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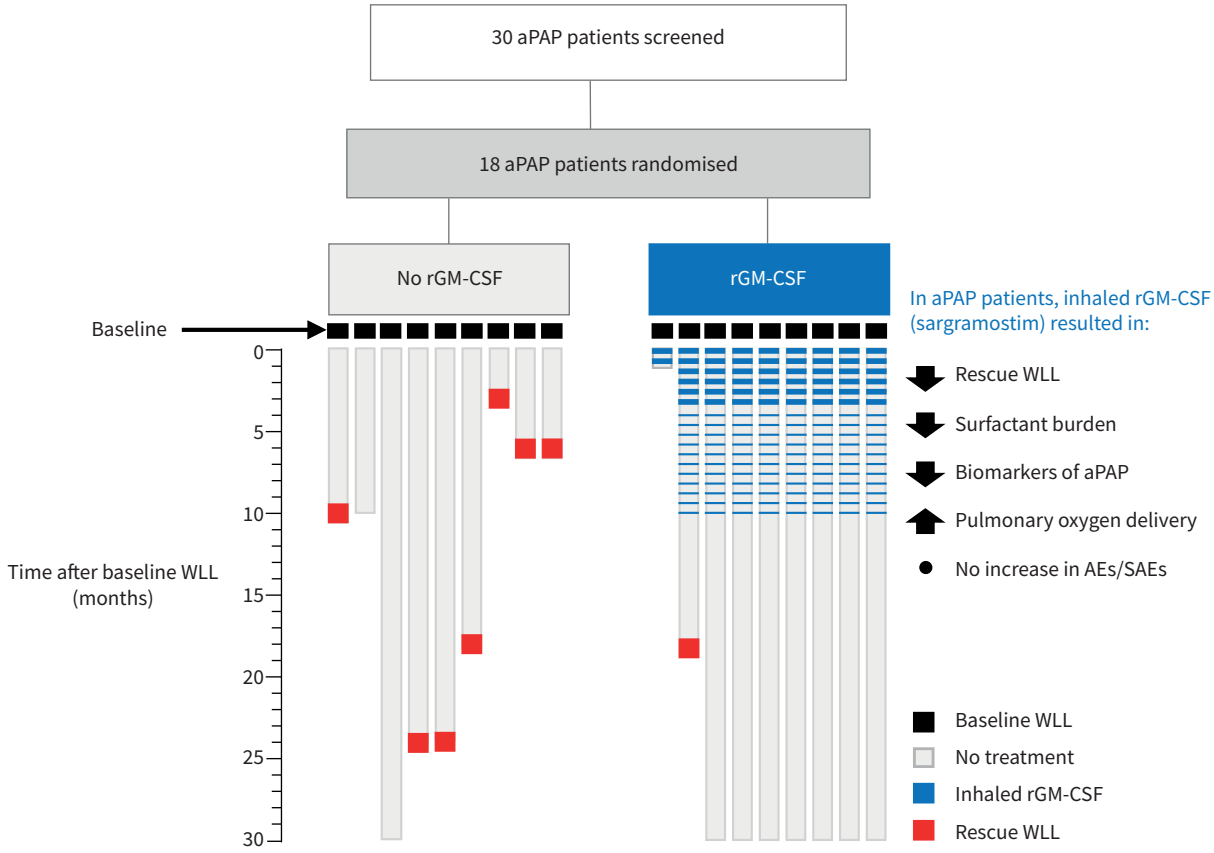

GRAPHICAL ABSTRACT Overview of the study. aPAP: autoimmune pulmonary alveolar proteinosis; rGM-CSF: recombinant granulocyte–macrophage colony-stimulating factor; WLL: whole lung lavage; AE: adverse event; SAE: serious adverse event.

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Ilaria Campo [1], Brenna C. Carey [2,3], Elena Paracchini [1], Zamir Kadija [1], Annalisa De Silvestri [4], Giuseppe Rodi [5], Mara De Amici [6], Cristina Torre [6], Michele Zorzetto [1], Matthias Griese [7], Federica Meloni [1,8], Angelo Guido Corsico [1,8], Bruce C. Trapnell [2,3,9] and Francesca Mariani [1]

[1]Pneumology Unit, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Policlinico San Matteo, Pavia, Italy. [2]Translational Pulmonary Science Center, Cincinnati Children's Hospital, Cincinnati, OH, USA. [3]Department of Pediatrics, University of Cincinnati, College of Medicine, Cincinnati, OH, USA. [4]Clinical Epidemiology and Biometric Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy. [5]Anesthesiology and Intensive Care Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy. [6]Pediatric Clinic, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy. [7]Dr. von Hauner Children's Hospital, University of Munich, German Center for Lung Research, Munich, Germany. [8]Department of Internal Medicine, University of Pavia, Pavia, Italy. [9]Division of Pulmonary, Critical Care, and Sleep Medicine, Department of Medicine, University of Cincinnati, Cincinnati, OH, USA.

Corresponding author: Bruce C. Trapnell (Bruce.Trapnell@cchmc.org)

Shareable abstract (@ERSpublications)
Following whole lung lavage (WLL), inhaled recombinant GM-CSF reduces the requirement for further WLL in aPAP patients, resulting in greater improvement in lung function, and is safe https://bit.ly/3MD2Klh

Cite this article as: Campo I, Carey BC, Paracchini E, *et al*. Inhaled recombinant GM-CSF reduces the need for whole lung lavage and improves gas exchange in autoimmune pulmonary alveolar proteinosis patients. *Eur Respir J* 2024; 63: 2301233 [DOI: 10.1183/13993003.01233-2023].

This article has an editorial commentary: https://doi.org/10.1183/13993003.01982-2023

Received: 26 April 2023
Accepted: 17 Oct 2023

Abstract

Rationale Whole lung lavage (WLL) is a widely accepted palliative treatment for autoimmune pulmonary alveolar proteinosis (aPAP) but does not correct myeloid cell dysfunction or reverse the pathological accumulation of surfactant. In contrast, inhaled recombinant granulocyte–macrophage colony-stimulating factor (rGM-CSF) is a promising pharmacological approach that restores alveolar macrophage functions including surfactant clearance. Here, we evaluate WLL followed by inhaled rGM-CSF (sargramostim) as therapy of aPAP.

Methods 18 patients with moderate-to-severe aPAP were enrolled, received baseline WLL, were randomised into either the rGM-CSF group (receiving inhaled sargramostim) or control group (no scheduled therapy) and followed for 30 months after the baseline WLL. Outcome measures included additional unscheduled "rescue" WLL for disease progression, assessment of arterial blood gases, pulmonary function, computed tomography, health status, biomarkers and adverse events. Patients requiring rescue WLL were considered to have failed their assigned intervention group.

Results The primary end-point of time to first rescue WLL was longer in rGM-CSF-treated patients than controls (30 *versus* 18 months, n=9 per group, p=0.0078). Seven control patients (78%) and only one rGM-CSF-treated patient (11%) required rescue WLL, demonstrating a 7-fold increase in relative risk (p=0.015). Compared to controls, rGM-CSF-treated patients also had greater improvement in peripheral arterial oxygen tension, alveolar–arterial oxygen tension difference, diffusing capacity of the lungs for carbon monoxide and aPAP biomarkers. One patient from each group withdrew for personal reasons. No serious adverse events were reported.

Conclusions This long-term, prospective, randomised trial demonstrated inhaled sargramostim following WLL reduced the requirement for WLL, improved lung function and was safe in aPAP patients. WLL plus inhaled sargramostim may be useful as combined therapy for aPAP.