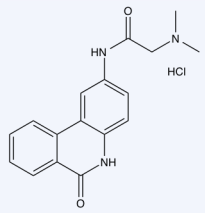
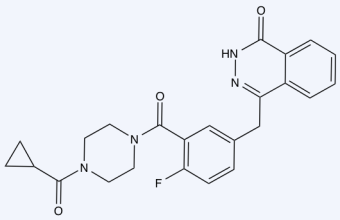
FOCUS on...

PARP Inhibitors

Poly (ADP-ribose) polymerases (PARP) catalyze the synthesis of poly ADP-ribose chains on DNA and protein targets. The involvement of PARP1 and 2 in single strand break repair has made PARPs attractive targets for breast and ovarian cancer[1]. Rapidly dividing mitotic cancer cells or tumors with mutations in DNA-repair pathways (BRCA1, BRCA2 or PALB2) are sensitive to PARP inhibitors whereas normal cells with intact DNA repair pathways can survive inhibition of PARP. Interestingly, certain classes of PARP inhibitors can trap PARP proteins on damaged DNA, a novel mechanism of action that leads to apoptosis distinct from inhibiting PARP catalytic activity [2].



PJ-34



Olaparib

PJ-34 HCl

Potent and selective inhibitor of PARP1 & 2. EC_{50} = 20 nM[3]. Causes PARP1 independent, p21 dependent mitotic arrest.[4]

10-2395 5 mg , 25 mg

Olaparib

A single digit nM inhibitor of PARP1 & 2[5]. Inhibition of PARP1 by olaparib prevents repair of single-strand breaks, which is tolerated in normal cells that efficiently repair double-strand repair pathways. Olaparib has progressed in and out of clinical trials. Most recently, it is undergoing a phase III trial for BRCA-mutated ovarian cancer[6].

10-2154 5 mg , 25 mg

4-HQN

Inhibitor of poly(ADP-ribose) polymerase (IC_{50}= 9.5 µM); displays mixed inhibition with respect to NAD+[7]. 4-HQN decreases the NFkappaB activation in LPS-induced endotoxic shock in a PI3K/Akt pathway dependent manner[8].

10-1307 1 g

4-Aminonaphthalimide

PARP inhibitor (IC_{50} = 0.18 µM) [9]. PARP inhibition sensitizes cells to damage by radiation or cytotoxic agents and reduces cell death related to ischemia/reperfusion.

10-1320 20 mg ,100 mg

ME-0328

A potent and selective PARP3 inhibitor (IC_{50}=0.89 µM). Selective over PARP1, PARP2 and other ARDT enzymes (IC_{50}=6.3, 10.8 and >30 µM respectively)[10].

10-1484 5 mg , 25 mg

Iniparib

Iniparib has been reported to inhibit PARP by covalent binding to the DNA binding domain but this result has been controversial[11].

10-2574 10 mg, 50 mg

References

1. J. Morales *et al.* (2014) Crit. Rev. Eukaryot. Gene Expr., **24** 15
2. J. Murai *et al.* (2012) Cancer Res., **72** 5588
3. Pellicciari *et al.* (2008) Chem. Med. Chem., **3** 914
4. Madison *et al.* (2011) DNA Repair, **10** 1003
5. Meaner *et al.* (2008) J. Med. Chem. **51** 6581
6. Shaw and Hall (2013) Ther. 6 1197
7. Banasik et al. (1992) J. Biol. Chem. **267** 1569
8. Veres et al. (2004) J. Pharmacol. Exp. Ther. **310** 247
9. Banasik *et al.* (1992) J. Biol. Chem., **267** 1569
10. Lindgren *et al.* (2013) ACS Chem. Biol. **8** 1698
11. Yuan *et al.* (2011) J. Hematol. Oncol. **4** 16

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