

## Supplementary materials

Source: PubMed (Searched on: 5 June 2018)		
Search	Query	Items found
#118	Search #117 AND #95 AND #93	249
#117	Search #96 OR #97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105 OR #106 OR #107 OR #108 OR #109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116	1194648
#116	Search tripleblind*[Title/Abstract]	3
#115	Search trebleblind*[Title/Abstract]	0
#114	Search doubleblind*[Title/Abstract]	227
#113	Search singleblind*[Title/Abstract]	14
#112	Search blind*[Title/Abstract]	266997
#111	Search random*[Title/Abstract]	978600
#110	Search "Double-Blind Method"[Mesh]	145896
#109	Search "Single-Blind Method"[Mesh]	25194
#108	Search "Pragmatic Clinical Trials as Topic"[Title/Abstract]	4
#107	Search "Randomized Controlled Trials"[Publication Type]	0
#106	Search "Controlled Clinical Trials"[Publication Type]	0
#105	Search "Clinical Trials, Phase IV"[Publication Type]	0
#104	Search "Clinical Trials, Phase III"[Publication Type]	0
#103	Search "Clinical Trials, Phase II"[Publication Type]	0
#102	Search "Pragmatic Clinical Trials as Topic"[Mesh]	188
#101	Search "Intention to Treat Analysis"[Mesh]	2048
#100	Search "Randomized Controlled Trials as Topic"[Mesh]	118445
#99	Search "Controlled Clinical Trials as Topic"[Mesh]	123315
#98	Search "Clinical Trials, Phase IV as Topic"[Mesh]	267
#97	Search "Clinical Trials, Phase III as Topic"[Mesh]	8231
#96	Search "Clinical Trials, Phase II as Topic"[Mesh]	7024
#95	Search #5 OR #9 OR #18 OR #29 OR #32 OR #40 OR #49 OR #56	8941
#94	Search #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93	335222
#93	Search "Mammary Neoplasm, Human"[Title/Abstract]	0
#92	Search "Neoplasms, Human Mammary"[Title/Abstract]	0
#91	Search "Neoplasm, Human Mammary"[Title/Abstract]	0
#90	Search "Human Mammary Neoplasms"[Title/Abstract]	4
#89	Search "Human Mammary Neoplasm"[Title/Abstract]	0
#88	Search "Mammary Neoplasms, Human"[Title/Abstract]	0
#87	Search "Mammary Carcinomas, Human"[Title/Abstract]	0
#86	Search "Human Mammary Carcinomas"[Title/Abstract]	155

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#85	Search "Carcinomas, Human Mammary"[Title/Abstract]	0
#84	Search "Carcinoma, Human Mammary"[Title/Abstract]	0
#83	Search "Mammary Carcinoma, Human"[Title/Abstract]	0
#82	Search "Carcinomas, Breast"[Title/Abstract]	0
#81	Search "Carcinoma, Breast"[Title/Abstract]	1
#80	Search "Breast Carcinomas"[Title/Abstract]	7831
#79	Search "Breast Carcinoma"[Title/Abstract]	23270
#78	Search "Cancer of Breast"[Title/Abstract]	98
#77	Search "Breast Malignant Tumors"[Title/Abstract]	17
#76	Search "Breast Malignant Tumor"[Title/Abstract]	10
#75	Search "Malignant Tumor of Breast"[Title/Abstract]	3
#74	Search "Breast Malignant Neoplasms"[Title/Abstract]	2
#73	Search "Breast Malignant Neoplasm"[Title/Abstract]	2
#72	Search "Malignant Neoplasm of Breast"[Title/Abstract]	3
#71	Search "Mammary Cancers"[Title/Abstract]	426
#70	Search "Cancers, Mammary"[Title/Abstract]	0
#69	Search "Cancer, Mammary"[Title/Abstract]	3
#68	Search "Mammary Cancer"[Title/Abstract]	2993
#67	Search "Cancer of the Breast"[Title/Abstract]	2778
#66	Search "Cancer, Breast"[Title/Abstract]	10
#65	Search "Breast Cancer"[Title/Abstract]	235278
#64	Search "Neoplasm, Breast"[Title/Abstract]	1
#63	Search "Breast Neoplasm"[Title/Abstract]	597
#62	Search "Neoplasms, Breast"[Title/Abstract]	0
#61	Search "Tumor, Breast"[Title/Abstract]	1
#60	Search "Breast Tumor"[Title/Abstract]	8653
#59	Search "Breast Tumors"[Title/Abstract]	10255
#58	Search "Tumors, Breast"[Title/Abstract]	1
#57	Search "Breast Neoplasms"[Mesh]	263603
#56	Search #50 OR #51 OR #52 OR #53 OR #54 OR #55	299
#55	Search "PD-0332991"[Title/Abstract]	75
#54	Search "PD0332991"[Title/Abstract]	65
#53	Search "PD 0332991"[Title/Abstract]	75
#52	Search "Ibrance"[Title/Abstract]	14
	Search	
#51	"6-acetyl-8-cyclopentyl-5-methyl-2-(5-piperazin-1-ylpyridin-2-ylamino)-8H-pyrido(2,3-d)pyrimidin-7-one"[Title/Abstract]	0
#50	Search "palbociclib" [Supplementary Concept]	245
#49	Search #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48	3368
#48	Search "Faslodex"[Title/Abstract]	214
#47	Search "ZM-182780"[Title/Abstract]	18
#46	Search "ZM 182780"[Title/Abstract]	18
#45	Search "ICI-182780"[Title/Abstract]	456

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#44	Search "ICI 182,780"[Title/Abstract]	1767
#43	Search "ICI 182780"[Title/Abstract]	456
#42	Search "7-(9-(4,4,5,5,5-pentafluoropentylsulfanyl)nonyl)estra-1,3,5(10)-tri ene-3,17-diol"[Title/Abstract]	0
#41	Search "fulvestrant" [Supplementary Concept]	2123
#40	Search Search #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39	819
#39	Search Zactima[Title/Abstract]	38
#38	Search vandetanib[Title/Abstract]	603
#37	Search "ZD-6474"[Title/Abstract]	10
#36	Search "ZD6474"[Title/Abstract]	190
#35	Search "ZD 6474"[Title/Abstract]	10
#34	Search caprelsa[Title/Abstract]	12
#33	Search "N-(4-bromo-2-fluorophenyl)-6-methoxy-7-((1-methylpiperidin-4- yl)methoxy)quinazolin-4-amine" [Supplementary Concept]	458
#32	Search #30 OR #31	68
#31	Search LEE011[Title/Abstract]	38
#30	Search "ribociclib" [Supplementary Concept]	50
#29	Search #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28	4057
#28	Search "Certican"[Title/Abstract]	70
#27	Search "Afinitor"[Title/Abstract]	53
#26	Search "RAD001"[Title/Abstract]	478
#25	Search "001, RAD"[Title/Abstract]	2
#24	Search "RAD 001"[Title/Abstract]	32
#23	Search "40-O-(2-hydroxyethyl)-rapamycin"[Title/Abstract]	25
#22	Search "SDZ-RAD"[Title/Abstract]	66
#21	Search "RAD, SDZ"[Title/Abstract]	0
#20	Search " SDZ RAD"[Title/Abstract]	66
#19	Search "Everolimus"[Mesh]	3838
#18	Search #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17	165
#17	Search "CHIR-258"[Title/Abstract]	11
#16	Search "CHIR258"[Title/Abstract]	5
#15	Search "CHIR 258"[Title/Abstract]	11
#14	Search "dovitinib"[Title/Abstract]	122
#13	Search "TKI-258"[Title/Abstract]	10
#12	Search TKI258[Title/Abstract]	50
#11	Search "TKI 258"[Title/Abstract]	10
#10	Search "4-amino-5-fluoro-3-(5-(4-methylpiperazin-1-yl)-1H-benzimidazol -2-yl)quinolin-2(1H)-one" [Supplementary Concept]	96

