

# Randomized Comparison of Adjuvant Aromatase Inhibitor Exemestane plus Ovarian Function Suppression vs Tamoxifen plus Ovarian Function Suppression in Premenopausal Women with HR+ Early Breast Cancer: Update Of The Combined TEXT and SOFT Trials

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on behalf of Olivia Pagani, MD

**TEXT and SOFT Investigators and  
International Breast Cancer Study Group (IBCSG)**



# Premenopausal Endocrine Therapy

- The combined analysis of TEXT and SOFT, after 5.7 years median follow-up, found adjuvant E+OFS significantly improved disease-free survival vs T+OFS in premenopausal women with HR+ BC (*NEJM 2014*)  
Follow-up was immature for overall survival
- Those results have been incorporated into treatment guidelines (St. Gallen, ASCO, NCCN, BCY) to help oncologists tailor adjuvant endocrine therapy in this patient population
- We report today the planned update after 9 years median follow-up

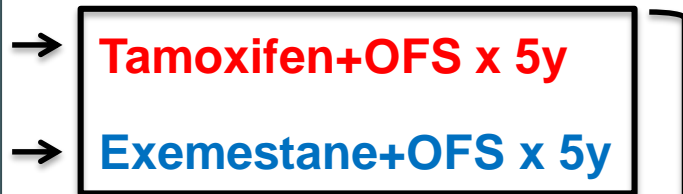


# TEXT and SOFT Designs

Enrolled: Nov03-Apr11

- Premenopausal HR+
- ≤12 wks after surgery
- Planned OFS
- No planned chemo  
OR planned chemo

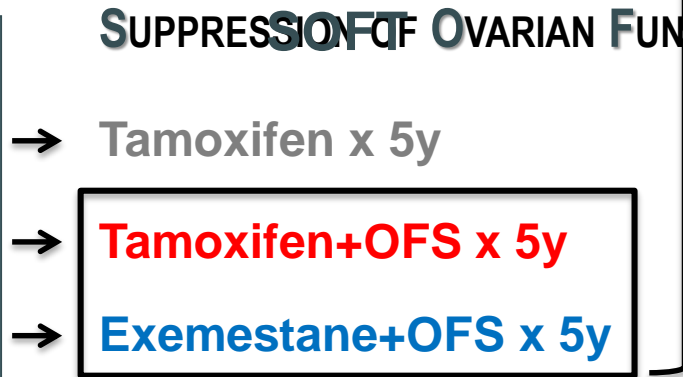
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TAMOXIFEN AND EXEMESTANE TRIAL (N=2672)

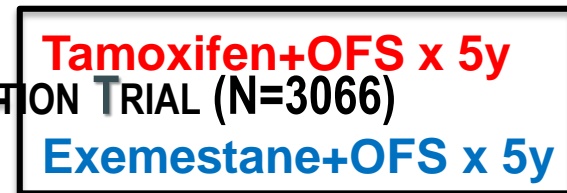
- Premenopausal HR+
  - ≤12 wks after surgery
  - No chemo
- OR
- Remain premenopausal  
≤ 8 mos after chemo

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SUPPRESSION OF OVARIAN FUNCTION TRIAL (N=3066)

Joint Analysis  
(N=4690)



Median follow-up 9 years

OFS=ovarian function suppression



# Endpoints

## Primary:

- **Disease-free survival (DFS)**
  - Invasive recurrence (local, regional, distant)
  - Invasive contralateral breast cancer
  - Second (non-breast) invasive malignancy
  - Death without prior cancer event

## Secondary:

- **Breast cancer-free interval (BCFI)**
  - Invasive recurrence or contralateral breast cancer
- **Distant recurrence-free interval (DRFI)**
  - Distant recurrence
- **Overall survival (OS)**
  - Death from any cause

