

Table SI. Clinical trials using modulators of P-class pumps (retrieved from clinicaltrials.gov).

A, Completed			
Study identifier and status	Study title	Type of malignancy	Compound studied
Na/K ATPases			
NCT00002862	Perillyl Alcohol in Treating Patients With Refractory Cancer	Lymphoma, unspecified adult solid tumor	Perillyl alcohol
NCT00003219	Perillyl Alcohol in Treating Patients With Metastatic Breast Cancer	Breast cancer	Perillyl alcohol
NCT00003238	Perillyl Alcohol in Treating Patients With Metastatic Prostate Cancer That Has Not Responded to Hormone Therapy	Prostate cancer	Perillyl alcohol
NCT00003769	Perillyl Alcohol Followed by Surgery in Treating Patients With Stage II or Stage III Pancreatic Cancer	Pancreatic cancer	Perillyl alcohol
NCT00650910	Study To Examine The Effects Of Lapatinib On The Pharmacokinetics Of Digoxin In Subjects w/ ErbB2 Positive Breast Cancer	Breast cancer	Digoxin
NCT00837239	Huachansu & Gemcitabine in Pancreatic Cancer	Pancreatic cancer	Huachansu
NCT01162135	Digoxin for Recurrent Prostate Cancer	Prostate cancer	Digoxin
NCT01517399	Drug-drug Interaction Study of Tivantinib (ARQ 197) With Omeprazole, S-warfarin, Caffeine, Midazolam, and Digoxin in Cancer Subjects	Advanced solid tumors	Digoxin, Omeprazole
NCT01763931	DIG-HIF1 Pharmacodynamic Trial in Newly Diagnosed Operable Breast Cancer	Breast cancer	Digoxin
NCT01765569	A Pharmacokinetics Study to Investigate the Effect of Vemurafenib on Digoxin in Patients With BRAFV600 Mutation-Positive Metastatic Melanoma	Melanoma	Digoxin
NCT01887288	Capecitabine With Digoxin for Metastatic Breast Cancer	Breast cancer	Digoxin
NCT02106845	Effect of Regorafenib on Digoxin and Rosuvastatin in Patients With Advanced Solid Malignant Tumors.	Locally advanced or metastatic solid tumors	Digoxin
NCT02138292	A Phase 1B Clinical Trial of Trametinib Plus Digoxin in Patients With Unresectable or Metastatic BRAF Wild-type Melanoma	Melanoma	Digoxin
NCT02626234	A Drug-drug Interaction (DDI) Study to Assess the Effect of INC280 on the Pharmacokinetics of Digoxin and Rosuvastatin in Patients With cMET-dysregulated Advanced Solid Tumors	Advanced solid tumors	Digoxin
NCT02740712	Pharmacokinetic Drug-Drug Interaction Study of Rucaparib	Digoxin, Omeprazole Advanced solid tumors	
SERCA			
NCT00256334	Resveratrol for Patients With Colon Cancer	Colon cancer	Resveratrol
NCT00433576	Resveratrol in Treating Patients With Colorectal Cancer That Can Be Removed By Surgery	Colorectal cancer	Resveratrol
NCT00920803	A Clinical Study to Assess the Safety, Pharmacokinetics, and Pharmacodynamics of SRT501 in Subjects With Colorectal Cancer and Hepatic Metastases	Colorectal neoplasms	Resveratrol
NCT01476592	A Biological Study of Resveratrol's Effects on Notch-1 Signaling in Subjects With Low Grade Gastrointestinal Tumors	Neuroendocrine tumor	Resveratrol
NCT01056029	Dose-Escalation Phase 1 Study of G-202 (Mipsagargin) in Patients With Advanced Solid Tumors	Advanced solid tumors	Mipsagargin
NCT01777594	Study of G-202 (Mipsagargin) as Second-Line Therapy Following Sorafenib in Hepatocellular Carcinoma (G-202-003)	Hepatocellular carcinoma	Mipsagargin
NCT02067156	Efficacy, Safety and CNS Exposure of G-202 (Mipsagargin) in Patients With Recurrent or Progressive Glioblastoma	Glioblastoma multiforme	Mipsagargin

Table SI. Continued.

