

**Table S1.** Select clinical trials of DNA-damage repair targeted agents in clinical trials in solid tumors including non-small cell lung cancer.

Clinical Trial	Medication	DNA-Damage Repair Target by Novel Medication	Tumor Type	Inclusion Criteria	Exclusion Criteria	Selective Biomarkers	End Point
NCT04216316	Addition of Berzosertib (M6620, VX-970) to carboplatin and gemcitabine and pembrolizumab Phase IB, II	ATR inhibitor	Squamous NSCLC	Stage IV disease, Age $\geq$ 18, ECOG 0-1	Prior chemo/immuno therapy for advanced disease, Autoimmune disease	ATM mutation	<i>Primary:</i> RP2D PFS <i>Secondary:</i> PFS (in ATM-deficient), OR, worse grade of adverse events
NCT02589522	Berzosertib (M6620,(VX-970)) with WBRT Phase I	ATR inhibitor	NSCLC, neuroendocrine, small cell lung cancer	Stage IV disease, CNS disease eligible for palliative WBRT, ECOG 0-1 Life expectancy > 2 months	Patients with 1-3 brain mets, eligible for SRS/SRT, greater than 1cm mid-line shift	Germline DDR defects excluded	<i>Primary:</i> Incidence of dose limiting toxicity <i>Secondary:</i> icPFS, OS, QoL, RRR
NCT05450692	Ceralasertib (AZD6738) plus durvalumab versus docetaxel Phase III	ATR inhibitor	NSCLC	Locally advanced or metastatic disease, PD on last line of treatment, life expectancy > 3 months	Persistent toxicity from prior treatment, history of autoimmune disorders	EGFR/ALK wild type	<i>Primary:</i> OS <i>Secondary:</i> PFS, ORR, DoR, TTR, DCR, PFS2, TTD of QoL, AEs
NCT02264678	Ascending dosing of ceralasertib in combination with chemo or novel agents Phase I	ATR inhibitor	NSCLC, H&N SCC, gastric, breast, ovarian ca	Presence of solid tumor not considered appropriate for further standard treatment	Prior exposure to ATM inhibitors, prior treatment with PARPi	ATM	<i>Primary:</i> AE, sAE <i>Secondary:</i> Cmax, PFS, ORR
NCT03334617	Umbrella study of novel agents (ceralasertib) +Durvalumab Phase II	ATR inhibitor	NSCLC	Stage IV, progressed on anti PD1/PD-L1, life expectancy $\geq$ 3 months	History of primary immunodeficiency or autoimmune disorders, CNS disease	EGFR mutation negative ALK fusions negative ROS1, BRAF, MET, RET negative	<i>Primary:</i> ORR <i>Secondary:</i> DCR, DoR, PFS, OS
NCT03833440	Precision Immunology for Advanced Non-small Cell Lung Cancer Patients	ATR Inhibitor	NSCLC	ECOG 0-1, progression after second- or third-line PD-1, PDL-1 inhibitor	Symptomatic or untreated CNS disease, prior autoimmune disease	N/A	<i>Primary:</i> 12w disease control rate <i>Secondary:</i> ORR, PFS, OS, duration of response

	With PD-1 ICI Resistance Phase 2						
NCT02588105	Safety and efficacy of AZD0156 at increase alone or in combination with other anti-cancer treatment in patients with advanced cancer Phase I	ATM inhibitor	Solid tumors	Locally advanced or metastatic cancer, refractory to standard therapy, ECOG 0-1,	Prior treatment with ATM inhibitor, poor lung reserve, symptomatic CNS disease	N/A	<i>Primary:</i> AE rate <i>Secondary:</i> OS, MTD, RAC, CLR,
NCT04550104	Platform of novel agents (AZD0156) in combination with radiotherapy Phase I	ATM inhibitor	NSCLC	Stage IIB, IIIA/IIIB planned to receive curative RT, ECOG 1-2, life expectancy > 6 months	Progression during induction chemotherapy, prior thoracic RT, treatment with pneumotoxic drugs	N/A	<i>Primary:</i> Dose limiting toxicities <i>Secondary:</i> OS, PFS, QLQ-C30, ORR, treatment compliance
NCT00006464	UCN-01 and Cisplatin Phase I	Protein Kinase C inhibitor	Solid tumors	Advanced or metastatic disease without standard curative or palliative measures, ECOG 0-2	Pulmonary dysfunction, NYHA III-IV CHF, DM	N/A	<i>Primary:</i> Dose-limiting toxicities of cisplatin w/ UCN-01 <i>Secondary:</i> ORR, peak plasma concentration
NCT00004059	UCN-01 and Fluorouracil Phase I	Protein Kinase C inhibitor	Solid tumors	Advanced or metastatic disease without standard curative or palliative measures, Karnofsky 60-100%	CAD, DLCO <60% of predicted, CNS disease	N/A	<i>Primary:</i> Dose-limiting toxicities of 5-FU w/ UCN-01 <i>Secondary:</i> ORR, peak plasma concentration
NCT00047242	UCN-01 and Irinotecan Phase I	Protein Kinase C inhibitor	Solid tumors	Advanced or metastatic disease without standard curative or palliative measures ECOG 0-2 Life expectancy > 3 months	CAD, LVEF < 50%, DLCO < 75%	N/A	<i>Primary:</i> Maximum tolerated dose of UCN-01 + irinotecan <i>Secondary:</i> ORR, peak plasma concentration
NCT00551512	CBP501 and Cisplatin Phase I	CHEK1/2 Inhibitor	Solid tumors	Advanced or metastatic disease without standard curative or	Prior chemotherapy with nitrosoureas or high dose carboplatin,	N/A	<i>Primary:</i> Dose limiting toxicity <i>Secondary:</i> AE, sAE, ORR, PFS

