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HIGHLIGHTS

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Highlights of International Congresses. Report from our Representatives at the Following International Events

Highlights de los Congresos Internacionales. Informe de nuestros representantes en los siguientes eventos internacionales

HIGHLIGHTS OF 2025 EUROPEAN CONGRESS

During the 2025 European Congress, numerous scientific advances of great clinical relevance were introduced, with notable participation from Argentine researchers and pulmonologists in oral and poster sessions. From this section, we would like to congratulate all the members who actively contributed with their work, reflecting the high academic level and excellence of national respiratory medicine. Amid the abundant scientific production, we wish to highlight three novelties of special interest, presented in various thematic sessions of the congress.

1. TETON-2 Study results: inhaled treprostinil therapy in idiopathic pulmonary fibrosis

The phase 3 TETON-2 trial evaluated the use of inhaled treprostinil (Tyvaso®) in patients with idiopathic pulmonary fibrosis (IPF). The results showed a significant improvement in forced vital capacity (FVC) after 52 weeks, reaching a difference of 95.6 mL compared to placebo ($p < 0.0001$). Additionally, a 29% reduction in the risk of clinical worsening was observed, along with a favorable trend in quality of life parameters (KBILD, King's Brief Interstitial Lung Disease questionnaire) and diffusing capacity of the lung for carbon monoxide (DLCO).

The drug demonstrated a safety profile consistent with previous studies, consolidating its role as a potential therapeutic option for IPF.

2. Update of the Multidisciplinary Classification of Interstitial Pneumonias (ERS/ATS 2025)

The new ERS/ATS 2025 international consensus proposed a comprehensive revision of the classification of interstitial pneumonias, incorporating both idiopathic and secondary causes. Three main innovations are recognized:

- The inclusion of the bronchiolocentric pattern (BIP) as a major entity, alongside the classic UIP (usual interstitial pneumonia) and NSIP (nonspecific interstitial pneumonia) patterns.
- The replacement of the terms "acute interstitial pneumonia" with idiopathic diffuse alveolar damage and "desquamative interstitial pneumonia" with alveolar macrophage pneumonia, in order to better reflect the underlying pathophysiology.
- The differentiation between fibrosing and non-fibrosing interstitial disorders, as well as between interstitial and alveolar filling patterns, with clear prognostic and therapeutic implications.

The document emphasizes the importance of the level of diagnostic confidence and a standardized multidisciplinary approach to optimize clinical decision-making.

3. ERS/EULAR 2025 Guidelines on Interstitial Lung Disease Associated with Connective Tissue Diseases (CTD-ILD)

The new guidelines of the ERS/EULAR (European Respiratory Society/European Alliance of Associations for Rheumatology) developed using the GRADE methodology, provide evidence-based recommendations for the screening, diagnosis,

monitoring, and treatment of interstitial lung disease associated with connective tissue diseases. Among the most notable recommendations are:

- Systematic use of high-resolution CT (HRCT) for initial detection in systemic sclerosis, inflammatory myopathies, and mixed connective tissue disease (MCTD). In the context of rheumatoid arthritis, its use remains restricted to "high-risk" patients.
- Periodic lung function testing every 3–6 months during the first years.
- Use of immunosuppressive treatments (mycophenolate, rituximab, cyclophosphamide) and antifibrotic agents such as nintedanib or pirfenidone in cases of progressive fibrosis. These guidelines promote an individualized and multidisciplinary approach, integrating the expertise of pulmonologists and rheumatologists to optimize clinical outcomes.

Non-CF Bronchiectasis (Miguel Penizzotto)

We were present at various activities where the topic of non–cystic fibrosis bronchiectasis was widely addressed at this congress. From my point of view, the importance of this topic in the program increased notably compared to previous years. The activities were divided into courses, symposia (including patient testimonies), oral presentations, and –undoubtedly– the most relevant highlight was the presentation of the ERS 2025 Guidelines. The importance of EMBARC was consistently emphasized across multiple activities and initiatives.

In summary, I believe the following are the most important insights to consider after the different sessions (including the ERS 2025 Guidelines presentation):

