PS1-11-29• Factors predicting the efficacy of CDK4/6 inhibitor rechallenge following progression on first-line CDK4/6 inhibitor and endocrine therapy in HR+ metastatic breast cancer in the French ESME Database

T. Papazyan[1], A. Lusque[2], A. Mailliez[3], T. Bachelot[4], T. Grinda[5], A. Goncalves[6], E. Brain[7], A.-M. Savoye[8], M. Arnedos[9], C. Levy[10], I. Desmoulins[11], T. De la Motte Rouge[12], C. Pflumio[13], C. Bailleux[14], M.-A. Mouret-Reynier[15], V. Massard[16], M. Leheurteur[17], L. Bosquet[18], W. Jacot[19], M. Campone[1], J.-S. Frenel[1]

[1]Medical oncology, ICO Nantes, Saint Herblain, France; [2] Biostatistics & Health Data Science Unit, Oncopole Claudius Regaud, Toulouse, France; [3] Medical oncology, Centre Oscar Lambret, Lille, France; [4] Medical oncology, Centre Léon Bérard, Lyon, France; [5] Medical oncology, Institut Gustave Roussy, Villejuif, France; [6] Medical oncology, IPC, Marseille, France; [7] Medical oncology, Institut Curie, Paris, France; [8] Medical oncology, Institut Godinot, Reims, France; [9] Medical oncology, Institut Bergonié, Bordeaux, France; [10] Medical oncology, Centre François Baclesse, Caen, France; [11] Medical oncology, CGFL, Dijon, France; [12] Medical oncology, Centre Eugène Marquis, Rennes, France; [13] Medical oncology, ICANS, Strasbourg, France; [14] Medical oncology, Centre Antoine-Lacassagne, Nice, France; [15] Medical oncology, Centre Jean Perrin, Clermont-Ferrand, France; [16] Medical oncology, Institut de Cancérologie de Lorraine – Alexis Vautrin, Vandœuvre-lès-Nancy, France; [17] Medical oncology, CHB, Rouen, France; [18] Department of Health Data and Partnerships, UNICANCER, Paris, France; [19] Medical oncology, ICM, Montpellier, France.

BACKGROUND

- Few data are available regarding the clinical benefit of rechallenging with a CDK4/6 inhibitor (CDK4/6i), either by continuing the same agent or switching to another, after progression on first-line treatment remains unclear. To date, only the MAINTAIN and post-MONARCH study have shown Progression free survival benefits.
- Our study aimed to assess the real-world efficacy of CDK4/6i rechallenge after progression on first-line therapy , using data from the ESME cohort, a large real-world database.

METHODS

Data source

- ESME MBC database (NCT03275311), a multicenter real-world cohort collecting data from patients treated for metastatic breast cancer (MBC) across 18 French Comprehensive Cancer Centers from 2008 onwards.
- The ESME MBC database includes a total of 38,285 patients diagnosed for MBC between 2008 and 2023 with data updated early 2025.

Patient selection

- For this study, we included all patients aged 18 years or older with HR+/HER2- MBC treated with 1L CDK4/6i in combination with endocrine therapy (ET) between January 2008 and December 2023 and rechallenged with CDK4/6i + ET during their treatment course.

Enpoints

- Real world Progression-free survival (rwPFS) and real world Overall survival (rwOS) following the second CDK4/6i exposure.
- Multivariable analysis was performed using a cox model

RESULTS

Flow Chart

5553 women HR+/HER2- treated with CDK4/6i + ET as first line **(Population #1)**

↓

2711 women HR+/HER2- who stopped first CDK4/6i for progression **(Population #2)**

↓

177 patients rechallenged with CDK4/6i + ET in their treatment course **(Population #3)**

Patient's Characteristics

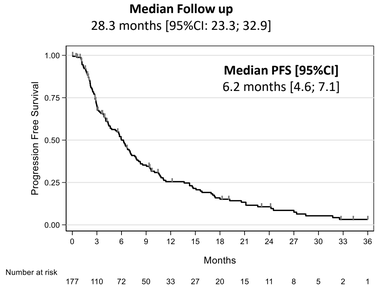
	Population #1	Population #3
Age at MBC	64 (22-95)	61 (27-87)
Menopausal (%)	4126 (74.3)	122 (68.9)
ER+/PR- (%)	1901 (34.9)	63 (36.6)
BMI median (range)	25.4 (11.2-64.2)	25.4 (18.2-40.5)
Metastatic de novo (%)	2023 (36.6)	63 (36.6)
Metastatic bone only (%)	2194 (39.5)	62 (35.0)
Visceral metastasis (%)	2101 (37.8)	61 (34.5)
Metastatic sites < 3 (%)	4384 (78.9)	138 (78.0)

