



Lo Mejor de San Antonio 2017

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Randomized Comparison of Adjuvant Tamoxifen plus Ovarian Function Suppression vs Tamoxifen in Premenopausal Women with HR+ Early Breast Cancer: Update of the SOFT Trial

Gini Fleming, MD
on behalf of SOFT Investigators and
International Breast Cancer Study Group (IBCSG)



International Breast Cancer Study Group (IBCSG)



IBCSG

2003

SOFT

TEXT

PERCHE

IBCSG

SOFT

- **Suppression of Ovarian Function Trial**
- ¿Cuál es el rol de la supresión de la función ovárica en mujeres premenopáusicas tratadas con Tamoxifeno?

TEXT

- **Tamoxifen and Exemestane Trial**
- ¿Cuál es el rol de los IA en mujeres tratadas con supresión de la función ovárica?

PERCHE

- **Premenopausal Endocrine Responsive Chemotherapy Trial**
- ¿Cuál es el rol de QMT adicional a la terapia endocrina combinada?
- CIERRE PREMATURO DEL ESTUDIO

SOFT:

Suppression of Ovarian Function Trial

- Periodo: dic 2003 - enero 2011
- Categorización:
QMT (neo) adyuvante
 - Sin QMT, incluidas dentro de las 12 semanas de la cirugía (47%)
 - QMT previa, paciente premenopáusicas, incluidas dentro de 8 semanas (53%)
- Ganglios: Positivos (34,5%)
- Método de supresión ovárica: Triptorelina

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- Mediana seguimiento: 8 años
- Tamoxifeno x 5a (n: 1018)
- Tamoxifeno + SFO x 5a (n: 1015)
- Exemestano + SFO x 5a (n: 1014)

Patient Characteristics

	No Chemotherapy N=1419	Prior Chemotherapy N=1628	All N=3047
Age (median)	46 yr	40 yr	43 yr
<35 years	1.5%	20.2%	11.5%
Nodal status			
positive	8.8%	56.9%	34.5%
negative	91.2%	43.1%	65.5%
Grade			
1	39.7%	13.8%	25.9%
2	52.8%	49.5%	51.0%
3	6.5%	33.7%	21.0%
HER2+	3.7%	19.2%	12.0%



Endpoints

Primarios:

- Sobrevida libre de enfermedad (SLE)
 - ✧ Recurrencia invasora (local, regional o a distancia)
 - ✧ Ca de mama invasor contralateral
 - ✧ Segundo cáncer invasor (no mama)
 - ✧ Muerte sin evento cancerígeno previo

Secundarios:

- Intervalo libre de cáncer
 - ✧ Recurrencia invasiva o ca de mama contralateral
- Intervalo libre de recurrencia a distancia
 - ✧ Recurrencia a distancia
- Sobrevida General (SG)
 - ✧ Muerte por cualquier causa

Resultados primarios

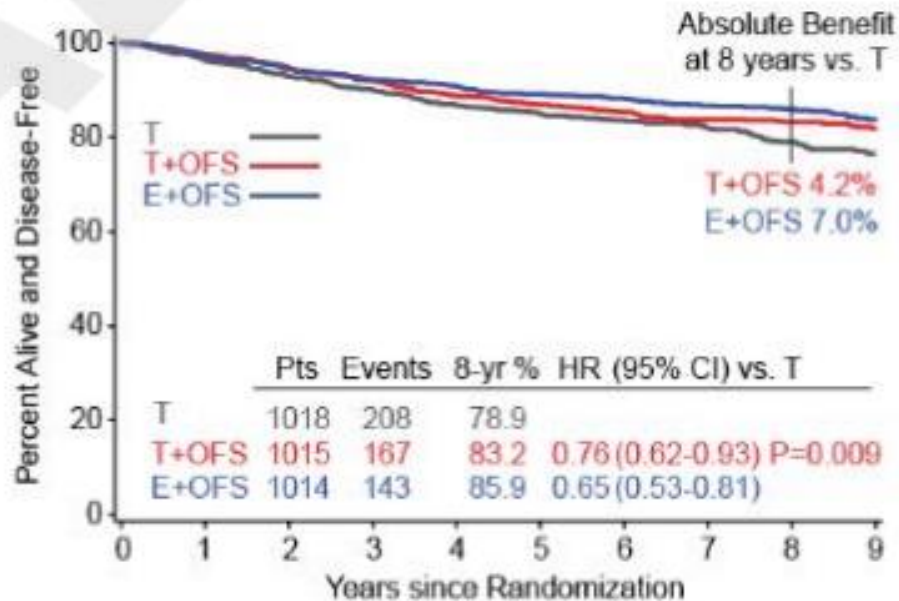
- Luego de 5,6 años de seguimiento no se encontró beneficio significativo en general al adicionar SFO a tamoxifeno en mujeres premenopáusicas con cáncer de mama RH (+)
- Para aquellas mujeres con riesgo de recurrencia suficiente para justificar QMT y se mantuvieron premenopáusicas, la adición de SFO mejoró outcomes de enfermedad
- El seguimiento fue insuficiente para Sobrevida general

