**Supplementary tables for:**

**The novel ATR inhibitor BAY 1895344 is efficacious as monotherapy and combined with DNA damage-inducing or repair-compromising therapies in preclinical cancer models**

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**Supplementary Tables**

**Table S1.** In-house kinase selectivity profile of BAY 1895344.

|  |  |
| --- | --- |
| Kinase | IC50 [nM] with 10 µM ATP  (median ± SD) |
| ATR/ATRIP | 7 ± 3.7 |
| mTOR | 35 ± 32 |
| DNA-PK | 332 ± 756 |
| ATM | 1420 ± 325 |
| PI3Kß | 3270 ± 1270 |
| EGFR | 3660 ± 5110 |
| PDGFRß | 18200 ± 3690 |

ATR, ataxia telangiectasia and Rad3-related kinase; ATRIP, ATR-interacting protein; mTOR, mechanistic target of rapamycin; DNA-PK, DNA-dependent protein kinase; ATM, ataxia telangiectasia mutated kinase; PI3Kß, phosphoinositide 3-kinase beta; EGFR, epidermal growth factor receptor; PDGFRß, Platelet-derived growth factor receptor beta.

**Table S2.** Binding of BAY 1895344 to kinases identified in the KINOME*scan*® Profiling Service at DiscoverX.

|  |  |  |
| --- | --- | --- |
| Kinase | BAY 1895344  Kd [nM] | % of control signal at  1 µM of BAY 1895344 |
| DYRK1B | 25000 | 11 |
| mTOR | 24 | 2.2 |
| GAK | 580 | 27 |
| GSK3A | >30000 | 31 |
| RIOK2 | 660 | 24 |
| VPS34 | 3200 | 17 |

DYRK1B, dual specificity tyrosine phosphorylation regulated kinase 1B; mTOR, mechanistic target of rapamycin; GAK, cyclin G-associated kinase; GSK3A, glycogen synthase kinase-3 alpha; RIOK2, right open reading frame (3) kinase 2; VPS34, class III PI3-kinase.