Study identifier and status	Study title	Type of malignancy	Compound studied
H/K ATPases			
NCT00001191	The Use of Oral Omeprazole and Intravenous Pantoprazole in Patients With Hypersecretion of Gastric Acid	Gastrinoma	Pantoprazole, Omeprazole
NCT00002682	Antibiotic Therapy and Antacids in Patients With Malt Lymphoma of the Stomach	Gastric MALT lymphoma	Omeprazole
NCT00003151	Antibiotic Therapy in Treating Patients With Low Grade Gastric Lymphoma	Gastric lymphoma	Omeprazole
NCT00079833	Esomeprazole In Patients With Gastric Acid Hypersecretory States Including Idiopathic Hypersecretion and Zollinger-Ellison Syndrome	Zollinger-Ellison syndrome	Esomeprazole
NCT00201422	Eradication of Helicobacter Pylori in the Management of Stage IE & IIE-1 Primary Low-grade B Cell Lymphoma of MALToma	MALT lymphoma	Omeprazole
NCT00298779	Open-Label Study to Assess the Effect of Omeprazole. on the Pharmacokinetics of VELCADE in Patients With Either Advanced Solid Tumors or Non-Hodgkin's Lymphoma	Non-Hodgkin's lymphoma	Omeprazole
NCT00327132	Prospective Study of First-line Antibiotic Therapy for Early-stage Gastric MALT Lymphoma for Treatment Outcome	Early-stage gastric MALT lymphoma	Omeprazole
NCT00339768	A Randomized Multi-Intervention Trial to Inhibit Precancerous Gastric Lesions in Lingu, Shandong Province	Precancerous gastric lesions	Omeprazole
NCT00420615	Evaluate the Effects of Patupilone on the Pharmacokinetics of Midazolam and Omeprazole in Patients With Advanced Malignancies	Advanced solid tumor	Omeprazole
NCT00473980	Preoperative Non-steroidal Anti-inflammatory Drugs(NSAID) to Colorectal Cancer Patients	Colorectal cancer	Esomeprazole
NCT00474903	Esomeprazole Magnesium With or Without Aspirin in Preventing Esophageal Cancer in Patients With Barrett Esophagus	Esophageal cancer	Esomeprazole
NCT00559182	A Study of MK-8033 in Patients With Advanced Solid Tumors (MK-8033-001)	Omeprazole Advanced solid tumor	
NCT00844675	Effects of Oral Rabeprazole on the Prevention of Ulcer Bleeding Following Endoscopic Mucosal Resection	Early gastric adenocarcinoma	Rabeprazole
NCT00849329	A Study to Examine the Effects of Esomeprazole on the Pharmacokinetics of Orally Administered Lapatinib in Subjects With Metastatic ErbB2 Positive Breast Cancer	Breast cancer	Esomeprazole
NCT01042704	Bendamustine in Combination With Lenalidomide and Dexamethasone in Refractory or Relapsed Multiple Myeloma	Multiple myeloma	Omeprazole
NCT01069081	Docetaxel and Cisplatin Chemotherapy With or Without High Dose Proton Pump Inhibitor in Metastatic Breast Cancer	Breast cancer	Esomeprazole
NCT01163903	Pantoprazole With Doxorubicin for Advanced Cancer Patients With Extension Cohort of Patients With Solid Tumours	Advanced solid tumors	Pantoprazole
NCT01205230	VEG113971: An Open-Label Study of the Effects of Ketoconazole or Esomeprazole on Pazopanib PK	Advanced solid tumor malignancy	Esomeprazole
NCT01216267	Evaluation of Methods for the Determination of Chromogranin A in Routine Blood Samples	Neuroendocrine carcinoma (carcinoid)	Lansoprazole
NCT01218620	Gamma-Secretase/Notch Signalling Pathway Inhibitor RO4929097 in Treating Patients With Advanced Solid Tumors	Advanced solid tumor	Omeprazole

Table SI. Continued.