Sobrevida Libre de Enfermedad 8 años de seguimiento

2017 SAN ANTONIO BREAST CANCER SYMPOSIUM

December 5-9, 2017

SOFT DFS 8 years median follow-up



T+OFS significantly improves DFS vs T-alone in the overall population



INTERNATIONAL BREAST CANCER S

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Sites of First DFS Event

	T (n=1018)	T + OFS (n=1015)	E + OFS (n=1014)
<i>DFS events (n total = 518)</i>	208	167	143
Local	29	17	18
Contralateral breast \pm above	25	14	12
Regional \pm above	19	15	7
Distant \pm above	102	96	81
2 nd non-breast malignancy	25	24	21
Death, no cancer	6	1	2
Death, incomplete info	2	0	2

54% of first DFS events involved distant sites



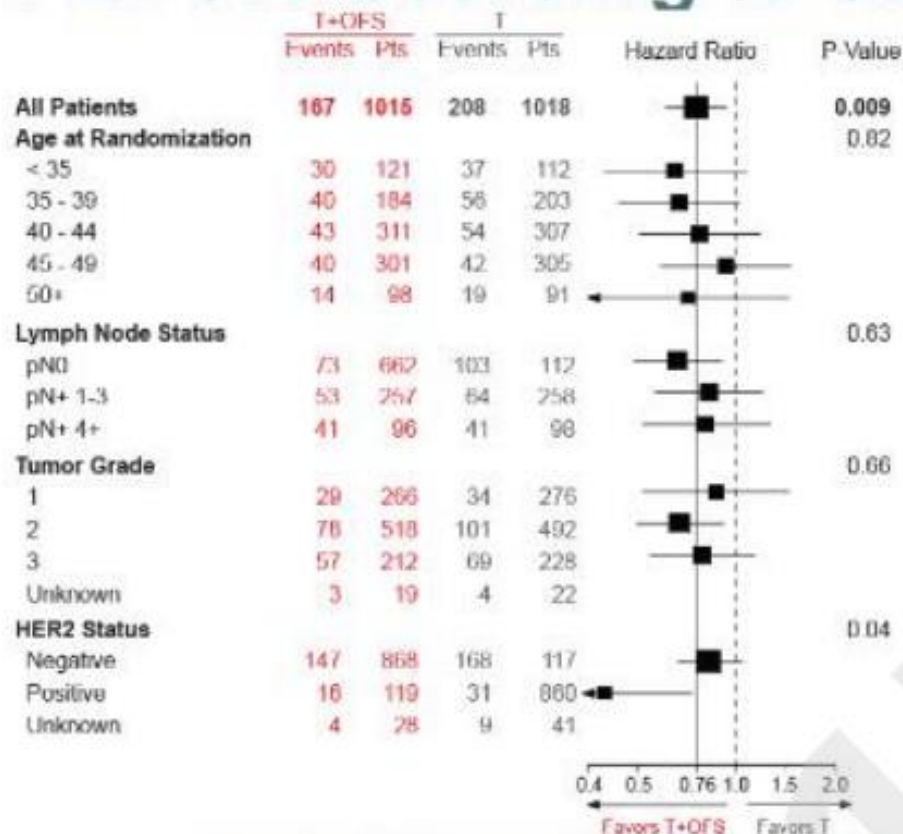
SOFT DFS

8 years median follow-up

	8-yr DFS T	8-yr DFS T + OFS	HR: T + OFS vs T	8-yr DFS E + OFS	HR: E + OFS vs T
All	78.9%	83.2%	0.76 (0.62-0.93)	85.9%	0.65 (0.53-0.81)
No chemo	87.4%	90.6%	0.76 (0.52-1.12)	92.5%	0.58 (0.38-0.88)
Prior chemo	71.4%	76.7%	0.76 (0.60-0.97)	80.4%	0.68 (0.53-0.88)
<35 years (n=350)	64.3%	73.0%	0.66 (0.41-1.07)	77.4%	0.52 (0.31-0.87)