- *The relevance of the HRCT (with an appropriate protocol) as the diagnostic standard was reinforced, along with severity stratification using validated scores (BSI and EFACED).*
- *The importance of identifying the underlying cause was highlighted, including ciliary dyskinesia, where global diagnostic challenges were discussed.*
- *The importance of distinguishing endotypes was emphasized, with particular focus on phenotypes (eosinophilic, Pseudomonas infection, non-tuberculous mycobacteria [NTM], and asthma/COPD overlap) to optimize patient management.*
- *The need to identify frequent exacerbators (≥2/year or ≥1 severe) was stressed due to their impact on prognosis. Attention was also given to treatable traits such as chronic infection, type of inflammation, mucociliary dysfunction, bronchospasm, and comorbidities.*
- *There was a positive recommendation for the use of macrolides in frequent exacerbators after optimizing physiotherapy and infection management.*
- *New EMBARC data suggest that patients with childhood onset may reach adulthood with more severe disease compared to adult-onset cases, underscoring the value of structured transition from pediatric to adult care. Hence, the importance of documenting age at onset.*
- *Pseudomonas aeruginosa remains a marker of worse prognosis and higher exacerbation risk. The 2025 guidelines prioritize early eradication strategies and consider inhaled antibiotics in chronic colonization with frequent exacerbations.*
- *With regard to eradication strategies, a local eradication protocol is suggested at the first isolation, followed by reassessment at 3 and 6 months.*
- *As a new concept, the resistome/microbiome concept was discussed, with emphasis beyond traditional cultures (i.e., sequencing) to better understand resistance and dysbiosis, with future implications for targeted therapies.*
- *In my opinion, the most important novelty is the use of DPP-1 inhibitors (dipeptidyl peptidase 1), especially brensocatib, which is already approved by the Food and Drug Administration (FDA). Additionally, other drugs currently under investigation were presented and are expected to become available in the coming years for patients with non–CF bronchiectasis who are frequent exacerbators with a neutrophilic profile.*
- *Another key point was the growing importance of atypical mycobacteria, emphasizing close monitoring and treatment when indicated.*
- *The importance of continuing respiratory physiotherapy and mucociliary clearance through education and individualized techniques was highlighted.*
- *Regarding hypertonic saline solutions and mannitol, an individual trial-and-response approach was recommended. A lack of efficacy of dornase alfa in this group of patients was suggested.*
- *Bronchodilators and inhaled corticosteroids remain useful in phenotypes with obstruction/hyperreactivity.*

- *Routine use of inhaled corticosteroids should be avoided unless there is coexisting asthma and/or elevated eosinophils. Elevated FeNO (fractional exhaled nitric oxide) may be helpful in guiding this type of treatment.*

Dr. Maria Otaola - Coordinator, Interstitial Lung Diseases Section

EARCO: Meetings of the CRC (Clinical Research Collaboration) called EARCO, sponsored by the European Respiratory Society, were held. Updated data were provided on the number of patients included in the alpha-1 antitrypsin deficiency registry, as well as the need to increase patient follow-up. More than 4,300 patients had been enrolled as of September 2025. The discussion also covered the idea of incorporating a CT scan platform for patients. This initiative is contributing to a better understanding of the natural history of the disease.

A review was presented of all clinical studies published based on data from the registry.

In addition, the session discussed progress on new **European guidelines for the diagnosis and treatment of this condition**, based on the GRADE methodology.

A total of 52 **posters** related to alpha-1 antitrypsin deficiency (AATD) were presented. One of them showed the follow-up of a cohort of more than 3,000 patients in Denmark in relation to thromboembolic disease.

Clinical trial results for new therapies in AATD

- BEAM-302 – Beam Therapeutics: BEAM-302, a DNA base-editing therapy for AATD, demonstrated its ability to correct the PiZ mutation responsible for the disease. It uses CRISPR technology. Initial data from a phase 1 and phase 2 trial showed promising results, marking an important step toward a potential cure.
- INBRX-101 – Inhibrx (now Sanofi): Sanofi presented ongoing data on INBRX-101, a recombinant human AAT-Fc fusion protein designed to normalize serum AAT levels with less frequent dosing. An open-label phase 2 extension trial is currently evaluating its long-term safety and efficacy in patients with AATD-related emphysema. The drug, now known as **SAR447537**, is a recombinant fusion protein aimed at improving AATD treatment.
- Fazirsiran for liver disease: Updates were provided on fazirsiran, an RNA interference therapy being investigated for its effect on liver disease associated with AATD. Fazirsiran is a small interfering RNA (siRNA) that silences the gene responsible for producing the mutant AAT protein in the liver. By reducing production of this defective protein, the drug prevents its accumulation. A phase 3 trial is currently recruiting patients with liver fibrosis to determine whether the drug can reduce scarring.
- The clinical trial of Kamada's inhaled formulation for AATD is ongoing and could eliminate the need for intravenous infusions in the specific treatment of the disease. It is currently in an advanced phase of enrollment of patients with severe AATD. **Phase 3 (InnovAATe study):** A double-blind, placebo-controlled trial evaluating the long-term safety and efficacy of inhaled AAT in patients with AATD.

Dr. Mariano Fernández Acquier Best of ERS in Pulmonary Circulation

The latest Task Forces from the 7th World Symposium on Pulmonary Hypertension (7WSPH), held in Barcelona in July 2024, were recently published, underscoring the importance of early diagnosis, defined as detection in patients with risk conditions (such as scleroderma or portal hypertension). A key challenge remains in those patients who were diagnosed late, often because they were asymptomatic—yet by that time, up to 60% of the disease has already progressed. This raises an important question: should we treat presymptomatic patients, or should we aim to detect the disease even earlier?