Study identifier and status	Study title	Type of malignancy	Compound studied
NCT01264822	Prognostic Study of Gastric MALT Lymphoma After Eradication of <i>Helicobacter Pylori</i>	Gastric low-grade MALT lymphoma with <i>Helicobacter pylori</i> infection	Rabeprazole
NCT01287598 NCT01322633	BAY73-4506 Probe Substrate Study Risk of Cancer Among Pantoprazole Users	Advanced Solid Tumour Gastric cancer, gastrointestinal cancer, any cancer	Omeprazole Pantoprazole
NCT01434485	Nexium Capsules Clinical Experience Investigation	Zollinger-Ellison syndrome	Esomeprazole
NCT01435525	Nexium Capsules <i>Helicobacter Pylori</i> Specific Clinical Experience Investigation	Gastric MALT lymphoma, early gastric cancer	Esomeprazole
NCT01539655	Study in Healthy Volunteers to Assess Effect of Omeprazole and Ranitidine on the Pharmacokinetics of Vandetanib (Vandetanib)	Medullary thyroid cancer	Omeprazole
NCT01585623	Drug Interaction Study of SAR302503 in Patients With Solid Tumor	Advanced solid tumor	Omeprazole
NCT01596647	Pharmacokinetic Drug-drug Interaction Study of Dovitinib (TKI258) in Patients With Advanced Solid Tumors	Advanced solid tumors, excluding breast cancer	Omeprazole
NCT01844583	Safety, Tolerability and PK of Concomitant Esomeprazole and Rifampin, and QT Study on Single and Multiple-doses of Alisertib	Metastatic tumors, advanced solid tumors, lymphomas	Esomeprazole
NCT01911728	Drug-drug Interaction Study With MDV3100 and a Cocktail of Substrates	Prostate cancer	Omeprazole
NCT01954043	A Pharmacokinetics (PK) Study of the Effects Rabeprazole and Rifampin on Dabrafenib in Subjects With BRAF V600 Mutation Positive Tumors	BRAF V600 mutation-positive tumor	Rabeprazole
NCT02254889	Pain After Endoscopic Submucosal Dissection	Gastric neoplasm	Proton pump inhibitor Omeprazole
NCT02518373	Effect of G17DT in Patients With Stage II/III Colorectal Cancer (CC5)	Colorectal Cancer	Omeprazole
NCT02666976	The Prospective Study on the Effect of Ilaprazole in Non-erosive Reflux Disease Patients; Focused on Histologic Findings and Inflammatory Biomarker	Upper gastrointestinal subepithelial tumors	Ilaprazole
NCT02682446	The Efficacy of Serum Pepsinogen for Prediction of Metachronous Gastric Neoplasm	Gastric cancer	Lansoprazole
NCT02730533	The Efficacy of Esomeprazole Premedication on Intraoperative Bleeding During Gastric ESD	Gastric neoplasms	Esomeprazole
NCT02800330	The Effects of the Proton Pump Inhibitor Esomeprazole on the Bioavailability of Regorafenib (REGORA)	Colorectal neoplasms, gastrointestinal stromal tumors	Esomeprazole
NCT03219723	Drug Use Surveillance of Takecab for 'Supplement to <i>Helicobacter Pylori</i> Eradication'	Gastric MALT lymphoma	Vonoprazan

## B, Recruiting

Study identifier and status	Study title	Type of malignancy	Compound studied
Na/K ATPases NCT02212639	Phase II Multicentric Study of Digoxin Per os in Classic or Endemic Kaposi' s Sarcoma (KADIG 01)	Kaposi's sarcoma	Digoxin

Table SI. Continued.

Study identifier and status	Study title	Type of malignancy	Compound studied
NCT02530398	A Tolerance Trial of Cinobufacini Injection Intraperitoneal Perfusion on Digestive System Cancer With Ascites	Digestive system cancer with malignant ascites	Cinobufacini
NCT02647125	A Study of Comparing Huachansu Plus Thoracic RT Versus RT Alone For ESCC	Esophageal squamous cell carcinoma	Huachansu
NCT02871869	Cinobufacini Tablets Combined With Chemotherapeutic Protocol in Treatment of Diffuse Large B Cell Lymphoma	Diffuse large B cell lymphoma	Cinobufacini
NCT02906800	Potential of Cisplatin-based Chemotherapy by Digoxin in Advanced Unresectable Head and Neck Cancer Patients (DIGHANC)	Head and neck cancer	Digoxin
NCT03843229	Clinical Trial of Cinobufacini Combined With Transarterial Chemoembolization (TACE) on Primary Liver Cancer	Liver cancer	Cinobufacini
SERCA			
NCT00920556	A Clinical Study to Assess the Safety and Activity of SRT501 Alone or in Combination With Bortezomib in Patients With Multiple Myeloma	Multiple myeloma (Resveratrol)	SRT501
H/K ATPases			
NCT02387203	Antibiotic Treatment and Long-term Outcomes of Patients With Pseudomyxoma Peritonei of Appendiceal Origin	Pseudomyxoma peritonei, appendiceal neoplasms	Lansoprazole
NCT02388581	First-line Antibiotic Therapy for Early-stage HP(+) Gastric Pure DLBCL	Gastric diffuse large b-cell lymphoma	Lansoprazole
NCT02595372	Inhibiting Fatty Acid Synthase to Improve Efficacy of Neoadjuvant Chemotherapy	Breast cancer	Omeprazole
NCT03028103	Open-Label, Multicenter, Two-Part, Phase 1 Study to Characterize Effects of a Moderate CYP3A Inhibitor on PK of Tazemetostat, Effects of Tazemetostat on PK of CYP2C8 and CYP2C19 Substrates, and Effect of Increased Gastric pH on PK of Tazemetostat in B-cell Lymphoma or Advanced Solid Tumor Patients	Diffuse large B cell lymphoma, primary mediastinal lymphoma, mantle cell lymphoma, advanced solid tumor, marginal zone lymphoma	Omeprazole
NCT03192059	Study of Pembrolizumab, Radiation and Immune Modulatory Cocktail in Cervical/Uterine Cancer (PRIMMO)	Cervical cancer, endometrial carcinoma or uterine sarcoma	Lansoprazole
NCT03267680	IRX-2 Regimen in Treating Women With Cervical Squamous Intraepithelial Neoplasia 3 or Squamous Vulvar Intraepithelial Neoplasia 3	Cervical squamous cell carcinoma in situ, vulvar high grade squamous intraepithelial lesion	Omeprazole
NCT03537833	Association Between Proton Pump Inhibitors and Hematologic Toxicity of Pemetrexed (IPPEM)	Non-small cell lung cancer or mesothelioma	Proton pump inhibitors
NCT03647072	PPI Versus Histamine Antagonists as Adjuvant to Chemotherapy	Non-Hodgkin's Lymphoma	Lansoprazole
NCT03864042	Pharmacokinetic Drug-drug Interaction Study of Encorafenib and Binimetinib on Probe Drugs in Patients With BRAF V600-mutant Melanoma or Other Advanced Solid Tumors	Advanced solid tumors, metastatic melanoma	Omeprazole

