

Progetto **CANOA**
**CARCINOMA
MAMMARIO:**

QUALI NOVITÀ PER IL 2013?

“Saper leggere” uno studio clinico per migliorare la pratica clinica

Coordinatori scientifici:

Stefania Gori
Giovanni L. Pappagallo

Comitato Scientifico:

Emilio Bria
Massimo Di Maio
Jennifer Foglietta
Alessia Levaggi

Negrar - Verona 22-23 marzo 2013
Ospedale Sacro Cuore - Don Calabria

**METASTASI
VISCERALI: ALTRE
OPZIONI OLTRE LA
CHEMIOTERAPIA
FULVESTRANT**

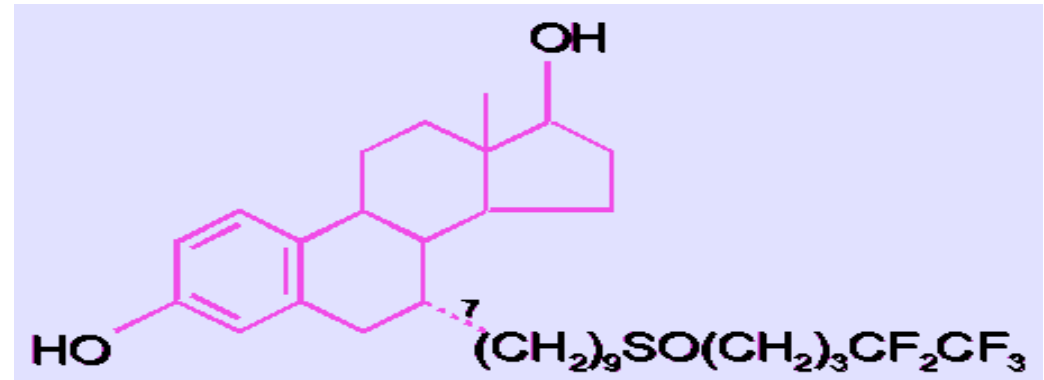
Marta Pestrin

**“Sandro Pitigliani” Medical
Oncology Dept.
Hospital of Prato
Istituto Toscano Tumori,
Prato, Italy**



Fulvestrant

- Steroid structure
- High affinity for ER (100 > Tam)
- Antiestrogen devoid of agonist activity
- Full inhibition ER pathway



Fulvestrant Pivotal Phase III Trials

- **First line setting**

0025: multicenter, double-blind, randomized trial.

- 587 pts with untreated M or LA BC were randomly assigned to receive either fulvestrant (250 mg/mo) or tamoxifen (20 mg/d)
- In the overall population efficacy end points (TTP, ORR and CBR) favored tamoxifen

Howell et al, JCO 2004

- **Second line setting**

0020-0021: prospectively planned comparative Phase III trials

- 851 pts with MBC previously treated with endocrine therapy were randomly assigned to receive fulvestrant (250 mg/mo) or anastrozole (1 mg/d)
- Fulvestrant was found to be at least as effective as anastrozole in the second line setting for MBC ER+ pts

