**Supplementary Table 1: Selected DNA repair targeted therapies currently in clinical trials**

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| **Agent** | **Phase** | **Clinical context** | **CT ID\*** | **Single/combination** | **Selected exploratory biomarkers** |
| **PARP inhibitors** |  |  |  |  |  |
| Olaparib | I | Recurrent ovarian or triple-negative breast | NCT01623349 | Olaparib + BKM120/BYL719 (MEKi) | BRCA1 IHC, methylation; *BRCA1/2* mutations |
|  | II | Recurrent ovarian | NCT02345265 | Olaparib + cediranib (VEGFRi) | HRR gene mutations (BROCA assay), VEGFR3 expression, circulating endothelial cells |
|  | I/II | Recurrent ovarian, germline *BRCA1/2* mutation | NCT02571725 | Olaparib + tremelimumab (anti-CTLA4) |  |
|  | I | Recurrent Ewing Sarcoma | NCT01858168 | Olaparib + temozolomide | gamma-H2AX and RAD51 foci, apoptosis and DNA repair gene/protein expression |
|  | III | Recurrent ovarian, platinum-sensitive | NCT02446600 | Olaparib or olaparib + cediranib (VEGFRi) | Germline *BRCA1/2*, HRR gene mutations (BROCA assay) |
|  | III | Met. pancreatic,  germline *BRCA1/2* mutation | NCT02184195 | Olaparib |  |
|  | II/III | Recurrent ovarian, platinum-resistant/refractory | NCT02502266 | Olaparib + cediranib vs. chemotherapy | HRR gene mutations (BROCA assay), circulating endothelial cells |
|  | I/II | Recurrent endometrial, ovarian, triple negative breast | NCT02208375 | Olaparib + AZD2014 (mTORC1/2 inhibitor) or AZD5363 (AKT inhibitor) | HRR and PI3K/mTOR alterations |
|  | II | AST; eligibility by arm:  1. DNA repair genes for olaparib only  2. PI3K/AKT alterations for AKT inhibitor  3. TP53 and/or KRAS mutation for Wee1 inhibitor  4. TORC1/2, TSC1/2, LKB1, PTEN loss for mTORC1/2 inhibitor | NCT02576444 | Olaparib + AZD5363 (AKT inhibitor) or AZD1775 (Wee1 kinase inhibitor) or AZD2014 (mTORC1/2 inhibitor) |  |
|  | II | Recurrent/metastatic or unresectable NSCLC, SCLC, triple-negative breast, pancreatic | NCT02498613 | Olaparib + cediranib (VEGFRi) | Various biomarkers including miRNA |
|  | I/II | AST (phase I), recurrent ovarian or triple-negative breast (germline *BRCA1/2* mutation) or advanced NSCLC (phase II) | NCT02484404 | Olaparib or cediranib (VEGFRi) + MEDI4736 (anti-PD-L1) | HRR mutations (BROCA assay) |
| Niraparib | III | Adv. ovarian,  Myriad HRD high score | NCT02655016 | Niraparib maintenance after front-line platinum therapy | *BRCA1/2* mutations |
|  | II | Recurrent ovarian | NCT02354586 | Niraparib | Myriad HRD assay, germline *BRCA1/2* mutations |
|  | I | Recurrent Ewing sarcoma | NCT02044120 | Niraparib + temozolomide |  |
|  | I/II | Recurrent ovarian or adv./met. triple-negative breast | NCT02657889 | Niraparib + pembrolizumab (anti-PD-1) | Myriad HRD immune response studies |
|  | III | Adv./met. breast, germline *BRCA1/2* mutations | NCT01905592 | Niraparib vs. physician’s choice |  |
| Veliparib | III | Met. breast, germline *BRCA1/2* mutations, HER2 negative | NCT02163694 | Carboplatin/paclitaxel +/- veliparib |  |
|  | I | Recurrent ovarian, met. breast | NCT01145430 | Veliparib + liposomal doxorubicin |  |