**Table S3:** The efficacy of the ATRi BAY 1895344 in inhibiting cell proliferation in a panel of human cancer cell lines covering various types of cancer.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Tumor type | Cell line | Provider | DDR/MMR defects | Oncogenic replication stress or  TP53/tumor suppressors | *In vitro* IC50 (nM) |
| Mammary carcinoma | HCC70 | ATCC  CRL-2315 | *MSH3PPA66-68-, RB1DN479-480D* | *PTENfs, TP53R248Q* | 27 |
| Mammary carcinoma | MDA-MB-436 | CLS  300278 | *BRCA1splice\_donor, FANCIS812G, MLH3F92L, PRKDCL1824F;fs* | *TMPRSS2V101F*, *MYCamp+, TP53fs* | 120 |
| Mammary carcinoma | MDA-MB-468 | ATCC  HTB-132 | *BLMD554V, BRCA2M965I, FANCAQ869\*,*  *FANCEGG245-246G, FBXO18G193A, SLX4E1784Q, XRCC5L536F* | *ERBB2fs, ATR(2633+5A>G, Substitution-intronic), PTENsplice\_donor, TP53R273H* | 130 |
| Colorectal carcinoma | LOVO | DSMZ  ACC-350 | *MSI-H, ARID1AF2141fs\*59, BLMfs, CCNT1S431N, DDB1V637I, ERCC3Q711R, FANCAR350W, FBXW7R505C, GTF2H1T503M, MSH3L795H, NBNfs, NEIL1fs, truncation, PNKPP7S, POLHT477I, BLMfs, POLQfs, PRKDCfs, RAD50fs, XRCC5F183L* | *APCR1114\*; R2816Q;fs, CCNT1S431N, CDK5R1T138M, KRASG13D, CDK5R1T138M* | 71 |
| Colorectal carcinoma | HT-29 | DSMZ  ACC-299 | *FANCMfs, POLNR761\*, POLQS1819\*, PRKDCfs, RFC1spliceRegion, WRNL1255V* | *APCE853\*, fs, MYCamp, BRAFV600E, T119S, CDKL5P295H, PIK3CAP449T, TP53R273H`* | 160 |
| Colorectal carcinoma | Caco2 | DSMZ  ACC-169 | *ERCC8Q326H* | *APCQ1367\*, ERBB3D857N* | 240 |
| Colorectal carcinoma | HCT-116 | DSMZ  ACC-581 | *ATMA1127V, ATRXTK1529-1530K, BRCA2fs, CDK12P250H, CHEK2L398P, ERCC4\_T221A, ERCC5splice\_donor, FANCAfs, FBXO18A1062V, GEN1R401Q, GTF2H1R16C, LIG1D410N, MLH1S252\*, MSH2spliceRegion, intron, truncation, MMS19Q443K, MSH3fs, MSH6fs, POLHA112T, POLQK2571N, PRKDCY2964C, RAD50fs, REV3Lfs, SLX4A1461fs\*2, TRRAPH3023Y; T3663A, USP1R180\*, WRNE480V* | *CCNKA469V, CDK8V195A, ERBB3Q261\*, TOP2Afs, TOP2BR651H, KRASG13D, PIK3CAH1047R* | 25 |
| Glioblastoma | U-87MG | ATCC  HTB-14 | *RAD50D515G, RAD54LR691Q* | *ATRXN564S, PTENsplice\_donor* | 64 |
| Glioblastoma | M059J | ATCC  CRL-2366 | *FANCAR1409W, NEIL1P233R, PRKDCfs, RAD54BP98L, TDP2R317\** | *CCNE1R95L, ERBB2W452S, PTENfs, RB1spliceRegion, intron, TP53E286K* | 80 |
| Human cervical adenocarcinoma | HeLa | ATCC  CCL-2 | *BRIP1R855H, REV3LQ2891\*, UIMC1R536W* | *ARLQQQQQQQQQQQ57-68L, EGFRI646L* | 150 |