**Registration of fulvestrant 250 mg
as an additional treatment option
for MBC ER+ pts**

Robertson JFR et al. Cancer 2003

Previous data suggesting an interaction between fulvestrant dose and activity

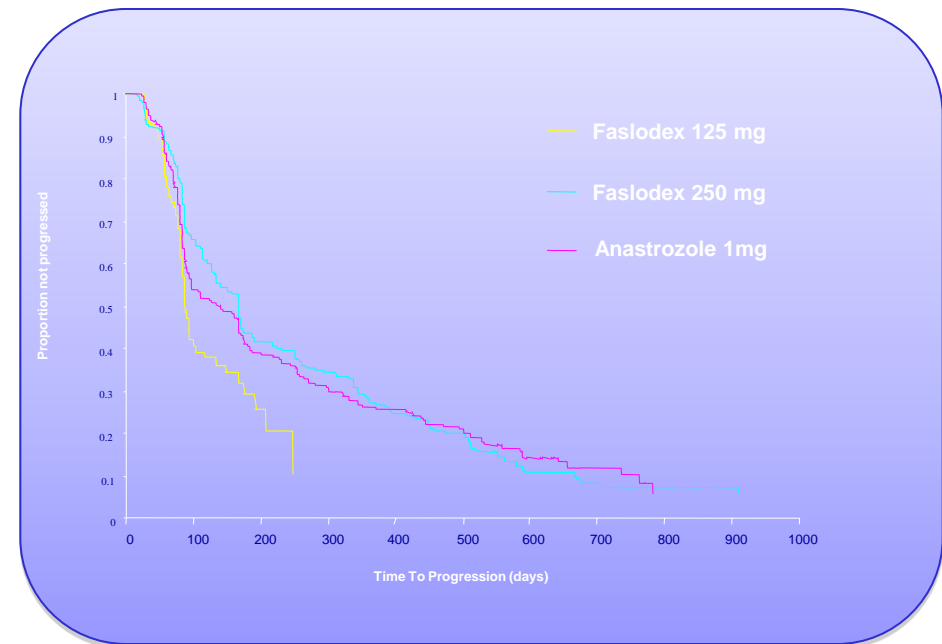
- **Neoadjuvant setting**

- Two studies, where pts were exposed short term to different doses of F indicated that ER, PgR, and Ki-67 were downregulated in a dose-dependent manner after treatment with fulvestrant.

Robertson J et al, Cancer Research 2001
DeFriend DJ et al, Cancer Research 1994

- **20/21: Prospective Combined Analysis**

- The pooled analysis of the 2 trials suggested a dose-response effect might exist because the two trials initially included a F lower dose arm (125 mg) which was discontinued after a first interim analysis



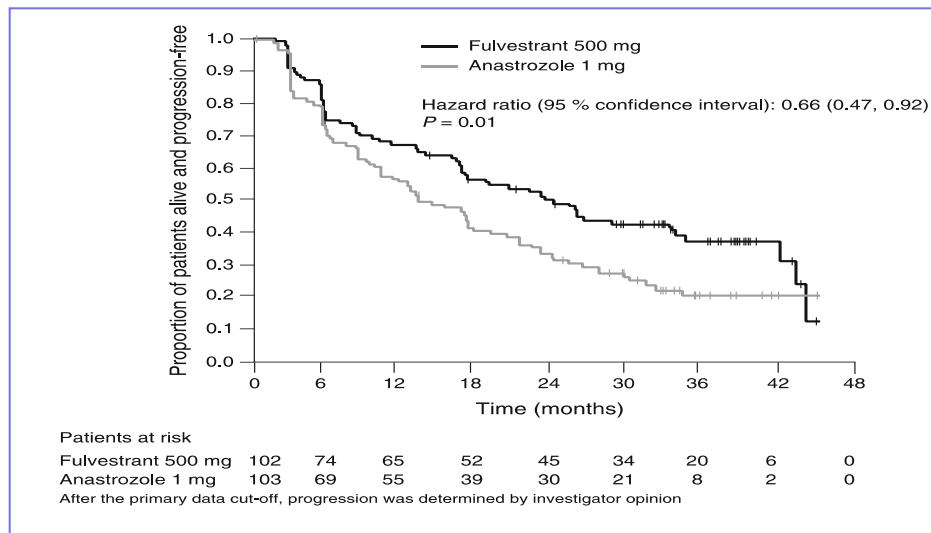
Previous data from a study testing fulvestrant 500 mg

- **First line setting**

FIRST trial: phase II, randomized, open-label, multicenter study

- 205 pts with untreated M or LABC were randomly assigned to receive a F high dose regimen (500 mg/mo + 500 mg on day 14 of mo 1) versus anastrozole (1 mg/d)

Robertson JFR et al, J Clin Oncol 2009



- First-line F HD was at least as effective as anastrozole for CBR and ORR and was associated with significantly longer TTP

