Amsterdam UMC
Universitair Medische Centra

PVRI Drug Discovery and Development Symposium

Impressions and lessons learned

Harm Jan Bogaard and Louise Bouman

08:25-08:30 **Welcome**
Anna Hemnes, PVRI President 2024-2026

SESSION 1: New standards of care
Moderators: Anna Hemnes, Harm Jan Bogaard

08:30-09:00 **Global perspective on regulatory approval of Sotatercept**
Mitchell Psotka, FDA (virtual) & Illiana Meurs, Dutch Medicines Evaluation Board (CBG-MEB)

09:00-09:20 **How Sotatercept will change the treatment algorithm**
Luke Howard

09:20-09:40 **Implications of a new background therapy for drug development**
Marion Delcroix

08:30-09:00 **Global perspective on regulatory approval of Sotatercept**
Mitchell Psotka, FDA (virtual) & Illiana Meurs, Dutch Medicines Evaluation Board (CBG-MEB)

Sotatercept **to improve exercise capacity** vs. **to improve outcomes**

08:30-09:00 Global perspective on regulatory approval of Sotatercept
Mitchell Psotka, FDA (virtual) & Illiana Meurs, Dutch Medicines Evaluation Board (CBG-MEB)

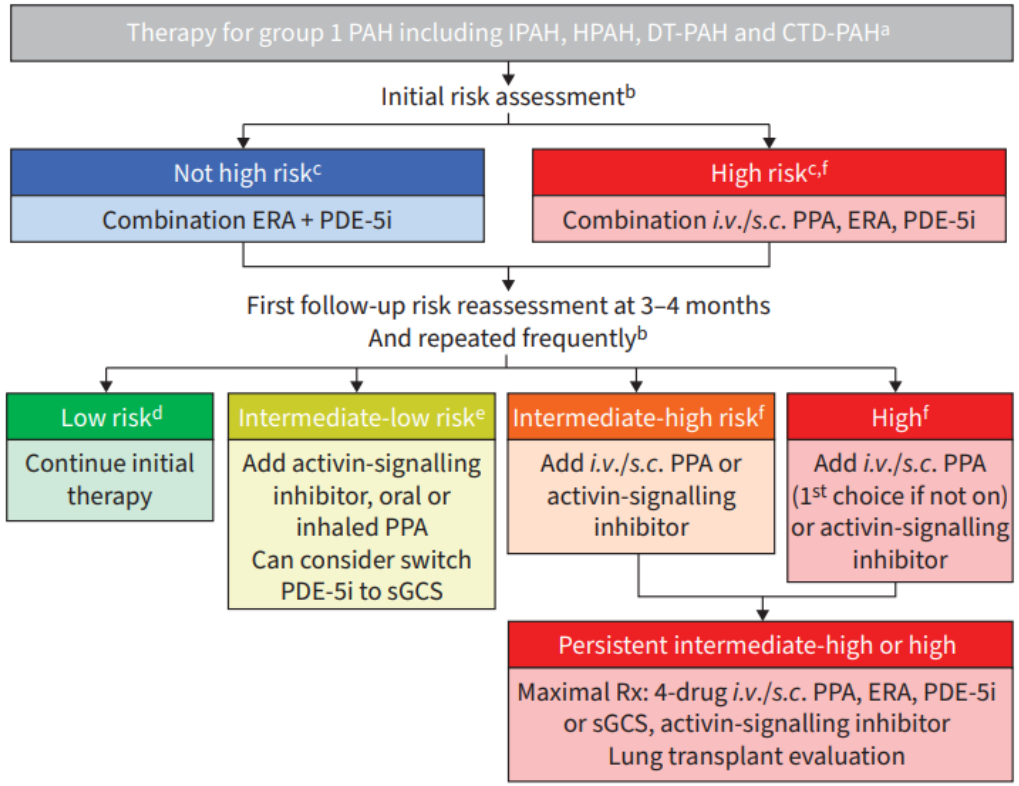
Comment from patient perspective:

The final approved indication was narrowed to improving **exercise capacity only**, removing all references to secondary endpoints.

The lack of consistency in how health-related quality of life has been measured across clinical trials in PAH.