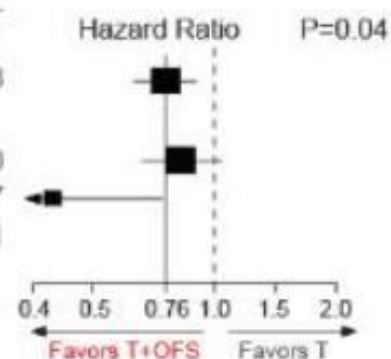
SOFT DFS: According to Subgroups



SOFT DFS: Effect of HER2 Status

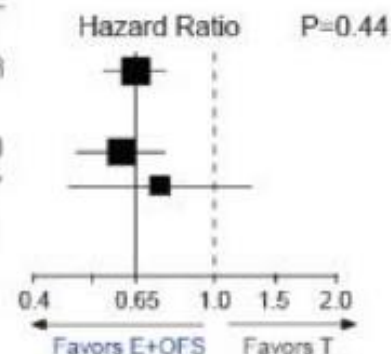
T + OFS vs T

	T+OFS		T	
	Events	Pts	Events	Pts
All Patients	167	1015	208	1018
HER2 Status				
Negative	147	868	168	860
Positive	16	119	31	117
Unknown	4	28	9	41



E + OFS vs T

	E+OFS		T	
	Events	Pts	Events	Pts
All Patients	143	1014	208	1018
HER2 Status				
Negative	105	858	168	860
Positive	31	130	31	117
Unknown	7	26	9	41