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#9	Search #6 OR #7 OR #8	248
#8	Search BKM120[Title/Abstract]	169
#7	Search buparlisib[Title/Abstract]	78
#6	Search "NVP-BKM120" [Supplementary Concept]	135
#5	Search #1 OR #2 OR #3 OR #4	104
#4	Search LY2385219[Title/Abstract]	0
#3	Search LY2835210[Title/Abstract]	0
#2	Search abemaciclib[Title/Abstract]	97
#1	Search "5-(4-ethylpiperazin-1-ylmethyl)pyridin-2-yl)-(5-fluoro-4-(7-fluoro-3-isopropyl-2-methyl-3H-benzimidazol-5-yl)pyrimidin-2-yl)amine" [Supplementary Concept]	34

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Source: EMBASE (Searched on: 5 June 2018)

No.	Query	Results
#151	#125 AND #135 AND #150	1814
#150	#136 OR #137 OR #138 OR #139 OR #140 OR #141 OR #142 OR #143 OR #144 OR #145 OR #146 OR #147 OR #148 OR #149	1605765
#149	'tripleblind*':ab,ti	7
#148	'trebleblind*':ab,ti	0
#147	'doubleblind*':ab,ti	2801
#146	'singleblind*':ab,ti	227
#145	'blind*':ab,ti	369624
#144	'random*':ab,ti	1293251
#143	'double blind procedure'/exp	149249
#142	'single blind procedure'/exp	31422
#141	'randomized controlled trial (topic)'/exp	142073
#140	'controlled clinical trial (topic)'/exp	147995
#139	'phase 4 clinical trial (topic)'/exp	1374
#138	'phase 3 clinical trial (topic)'/exp	31042
#137	'phase 2 clinical trial (topic)'/exp	30556
#136	'multicenter study (topic)'/exp	26177
#135	#126 OR #127 OR #128 OR #129 OR #130 OR #131 OR #132 OR #133 OR #134	412000
#134	'mammary gland cancer':ab,ti	205
#133	'mammary cancer':ab,ti	3767
#132	'mamma cancer':ab,ti	18
#131	'cancer, breast':ab,ti	2639
#130	'breast gland neoplasm':ab,ti	0
#129	'breast gland cancer':ab,ti	0
#128	'breast cancer recurrence':ab,ti	2121
#127	'advanced breast cancer':ab,ti	11292
#126	'breast cancer'/exp	408502
#125	#9 OR #26 OR #44 OR #58 OR #77 OR #88 OR #108 OR #124	37127
#124	#109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118 OR #119 OR #120 OR #121 OR #122 OR #123	22992
#123	'everolimus'/exp	22934
#122	'zortress':ab,ti	5
#121	'votubia':ab,ti	5
#120	'sdz rad':ab,ti	67
#119	'rad001a':ab,ti	0
#118	'rad001':ab,ti	1041
#117	'rad 001a':ab,ti	0
#116	'rad 001':ab,ti	55
#115	'nvp rad001':ab,ti	2

#114	'nvp rad 001':ab,ti	0
#113	'certican':ab,ti	122
#112	'afinitor disperz':ab,ti	0
#111	'afinitor':ab,ti	104
#110	'affinitor':ab,ti	4
#109	'40 o (2 hydroxyethyl) rapamycin':ab,ti	28
#108	#89 OR #90 OR #91 OR #92 OR #93 OR #94 OR #95 OR #96 OR #97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105 OR #106 OR #107	1919
#107	'pf00080665-73':ab,ti	0
#106	'pf00080665 73':ab,ti	0
#105	'pf 00080665-73':ab,ti	0
#104	'pf 00080665 73':ab,ti	0
#103	'pd332991':ab,ti	9
#102	'pd0332991-0054':ab,ti	0
#101	'pd0332991 0054':ab,ti	0
#100	'pd0332991':ab,ti	131
#99	'pd 332991':ab,ti	3
#98	'pd 0332991-0054':ab,ti	0
#97	'pd 0332991 0054':ab,ti	0
#96	'pd 0332991':ab,ti	206
#95	'palbociclib isethionate':ab,ti	0
#94	'ibrance':ab,ti	29
#93	'6 acetyl 8 cyclopentyl 5 methyl 2 [[5 (piperazin 1 yl) pyridin 2 yl] amino] pyrido [2, 3 d] pyrimidin 7 (8h) one':ab,ti	1
#92	'6 acetyl 8 cyclopentyl 5 methyl 2 [[5 (1 piperazinyl) 2 pyridinyl] amino] pyrido [2, 3 d] pyrimidin 7 (8h) one':ab,ti	0
#91	'6 acetyl 8 cyclopentyl 5 methyl 2 [5 (piperazin 1 yl) pyridin 2 ylamino] 8h pyrido [2, 3 d] pyrimidin 7 one':ab,ti	0
#90	'6 acetyl 8 cyclopentyl 5 methyl 2 [5 (1 piperazinyl) 2 pyridinylamino] 8h pyrido [2, 3 d] pyrimidin 7 one':ab,ti	0
#89	'palbociclib'/exp	1910
#88	#78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87	4098
#87	'zd6474':ab,ti	240
#86	'zd 6474':ab,ti	17
#85	'zactima':ab,ti	57
#84	'vandetinib':ab,ti	22
#83	'n (4 bromo 2 fluorophenyl) 6 methoxy 7 (1 methylpiperidin 4 ylmethoxy) quinazolin 4 amine':ab,ti	0

#82	'n (4 bromo 2 fluorophenyl) 6 methoxy 7 (1 methyl 4 piperidinylmethoxy) 4 quinazolinamine':ab,ti	0
#81	'caprelsa':ab,ti	24
#80	'azd6474':ab,ti	0
#79	'azd 6474':ab,ti	0
#78	'vandetanib'/exp	4073
#77	#59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76	545
#76	'ribociclib succinate':ab,ti	0
#75	'ribociclib butanedioate':ab,ti	0
#74	'lee11bba':ab,ti	0
#73	'lee11a':ab,ti	0
#72	'lee11':ab,ti	0
#71	'lee011bba':ab,ti	0
#70	'lee011a':ab,ti	0
#69	'lee011':ab,ti	111
#68	'lee 11bba':ab,ti	0
#67	'lee 11a':ab,ti	0
#66	'lee 11':ab,ti	1
#65	'lee 011bba':ab,ti	0
#64	'lee 011a':ab,ti	0
#63	'lee 011':ab,ti	2
#62	'kisqali':ab,ti	8
#61	'7 cyclopentyl n, n dimethyl 2 [[5 (piperazin 1 yl) pyridin 2 yl] amino] 7h pyrrolo [2, 3 d] pyrimidine 6 carboxamide':ab,ti	0
#60	'7 cyclopentyl n, n dimethyl 2 [[5 (1 piperazinyl) 2 pyridinyl] amino] 7h pyrrolo [2, 3 d] pyrimidine 6 carboxamide':ab,ti	0
#59	'ribociclib'/exp	528
#58	#45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57	8204
#57	'zm182780':ab,ti	0
#56	'zm 182780':ab,ti	18
#55	'zd9238':ab,ti	0
#54	'zd182780':ab,ti	0
#53	'zd 9238':ab,ti	0
#52	'zd 182780':ab,ti	0
#51	'ici182780':ab,ti	236
#50	'ici 182780':ab,ti	530
#49	'ici 182, 780':ab,ti	2274
#48	'ici 182 780':ab,ti	2274
#47	'faslodex':ab,ti	307