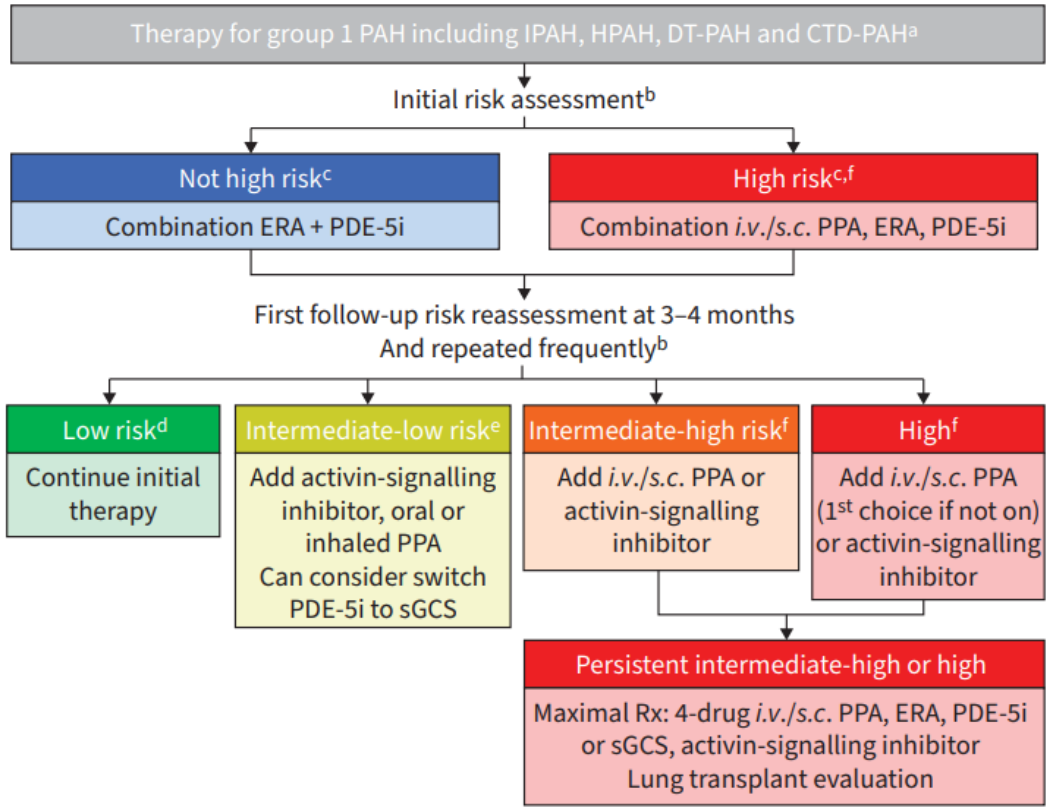
How Sotatercept will change the treatment algorithm

Luke Howard



Chin, ERJ 2024

- Based on Stellar… But what are the implications of the **Zenith** and **Hyperion** studies?
- Low Risk is not **No Risk**…. Should we aim for **normalization of hemodynamics**?
- When can we think of treatment **withdrawl?**



Chin, ERJ 2024

How Sotatercept will change the treatment algorithm

Luke Howard

Will future evidence also support the immediate use of sotatercept in patients diagnosed at high risk???

Or starting with quadruple therapy, with an extra option for later to stop the IV and replace it with selexipag if needed?

Implications of a new background therapy for drug development

Marion Delcroix

- Many new questions, new trial designs and endpoints are required
- Will we require Sotatercept in control arm to register new drug?
- Enrichment strategies based on biomarkers?
- New kinds of drug interactions and side effects
- Clinical trial network
- Patient involvement

Implications of a new background therapy for drug development

Marion Delcroix

During the discussion, Prof. Delcroix was asked about the use of quality of life as a potential outcome measure in clinical trials.

Only 20% of her patients complete these questionnaires before follow up and suggested this might mean patients are not interested in them.