Treatment Characteristics

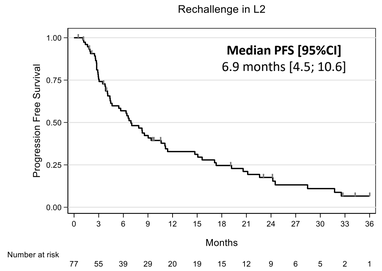
	Population #1	Population #3	
Median duration of first CDK4/6i (months, 95%CI)			
	16.5 (15.9; 17.4)	16.6 (0.6-72.2)	
Reason of CDK4/6i discontinuation (%)			
	1st CDK4/6i	2nd CDK4/6i	
Progression	2711 (66.8)	100 (82.6)	
Toxicity	656 (16.2)	12 (10.0)	
Other	691 (17.0)	9 (7.4)	
Line of rechallenge (%)			
Second line	-	77 (43.5)	
Third line & beyond	-	100 (56.5)	
CDK4/6i at rechallenge (%)			
Same CDK4/6i	-	35 (19.8)	
Groups of ET type concomitant to CDK4/6i			
	1st CDK4/6i	1st CDK	2nd CDK
Anti-aromatase	4436 (79.9)	150 (84.7)	59 (33.3)
Fulvestrant	985 (17.7)	23 (13.0)	104 (58.8)
Other	132 (2.4)	4 (2.3)	14 (7.9)

Progression free survival and overall survival depending on treatment strategies

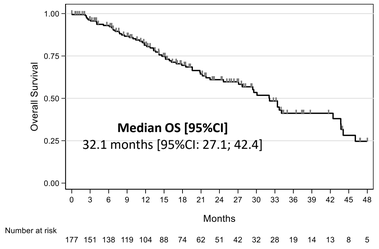
rwPFS for rechallenge in all lines



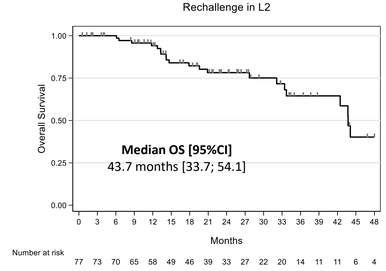
rwPFS for rechallenge in 2nd line



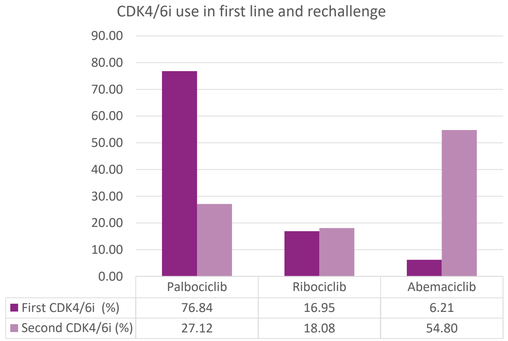
rwOS for rechallenge in all lines



rwOS for rechallenge in 2nd line



Profile of CDK4/6i switch



Multivariable analysis of PFS

Variable	Univariate HR [IC95%]	p-value	Multivariate HR [IC95%]	p-value
Diagnosis metastatic De Novo (<6 mois)				
No	1.00		1.00	
Yes	0.93 [0.65–1.31]	0.670	0.96 [0.67–1.37]	0.824
Type of Metastases at Rechallenge				
Non-visceral	1.00		1.00	
Visceral	1.52 [1.07–2.16]	0.020	1.18 [0.75–1.86]	0.472
Number of metastatic sites at Rechallenge				
<3 sites	1.00		1.00	
≥3 sites	1.63 [1.16–2.30]	0.005	1.31 [0.86–2.00]	0.214
Line of rechallenge				
L2	1.00		1.00	
L3 or more	1.69 [1.19–2.40]	0.003	1.39 [0.94–2.07]	0.101
Duration of First CDK4/6				
<24 months	1.00		1.00	
>24 months	0.64 [0.44–0.93]	0.019	0.77 [0.51–1.15]	0.202
Type of Second CDK4/6i				
Same	1.00		1.00	
Different	1.28 [0.85–1.95]	0.239	1.29 [0.82–2.01]	0.267

CONCLUSION

- This large multicenter retrospective study provides real-world evidence that switching with a second CDK4/6 inhibitor after progression is feasible.
- These results support the rechallenge with CDK4/6i in selected patients. The rwPFS was comparable to that reported in post-MONARCH and MAINTAIN studies.

Contact: Jean-sebastien.frenel@ico.unicancer.fr

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