Supplementary Materials

Clinical Outcomes of Everolimus Plus Exemestane Versus Fulvestrant in Patients with Metastatic Breast Cancer after Progression on Cyclin-Dependent Kinase 4/6 Inhibitors

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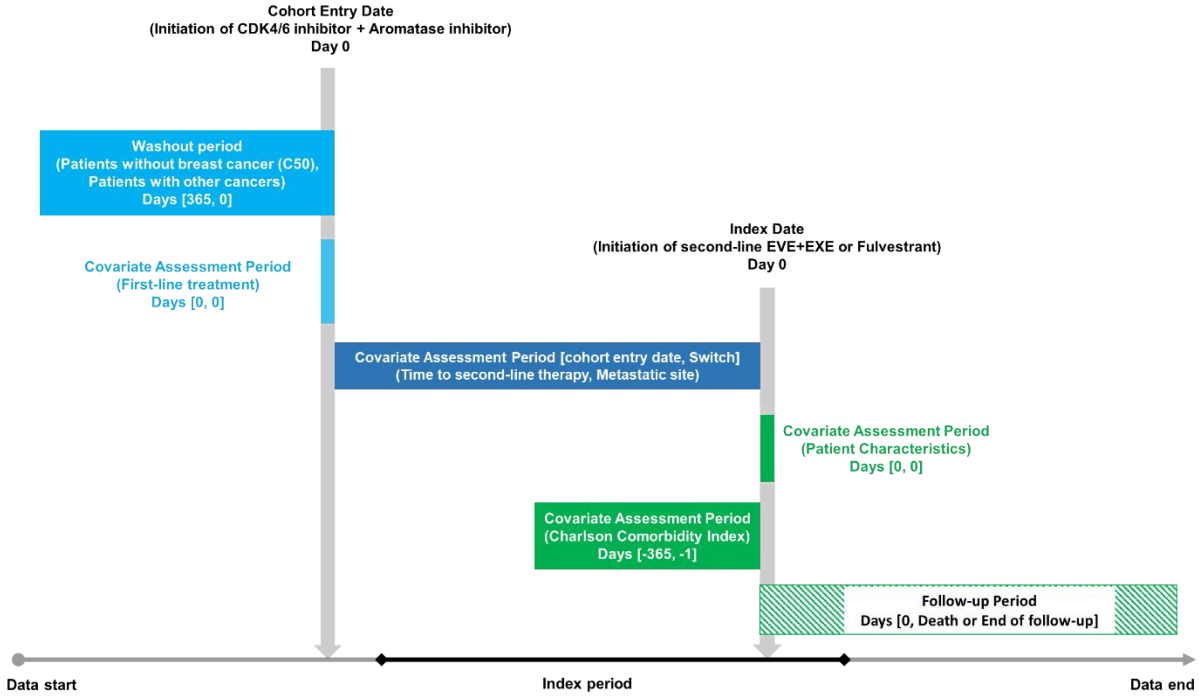


Supplementary Fig. 1 Study design

CDK, cyclin-dependent kinase; EVE+EXE, everolimus plus exemestane

Supplementary Table 1

List of third-line regimen according to the HIRA reimbursement list

Third-line regimen	
Albumin-bound paclitaxel	Etoposide
Anastrozole	Etoposide+Cisplatin
Capecitabine	Everolimus+Exemestane
Capecitabine+Carboplatin	Exemestane
Capecitabine+Cisplatin	Fulvestrant
Capecitabine+Vinorelbine	Gemcitabine
Carboplatin	Gemcitabine+Carboplatin
Cisplatin	Gemcitabine+Cisplatin
Cyclophosphamide	Gemcitabine+Paclitaxel
Cyclophosphamide+Doxorubicin	Gemcitabine+Vinorelbine
Cyclophosphamide+Doxorubicin+Fluorouracil	Ifosfamide
Cyclophosphamide+Epirubicin+Fluorouracil	Ifosfamide+Epirubicin
Cyclophosphamide+Methotrexate+Fluorouracil	Ifosfamide+Vinorelbine
Docetaxel	Letrozole
Docetaxel+Capecitabine	Paclitaxel
Docetaxel+Carboplatin	Paclitaxel+Carboplatin
Docetaxel+Cisplatin	Paclitaxel+Cisplatin
Doxorubicin	Tamoxifen
Epirubicin	Vinorelbine
Epirubicin+Cyclophosphamide	Vinorelbine+Carboplatin
Eribulin	Vinorelbine+Cisplatin

