

# The effect of (neo)adjuvant chemotherapy on long-term survival outcomes in invasive lobular breast cancer patients treated with endocrine therapy: a retrospective cohort study

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## BACKGROUND

Invasive lobular carcinoma (ILC) may be less sensitive to chemotherapy than carcinoma of no special type (NST). However, studies on the long-term outcome of chemotherapy in ILC patients are scarce and inconclusive.

## CONCLUSION

**Chemotherapy is not associated with improved survival for ER+/HER2- ILC patients treated with endocrine therapy and who had an indication for chemotherapy.**

## PATIENTS AND METHODS

ILC patients registered in Erasmus MC Breast Cancer database from 1990 to 2022 (n=1326)

Excluded:

- ER negative/unknown (n=192)
- HER2 negative/unknown/determined at recurrence (n=215)
- Other tumor before ILC (n=23)
- No endocrine therapy (n=180)
- Age ILC > 70 (n=50)
- No indication for chemotherapy (n=146)

ER+/HER2- ILC patients treated with endocrine therapy and who had an indication for chemotherapy (n=520)

- Multivariable Cox proportional hazards models adjusted for T-status, N-status, year of diagnosis, age at diagnosis
- Inverse Probability of Treatment Weighting (IPTW) to obtain the average treatment effects (ATE) of chemotherapy on survival

## RESULTS

	No chemotherapy	Chemotherapy	
N (%)	141 (27%)	379 (73%)	
Years FU (IQR)	5.2 (3.8-8.1)	7.8 (4.8-11.3)	<i>p</i> <.001
Median age (IQR)	61 (55-66)	51 (46-58)	<i>p</i> <.001
Year ILC (IQR)	2015 (2010-2018)	2010 (2006-2013)	<i>p</i> <.001
<b>Tumor characteristics</b>			
T1	15%	18%	<i>p</i> <.001
T2	71%	49%	
T3/4	14%	5%	
N0	51%	20%	<i>p</i> <.001
N+	49%	80%	
Grade I/II	89%	85%	<i>p</i> =.133
Grade III	11%	15%	
<b>Long-term outcome</b>			
Recurrent disease	11%	30%	<i>p</i> <.001
Years after ILC (IQR)	5.5 (3.8-9.5)	6.2 (3.5-9.6)	<i>p</i> =.649
Local	0%	6%	<i>p</i> =.174
Regional	7%	1%	
Distant	93%	93%	
Death all causes	23%	31%	<i>p</i> =.056
Death breast cancer	14%	27%	<i>p</i> <.001

IQR, inter-quartile range; FU, follow-up

	ATE	95% CI
RFS	1.74	-0.54 – 4.02
BCSS	0.84	-1.21 – 2.89
OS	-0.99	-2.70 – 0.72

Abbreviations: ATE, average treatment effect; RFS, recurrence free survival; BCSS, breast cancer-specific survival; OS, overall survival

Interpretation of the ATE for BCSS (as example): When every woman in the population would receive chemotherapy, the average time to death due to breast cancer is estimated to be 0.84 years longer than when no woman in the population would receive chemotherapy. Since the 95% CI includes 0, this effect is non-significant

## LAY ABSTRACT

Invasive lobular breast cancer (ILC) may be less sensitive to chemotherapy than carcinoma of no special type (NST). We aimed to investigate whether adding chemotherapy upon endocrine therapy lowers the risks of disease recurrence and of dying from breast cancer, and additionally improves overall survival for ILC patients. We selected 520 women from our institutional breast cancer registry with a history of hormone-sensitive ILC who were treated with endocrine therapy and who had an indication for chemotherapy according to the national guidelines. We compared patients actually treated with chemotherapy (n=379) with those who received no chemotherapy (n=141). We used two different statistical approaches to estimate the added value of chemotherapy. We observed **no differences in the risk of recurrence of breast cancer and dying from BC**, nor a difference in overall survival **between patients with and without chemotherapy**, indicating no added value of chemotherapy.