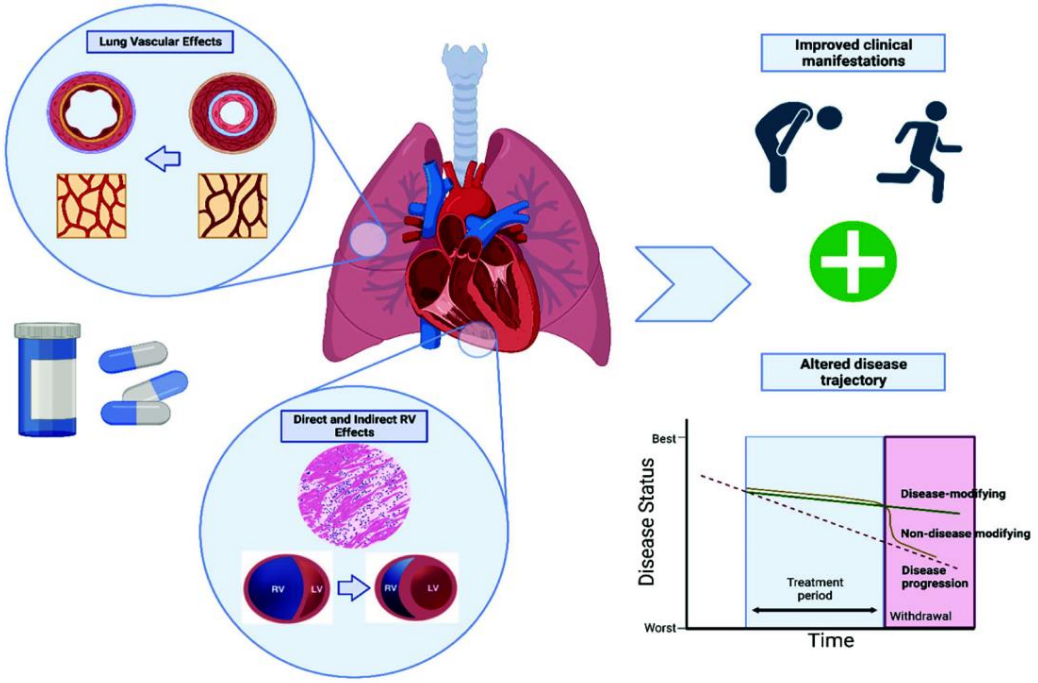
SESSION 2: Disease modification

Moderators: Zhi-Cheng Jing, Martin Wilkins

10:00-10:20	How to define or prove disease modification Mark Toshner
10:20-10:40	The role of imaging in establishing disease modifying effects of a trial drug Sudarshan Rajagopal

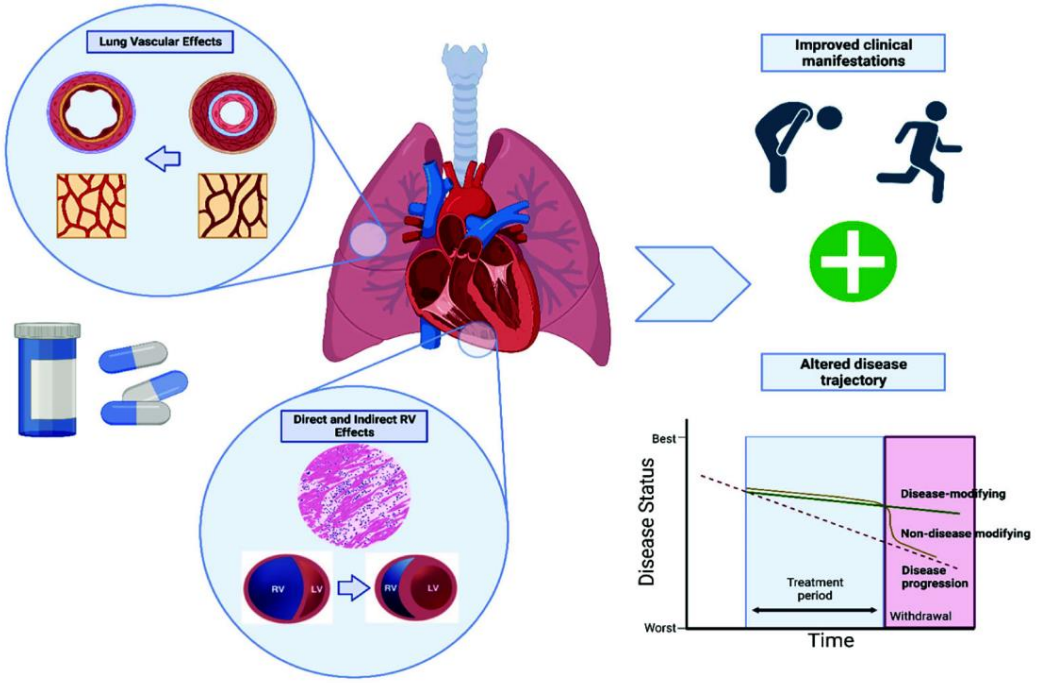
How to define or prove disease modification

Mark Toshner



- Concept pioneered in rheumatology
- Persistent effect on the course of a disease
- How to define disease status?
- What is the patients perspective?