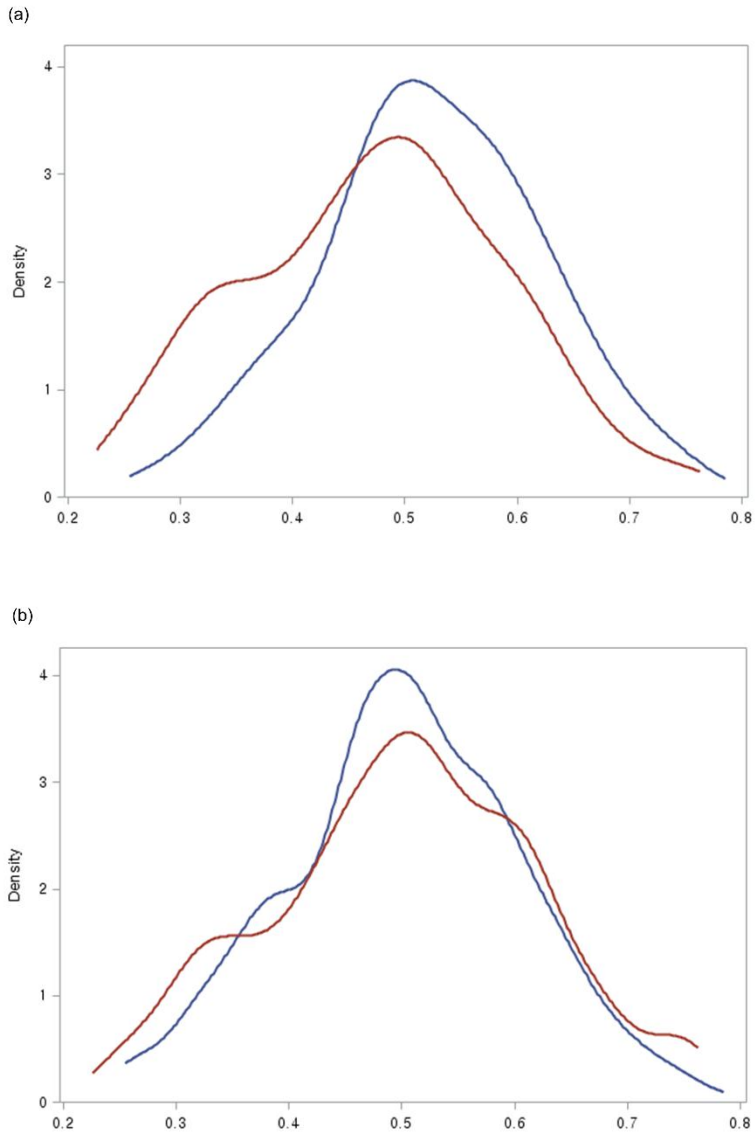
HIRA, Health Insurance Review and Assessment Service

