cambiare la via di somministrazione :ip
 - GOG-172
- Cambiare la dose intensita'
 - JGOG (NOVEL)

Trabectedina (ET743)



Ecteinascidia turbinata

Ere della terapia per il cancro

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Futuro

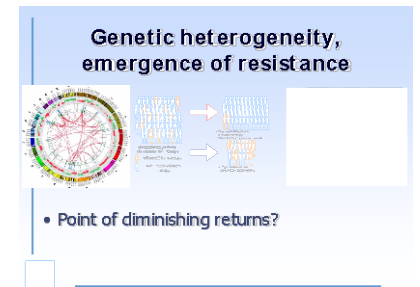
Terapia Mirata



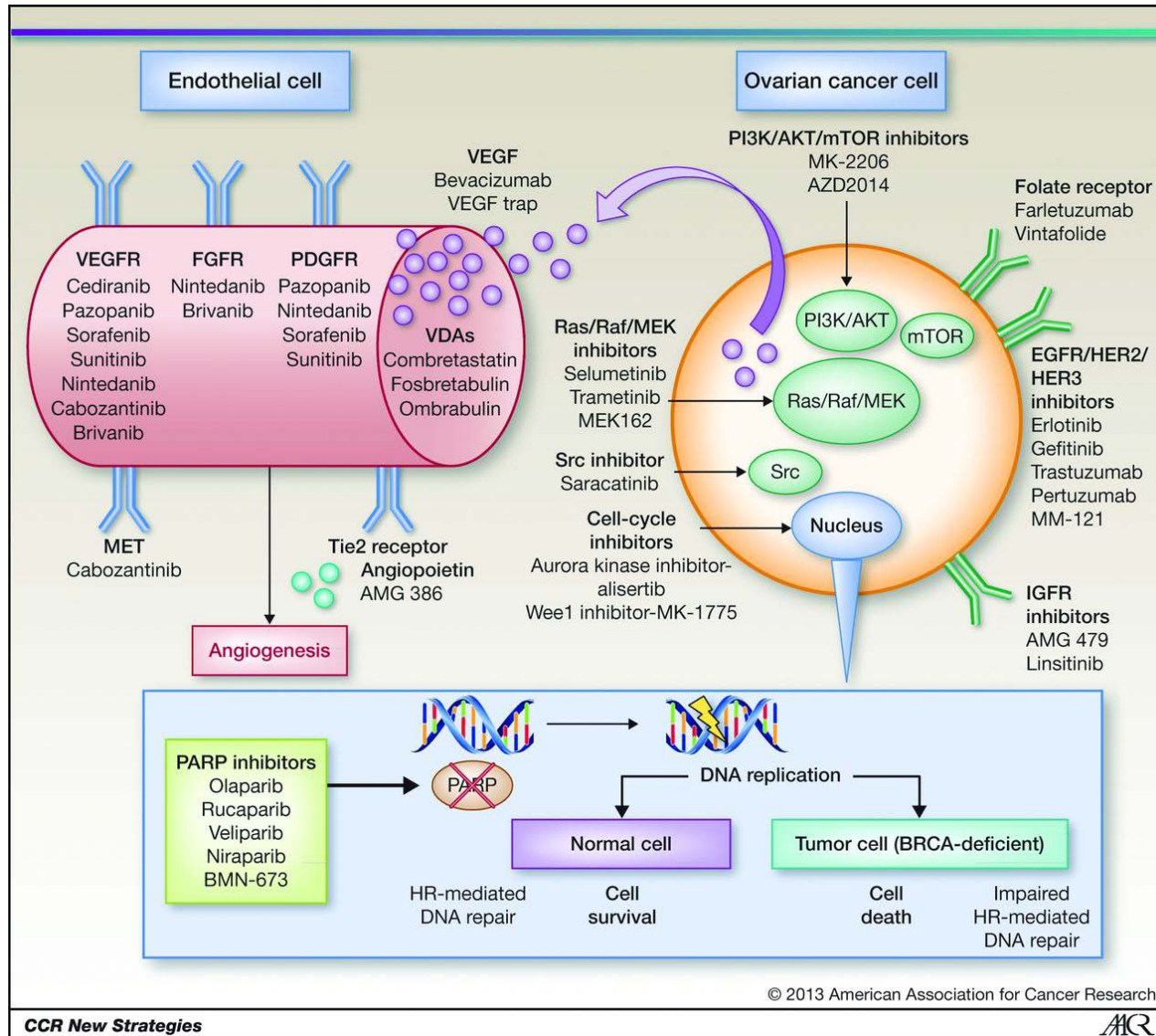
Terapia Mirata

Mirata contro uno specifico meccanismo alterato nella cellula o nel microambiente

Mirata contro la cellula tumorale



Terapie mirate nel carcinoma ovarico



Banerjee S , and Kaye S B Clin Cancer Res 2013;19:961-968

Lo switch angiogenico nello sviluppo del tumore

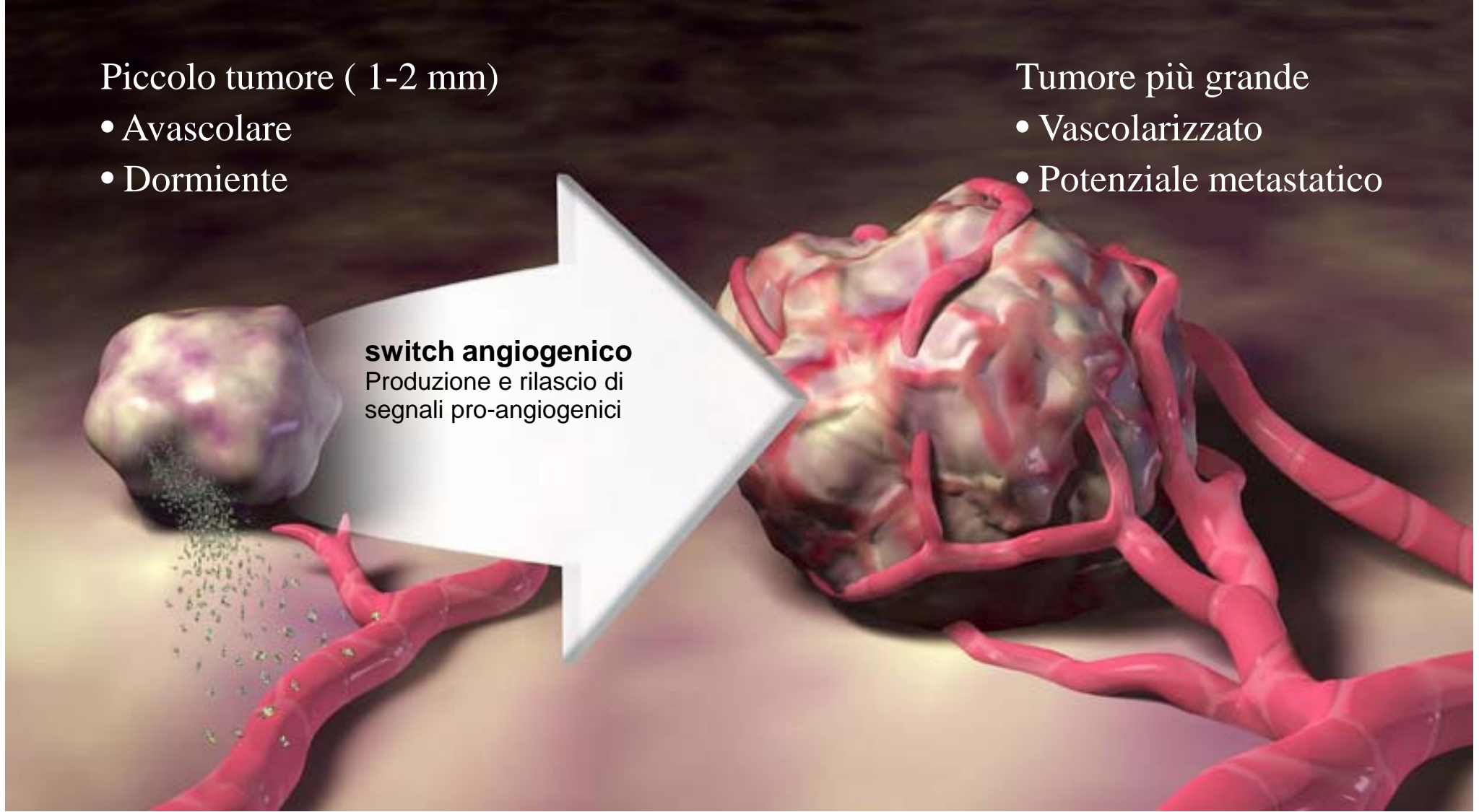
Piccolo tumore (1-2 mm)