## C, Not yet recruiting

Study identifier and status	Study title	Type of malignancy	Compound studied
Na/K ATPases			
NCT03236636	The Phase III Study of Icaritin Versus HUACHANSU PIAN in Hepatocellular Carcinoma Subjects	Hepatocellular carcinoma	Huachansu

Table SI. Continued.

Study identifier and status	Study title	Type of malignancy	Compound studied
NCT03720366	A Study of Perpetrator Drug Interactions of Enasidenib in AML Patients	Acute myeloid leukemia	Digoxin, Omeprazole
D, Withdrawn			
Study identifier and status	Study title	Type of malignancy	Compound studied
Na/K ATPases NCT01562301	Sublingual Anvirzel in Advance Non-Small Cell Lung Cancer (NSCLC)	Lung cancer	Anvirzel
NCT02915666 SERCA	A Clinical Trial of Patients With Melanoma	Melanoma	Digoxin
NCT02261844	Resveratrol and Human Hepatocyte Function in Cancer	Liver cancer	Resveratrol
E, Status unknown			
Study identifier and status	Study title	Type of malignancy	Compound studied
Na/K ATPases NCT00022425	Perillyl Alcohol in Preventing Recurrent Breast Cancer in Women Who Have Been Treated With Surgery With or Without Adjuvant Therapy	Breast cancer	Perillyl Alcohol
NCT01715532	Role of Huachansu in Treating Hepatocellular Carcinoma and the Correlation With Na <sup>+</sup> /K <sup>+</sup> -ATPase	Hepatocellular carcinoma	Huachansu
NCT02860429	Clinical Trial of Cinobufacini Injection Combined With Oxaliplatin Regimen on Gastrointestinal Carcinoma	Gastrointestinal cancer	Cinobufacini
NCT01236690	Study of Hepatoma Treated by Perfusing Cinobufacin Through Hepatic Artery Combining Embolotherapy	Hepatoma	Cinobufacin
F, Terminated			
Study identifier and status	Study title	Type of malignancy	Compound studied
H/K ATPases NCT00332748	A Phase I Study of BMS-275183 (Oral Taxane) Given on a Daily Schedule in Combination With Esomeprazole (Nexium) in Patients With Advanced Cancer	Advanced malignancies	Esomeprazole
NCT01290380	A Study to Evaluate the Effects of ASA404 Alone or in Combination With Taxane-based Chemotherapies on the Pharmacokinetics of Drugs in Patients With Advanced Solid Tumor Malignancies	Solid tumor malignancies	Omeprazole
Na/K ATPases NCT00281021	Second Line Erlotinib (Tarceva) Plus Digoxin in Non-Small Cell Lung Cancer	Non-small cell lung cancer	Digoxin
NCT03113071	Safety and Activity of Digoxin With Decitabine in Adult AML and MDS	Acute myeloid leukemia, myelodysplastic syndromes	Digoxin

SERCA, sarcoendoplasmic reticulum calcium ATPase; MALT, mucosa-associated lymphoid tissue.