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Real-world outcomes of second-line therapies in HR+/HER2- metastatic breast cancer after progression on CDK4-6 inhibitors

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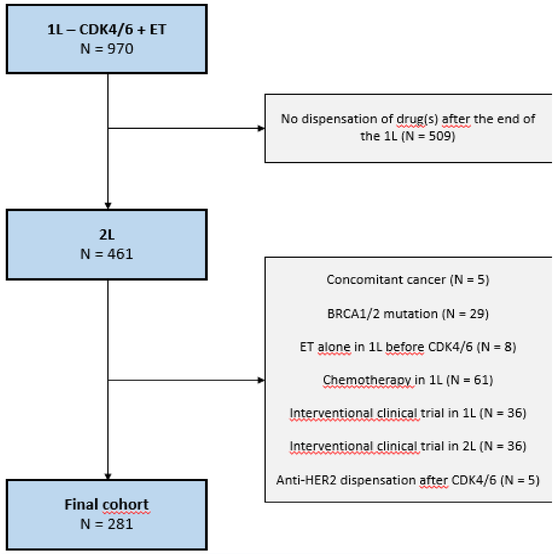
Introduction

- Following progression on CDK4-6 inhibitors and endocrine therapy (ET), treatment options include further lines of endocrine-based regimens alone or in combination with targeted therapies such as PI3K inhibitors or Everolimus, and chemotherapy.
- To date, no reliable predictive markers for response to second-line (2L) therapy have been established.

Materials and Methods

- We performed a single center cohort study of all patients with HR+/HER2- MBC who initiated 2L therapy following progression on first line (1L) treatment with CDK4-6 inhibitors and ET.
- Primary objective was to describe PFS and OS according to the type of 2L treatment and to identify prognostic factors associated with PFS and OS according to the type of therapy.
- Outcomes were assessed using the Kaplan-Meier method alongside multivariable cause-specific Cox regression models, which included factors such as the type of 2L treatment, duration of 1L CDK4-6 inhibitors , metastatic sites, and HER2 expression.

Figure 1 : Flowchart of the study



Results

Table 1 : Quantitative socio-demographic and clinical characteristics

	NA	n	mean (95% CI)	SD	median	min	max
Patient age (years)	0	281	65.9 (64.3-67.4)	13.2	66.9	28.8	92.0
Duration of CDK4-6 inhibiin L1 (months)	0	281	17.6 (16.1-19.2)	13.3	14.2	0.4	73.3
Estrogen receptor (%)	36	245	86.3 (83.1-89.4)	25.1	100.0	0.0	100.0
Progesterone receptor (%)	37	244	32.2 (27.5-36.9)	37.4	10.0	0.0	100.0
Ki67 (%)	169	112	25.8 (22.0-29.7)	20.6	19.5	0.0	90.0

CI: confidence interval; L1: first line treatment; NA: not available (missing); n: effective; SD, standard deviation

Table 2 : Categorical socio-demographic and clinical characteristics

	NA	n	% (95% CI)
Post-menopausal (vs pre- or peri-menopausal)	8	218	79.9 (74.5-84.3)
ECOG-PS	66		
0		52	24.2 (18.7-30.6)
1		122	56.7 (49.8-63.4)
2		31	14.4 (10.1-20.0)
3		10	4.7 (2.4-8.6)
Metastatic sites	0		
Other		112	39.9 (34.1-45.9)
Bone only		55	19.6 (15.2-24.8)
Brain or liver		114	40.6 (34.8-46.6
De novo metastatic	0	81	28.8 (23.7-34.6)
CDK4-6 inhibitor in 1L	0		
Abemaciclib		52	22.5 (17.4-28.6)
Palbociclib		107	46.3 (39.8-53.0)
Ribociclib		72	31.2 (25.3-37.6)
Kind of ET prescribed in combination with CDK4-6 inhibitor in L1	0		
Aromatase inhibitor		203	72.2 (66.5-77.3)
Fulvestrant		73	26.0 (21.0-31.6)
Tamoxifen		2	0.7 (0.1-2.8)
Other		3	1.1 (0.3-3.3)
HER2	32		
0		138	55.4 (49.0-61.7)
1+ or 2+		111	44.6 (38.3-51.0)
Second-line treatment category	0		
CT alone		139	49.5 (43.5-55.5)
ET alone		31	11.0 (7.7-15.4)
ET + mTOR inhibitor		84	29.9 (24.7-35.7)
CT -> ET		10	3.6 (1.8-6.6)
Other		17	6.0 (3.7-9.7)

