
Supplementary information

At a crossroads: how to translate the roles of PI3K in oncogenic and metabolic signalling into improvements in cancer therapy

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Supplementary Table 1 | Examples of trials testing PI3K-pathway inhibitors in new combinations and/or new cancer settings

Therapeutic strategy and interventions tested	Patient population	Study phase	ClinicalTrials.gov identifier (trial name)
PI3K inhibition plus metabolic modulation			
Alpelisib (PI3K α inhibitor) and fulvestrant + a ketogenic diet vs a low-carbohydrate diet vs canagliflozin (SGLT2 inhibitor)	Metastatic <i>PIK3CA</i> -mutant ER ⁺ HER2 ⁻ breast cancer	II	NCT05090358 (TIFA)
PI3K inhibition for tumours with multiple <i>PIK3CA</i> mutations			
Inavolisib	Advanced-stage cancers with multiple co-existing <i>PIK3CA</i> mutations	II	NCT04589845 (TAPISTRY cohort H)
PI3K-pathway inhibition plus hormone therapy			
Alpelisib + enzalutamide (ar inhibitor)	AR ⁺ PTEN ⁺ metastatic breast cancer	Ib	NCT03207529
Abiraterone (anti-androgen) and androgen-deprivation therapy + capivasertib (AKT inhibitor) or placebo	Metastatic <i>PTEN</i> -deficient castration-sensitive prostate cancer	III	NCT04493853 (CAPItello-281)
Fulvestrant (SERD) + capivasertib or placebo	Previously treated advanced-stage ER ⁺ HER2 ⁻ breast cancer	III	NCT04305496 (CAPItello-291)
PI3K-pathway and CDK4/6 inhibition			
Alpelisib + ribociclib (CDK4/6 inhibitor) + letrozole (AI)	Advanced-stage ER ⁺ HER2 ⁻ breast cancer	Ib/II	NCT01872260
Palbociclib (CDK4/6 inhibitor) and fulvestrant + capivasertib or placebo	Advanced-stage ER ⁺ HER2 ⁻ breast cancer (endocrine-resistant disease only in phase III part)	Ib/III	NCT04862663 (CAPItello-292)
Palbociclib and fulvestrant + ipatasertib (AKT inhibitory) or placebo	Metastatic ER ⁺ HER2 ⁻ breast cancer without ctDNA suppression after 15 days of CDK4/6i + fulvestrant	II	NCT04920708 (FAIM)
Gedatolisib (dual PI3K/mTOR inhibitor) + palbociclib	Various advanced-stage solid tumours	I	NCT03065062
PI3K inhibition plus anti-HER2 therapy			
Alpelisib + trastuzumab (anti-HER2 antibody) \pm fulvestrant vs trastuzumab + chemotherapy	Previously treated advanced-stage <i>PIK3CA</i> -mutant HER2 ⁺ breast cancer	III	NCT05063786 (ALPHABET)
Trastuzumab and pertuzumab (anti-HER2 antibody) + alpelisib or placebo	Advanced-stage <i>PIK3CA</i> -mutant HER2 ⁺ breast cancer, as maintenance therapy	III	NCT04208178 (EPIK-B2)
PI3K and PARP inhibition			
Alpelisib and olaparib vs chemotherapy	Platinum-resistant/refractory ovarian cancer without germline <i>BRCA</i> mutations	III	NCT04729387 (EPIK-O)
PI3K-pathway inhibition plus chemotherapy			
Nab-paclitaxel + alpelisib or placebo	Advanced-stage <i>PIK3CA</i> -mutant and/or <i>PTEN</i> -deficient triple-negative breast cancer	III	NCT04251533 (EPIK-B3)
Paclitaxel + capivasertib or placebo	Previously untreated advanced-stage triple-negative breast cancer	III	NCT03997123 (CAPItello-290)

AI, aromatase inhibitor; AR, androgen receptor; ER, oestrogen receptor; SERD, selective oestrogen receptor degrader; SGLT2, sodium–glucose co-transporter 2.