Zoladex®
goserelin

Zoladex® 3.6mg: Early and advanced breast cancer[1*]

* Pre and perimenopausal women suitable for hormone manipulation.

PBS Information: Restricted Benefit. Breast Cancer.
The condition must be hormone receptor positive.

PI

References:

1. Zoladex 3.6mg Approved Product Information. Date of TGA approval 11 November 2010. Date of most recent amendment 25 June 2015

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Zoladex® 3.6mg in Early Premenopausal Breast Cancer

Zoladex® 3.6mg in Early Premenopausal Breast Cancer[1-5#]

#Pre and perimenopausal

- As effective as CMF* (chemotherapy) for disease-free survival (DFS) in ER+ early breast cancer[2,3]
  - HR=1.05; 95% CI:0.88–1.24; P=0.597[3]
- Improved overall quality of life (QoL) compared to CMF# during the first six months of therapy[4†]

†QoL was evaluated using a written, self-administered questionnaire (Rotterdam Symptom Checklist (RSCL))[4]

- Improved tolerability compared with CMF*[2‡]

‡Zoladex had a lower incidence of side effects usually associated with chemotherapy, including nausea/vomiting, alopecia and infections, during CMF treatment period. Zoladex causes a higher incidence of side effects related to oestrogen suppression, such as hot flushes, vaginal dryness and soreness, but these incidences decrease below those seen in CMF patients within 6 months of completing therapy.[2]

- The majority of patients have a return to menses within a year of completing Zoladex therapy[2]

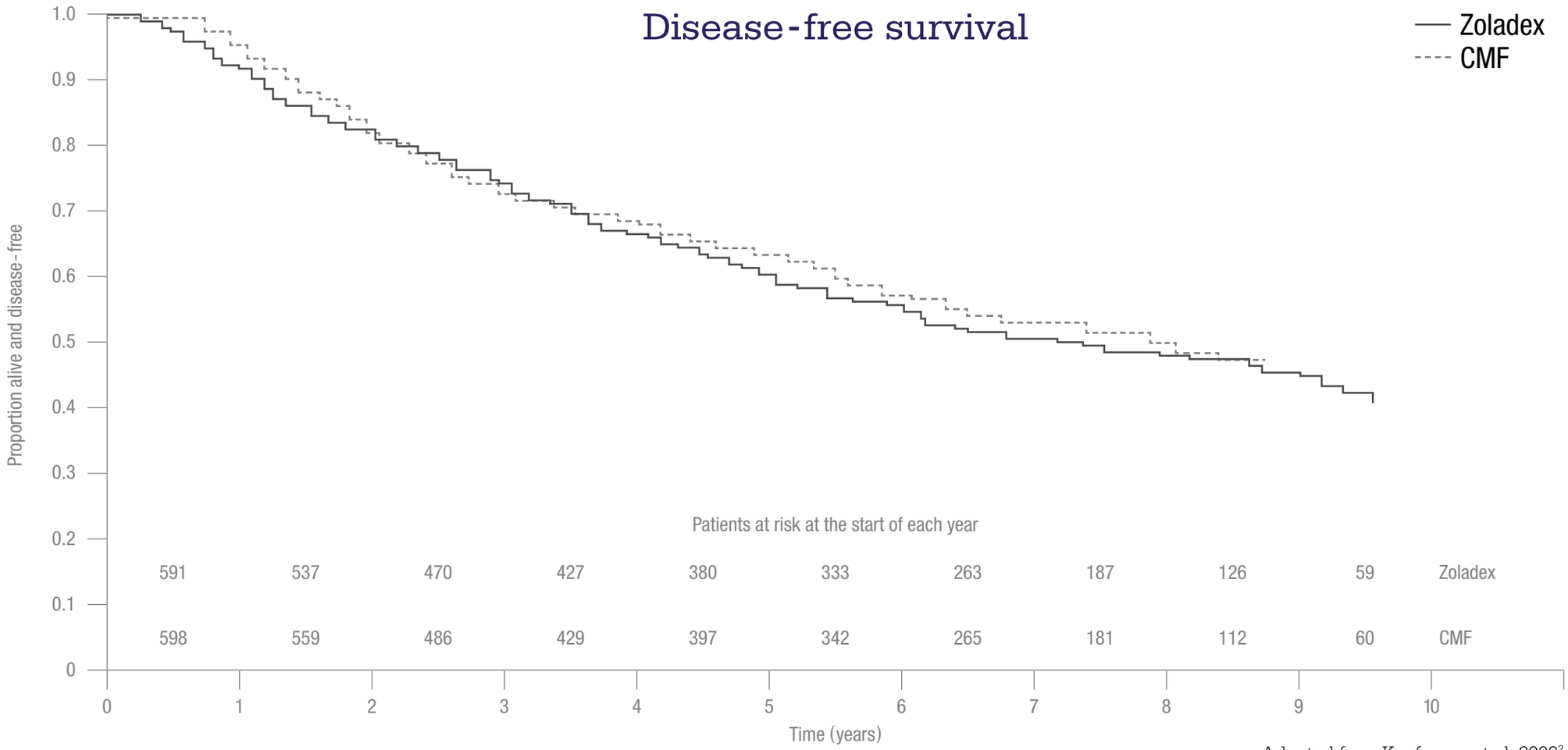
*cyclophosphamide, methotrexate and fluorouracil