AI: aromatase inhibitor; CI: confidence interval; ET: endocrine therapy; L1: first line treatment; NA: not available (missing); n: effective

Figure 2 : Survival in 2L : chemotherapy versus Everolimus + ET in patients previously treated ≥ 6 Months with 1L CDK4-6 Inhibitors

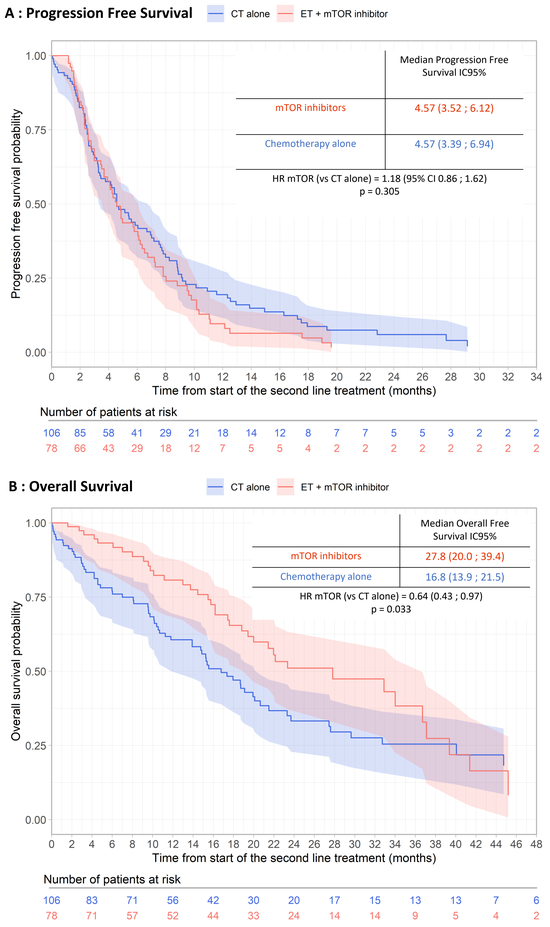


Figure 3: Overall survival in the whole population versus patients treated ≥ 6 months with CDK4-6 Inhibitors in 1L

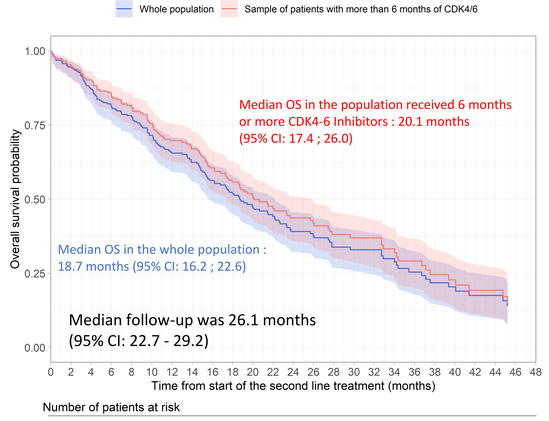


Table 3 : Results of the multivariable Cox model associated with the overall survival

	HR	95% CI	p-value
Second-line treatment category			0.0822
ET + mTOR inhibitor (vs. CT alone)	0.59	(0.34-1.03)	
ET alone (vs. CT alone)	0.45	(0.20-1.02)	
Other (vs. CT alone)	0.59	(0.28-1.28)	
ECOG-PS			<0.0001
1 (vs. 0)	2.12	(1.14-3.94)	
>= 2 (vs. 0)	6.11	(2.72-13.72)	
Metastatic sites			0.0121
Brain or liver (vs. bone only)	2.59	(1.26-5.29)	
Other (vs. bone only)	2.86	(1.41-5.80)	
HER2 1+ or 2+ (vs 0)	1.00	(0.62-1.59)	0.9870

CI: confidence interval; HR: hazard ratio; ET endocrine therapy; CT: Chemotherapy

Conclusion

- These preliminary results suggest Everolimus with ET is an option for patients with HR+/HER2- metastatic breast cancer in 2L who received more than 6 months of CDK4-6 inhibitors in 1L, have an ECOG-PS score < 2, and present with bone-only metastasis. Chemotherapy may be considered otherwise.
- This database enabled the development of a prognostic model that identifies different patient profiles and helps clinicians choose the best treatment option

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