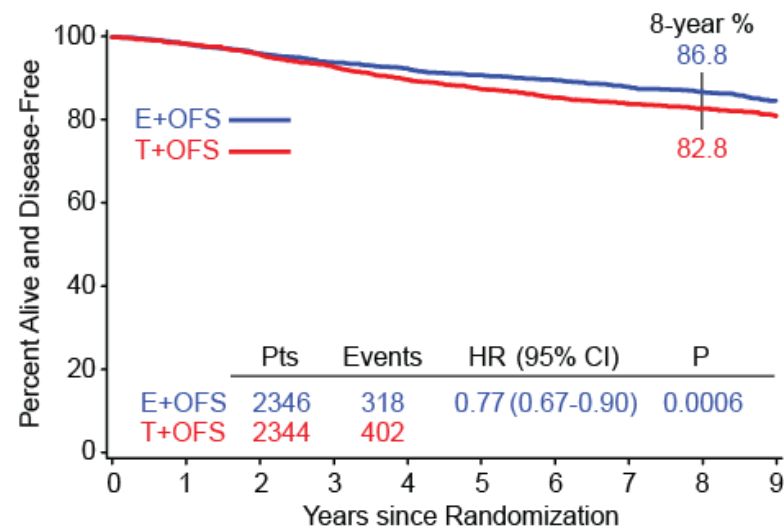


# Patient Characteristics

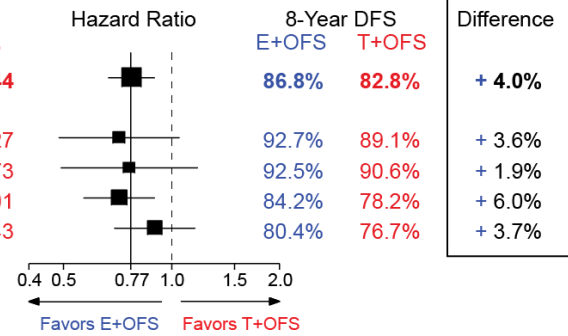
	No chemo TEXT (N=1053)	No chemo SOFT (N=943)	Chemo TEXT (N=1607)	Prior chemo SOFT (N=1087)	Overall (N=4690)
Age <40 yr	16%	9%	30%	49%	27%
LN +	21%	8%	66%	57%	42%
T-size >2cm	19%	15%	53%	47%	36%
HER2 +	5%	3%	17%	20%	12%
Surgery to random. (median)	1.5 mo	1.8 mo	1.2 mo	8.0 mo	1.6 mo



# Sustained Improvement in DFS



Cohort	E+OFS		T+OFS	
	Events	Pts	Events	Pts
<b>All Patients</b>	<b>318</b>	<b>2346</b>	<b>402</b>	<b>2344</b>
No Chemotherapy TEXT	44	526	62	527
No Chemotherapy SOFT	35	470	47	473
Chemotherapy TEXT	131	806	173	801
Prior Chemotherapy SOFT	108	544	120	543

