DRUG–DRUG INTERACTIONS FOR NUCLEIC ACID-BASED DERIVATIVES

JIAN WANG and HONG ZHAO

15.1 INTRODUCTION

In the last decade, oligonucleotide-based therapeutics have been under active development for treatment of diseases such as cancers, genetic disorders, and or infections. Fomivirsen was the first antisense oligonucleotide drug approved by the FDA in 1998 for the treatment of cytomegalovirus retinitis in AIDS patients who have failed therapy with other anticytomegalovirus drugs or who are intolerant or have a contraindication to other therapies. Six years later, pegaptanib (pegylated aptamer), a selective vascular endothelial growth factor (VEGF) antagonist was approved for the treatment of neovascular (wet) age-related macular degeneration (AMD). Both drugs are administered via intravitreal injection.

Antisense oligonucleotides (ASOs) are perhaps the most direct therapeutic strategy to target RNA. Currently ASOs make up the major investigational new drug (IND) submissions for oligonucleotide drug development. These ASOs are designed to bind to the target RNA by well-characterized Watson-Crick base pairing, and once bound to the target RNA, modulate its function through a variety of postbinding events. In this chapter, the primary information used for summarizing drug–drug interactions (DDIs) of oligonucleotides comes from the first- and second-generation ASOs because the currently published DDI studies are mostly focused on these classes of oligonucleotides. When possible, information on other classes of oligonucleotides is presented in the context of these base classes. Caution should be taken in making generalized conclusions based on the limited number of reported studies due to the fact that most of the oligonucleotides are still in the development stage. More information needs to be accumulated to better define the DDI potential between oligonucleotides and other drugs.

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