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Adaptive multi-interventional trial platform to improve patient care for fibrotic interstitial lung diseases

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ABSTRACT

Background Fibrotic interstitial lung diseases (fILDs) are a heterogeneous group of lung diseases associated with significant morbidity and mortality. Despite a large increase in the number of clinical trials in the last 10 years, current regulatory-approved management approaches are limited to two therapies that prevent the progression of fibrosis. The drug development pipeline is long and there is an urgent need to accelerate this process. This manuscript introduces the concept and design of an innovative research approach to drug development in fILD: a global Randomised Embedded Multifactorial Adaptive Platform in fILD (REMAP-ILD).

Methods Description of the REMAP-ILD concept and design: the specific terminology, design characteristics (multifactorial, adaptive features, statistical approach), target population, interventions, outcomes, mission and values, and organisational structure.

Results The target population will be adult patients with fILD, and the primary outcome will be a disease progression model incorporating forced vital capacity and mortality over 12 months. Responsive adaptive randomisation, prespecified thresholds for success and futility will be used to assess the effectiveness and safety of interventions. REMAP-ILD embraces the core values of diversity, equity, and inclusion for patients and researchers, and prioritises an open-science approach to data sharing and dissemination of results.

Conclusion By using an innovative and efficient adaptive multi-interventional trial platform design, we aim to accelerate and improve care for patients with fILD. Through worldwide collaboration, novel analytical methodology and pragmatic trial delivery, REMAP-ILD aims to overcome major limitations associated with conventional randomised controlled trial approaches to rapidly improve the care of people living with fILD.

BACKGROUND

Interstitial lung diseases (ILDs) are a group of pulmonary disorders that occur due to a variety of causes, including many different environmental and genetic factors.[1–4] ILDs are often subcategorised as fibrotic, inflammatory or fibroinflammatory based on clinical and radiological features, and in some cases, supplemented with immunological and histological data. Patients with fibrotic ILD (fILD) typically have a poor prognosis, with significant morbidity and mortality.[5–8] There is an urgent unmet need for better pharmacological and non-pharmacological therapies for patients affected by fILD.[9]

Standard of care for fILD varies substantially, even for those fILDs where guidelines exist. The heterogeneity in the management of fILD reflects the lack of robust evidence in the field.[10–13] Conversely, development of new therapeutic agents has been limited by the complexity and heterogeneity of disease pathophysiology. These challenges require changes to conventional drug development, including other non-pharmacological treatment modalities.

PREVIOUS CLINICAL TRIAL DESIGNS IN FILD

Previous clinical trials in fILD have typically been conventional placebo-controlled randomised controlled trials (RCTs) that usually evaluated a single investigational product, with a treatment and a control arm, and a prespecified fixed sample size. Previous RCTs initially focused on idiopathic pulmonary fibrosis (IPF),[14 15] with more recent attention on non-IPF fILD.[16–18] However, the traditional research protocol misses several opportunities to increase efficiency such as investigating multiple interventions simultaneously, testing for interaction among treatment combinations and early stopping for non-promising interventions (tables 1 and 2).[19–21] Alternative study designs such as the Randomised Embedded Multifactorial

Table 1 Limitations of traditional randomised controlled trials in interstitial lung disease

	Typical limitations
Trial design	► Need for large, fixed and dedicated sample sizes to independently address each research question or intervention in separate studies ► Fixed study duration ► Lack of generalisability of data from homogeneous study cohorts to real-world populations ► Equally likely for patients to receive control or active treatment ► Limited incentive to design head-to-head trials of approved treatments
Operational factors	► Site related: – Infrastructural barriers to conducting clinical trials in a broad and diverse geographical area, particularly in small centres and under-resourced settings (reduced equity) ► Sponsor related: – High operational costs, including costs to build study infrastructure for each trial and support extensive tests that fall outside patient care ► Study related: – Lack of open data – Slow identification of new successful interventions – Delays in translating results into clinical practice
Patient factors	► Extensive inclusion and exclusion criteria and disease-specific focus (reducing opportunities to participate and equity of access to new treatments/interventions) ► Burden of patient schedule, including additional travel requirements ► Limited access to trials and increased inequality due to frequent focus on only a few specialist trial sites

Adaptive Platform (REMAP) trials may be better equipped to efficiently explore potential treatments. Adaptive platform trials have successfully been implemented to investigate treatments in pancreatic cancer,[22] Alzheimer's disease,[23] amyotrophic lateral sclerosis,[19] community-acquired pneumonia (CAP) and COVID-19.[24]

REMAP TRIALS AS A SOLUTION TO CHALLENGES IN IDENTIFYING EFFECTIVE ILD TREATMENTS

REMAP trials are characterised by five key features as described in table 2. These key features provide multiple advantages over conventional RCTs, collectively maximising trial efficiency and supporting rapid generation of new knowledge.[25] These advantages are particularly impactful for rare diseases such as fILD that have a poor prognosis, few evidence-based treatment options and numerous potential treatments/interventions at the clinical trial phase of development.[26]

Table 2 Key features of REMAP trials

Key features		Description
R	Randomised	Patients are randomised to all interventions for which they are eligible and consent to.
E	Embedded	The study protocol is embedded within routine clinical care, reflecting standard practice,and minimising additional study procedures.
M	Multifactorial	Multiple interventions (factors) are tested concurrently, with patients randomised to multiple treatment domains, increasing the probability of receiving at least one active treatment rather than control.
A	Adaptive	Information acquired during the trial is used to adaptively determine how the study should progress based on prespecified procedures in the protocol, such as a randomisation algorithm to determine randomisation weights to factors and stopping rules defining early success or futility.
P	Platform	A perennial infrastructure is developed with the objective to generate a continuous learning system.