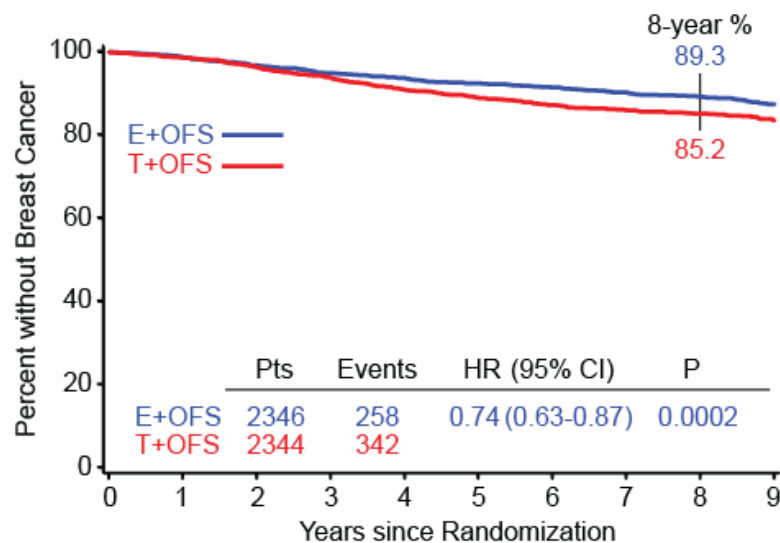


**4.0% absolute improvement in 8-yr DFS for E+OFS after 9 years median follow-up**

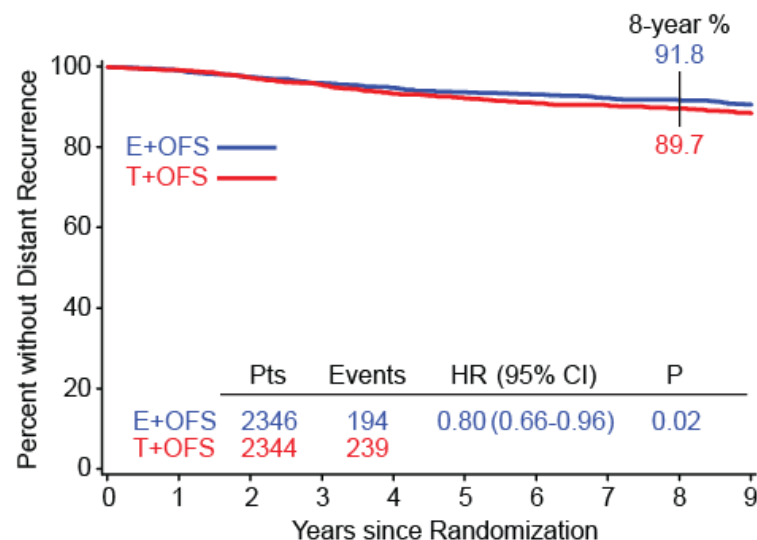


# Significant Reductions in Recurrence

## Breast Cancer-Free Interval



## Distant Recurrence-Free Interval

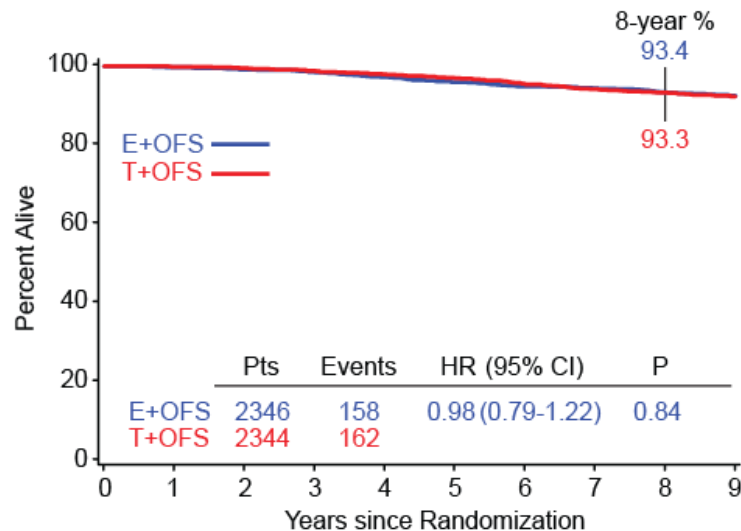


**4.1% absolute improvement in 8-yr freedom from breast cancer for E+OFS**

**2.1% absolute improvement in 8-yr freedom from distant recurrence for E+OFS**



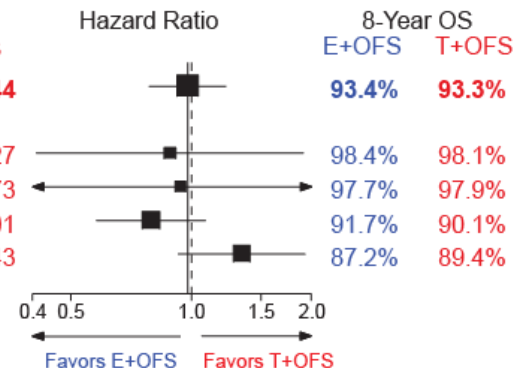
# Overall Survival



**All Patients**

**Cohort**

	E+OFS Events	Pts	T+OFS Events	Pts
<b>All Patients</b>	<b>158</b>	<b>2346</b>	<b>162</b>	<b>2344</b>
No Chemotherapy TEXT	12	526	14	527
No Chemotherapy SOFT	9	470	10	473
Chemotherapy TEXT	70	806	87	801
Prior Chemotherapy SOFT	67	544	51	543