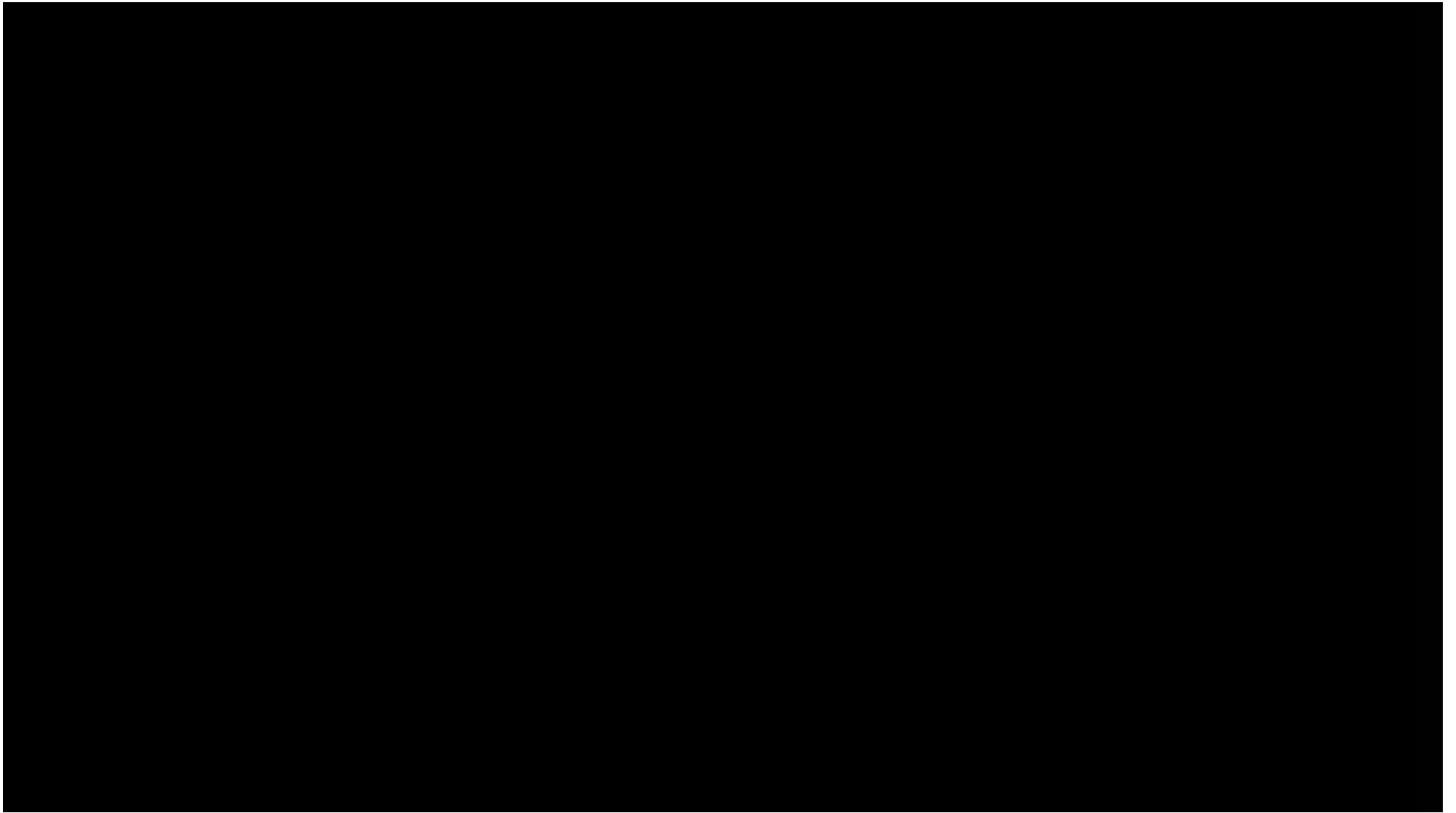
- Avascolare
- Dormiente

Tumore più grande

- Vascolarizzato
- Potenziale metastatico

switch angiogenico
Produzione e rilascio di
segnali pro-angiogenici





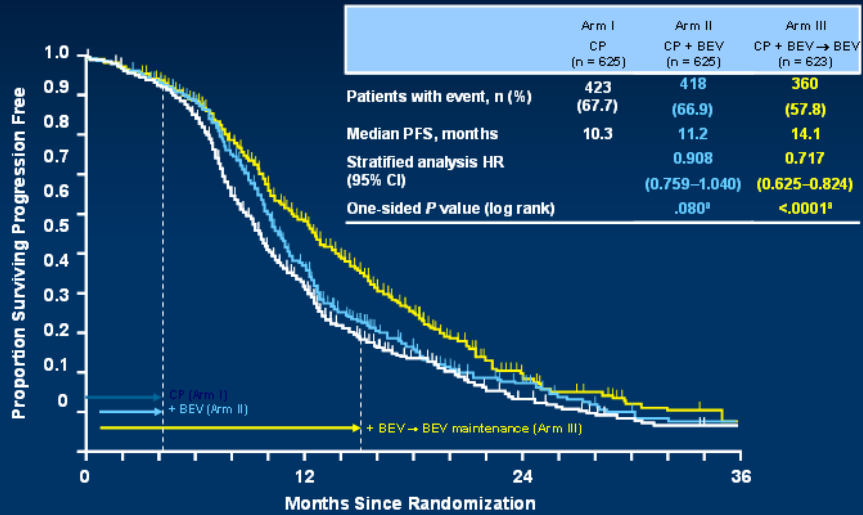
terapia Anti-VEGF

Bevacizumab



Quattro studi positivi con Bev nel carcinoma ovarico

GOG-0218: Investigator-Assessed PFS



Burger RA, et al. *J Clin Oncol*. 2010;28(18s): Abstract LBA1. Burger RA, et al. ESMO 2010.

