Table S1. Ongoing cancer clinical trials of drugs targeting the PI3K/mTOR signalling network (source: ClinicalTrials.gov).

Tested regimens	Pathology characteristics	Setting	Phase	Primary outcome measures	No. of patients	Trial identifier
Gedatolisib / PF-05212384 (dual PI3K/mTOR inhibitor)						
Gedatolisib + Palbociclib (CDK4/6i)	N/A	Advanced squamous cell lung cancer Advanced pancreatic cancer Advanced head and neck cancer	I	Maximum tolerated dose Incidence of treatment-emergent adverse events	96	NCT03065062
Gedatolisib + Talazoparib (PARP1/2i)	Triple-negative HER2 negative and BRCA1/2 mutation	Advanced or metastatic breast cancer	I and II	Maximum tolerated dose Objective response rate	54	NCT03911973
Gedatolisib + Faslodex (ERi) + Palbociclib (CDK4/6i)	ER positive, HER2 negative	Stage I-IV non-inflammatory invasive breast cancer	Ib	Treatment-related adverse events	18	NCT02626507
Vistusertib / AZD2014 (mTOR inhibitor)						
Vistusertib	N/A	Grade II-III intracranial meningioma	II	Progression-free survival	28	NCT03071874
1. Fulvestrant (ERi) 2. Vistusertib (continuous schedule) + Fulvestrant (ERi) 3. Vistusertib (intermittent schedule) + Fulvestrant (ERi) 4. Everolimus (mTORi) + Fulvestrant (ERi)	ER positive, HER2 negative	Advanced or metastatic breast cancer	II	Progression-free survival	333	NCT02216786
1. Vistusertib (continuous schedule) + Olaparib (PARPi) 2. Vistusertib (intermittent schedule) + Olaparib (PARPi) 3. Capivasertib (AKTi) + Olaparib PARPi)	BRCA1/2 mutation carrier Triple-negative	Endometrial, breast cancer, ovarian, primary peritoneal, or fallopian tube cancer	I and II	Maximum tolerated dose	159	NCT02208375

Everolimus (mTOR inhibitor)						
(1. Everolimus 2. Placebo	N/A	Invasive unilateral or bilateral breast cancer	III	Benefit from adding everolimus to standard endocrine treatments	1279	NCT01805271
Everolimus + Sorafenib (multikinase inhibitor)	N/A	Thyroid carcinoma	II	Response rate	41	NCT01141309
1. Everolimus followed by STZ-5FU (thymidylate synthetase inhibitor) 2. STZ-5FU (thymidylate synthetase inhibitor) followed by Everolimus	N/A	Metastatic or advanced pancreatic neuroendocrine tumours	III	First progression-free survival	141	NCT02246127
Alpelisib / BYL719 (PI3K inhibitor)						
1. LSZ102 (ER degrader) 2. LSZ102 (ER degrader) + LEE011 (CDK4/6i) 3. LSZ102 (ER degrader) + BYL719	ER positive, HER2 negative	Locally recurrent or metastatic breast cancer	I	Incidence of dose limiting toxicities Safety and tolerability	199	NCT02734615
Alpelisib + Letrozole (aromatase inhibitor)	ER positive and/or PR positive and HER2 negative A minimum of 10 patients will need to have a PIK3CA mutation	Stage IV invasive mammary carcinoma	I	Maximum tolerated dose	46	NCT01791478
Alpelisib (250, 300, 350 mg) + Nab-paclitaxel (mitosis inhibitor)	HER2 negative	Locally recurrent or metastatic breast cancer	I and II	Recommended phase II dose of BYL719 + Nab-paclitaxel Overall response rate	44	NCT02379247
Copanlisib / BAY 80-6946 (PI3K inhibitor)						
Copanlisib	N/A	Recurrent/refractory solid tumors or lymphoma in pediatric patients	I and II	Maximum tolerated dose Dose-limiting toxicities Treatment-emergent adverse events	142	NCT03458728