Terminology

The distinct features of REMAP trials necessitate precise and standardised terminology. As defined in table 3, REMAP trials contain multiple mutually exclusive treatment *factors*. A factor describes the intervention being studied, which could be a medicinal or non-medicinal product. Examples of factors include existing standard of care treatments or active treatments. One or more factors may be grouped together into a treatment *domain*, with a domain describing a specific approach to clinical management. For example, an antifibrotic domain could include standard of care and one or more antifibrotic treatments, while an immunomodulatory domain could contain standard of care and one or more immunomodulatory treatments. A patient is randomised to a single factor within each domain of the adaptive platform trial and receives treatments in active domains for which they are eligible. Thus, a patient can be randomised to multiple factors across multiple domains. This collection of factors coming from separate domains administered to the individual patient is referred to as that patient's *regimen* (figure 1). A *stratum* (for example, a diagnosis of IPF) captures a specific baseline disease characteristic that makes patients eligible or ineligible for particular domains, and can be used for stratified randomisation and/or strata-specific analyses. This means that not all patients entering the platform are eligible to be randomised to all platform domains. For example, an immunomodulatory domain is made unavailable for patients with IPF. REMAP trials also possess specific analytical characteristics, as described below, that can increase study efficiency.

Principles of REMAP trials

REMAP trials are intended to operate as a perennial platform where new domains and/or factors (interventions) are added when understood to be a research priority and when additional funding to support such an addition is acquired (figure 2). They are randomised clinical trials centred around a core protocol that is embedded in routine patient care,[15 17] reducing recruitment burden and increasing recruitment rate.[27] The core protocol provides global details on trial design and conduct that is supplemented with domain-specific and region-specific appendices. These appendices describe prespecified protocol details for specific interventions and geographical regions; for example, details may include adaptations to treatment-specific exclusion criteria or specific healthcare system requirements.[15] This modular structure allows rapid and efficient modification to individual components of the study with minimal disruption to overall study conduct, which includes the addition of new interventions or removal of ineffective interventions.

Multifactorial design

The multifactorial aspect of a REMAP trial permits simultaneous assessment of several interventions across multiple therapeutic domains and different disease strata.[25 28] Multifactorial designs facilitate efficient use of resources, leveraging patient data across multiple domains and providing support for important, but potentially less commercially appealing, research questions enabling these research questions to be answered simultaneously with questions for which funding may be more readily obtainable. A patient can be assigned to the control arm in one domain