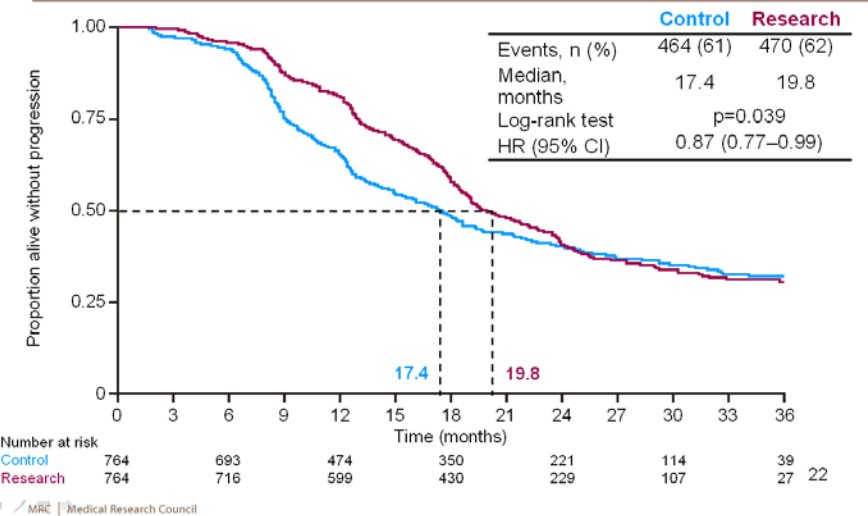
*value boundary = 0.0116

ICON7

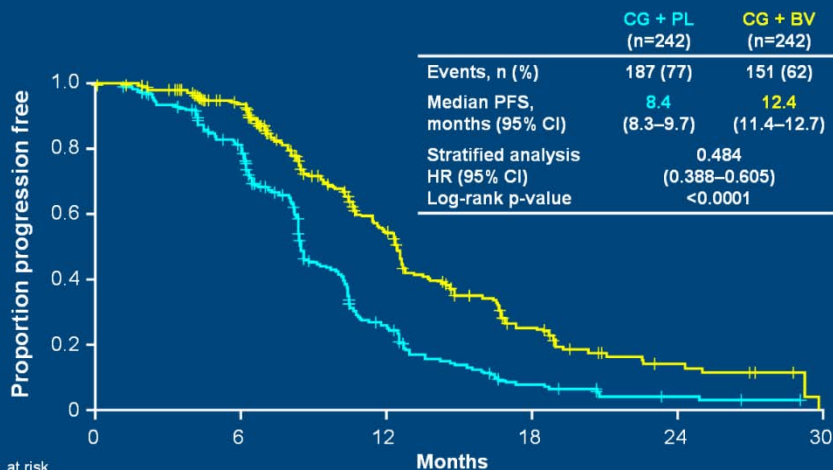
Bevacizumab in Ovarian Cancer

Updated PFS

MRC Clinical Trials Unit



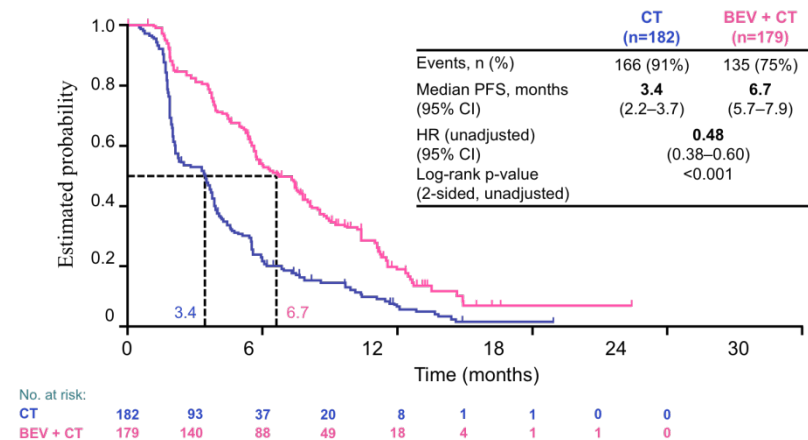
OCEANS: Primary analysis of PFS



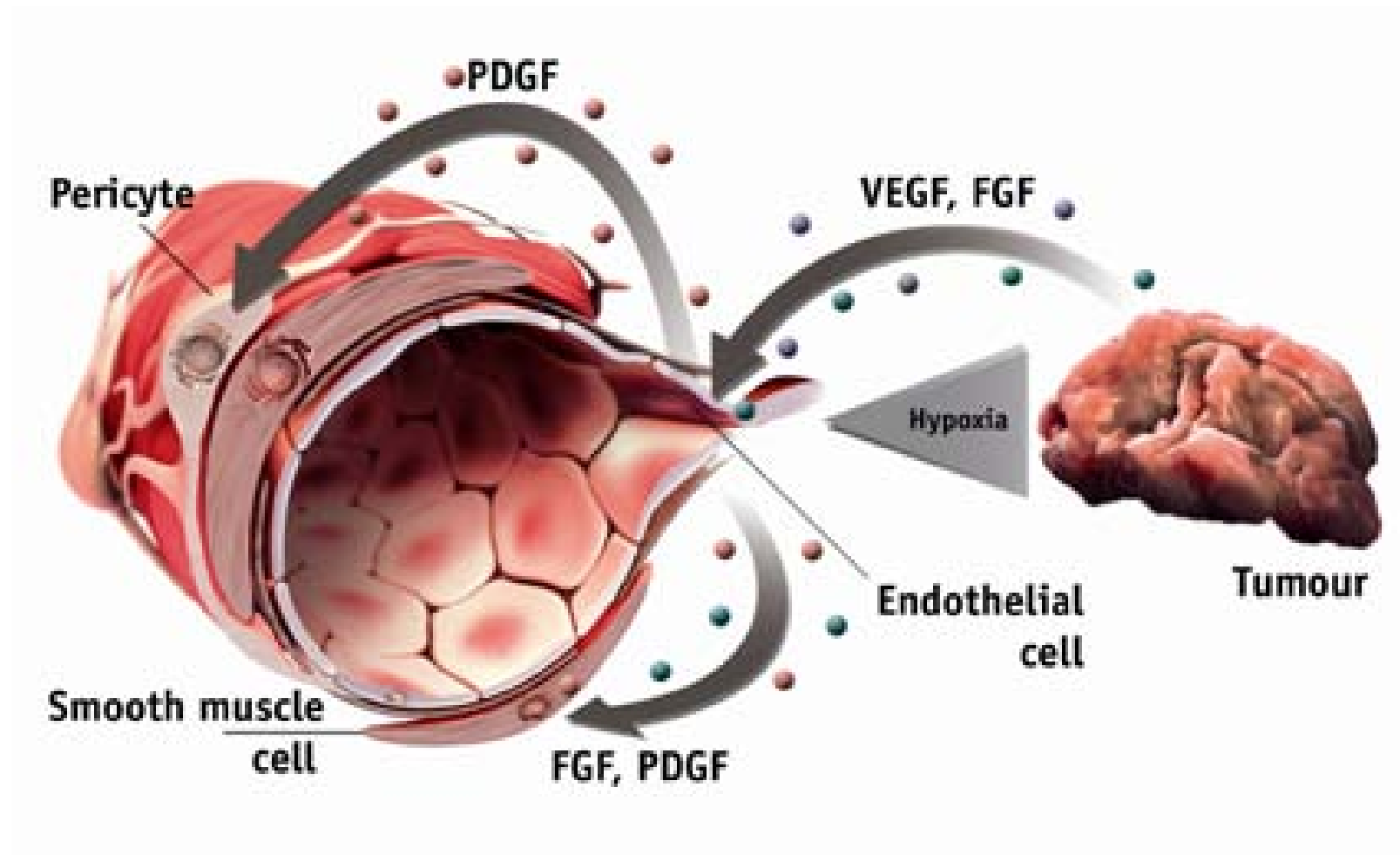
PRESENTED AT: ASCO Annual Meeting

AURELIA

Progression-free survival



Angiogenesi: Un processo complesso



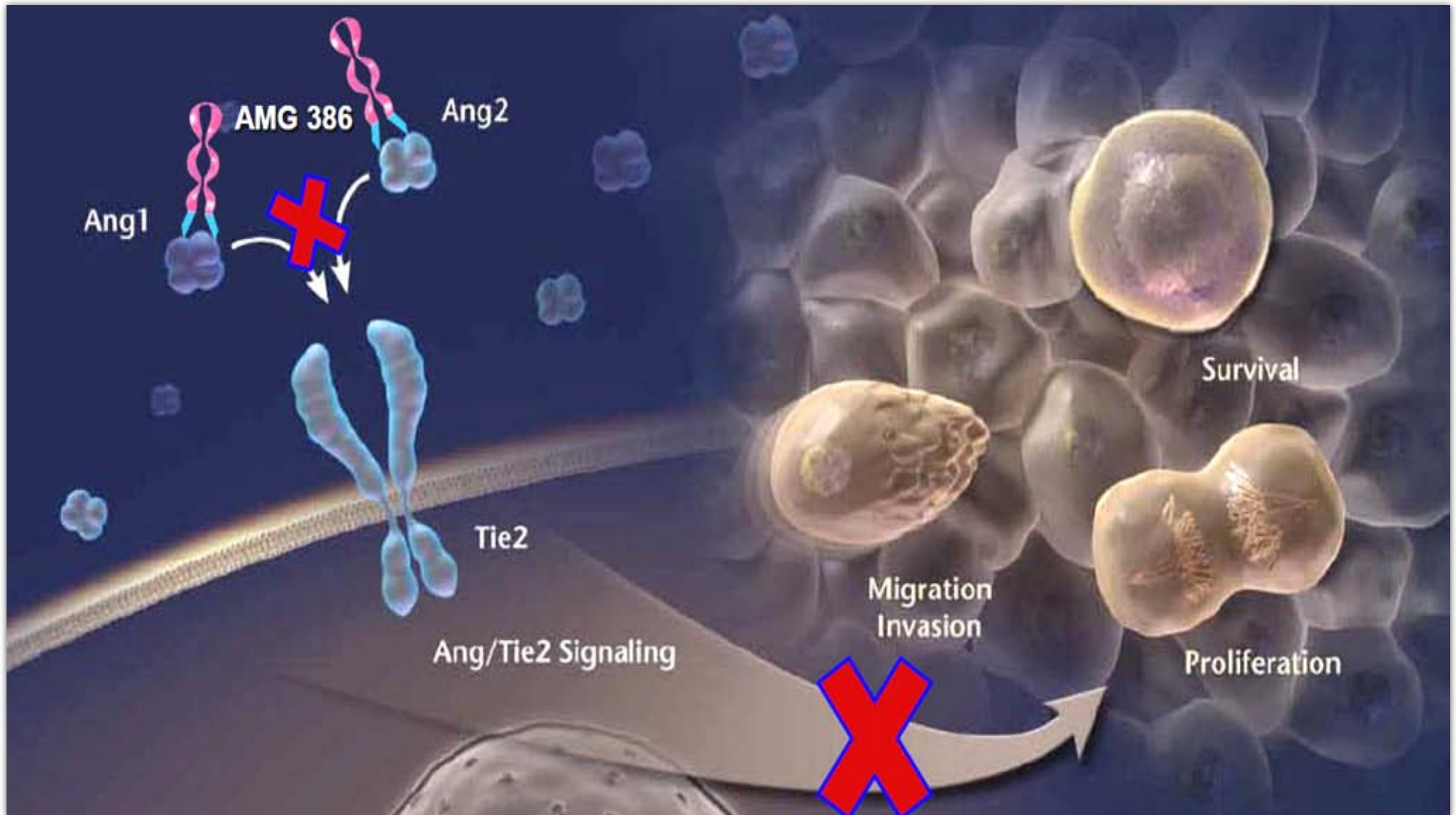
Nuovo paradigma: Terapia a bersagli multipli

Farmaci in fase di sviluppo II/III

Farmaco	Classe	Target	Fase
Nintedanib (BIBF 1120)	Small-molecule TKI	VEGFR + PDGFR + FGFR	III
Cediranib	Small-molecule TKI	VEGFR + PDGFR + FGFR + c-kit	III
Pazopanib	Small-molecule TKI	VEGFR + PDFGR + c-kit	III
Sunitinib	Small-molecule TKI	VEGFR + PDGFR + c-kit	II
Sorafenib	Small-molecule TKI	VEGFR + PDGFR + Flt-3 + c-kit + b-Raf	II
Vandetanib	Small-molecule TKI	VEGFR + EGFR	II
Motesanib	Small-molecule TKI	VEGFR + PDFGR + c-kit	II

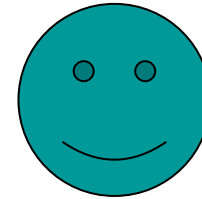
Altri farmaci?

