Précis: Coamplification of EGFR and ERBB2 is associated with afatinib response in patients with trastuzumab-refractory esophagogastric cancer, whereas selection for MET amplification or loss of EGFR amplification is associated with resistance.

See commentary, p. 166

**BRCA Reversion Mutations in Circulating Tumor DNA Predict Primary and Acquired Resistance to the PARP Inhibitor Rucaparib in High-Grade Ovarian Carcinoma**


Précis: Analysis of cfDNA from 112 patients with high-grade ovarian carcinoma showed that BRCA reversion mutations may be associated with reduced clinical benefit from the PARP inhibitor rucaparib.

**PPT1 Promotes Tumor Growth and Is the Molecular Target of Chloroquine Derivatives in Cancer**


Précis: Chloroquine derivatives exert their antiautophagic and antitumor effects by binding palmitoyl-protein thioesterase 1 (PPT1) and inhibiting its enzymatic activity.
Aurora kinase A (AURKA) and Aurora kinase B (AURKB) were found to be synthetic lethal with RB1 loss using a "gene–gene" interaction CRISPR/Cas9-based screening approach initiated by Oser and colleagues and a "gene–drug" interaction approach involving a screen of cell-cycle inhibitors performed by Gong, Du, Parsons, and colleagues. Both an AURKB-specific inhibitor, AZD2811, and the developed AURKA-specific inhibitor, LY3295668, specifically eliminated RB1-mutant but not RB1–wild-type cells and had in vivo efficacy against RB1-mutant tumors. Mechanistic studies suggested that RB1 and AURKA or AURKB have partially redundant roles in mitosis, explaining their synthetic lethal interaction. These findings suggest a potential therapeutic vulnerability caused by RB1 loss and a possible way forward for treatment of RB1-mutant tumors. For details, please see the article by Oser and colleagues on page 230 and the article by Gong, Du, Parsons, and colleagues on page 248.