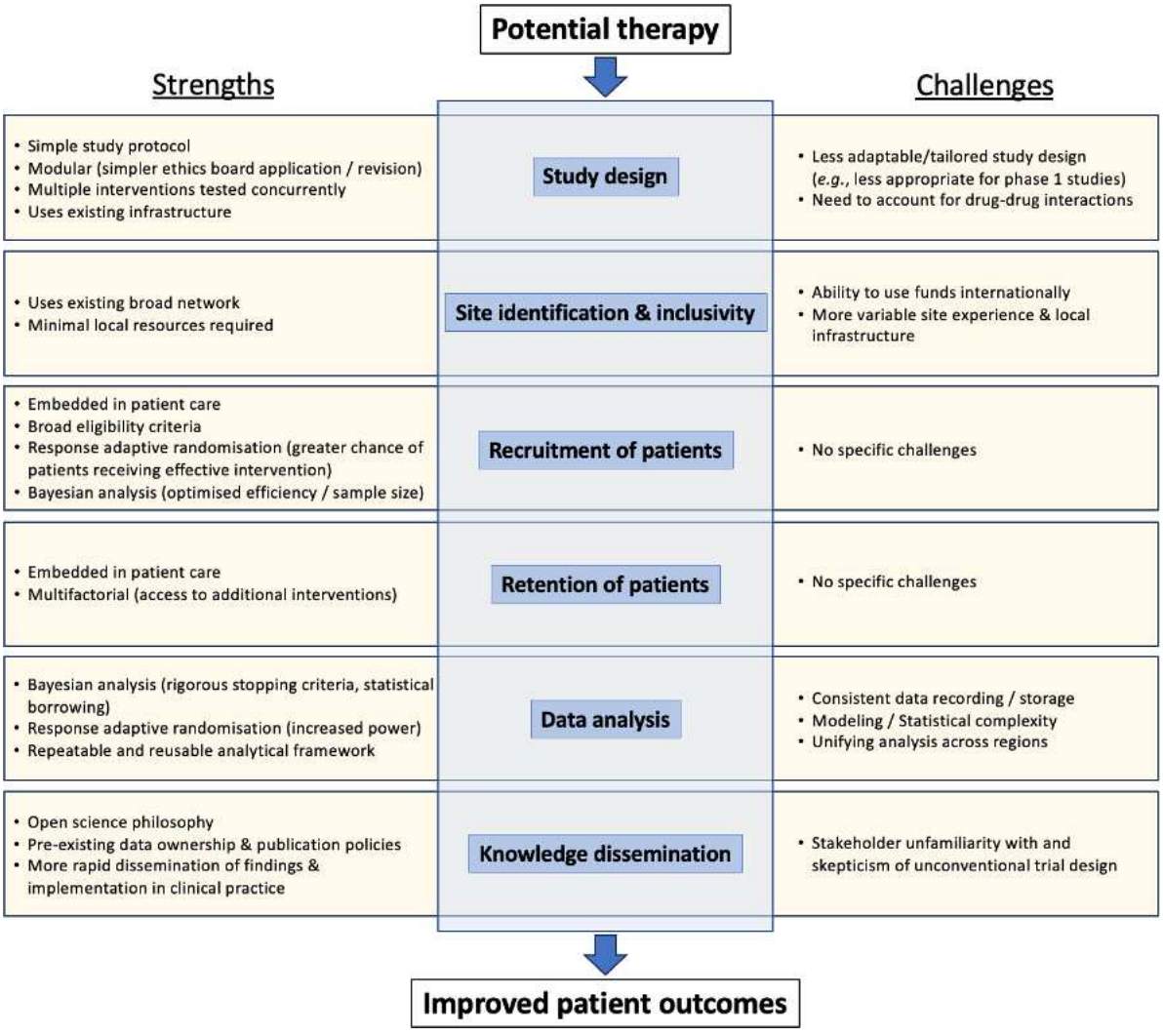

Figure 1 Strengths and challenges of REMAP trials as compared with conventional randomised controlled trials. REMAP, Randomised Embedded Multifactorial Adaptive Platform.

but to active treatments in other domains. This patient-centred approach decreases the number of trial participants who receive only standard of care or placebo, ensuring that more patients receive active treatments, which appeals to patients and increases trial attractiveness.

Adaptive features

REMAP trials, like all RCTs, require a comprehensive statistical analysis plan (SAP) addressing typical issues, while also requiring additional work to arrive at the best adaptive features to be used prior to initiation of the trial. These design decisions are informed by extensive simulations whenever possible using real-world data.[25] Design decisions are supported by the analysis of the trial performance characteristics under different simulated circumstances.

Multiple adaptive features can be employed, with the Bayesian statistical framework leveraging all available data, naturally enabling prespecified adaptations. These adaptive features include response-adaptive randomisation (RAR), which concentrates recruitment to therapies that appear to be beneficial, while minimising resource use and risks for enrolled patients.[28] There is also greater potential to terminate a given factor or domain based on predetermined thresholds for success or futility.[29] Similarly, should targeted therapies become available at some time in the future, the protocol can be adapted to incorporate stratified randomisation. All of these adaptive features are supported within a platform infrastructure that, once study start-up and site initiation are established, leverages the ongoing infrastructure to assess numerous therapies over time.

Recruitment and retention of patients

Not infrequently many patients are excluded from traditional clinical trials due to extensive inclusion and exclusion criteria.[30] REMAP trials typically have broad eligibility criteria and simple study procedures that maximise patient recruitment while also retaining the ability to test heterogeneity of treatment effects across prespecified strata.[29] Embedding the trial in routine clinical practice with minimal additional study visits also increases the likelihood that patients residing in more remote areas can participate. The simplified study protocol embedded within routine clinical care and the ability to randomise patients to multiple domains facilitate the retention of patients by reducing the burden of study visits and increasing the incentive to ongoing participation, respectively. To ensure that patients from low/middle-income countries can participate in REMAP-ILD, the core protocol is pragmatic, with minimally required data collection required to ensure successful delivery of the trial. This will reduce the burden of delivery and cost to ensure that more

Table 3 Common terminology used in REMAP trials

Term	Definition	Examples
Factor	The mutually exclusive interventions, categorised within domains, to which a patient can be randomised.	▶ Pirfenidone ▶ Nintedanib ▶ New antifibrotic ▶ Control
Domain	A distinct category of mutually exclusive interventions called factors; patients can be randomised to receive a factor from a domain for which they are eligible.	▶ Antifibrotic ▶ Immunomodulatory ▶ Senolytic ▶ Corticosteroids
Regimen	The collection of factors that a patient is randomised to across domains; patients receive one unique factor from each domain for which they are eligible.	▶ Pirfenidone, mycophenolate, metformin and corticosteroid ▶ Nintedanib, control (no immunomodulation), metformin and control (no corticosteroid)
Stratum	Baseline disease characterisation that defines which domain(s) a patient is potentially eligible to participate in; strata can be used for stratified randomisation and strata-specific analyses.	▶ IPF ▶ Non-IPF fILD

fILD, fibrotic interstitial lung disease; IPF, idiopathic pulmonary fibrosis; REMAP, Randomised Embedded Multifactorial Adaptive Platform.