AMG386, Angiopoietine e Angiogenesi



Angiogenesi e carcinoma ovarico

- Bevacizumab



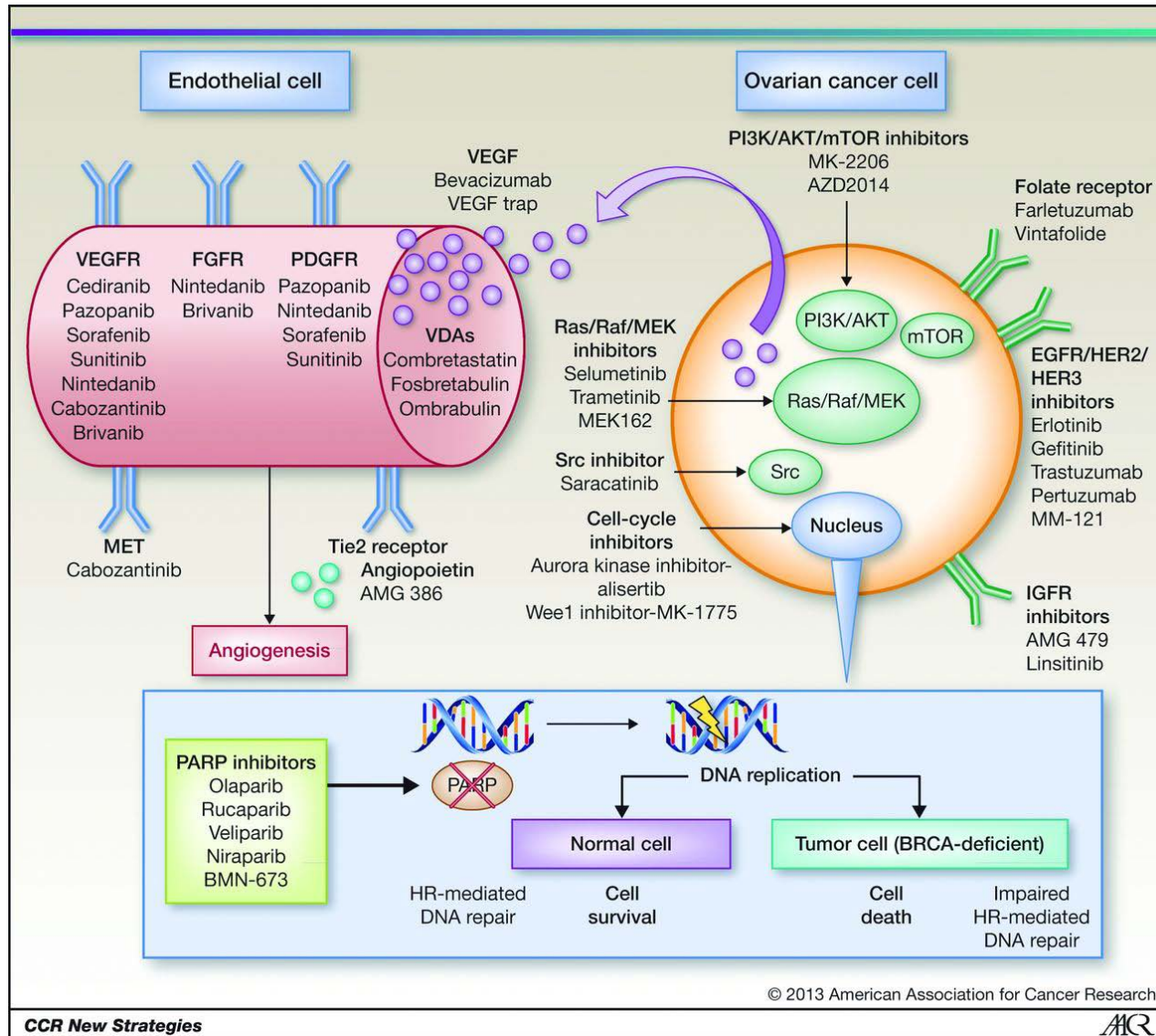
- Pazopanib

- Nintedanib

- Trebananib

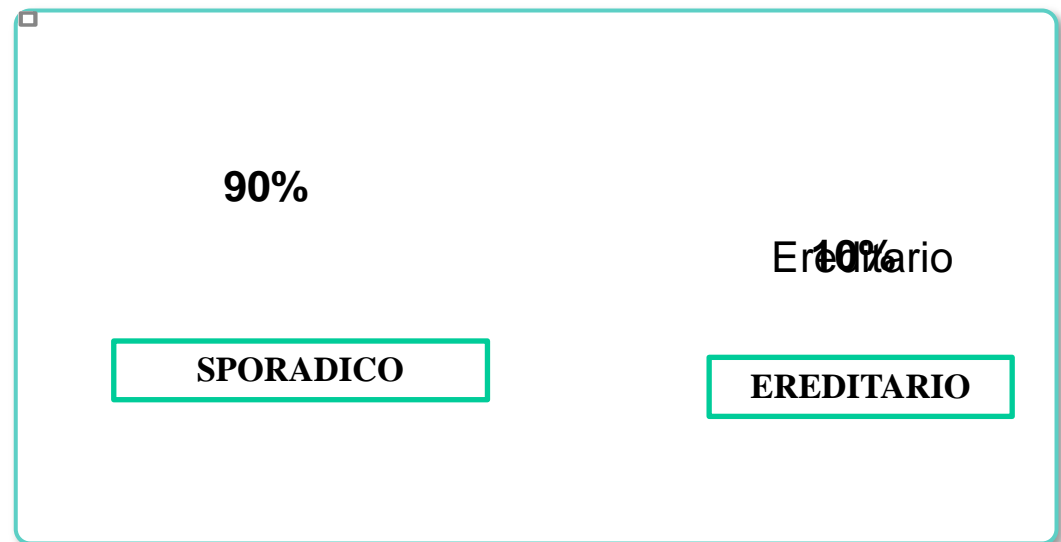
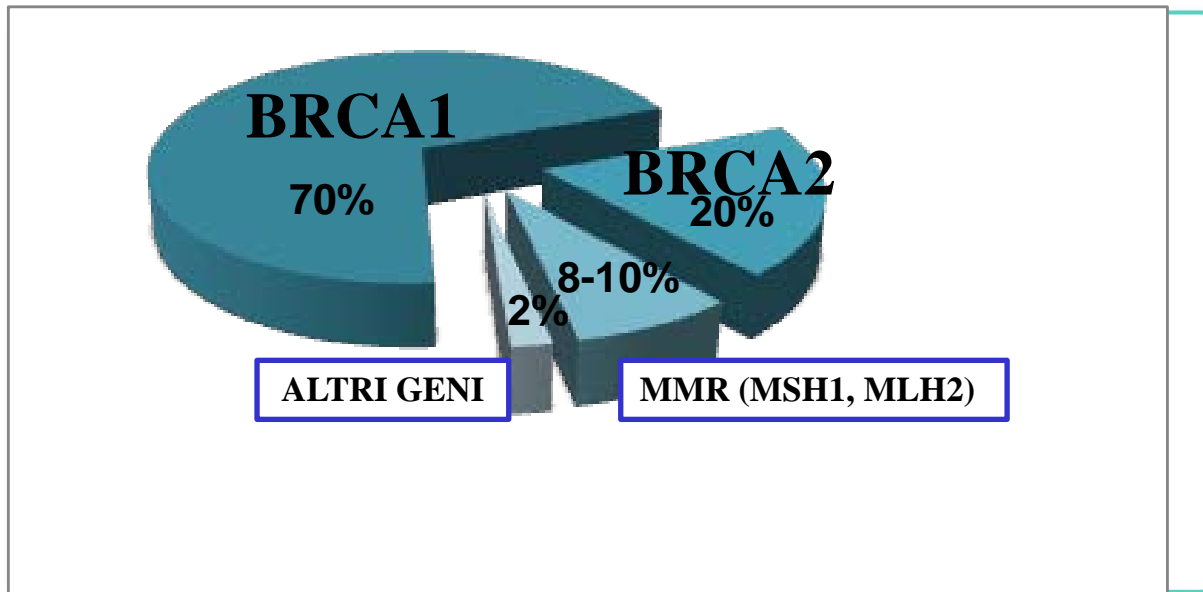


Terapie mirate nel carcinoma ovarico

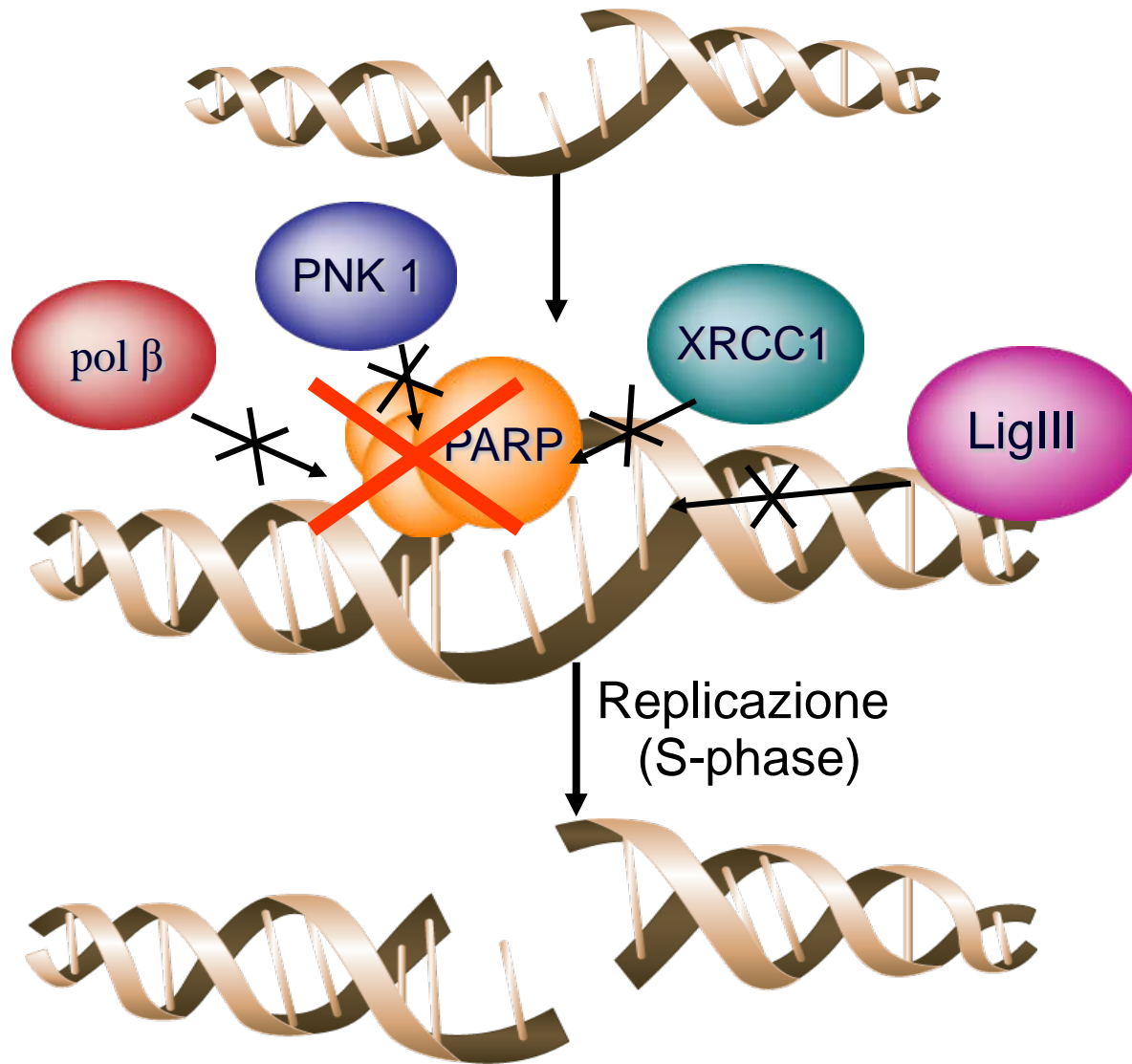


Banerjee S , and Kaye S B Clin Cancer Res 2013;19:961-968

Carcinoma ovarico: sporadico vs ereditario



Come funzionano I PARPi



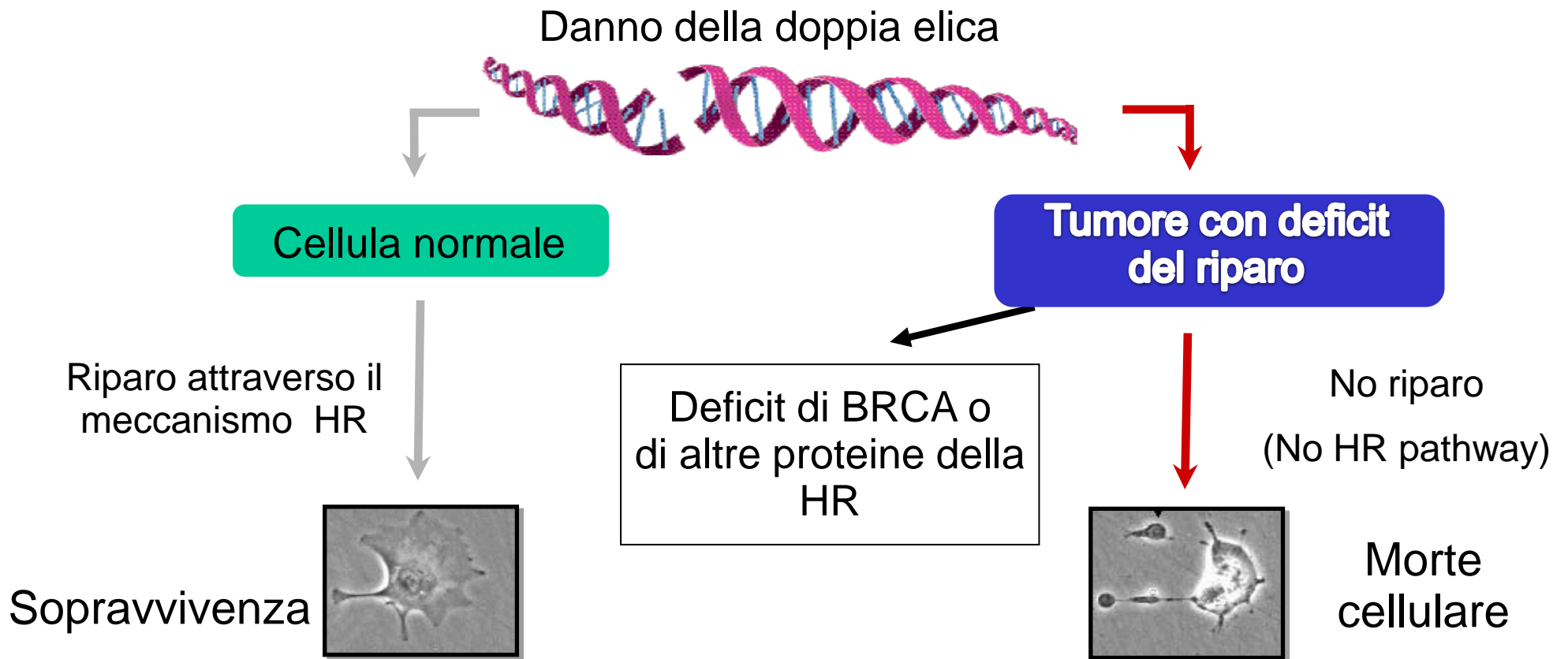
DNA SSB

L'inibizione di PARP-1
previene il
reclutamento di fattori
del riparo della
singola elica

