Loading Dose Schedule of Fulvestrant Combined with Anastrozole for the Treatment of Patients with Breast Cancer at First Relapse

Presentation discussed in this issue:

Bergh J et al. **First results from FACT — An open-label, randomized Phase III study investigating loading dose of fulvestrant combined with anastrozole versus anastrozole at first relapse in hormone receptor positive breast cancer.** SABCS 2009;**Abstract 23**.

Slides from a presentation at SABCS 2009

Introduction

- Many patients with advanced hormone-dependent breast cancer develop resistance to aromatase inhibitors such as anastrozole.
- Fulvestrant down regulates estrogen receptors and has similar single agent activity as anastrozole in pre-clinical studies (*Cancer Res* 2008;68:3516).
- The combination of anastrozole (A) and fulvestrant (F) may counteract resistance by increasing the level of estrogen blockade through synergistic modes of action.
- **Current study objectives:**
  - Examine the safety and efficacy of the combination of F + A using a loading dose schedule of F in patients with relapsed hormone receptor positive breast cancer.

Source: Bergh J et al. SABCS 2009;Abstract 23.

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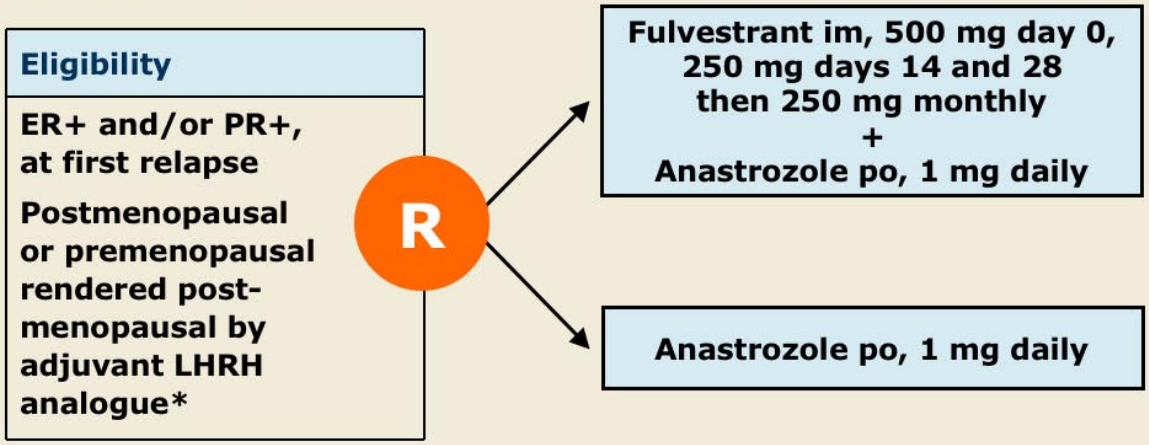
FACT: Phase III, Open-Label, Multicenter Trial of Combined Fulvestrant and Anastrozole Therapy

Accrual: 514



**In these cases, the LHRH analog must be continued throughout the study period*

Source: Bergh J et al. SABCS 2009;Abstract 23.

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Efficacy – Full Analysis Set

Efficacy parameter	F + A (n=258)	A (n=256)	HR (95% CI) *p*-value
Best objective response[1] Complete response (CR) Partial response (PR) Stable disease (SD) ≥ 24 weeks	 1.6% 14.3% 39.1%	 1.6% 13.3% 40.2%	—
Median time to progression (months)	10.8	10.2	0.99 (0.81, 1.20) *p* = 0.91
Overall survival (months)	37.8	38.2	1.00 (0.76, 1.32) *p* = 1.00

[1]*Programmatically derived to RECIST criteria*

Source: Bergh J et al. SABCS 2009;Abstract 23.

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Pre-specified Adverse Events* (Safety Population)

Grouped event type	F + A (n=256)	A (n=254)	*p*-value
GI disturbances	28.9%	25.2%	0.37
Hot flushes	24.6%	13.8%	< 0.01
Joint disorders	26.6%	27.6%	0.84
Thromboembolic events	2.3%	1.6%	0.75
Urinary tract infection	7.8%	5.9%	0.48
Weight gain	2.3%	2.4%	1.00

**Shown are only those adverse events with an incidence of 2% or greater.*

Source: Bergh J et al. SABCS 2009;Abstract 23.

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Conclusions

- Time to progression, overall survival and the clinical benefit rate were almost identical between the two study arms.
  - Time to progression: 10.8 mos vs 10.2 mos
  - Overall survival: 37.8 mos vs 38.2 mos
  - Clinical benefit rate: 55.0% vs 55.1%
- F+A is well tolerated, however patients receiving the combination experienced significantly more hot flushes.
- Combining A with F offers no clinical efficacy advantage over anastrozole alone and should not be used.

Source: Bergh J et al. SABCS 2009;Abstract 23.

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