ERS Congress 2024: highlights from the Respiratory Infections Assembly

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Shareable abstract (@ERSpublications)
This highlights article shares key updates in the field of respiratory infections from the 2024 #ERSCongress, focusing on new research and the need for fair access to care to help tackle global challenges in respiratory infections and improve patient care https://bit.ly/40gDmrj

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The 2024 European Respiratory Society (ERS) Congress in Vienna, Austria, brought together leading experts worldwide to address some of the most pressing challenges in respiratory medicine. In the field of respiratory infections, the congress highlighted notable advancements, particularly regarding pulmonary aspergillosis, tuberculosis (TB) and cystic fibrosis (CF), reflecting the rapidly evolving landscape in this area. This article aims to provide an overview of the key highlights from the congress in the field of respiratory infections, offering insights into the latest research, treatment innovations and ongoing challenges in managing these complex respiratory diseases.

A key session was the symposium on chronic pulmonary aspergillosis, which presents a high incidence and significant mortality worldwide, mainly due to challenges in diagnosis and treatment [1]. While *Aspergillus* spores are ubiquitous in the environment, they only become pathogenic in the presence of impaired immune defences or compromised lung structures [2]. In this context, Eva Van Braeckel (Ghent, Belgium) provided an overview of the spectrum of pulmonary aspergillosis, ranging from respiratory colonisation to invasive disease and hypersensitivity reactions. She highlighted risk factors including impaired cell-mediated immunity, mucosal barrier integrity, structural lung disease and hyperresponsiveness [3]. The different diagnostic approaches for invasive, chronic pulmonary and allergic bronchopulmonary aspergillosis were outlined by Paul Verweij (Nijmegen, the Netherlands). Detection of *Aspergillus* infection often relies on microscopy, *Aspergillus* antigen, and antibody testing, while species and antimicrobial susceptibility are identified using culture and PCR. Depending on the host profile and the clinical entity, *Aspergillus* antigen and PCR generally demonstrate high sensitivity, complemented by serology [4]. Emerging diagnostic tools and techniques are expected to improve sensitivity and accuracy, although resistance mutations, mixed-genotype infections, tolerance and biofilm formation continue to complicate both diagnosis and treatment [5].

Martin Hoenigl (Graz, Austria) pointed out that climate change and agriculture are key contributors to the rising pathogenicity of fungi, including *Aspergillus* [6]. Resistance patterns are becoming increasingly complex, underscoring the need for new antifungal agents [7]. In this light, fosmanogepix, olorofim and opelconazole are promising candidates in late-stage development. Additionally, immunotherapies such as

recombinant interferon-γ and anti-*Aspergillus* antibodies show promise in enhancing immune responses against the fungus. Lastly, Helmut Salzer (Linz, Austria) discussed the burden of chronic pulmonary aspergillosis in people with post-TB lung disease. This growing patient cohort, constituting 5–18% of those with post-TB complications, faces high mortality and disability, necessitating interdisciplinary follow-up and close monitoring of lung function and radiological abnormalities [8, 9].

Another relevant session addressed advancements in short regimens for treating drug-susceptible (DS) and drug-resistant TB. Carla Winston (Atlanta, GA, USA) presented a new regimen for DS-TB, based on a 4-month combination of isoniazid, rifapentine, pyrazinamide and moxifloxacin, for adults and children over 12 years of age. This regimen was included in the new guidelines paper from the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) and is based on findings from clinical trials showing non-inferiority of these shortened treatments compared to the traditional 6-month regimen [10–13]. The session concluded with a call for further research in areas such as extrapulmonary TB, improved diagnostic methods for drug resistance, and the development of even shorter regimens.