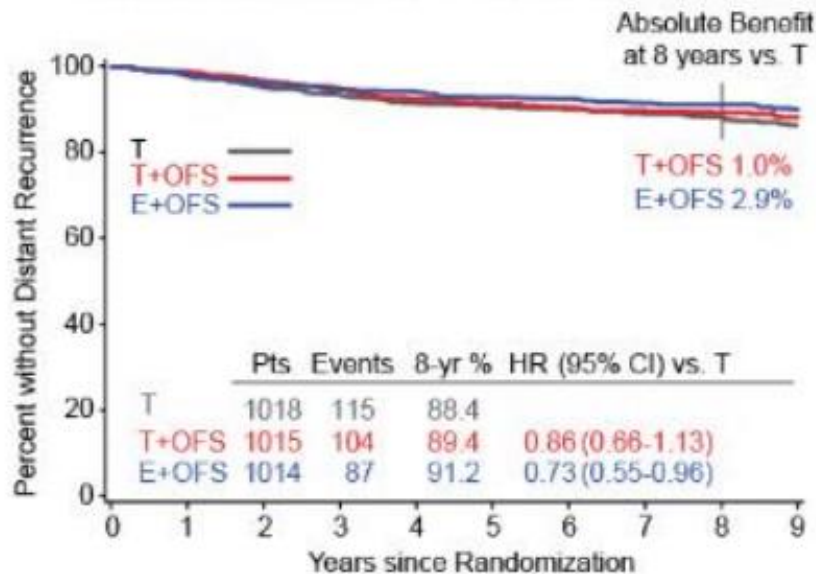
61% of HER2+
received trastuzumab



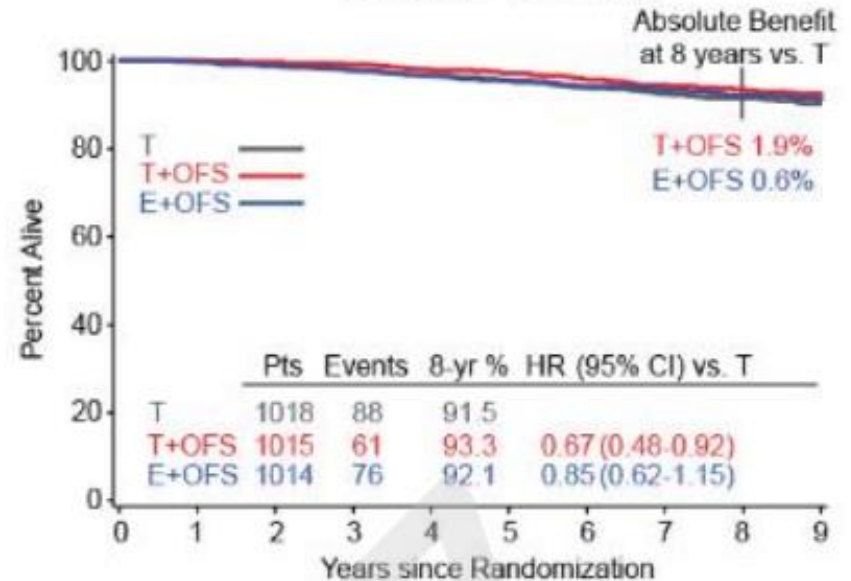
Endpoints Secundarios

SOFT Secondary Endpoints

Distant Recurrence-Free Interval



Overall Survival



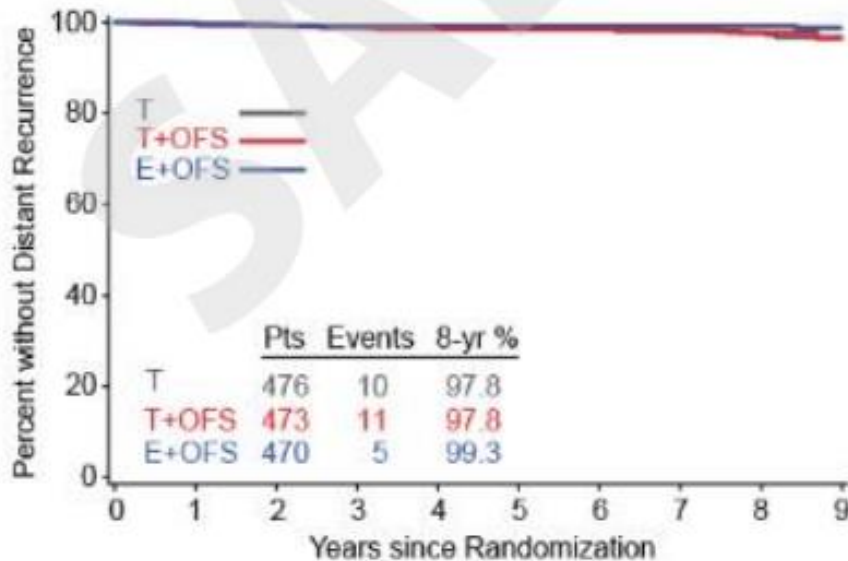
A small overall survival benefit is seen with T+OFS vs T, at 8 yrs median follow-up