References:
1. Zoladex 3.6mg Approved Product Information. Date of TGA approval 11 November 2010. Date of most recent amendment 25 June 2015
2. Jonat W et al. *J Clin Oncol 2002*;20(24):4628-35
3. Kaufmann M et al. *Eur J Cancer 2003*;39:1711-1717
4. De Haes H et al. *J Clin Oncol 2003*; 21 (24): 4510-4516
5. LHRH-agoints in Early Breast Cancer Overview group. Lancet 2007; 369: 1711-23

Zoladex® is as effective as CMF* chemotherapy for disease-free survival (DFS) in ER+ early premenopausal breast cancer[1,2]

- In ER positive, pre and perimenopausal patients (at a median follow-up of 7.3 years)[2]
- Disease-free survival was equivalent between Zoladex and CMF*[2]
  - HR=1.05; 95% CI:0.88–1.24; P=0.597[2]

DFS



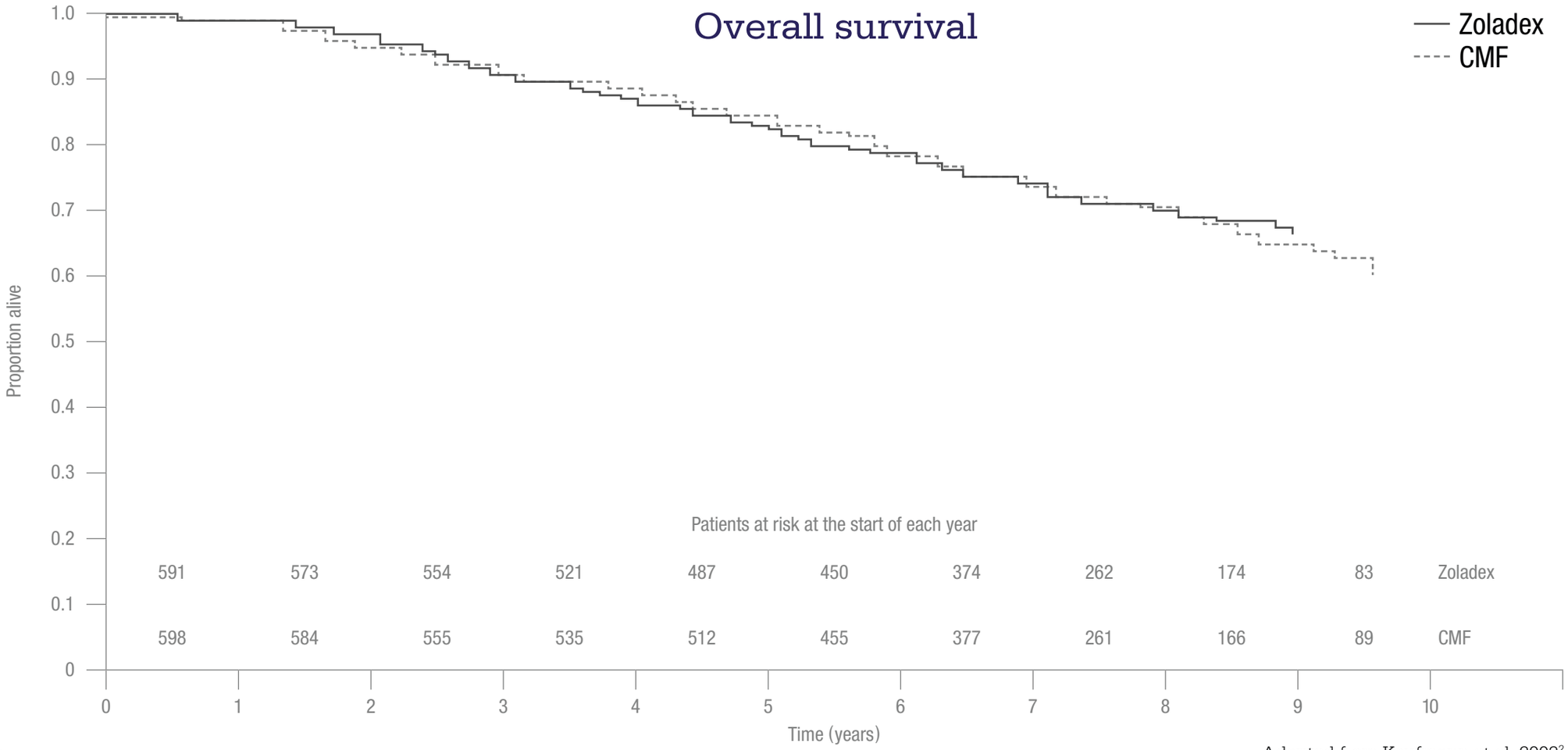
Adapted from Kaufmann et al. 2003[2]

