

Supplementary Table 1. Patient characteristics at time of advanced breast cancer diagnosis for patients with metachronous metastases, in total and per period of diagnosis.

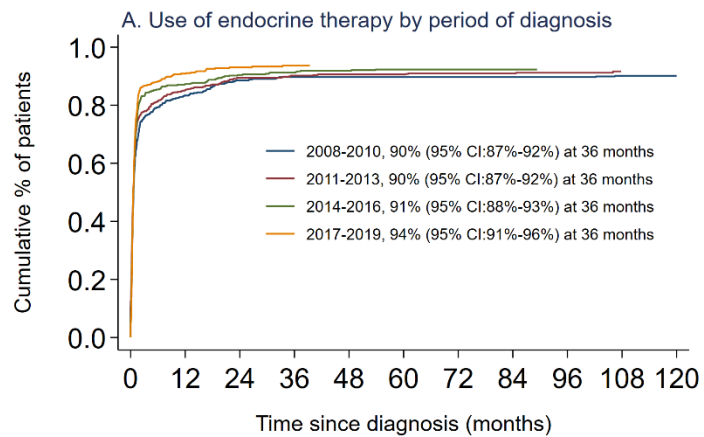
Characteristics	Total (n=1503)	2008-2010 (n=362)	2011-2013 (n=399)	2014-2016 (n=366)	2017-2019 (n=376)	p-value for Trend
Sex						0.33
Female	1489 (99)	358 (99)	394 (99)	363 (99)	374 (100)	
Age (in years)						0.04
Median (range)						
<70 years	888 (59)	227 (63)	247 (62)	215 (59)	199 (53)	
≥70 years	615 (41)	135 (37)	152 (38)	151 (41)	177 (47)	
WHO status						<0.001
0-1	923 (83)	122 (88)	245 (82)	256 (82)	300 (83)	
2-4	184 (17)	16 (12)	53 (17)	55 (18)	60 (17)	
Unknown	396	224	101	55	16	
Comorbidities						<0.001
Any	890 (59)	189 (52)	231 (58)	233 (64)	237 (63)	
Histology						0.152
Ductal	1087 (72)	260 (72)	291 (73)	256 (70)	280 (75)	
Lobular	317 (21)	73 (20)	88 (22)	85 (23)	71 (19)	
Other/unknown	99 (7)	29 (8)	20 (5)	25 (7)	25 (7)	
MFI						0.07
3-60 months	510 (34)	147 (41)	117 (29)	120 (33)	126 (34)	
60-120 months	443 (30)	101 (28)	122 (31)	119 (33)	101 (27)	
>120 months	550 (37)	114 (32)	160 (40)	127 (35)	149 (40)	
Number of metastatic sites						0.002
Single	680 (45)	183 (51)	193 (48)	148 (40)	156 (42)	
Multiple	823 (55)	179 (49)	206 (52)	218 (60)	220 (59)	
Sites of metastases						
Bones	1120 (75)	272 (75)	307 (77)	262 (72)	279 (74)	0.41
Bone-only	466 (31)	127 (35)	138 (35)	101 (28)	100 (27)	0.002
Soft tissue ^a	507 (34)	104 (29)	116 (29)	140 (38)	147 (39)	<0.001
Visceral ^b	846 (56)	193 (53)	216 (54)	215 (59)	222 (59)	0.06
CNS ^c	57 (4)	17 (5)	13 (3)	15 (4)	12 (3)	0.42

Data are given as number (%) unless otherwise indicated.

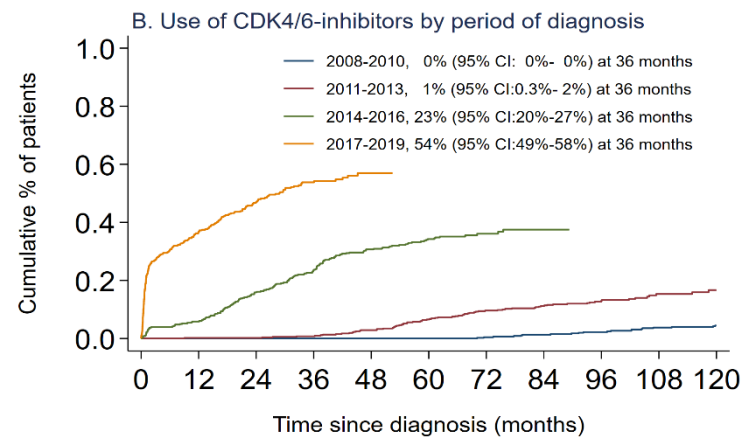
Abbreviations: ABC, advanced breast cancer; CNS, central nervous system; MFI, metastatic-free interval; WHO, World Health Organization

