Brincidofovir Decreases Adenovirus Viral Burden, Which is Associated With Improved Mortality in Pediatric Allogeneic Hematopoietic Cell Transplant Recipients

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Abstract

Background

Adenovirus (AdV) infections are an important cause of morbidity and mortality following hematopoietic stem cell transplantation (HSCT). While significant advances have been made in the management of AdV infections with cidofovir (BCV), the drug limits the concentration of cidofovir in plasma, and together with 1-deoxy-D-ribose, results in a higher intracellular concentration of cidofovir diphosphate. BCV limits the concentration of cidofovir in plasma and, together with 1-deoxy-D-ribose, results in a higher intracellular concentration of cidofovir diphosphate. BCV is associated with significant dose-limiting nephrotoxicity.

Objectives

To evaluate the safety and efficacy of Brincidofovir (BCV) in a single-blind, multicenter, Phase 2 study in pediatric and adult allogeneic hematopoietic stem cell transplant recipients with AdV viremia.

Methods

Nonrandomized, single-arm study of 47 HSCT recipients aged ≥2 months who received BCV as per institutional protocol for anytime AdV viremia. Patient demographics and clinical characteristics are described in Table 1. Virologic and clinical endpoints are described in Table 2. Primary endpoint was the number of days AdV became undetectable during BCV treatment.

Results

In total, 32/47 (68%) patients achieved undetectable AdV viremia during BCV treatment. The median (IQR) time to undetectable AdV viremia was 7 (3-15) days post first BCV dose. Significant improvements were observed in 12-week mean AdV AAUC compared with baseline. Patients with the highest 12-week AdV AAUC values had the lowest 36-week survival rates (Figure 2).

Conclusions

BCV is a safe and effective antiviral for the treatment of AdV viremia. Improvements in AdV viremia between groups with the highest and lowest 12-week AdV AAUC were the lowest in survival. Significant association was observed between lower AdV AAUC and improved survival.

References


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