

# THE IMPACT OF DE-ESCALATION OF ADJUVANT SYSTEMIC THERAPY ON THE OUTCOME OF WOMEN WITH EARLY ER+/HER2+ BREAST CANCER

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## BACKGROUND

Adjuvant systemic therapy in women with early ER+/HER2+ breast cancer includes chemotherapy (ChT), one year of anti-HER2 therapy and at least five years of hormonal therapy (HT). Here, we explore the impact of de-escalation of adjuvant therapy on the outcome in women with early ER+/HER2+ breast cancer.

## METHODS

All women with ER+ (IHC ≥ 1%) and HER2+ (IHC3+ and/or FISH ratio ≥ 2.0) early breast cancer who received adjuvant systemic therapy at the Institute of Oncology Ljubljana between year 2006 and 2016 were retrospectively included in this study. For various reasons ChT, anti-HER2 therapy (trastuzumab) or HT were omitted or administered for shorter duration (i.e. de-escalated) in some women. An association between de-escalated therapy and distant disease-free survival (DDFS) was analysed using a multivariate Cox proportional-hazards model (Table 1).

## RESULTS

followed up to 10 years (median time 6.6 years) and death or distant recurrence occurred in 58 (19.9%) women. The estimated DDFS at 5 and 10 years was 86% and 74%, respectively. A total of 84 (28.9%), 92 (31.5%) and 45 (15.4%) women did not receive adjuvant ChT, received no or < 1yr of trastuzumab and discontinued HT prematurely. De-escalation of HT (HR 4.44; p<0.001) and trastuzumab (HR 3.42; p=0.02) had a significant detrimental effect on DDFS. In contrast, there was a non-significant effect of de-escalated ChT on DDFS (HR 1.15; p=0.78) (Table 1).

Table 1

Covariate		N	HR	95% CI	P
Age		292	1.01	0.99-1.04	0.29
Stage	Stage I (ref.)	107			
	Stage II	118	3.65	1.64-8.12	< 0.01
	Stage III	67	10.04	4.22-23.85	< 0.001
Trastuzumab	1yr of therapy (ref.)	200			
	No or <1 yr.	92	3.42	1.26-9.27	0.02
HT	Yes (ref.)	247			
	No or discontinued	45	4.44	2.39-8.25	< 0.001
ChT	Yes (ref.)	208			
	No	84	1.15	0.44-3.01	0.78
Treatment period	2006-2010 (ref.)	133			
	2011-2016	159	0.58	0.32-1.04	0.07

## CONCLUSIONS

Women with early ER+/HER2+ breast cancer should be strongly encouraged not to omit or discontinue HT and anti-HER2 therapy prematurely. De-escalation of adjuvant ChT might not be detrimental for some women with this subtype of breast cancer.