| Non-small cell lung carcinoma | NCI-H1838 | ATCC  CRL-5899 | *ATMW1279\*, BRCA1C328Y, CDK12R1473Q, GTF2H1fs, truncation, RAD50L347P, MSH3AAAAAAAAPP55-64A; PPA66-68-, PRKDCfs* | *ATRP1991S, TP53R273L* | 24 |
| Non-small cell lung carcinoma | NCI-H1703 | ATCC  CRL-5889 | *ATMV1521L; G1998E, BRCA1G890V, FANCD2V97I, MSH3AAAAAAAAPP55-64A;PPA66-68-, PRKDCfs* | *TP53splice\_donor* | 46 |
| Non-small cell lung carcinoma | NCI-H460 | ATCC  HTB-177 | *ARID1ALI2134-2135-;LIL2134-2136L, FANCD2spliceRegion, intron, NBNG224A, REV3LQ1367L, MSH3AAAAAAAAPP55-64A, PRKDCfs* | *KRASQ61H, PIK3CAE545K, MYCamp* | 65 |
| Non-small cell lung carcinoma | NCI-H2030 | ATCC  CRL-5914 | *MSH3AAAAAAAAPP55-64A; PPA66-68-, PRKDCfs,*  *TDP1spliceRegion, intron* | *KRASG12C, TP53G262V* | 160 |
| Non-small cell lung carcinoma | NCI-H23 | ATCC  CRL-5800 | *ARID2M452V, ATMQ1919P, BARD1A168T, BRIP1E1054A, FANCID1048Y, LIG1Q654L, MSH3E251\*, MDC1N1233S, NBNV153I, PMS2E491K, PRKDCfs, SLX4ED1148-1149D* | *CCNE1D83N, CDK10I52F, KRASG12C/amp, TOP2BH977Y, MYCamp, NRASamp, TP53M246I* | 18 |
| Non-small cell lung carcinoma | A549 | DSMZ  ACC-107 | *ATRsplice\_acceptor, MSH3PPA66-68-, PRKDCfs,*  *SLX4spliceRegion, intron* | *KRASG12S, ATRsplice, CCNE1amp* | 29 |
| Germinal center B cell-like diffuse large B cell lymphoma | SU-DHL-8 | DSMZ  ACC-573 | *ATMK1964E, FANCD2R1165Q, FEN1L190V, REV3LV1004E, PRKDCfs* | *MYCp72S, Q10H, BRAFT599TT, CDC7K42N, TOP2AG1197E, TP53R249G; Y234N* | 9 |
| Activated B cell-like diffuse large B cell lymphoma | TMD-8 | Charité, Berlin, Germany | *BRIP1S59P, ERCC2H148R, MLH1V16L* | *APCK1170E, MYCF3L* | 179 |
| Lymphoma, mantle cell | REC-1 | ATCC  CRL-3004 | *ATMS707P/amp, PRKDCK3872R;fs, POLNN382S* | *KRASamp, TP53Q317\*; G245D* | 10 |
| Lymphoma, mantle cell | Jeko-1 | DSMZ  ACC-553 | *ATMamp, ATRXR246C, BAP1S609G, BRCA1N742S, C17orf70P93S, CHEK2V218A, DCLRE1AR1002C, ERCC2V231M, ERCC6V127I, MLH3I397-, PRKDCfs, RB1R621S, SLX4G395C* | *ATRT1751A, CCNA1F347L, TMPRSS2Y82D, TP53fs* | 18 |
| Lymphoma, mantle cell | GRANTA-519 | DSMZ  ACC-342 | *ATMR2832C;splice\_acceptor, ERCC8I189V, REV3LspliceRegion, intron* | *CCNKK137Q,*  *PRKDCfs, spliceRegion, intron, elongation* | 30 |
| Lymphoma, mantle cell | JVM-2 | ATCC  CRL-3002 | *FANCMQ1701\*, MSH3AAAAAAAAPP55-64A, PRKDCfs* | *CCNB1N12K* | 32 |
| Melanoma | HT-144 | ATCC  HTB-63 | *ATMW2845\*, FANCIspliceRegion, PRKDCfs, XRCC3E278K* | *BRAFV600E, CDK13A476T* | 40 |
| Neuroblastoma | SH-SY5Y | ATCC  CRL-2266 | *CHEK2fs, MSH3PPA66-68-, PRKDCfs* | *none* | 13 |