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#46	'7alpha [9 (4, 4, 5, 5, 5 pentafluoropentylsulfinyl) nonyl] estra 1, 3, 5 (10) triene 3, 17beta diol':ab,ti	0
#45	'fulvestrant'/exp	7511
#44	#36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43	904
#43	'tki258':ab,ti	116
#42	'tki 258':ab,ti	26
#41	'dovitinib lactate':ab,ti	5
#40	'chir258':ab,ti	8
#39	'chir 258':ab,ti	15
#38	'4 amino 5 fluoro 3 [6 (4 methylpiperazin 1 yl) 1h benzimidazol 2 yl] quinolin 2 (1h) one':ab,ti	0
#37	'4 amino 5 fluoro 3 [6 (4 methyl 1 piperazinyl) 1h benzimidazol 2 yl] 2 (1h) quinolinone':ab,ti	0
#36	'dovitinib'/exp	888
#35	#27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34	904
#34	'tki258':ab,ti	116
#33	'tki 258':ab,ti	26
#32	'dovitinib lactate':ab,ti	5
#31	'chir258':ab,ti	8
#30	'chir 258':ab,ti	15
#29	'4 amino 5 fluoro 3 [6 (4 methylpiperazin 1 yl) 1h benzimidazol 2 yl] quinolin 2 (1h) one':ab,ti	0
#28	'4 amino 5 fluoro 3 [6 (4 methyl 1 piperazinyl) 1h benzimidazol 2 yl] 2 (1h) quinolinone':ab,ti	0
#27	'dovitinib'/exp	888
#26	#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25	1413
#25	'nvp bkm120':ab,ti	106
#24	'nvp bkm 120':ab,ti	9
#23	'buparlisib hydrochloride':ab,ti	0
#22	'bkm120nx':ab,ti	0
#21	'bkm120aaa':ab,ti	0
#20	'bkm120 nx':ab,ti	0
#19	'bkm120 aaa':ab,ti	0
#18	'bkm120':ab,ti	528
#17	'bkm 120nx':ab,ti	0
#16	'bkm 120aaa':ab,ti	0
#15	'bkm 120 nx':ab,ti	0
#14	'bkm 120 aaa':ab,ti	0
#13	'bkm 120':ab,ti	63
#12	'5 [2, 6 bis (morpholin 4 yl) pyrimidin 4 yl] 4 (trifluoromethyl) pyridin 2 amine':ab,ti	0

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#11	'5 (2, 6 dimorpholino 4 pyrimidinyl) 4 (trifluoromethyl) 2 pyridinamine':ab,ti	0
#10	'buparlisib'/exp	1358
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	415
#8	'n [5 [(4 ethylpiperazin 1 yl) methyl] pyridin 2 yl] 5 fluoro 4 [4 fluoro 2 methyl 1 (propan 2 yl) 1h benzimidazol 6 yl] pyrimidin 2 amine':ab,ti	0
#7	'n [5 [(4 ethylpiperazin 1 yl) methyl] pyridin 2 yl] 5 fluoro 4 [4 fluoro 2 methyl 1 (1 methylethyl) 1h benzimidazol 6 yl] pyrimidin 2 amine':ab,ti	0
#6	'n [5 [(4 ethyl 1 piperazinyl) methyl] 2 pyridinyl] 5 fluoro 4 [4 fluoro 2 methyl 1 (1 methylethyl) 1h benzimidazol 6 yl] 2 pyrimidinamine':ab,ti	0
#5	'n [5 [(4 ethyl 1 piperazinyl) methyl] 2 pyridinyl] 5 fluoro 4 (4 fluoro 1 isopropyl 2 methyl 1h benzimidazol 6 yl) 2 pyrimidinamine':ab,ti	0
#4	'ly2835219':ab,ti	56
#3	'ly 2835219':ab,ti	0
#2	'bemaciclib':ab,ti	0
#1	'abemaciclib'/exp	407

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Source: Cochrane Library (Searched on: 5 June 2018)

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No.	Query
#1	abemaciclib:ti,ab,kw (Word variations have been searched)
#2	LY2835210:ti,ab,kw (Word variations have been searched)
#3	LY2385219:ti,ab,kw (Word variations have been searched)
#4	#1 or #2 or #3
#5	"NVP-BKM120":ti,ab,kw (Word variations have been searched)
#6	buparlisib:ti,ab,kw (Word variations have been searched)
#7	BKM120:ti,ab,kw (Word variations have been searched)
#8	#5 or #6 or #7
#9	"4-amino-5-fluoro-3-(5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl)quinolin-2(1H)-one":ti,ab,kw (Word variations have been searched)
#10	"TKI 258":ti,ab,kw (Word variations have been searched)
#11	TKI258:ti,ab,kw (Word variations have been searched)
#12	"TKI-258":ti,ab,kw (Word variations have been searched)
#13	dovitinib:ti,ab,kw (Word variations have been searched)
#14	"CHIR 258":ti,ab,kw (Word variations have been searched)
#15	CHIR258:ti,ab,kw (Word variations have been searched)
#16	"CHIR-258":ti,ab,kw (Word variations have been searched)
#17	#9 or #10 or #11 or #12 or #13 or #14 or #15 or #16
#18	MeSH descriptor: [Everolimus] explode all trees
#19	"SDZ RAD":ti,ab,kw (Word variations have been searched)
#20	"RAD, SDZ":ti,ab,kw (Word variations have been searched)
#21	"SDZ-RAD":ti,ab,kw (Word variations have been searched)
#22	"40-O-(2-hydroxyethyl)-rapamycin":ti,ab,kw (Word variations have been searched)
#23	"RAD 001":ti,ab,kw (Word variations have been searched)
#24	"001, RAD":ti,ab,kw (Word variations have been searched)
#25	"RAD001":ti,ab,kw (Word variations have been searched)
#26	"Afinitor":ti,ab,kw (Word variations have been searched)
#27	"Certican":ti,ab,kw (Word variations have been searched)
#28	#18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27