Jussi Saukkonen (Boston, MA, USA) focused on the challenges of treating multidrug-resistant (MDR) TB. New 6- and 9-month regimens involving bedaquiline, pretomanid and linezolid (BPaL) have shown promising results, significantly improving treatment outcomes with fewer adverse events compared to older, longer regimens [10]. Trials like ZeNix and TB-PRACTECAL demonstrated high success rates, particularly with BPaL(M) regimens (BPaL with/without moxifloxacin), but also highlighted concerns regarding adverse effects, particularly those linked to linezolid [14, 15]. Despite promising results, Jussi Saukkonen noted that the certainty of the evidence for these regimens remains low due to small sample sizes and the rarity of some adverse events. Additionally, specific populations, including pregnant women, children, and those with extrapulmonary TB, were excluded from these studies, limiting the generalisability of the findings. The WHO has also endorsed a 9-month regimen including bedaquiline, delamanid and linezolid with either levofloxacin, clofazimine or both for MDR-TB, expanding eligibility to previously excluded groups such as HIV-positive individuals and pregnant women. These regimens could soon replace traditional 18-month treatments, although further data are required to refine guidelines [11].

Finally, the session “CF beyond CF: recent advances and new perspectives” explored groundbreaking advancements in CF management, with a particular focus on the changes and challenges in the cystic fibrosis transmembrane conductance regulator (CFTR) modulator era. The introduction of elexacaftor–tezacaftor–ivacaftor (ETI) triple modulator therapy has significantly improved lung function in people with CF (pwCF), including those with advanced disease [16]. A French real-world study reported that in patients with advanced lung disease, percentage predicted forced expiratory volume in 1 s ($ppFEV_1$) improved from 30% to 45% within 1 month on ETI, with sustained benefits observed over 2 years [17]. Moreover, the expanded French compassionate use programme revealed that at least 60% of pwCF without the *F508del* variant respond to ETI, highlighting the urgent need to expand its therapeutic label [18]. However, as Pierre-Régis Burgel (Paris, France) noted, 25% of adults with advanced CF continue to have a $ppFEV_1$ below 40% post-ETI, emphasising the importance of careful long-term monitoring [17]. In this regard, in the session “The future of lung transplantation for CF”, Clémence Martin (Paris, France) explored the future of lung transplantation in pwCF, noting a substantial decline in transplant needs due to ETI [19]. During the French early access programme, the percentage of pwCF listed for lung transplantation dropped from 21% to 2% within 3 months of starting ETI [20]. Nevertheless, timely referral for lung transplantation remains crucial for pwCF with ETI-unresponsive CFTR variants and those with advanced lung disease despite treatment [17].

Nonetheless, the landscape for pwCF has changed and, as Michal Shteinberg (Haifa, Israel) highlighted in the “CF beyond CF” symposium, the ageing CF population now faces new challenges, including cardiovascular and oncological complications. Updated standards of care now emphasise the need for a multidisciplinary approach to address these emerging issues. While the evolving understanding of CF carrier status and its associated risks remain debated, genetic counselling continues to play a critical role in patient care [21–24].

On a global scale, Samia Hamouda (Tunis, Tunisia) addressed health disparities in CF care, stressing the urgent need for initiatives to improve diagnostics, enhance access to essential medications, and establish specialised CF centres in low- and middle-income countries [24–26]. Tackling these disparities is vital to ensure equitable care for pwCF worldwide.

Broadening the scope beyond CF, Marcus Mall (Berlin, Germany) discussed acquired CFTR dysfunction in chronic respiratory diseases such as COPD and bronchiectasis, highlighting evidence that environmental

factors such as cigarette smoke can impair CFTR function [27]. Interestingly, preclinical findings suggest that CFTR modulators may have therapeutic potential in treating other muco-obstructive lung diseases, with early clinical trials underway to validate these findings [28–30].

In conclusion, the 2024 ERS Congress underscored significant progress in managing various pulmonary infectious diseases, while identifying ongoing challenges such as rising fungal resistance, the need for more personalised TB treatments, and global disparities in CF care. The sessions highlighted the importance of continued research, innovation and equitable access to care, to improve patient outcomes worldwide.

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