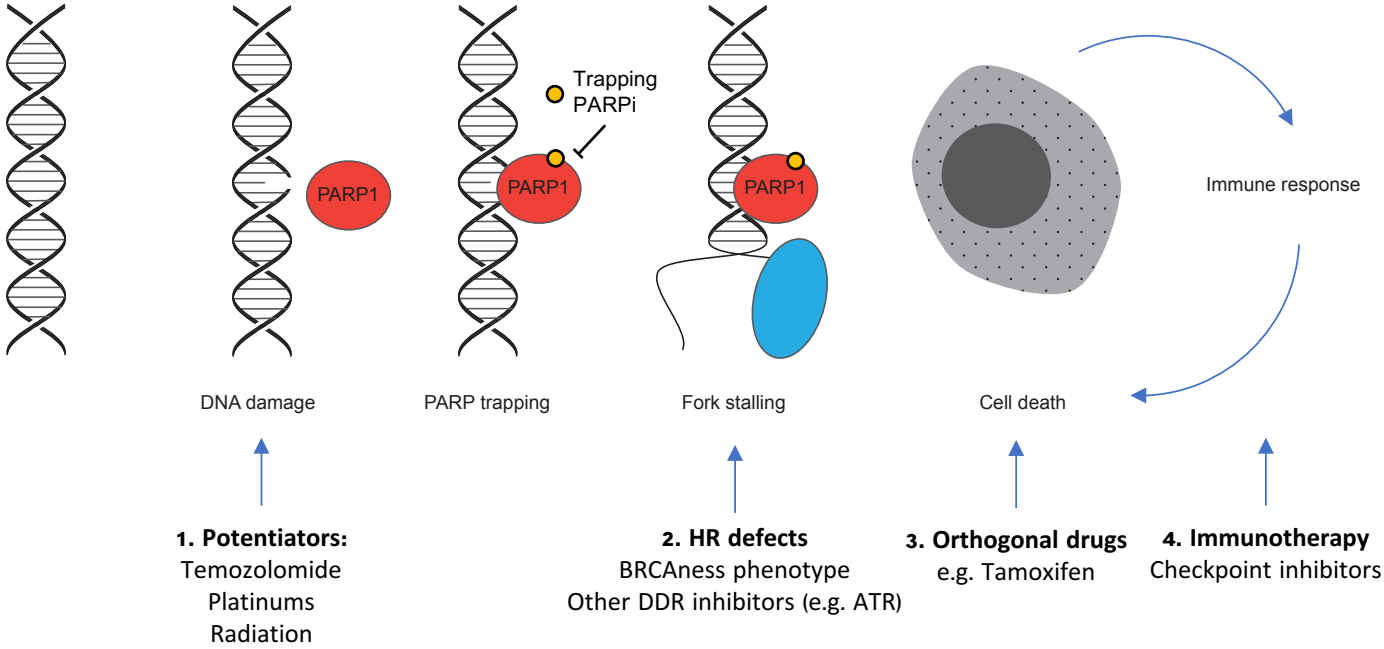

Figure 1 Strategies for PARP inhibitor combination therapy relating to the proposed "trapping" mechanism of tumour cell killing by PARPi. Killing can be enhanced at a number of steps: 1) Induction of more DNA damage, leading to higher levels of PARP1 trapping (and unrepaired SSBs in the case of certain agents). 2) HR defects, either via a *BRCA* or *BRCAness* gene mutation, that result in an inability to rescue stalled replication forks arising from trapped PARP1 and unrepaired SSBs. Other agents targeting DDR may have a similar effect. 3) Drugs that target tumour cells by an orthogonal method exploiting a further tumour-specific vulnerability, such as tamoxifen for ER-positive breast cancer. 4) Immune checkpoint inhibitors that may enhance immunogenic tumour cell death.

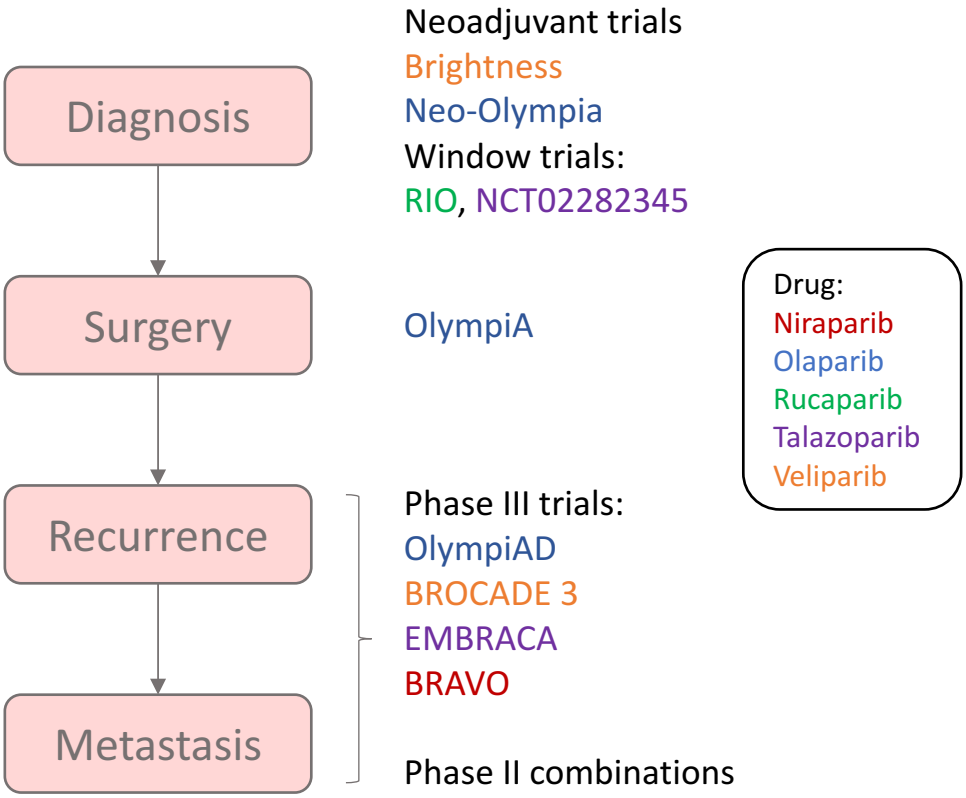

Figure 2 Schematic of recent and ongoing trials of PARPi in breast cancer at different stages.