				Objective response rate Disease control rate Progression-free survival		
Copanlisib + Nivolumab (PD-1i)	N/A	Relapsed/refractory solid tumors with expansions in mismatch-repair proficient colorectal cancer	I and II	Maximum tolerated dose Objective response rate	54	NCT03711058
1. Copanlisib + Trastuzumab (HER2i) + Pertuzumab (HER2i) 2. Trastuzumab (HER2i) + Pertuzumab (HER2i)	HER2 positive PIK3CA or PTEN mutation	Locally advanced or metastatic breast cancer	I and II	Incidence of adverse events and serious adverse events Dose limiting toxicities Progression-free survival	102	NCT04108858
Inavolisib / GDC-0077 / RG6114 (PI3K inhibitor)						
1. Inavolisib + Palbociclib (CDK4/6i) + Fulvestrant (ERi) 2. Placebo + Palbociclib (CDK4/6i) + Fulvestrant (ERi)	Hormone receptor positive, HER2 negative PIK3CA mutation	Metastatic or locally advanced breast cancer	II and III	Progression-free survival	400	NCT04191499
1. Inavolisib 2. Inavolisib + Palbociclib (CDK4/6i) + Letrozole (aromatase inhibitor) 3. Inavolisib + Letrozole (aromatase inhibitor) 4. Inavolisib + Fulvestrant (ERi) 5. Inavolisib + Palbociclib (CDK4/6i) + Fulvestrant (ERi) 6. Inavolisib + Palbociclib (CDK4/6i) + Fulvestrant (ERi) + Metformin (energetic stress inducer) 7. Inavolisib + Trastuzumab (HER2i) + Pertuzumab (HER2i)	PIK3CA mutation	Locally advanced or metastatic solid tumors	I	Percentage of participants with dose limiting toxicities Recommended phase II dose of Inavolisib Percentage of participants with adverse events and serious adverse events	256	NCT03006172

Ipatasertib / GDC-0068 (Akt inhibitor)						
Ipatasertib	N/A	Locally advanced or metastatic solid tumors	I	Maximum/minimum plasma concentration Time to maximum plasma concentration Terminal half-life Apparent clearance Accumulation ratio at steady state	20	NCT04341259
1. Ipatasertib + Fulvestrant (ERi) 2. Ipatasertib + Letrozole (aromatase inhibitor) 3. Ipatasertib + Fulvestrant (ERi) + Palbociclib (CDK4/6i)	Hormone receptor positive, HER2 negative	Metastatic or locally advanced breast cancer	I	Incidence of treatment-emergent adverse events	60	NCT03959891
1. Ipatasertib + Abiraterone (CYP17i) 2. Placebo + Abiraterone (CYP17i)	PTEN loss	Metastatic castrate-resistant prostate cancer	III	Radiographic progression-free survival	1101	NCT03072238
Capivasertib / AZD5363 (Akt inhibitor)						
Capivasertib	AKT mutation	Advanced refractory cancers/lymphomas/multiple myeloma	II	Objective response rate	35	NCT04439123
1. Capivasertib + Paclitaxel (ERi) 2. Placebo + Paclitaxel (ERi)	Triple-negative	Advanced or metastatic breast cancer	II	Progression-free survival	140	NCT02423603
1. Capivasertib + Paclitaxel (ERi) 2. Placebo + Paclitaxel (ERi)	Triple-negative	Locally advanced or metastatic breast cancer	III	Progression-free and overall survival	942	NCT03997123
MK2206 (Akt inhibitor)						
MK2206 + Hydroxychloroquine (lysosome inhibitor)	N/A	Advanced solid tumors, melanoma, prostate or kidney cancer	I	Maximum tolerated dose of MK2206 Dose-limiting toxicity rate	62	NCT01480154

1. Bicalutamide 2. MK2206 + Bicalutamide	N/A	Recurrent prostate carcinoma	II	The proportion of patients with undetectable prostate-specific antigen level	108	NCT01251861
1. Erlotinib (EGFRi) 2. AZD6244 (MEK1/2i) 3. MK2206 4. Lapatinib (HER1/2i) 5. Sunitinib (PDGF-R and VEGFR inhibitor)	EGFR mutation KRAS, BRAF, HRAS, or NRAF mutation PIK3CA, AKT, or PTEN mutation KIT or PDGFRA mutation ERBB2 mutation	Advanced non-small cell lung cancer Small cell lung lancer Thymic malignancies	II	Determine the feasibility of the use of tumor molecular profiling and Estimate the response rate of molecular-profile directed treatments targeted therapies	469	NCT01306045