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- #29 ribociclib:ti,ab,kw (Word variations have been searched)
- #30 LEE011:ti,ab,kw (Word variations have been searched)
- #31 #29 or #30
- #32 "N-(4-bromo-2-fluorophenyl)-6-methoxy-7-((1-methylpiperidin-4-yl)methoxy)quinazolin-4-amine":ti,ab,kw (Word variations have been searched)
- #33 caprelsa:ti,ab,kw (Word variations have been searched)
- #34 "ZD 6474":ti,ab,kw (Word variations have been searched)
- #35 ZD6474:ti,ab,kw (Word variations have been searched)
- #36 "ZD-6474":ti,ab,kw (Word variations have been searched)
- #37 "vandetanib":ti,ab,kw (Word variations have been searched)
- #38 "Zactima":ti,ab,kw (Word variations have been searched)
- #39 #32 or #33 or #34 or #35 or #36 or #37 or #38
- #40 fulvestrant:ti,ab,kw (Word variations have been searched)
- #41 "7-(9-(4,4,5,5,5-pentafluoropentylsulfinyl)nonyl)estra-1,3,5(10)-triene-3,17-diol":ti,ab,kw (Word variations have been searched)
- #42 "ICI 182780":ti,ab,kw (Word variations have been searched)
- #43 "ICI 182,780":ti,ab,kw (Word variations have been searched)
- #44 "ICI-182780":ti,ab,kw (Word variations have been searched)
- #45 "ZM 182780":ti,ab,kw (Word variations have been searched)
- #46 "ZM-182780":ti,ab,kw (Word variations have been searched)
- #47 "Faslodex":ti,ab,kw (Word variations have been searched)
- #48 #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47
- #49 palbociclib:ti,ab,kw (Word variations have been searched)
- #50 "6-acetyl-8-cyclopentyl-5-methyl-2-(5-piperazin-1-ylpyridin-2-ylamino)-8H-pyrido(2,3-d)pyrimidin-7-one":ti,ab,kw (Word variations have been searched)
- #51 "Ibrance":ti,ab,kw (Word variations have been searched)
- #52 "PD 0332991":ti,ab,kw (Word variations have been searched)
- #53 "PD0332991":ti,ab,kw (Word variations have been searched)
- #54 "PD-0332991":ti,ab,kw (Word variations have been searched)
- #55 #49 or #50 or #51 or #52 or #53 or #54
- #56 #4 or #8 or #17 or #28 or #31 or #39 or #48 or #55
- #57 MeSH descriptor: [Breast Neoplasms] explode all trees
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- #58 "Tumors, Breast":ti,ab,kw (Word variations have been searched)
- #59 "Breast Tumors":ti,ab,kw (Word variations have been searched)
- #60 "Breast Tumor":ti,ab,kw (Word variations have been searched)
- #61 "Tumor, Breast":ti,ab,kw (Word variations have been searched)
- #62 "Neoplasms, Breast":ti,ab,kw (Word variations have been searched)
- #63 "Breast Neoplasm":ti,ab,kw (Word variations have been searched)
- #64 "Neoplasm, Breast":ti,ab,kw (Word variations have been searched)
- #65 "Breast Cancer":ti,ab,kw (Word variations have been searched)
- #66 "Cancer, Breast":ti,ab,kw (Word variations have been searched)
- #67 "Cancer of the Breast":ti,ab,kw (Word variations have been searched)
- #68 "Mammary Cancer":ti,ab,kw (Word variations have been searched)
- #69 "Cancer, Mammary":ti,ab,kw (Word variations have been searched)
- #70 "Cancers, Mammary":ti,ab,kw (Word variations have been searched)
- #71 "Mammary Cancers":ti,ab,kw (Word variations have been searched)
- #72 "Malignant Neoplasm of Breast":ti,ab,kw (Word variations have been searched)
- #73 "Breast Malignant Neoplasm":ti,ab,kw (Word variations have been searched)
- #74 "Breast Malignant Neoplasms":ti,ab,kw (Word variations have been searched)
- #75 "Malignant Tumor of Breast":ti,ab,kw (Word variations have been searched)
- #76 "Breast Malignant Tumor":ti,ab,kw (Word variations have been searched)
- #77 "Breast Malignant Tumors":ti,ab,kw (Word variations have been searched)
- #78 "Cancer of Breast":ti,ab,kw (Word variations have been searched)
- #79 "Breast Carcinoma":ti,ab,kw (Word variations have been searched)
- #80 "Breast Carcinomas":ti,ab,kw (Word variations have been searched)
- #81 "Carcinoma, Breast":ti,ab,kw (Word variations have been searched)
- #82 "Carcinomas, Breast":ti,ab,kw (Word variations have been searched)
- #83 "Mammary Carcinoma, Human":ti,ab,kw (Word variations have been searched)
- #84 "Carcinoma, Human Mammary":ti,ab,kw (Word variations have been searched)
- #85 "Carcinomas, Human Mammary":ti,ab,kw (Word variations have been searched)
- #86 "Human Mammary Carcinomas":ti,ab,kw (Word variations have been searched)
- #87 "Mammary Carcinomas, Human":ti,ab,kw (Word variations have been searched)
-

- 
- #88 "Human Mammary Carcinoma":ti,ab,kw (Word variations have been searched)
- #89 "Mammary Neoplasms, Human":ti,ab,kw (Word variations have been searched)
- #90 "Human Mammary Neoplasm":ti,ab,kw (Word variations have been searched)
- #91 "Human Mammary Neoplasms":ti,ab,kw (Word variations have been searched)
- #92 "Neoplasm, Human Mammary":ti,ab,kw (Word variations have been searched)
- #93 "Neoplasms, Human Mammary":ti,ab,kw (Word variations have been searched)
- #94 "Mammary Neoplasm, Human":ti,ab,kw (Word variations have been searched)
- #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 or #65 or #66 or #67 or #68 or #69 or #70
- #95 or #71 or #72 or #73 or #74 or #75 or #76 or #77 or #78 or #79 or #80 or #81 or #82 or #83 or #84 or #85 or #86 or #87 or #88 or #89 or #90 or #91 or #92 or #93 or #94
- #96 #56 and #95
-

ID	study	clinicaltrials.gov	author	year
1	MONARCH2	NCT02107703	George W. Sledge	2017
2	---	NCT01528345	Antonino Musolino	2017
3	PrECOG 0102	---	NS Kornblum	2018
4	BELLE-2	NCT01610284	José Baselga	2017

5	FERGI	NCT01437566	Ian E Krop	2016
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6	PALOMA-3	NCT01942135	Massimo Cristofanilli	2016
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7	a New York Cancer Consortium trial	NCT01142401	Kerin Adelson	2016
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8	the OCOG ZAMBONEY study	NCT00811369	Mark J. Clemons	2014
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9	BELLE-3	NCT01633060	Angelo Di Leo	2017
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10	MONALEESA-3	NCT02422615	Dennis J. Slamon	2018
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11	SAKK 21/08	NCT01160718	Khalil Zamana	2015
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journal	foundation	study design
Journal of Clinical Oncology	Chugai Pharma (Inst), AstraZeneca (Inst), Kyowa- Kirin (Inst), MSD Oncology (Inst), Novartis (Inst), Pfizer (Inst), Eli Lilly (Inst)	phase III, randomized, double-blind, placebo-controlled study
Breast Cancer Research	Novartis Pharmaceuticals (Basel, Switzerland).	phase II, multicenter, international, randomized, double-blind, placebo- controlled trial
JOURNAL OF CLINICAL ONCOLOGY	---	randomized, double-blind, placebo-controlled phase II trial.
Lancet Oncology	Novartis	randomised, double-blind, placebo-controlled, phase 3 trial

Lancet Oncology

F Hoff mann-La Roche.

international,  
multicentre, randomised,  
double-blind, placebo-  
controlled, phase 2  
clinical trial

Lancet Oncology

Pfizer

prospective, randomised,  
double-blind,  
placebo-controlled phase 3  
trial done

Nature partner  
journals(Breast Cancer)

---

open-label, multicenter,  
randomized phase II trial

Breast Cancer Research and  
Treatment

---

a randomised, double-  
blind, multicentre,  
phase II study

Lancet Oncology

Novartis  
Pharmaceuticals  
Corporation

randomised, double-blind,  
placebo-controlled, phase  
3 trial

JOURNAL OF CLINICAL ONCOLOGY

Supported by Novartis  
Pharmaceuticals,  
which also funded  
medical writing  
assistance.

phase III, double-blind,  
placebo-controlled  
international  
study

European Journal of Cancer

AstraZeneca AG  
Switzerland,  
S.A. AstraZeneca N.V.  
and the Swiss  
State Secretariat

multicentre, double-blind,  
placebo-controlled  
and randomised phase II  
trial

randomization	country	M	Simple size
Using an interactive, web-based randomization scheme,	142 centers in 19 countries	379	669
a patient number, which was used as the primary identifier for the patient throughout the study.	---	64	97
Random assignment was conducted centrally using permuted blocks within strata.	---	98	131
Patients were assigned randomisation numbers with a validated interactive response technology	267centers in 29 countries	784	1147

<p>a computer-generated hierarchical randomisation algorithm</p>	<p>123 medical centres across countries</p>	<p>120</p>	<p>168</p>
<p>the investigator or another designated member of the research staff via a centralised interactive web-based and voice-based randomisation system(which also generated the random allocation sequence)</p>	<p>in 144 centres in 17 countries</p>	<p>259</p>	<p>521</p>
<p>---</p>	<p>---</p>	<p>---</p>	<p>116</p>
<p>A computer-generated randomization schedule was used to allocate patients using variable block sizes</p>	<p>13 Canadian cancer centres</p>	<p>---</p>	<p>129</p>

<p>Randomisation was done with a block size of six within each stratum. Patients and investigators (including local radiologists) remained <b>masked</b></p>	<p>200 trial centres in 22 countries</p>	<p>319</p>	<p>432</p>
		<p>361</p>	<p>726</p>
<p>Randomisation was stratified using the minimisation method for centre</p>	<p>—</p>	<p>15</p>	<p>42</p>

sex(women%)	Her-2 expression	disease stage	pathway inhibited
100%	(-)	ABC	CDK4/6
100%	(-)	locally advanced or metastatic breast cancer	FGFR
100%	(-)	unresectable locally advanced or metastatic, ER-positive, human epidermal growth factor receptor 2/neu negative breast cancer	mTOR
100%	(-)	inoperable locally advanced or metastatic disease	PI3K