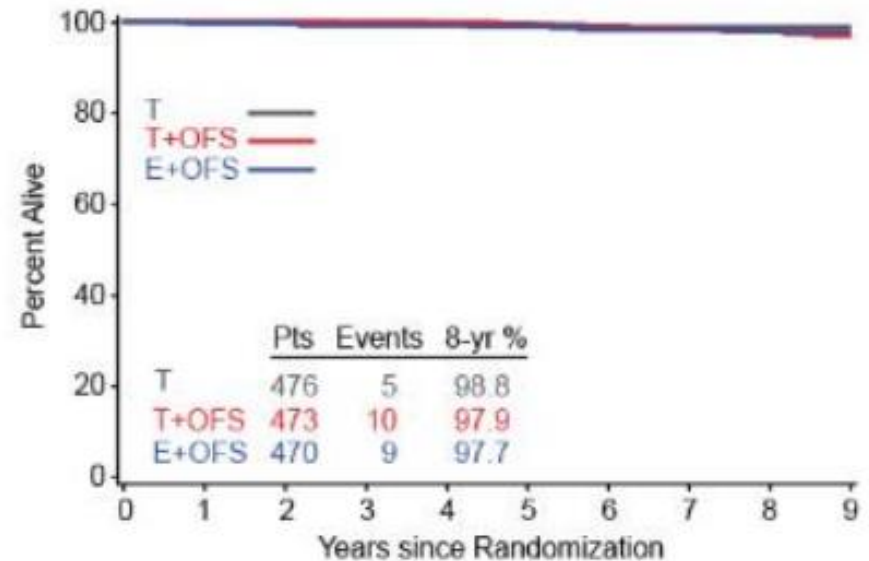
Endpoints Secundarios: Sin QMT

SOFT Secondary Endpoints: No Chemo

Distant Recurrence-Free Interval



Overall Survival

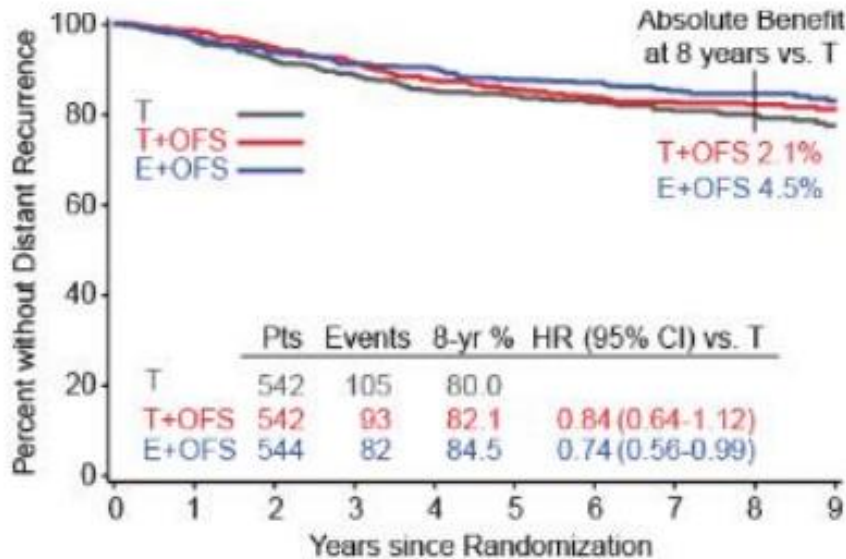


**No Chemo cohort remains at low risk of distant recurrence with T alone;
12 of 24 deaths were in setting of no distant recurrence**

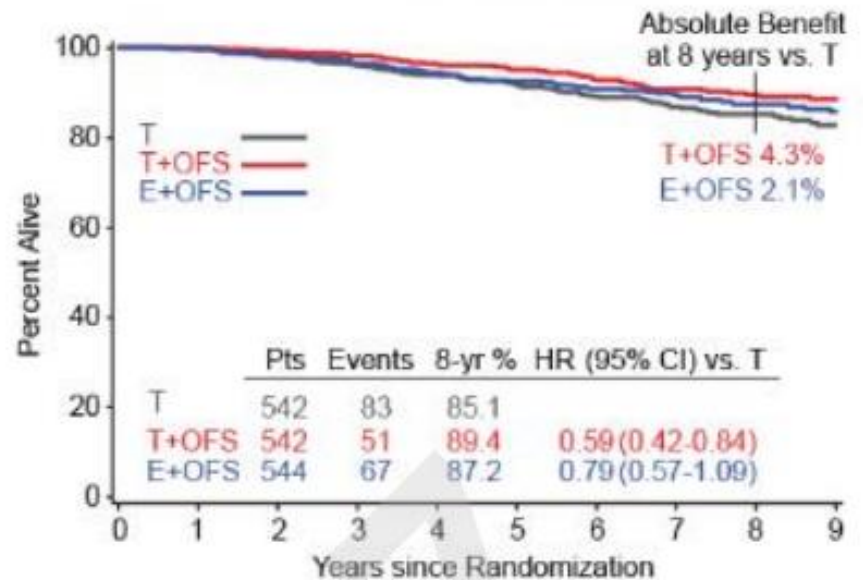
Endpoints Secundarios: QMT previa

SOFT Secondary Endpoints: Prior Chemo

Distant Recurrence-Free Interval



Overall Survival



Prior Chemo cohort has small absolute OS improvements in OFS arms at 8 yrs



Protocol and Non-protocol Therapy

	T	T + OFS	E + OFS
Stopped assigned oral endocrine therapy early	22.5%	18.5%	27.8%
Stopped triptorelin early*		21.4%	19.6%
Received OFS (in first 5 yrs)	15.5%		
Used oral endocrine therapy at ≥ 6 yr**	24.7%	24.3%	12.6%

*and did not undergo oophorectomy or ovarian irradiation

**as adjuvant therapy; denominator is patients alive and in follow-up at 6 yrs



Eventos Adversos

Selected Adverse Events

	T (N=1005)	T + OFS (N=1006)	E + OFS (N=1000)
Endometrial cancer (n)	N=7	N=4	N=3
Thrombosis/embolism (G2-4)	2.2%	2.2%	0.9%
Hot flashes (G3)	7.8%	13.2%	10.7%
Libido decrease (G2)	11.5%	15.9%	17.5%
Musculoskeletal symptoms (G3-4)	6.7%	5.9%	12.0%
Osteoporosis (G2-4; T score<-2.5)	3.9%	6.1%	11.9%
Depression (G3-4)	4.1%	4.5%	3.9%



Conclusiones

- Adicionar SFO a Tamoxifeno mejora significativamente la SLE a 8 años de seguimiento
 - En mujeres <35 años el HR en SLE es 0.66 (beneficio absoluto de 8.7%)
 - Los resultados de SLE mejoraron aún más con Exemestano + SFO
- Pequeño beneficio en Sobrevida General a 8 años
 - Evidente en mujeres que recibieron QMT
- Población que no recibió QMT tiene bajo riesgo de metástasis a distancia a 8 años con uso solo de Tamoxifeno
- El seguimiento continuara

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