PS1-10-21• Switching CDK4/6 inhibitors due to Toxicity in first-line treatment of HR+/HER2- metastatic breast cancer: Incidence and Outcomes from the ESME Cohort.

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

[1]Medical oncology, ICO Nantes, Saint Herblain, FRANCE, [2]Biostatistics Unit, Institut Claudius Regaud, Toulouse, FRANCE, [3]Medical oncology, ICM, Montpellier, FRANCE, [4]Medical oncology, Institut Gustave Roussy, Villejuif, FRANCE, [5]Medical oncology, Centre Oscar Lambret, Lille, FRANCE, [6]Medical oncology, Institut Curie, Paris, FRANCE, [7]Medical oncology, Centre Leon Berard, Lyon, FRANCE, [8]Medical oncology, Centre Francois Baclesse, Caen, FRANCE, [9]Medical oncology, Institut Bergonié, Bordeaux, FRANCE, [10]Medical oncology, IPC, Marseille, FRANCE, [11]Medical oncology, Institut de Cancérologie de Lorraine (ICL) - Alexis Vautrin, Vandœuvre-lès-Nancy, FRANCE, [12]Medical oncology, Centre Jean Perrin, Clermont-Ferrand, FRANCE, [13]Medical oncology, Centre Eugene Marquis, Rennes, FRANCE, [14]Medical oncology, ICANS, Strasbourg, FRANCE, [15]Medical oncology, Institut Gaudinot, Reims, FRANCE, [16]Medical oncology, CGFL Dijon, Dijon, FRANCE, [17]Medical oncology, CHB, Rouen, FRANCE, [18]Department of Health Data and Partnerships, UNICANCER, Paris, FRANCE.

BACKGROUND

- Guidelines recommend switching between CDK4/6 inhibitors (CDK4/6i) when patients experience unacceptable toxicity during therapy, however data are lacking.
- This study aimed to examine patterns of CDK4/6i switching strategies due to toxicity in the first-line setting, 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 MBC across 18 French Comprehensive Cancer Centers from 2008 onwards.

Patient selection

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

Endpoints

- Type of toxicity leading to first CDK4/6i stop.
- TTF1: Time to Treatment Failure for first CDK4/6i (or TTF2: Time to Treatment Failure for second CDK4/6i) is defined by the time between the first (or second) CDK4/6i initiation and treatment discontinuation for progression, toxicity or other reason.

RESULTS

Flow Chart

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

↓

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

↓

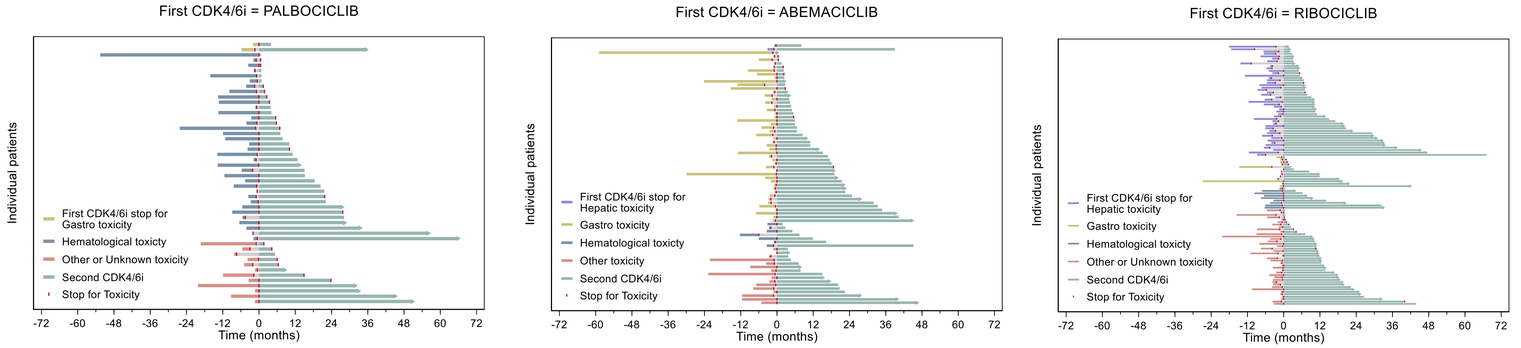
231 retrial of CDK4/6i + ET in first-line with a different cdk4/6i **(population#3)**