A study conducted at the Mayo Clinic, led by Steven Cassady and Bradley Cole, explored the use of artificial intelligence for early detection of pulmonary arterial hypertension (PAH) based on echocardiographic studies. The use of right heart catheterization during exercise was also highlighted as a tool for early disease detection.

Marc Humbert, MD
Universite Parie-Saclary
France

PULMONARY HYPERTENSION-IPF-SARCOIDOSIS

During the congress, relevant advances were presented in the therapeutic approach to pulmonary hypertension (PH) and interstitial lung diseases, highlighting the development of new pharmacological strategies and the consolidation of combination therapies.

NOVEL THERAPIES IN THE TREATMENT OF PULMONARY HYPERTENSION

In the field of pulmonary arterial hypertension (PAH), the emerging role of sotatercept was highlighted. This drug is an activin signaling inhibitor, currently in phase III, with consistent evidence of clinical efficacy and a favorable safety profile, based on the PULSAR and STELLAR studies. In addition, phase II studies are underway, evaluating new therapeutic alternatives in both adult and pediatric populations, thereby broadening treatment options for this condition.

TREATMENT OF PULMONARY HYPERTENSION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND INTERSTITIAL LUNG DISEASE

Regarding pulmonary hypertension (PH) associated with chronic lung diseases (Group III), the use of inhaled prostanoids was discussed, particularly in patients with idiopathic pulmonary fibrosis (IPF) and progressive pulmonary fibrosis (PPF), in line with the latest classification from the World Symposium on Pulmonary Hypertension held in Barcelona. In contrast, it was emphasized that PH-specific medications are not recommended in patients with COPD, due to the lack of solid clinical evidence supporting their use.

The treatment of chronic thromboembolic pulmonary hypertension (CTEPH) continues to be multimodal, with pulmonary endarterectomy as the cornerstone therapy, complemented by balloon pulmonary angioplasty (BPA) and medical treatment, targeting both proximal and distal lesions of the pulmonary microvasculature.

REFERENCES

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- Kiko T et al. Eur Resp J. 2025;65:2402268.

IDIOPATHIC PULMONARY FIBROSIS

In the field of idiopathic pulmonary fibrosis, innovative therapies under investigation were presented. Taladegib, currently in phase II studies, showed benefits by inhibiting the Hedgehog signaling pathway, reducing fibroblast activation and improving lung function. Similarly, nerandomilast, a selective phosphodiesterase 4B inhibitor, demonstrated antifibrotic and immunomodulatory effects.

References: ALAT–ATS, September 2025.

With regard to combined antifibrotic therapy, the TETON-1 and TETON-2 studies demonstrated that the use of inhaled treprostinil, in combination with pirfenidone and/or nintedanib, is associated with significant improvements in FVC and a reduction in time to clinical worsening. There was a 29% reduction in the probability of adverse clinical events, while maintaining an acceptable safety profile.

TETON-1, a phase III, randomized, double-blind, controlled clinical trial, supports the use of inhaled treprostinil in the treatment of IPF without pulmonary hypertension, according to data published by United Therapeutics. These results initiate a new era in combined antifibrotic treatment, including inhaled treprostinil associated with pirfenidone.

TETON-2 also demonstrated significant differences in the primary endpoint, evaluating the combination of inhaled treprostinil, nintedanib, and pirfenidone. Benefits were also observed in the secondary endpoint, corresponding to time to clinical worsening, defined by a combination of different variables: death, hospitalizations, and a decline in FVC of more than 10%.

The FIBRONEET-ILD study, a phase III, randomized, double-blind, placebo-controlled trial, evaluated doses of 9 mg and 18 mg in patients with progressive pulmonary fibrosis (PPF) receiving concomitant antifibrotic treatment (nintedanib or

pirfenidone) for more than 52 weeks. The study met its primary objective, demonstrating a significant reduction in the absolute change in FVC compared to baseline.

REFERENCES

- Zheng Q et al ERJ Open Research. 2022;8:00591-2021.
- Renninger D et al Am J Respir Cell Mol Biol. 2025. https://doi.org/10.1165/rcmb.2024-0614.

SARCOIDOSIS

In sarcoidosis, efzofitimod –currently in phase III– was highlighted as a promising therapeutic strategy. Its immunomodulatory mechanism, mediated by binding to the neuropilin-2 (NRP2) receptor on activated immune cells, represents a novel targeted therapeutic approach in this systemic inflammatory disease.

References: Richeldi L et al New England Journal of Medicine. 2025;392:2193-2202.

In conclusion, the data presented at the congress reflect significant progress toward more personalized, combination, and targeted treatments, both in pulmonary hypertension and interstitial lung diseases. This poses a paradigm shift in the management of these complex conditions.

Dr. Daniela Bustos - Coordinator, Pulmonary Circulation Section