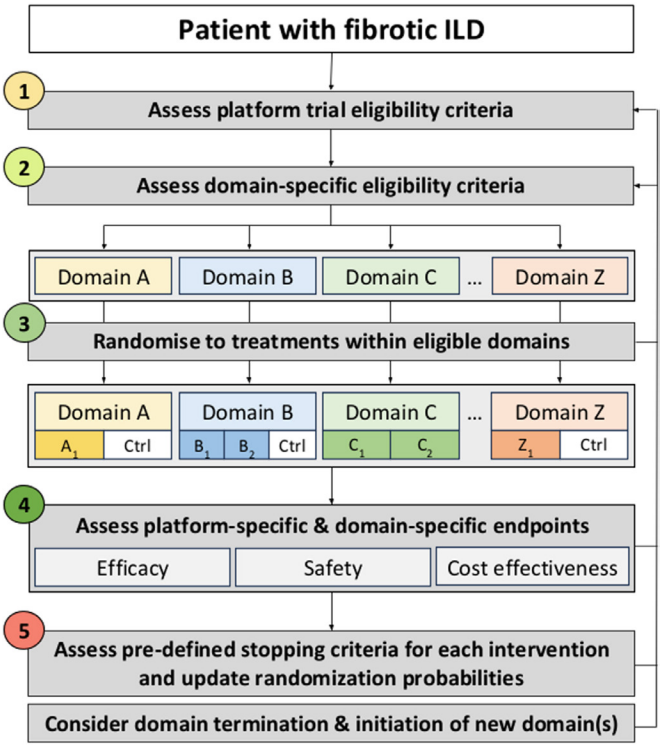

Figure 2 Study overview. Patients with fibrotic ILD will be assessed for platform eligibility criteria (step 1), after which, screening for domain-specific eligibility criteria will be performed (step 2). Patients who meet eligibility criteria for at least one domain will be randomised to an intervention (factor) from each domain (step 3), which could include a variety of different options depending on the available interventions (indicated by subscripts). Patients would then be initiated on therapy and complete study assessments that allow analysis of efficacy, safety and cost-effectiveness outcomes (step 4). Predefined stopping criteria for each intervention will be assessed throughout the study (step 5), with termination of completed interventions (factors) and/or domains and initiation of new interventions (factors) and/or domains. Patients will be continuously assessed throughout their participation in the study for eligibility of previously existing and newly added domains. Domain refers to a group of interventions that are mutually exclusive. Interventions are called factors in the REMAP terminology. Ctrl, control arm; ILD, interstitial lung disease; REMAP, Randomised Embedded Multifactorial Adaptive Platform.

people can participate even in resource-scarce scenarios. All information and data collection tools will be translated into the languages of participating centres.

Data analysis

Initial power calculations and number needed to recruit are based whenever possible on simulated trials using real-world data. REMAP trials include frequent prespecified adaptive analyses, the timing and frequency of which are based on data obtained from simulated trials.[28] Bayesian statistical methods are used during the trial to make prespecified changes to the protocol based on accruing data, including evaluation of differential treatment effects within prespecified strata, evaluation of prespecified intervention–intervention interactions and testing of multiple interventions.

An RAR algorithm may be used to preferentially randomise patients to interventions that have demonstrated a suggested benefit compared with other factors within a domain based on prespecified criteria that are assessed at interim analyses.[28] The study continues until a statistical stopping rule for success, futility or harm has been triggered, or until complete follow-up for the predefined maximum sample size has been reached. Although a priori sample size estimates are generated, the exact sample size of REMAP trials is not fixed as in conventional RCTs. Instead, predefined minimum and maximum sample sizes are defined, with the potential to quickly declare success or futility, using prespecified statistical rules, based on accumulating data. Reaching study conclusions before reaching the maximum sample size, through triggering a prespecified statistical rule for success or futility, allows more efficient use of funding and leads to better patient care.[21 31 32] This is an important advantage of REMAP trials, although it requires that regulatory agencies accept the employed analytical techniques.[33]

Funding structure

Funding global perennial adaptive platforms is a challenge as the current model for most funding organisations precludes fully integrated global collaboration by limiting the funds that can be transferred internationally. The funding structure is even more challenging for less-resourced countries and centres, as research funding is itself a source of research inequity. Further contributing to this challenge is the limited term for most funding sources, resulting in the need to frequently reapply for funding of a perennial international platform that tests multiple interventions over many years. Despite that, REMAP-CAP,[24] an investigator-initiated global platform, was able to thrive and succeed. REMAP-ILD is being planned to adapt the learning and principles of REMAP-CAP to investigate therapies for fILD as outlined below. As per January 2024, various funding applications have been submitted. A REMAP trial design proposal has been submitted to the National Institute for Health and Care Research (UK). An investigator-initiated interventional trial activating the steroid domain has been submitted to the Swiss National Science Foundation (SNF) (Switzerland). A proposal to activate the antifibrotic and steroid domain is under negotiation