100% (-) locally advanced or metastatic breast cancer PI3K-AKT-mTOR

100% (-) metastatic breast cancer CDK4/6

100% (-) unresectable locally advanced or metastatic breast cancer proteasome inhibitor

Primary tumour status: n (%) 3 (5)  
VS 3 (5)

100% Metastatic tumour status: n (%) 3 (5) vs 1 (2) metastatic breast cancer VEGF



100%	100%	locally advanced or metastatic breast cancer pretreated with aromatase inhibitors and resistant to endocrine and mTOR inhibitor combination therapy	PI3K
female:484, 100%	female:242, 100%	advanced (metastatic or locoregionally recurrent disease not amenable to curative treatment) breast cancer.	CDK4/6
100%	(-)	advanced-stage endocrine sensitive (ER and/or PgR $\geq 10\%$ ) breast cancer	MEK 1/2inhibitor (MAPK)

trt1	trt2	event	simple	
abemaciclib 200 mg twice daily+ fulvestrant 500mg, im	placebo+fulvestrant 500mg, im	222	157	446
dovitinib 500 mg +fulvestrant 500 mg, im	placebo+fulvestrant 500mg, im	30	34	47
everolimus 10mg+fulvestrant 500mg, im	placebo+fulvestrant 500mg, im	---	---	66
buparlisib 100 mg once daily, +fulvestrant 500 mg, im	placebo+fulvestrant 500mg, im	349	435	576

pictilisib 340 mg daily+  
fulvestrant 500 mg, im

placebo+fulvestrant 500mg,  
im

61

59

89

palbociclib 125 mg  
daily+fulvestrant 500 mg, im

placebo+fulvestrant 500mg,  
im

145

114

347

bortezomib+fulvestrant 500 mg  
, i. m

fulvestrant 500mg, im

---

---

57

vandetanib 100 mg, PO  
OD+fulvestrant 500 mg , im

placebo+fulvestrant 500mg,  
im

---

---

61

buparlisib 100 mg once daily, +fulvestrant 500 mg, im	placebo+fulvestrant 500mg, im	202	117	289
---	-------------------------------	-----	-----	-----

ribociclib 600mg orally per day, 3 weeks on, 1 week off+fulvestrant 500mgim, on day 1 of each 28-day cycle	placebo+fulvestrant 500mg, im	210	151	484
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selumetinib 75 mg + Fulvestrant	placebo+fulvestrant 500mg, im	5	10	22
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size	median age (years)		Prior endocr
223	59 (32-91)	62 (32-87)	AI:316 (70.9%)
50	63 (44 - 82)	63 (38 - 82)	Tam:27 (57.4%) Let:18 (38.3%) Ana:16 (34.0%) Exe:8 (17.0%) Other:1 (2.1%)
65	64 (39-92)	59 (35-85)	AI-resistant
571	62.0 (55.0 - 69.0)	61 (54.0 - 68.0)	AI:574 (100%)

79	60 (36 - 90) Aged $\geq$ 65 years: 29 (33%)	63 (40 - 82) Aged $\geq$ 65 years: 29 (37%)	AI: (98%)
174	57 (30 - 88)	56 (29 - 80)	AI:137 (39%) Tam:51 (15%) AI+Tam:159 (46%)
59	59 (31 - 80)	57 (31 - 83)	Endocrine therapy : 42 (74%) Mean no. of prior: 1.47 endocrine therapies for advanced disease
68	61.6 (SD: 8.9)	57.7 (SD: 8.7)	Tam or AI for metastatic disease: 42 (69%)  Tamoxifen or AI in adjuvant: 9 (15%)  Any prior adjuvant endocrine therapy: 10 (16%)

143	60.0 (54.0 - 68.0)	62.0 (55.0 - 69.0)	Lines of previous hormonal therapy in metastatic setting: 1:87 (30%) 2:166 (57%) 3:31 (11%) 4:4 (1%) ≥5:1 (<1%)
242	63.0 (31 - 89)	63.0 (34 - 86)	Tamoxifen: 41% AI: 53%
20	66 (40 - 79)	69 (46 - 79)	AI: Adjuvant 9 (41%) Advanced stage 13 (59%) Tam: 14 (64%)

line therapy (%)	HR status (%)	
AI:149 (66.8%)	PR(+):339 (76.0%) PR(-):96 (21.5%)	PR(+):171 (76.7%) PR(-):44 (19.7%)
Tam:21 (42.0%) Let:23 (46.0%) Ana:18 (36.0%) Exe:9 (18.0%) Other:4 (8.0%)	HR+:100%	HR+:100%
AI-resistant	HR+:100%	HR+:100%
AI:568 (99%)	(+)	(+)



<p>AI: (99%)</p>	<p>ER (+) PR (+) 58 (65%) PR (-) 21 (24%) PR (unknown) 10 (11%)</p>	<p>ER (+) PR (+) 58 (73%) PR (-) 14 (18%) PR (unknown) 7 (9%)</p>
<p>AI:70 (40%) Tam:23 (13%) AI+Tam:81 (47%)</p>	<p>ER, PR(+): ≥Median of distribution: 81 (23%) &lt;Median of distribution: 71 (20%) ER/PR (+): ≥Median of distribution: 179 (52%) &lt;Median of distribution: 165 (48%)</p>	<p>ER, PR(+): ≥Median of distribution: 40 (23%) &lt;Median of distribution: 29 (17%) ER/PR (+): ≥Median of distribution: 100 (57%) &lt;Median of distribution: 90 (52%)</p>
<p>Endocrine therapy : 39 (66%)</p> <p>Mean no. of prior: 1.43 endocrine therapies for advanced disease</p> <p>ER (+) 100%                      ER (+) 100%</p>		
<p>Tam or AI for metastatic disease: 53 (78%)</p> <p>Tamoxifen or AI in adjuvant: 10 (15%)</p> <p>Any prior adjuvant endocrine therapy: 5 (7%)</p>	<p>Primary tumour status: ER(+)56 (92%) PR(+)47 (77%)</p> <p>Metastatic tumour status: n (%) ER(+)19 (31%) PR(+)11 (18%)</p>	<p>Primary tumour status: ER(+)64 (94%) PR(+)47 (69%)</p> <p>Metastatic tumour status: n (%) ER(+)17 (25%) PR(+)7 (10%)</p>

Lines of previous hormonal therapy in metastatic setting:

1:48 (34%)  
2:48 (34%)  
3:16 (11%)  
4:3 (2%)  
≥5:0

Tamoxifen: 61%	ER+:481 (99.4%)	ER+:241 (99.6%)
AI:68%	PR+:353 (72.9%)	PR+:167 (69.0%)

AI: Adjuvant 8 (40%) Advanced stage 12 (60%) Tam:11 (55%)	(ER and/or PgR ≥ 10%)	(ER and/or PgR ≥ 10%)
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Metastatic site		Visceral disease		Measurabl
Bone only:123 (27.6%) Other:75 (16.8%)	Bone only:57 (25.6%) Other:38 (17.0%)	245 (54.9%)	128 (57.4%)	yes:318 (71.3%) no:128 (28.7%)
Bone 39 (83.0%) Lymph nodes 21 (44.7%) Liver 22 (46.8%) Other 19 (40.4%) Adrenal 3 (6.4%) Breast 0	Bone 36 (72.0%) Lymph nodes 26 (52.0%) Liver 16 (32.0%) Other 8 (16.0%) Adrenal 3 (6.0%) Breast 1 (2.0%)	35 (74.5%)	30 (60.0%)	---
Bone:44 (67%) Lung:28(42%) Liver:18 (27%) Lymph nodes:27 (41%)	Bone:46 (71%) Lung:23(35%) Liver:17 (26%) Lymph nodes:28 (43%)	---	---	44, 67%
---	---	341 (59%)	337 (59%)	---

