Extended Endocrine Therapy (eET) Following Five Years of Adjuvant LHRH-agonist (LHRHa) in Premenopausal Patients with Node-Positive, Hormone Receptor (HR)-Positive early Breast Cancer (eBC): a subanalysis according to surrogate subtypes

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Introduction

- In a previous cohort study analysis on 501 patients with node-positive early breast cancer (eBC) who remained premenopausal after 5 years of LHRHa treatment, we showed that the extension of endocrine therapy (eET) was associated with reduced invasive and distant breast cancer recurrences (Valenza, ASCO 2025).
- Due to the relative higher incidence of long-term recurrences in patients with luminal A-like eBC, the benefit of eET may differ according to surrogate breast cancer subtypes.

Methods and Materials

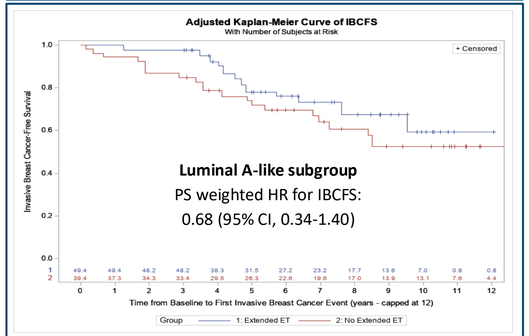
- We conducted a cohort study on two ongoing prospective datasets (Young Women's Study [YWS] and European Institute of Oncology [IEO]'s Breast Cancer Dataset) to evaluate the clinical benefit of eET in women who had completed 5 years of adjuvant LHRHa, remained premenopausal and had no evidence of distant or locoregional recurrence.
- This study included women <40y at diagnosis (from 2005-2016) with node-positive HR+ eBC, with ductal, lobular, or ductolobular histotype, receiving or not eET (tamoxifen monotherapy or LHRHa+tamoxifen/aromatase inhibitor [AI]).
- Endpoints included invasive breast cancer-free survival (IBCFS) and distant recurrence-free survival (DRFS) calculated from the 6th year of ET (study baseline) and assessed through the propensity score (PS) weighting analysis for: cohort, age at diagnosis, tumor histology, tumor dimension, nodal status, disease subtype, type of adjuvant ET received during the first 5 years, and receipt of adjuvant chemotherapy (yes vs. no).
- We performed a subgroup analysis according to the following surrogate breast cancer subtypes:
  - **luminal A-like (i.e., Ki67<20%, and PgR≥20%, and Grade 1/2, and HER2-negative),**
  - **luminal B-like/HER2-negative (i.e., Ki67≥20%, or PgR<20%, or Grade 3; and HER2-negative),**
  - **HER2-positive (i.e., HER2-positive per ASCO/CAP).**

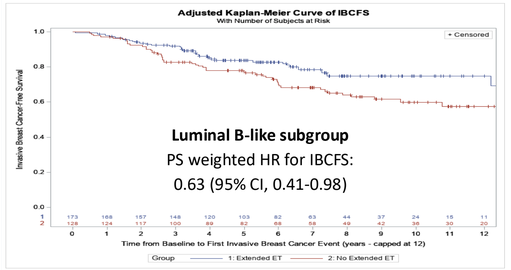
Results

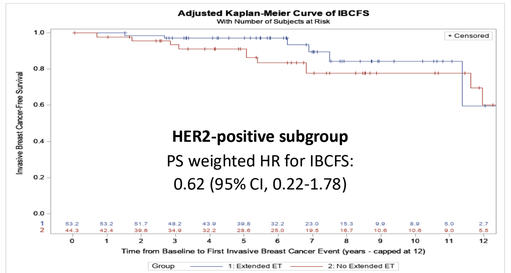
- 487 patients were included (see Table): 276 received eET for a median duration of 3.7 years (IQR: 2.2-5.0).
- Overall, 89 (18.3%), 298 (61.2%) and 100 (20.5%) had a luminal A-like, luminal B-like and HER2-positive disease.
- At a median follow-up of 7.3 years (from the study baseline), the PS weighted Hazard Ratio (HR) for IBCFS comparing the eET to the non-eET group was 0.64 (95% CI, 0.45-0.91) in all patients. The PS weighted cause-specific HR for DRFS was 0.50 (95% CI, 0.32-0.79) in all patients.

Characteristic	Extended endocrine therapy (N=276)	No extended endocrine therapy (N=211)
Age at diagnosis, median (IQR)	37 (35-39)	37 (33-39)
Dataset		
IEO, n (%)	273 (99)	210 (99)
YWS, n (%)	3 (1)	1 (1)
Histology		
Ductal, n (%)	253 (92)	201 (95)
Lobular, n (%)	12 (4)	6 (3)
Ductolobular, n (%)	11 (4)	4 (2)
pT		
pT1, n (%)	101 (37)	87 (41)
pT2, n (%)	137 (50)	110 (52)
pT3-4, n (%)	38 (13)	14 (7)
pN		
pN1, n (%)	175 (63)	155 (73)
pN2, n (%)	61 (22)	35 (17)
pN3, n (%)	40 (15)	21 (10)
Surrogate subtype		
Luminal A-like, n (%)	47 (17)	42 (20)
Luminal B-like (HER2-negative), n (%)	175 (63)	123 (58)
HER2-positive, n (%)	54 (20)	46 (22)
Endocrine therapy during the first 5 years		
LHRH-agonist plus tamoxifen, n (%)	179 (65)	163 (77)
LHRH-agonist plus AI, n (%)	95 (34)	45 (21)
LHRH-agonist only, n (%)	2 (1)	3 (2)
Previous chemotherapy, n (%)	212 (77%)	148 (70%)

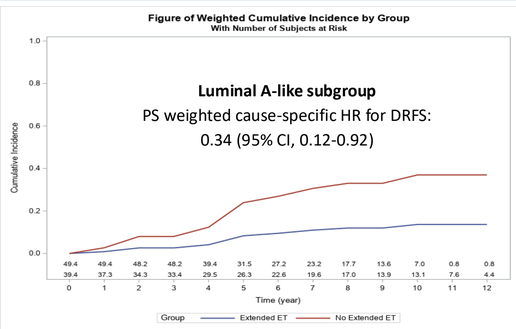
Results

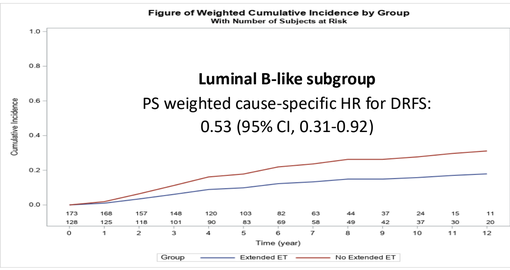


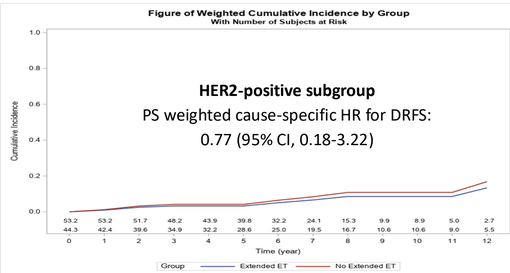




Results







Conclusions

In this subanalysis, the benefit of eET was observed across all surrogate breast cancer subtypes. Notably, the magnitude of clinical benefit in terms of DRFS appeared greater in patients with a luminal A-like disease, a finding that warrants confirmation in larger, prospective cohorts

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