**A**

[Graph showing cell viability over PARPi concentrations for UWB1+B1, UWB1, SYr2, SYr3, SYr8, SYr9, SYr12, SYr13, SYr14, SYr30, SYr37, SYrA, SYrB, and SYrC.]

**B**

[Graph showing cell viability over PARPi concentrations for UWB1+B1, UWB1, SYr2, SYr3, SYr8, SYr9, SYr12, SYr13, SYr14, SYr30, SYr37, SYrA, SYrB, and SYrC.]

**C**

- BRCA1 (N-term)
- BRCA1 (C-term)
- 53BP1
- Rif1
- Rev7
- PTIP
- KU70
- Tubulin
- GAPDH

**D**

- Relative levels of total BRCA1 mRNA
- Relative Δ11q BRCA1 mRNA

**E**

- BRCA1
- Full-length
- Δ11q
- Full + Δ11q
- GAPDH

*Fig. S1*
Fig. S1
Fig. S1
Fig. S2

[Graph showing the relationship between % Cell Viability and [PARPi], μM for different cell lines: HCC1937+B1, HCC1937+B1 + ATRi (0.5μM), HCC1937+B1 + ATRi (1μM), and HCC1937 (BRCA1-).]
Fig. S3

% RAD51+/H2AX after 10 Gy IR

A

B

C

D
**A**

| I-SceI | - | + |
|--------|---|---|
| **DMSO** | 0.13% | 8.21% |
| **ATM (KU55933)** | 0.10% | 7.96% |
| **ATRi (VE821)** | 0.06% | 3.34% |
| **ATRi (AZ20)** | 0.07% | 1.51% |

**B**

| CPT: | DMSO | VE821 (10 μM) | AZ20 (1 μM) | KU55933 (10 μM) |
|------|------|--------------|-------------|-----------------|
| **pChk1 (S345)** | - | + | + | + |
| **pChk2 (T68)** | - | + | + | + |
| **tChk1** | - | + | + | + |
| **tChk2** | - | + | + | + |

**C**

**D**

**E**

**F**
Fig. S5

% Cell RAD51 positive

- DMSO
- PARPi
- PARPi + ATRi

- HCC1937-B1
- HCC1937
A

% Fibers

0 1 2 3

idU/CldU Ratio

0 2 4 6 8

% Cell Viability

B

*** ****

idU/CldU Ratio

** ****

idU/CldU Ratio

ns ****

C

U+B1 U

siControl siMRE11

MRE11

GAPDH

D

SYr13 SYr13 HU SYr13 HU ATRi

[PARPi], μM

0 2 4 6 8

% Cell Viability

E

SYr13 SYr13 HU SYr13 HU ATRi

RAD51

KU70

Chromatin Fraction

F

SYr9 No HU SYr9 HU SYr9 HU+ATRi

SYr37 No HU SYr37 HU SYr37 HU+ATRi

IdU/CldU Ratio

*** ****

IdU/CldU Ratio

****ns

SYr14 SYr9

HU (4 mM, 5 hr): + + + +

ATRi (10 μM, 5 hr): + + ++

Relative mRNA level

0 0.2 0.4 0.6 0.8 1 1.2 1.4

sIControl sXRCC3 sXRCC2

Fig. S6
Fig. S7

A (In BRCA1-deficient cells)

ATR

PALB2-BRCA2

RAD51 loading

RPA

XRCC2

XRCC3

DSB repair (HR)

fork protection

Efficiency of RAD51 loading

A threshold for significant PARPi sensitivity

B

Efficiency of RAD51 loading

BRCA-proficient

BRCA1-deficient, PARPi-sensitive (UWB1)

BRCA1-deficient, acquired PARPi resistance (SYr12) or pre-existent PARPi resistance (HCC1937)

low ATR 

high PARPi sensitivity

- + - + - + low PARPi sensitivity

BRCA-proficient PARPi-sensitive PARPi-resistant