Bone-only disease: 19 (21%)	Bone-only disease: 17 (22%)			
≥3 metastatic sites: 24 (27%)	≥3 metastatic sites: 31 (39%)	51 (57%)	42 (53%)	51 (57%)

Lung involvement: 100 (29%)	Lung involvement: 45 (26%)			
Liver involvement: 127 (37%)	Liver involvement: 81 (47%)	206 (59%)	105 (60%)	Any measurable disease: 268 (77%)
Peritoneal involvement: 2 (1%)	Peritoneal involvement: 1 (1%)			
Brain or pleural involvement, or both: 4 (1%)	Brain or pleural involvement, or both: 4 (1%)			

Bone:46 (78%)	Bone:45 (76%)			
Lung:9 (15%)	Lung:23 (39%)	---	---	yes:31 (54%)
Liver:22 (37%)	Liver:21 (36%)			no:26 (46%)
Pleura:5 (8%)	Pleura:8 (14%)			

Liver: 14 (23%)				
Lung:12 (20%)				
Lymph node: 14 (23%)				
16 (24%)				
Skin: 3 (5%)	Liver:23 (34%)			
Other: 15 (25%)	Lung: 22 (32%)			
	Lymph node:16 (24%)	---	---	21 (34.4%)
	Skin:0 (0%)			
	Other:18 (27%)			

Bone:219 (76%) Liver:137 (47%) Lymph nodes:101 (35%) Lung:94 (33%)	Bone:111 (78%) Liver:76 (53%) Lymph nodes:49 (34%) Lung:43 (30%)	Visceral:21 2 (73%)	Visceral:103 (72%)	---
Bone:367 (75.8%) Bone only:103 (21.3%)  Lung:146 (30.2%) Liver:134 (27.7%) Lung or liver:242 (50.0%) Central nervous system:6 (1.2%) Other‡:102 (21.1%) Lymph nodes:199 (41.1%)	Bone:180 (74.4%) Bone only:51 (21.1%)  Lung:72 (29.8%) Liver:63 (26.0%) Lung or liver:121 (50.0%) Central nervous system:2 (0.8%) Other‡: 51 (21.1%) Lymph nodes:115 (47.5%)	Visceral:29 3 (60.5%)	Visceral: 146 (60.3%)	---
1 or 2: 13 (59%) ≥3: 9 (41%)	1 or 2: 13 (65%) ≥3: 7 (35%)	13 (59%)	11 (55%)	15 (68%)

e disease	Race		ECOG performe
yes:164 (73.5%) no:59 (26.5%)	Asian:149 (33.4%) Caucasian:237 (53.1%) Other:29 (6.5%)	Asian:65 (29.1%) Caucasian:136 (61.0%) Other:13 (5.8%)	0:264 (59.2%) 1:176 (39.5%)
-----	-----	-----	0:28 (59.6%) 1:18 (38.8%) 2:1 (2.1%)
42,65%	White 56 (85%) Black 8 (12%) Other 2 (3%)	White 49 (75%) Black 11 (17%) Other 5 (8%)	0:40 (61) 1: 26 (39)
-----	White:402 (70%) Asian:132 (23%) Black:5 (1%) Other:18 (3%) Unknown or missing: 19 (3%)	White:376 (66%) Asian:153 (27%) Black:16 (3%) Other:7 (1%) Unknown or missing: 19 (3%)	0:333 (58%) 1:231 (40%) 2:11 (2%) 3:1 (<1%)

43 (54%)	White: 78 (88%) Asian: 5 (6%) Black: 2 (2%) Other: 4 (4%) Multiple: 0	White: 68 (86%) Asian: 8 (10%) Black: 1 (1%) Other: 1 (1%) Multiple: 1 (1%)	0/1:100%
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Any measurable disease: 138 (79%)	White: 252 (73%) Asian: 74 (21%) Black and others: 21 (6%)	White: 133 (76%) Asian: 31 (18%) Black and others: 10 (6%)	0: 206 (59%) 1: 141 (41%)
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yes:38 (64%) no:21 (36%)	---	---	0:37 (65%) 1:19 (33%) 2:1 (2%)
-----------------------------	-----	-----	--------------------------------------

40 (58.8%)	---	---	0: 33 (54%) 1: 27 (44%) 2: 1 (2%)
------------	-----	-----	---

----	White 249 (86%)	White 121 (85%)	0: 173 (60%)
	Asian 20 (77%)	Asian 9 (6%)	1: 112 (39%)
	Black 4 (1%)	Black 4 (3%)	2: 2 (1%)
	Other 7 (2%)	Other 3 (2%)	Missing: 2 (1%)
	Unknown 9 (3%)	Unknown 6 (4%)	

----	White: 406 (83.9%)	White: 213 (88.0%)	0: 310 (64.0%)
	Asian: 45 (9.3%)	Asian: 18 (7.4%)	1: 173 (35.7%)
	Native American: 5 (1.0%)	Native American: 1 (0.4%)	Missing: 1 (0.2%)
	Black: 3 (0.6%)	Black: 2 (0.8%)	
	Unknown: 15 (3.1%)	Unknown: 5 (2.1%)	
	Other: 10 (2.1%)	Other: 3 (1.2%)	

15 (75%)

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0: 16 (73%)  
1/2: 6 (27%)



ance status	Postmenopausal (%)		median length of follow-up	primary endpoint
0:136 (61.0%) 1:87 (39.0%)	371 (83.2%)	180 (80.7%)	19.5 months	PFS
0:28 (56.0%) 1:20 (40.0%) 2:2 (4.0%)	未提及百分比 100%	未提及百分比 100%	—	PFS
0 :38 (58) 1:27 (42)	未提及百分比 100%	未提及百分比 100%	19.3 months (range, 0 to 36.3 months)	PFS
0:344 (60%) 1:211 (37%) 2:16 (3%) 3:0	postmenopausal 未提及百分比	postmenopausal 未提及百分比	13.73 months (IQR 5.45 - 19.81) versus 14.32 (10.64 - 21.62)	PFS、ORR

0/1:100%	postmenopausal 未提及百分比	postmenopausal 未提及百分比	17.5 months (IQR 15.4 - 19.4)	PFS
0: 116 (67%) 1: 58 (33%)	275 (79%)	138 (79%)	8.9 months (IQR 8.7 - 9.2).	PFS
0:38 (64%) 1:20 (34%) 2:1 (2%)	postmenopausal 未提及百分比	postmenopausal 未提及百分比	---	PFS
0: 36 (53) 1: 27 (40) 2: 5 (7)	postmenopausal 未提及百分比	postmenopausal 未提及百分比	---	uNTx response.