*cyclophosphamide, methotrexate and fluorouracil

Zoladex® is as effective as CMF* chemotherapy for overall survival (OS) in ER+ early premenopausal breast cancer[1,2]

- In ER positive, pre and perimenopausal patients (at a median follow-up of 7.3 years)[2]
- Overall survival was non-inferior to CMF*[2]
  - HR=0.94; 95% CI:0.75-1.18; P=0.622[2]

OS



Adapted from Kaufmann et al. 2003[2]

*cyclophosphamide, methotrexate and fluorouracil

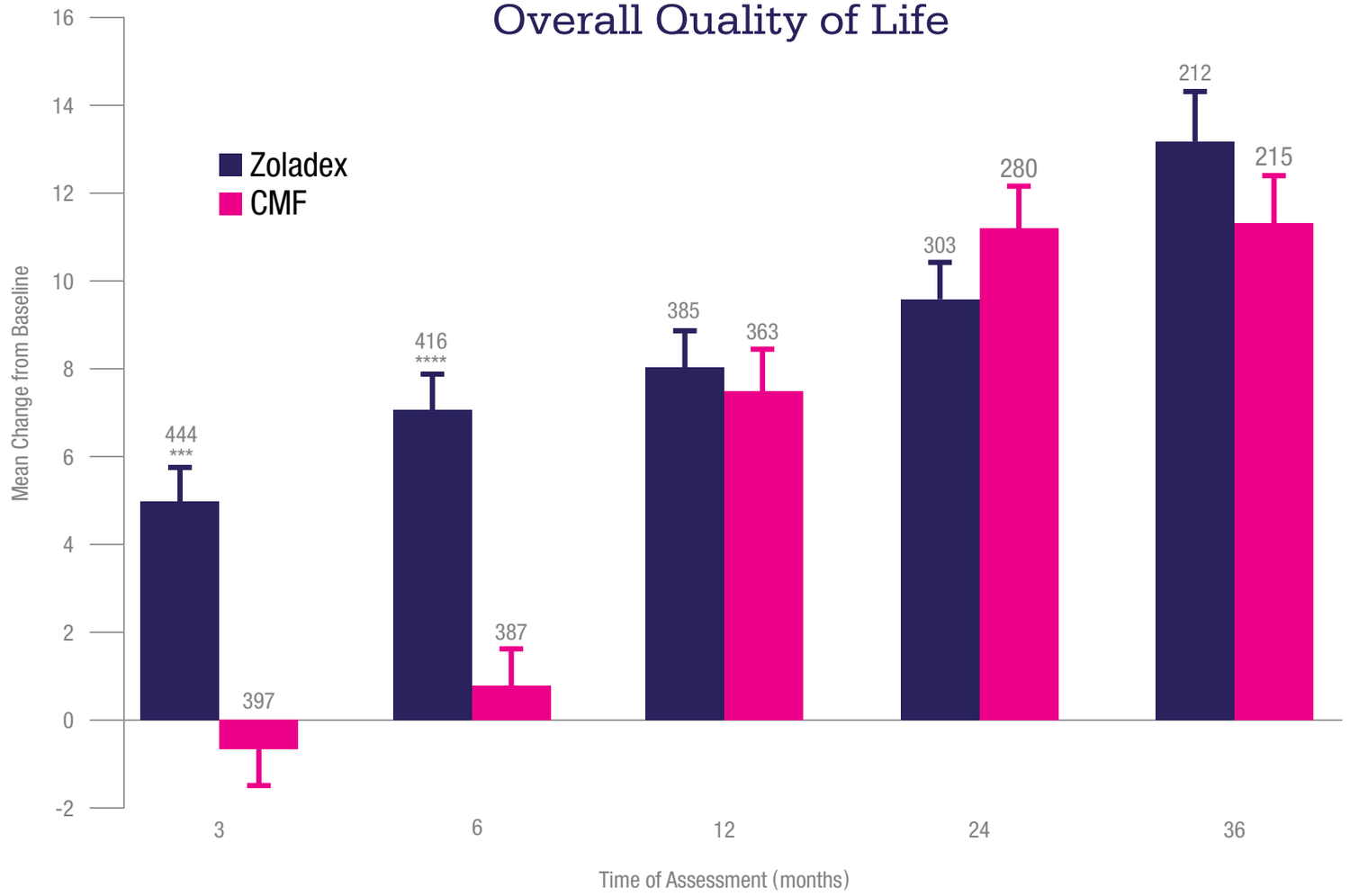
Zoladex® is well tolerated and shows improved quality of life† compared to CMF.*[1-3]