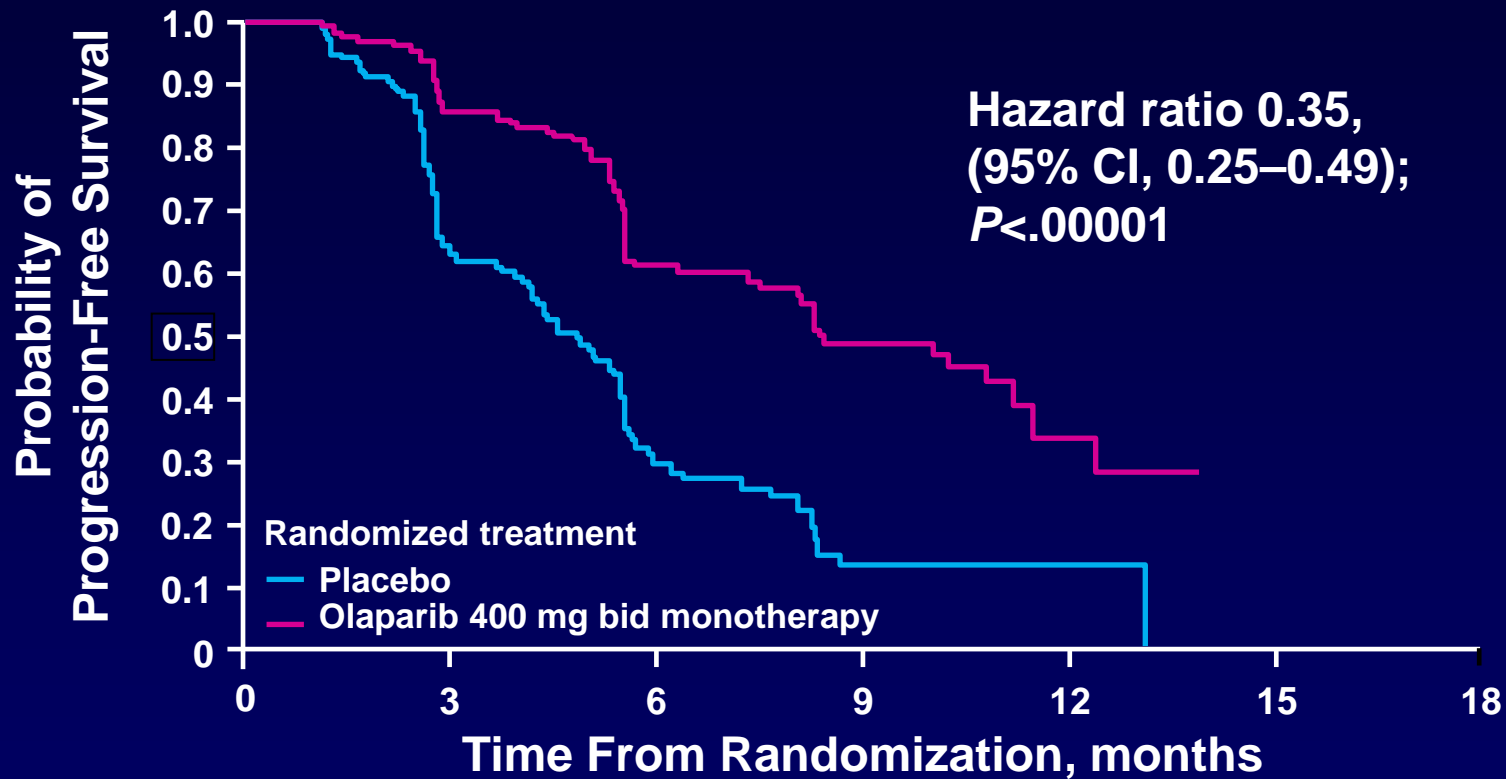
Replicazione
(S-phase)

DNA DSB

Uccisione mirata di cellule che hanno i meccanismi di riparo del DNA alterati

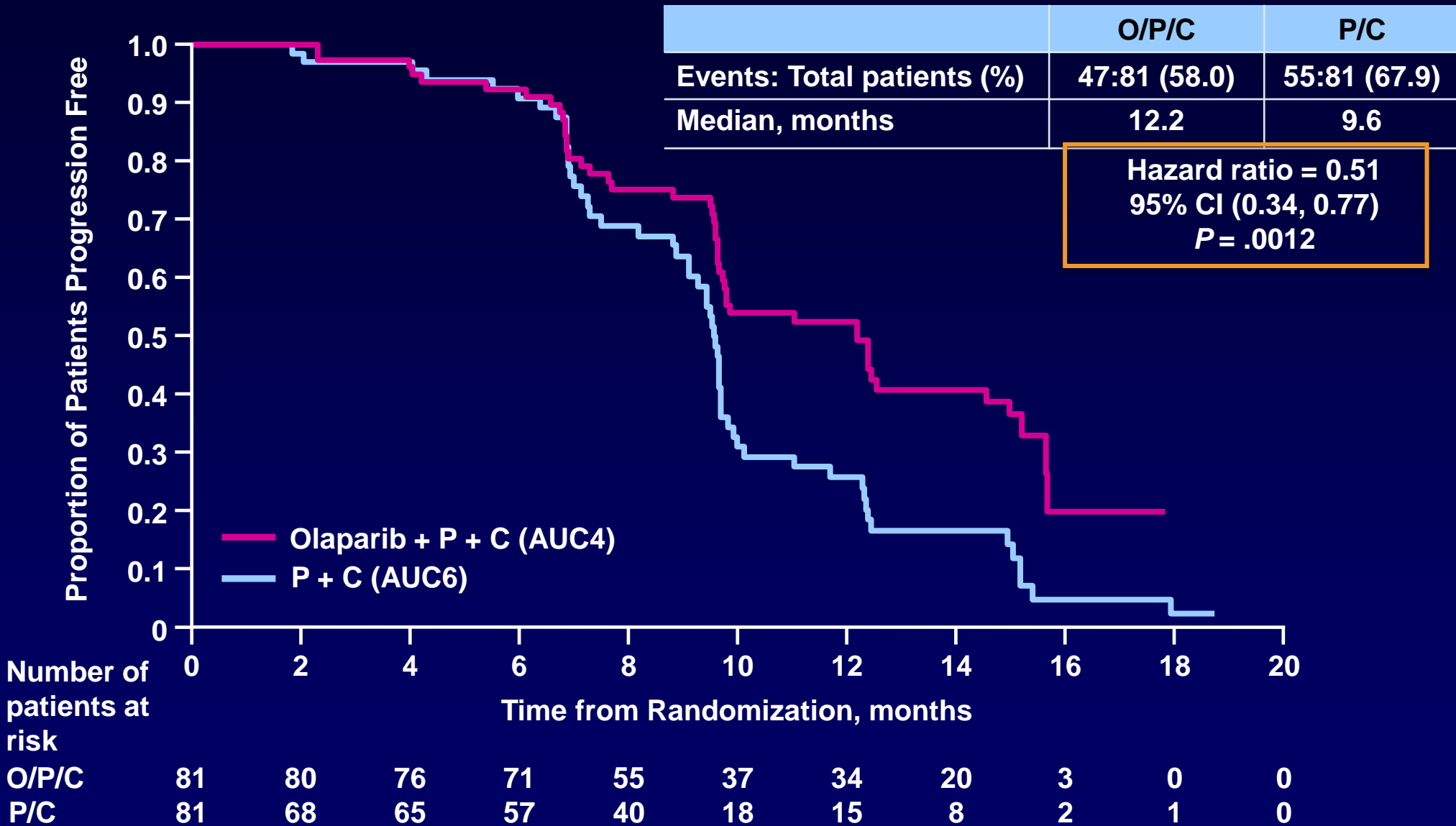


Terapia di mantenimento con Olaparib nelle recidive platino-sensibili



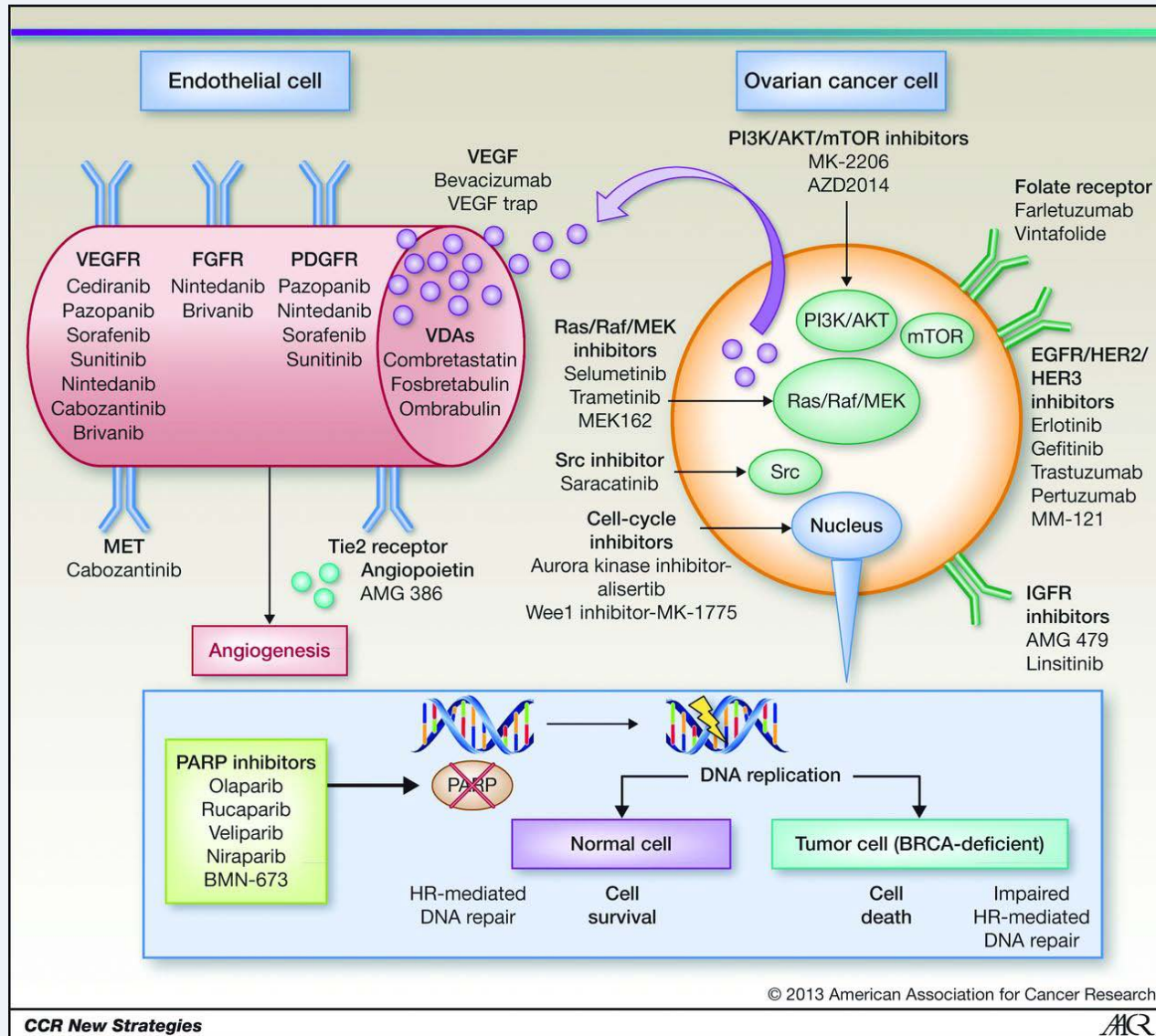
Miglioramento significativo di PFS (HR 0.35, $P < .00001$)

