

RSV has a seasonal incidence; it is highly predictable and occurs in the winters of both hemispheres, from September to May in Europe and North America, peaking in December and January, and can occur throughout the year in tropical countries. It affects >90% of infants and young children by the age of two years and as natural immunity is short-lived; many will be re-infected each year. As with influenza, in elderly people, RSV causes around 10% of winter hospitalisations with an associated mortality of 10%.

Current anti-RSV treatment involves the use of a monoclonal antibody to RSV, called palivizumab. Such use of palivizumab is a prophylactic, rather than therapeutic, treatment of RSV. Although this antibody is often effective, its use is restricted to preterm infants and infants at high risk. Indeed, its limited utility means that it is unavailable for many people in need of anti-RSV treatment. There is therefore an urgent need for effective alternatives to existing anti-RSV treatment.

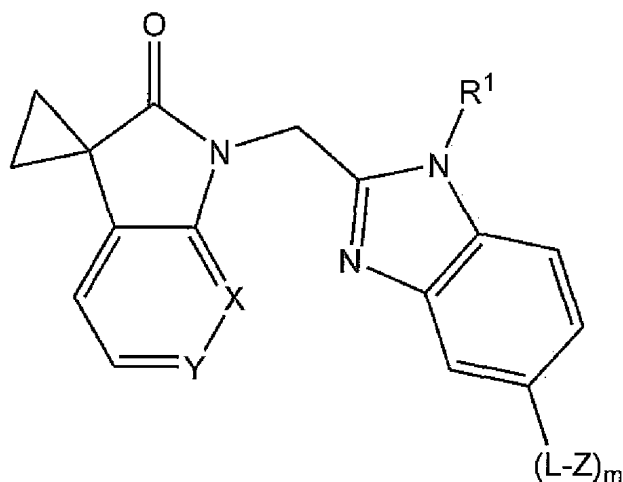
Additionally, several compounds have been proposed as inhibitors of RSV, including benzimidazole-based compounds. For example, K D Combrink et al., Bioorganic & Medicinal Chemistry Letters, 17 (2007), 4784-4790 discloses the compound BMS-433771 and variants thereof. Further benzimidazole-based compounds are disclosed in WO-02/062290, WO-03/053344 and WO-10/103306.

WO 2013/068769 discloses spirocyclic compounds having activity against RSV. However there exists a need to identify further compounds, and in particular compounds having favourable pharmacokinetic profiles.

Summary

It has now been found that a novel series of benzimidazoles are active as RSV inhibitors with favourable pharmacokinetics.

Accordingly, in one aspect of the present disclosure, there is provided a compound which is a benzimidazole of formula (I):



Formula (I)

wherein:

- 5 - one of X and Y is an N atom or a substituted C atom, and the other is CH;
- L is a single bond, C₁₋₃ alkylene, C₂₋₃ alkenylene or C₂₋₃ alkynylene;
- R¹ is C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, 3- to 10-membered cycloalkyl
10 5- to 10-membered heterocyclyl or 5- to 12- membered heteroaryl, each
 of which is unsubstituted or substituted;
- Z is halo, C₁₋₆ haloalkyl, nitro, -CN, -N(R²)₂, -OR², -SR², -S(=O)R², or -
 S(=O)₂R²;
- each R² is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl or C₂₋₆
15 alkynyl, wherein said alkyl, alkenyl and alkynyl groups are
 unsubstituted or substituted; and
- m is 0 or 1;

or a pharmaceutically acceptable salt thereof.

20 In another aspect of the present disclosure, there is provided a pharmaceutical
 composition which comprises a compound as defined herein and a pharmaceutically
 acceptable carrier or diluent.

 In yet another aspect of the present disclosure, there is provided a compound as defined
 herein, for use in the treatment of the human or animal body by therapy.

In a further aspect of the present disclosure, there is provided a compound as defined herein for use in the treatment or prevention of an RSV infection.

5 In another aspect of the present disclosure, there is provided a use of a compound as defined herein, in the manufacture of a medicament for use in the treatment or prevention of an RSV infection.

In yet another aspect of the present disclosure, there is provided a product containing:

- (a) a compound as defined herein; and
 - 10 (b) one or more further therapeutic agents;
- for simultaneous, separate or sequential use in the treatment of a subject suffering from or susceptible to an RSV infection.

15 In a further aspect of the present disclosure, there is provided a pharmaceutical composition which comprises (a) a compound as defined herein, and (b) one or more further therapeutic agents, as defined herein, together with a pharmaceutically acceptable carrier or diluent.

Detailed Description of the Invention

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When any group, ring, substituent or moiety defined herein is substituted, it is typically substituted by Q as defined below.

25 A C₁₋₆ alkyl group or moiety is linear or branched. A C₁₋₆ alkyl group is typically a C₁₋₄ alkyl group, or a C₄₋₆ alkyl group. Examples of C₁₋₆ alkyl groups and moieties include