				palliative measures	active CNS disease		
NCT00942825	First line triplet combination (CBP501, pemetrexed, and cisplatin) Phase II	CHEK1/2 Inhibitor	Non-squamous NSCLC	Locally advanced or metastatic disease, ECOG 0-1, Life expectance 0-1	Symptomatic CHF, peripheral neuropathy > grade 1, symptomatic CNS disease	N/A	<i>Primary:</i> PFS <i>Secondary:</i> ORR, OS, AE, sAE
NCT03113188	CBP501, Cisplatin, Nivolumab Phase IB	CHEK1/2 Inhibitor	Solid Tumor	Locally advanced or metastatic disease, prior treatment, ECOG 0-1, Life expectance > 3 months	Prior chemotherapy with nitrosoureas, peripheral neuropathy > grade 1, active CNS disease	N/A	<i>Primary:</i> RP2D <i>Secondary:</i> ORR
NCT00413686	AZD7762 alone and in combination with Gemcitabine Phase I	CHEK2 inhibitor	Solid Tumor	Locally advanced or metastatic disease without standard curative or palliative therapy, ECOG 0-1	NYHA II-IV CHD, prior anthracycline, impaired renal or liver function	N/A	<i>Primary:</i> Safety and tolerability <i>Secondary:</i> Single and combination dose PK
NCT00415636	Safety and tolerability of IC83/LY2603618 Phase 1	CHEK1 inhibitor	Solid tumor	At least one lesion that can be evaluated by RECIST, life expectancy > 3 months	CNS disease, pregnancy	N/A	<i>Primary:</i> AEs <i>Secondary:</i> Cmax, percentage of patients with best overall response,
NCT00988858	IC83/LY2603618 in combination with Pemetrexed	CHEK1 inhibitor	NSCLC	Advanced or metastatic disease that has progressed on prior treatment	Pregnancy, prior treatment with pemetrexed	N/A	<i>Primary:</i> ORR, percentage achieving CR, PR. <i>Secondary:</i> PFS, duration of response, LCSS, Cmax
NCT01139775	LY2603618 in Combination with Pemetrexed and Cisplatin Phase I/II	CHEK1 inhibitor	Non-squamous NSCLC	Eligible for first line treatment with platinum doublet, ECOG 0-1	CNS metastasis, serious co-morbidities, third space fluid collection	N/A	<i>Primary:</i> Recommended phase 2 dose, PFS <i>Secondary:</i> OS, ORR, Cmax, LCSS, mortality
NCT00437203	PF-00477736 in combination with gemcitabine Phase I	CHEK1 inhibitor	Solid tumors	Advanced/metastatic disease refractory to standard therapy, ECOG 0-1	Prior treatment with metastasis, uncontrolled CNS disease,	N/A	<i>Primary:</i> MTD with gemcitabine <i>Secondary:</i> OR, Cmax,

NCT02860780	Prexasertib (LY2606368) in combination with Ramlimetinib Phase I	CHEK1/2 inhibitor	Solid tumor	Advanced or metastatic disease, able to swallow tablets	Active infection, active CNS disease, autoimmune disorders.	KRAS and or/BRAF mutations	<i>Primary:</i> MTD <i>Secondary:</i> PK – Cmax, AUC, BOR, DCR, DOR, PFs
NCT02087176	AZD1775 + docetaxel vs placebo + docetaxel Phase II	WEE1 inhibitor	NSCLC	Failure of one platinum-based doublet, ECOG 0-1	Known CNS disease, active infection, NYHA II-IV CHF	N/A	<i>Primary:</i> ORR <i>Secondary:</i> Pharmacokinetic profile
NCT02087241	Carboplatin and Pemetrexed with or without AZD1775 Phase II	WEE1 inhibitor	NSCLC	Recurrent of Stage IV disease, egfr/alk mut patients prior treatment w/ inhibitor ECOG 0-1	Known CNS disease, NYHA II-IV CHF, presence of other active cancers	EGFR mutation, ALK mutation	<i>Primary:</i> PFS <i>Secondary:</i> ORR, Disease control rate, duration of response, OS
NCT02513563	AZD1775 plus carboplatin-paclitaxel Phase II	WEE1 inhibitor	SquamousCLC	Advanced/metastatic disease without curative options, ECOG 0-1	Progressive/symptomatic brain mets, use of platinum or paclitaxel for stage IV disease NYHA II-IV CHF	N/A	<i>Primary:</i> PFS <i>Secondary:</i> OS, OR, SD, DCR
NCT01748825	AZD1775 for Advanced Solid Tumors Phase I	WEE1 inhibitor	Solid tumor	Advanced or metastatic disease without or refractory to standard therapy, ECOG 0-1, Life expectancy > 3 months	Known CNS disease, uncontrolled illness, pregnant women	N/A	<i>Primary:</i> Safety and tolerability, pharmacokinetics <i>Secondary:</i> ORR
NCT02511795	AZD1775 combined with olaparib Phase I	WEE1 inhibitor	Solid tumor	Advanced or metastatic disease without standard treatment, ECOG 0-1	Prior treatment with PARP inhibitor, persistent Grade > 1 toxicity from prior cancer therapy, known CNS disease	N/A	<i>Primary:</i> DLTs, TEAEs <i>Secondary:</i> Cmax, AUC, ORR, PFS, OS, DCR