0: 91 (64%) 1: 48 (34%) 2: 1 (1%) Missing: 3 (2%)	postmenopausal 未提及百分比	postmenopausal 未提及百分比	8.3 months (IQR 4.2 - 20.7) VS 12.0 months (IQR 4.7 - 13.7)	progression-free survival
0: 158 (65.3%) 1: 83 (34.3%) Missing: 1 (0.4%)	——	——	20.4 months	locally assessed PFS
0: 13 (65%) 1/2: 7 (35%)	postmenopausal 未提及百分比	postmenopausal 未提及百分比	22 months	DCR

secondary endpoint	PFS	ORR (CR+PR)
ORR, duration of response, CBR	PFS:16.4 VS 9.3months HR: 0.553; 95% CI: (0.449 , 0.681) P<0.001	OR:2.82 ,P<.001) 157 (35.2%) 95%CI: (30.8% to 39.6%) vs 36 (16.1%) 95%CI: (11.3% to 21.0%)
ORR, Median time to first response;DOR	PFS: 5.5months(3.8 - 14.0) vs 5.5months(3.5 - 10.7) HR:0.68 95% CI: (0.41, 1.14)	13 (27.7%) 95%CI: [15.6 - 42.6] 5 (10.0%) 95%CI: [3.3 - 21.8]
objective response rate, clinical benefit rate, OS	10.3 (95% CI, 7.6 to13.8 months; 5.1 (95% CI, 3.0 to 8.0 months) P=0.02; HR=0.61 [95% CI: 0.40 to 0.92]	12, 18.2%, 95%CI:9.8, 29.6 8, 12.3%, 95%CI:5.5, 22.8
OS, overall response, clinical benefit	PFS:6.9(6.8 - 7.8) 5.0 months(4.0 - 5.2) HR:0.78 95% CI: (0.67-0.89) p=0.00021	overall response: 11.8% (95% CI9.3 - 14.7) 7.7% (5.7 - 10.2)

	(6.6 months [95% CI 3.9 - 9.8])	7 (7.9% [95% CI 3.2 - 15.5])
OR, clinical benefit, duration of response, the prognostic effect	(5.1 months [3.6 - 7.3]) [HR] 0.74 [95% CI 0.52 - 1.06]; p=0.096	5 (6.3% [2.1 - 14.2]) (p=0.70)

	PFS: 9.5 (95% CI 9.2 - 11.0)	66, 19% (15.0 - 23.6) VS 15, 9% (4.9 - 13.8)
ORR, clinical benefit, tumour tissue biomarkers,	4.6 (95%CI: 3.5 - 5.6) HR: 0.46 95%CI:0.36 - 0.59, p<0.0001	OR: 2.47 (1.36 - 4.91)
		CR: 0.0% VS 4.2% (n, %) PR: 66.19% VS 11.6% Stable disease: 213.61% vs 94.54% Progressive disease: 58.17% 57.33%

CBR (for cross over trial)	2.73 vs 2.69 HR:0.73 (95% (CI)=0.49, 1.09) P=0.06	---
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PFS, OS, RECIST response,	PFS: 5.8 months (95% CI 2.7 - 8.1) and 4.8 months (95% CI 2.7 - 5.4), HR=0.94 (95% CI 0.64 - 1.36), P=0.73	RECIST best response: n (%) PR: 0 (0) vs 3 (75) P=0.47 SD: 9 (41) VS 14 (35) PD: 11 (50) VS 18 (45) NE: 2 (9) VS 5 (13)
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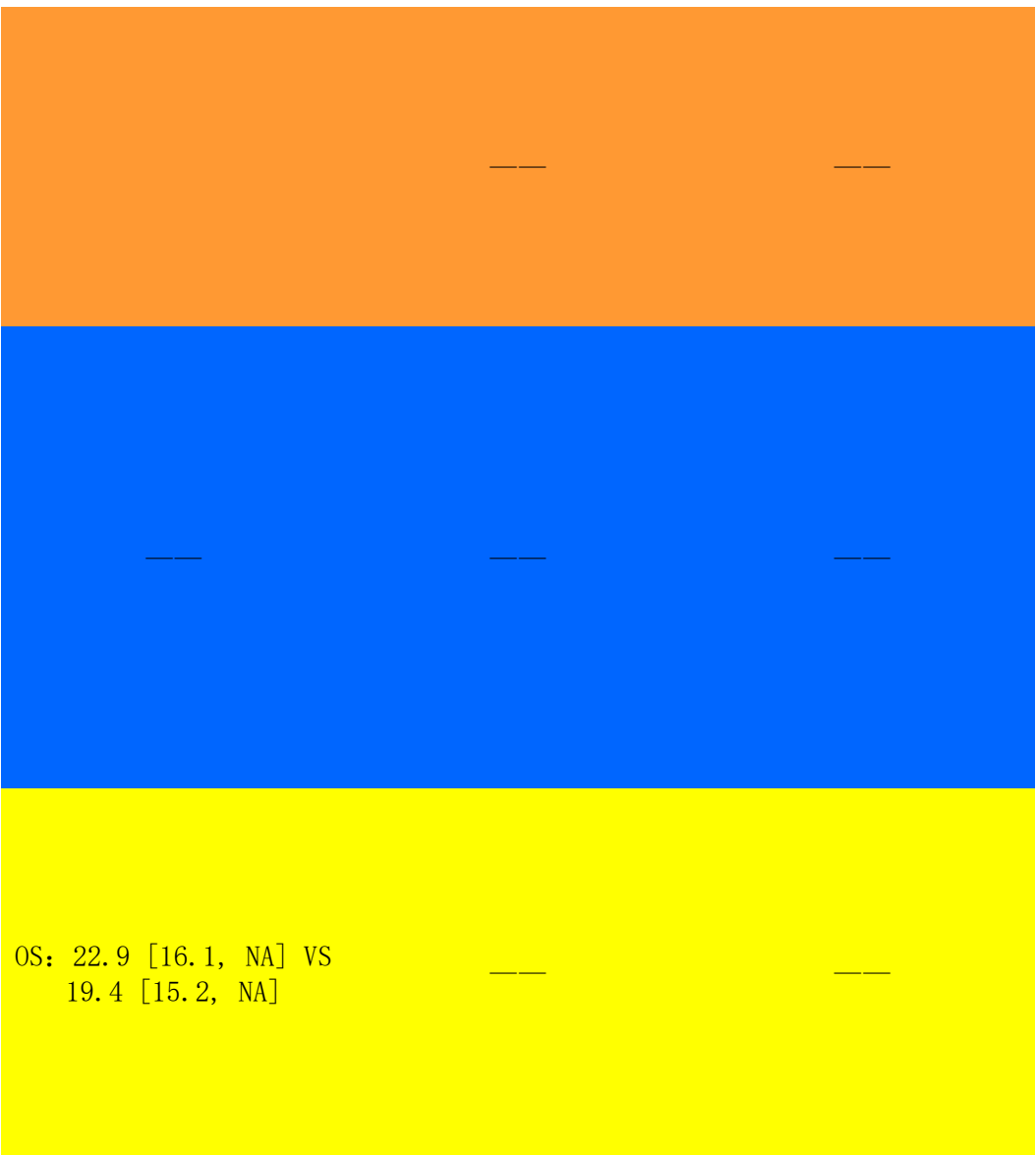
overall survival, safety	3.9 months [95% CI 2.8 - 4.2] vs 1.8 months [1.5 - 2.8] HR=0.67, 95% CI 0.53 - 0.84, one-sided p=0.00030	CR:1 PR:21 Overall response:22,8%, 95%CI:5-11 CR:0 PR:3 Overall response:3,2%, 95%CI:0-6
overall survival (OS), overall response rate (ORR), clinical benefit rate, and safety and tolerability	20.5 months (95% CI, 18.5 to 23.5 months) versus 12.8 months (95% CI, 10.9 to 16.3 months) HR=0.593 (95% CI, 0.480 to 0.732; P =0.001 {up to line:HR=0.565, 95%CI: 0.428-0.744}	155, 32.4% (95% CI, 28.3% to 36.6%) versus 52, 21.5% (95% CI, 16.3% to 26.7%)
overall response rate (OR, best response i.e. CR or PR), time to treatment failure (TTF, from randomisation to discontinuation of all trial treatment), duration	PFS:3.7 months (95% CI 1.9, 5.8) and 5.6 months (95% CI 3.4, 13.6)	CR: 0 (0%) VS 0 (0%) PR: 1 (5%) VS 3 (15%)

OS	Median time to first response	duration of response rate
	---	67.8% vs 66.9%
	months: 2.0(1.5 - 18.8) 3.7(1.6 - 9.1)	months: 13.5 [5.5 - 16.6] 14.7 [3.3 - NE]
28.3 months (95% CI, 19.5 to 29.6 months) 31.4 months (95% CI, 21.8 to month not reached) HR=1.31 [95% CI:0.72, 2.38] P=0.37	---	---
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(9.43 months [4.1 to not estimable] vs 6.5 months [3.7 months to not estimable]; p=0.65

