PC945, a novel inhaled azole for treatment of fungal tracheobronchitis post-lung transplantation: a case report.

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The median incidence of Aspergillus infections in lung transplant recipients has been reported in up to 20%1. The commonest site for infection is the tracheobronchial area, most commonly at the anastomotic site which is particularly vulnerable due to blood supply disruption to the donor airway and the presence of the sutures, a point of adhesion for pathogens. Bronchial anastomotic infections are a major risk factor for dehiscence, bronchial stenosis, fistulas and granulation tissue, with the potential of limiting the lung capacity and facilitate secretion retention2.

The treatment of bronchial anastomotic infections with triazoles is challenging due to the drug-drug interaction with CNIs and risk of liver toxicity. The use of systemic amphotericin B is usually avoided in lung transplant recipients due to the increased nephrotoxicity while the nebulised administration is often hindered by tolerability issues. Furthermore, the bronchial anastomosis remains quite ischemic post-transplantation, therefore the penetration at the site of infection of systemically administered antifungal agents is limited.

The aim of this report is to describe our experience in using a potent, novel inhaled azole agent PC945 (Pulmocide) to treat a proven fungal bronchial anastomotic infection3, refractory to systemic antifungal treatment. PC945 is designed to deliver high pulmonary concentrations with retention in cells offering a long duration of action and minimal systemic exposure4.

A 29-year-old woman who underwent a bilateral lung transplant in September 2018 for end stage cystic fibrosis developed an infection of the right main bronchial anastomosis four weeks after the transplant. Grocott staining on a biopsy of the affected bronchial mucosa highlighted fungal hyphae. Aspergillus fumigatus complex grew from a bronchoalveolar lavage sample.
A treatment with isavuconazole and inhaled amphotericine B was started, switched to posaconazole and terbinafine due poor tolerance of the first two agents.

A follow up bronchoscopy after six weeks of treatment showed worsening of the fungal ball attached to the sutures and endobronchial erythema.

A treatment with nebulized PC945 5mg daily aqueous suspension was initiated under a special needs program. The patient reported excellent toleration with no adverse local nor systemic effects. Further follow up bronchoscopies showed progressive improvement with complete resolution of fungal ball and mucosal erythema after eight weeks of treatment.

This is the first report of using PC945 as part of a combination treatment for a refractory fungal bronchial anastomotic infection and tracheobronchitis. It showed excellent tolerability profile and had promisingly proven effective in controlling the active infection.

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