Robertson JFR et al, BCRT 2012

Comparison between fulvestrant 250 and 500 mg: CONFIRM trial

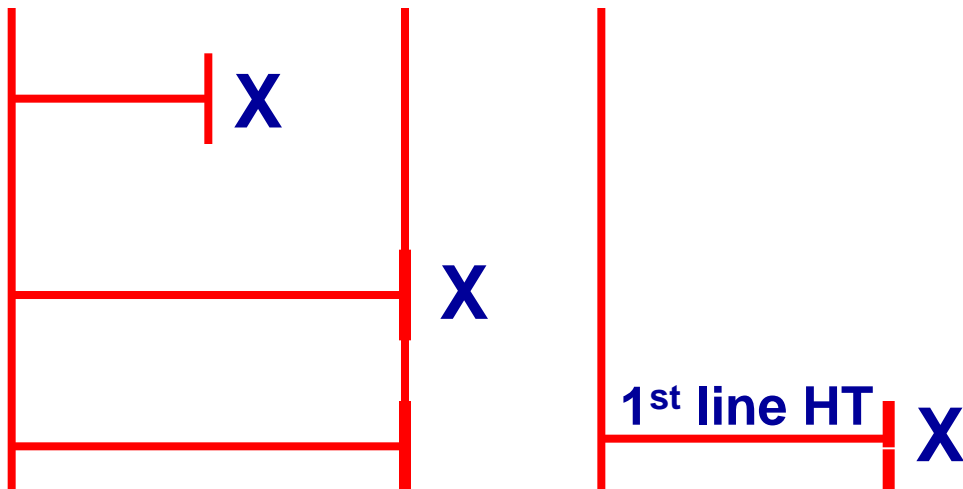
- **First-second line setting**

CONFIRM: a double-blind, parallel-group, multicenter, phase III study

- 736 pts were randomly assigned to fulvestrant 500 mg or 250 mg
- Primary end point was PFS. Secondary end points included ORR, CBR, DoCB, OS, and QoL

Allowed prior hormonotherapy (HT)

Relapsing pts.

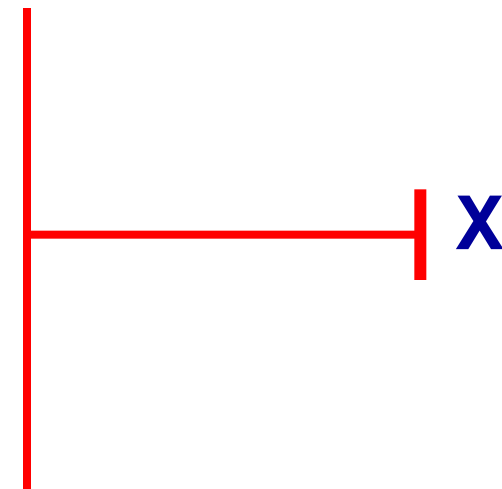


Start adj. HT

5 yrs.

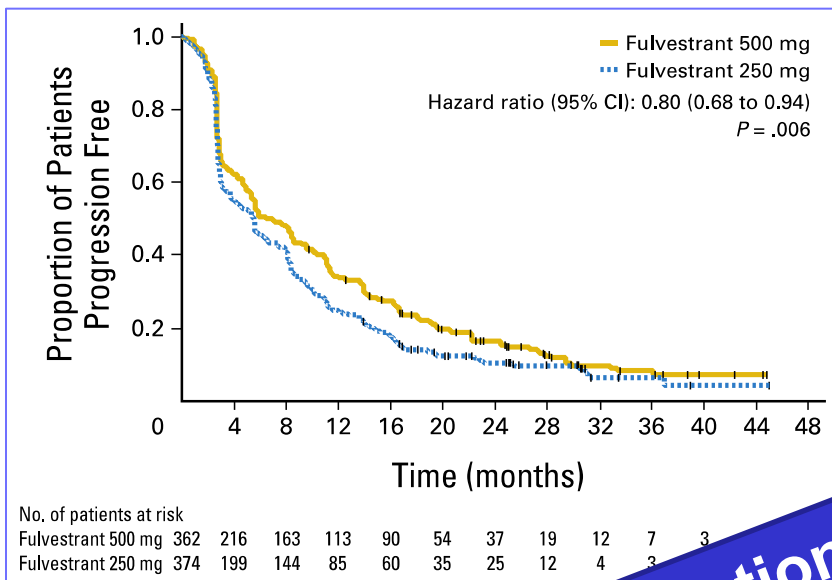
12 mos. gap

“de novo” advanced pts.