†during the first six months of therapy.

- The incidence of elicited side effects of cytotoxic chemotherapy including nausea, vomiting, alopecia and infection, was substantially higher with CMF than with Zoladex during the 6-month CMF treatment period[1]
- Improved overall quality of life compared to CMF during the first six months of treatment ($p<0.0001$)[3]
- Only 22.6% of Zoladex patients remained amenorrhoeic one year after completion of therapy[1]
  - 3 years after the start of treatment (includes 1 year post treatment for goserelin, 2½ years post treatment for CMF where 76.9% of patients remained amenorrhoeic)

*cyclophosphamide, methotrexate and fluorouracil

Overall Quality of Life



Improvement in overall quality-of-life (least square mean) after treatment with Zoladex or cyclophosphamide + methotrexate + fluorouracil (CMF). ***P<.0001 for goserelin versus CMF.

Adapted from De Haes M et al. 2003[3]

References:
1. Jonat W et al. *J Clin Oncol 2002*;20(24):4628-35
2. Kaufmann M et al. *Eur J Cancer 2003*;39:1711-1717
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Study Design (ZEBRA study[1,2])
International, multicentre, open, randomised study in premenopausal patients with node-positive early breast cancer.
After local therapy for breast cancer (mastectomy or breast-conserving therapy with or without radiotherapy, according to local practice), patients were randomised in a 1:1 ratio to receive goserelin 3.6mg every 28 days for 2 years or 6 x 28 day cycles of CMF chemotherapy (cyclophosphamide 500mg/m^2 intravenously (IV) on days 1 and 8, or 100mg/m^2 orally on days 1 through 14, methotrexate 40mg/m^2 IV on days 1 and 8 and fluorouracil 600mg/m^2 IV on days 1 and 8)
The primary efficacy parameters were disease-free survival (DFS) and overall survival (OS).
Safety was assessed by overall therapy tolerance and the occurrence of adverse events.

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Zoladex® 3.6mg in Advanced Premenopausal Breast Cancer