|  | III | Adv. ovarian (new diagnosis) | NCT02470585 | Carboplatin/paclitaxel + veliparib, veliparib maintenance |  |
|  | I | Met. ovarian | NCT01749397 | Veliparib + floxuridine | Mutations in HRR and NHEJ |
|  | I | Adv./met. breast | NCT01351909 | Veliparib + cyclophosphamide | macroH2A1.1 and PARP1 expression |
|  | II/III | Glioblastoma (new diagnosis) | NCT02152982 | Temozolomide +/- veliparib | MGMT methylation; DNA repair/replication gene alterations; polymorphisms in MGMT, PARP1, and DNA repair genes |
|  | I/II | Adv Head & neck | NCT01711541 | Chemotherapy +/- veliparib |  |
|  | I | AST | NCT02723864 | Veliparib + VX-970 (ATR inhibitor) + cisplatin | Markers of DNA damage and apoptosis |
|  | II | Stage III NSCLC | NCT02412371 | Veliparib + carboplatin + paclitaxel + XRT |  |
|  | I | Adv. ovarian (new diagnosis) | NCT00989651 | Veliparib + carboplatin + paclitaxel + bevacizumab (anti-VEGF) | Germline *BRCA1/2* mutations, PARP inhibition in peripheral blood mononuclear cells |
|  | I | AST, hepatic/renal dysfunction | NCT01366144 | Veliparib + carboplatin + paclitaxel | Gamma-H2AX foci, PAR levels |
|  | II | Adv./met. pancreatic, *BRCA1/2* or *PALB2* mutation | NCT01585805 | Veliparib or gemcitabine + cisplatin +/- veliparib | PAR levels, BRCA reversion, expression profiles, DNA and RNA sequencing |
|  | I | AM | NCT00576654 | Veliparib + irinotecan | Gamma-H2AX foci, RAD51 levels, PARP levels, PAR activity, Pharmacogenomic biomarker for irinotecan:UGT1A1\*28 allele |
|  | I | Extensive stage SCLC | NCT02289690 | Veliparib + carboplatin + etoposide |  |
|  | I | AST | NCT01434316 | Veliparib + dinaciclib (CDK inhibitor) | *BRCA1/2* mutation, Myriad HRD score, CDK and PARP1 activity, HRR protein expression including BRCA1 and RAD51, DNA damage levels |
|  | I | Adv./met. NSCLC | NCT02264990 | Veliparib + carboplatin/paclitaxel or other chemotherapy |  |
|  | I | AST | NCT02631733 | Veliparib + liposomal irinotecan |  |
|  | II | Met. breast, triple-negative or germline *BRCA1/2* mutation | NCT02595905 | Cisplatin +/- veliparib | Myriad HRD score, , PAM50 expression profile score, BRCA1 mRNA expression |
|  | I/II | Met. pancreatic, personal or family history of germline mutation in *BRCA1/2*, *PALB2*, or *FANC* genes, or family history suggesting breast/ ovarian cancer syndrome | NCT01489865 | Veliparib + modified FOLFOX6 chemotherapy (5-FU, oxaliplatin) |  |
| Rucaparib | I/II | AST, ovarian; germline or somatic *BRCA1/2* mutation | NCT01482715 | Rucaparib |  |
|  | III | Recurrent ovarian platinum-sensitive | NCT01968213 | Rucaparib after platinum chemotherapy | Foundation Medicine LOH profiling, HRR gene mutations |
|  | II | Recurrent ovarian | NCT01891344 | Rucaparib | Foundation Medicine LOH profiling |
| Talazoparib (BMN673) | III | Adv./met. breast, germline *BRCA1/2* mutation | NCT01945775 | Talazoparib |  |
|  | I/II | AST with *BRCA1/2* mutations | NCT01989546 | Talazoparib | PAR levels, DNA damage response markers, CHK1/2 levels |
|  | II | Adv./met. breast, germline *BRCA1/2* mutations | NCT02034916 | Talazoparib |  |