1st line HT

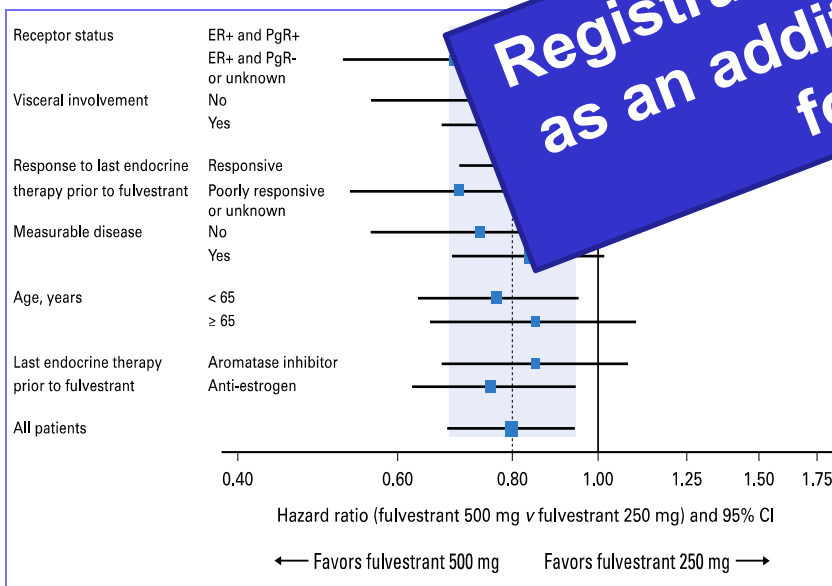
Time to progression



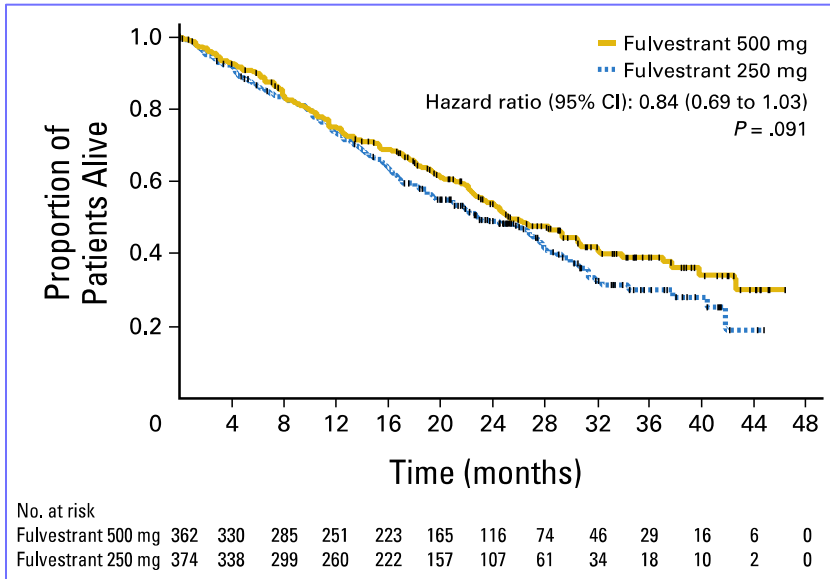
PFS was significantly longer for F 500 mg than 250 mg (HR = 0.80; 95% CI: 0.68-0.94; P = .006), corresponding to a 20% reduction in risk of progression

Registration of fulvestrant 500 mg as an additional treatment option for MBC ER+ pts

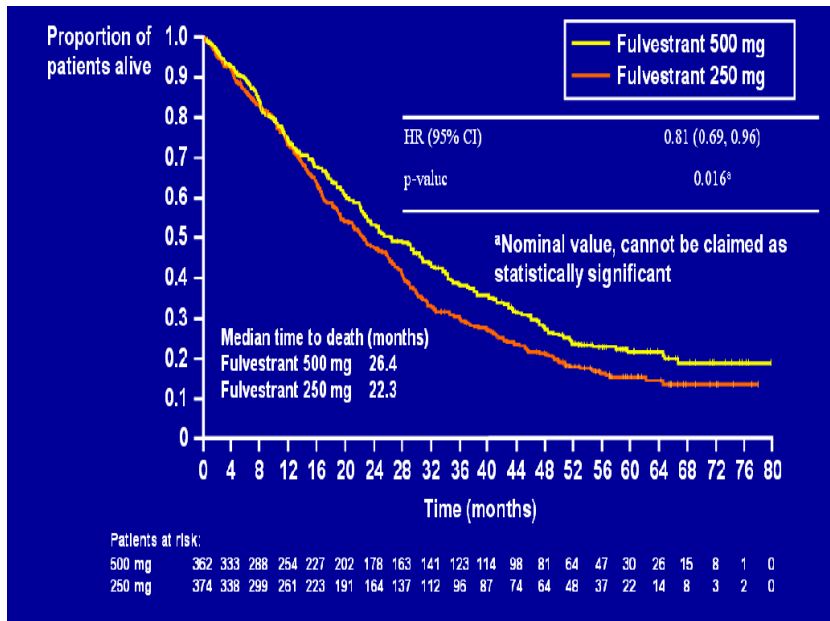
of treatment effect seems to be consistent across all subgroups



Overall survival



Median OS were 25.1 and 22.8 mos for F 500 mg and 250 mg, respectively (HR= 0.84; 95% CI, 0.69-1.03; P= .091)



Final OS analysis at 75% maturity shows that F 500 mg is associated with 4.1 mo. increase in median OS and a 19% reduction in the risk of death compared with F 250 mg

Possible treatment algorithm

<u>Adjuvant</u>	<u>1° line</u>	<u>2° line</u>
AI	1° TAM 2° Fulvestrant	1° Fulvestrant 2° TAM 3° AI*
TAM	AI or Fulvestrant	Fulvestrant or AI*
TAM → AI	Fulvestrant	AI*

* + Everolimus