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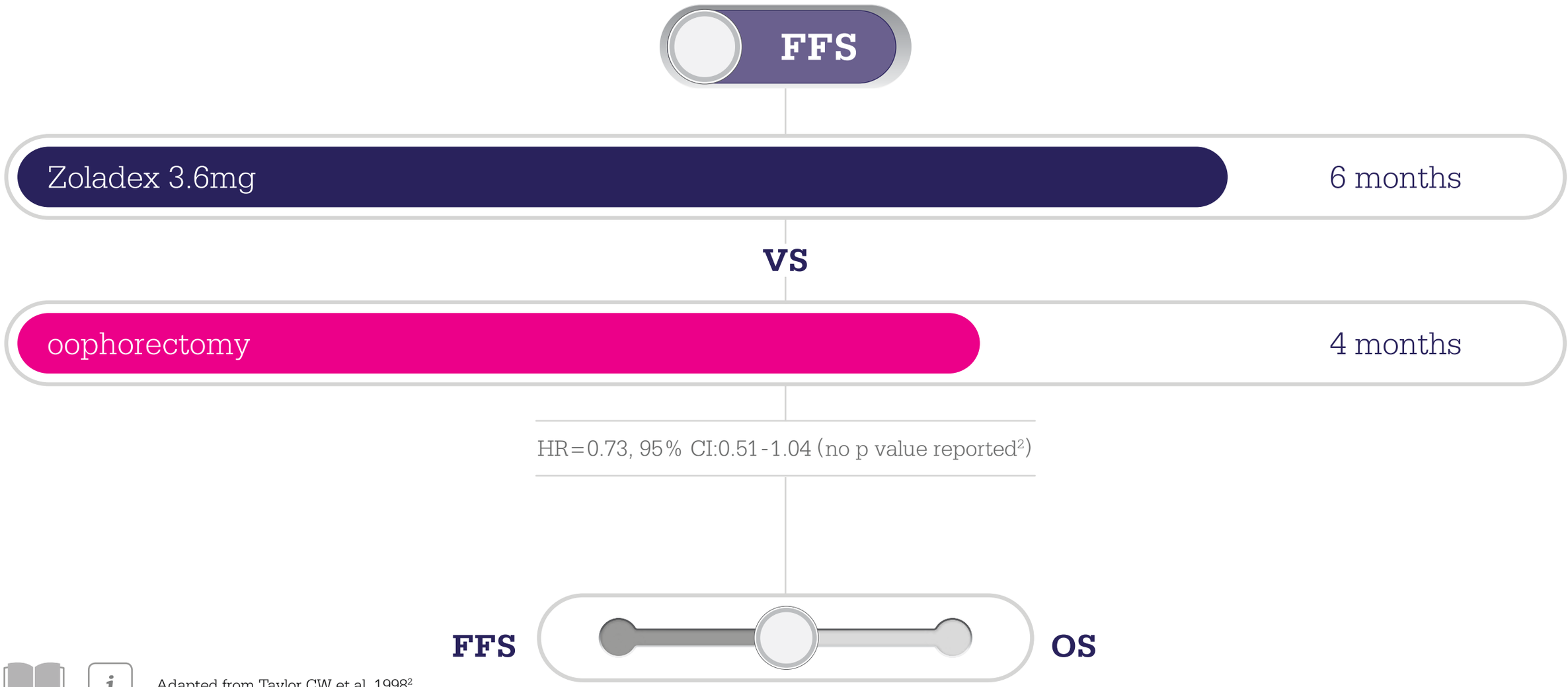
Zoladex® 3.6mg in Advanced Premenopausal Breast Cancer[1,2]

- Zoladex achieved similar median failure-free survival (FFS) compared to oophorectomy in premenopausal patients with advanced breast cancer[2]



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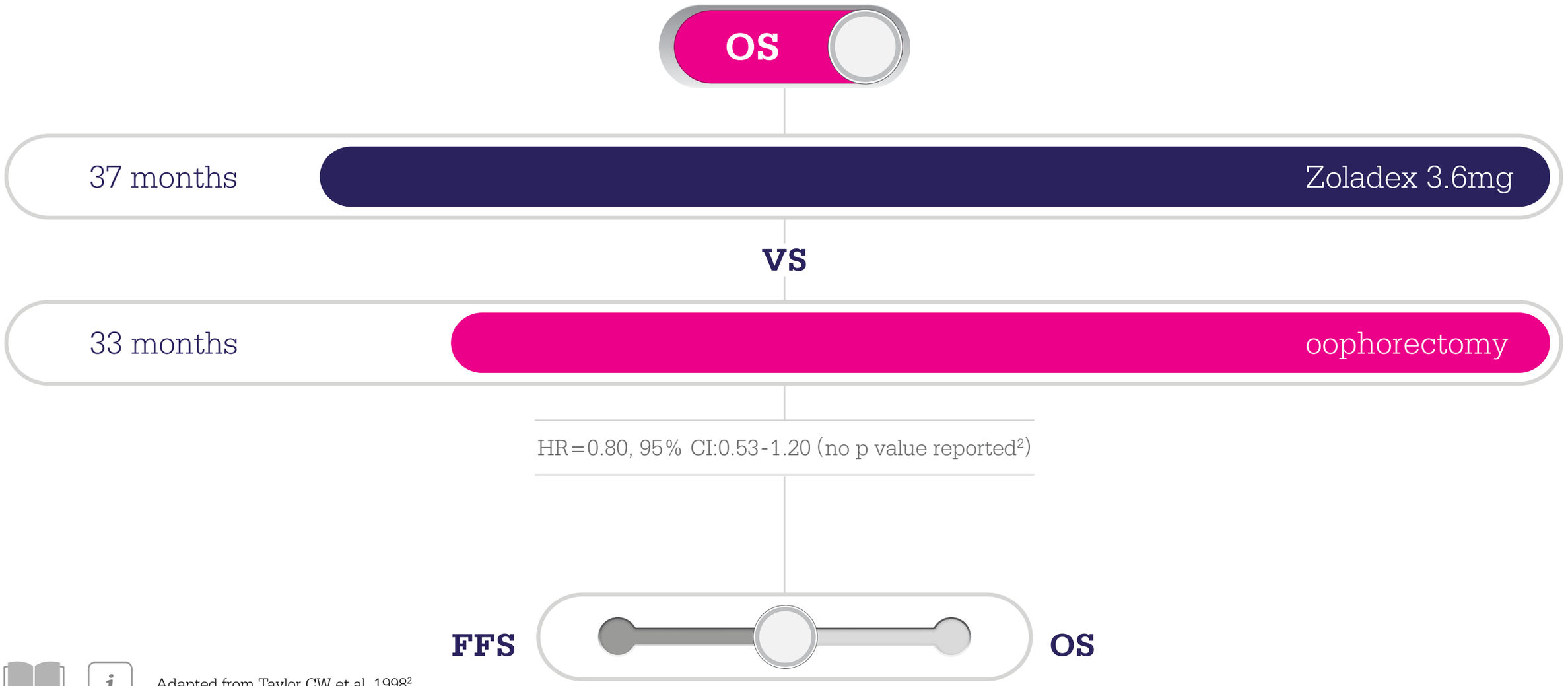