OS: 31.0 (23.3 - NR) vs  
NR, p=0.30





Disease control rate (CR + PR + SD)	Clinical benefit rate (CR+PR+SD $\geq$ 6 months)
OR:1.56 P=0.025 370 (83.0%) 95%CI: (79.5 to 86.4) 169 (75.8%) 95%CI: (70.2 to 81.4)	OR:2.04 , P<.001 322 (72.2%) 95%CI: (68.0 to 76.4) 125 (56.1%) 95%CI: (49.5 to 62.6)
———	———
———	42, 63.6%, 95%CI: 50.9, 75.1 27, 41.5% 95%CI: 29.4, 54.4
———	43.8% (95% CI 39.7 - 47.9) 42.0% (37.9 - 46.2)

—— 22 (24.7%) (95% CI  
16.2 - 35.0) versus 14  
(17.7%) (p=0.27)

—— 231, 67%  
(61.3 - 71.5) VS 69, 40%  
(32.3 - 47.3)  
OR: 3.05 (2.07 - 4.61)

—— ———

—— ———

71, 25%, 95%CI:20-30  
VS 22, 15%, 95%CI:10-22

340 (70.2%) 95% CI:66.2  
to 74.3 VS 152 (62.8%)  
95% CI:56.7 to 68.9

DCR:5 23% (95% CI:  
8 - 45%) VS  
10 50% (95% CI 27 - 75%)

safety(adverse events)	safety simple size	Grade
<p>abemaciclib versus placebo arms were diarrhea (86.4% v 24.7%), neutropenia (46.0% v 4.0%), nausea (45.1% v22.9%), and fatigue (39.9% v 26.9%).</p>	<p>441      223</p>	<p>all:435 (98.6%) 3级: 241 (54.6%) 4级: 26 (5.9%)</p>
<p>The most common grade 3 AEs (occurring in <math>\geq</math> 10% of patients) in the dovitinib vs placebo arms were hypertension (21.3% vs 6.0%), diarrhea (14.9% vs 4.0%), alanine aminotransferase increase (14.9% vs 2.0%), fatigue (12.8%vs 2.0%), blood alkaline phosphatase increase (12.8% vs 0%), and <math>\gamma</math>-glutamyltransferase increase (10.6% vs 6.0%)</p>	<p>47      50</p>	<p>47 (100%) 3级: 32 (68.1%) 4级: 8, 17%</p>
<p>hyperglycemia (16%/0% vs. 0%), stomatitis (11%/0% vs. 0%), hypertriglyceridemia (9%/2% vs. 0%), lymphopenia (9%/0% vs. 0%), and pneumonitis (6%/2% vs. 0%)</p>	<p>64      65</p>	<p>3/4级: 53%/3%</p>
<p>The most common grade 3-4 adverse events in the buparlisib group versus the placebo group were increased alanine aminotransferase (146 [25%] of 573 patients vs six [1%] of 570), increased aspartate aminotransferase (103 [18%] vs 16 [3%]), hyperglycaemia (88 [15%] vs one[&lt;1%]), and rash (45 [8%] vs none)</p>	<p>573      570</p>	<p>---</p>

<p>grade 3 or 4 adverse events were neutropenia (223 [65%] in the fulvestrant plus palbociclib group and one [1%] in the fulvestrant plus placebo group), anaemia (ten [3%] and three [2%]), and leucopenia (95 [28%] and two [1%]).</p>	<p>89</p>	<p>79</p>	<p>Grade <math>\geq 3</math>: 54, 61%</p>
<p>The most common adverse events in the fulvestrant/bortezomib combination arm compared with the fulvestrant alone arm included nausea (63 vs. 29%), diarrhea (47 vs. 8%), sensory neuropathy (46 vs. 29%), and limb edema (37 vs. 19%)</p>	<p>345</p>	<p>172</p>	<p>3/4级: 251 (73%) of 345</p>
<p>14 (23.0 %) patients on FV and 9 (13.2 %) on FP experienced a grade 3 or greater serious or clinically significant AE (p= 0.17). 6 patients experienced a serious adverse event, 2 who received FV (diarrhoea and mucositis/stomatitis) and 4 who received FP (dehydration, pericarditis and 2 cases of pulmonary infection).</p>	<p>61</p>	<p>68</p>	<p>14, 23.0%</p>

— 288 140 177, 61%

— 483 241

selumetinib - fulvestrant arm:

skin disorders (17 (73.9)), fatigue (12 (52.2)), nausea/vomiting(12 (52.2)), oedema(11 (47.8)), diarrhoea(10 (43.5)), mouth disorders(9 (39.1)) and muscle disorders(6 (26.1)).

Placebo: Nausea/vomiting: 9 (40.9)、Fatigue: 7 (31.8)、Diarrhoea: 7 (31.8)、Pain: 7 (31.8)、Eye disorders: 5 (22.7)、Skin disorders: 5 (22.7)

23

22

1级: 1 (4.3%)  
2级: 11 (47.8%)  
3级: 11 (47.8%)  
4级: 0 (0.0%)

3/4级

all:199 (89.2%)

3级 46 (20.6%)

4级: 5 (2.2%)

47 (94.0%)

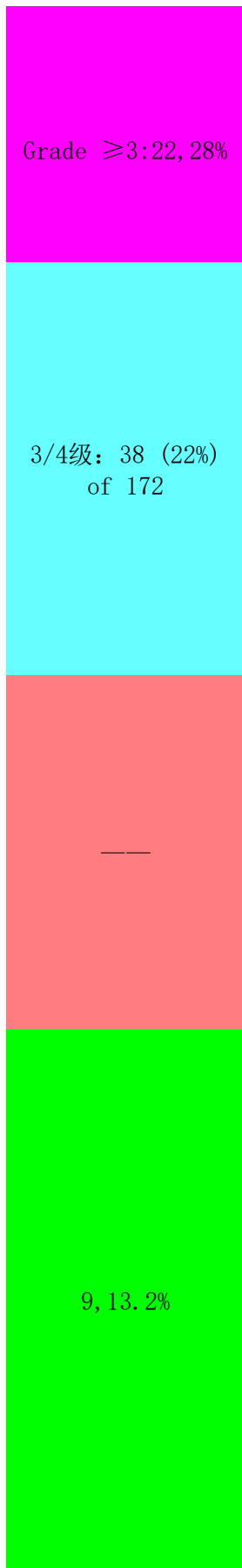
3级: 19 (38.0)

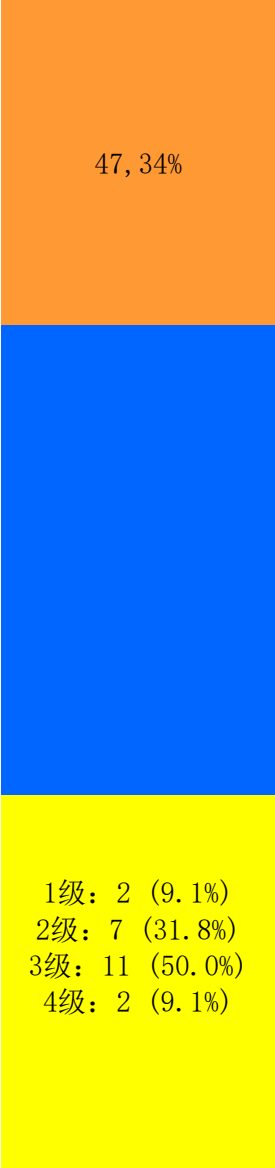
4级: 6, 12%

3/4级: 23%/3%

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47, 34%

1级: 2 (9.1%)

2级: 7 (31.8%)

3级: 11 (50.0%)

4级: 2 (9.1%)