| Ovarian carcinoma | A2780 | ECACC-93112519 | *ARID1AQ1430\*, R1721fs\*4, ATMP604S, FANCMfs, PARP4G630E, POLHR356Q, PRKDCfs, RBBP8K676N* | *ATRI123V, ERBB3V1082I, PTENK128;R130del, TOP2BV530I, BRAFV226M, PIK3CAE365K* | 21 |
| Ovarian carcinoma | SK-OV-3 | ATCC  HTB-77 | *ARID1AQ586\*, ATMsplice\_acceptor, FANCMA205V, FBXW7R505L, TDP1Y46C, TOPBP1N295S* | *APCfs, TOPBP1N295S, PIK3CAH1047R, KRASamp, CDC7del, TP53fs* | 33 |
| Ovarian carcinoma | IGROV-1 | NCI-60 panel; Sample ID No. 26 | *MSI-H, ARID1AD1850fs\*4,G276fs\*87, ATMR248Q, BRCA1K654fs\*47, BRCA2P3150T, C1orf86W180C, CHEK1fs, DDB1D1115N, LIG3fs; truncation, MLH1S505fs\*3;A586V, MRE11AR525K, MSH3G539V; F780L; D943N, MSH6fs, MUTYHspliceRegion, PALB2T787I, POLQfs; L45I, POLNfs, PNKPT490A, PRKDCC1454Y;Y155C, PTENY155C, RAD50fs, RAD52E130K, RBBP8fs, TDP1N179S, TRRAPS2051F, USP1V636I,UIMC1A418T* | *ARA400V, CCNB1D47N, ERBB3K742, PIK3CAR38C;\*1069W, PTENfs, RB1fs, TOP2AH605Q, TOPBP1D395G, TP53Y126C;fs* | 96 |
| Ovarian carcinoma | OVCAR-8 | NCI-60 panel; Sample ID No. 25 | *ATMV613L, GTF2H4L327F, MGMTP233L, MSH6T727S, PRKDC\_fs, REV3LL3040V, XPCA193V* | *APCA1225S, ERBB2G776V, KRASP121H, MYCamp, TP53splice\_acceptor* | 110 |
| Pancreatic carcinoma | BxPC3 | ATCC  CRL-1687 | *ERCC2R156Q, PRKDCfs* | *BRAFVTAPTP487-492A, TP53Y220C* | 44 |
| Pancreatic carcinoma | AsPc-1 | ATCC  CRL-1682 | *FBXW7R465C, PARP4M1110L, PRKDCfs* | *DYRK1AS14C, KRASG12D, TP53fs* | 49 |
| Pancreatic carcinoma | MIA Pa-Ca2 | ATCC  CRL-1420 | *ARID1AP1940L, ERCC6E1351D, MLH1T270I, PALB2S64L* | *CCNB3K347E, KRASG12C, TP53R248W* | 380 |
| Prostate carcinoma | LNCaP | DSMZ  ACC-256 | *ARID1Afs, ATG5fs, ATMA1119V/K1572N, ATRXEE2264-2265E, BAP1V569M, BARD1V297L, BLMP465H, BRCA2fs, BRIPQ322R, CHEK2T430N, DCLRE1BR207C/E223D, DDB1R198\*, DYRK1AK481\*, ERCC3A740T/R391W/P335S, ERCC5R420S/G1080R, EXO1E170\*, FANCAE369D;Q652\*;spliceRegion, intron;Q652\*, FANCD2N405S/spliceRegion, FANCFL157F, HDAC2A62V, LIG3A780V, LIG4N827T, MMS19R316Q;L104I;M1V, MLH3I541V, MSH3PPA66-68-; fs;K381X, MSH6P1073S, NBNN534K, PARP3W105\*, PARP4T1170I/V1065A/F714L/A2013T, POLA1A422T, POLBfs;R126X, POLHA461S/D631G, POLLQ270K, PRKDCfs, PTENfs, truncation, RAD17A119V/D610G, RAD18V82I, RAD50fs, RAD52A75P, RAD54LL532M, RB1splice\_acceptor, RBBP8fs, elongation, REV3LS2751G/R2212M/P2095S, SLX4S605N/K1576E/K1575KX/G141W, TDP1E99G,*  *TOP2Afs, truncation/R1435X, TOP2BV889A;G323\*;D1383N;L1225S, TDP2T308S, TP53BP1R639Q; Q111\*, TRRAPV503A/Q587\*/K1512N/R2390Q/R2665W, WDR48G107\*,A632V, XRCC2T83I, XRCC3P87L, XRCC4L70M* | *APCR2714C, ATRK1379N, BRAFV639A/T241X, CCNB3V402L, CCNE1D79N, CDC7L28X/Q80\*, CDK11AK476T, CDK12D159EX/G750R, CDKL5spliceRegion, intron;spliceAccept, EGFRV292A, ERBB2E325K/V910E/E930D, ERBB3K177N/R388W, HDAC2A62V/K11X, MYCN45S, NRASA91V, PIK3CAA442V, PTENfs, RB1spliceRegion/K765I, TOP2Afs, TOP2BG323\*/V889A, TP53E336K, TP53BP1L1425FX/R639Q/M267I/Q111\** | 18 |
| Prostate carcinoma | 22Rv1 | ATCC  CRL-2505 | *ATMK1101E, ARID1Afs, BARD1fs, BRCA2V1810Ifs, DCLRE1Cfs, FANCAfs, MSH3fs, NBNR43Q, PALB2V1123M, PARP4R970W, PRKDCfs, RAD18L314V, RAD50T532I, SLX4fs, TP53BP1fs, USP1fs, WRNfs, XRCC2fs* | *PIK3CAQ546R, ATRfs, BRAFL597R, ERBB3R683Q, TP53Q331R* | 36 |
| Prostate carcinoma | VCaP | VTT | *MSH3PPA66-68-, MSH6fs* | *CCND1S219N, TMPRSS2-ERG, MYCamp, TP53R248W* | 51 |
| Prostate carcinoma | LAPC-4 | VTT | *ARID1A-2138-2139X, ATMsplicedonor, BAP1P723L, BRCA2fs, CDK12W1459X, ERCC2E313K, ERCC3R642Q/ V443A/E259D, ERCC5G1080R, FANCD2N405S;P714L, FANCMF1612L, P1081X, splice\_donor, GEN1K42E, H2AFXN95S, LIG4T219A, MLH3K585X, MSH2M300R, splice\_donor, MSH3K381X, PALB2V398A, PARP1W589C, PARP3H441R, PARP4T1170I, V1065A, Q1059R, I1039T, V626D, POLHD140N, POLQS1797I, M587I, PRKDCQ4041H, RAD17R49X, RAD51C320Y, RAD54BI164T, REV3LS2862T, P2172L, TRRAPD394G, M1087I, P2026L, H3174Y, A3655V, WDR48S611P, WRNE3X, K1126X* | *ATRR1951\*stop/amp, CDC7A342V/D571G, EGFRV980D, TP53H178PX, R175H* | 55 |
| Prostate carcinoma | DU-145 | DSMZ  ACC-261 | *ATG5splice\_donor, BRCA1E962K, BRCA2S2284L, BRIP1T132N, C17orf70L841Q, CCNHspliceRegion, DDB1V510A, DYRK1AR226H, ERCC6F1437I;Q794H, EXO1spliceRegion, FANCBG702W, FANCIfs, GEN1Q554H, LIG4R32C;spliceRegion, MLH1A586V, splice, MMS19A330V, MSH2L736I, MSH3fs, MSH6S1067I, PMS2H189Y, POLA1A550S, POLLA285T, POLQV124M, PRKDCfs, RAD50N509K, RB1K715\*, RBBP8S679G, REV3LR2523C, RFC1Y830C, RPA2E252D, TP53BP1splice\_acceptor, TRRAPfs; A1389T, UIMC1A96D, UBE2Nfs, USP1fs, WDR48spliceRegion, XPAfs, XRCC1splice\_acceptor, XRCC2fs* | *CDK7spliceAccept, CDK9fs, CDKL5R822S;R822I, KRASamp, DYRK1R226H, TMPRSS2splice\_acceptor, TP53V274F; P223L* | 110 |
| Prostate carcinoma | PC-3 | DSMZ  ACC-465 | *MSH3AAAAAAAAPP55-64A; PPA66-68, PRKDCfs* | *CDK11Afs, MYCamp, TP53fs, TRRAPR696H* | 490 |
| Prostate carcinoma | C4-2B | MD Anderson Cancer Center | *MSI-H, ARID1Ac.854delG\_p. G285fs\*78, ATRXE2265del, MSH2loss, TRRAPQ1984\** | *PTENdel* | 50 |