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Zoladex® 3.6mg in Advanced Premenopausal Breast Cancer[1,2]

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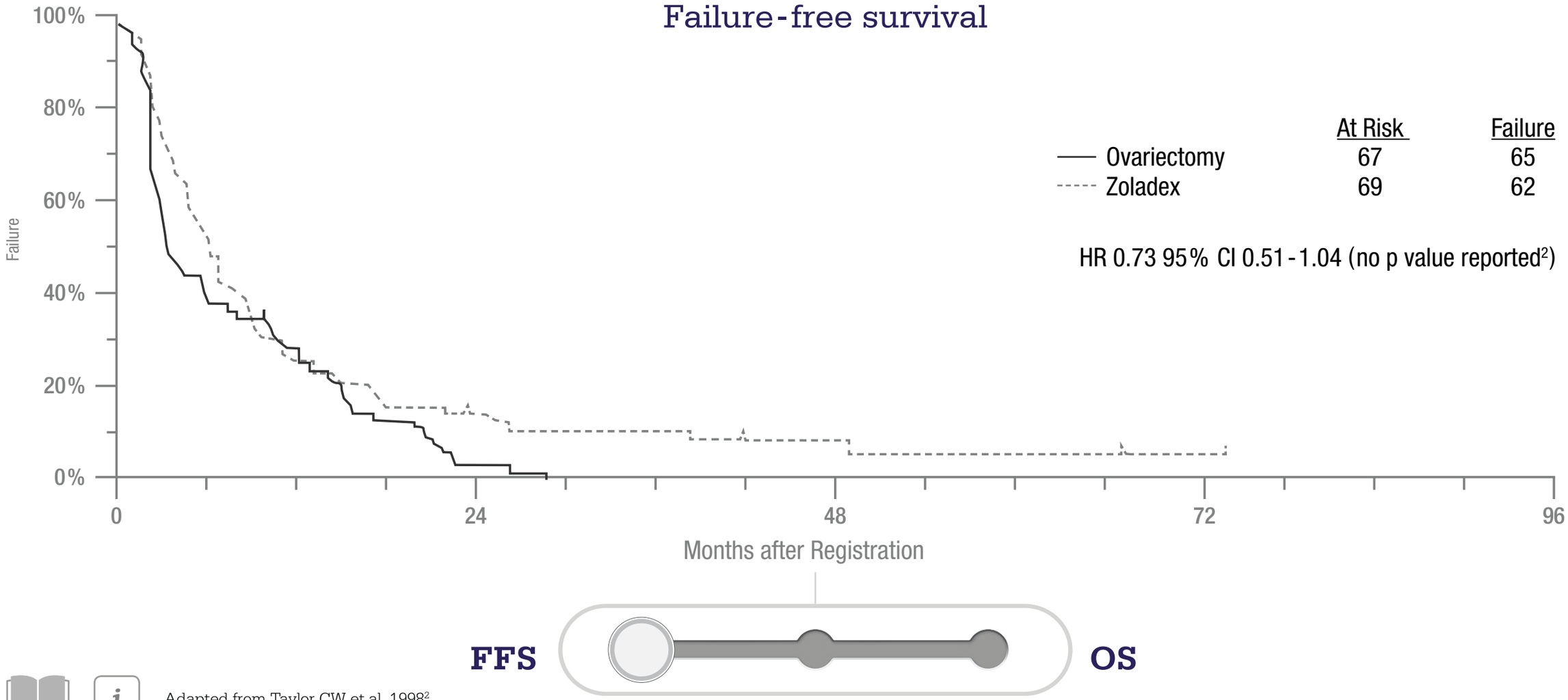
- There was no statistically significant differences between Zoladex and oophorectomy[2]