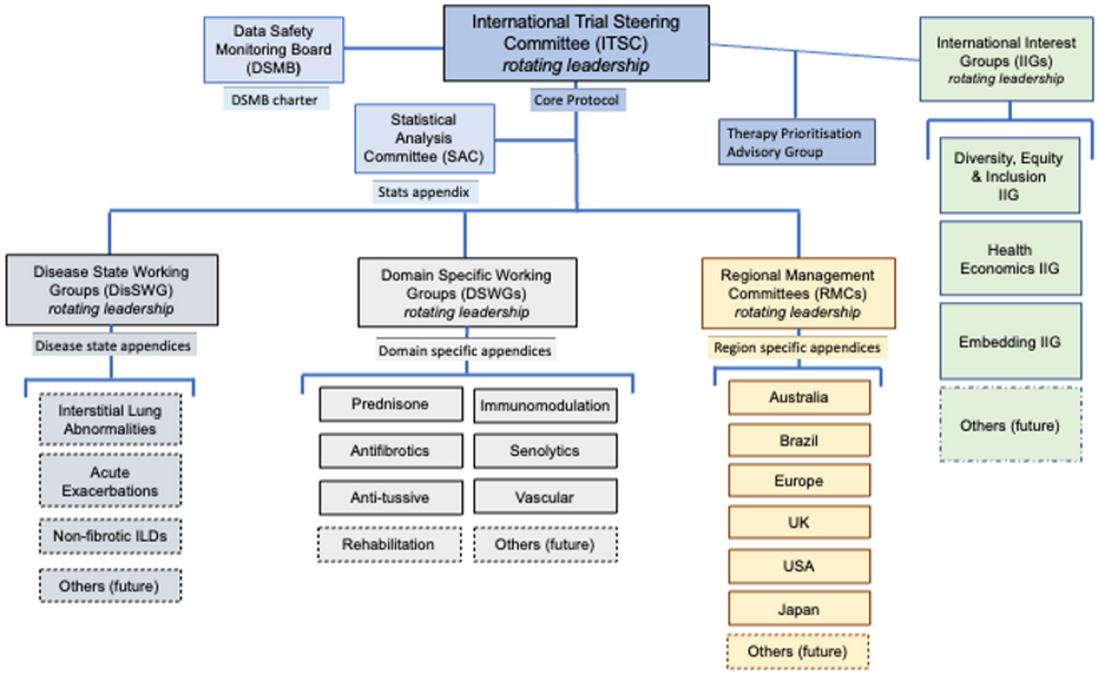

Figure 3 REMAP-ILD governance structure and their related documents. Dotted line boxes: desirable but not yet activated. Embedding refers to scenarios where REMAP-ILD will be embedded in clinical registries. Of note, if we succeed to embed REMAP-ILD in a clinical registry, patients will still be randomised to interventions within the registry. ILD, interstitial lung disease; REMAP, Randomised Embedded Multifactorial Adaptive Platform; Stats, statistical.

with the Brazilian Ministry of Health, PROADI-SUS Programme (Brazil). In addition, the European Patient-driven Research Hub for Effective Interventions in Interstitial Lung Diseases analogue to the REMAP-ILD structure has been proposed in a first stage Horizon call submission (HORIZON-HLTH-2024-DISEASE-03-08-two-stage Comparative effectiveness research for health-care interventions in areas of high public health need—European Union (EU)). The respective responses are currently pending. Additional submissions are currently under way to fund this global initiative and further sources of funding will be sought depending on the outcomes of these applications.

Knowledge dissemination

Governance policies within platform trials emphasise rapid and widespread dissemination of new knowledge through agreements on data sharing, data ownership and publication. The potential to reach earlier conclusions for success or futility contributes to the timely dissemination of evidence-based knowledge.

RANDOMISED EMBEDDED MULTIFACTORIAL ADAPTIVE PLATFORM IN FILD

Mission and values

REMAP-ILD is an international collaborative network (see online supplemental file 1) with the goal of rapidly and efficiently testing treatment options for patients with fILD, particularly therapies that are suitable for repurposing and thus less likely to be prioritised by pharmaceutical companies. REMAP-ILD is also interested in testing new drugs through phase II studies, which may be nested in the platform once it is established. The primary objective of REMAP-ILD is to test the effectiveness and safety of potential pharmacological and non-pharmacological treatments for fILD. Secondary objectives include assessment of specific subgroups of interest (eg, IPF vs non-IPF fILD) and cost-effectiveness, the latter will be specifically adapted at each regional level.

REMAP-ILD embraces the core values of diversity, equity and inclusion (DEI), and prioritises an open-science approach to data sharing and dissemination of results (see online supplemental file 2 for REMAP-ILD DEI statement).[34] There are four key principles underpinning the work performed by the REMAP-ILD consortium: first, DEI is at the core, and as such REMAP-ILD has embedded these values throughout the study. REMAP-ILD policies, documents and a governance structure prioritise DEI for participants, staff and collaborators. Second, non-discrimination in any form. We will be proactive in fostering inclusion both for patient participants and research staff and collaborators. Third, global involvement and representation. We will actively engage with under-represented communities worldwide. Fourth, accountability and continuous improvement. We will work across the board to gain feedback and iteratively improve our efforts.