Sopravvivenza libera da progressione



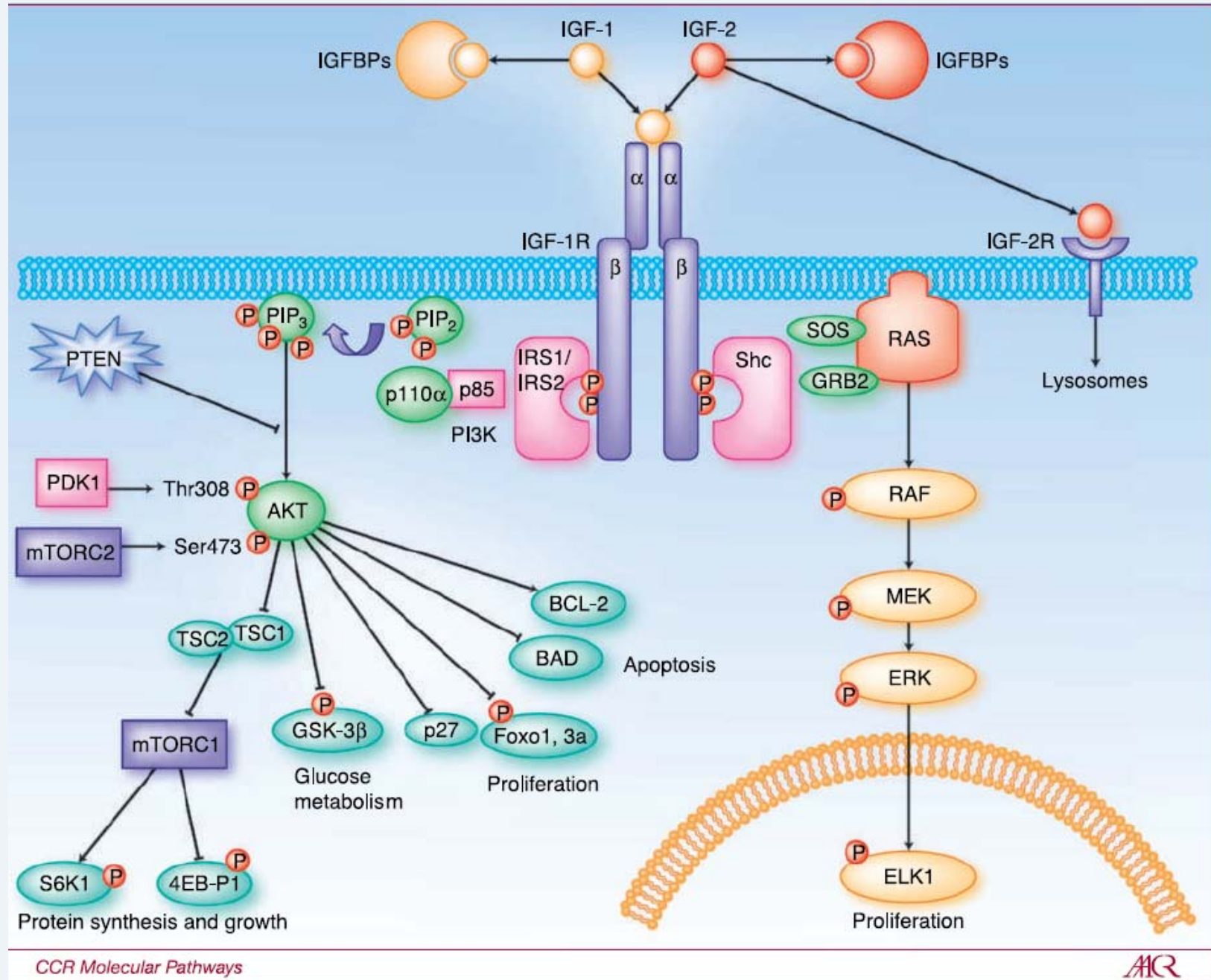
*Central review data

Terapie mirate nel carcinoma ovarico

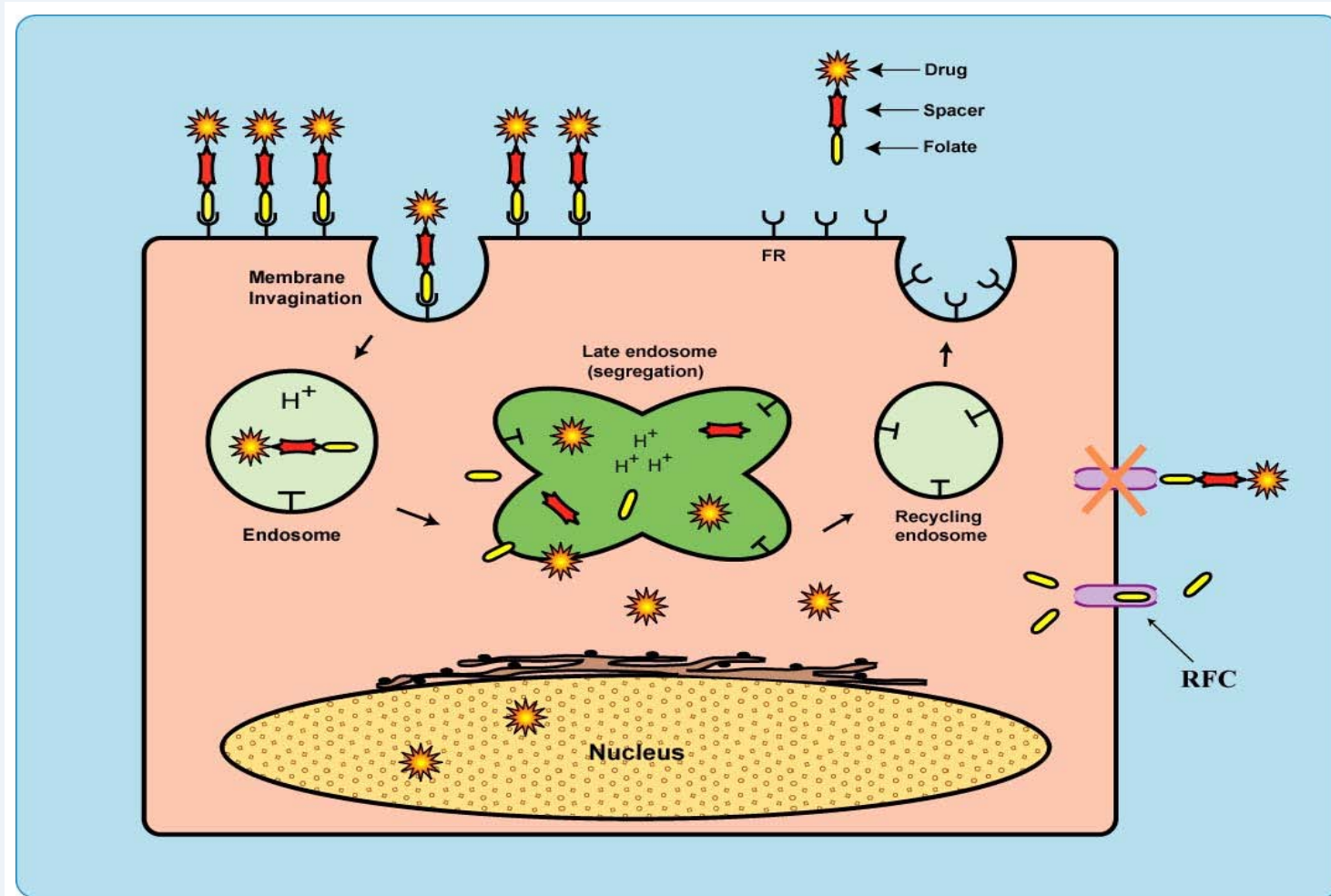


Banerjee S , and Kaye S B Clin Cancer Res 2013;19:961-968

IGF-1R : OSI 906



Recettore per l'alfa-folato



EC 145 (vintafolide) in ovarian cancer



EC145 (vintafolide)

Folic acid conjugated to
desacetylvinblastine hydrazide

19 patients in Phase I trial:

- received EC145 days 1,3,5 on alternate weeks
- DLT at 4mg – neuropathy, reversible ileus
- Main toxicity – fatigue, constipation, neuropathy
- 2 ovarian cancer patients had signs of clinical benefit
- Dose of 2.5mg taken into randomised trial (PRECEDENT)