ATCC, American Type Culture Collection; ECACC, European Collection of Authenticated Cell Cultures; NCI, National Cancer Institute; CLS, Cell Line Service GmbH, Germany; DSMZ, Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH, Germany; MD Anderson Cancer Center, Houston, USA; VTT, VTT Technical Research Centre of Finland Ltd.

DDR, DNA damage response; IC50, half-maximal inhibitory concentration; MMR, mismatch repair.

**Table S4:** Calculated EC50 values and combination indexes (CI) from proliferation assays of cancer cell lines treated with combinations of the ATRi BAY 1895344 and the DNA-damaging agents cisplatin, bleomycin, and SN-38 (active metabolite of irinotecan), the tubulin stabilizer docetaxel, and DNA damage response pathway inhibitors AZD0156 (ATM inhibitor), M9831 (VX-984, DNA-PKcs inhibitor), AZD7762 (CHEK1/2 inhibitor), PF 00477736 (CHEK1 inhibitor), MK-8776 (CHEK1 inhibitor), and AZD1775 (WEE1 inhibitor). Listed is in case of synergism the lowest CI50, in case of antagonism the highest CI50, and in case of additivity the CI50 range.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cell line** | **Single agent EC50** | | **Combination** | | |
|  | **BAY 1895344** | **Cisplatin** | **BAY 1895344 EC50 *plus* Cisplatin EC50** | | **CI50** |
| HT-29 | > 5.9·10-7 M | 8.0·10-6 M | 4.0·10-8 M | 5.6·10-7 M | 0.14 |
| LOVO | 3.0·10-8 M | 3.4·10-6 M | 3.6·10-9 M | 1.6·10-7 M | 0.17 |
| PC-3 | 3.9·10-7 M | 1.0·10-5 M | 2.0·10-8 M | 4.0·10-7 M | 0.15 |
| HeLa | 2.0·10-7 M | 3.0·10-6 M | 1.8·10-8 M | 2.4·10-7 M | 0.17 |
| HT-144 | 7.2·10-8 M | 1.3·10-6 M | 9.2·10-9 M | 1.8·10-7 M | 0.27 |
| NCI-H460 | > 3.6·10-7 M | 2.4·10-6 M | 5.7·10-8 M | 4.8·10-7 M | 0.36 |
|  | **BAY 1895344** | **Bleomycin** | **BAY 1895344 EC50 *plus* Bleomycin EC50** | | **CI50** |
| HT-29 | 1.5·10-7 M | 2.7·10-5 M | 6.4·10-8 M | 4.5·10-6 M | 0.59 |
| LOVO | 2.8·10-8 M | 1.2·10-7 M | 7.7·10-9 M – 2.7·10-8 M | 3.0·10-9 M – 6.9·10-8 M | 0.80 – 1.0 |
| PC-3 | 2.7·10-7 M | 3.8·10-6 M | 2.4·10-8 M | 4.7·10-7 M | 0.21 |
| HT-144 | 5.5·10-8 M | 1.0·10-6 M | 3.8·10-9 M | 2.7·10-7 M | 0.32 |
| MDA-MB-231 | 1.5·10-7 M | 7.8·10-6 M | 1.4·10-8 M | 1.9·10-6 M | 0.33 |
|  | **BAY 1895344** | **SN-38** | **BAY 1895344 EC50 *plus* SN-38 EC50** | | **CI50** |
| HT-29 | 1.5·10-7 M | 1.2·10-8 M | 1.8·10-8 M | 3.7·10-9 M | 0.43 |
| LOVO | 2.9·10-8 M | 6.8·10-9 M | 8.6·10-9 M | 1.7·10-9 M | 0.55 |
| PC-3 | 1.8·10-7 M | 1.2·10-8 M | 2.3·10-8 M | 1.7·10-9 M | 0.27 |