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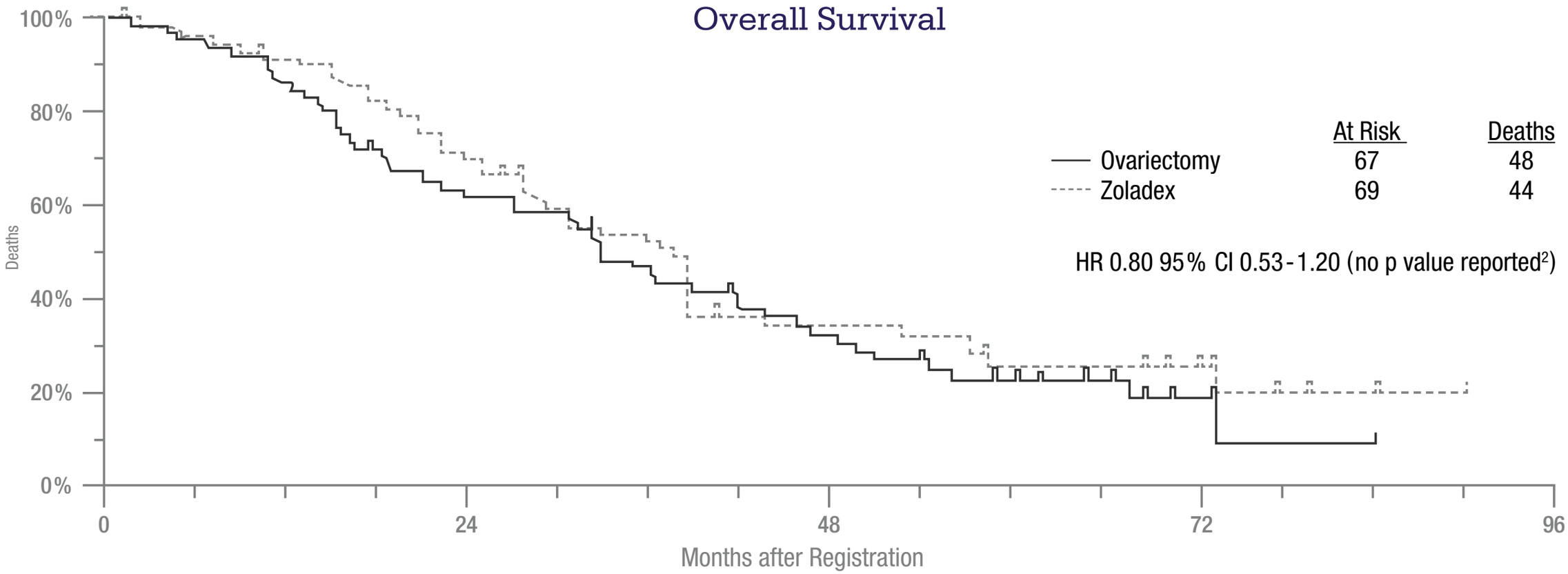

FFS OS

Adapted from Taylor CW et al. 1998[2]

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2. Taylor CW et al. *J Clin Oncol 1998*; 16 (3): 994-9

Study Design (Taylor C W et al.[2])
Patients were randomly assigned to treatment with surgical oophorectomy versus monthly goserelin 3.6mg.
The primary objective of the study was to compare the failure-free survival (FFS) and overall survival (OS) of premenopausal patients with metastatic breast cancer.
The study was initially designed as an equivalence study with 80% power to rule out a 50% improvement in survival due to oophorectomy. Due to slow accrual the study was terminated early which resulted in a final power of 60% for the alternative hyposthesis of equal survival distributions.