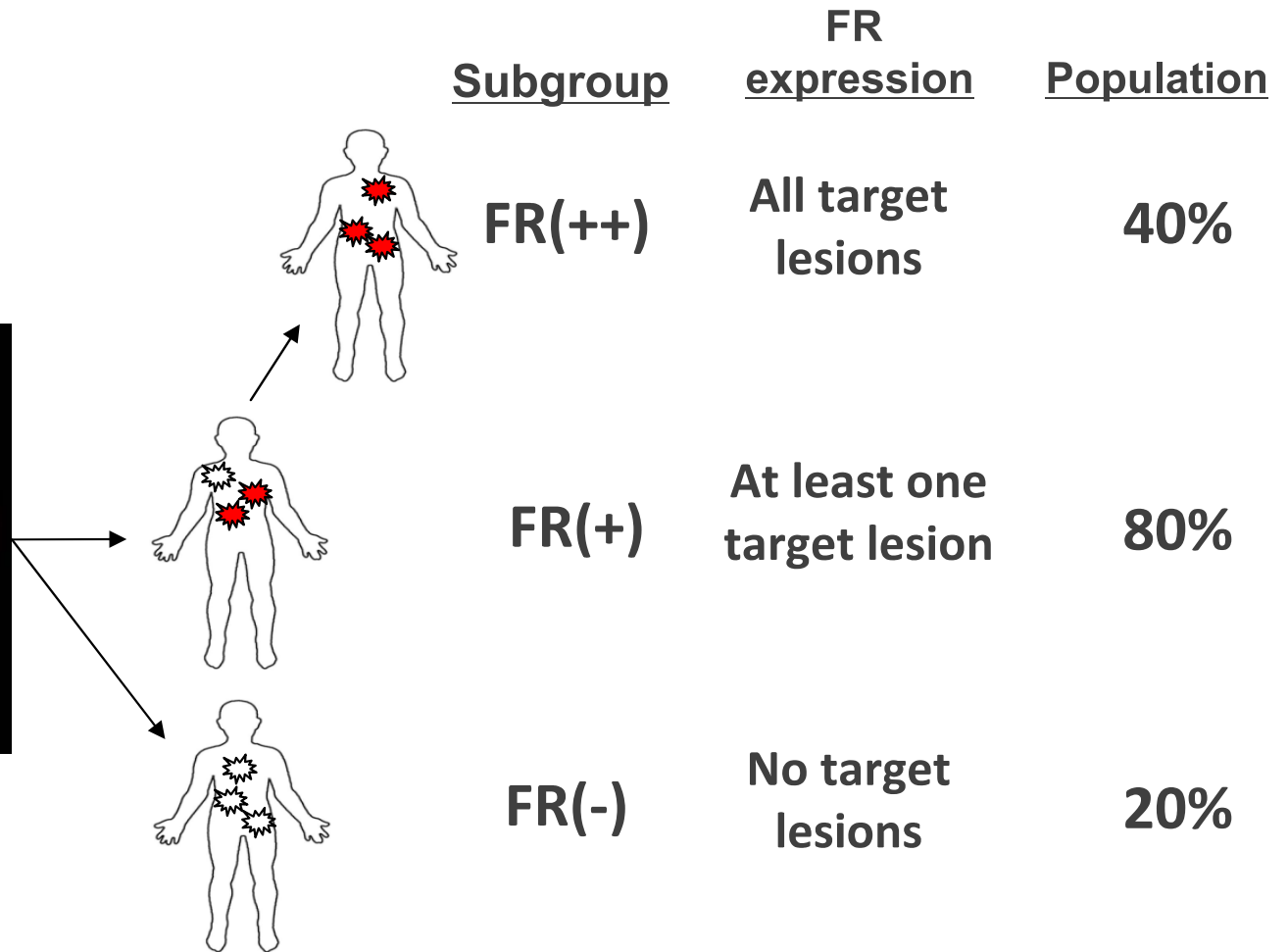
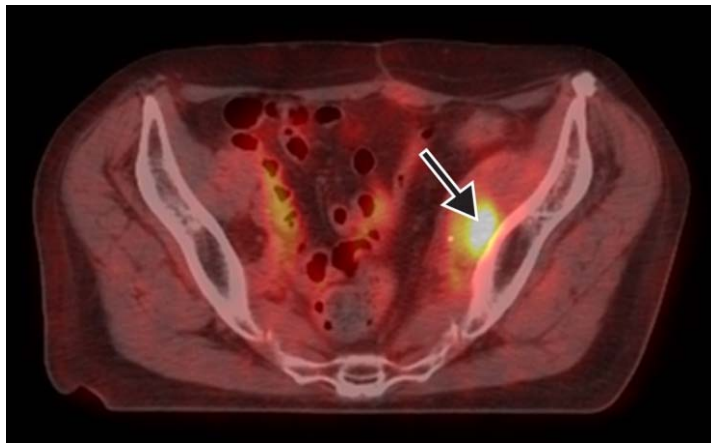
PRECEDENT

- Randomised phase II Trial in platinum resistant patients
- PLD ± EC145 (50mg/m² ± 2.5mg tiw)
- primary end point PFS n=149
- exploratory correlation with ^{99m}Tc-EC20 folate scan

Le Russo et al J. Clin Onc Oct 2012

^{99m}Tc Etarfolatide (EC20) Status of the Tumors

- Image 1 hour after injection of EC20



Perche' il carcinoma ovarico e' rimasto indietro ?

Terapia generica
1990

Terapia stratificata
2010

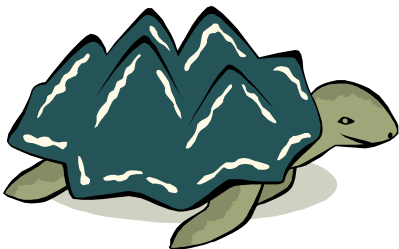
Terapia individualizzata
2020

Carcinoma della mammella

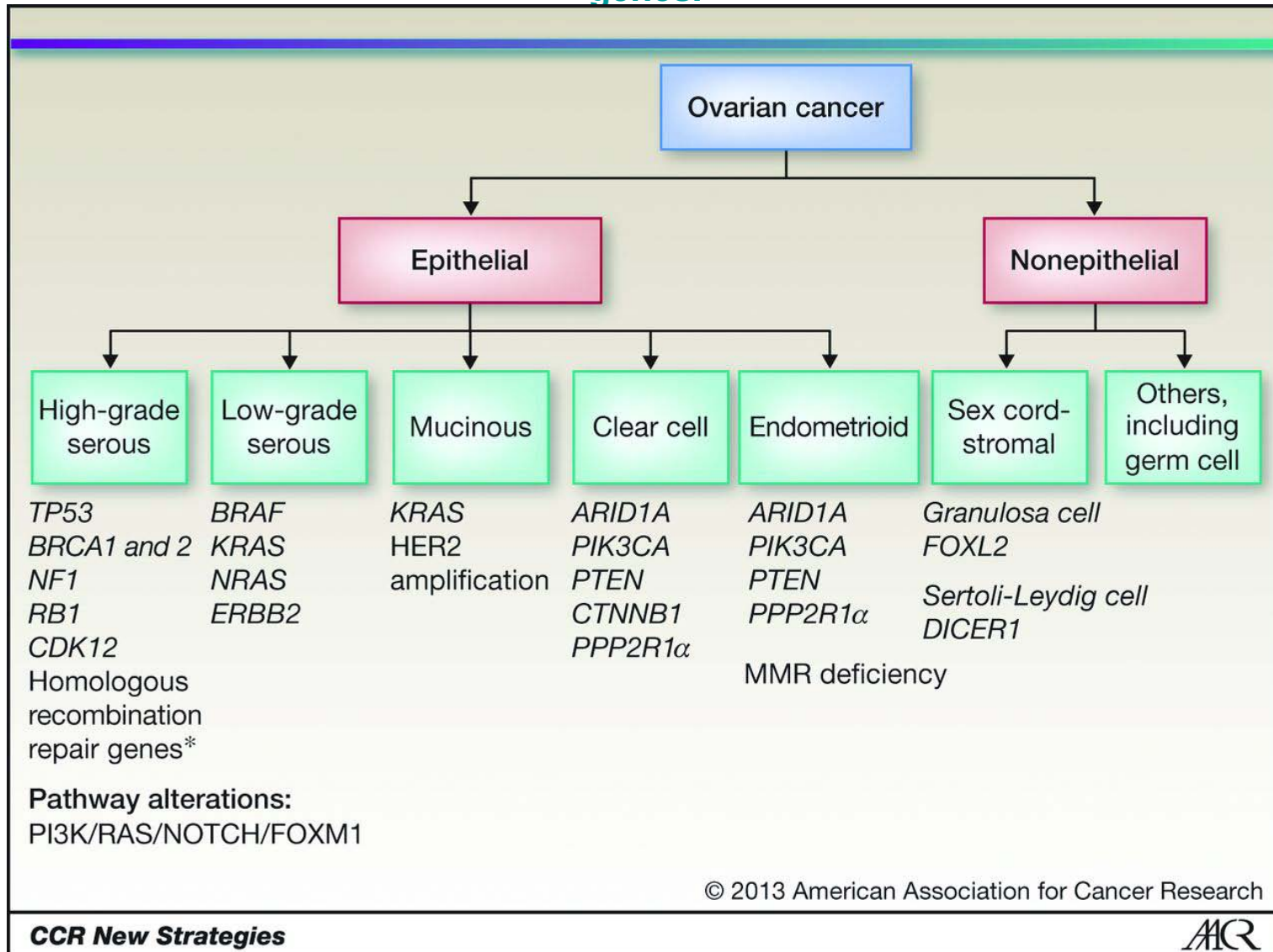
Linfoma

Carcinoma ovarico

Carcinoma pancreatico



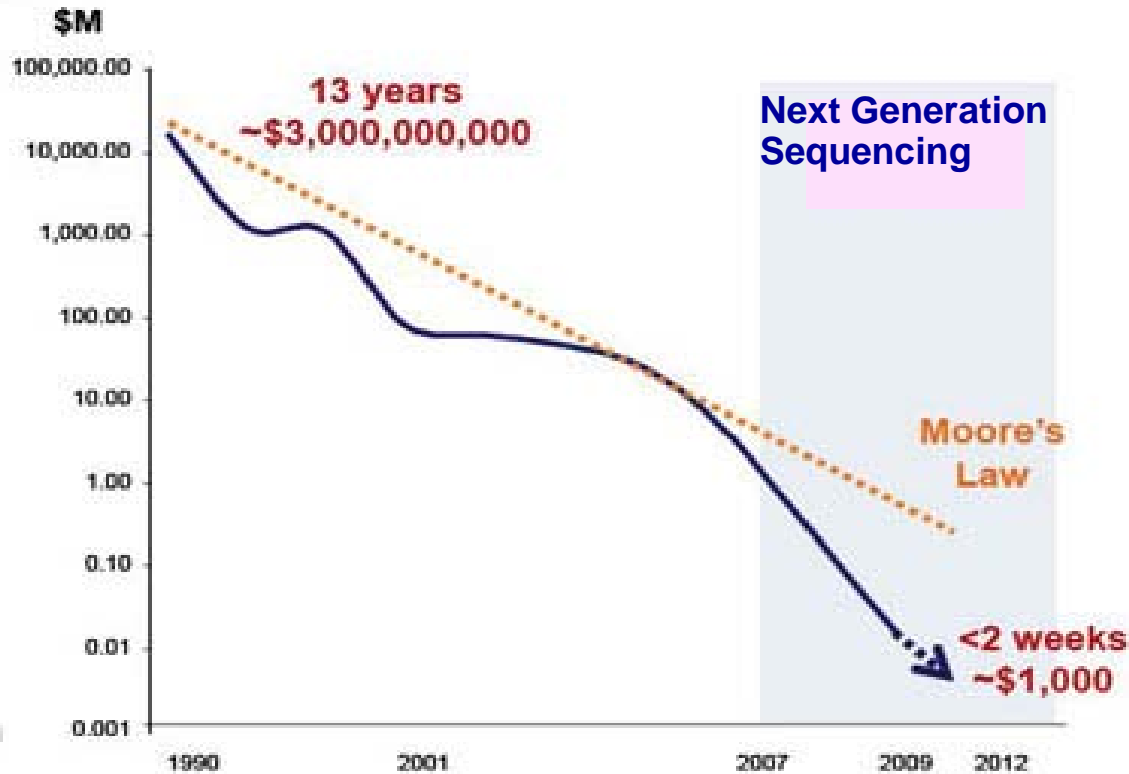
Histologic subtypes of epithelial ovarian carcinoma and associated mutations/molecular aberrations. *, CHK2, BARD1, BRIP1, PALB2, RAD50, RAD51C, ATM, ATR, EMSY, Fanconi anemia genes.