Patient population

REMAP-ILD will aim to focus on all adults with fILD, using eligibility criteria that are as broad and inclusive as possible. To ensure the presence of clinically meaningful fibrosis, patients will be required to have CT evidence of pulmonary fibrosis (ie, traction bronchiectasis, or reticulation, and/or honeycombing) affecting ≥10% of the lungs on CT visual assessment. Patients will not be required to have evidence of progression, which simplifies enrolment and broadens application to a clinically relevant patient population. Of note, the implications of including progressive and non-progressive fILD on trial design are being carefully simulated and will be described in a separate manuscript and in the SAP. Stable background therapy for ≥8 weeks will be required to minimise the influence of recently adjusted treatment. Exclusion criteria for the core protocol are

minimal, with exclusion of only inflammatory-predominant ILD requiring urgent treatment, sarcoidosis or asbestosis as the primary ILD diagnosis, inability to perform forced pulmonary function test manoeuvres and expected survival <3 months. The exclusion of asbestosis and sarcoidosis is due to preliminary data demonstrating difference in disease progression in these groups compared with others. All other exclusion criteria will be in relation to patient safety. Domain-specific exclusions will apply.

Multifactorial design in REMAP-ILD

REMAP-ILD is intended to have multiple concurrently enrolling domains, each testing a distinct set of mutually exclusive interventions (figure 2). Patients will be randomised within each domain, receiving interventions for which they are eligible, potentially receiving multiple interventions (from different domains) under study. Several funding applications are under review across several countries, intended to initially support testing of antifibrotic therapy (pirfenidone and nintedanib), oral corticosteroids, immunomodulatory drugs (mycophenolate and azathioprine) and senolytics (metformin). Additional planned domains (eg, antitussive, pulmonary rehabilitation, diet, pulmonary vasodilators and possibly palliative care) will be activated as funding becomes available.

Primary outcome

The primary outcome will be a disease progression model over 12 months that incorporates measures of forced vital capacity (FVC) and mortality.

Study measurements

Protocol-specific tests will be minimal and will relate only to the baseline and 1-year assessments. All other study measurements will be those embedded in standard clinical care to minimise the burden on patients and healthcare staff, increase patient recruitment and retention, and reduce costs. These most notably include pulmonary function tests, patient-reported outcome measures (PROMs) and adverse effect monitoring. PROMs focus on dyspnoea, cough and quality of life, including health utilities that support cost-effectiveness analyses. Additional domain-specific protocolised measurements may be required. Adverse effects will be monitored and reported throughout the study and will be intervention dependent as performed in conventional trials.

Statistical analysis

REMAP-ILD will use RAR and prespecified rules for early stopping for success, harm or futility during preplanned interim analyses. REMAP-ILD power calculations and design decisions/choices are being informed by extensive simulations using real-world data coming from the PROFILE, INJUSTIS and CARE-PF Studies.[35–37] The primary analysis for these domains is a joint model of the FVC per cent-predicted trajectory combined with the HR for mortality and will be detailed in future publications.

Governance structure

The governance structure of REMAP-ILD facilitates oversight and management of all aspects of the study (figure 3). The International Trial Steering Committee takes overall responsibility for the trial design and conduct. An international Domain-Specific Working Group exists for each domain and is responsible for design and oversight of each domain, while a Regional Management Committee takes primary responsibility for trial execution in each participating region and any adaptations that are described in the corresponding regional-specific appendix. While interim analyses and assessment of potential stopping rules will be overseen by an independent Data Safety Monitoring Board (DSMB), the DSMB will not make design decisions unless the trial's algorithms are no longer acceptable from an ethical, safety or scientific point of view. To ensure appropriate prioritisation of interventions for REMAP-ILD domains, evidence will be assessed by an independent Therapy Prioritisation Advisory Group. Additional groups are responsible for other aspects of trial success (eg, DEI committee, health economics committee, patient and public advisory board) and all groups meet regularly to support study design and delivery. Patient participants are embedded throughout these committees and provided a platform for input on study design and conduct. REMAP-ILD is committed to adhering to all relevant data privacy regulations and guidelines to maintain patient confidentiality. Protection of patient data from unauthorised access will be ensured through the use of encrypted data collection tools such as OpenClinica, but with a federated data sharing model where regions own their own data. Overall, this integrated and scalable structure is designed to support REMAP-ILD's mission of rapidly answering clinically relevant questions and facilitates the continual evolution required to meet the needs of people living with fILD.