Safety & Tolerability[1]

FREQUENCY	SYSTEM ORDER CLASS	EVENT (FEMALES)
Very Common (≥10%)	Psychiatric disorders	Libido decreased[a] Mood altered, depression
	Vascular disorders	Hot flush[a] Blood pressure abnormal[b]
	Skin and subcutaneous tissue disorders	Hyperhidrosis[a], acne[c]
	Reproductive system and breast disorders	Vulvovaginal dryness Breast enlargement
	General disorders	Injection site reactions
	Nervous system disorders	Paraesthesia Headache
	Investigations	Bone density decreased
Common (≥ 1% and <10%)	Skin and subcutaneous tissue disorders	Rash[d] Alopecia[e]
	Musculoskeletal, connective tissue and bone disorders	Arthralgia
	General disorders	Tumour flare, tumour pain
	Investigations	Weight increased
Uncommon (≥0.1% and <1%)	Immune system disorders	Drug hypersensitivity
	Metabolism and nutrition disorders	Hypercalcaemia
	Neoplasms benign, malignant and unspecified (including cysts and polyps)	Degeneration of uterine fibroid
Rare (≥0.01% and <0.1%)	Immune system disorders	Anaphylactic reaction
	Reproductive system and breast disorders	Ovarian cyst Ovarian hyperstimulation syndrome
	Endocrine disorders	Pituitary haemorrhage/infarction
Very rare (<0.01%)	Neoplasms benign, malignant and unspecified (including cysts and polyps)	Pituitary tumour
	Psychiatric disorders	Psychotic disorders

a These are pharmacological effects which seldom require withdrawal of therapy.

b These may manifest as hypotension or hypertension, have been occasionally observed in patients administered ZOLADEX. The changes are usually transient, resolving either during continued therapy or after cessation of therapy with ZOLADEX. Rarely, such changes have been sufficient to require medical intervention, including withdrawal of treatment from ZOLADEX

c In most cases acne was reported within one month after the start of ZOLADEX.

d These are generally mild, often regressing without discontinuation of therapy.

e Loss of head hair has been reported in females, including younger patients treated for benign conditions. This is usually mild but occasionally can be severe.

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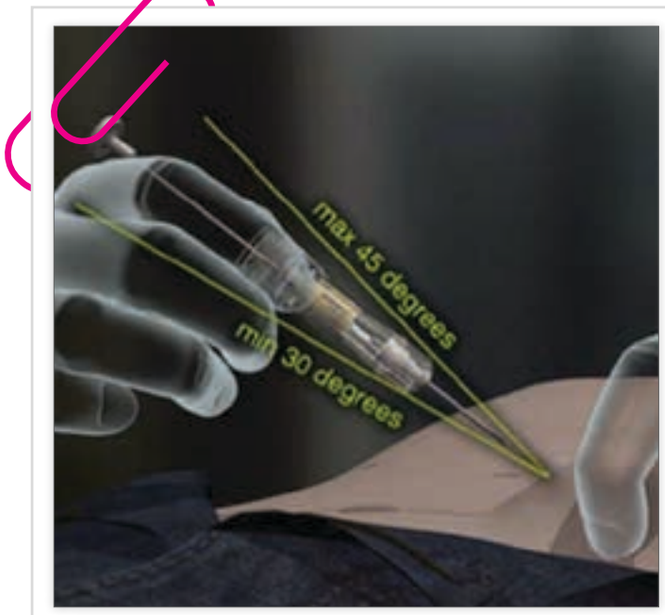
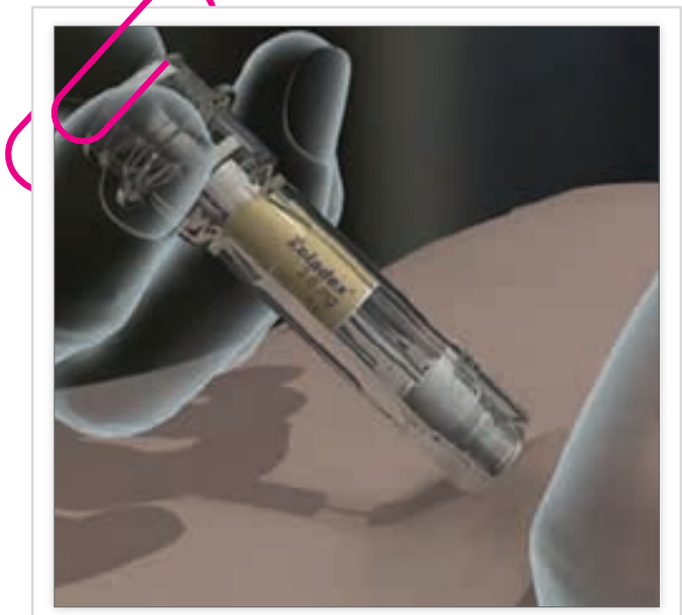
Zoladex SafeSystem®
Simple, one-step delivery[1]

- ✔ No pre-mixing
- ✔ No refrigeration
- ✔ No need to change needles





SEE ZOLADEX® SAFESYSTEM® IN ACTION

SafeSystem®

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