**E+OFS did not improve Overall Survival vs T+OFS, after 9 years median follow-up**





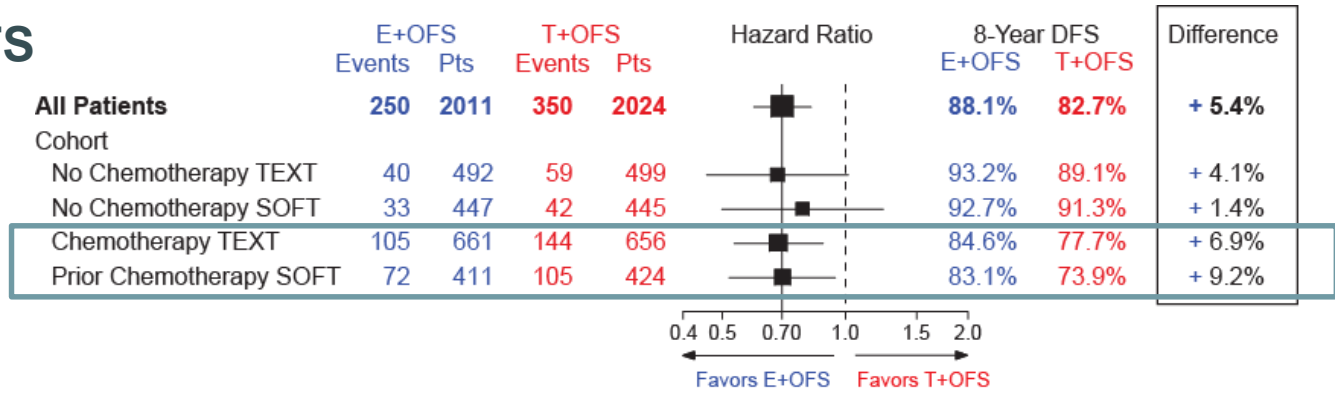
# HER2 Status

- HER2-negative and HER2-positive cancers are now considered clinically relevant subgroups for treatment decision-making
- The HER2-negative subgroup was the large majority of the trials' population: 4035 patients (86%)
- Results for the HER2-positive subgroup require further investigation:
  - Trials enrolled both before and after use of adjuvant trastuzumab



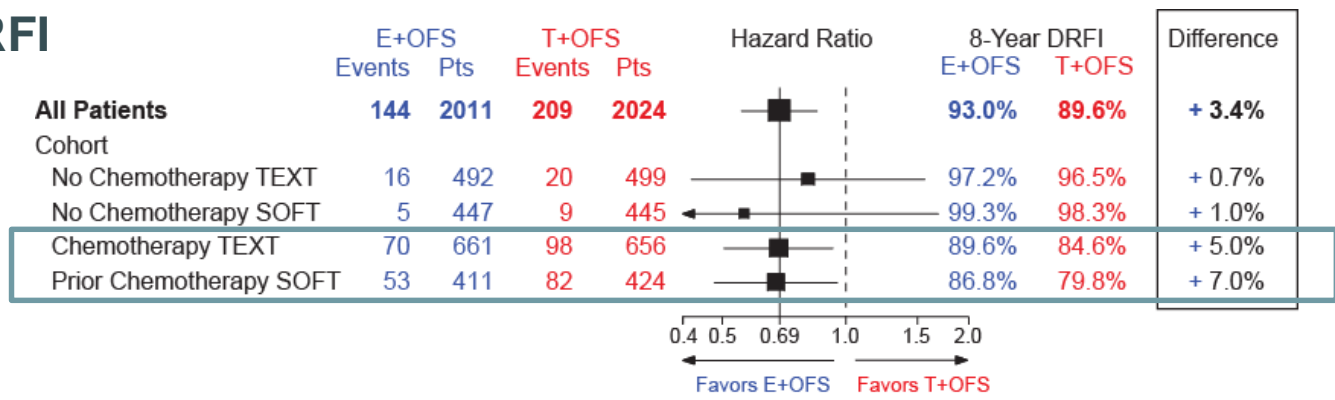
# HER2-negative Patients (N=4035)

## DFS



- Consistent relative treatment effects in all cohorts

## DRFI



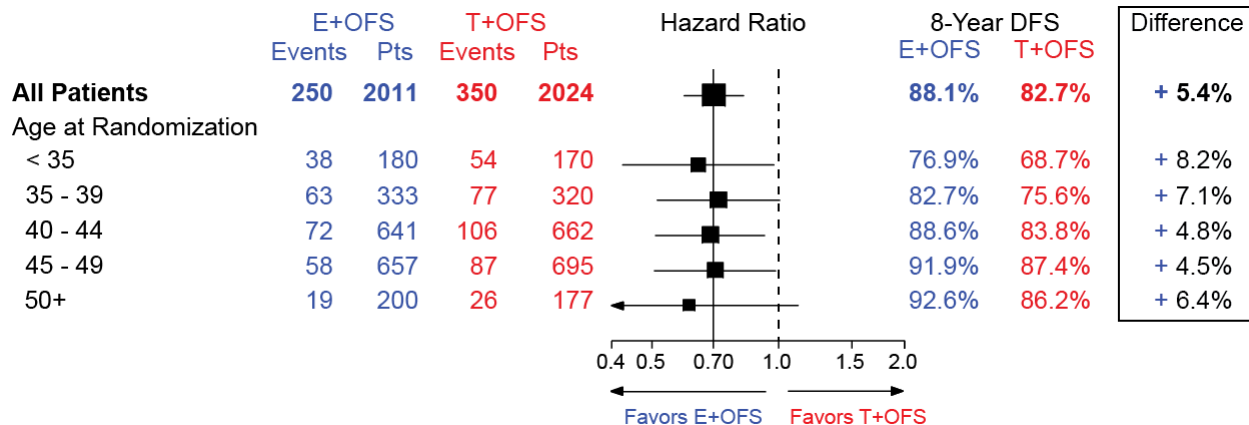
- Larger absolute benefits of E+OFS in chemo cohorts

- Overall Survival HR=0.86 (0.68-1.10)