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Tecnologia e costi

Cost per Human Genome

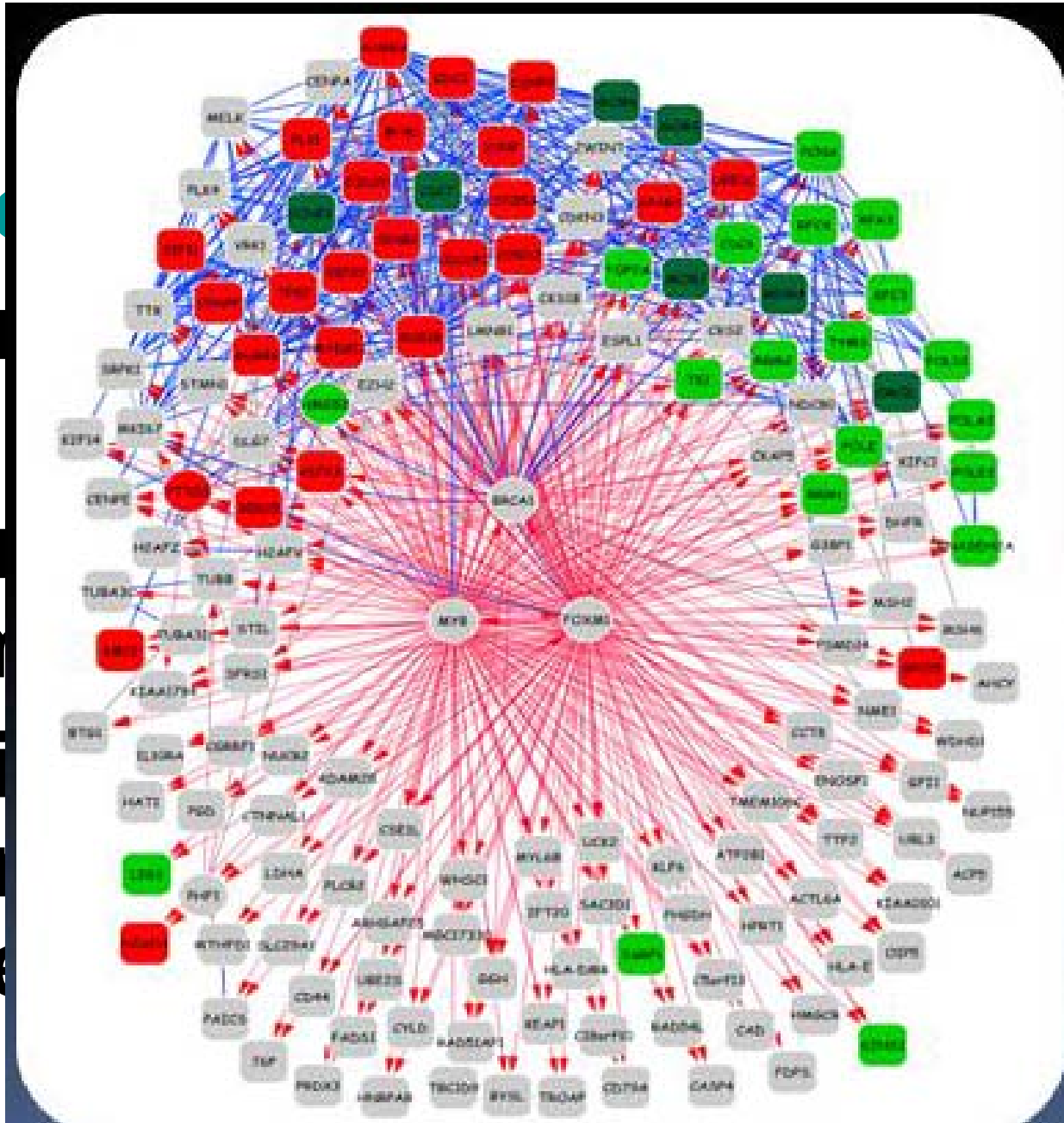


\$795 in 1977
(=\$2,800 in current \$)



Il tumore

- 1) Molti
- 2) Non
do
sim
- 3) Es
con
alte

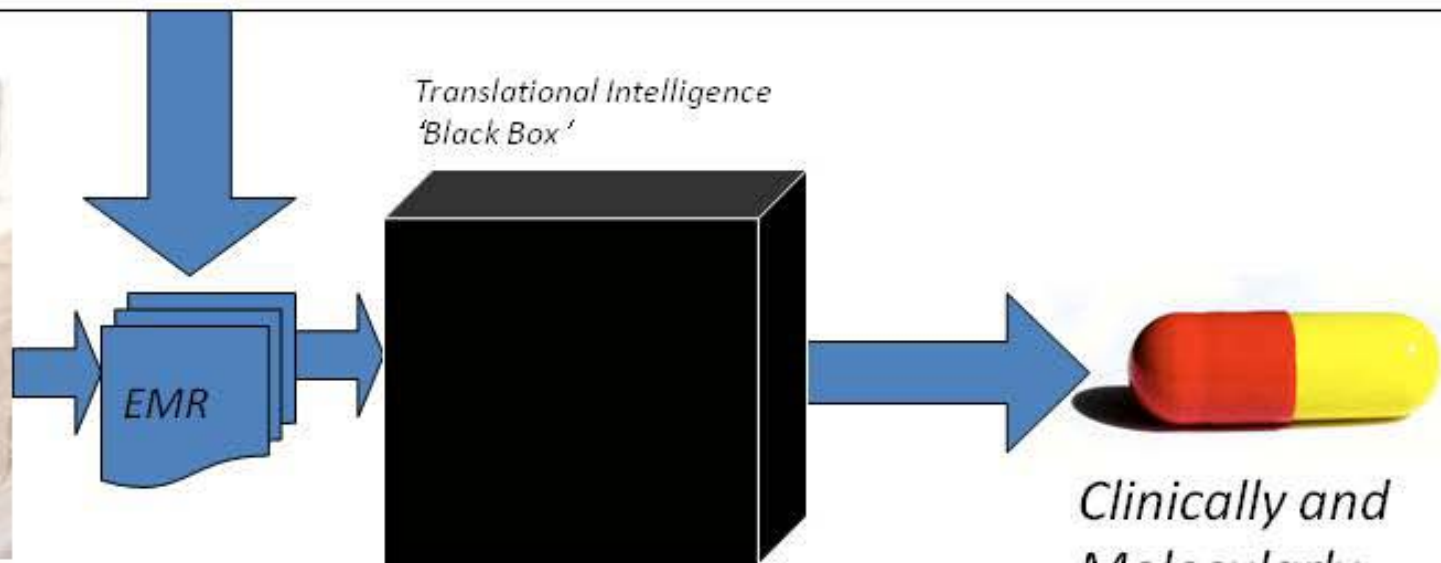
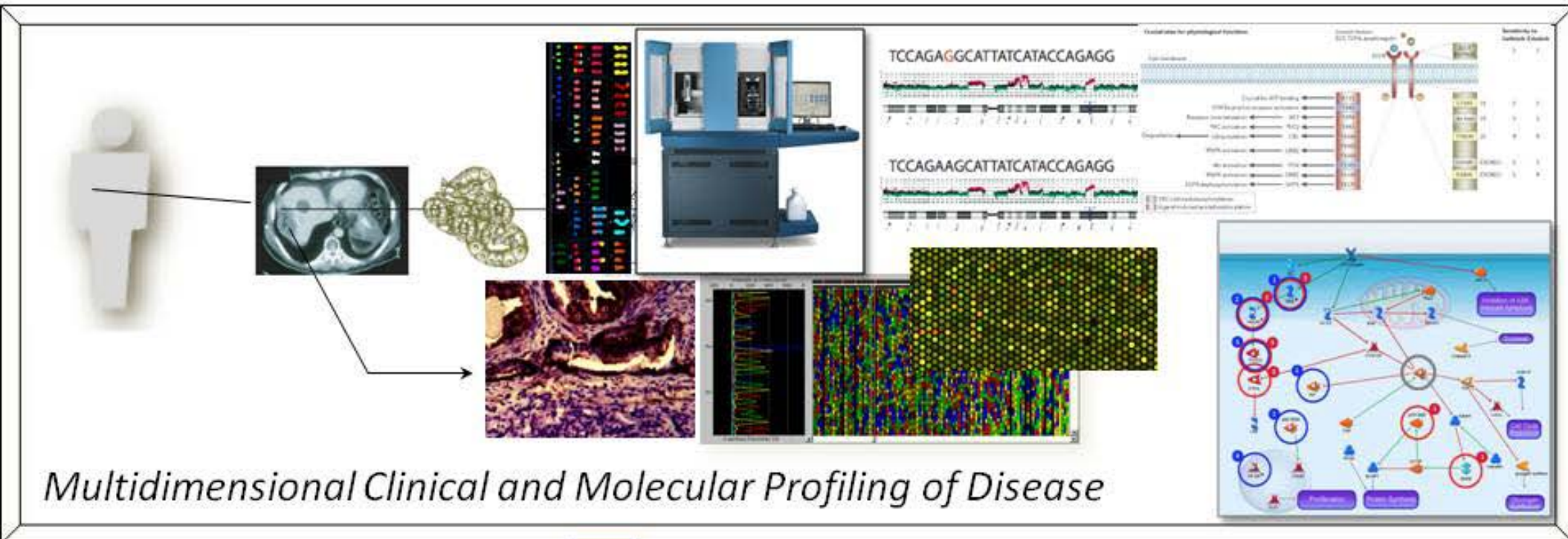


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Medicina personalizzata



*Precision Genomics
Based Medical Care*

*Clinically and
Molecularly
Appropriate
Therapy*



THE FUTURE LOOKS BRIGHT...

Serial killer or homosexual...yeah