Challenges

Regulatory approvals

A major challenge associated with global platform trials such as REMAP relates to harmonisation of regulatory, data protection, ethical and governance procedures. Each region will have its own process for regulating trial conduct (eg, Food and Drug Administration, USA; European Medicine Agency, EU; Medicines and Healthcare products Regulatory Agency, UK) as well as procedures for implementation (eg, National Institute for Health and Care Excellence). Furthermore, implementation will depend on health economic assessments which will also be dependent on the nature of the intervention (high-cost therapy under patent vs repurposed generic drug vs non-pharmacological therapy). To overcome these challenges, numerous regional and special interest working groups are required (described in the Governance structure section) as well as iterative discussions with regulatory bodies to ensure that the simplest, most broadly applicable protocols align with their requirements.

Funding

Most funding agencies allow use of allocated funds only within specific regions, which presents a major challenge for a global investigator-driven network such as REMAP-ILD. This may lead to some components of the study being activated in only distinct regions depending on funding opportunities. This also highlights the need for improved international collaboration among funding organisations, particularly in the study of rare diseases such as fILD, so that international networks such as REMAP-ILD can function on a global scale. It is anticipated that initiation of REMAP-ILD and other similar platform trials will call attention to the need for major granting agencies to support research for rare diseases in a more sustainable and globally equitable manner.

CONCLUSION

REMAP-ILD is an innovative and efficient approach for investigating treatment efficacy and safety in fILDs, which will result in improved, evidence-based patient care. Through global collaboration, novel analytical methodology and pragmatic clinical trial delivery, we anticipate that the REMAP-ILD design will overcome major limitations associated with conventional development of

therapeutic and non-pharmacological strategies in fILD, thereby improving the care of patients living with fILD across the world.

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Collaborators Members of the REMAP-ILD consortium are listed in online supplemental file 1.

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SUPPLEMENT FILE 2

Diversity, Equity, and Inclusion (DEI) Mission Statement for REMAP-ILD, a Randomised Embedded Multifactorial Adaptive Platform for Interstitial Lung Diseases

The members of the Randomised Embedded Multifactorial Adaptive Platform for Interstitial Lung Diseases (REMAP-ILD) consortium are committed to fostering a diverse, equitable, and inclusive research community. We recognize that diversity in all its forms is essential to advancing our understanding of fibrotic interstitial lung diseases (FILDs) and improving patient outcomes. This mission statement outlines our shared goals of DEI in research, with a focus on eliminating discrimination, promoting global involvement, and considering feasibility across regions.

1 Diversity Equity and Inclusion for REMAP-ILD Patients, Resources, and Countries

- We will work to ensure that all patients, researchers, and countries involved in REMAP-ILD experience equitable treatment, access, and opportunities.
- We are dedicated to addressing any disparities in participation, access to resources, or benefits that may arise during the course of our research.
- We acknowledge that the feasibility of certain study components may vary across regions due to differences in resources, infrastructure, and capacity.
- We commit to assessing these challenges and actively working to address them through capacity-building initiatives, collaborations, and resource allocation.
- Our goal is to enable equitable participation and contribution from all regions, supporting the development of critical research infrastructure.

2 Non-Discrimination

- We reject all forms of discrimination, including but not limited to race, ethnicity, nationality, gender, sexual orientation, religion, and other personal characteristics.
- We actively encourage the inclusion of individuals from diverse backgrounds in our patient populations and in our research teams.
- Discrimination in any form conflicts with our mission and should not be tolerated within our network.

3. Global Involvement and Representation

- We recognize that interstitial lung diseases (ILDs) affect individuals worldwide, and our research must reflect this global reality.
- We are committed to ensuring equitable representation of patients, researchers, and countries from all regions of the world within our network.
- We actively seek to engage with underrepresented communities and regions to amplify diverse voices in our research efforts

4. Accountability and Continuous Improvement

- We will be accountable for our commitments and make necessary adjustments to achieve our DEI goals.
- We welcome feedback and input from all members of the REMAP-ILD community to iteratively improve our DEI efforts.

By agreeing to participate in REMAP-ILD we affirm our commitment to creating a research environment that is diverse, inclusive, equitable, and respectful of all individuals. Together, we will strive to make meaningful advancements in our understanding of ILDs and improve the lives of those affected by these diseases worldwide.

INTRODUCTION : Les pneumopathies interstitielles diffuse fibrosantes (PIDf) sont un groupe hétérogène de maladies pulmonaires associées à une morbidité et une mortalité significative. Malgré une forte augmentation du nombre d'essais cliniques au cours des 10 dernières années, les traitments actuellement approuvées par les régulateurs se limitent à deux thérapies antifibrotique. Le « pipeline » de développement de médicaments est long et il est urgent d'accélérer ce processus. Ce manuscrit présente le concept et la conception d'une approche de recherche innovante pour le développement de médicaments dans les PIDf : une Plateforme Adaptative Multifactorielle Intégrée Randomisé Mondiale dans les PIDf (REMAP-ILD).
MÉTHODES : Description du concept et de la conception du REMAP-ILD : la terminologie spécifique, les caractéristiques de conception (multifactorielle, fonctionnalités adaptatives, approche statistique), la population cible, les interventions, les résultats, la mission et les valeurs, ainsi que la structure organisationnelle.
RÉSULTATS : La population cible sera constituée de patients adultes atteints de PIDf, et le critère principal sera un modèle de progression de la maladie intégrant la CVF (capacité vitale forcée) et la mortalité sur 12 mois. Une randomisation adaptative réactive, des seuils prédéfinis pour le succès et la futilité seront utilisés pour évaluer l'efficacité et la sécurité des interventions. REMAP-ILD embrasse les valeurs fondamentales de la diversité, de l'équité et de l'inclusion pour les patients et les chercheurs, et privilégie une approche de science ouverte pour le partage des données et la diffusion des résultats.
CONCLUSION : En utilisant un design innovant et efficace de plateforme d'essai multi-intervention adaptative, nous visons à accélérer et à améliorer les soins aux patients atteints de PIDf. Grâce à une collaboration mondiale, une méthodologie analytique novatrice et une livraison pragmatique d'essais, REMAP-ILD vise à surmonter les principales limitations associées aux approches classiques d'essays randomisé pour améliorer rapidement les soins des personnes vivant avec PIDf.