Supplementary Table 2

ICD-10 code of metastatic sites of cancer

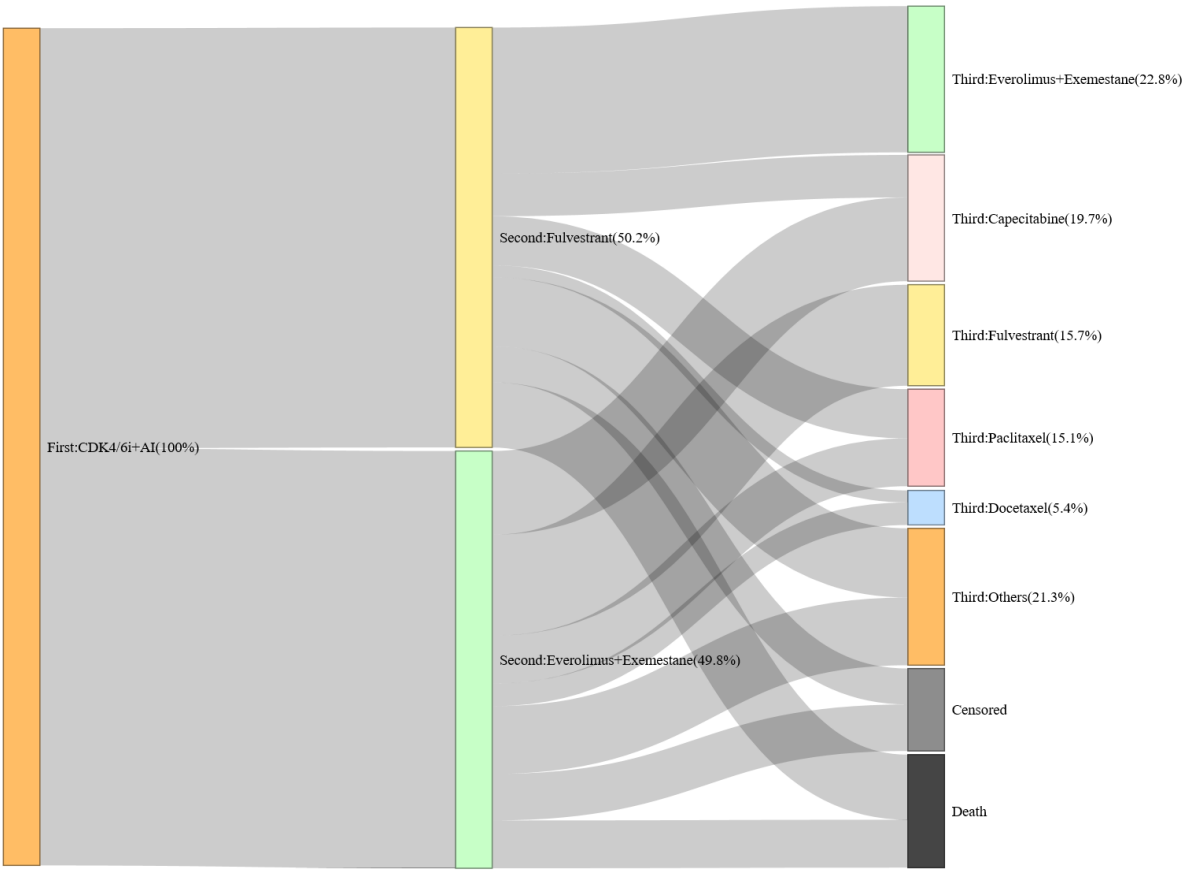
Metastatic site of cancer	ICD-10 code	Description
Lung	C78.0	Secondary malignant neoplasm of lung
	C78.1	Secondary malignant neoplasm of mediastinum
Liver	C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
Other visceral	C78.2	Secondary malignant neoplasm of pleura
	C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
	C79.0	Secondary malignant neoplasm of kidney and renal pelvis
	C79.6	Secondary malignant neoplasm of ovary
	C79.7	Secondary malignant neoplasm of adrenal gland
Bone	C79.5	Secondary malignant neoplasm of bone and bone marrow
Brain	C79.3	Secondary malignant neoplasm of brain and cerebral meninges
Others	C77	Secondary and unspecified malignant neoplasm of lymph nodes
	C78.3	Secondary malignant neoplasm of other and unspecified respiratory organs
	C78.4	Secondary malignant neoplasm of small intestine
	C78.5	Secondary malignant neoplasm of large intestine and rectum
	C78.8	Secondary malignant neoplasm of other and unspecified digestive organs
	C79.1	Secondary malignant neoplasm of bladder and other and unspecified urinary organs
	C79.2	Secondary malignant neoplasm of skin
	C79.4	Secondary malignant neoplasm of other and unspecified parts of nervous system
	C79.9	Secondary malignant neoplasm, unspecified site
	C79.81	Secondary malignant neoplasm of genital organs
	C79.88	Secondary malignant neoplasm of other specified sites

ICD-10, International Classification of Disease-10th revision
Metastatic sites were operationally defined using claims-based ICD-10 diagnostic codes and may not fully capture all clinically documented metastatic lesions.



Supplementary Fig. 2 Distributions of propensity scores before IPTW (a) and after IPTW (b). The blue line indicates the everolimus plus exemestane cohort, and the red line indicates the fulvestrant cohort.

IPTW, inverse probability of treatment weighting



Supplementary Fig. 3 Sankey diagram of treatment transitions after second-line therapy.

CDK, cyclin-dependent kinase; AI, aromatase inhibitor

Supplementary Table 3

Sensitivity analysis for overall survival after IPTW

	Adjusted hazard ratio for overall survival[a] (95% CI)	
	Sensitivity analysis 1 (3 months)	**Sensitivity analysis 2 (12 months)**
Second-line therapy		
Everolimus+Exemestane	reference	reference
Fulvestrant	1.09 (0.88–1.36)	1.10 (0.88–1.39)
Cohort age, years	**1.03 (1.02–1.04)**	**1.02 (1.01–1.03)**
Charlson comorbidity index	**1.04 (1.00–1.08)**	1.04 (1.00–1.08)
Time to second-line therapy, months	**0.98 (0.97–0.99)**	**0.97 (0.96–0.99)**
Insurance type		
National health insurance	reference	reference
Medical aid or veterans	1.07 (0.75–1.55)	1.09 (0.75–1.60)
Visceral metastasis		
No	reference	reference
Yes	0.95 (0.74–1.20)	0.93 (0.72–1.19)

CI, confidence interval; IPTW, inverse probability of treatment weighting

[a] Inverse probability of treatment weighting on the propensity score was used to balance the baseline characteristics.