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Fomivirsen
A Viewpoint by Erik de Clercq

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Fomivirsen (ISIS 2922) is an antisense oligodeoxynucleotide (composed of 21 phosphorothioate nucleotides), that is complementary to the human cytomegalovirus (CMV) immediate early 2 (IE) mRNA. The sequence of the nucleotides is as follows: 5′-GCGTTTGCTCTTCTTCTTGCG-3′. All nucleotides are the 2′-deoxy type and the phosphate backbone is replaced by phosphorothioates throughout. Following phase III clinical trials, fomivirsen has been approved by the US FDA for the topical treatment (by intravitreal injection) of cytomegalovirus retinitis in immunocompromised patients with AIDS. Fomivirsen has been found to inhibit IE gene expression in cytomegalovirus-infected cells, as could be expected if it were to act according to the antisense concept.[1,2] However, nonantisense mechanisms, such as inhibition of virus adsorption, may also contribute to the antiviral activity of this type of polyanions. In this respect, the isolation of a cytomegalovirus mutant with sequence-specific resistance to fomivirsen[3] might be reassuring that fomivirsen, at least in part, acts by a truly antisense mechanism. The clinical utility of fomivirsen, and in particular its tolerability and efficacy relative to those of the more 'conventional' anti-cytomegalovirus drugs, such as ganciclovir and cidofovir, remain the subject of further investigation. ▲

References

1. Azad RF, Driver VB, Tanaka K, et al. Antiviral activity of a phosphorothioate oligonucleotide complementary to RNA of the human cytomegalovirus major immediate-early region. Antimicrob Agents Chemother 1993 Sep; 37: 1945-54
2. Anderson KP, Fox MC, Brown-Driver V, et al. Inhibition of human cytomegalovirus immediate-early gene expression by an antisense oligonucleotide complementary to immediate-early RNA. Antimicrob Agents Chemother 1996 Sep; 40: 2004-11
3. Mulamba GB, Hu A, Azad RF, et al. Human cytomegalovirus mutant with sequence-dependent resistance to the phosphorothioate oligonucleotide fomivirsen (ISIS 2922). Antimicrob Agents Chemother 1998 Apr; 42: 971-3