Combining PARP inhibition with platinum, ruthenium or gold complexes for cancer therapy

ABSTRACT

Platinum drugs are heavily used first-line chemotherapeutic agents for many solid tumours and have stimulated substantial interest in the biological activity of DNA-binding metal complexes. These complexes generate DNA lesions which trigger the activation of DNA damage response (DDR) pathways that are essential to maintain genomic integrity. Cancer cells exploit this intrinsic DNA repair network to counteract many types of chemotherapies. Now, advances in the molecular biology of cancer has paved the way for the combination of DDR inhibitors such as poly (ADP-ribose) polymerase (PARP) inhibitors (PARPi) and agents that induce high levels of DNA replication stress or single-strand break damage for synergistic cancer cell killing. In this review, we summarise early-stage, preclinical and clinical findings exploring platinum and emerging ruthenium anti-cancer complexes alongside PARPi in combination therapy for cancer and also describe emerging work on the ability of ruthenium and gold complexes to directly inhibit PARP activity.

Keyword: PARP inhibitors; Cancer; Combination therapy; Platinum drugs; Ruthenium