^a Soft tissue, lymph nodes, skin and eye; ^b Liver, lung, pleura, peritoneum, gastrointestinal track, other; ^c Brain and leptomeningeal

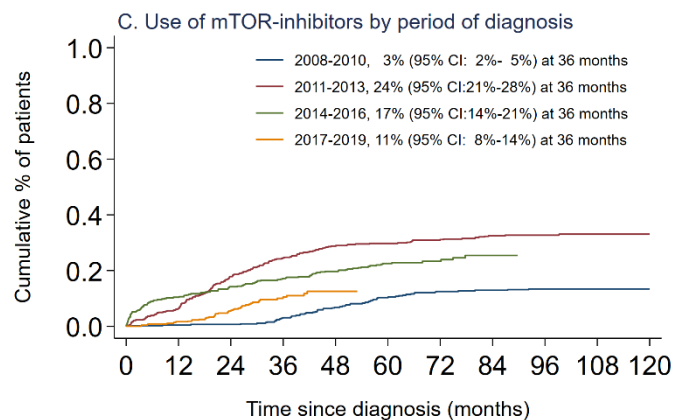
Supplementary Figure 1. Graphs of the cumulative use of systemic therapies (A. Endocrine therapy, B. CDK4/6 inhibitors, C. mTOR-inhibitors, D. Chemotherapy) by period of diagnosis.



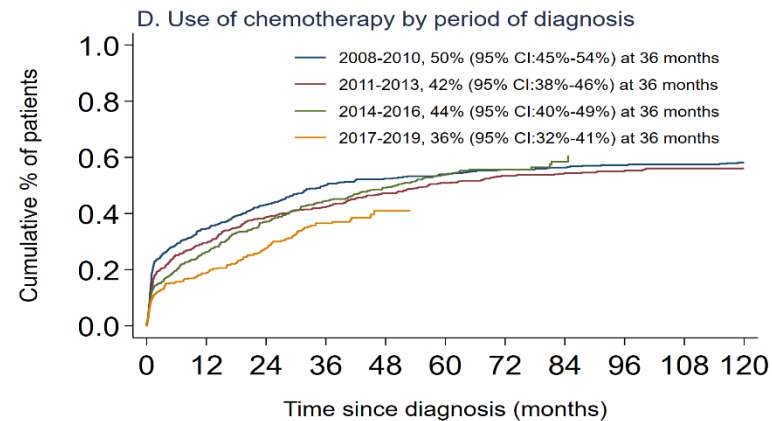
Number at risk	0	12	24	36	48	60	72	84	96	108	120
2008-2010	456	58	22	9	8	6	6	6	6	4	3
2011-2013	521	55	20	14	12	9	6	6	3	0	0
2014-2016	480	47	20	13	9	6	4	1	0	0	0
2017-2019	493	26	8	3	0	0	0	0	0	0	0



Number at risk	0	12	24	36	48	60	72	84	96	108	120
2008-2010	456	366	275	200	145	97	75	54	37	25	17
2011-2013	521	433	343	255	179	114	77	54	29	10	4
2014-2016	480	374	236	157	88	51	16	3	0	0	0
2017-2019	493	237	129	50	5	0	0	0	0	0	0



Number at risk	0	12	24	36	48	60	72	84	96	108	120
2008-2010	456	364	274	191	125	73	50	41	32	26	21
2011-2013	521	405	272	184	124	93	77	60	36	13	8
2014-2016	480	358	259	191	137	80	30	6	0	0	0
2017-2019	493	382	252	99	11	0	0	0	0	0	0



Number at risk	0	12	24	36	48	60	72	84	96	108	120
2008-2010	456	243	173	121	87	64	45	37	28	23	15
2011-2013	521	317	228	180	122	83	65	52	28	12	8
2014-2016	480	306	215	159	112	57	21	3	0	0	0
2017-2019	493	332	205	73	9	0	0	0	0	0	0