|  | II | Adv./met. breast, triple-negative with Myriad HRD high score or HER2-negative with germline or somatic mutation in a non-*BRCA1/2* HRR gene; NO known deleterious germline *BRCA1/2* mutation | NCT02401347 | Talazoparib |  |
| **ATM/ATR inhibitors** |  |  |  |  |  |
| VX-970 (ATR) | II | Recurrent ovarian, platinum-resistant | NCT02595892 | VX-970 + gemcitabine |  |
|  | II | Recurrent ovarian, platinum-sensitive | NCT02627443 | VX-970 + carboplatin + gemcitabine | DNA damage by multiplex assay, HRR gene mutations |
|  | II | Met. urothelial | NCT02567409 | VX-970 + cisplatin + gemcitabine | p53, p21, and *ERCC2* mutations |
|  | I/II | I: SCLC, NSCLC, ovarian, cervical, neuroendocrine  II: SCLC | NCT02487095 | VX-970 + topotecan |  |
|  | I | Adv. head & neck | NCT02567422 | VX-970 + cisplatin + XRT | Tissue-based biomarkers of DNA damage |
|  | I | NCLC with brain metastases | NCT02589522 | VX-970 + WBRT | pATR T1989, pCHK1 S345 and RAD51 in cerebral spinal fluid; ATR, cyclin E amplification, pCHK1 S345, and DNA-PK expression status in tumor biopsy |
|  | I | AST | NCT02595931 | VX-970 + irinotecan |  |
|  | I | AST | NCT02723864 | VX-970 + veliparib (PARPi) + cisplatin | Markers of DNA damage and apoptosis |
|  | I | AST; specific cohorts for NSCLC and triple-negative breast | NCT02157792 | VX-970 + chemotherapy | TP53 mutation or ATM loss of expression in tumor |
| AZD6738 (ATR) | I/II | AST (selected tumors for expansion cohorts) | NCT02264678 | AZD6738 +/- carboplatin, olaparib (PARPi), or MEDI4736 (anti-PD-L1) | ATM deficiency for lung and gastric/gastroesophageal junction tumors in expansion cohorts |
| AZD0156 (ATM) | I | AM | NCT02588105 | AZD0156 +/- olaparib | Expression of ATM-related proteins |
| **NHEJ inhibitors** |  |  |  |  |  |
| CC-122 | I | AM | NCT01421524 | CC-122 |  |
| MSC2490484A |  | AM | NCT02516813 | MSC2490484A + XRT |  |
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Selected DNA repair targeted agents (PARP inhibitors, ATM/ATR inhibitors, and NHEJ inhibitors) currently in clinical trials in the United States. Trials were identified via keyword search (agent and target) of clinicaltrials.gov (April/May 2016) with search limited to United States, Phase I/II/III, age >18, and open studies. Biomarkers are limited to those reported on the clinicaltrials.gov website or by personal communication and may not be comprehensive. See clinicaltrials.gov for updated trial information and eligibility.

\*CT ID – Trial ID in clinicaltrials.gov

*BRCA1/2:* BRCA1 and BRCA2

IHC: immunohistochemistry

XRT: radiation therapy

AM: advanced malignancies (may include some hematologic cancers); AST: advanced solid tumors

Ovarian cancer: includes ovarian, fallopian tube, primary peritoneal cancers

Met.: metastatic

Adv.: advanced

WBRT: whole brain radiation therapy

SCLC: small cell lung cancer; NSCLC: non-small-cell lung cancer

CRPC: castration resistant prostate cancer

BROCA assay: Targeted next-generation sequencing assay including genes involved in homologous recombination repair

Myriad HRD: Myriad Genetics assay for HRR deficiency based on several copy number indices

“i” indicates inhibitor (e.g. PARPi = PARP inhibitor)