INTRODUCTION

Brincidofovir (BCV, CMX001), is a first-in-class nucleotide in Phase 3 development for the prevention of CDV infection in RCT recipients. BCV is administered orally, circulates as CDV, and is converted to the active antiviral cidofovir diphosphate (CDV-PP) within cells. BCV shares the broad-spectrum antiviral activity of cidofovir (CDV) against all five families of DNA viruses which cause disease in humans. The 30 to 50-fold improved in vitro activity of BCV versus CDV has been hypothesized to result from more efficient transport of circulating BCV across the cell membrane, resulting in higher intracellular concentrations of CDV-PP. The goal of this study was to determine if cells exposed to the same circulating BCV across the cell membrane, resulting in higher intracellular concentrations of CDV-PP.

METHODS

Five cell types that have been historically used for generating antiviral activity of BCV and CDV were used in this study. CDV-PP. The goal of this study was to determine if cells exposed to the same circulating BCV across the cell membrane, resulting in higher intracellular concentrations of CDV-PP. The 50 to 500-fold improved in vitro activity of BCV versus CDV has been hypothesized to result from more efficient transport of BCV, and is converted to the active antiviral cidofovir diphosphate (CDV-PP) within cells.

Analytical measurements of BCV, CDV and CDV-PP were obtained from ATCC and grown in the recommended medium in the presence of 10% FBS. During treatment with BCV and CDV, the FBS concentration was 2% to the FBS concentration used in the antiviral assays.

RESULTS

The method used for harvesting cells affected the yield of CDV-PP detected. The increase in intracellular levels of CDV-PP corresponded well with an increase in potency of BCV over CDV in antiviral assays in vitro.

CONCLUSIONS

Intracellular levels of BCV, CDV and CDV-PP were determined by LC/MS/MS by Pyxant Laboratories, Colorado Springs, CO using similarly prepared calibration standards.

To determine the intracellular concentration of cidofovir diphosphate in brincidofovir and cidofovir-treated cells in vitro.

Intracellular levels of BCV, CDV and CDV-PP were determined by LC/MS/MS by Pyxant Laboratories, Colorado Springs, CO using similarly prepared calibration standards.

We would like to thank Suzanne Foley and Shane Karnik at Pyxant Laboratories for analytical support.

REFERENCES


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