| HT-144 | 4.7·10-8 M | 7.5·10-9 M | 6.7·10-9 M | 5.0·10-10 M | 0.21 |
| MDA-MB-231 | 1.5·10-7 M | 2.1·10-8 M | 7.1·10-9 M | 1.7·10-9 M | 0.13 |
|  | **BAY 1895344** | **Docetaxel** | **BAY 1895344 EC50 *plus* Docetaxel EC50** | | **CI50** |
| 22Rv1 | 8.6·10-8 M | 7.4·10-10 M | 5.9·10-9 M | 8.9·10-10 M | 1.27 |
|  | **BAY 1895344** | **AZD0156** | **BAY 1895344 EC50 *plus* AZD0156 EC50** | | **CI50** |
| HT-29 | 3.3·10-7 M | 2.4·10-6 M | 1.3·10-7 M | 1.4·10-7 M | 0.45 |
| LOVO | 1.9·10-8 M | 1.5·10-6 M | 9.3·10-9 M | 6.2·10-8 M | 0.52 |
| PC-3 | 3.5·10-7 M | 1.5·10-6 M | 1.3·10-7 M | 1.5·10-7 M | 0.48 |
| HT-144 | 4.0·10-8 M | 2.6·10-6 M | 2.0·10-8 M – 4.0·10-8 M | 4.5·10-8 M – 1.8·10-6 M | 1.0 – 1.2 |
|  | **BAY 1895344** | **M9831** | **BAY 1895344 EC50 *plus* M9831 EC50** | | **CI50** |
| HT-29 | 3.7·10-7 M | > 3.0·10-5 M | 7.3·10-8 M | 2.0·10-5 M | < 0.61 |
| LOVO | 2.4·10-8 M | 1.9·10-5 M | 1.5·10-8 M – 2.5·10-8 M | 8.4·10-8 M – 4.1·10-6 M | 0.85 – 1.16 |
| PC-3 | 4.5·10-7 M | > 3.0·10-5 M | 2.8·10-7 M | 3.6·10-6 M | < 0.69 |
| HT-144 | 5.0·10-8 M | > 3.0·10-5 M | 3.3·10-8 M | 3.9·10-6 M | < 0.72 |
|  | **BAY 1895344** | **AZD7762** | **BAY 1895344 EC50 *plus* AZD7762 EC50** | | **CI50** |
| LOVO | 2.9·10-8 M | 9.1·10-8 M | 8.1·10-9 M | 1.9·10-8 M | 0.49 |
| PC-3 | 3.1·10-7 M | 8.3·10-7 M | 4.3·10-8 M | 4.3·10-8 M | 0.19 |
|  | **BAY 1895344** | **PF 00477736** | **BAY 1895344 EC50 *plus* PF 00477736 EC50** | | **CI50** |
| LOVO | 3.5·10-8 M | 1.6·10-7 M | 1.6·10-8 M | 3.7·10-8 M | 0.69 |
| PC-3 | 3.8·10-7 M | > 1.0·10-6 M | 1.2·10-7 M | 1.7·10-7 M | < 0.43 |
|  | **BAY 1895344** | **MK-8776** | **BAY 1895344 EC50 *plus* MK-8776 EC50** | | **CI50** |
| LOVO | 5.4·10-8 M | 5.4·10-7 M | 2.7·10-8 M | 1.2·10-7 M | 0.72 |
| PC-3 | 5.2·10-7 M | > 1.0·10-5 M | 3.0·10-7 M | 7.4·10-7 M | 0.63 |
|  | **BAY 1895344** | **AZD1775** | **BAY 1895344 EC50 *plus* AZD1775 EC50** | | **CI50** |
| LOVO | 3.5·10-8 M | 2.5·10-7 M | 1.9·10-8 M | 2.8·10-8 M | 0.64 |
| PC-3 | 6.7·10-7 M | > 3.0·10-6 M | 1.4·10-7 M | 2.8·10-7 M | < 0.29 |

CI50 interpretation code: CI50 ≤0.8, synergism; 0.8< CI50 <1.2, additivity; CI50≥1.2, antagonism

ATM, ataxia-telangiectasia mutated kinase; CHEK1/2, checkpoint kinase ½ (Chk1/2); CI50, combination index calculated when using the EC50 concentrations of the drugs; DNA-PKcs, DNA-dependent protein kinase, catalytic subunit; EC50, half-maximal effective concentration; WEE1, WEE1 G2 checkpoint kinase.