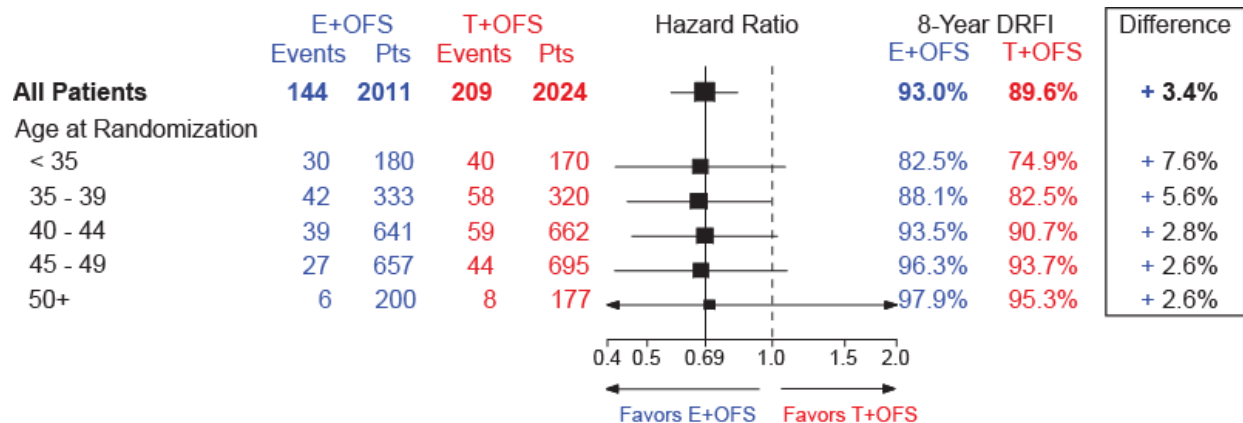


# Treatment Effect by Age (HER2-neg)

## DFS



## DRFI



# Selected Adverse Events (all patients)

	E + OFS (N=2317)	T + OFS (N=2326)
Endometrial cancer	<b>n=4</b>	<b>n=9</b>
Musculoskeletal symptoms (G3-4)	<b>11%</b>	<b>6%</b>
Osteoporosis (G2-4; T score < -2.5)	<b>15%</b>	<b>7%</b>
Fractures (G3-4)	<b>1.6%</b>	<b>1.0%</b>
Hot Flashes (G3)	10%	12%
Libido decrease (G2)	15%	12%
Vaginal dryness (G2)	27%	22%
Depression (G3-4)	4.1%	4.6%
Thrombosis/embolism (G2-4)	<b>1.2%</b>	<b>2.3%</b>



# Adverse Events and Treatment Adherence

- Incidence of grade 3-4 targeted AEs was similar in the two groups (32% and 31%)
- Overall, 15% of patients stopped all protocol-assigned treatment early
  - **More patients on E+OFS stopped assigned oral ET early**
    - 14% vs 6% by 1 year
    - 25% vs 19% by 4 years
  - **No difference in the rate of triptorelin cessation**
    - 18% vs 19% by 4 years



# Conclusions 1

- After longer follow-up (median 9 years), results confirm statistically significant improvements in disease outcomes with E+OFS
- Adjuvant E+OFS, compared with T+OFS, shows a sustained absolute improvement in DFS (4%) and reduction in distant recurrence (2.1%)
- In patients with HER2-negative tumors (86% of the population) E+OFS improved disease outcomes in all treatment cohorts
- For HER2-negative deemed at sufficient risk to receive chemotherapy, clinically meaningful benefits are observed with E+OFS, with absolute improvements in DFS of 7% - 9%, and absolute improvements in DRFI of 5% - 7%, across TEXT and SOFT respectively



# Conclusions 2

- Relative treatment effect was independent of age, although absolute benefit larger in very young women
- No difference in overall survival after 9 years median follow-up
- **Follow-up continues** (very few deaths in no chemo patients)
  
- **To optimally translate absolute trial improvements into clinical practice, oncologists need to discuss and weigh benefits and toxicity in each individual HR+ premenopausal patient**





# IBCSG Thanks



5738 women who participated in TEXT,SOFT



- Physicians, nurses, data and trial coordinators, and pathologists in 510 centers worldwide
- Pfizer and Ipsen for drug supply and financial support
- US NCTN, BCRF for financial support of long-term follow-up
- IBCSG central offices
- STP Steering Committee, DSMC

IBCSG  
BCT-ANZ  
SAKK  
GOCCHI  
CEEQG  
EORTC  
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CTI  
NCRI/ICR-CTSU  
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