Patient's Characteristics

Characteristics	Population #1 (n=5553)	Population #2 (n=656)	Population #3 (n=231)
Age at metastatic diagnosis: Median (range)			
	64 (22-95)	67 (26-91)	65 (31–89)
Menopausal (%)			
	4126 (74.3)	521 (79.4)	172 (74.5)
ER+/PR- (%)			
	1901 (34.9)	221 (34.3)	82 (36.1)
Diagnosis metastatic de novo (<6 months) (%)			
	2023 (36.6)	243 (37.1)	85 (36.8)
Patients with <3 metastatic sites (%)			
	4384 (78.9)	528 (80.5)	187 (81.0)
Patients with bone metastasis only (%)			
	2194 (39.5)	273 (41.6)	99 (42.9)
Patients with visceral metastasis (%)			
	2101 (37.8)	233 (35.5)	79 (34.2)
1st CDK4/6i (%) (P = Palbociclib, R= Ribociclib, A= Abemaciclib)			
	P: 3542 (63.8) R: 1192 (21.5) A: 819 (14.7)	P: 300 (45.7) R: 207 (31.6) A: 149 (22.7)	P: 50 (21.6) R: 108 (46.8) A: 73 (31.6)
Duration of first CDK4/6i: Median (range)			
	16.5 (15.9; 17.4) (TTF1)	3.71 (0.03-71.10)	2.89 (0.10-57.59)
Time from end of first CDK4/6i to rechallenge (months)			
Median (Range)	-	-	0.5 (0.0;10.7)

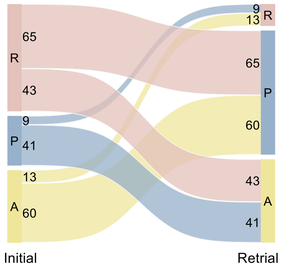
Profile of toxicity leading to first CDK4/6i stop in Population #3 (n=231)

Swimmer plot shows the duration of first CDK4/6i administration on the left side, colored by toxicity, and the duration of the second CDK4/6i administration on the right side.



Profile of CDK4/6i switch

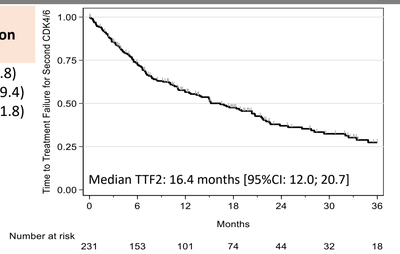
Sankey plot shows the CDK4/6i type used after first stop for toxicity.



Abbreviation: R, Ribociclib; P, Palbociclib; A, Abemaciclib.

Time to treatment failure for second CDK4/6i after toxicity and multivariable analysis

Reason of second iCDK4/6 termination (n=136)(%)	
Other	12 (8.8)
Toxicity	40 (29.4)
Progression	84 (61.8)



	HR [95%CI]	p-value
Age at metastatic diagnosis (years): ≥ 65 versus < 65	1.19 [0.83; 1.71]	0.334
Histological grade at primary diagnosis: III versus I/II	1.64 [1.10; 2.46]	0.016
Metastatic diagnosis: De Novo (<6 months) versus Recurrent	0.55 [0.37; 0.83]	0.005
Main toxicity for first CDK4/6i termination		
Hepatic	1.00	
Gastrointestinal	1.66 [0.95; 2.88]	0.075
Hematological	2.04 [1.18; 3.52]	0.010
Other	1.00 [0.56; 1.79]	0.991

	Population #1	Population #2	Population #3	
Groups of concomitant ET type				
	1st CDK4/6i	1st CDK4/6i	1st/2nd	
AA	79.9	80.8	83.5	81.0
Fulvestrant	17.7	18.3	16.0	17.7
Other	2.4	0.9	0.4	1.3

CONCLUSION

- This extensive multicenter retrospective study offers real-world evidence that switching with a second CDK4/6 inhibitors after toxicity in first-line treatment is feasible.
- Toxicity causing discontinuation of the second CDK4/6 inhibitor is not uncommon.

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

This presentation is the intellectual property of PAPAZYAN Thomas and FRENEL Jean Sebastien. Contact him/her at **Jean-sebastien.frenel@ico.unicancer.fr** for permission to reprint and/or distribute

San Antonio Breast Cancer Symposium • December 9-12, 2025