INTRODUÇÃO: As doenças pulmonares intersticiais fibrosantes (DPIf) constituem um grupo heterogêneo de doenças pulmonares associadas a significativa morbidade e mortalidade. Apesar do grande aumento no número de ensaios clínicos nos últimos 10 anos, os tratamentos farmacológicos atualmente aprovados por órgãos reguladores são limitadas a dois antifibróticos. O "pipeline" de desenvolvimento de medicamentos é longo e há uma necessidade urgente de acelerar esse processo. Este manuscrito introduz o conceito e o design de uma abordagem inovadora para acelerar o desenvolvimento de tratamentos em DPIf: uma Plataforma Adaptativa Multifatorial Inserida (na prática clínica) Randomizada Global em DPIf (REMAP-ILD).

MÉTODOS: Descrição do conceito e design do REMAP-ILD: terminologia específica, características do design (multifatorial, recursos adaptativos, abordagem estatística), população-alvo, intervenções, resultados, missão e valores, e estrutura organizacional.

RESULTADOS: A população-alvo serão pacientes adultos com DPIf, e o desfecho primário será um modelo de progressão da doença que incorpora a CVF (capacidade vital forçada) e mortalidade ao longo de 12 meses. A randomização adaptativa responsiva, limiares pré-especificados para sucesso e futilidade serão utilizados para avaliar a eficácia e segurança das intervenções. O REMAP-ILD abraça os valores fundamentais da diversidade, equidade e inclusão para pacientes e pesquisadores, e prioriza uma abordagem de ciência aberta para compartilhamento de dados e divulgação de resultados.

CONCLUSÃO: Ao utilizar um design de plataforma de ensaio inovador e eficiente, com múltiplas intervenções adaptativas, buscamos acelerar e melhorar o cuidado com pacientes com DPIf. Através da colaboração global, metodologia analítica inovadora e pragmatismo em pesquisa, o REMAP-ILD visa superar as principais limitações associadas às abordagens convencionais dos ensaios clínicos randomizados (ECR) com vistas a melhorar a assistência em saúde das pessoas que vivem com DPIf.

INTRODUCCIÓN: Las enfermedades pulmonares intersticiales difusas fibrosantes (EPIDf) son un grupo heterogéneo de enfermedades pulmonares asociadas con una morbilidad y mortalidad significativas. A pesar del incremento en el número de ensayos clínicos en los últimos 10 años, los tratamientos actualmente aprobados por las autoridades reguladoras se limitan a dos fármacos anti-fibróticos. El desarrollo de medicamentos es largo y existe una necesidad urgente de acelerar este proceso. Este manuscrito presenta un método de investigación farmacológica con concepto y diseño innovador en EPIDf: una Plataforma Adaptativa Multifactorial Randomizada Integradora y Global en EPIDf (REMAP-ILD).

MÉTODOS: Descripción del concepto y diseño de REMAP-ILD: terminología específica, características del diseño (multifactorial, características adaptativas, enfoque estadístico), población objetivo, intervenciones, resultados, misión y valores, y estructura organizativa.

RESULTADOS: La población objetivo serán pacientes adultos con EPIDf, y el objetivo principal a evaluar es la progresión de la enfermedad (reducción de la capacidad vital forzada (CVF), combinando un modelo bayesiano control) y la mortalidad a los 12 meses. Se utilizará una randomización adaptativa, límites preestablecidos para el éxito y la futilidad para evaluar la eficacia y seguridad de las intervenciones. REMAP-ILD abraza los valores fundamentales de diversidad, equidad e inclusión para pacientes e investigadores, y prioriza un enfoque de ciencia abierta para el intercambio de datos y la difusión de resultados.

CONCLUSIÓN: Al utilizar un diseño de plataforma de ensayos multi-intervencionales adaptativos e innovadores, buscamos acelerar y mejorar la atención a los pacientes con EPIDf. A través de la colaboración mundial, metodología analítica novedosa y entrega pragmática, REMAP-ILD tiene como objetivo superar las principales limitaciones asociadas con los ensayos clínicos randomizados para mejorar rápidamente la atención de las personas que viven con EPIDf.