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Nitazoxanide: a first-in-class broad-spectrum antiviral agent

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Abstract

Originally developed and commercialized as an antiprotozoal agent, nitazoxanide was later identified as a first-in-class broad-spectrum antiviral drug and has been repurposed for the treatment of influenza. A Phase 2b/3 clinical trial recently published in *The Lancet Infectious Diseases* found that oral administration of nitazoxanide 600mg twice daily for five days reduced the duration of clinical symptoms and reduced viral shedding compared to placebo in persons with laboratory-confirmed influenza. The same study also suggested a potential benefit for subjects with influenza-like illness who did not have influenza or other documented respiratory viral infection. From a chemical perspective, nitazoxanide is the scaffold for a new class of drugs called thiazolides. These small-molecule drugs target host-regulated processes involved in viral replication. Nitazoxanide is orally bioavailable and safe with extensive post-marketing experience involving more than 75 million adults and children. A new dosage formulation of nitazoxanide is presently undergoing global Phase 3 clinical development for the treatment of influenza. Nitazoxanide inhibits a broad range of influenza A and B viruses including influenza A(pH1N1) and the avian A(H7N9) as well as viruses that are resistant to neuraminidase inhibitors. It is synergistic with neuraminidase inhibitors, and combination therapy with oseltamivir is being studied in humans as part of ongoing Phase 3 clinical development. Nitazoxanide also inhibits the replication of a broad range of other RNA and DNA viruses including respiratory syncytial virus, parainfluenza, coronavirus, rotavirus, norovirus, hepatitis B, hepatitis C, dengue, yellow fever, Japanese encephalitis virus and human immunodeficiency virus in cell culture assays. Clinical trials have indicated a potential role for thiazolides in treating rotavirus and norovirus gastroenteritis and chronic hepatitis B and chronic hepatitis C. Ongoing and future clinical development is focused on viral respiratory infections, viral gastroenteritis and emerging infections such as dengue fever.

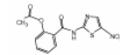
Keywords: Antiviral therapy; Broad-spectrum; Influenza; Nitazoxanide; Thiazolides.

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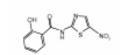
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Figures

Nitazoxanide



Tizoxanide



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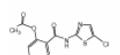


Fig. 1 Chemical structures of nitazoxanide, tizoxanide...

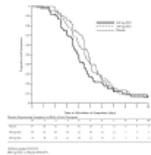


Fig. 2 Kaplan-Meier plot of time from...

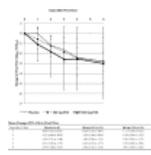


Fig. 3 Mean change in influenza TCID...

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