How to define or prove disease modification
Mark Toshner



Harm | No Response | Modest Response | Strong Response | Disease Modification | Cure

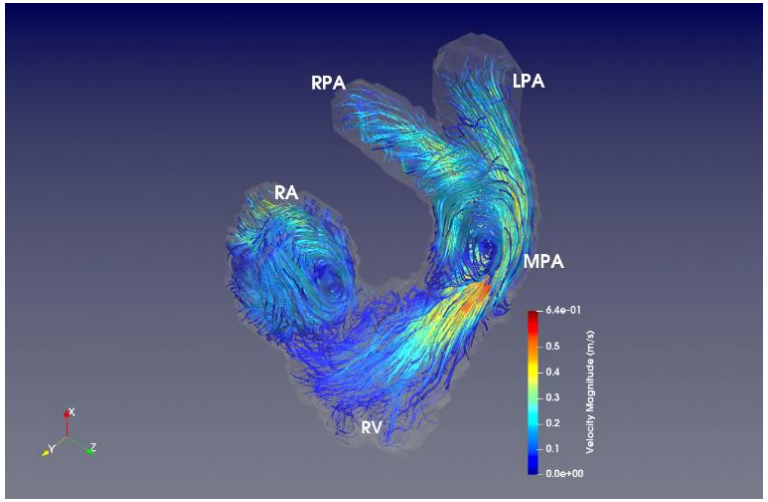
What is the patients perspective?

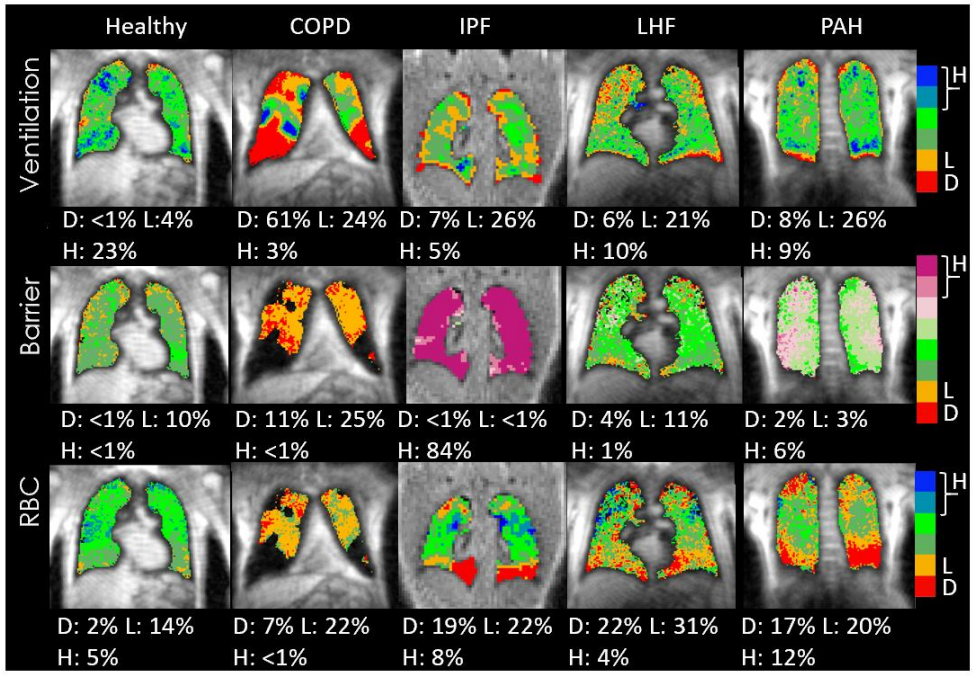
- remission is not just a medical term
- reclaiming a sense of normal life
- stability, fewer symptoms, and most importantly, more freedom

The role of imaging in establishing disease modifying effects of a trial drug

Sudarshan Rajagopal

- Pathophysiology of the disease can be imaged, both in the lungs and in the heart
- Correlation with how a patient functions, feels or survives, but not formerly validated





Patient perspective:

- Innovative methods offer promise in assessing microvascular changes, further validation is needed.
- AI potential in pattern recognition, helping extract features from MRI?

SESSION 3: Diversity & inclusion
Moderators: Gergely Meszaros, Esther Nossent

11:10-11:30	Addressing sex differences in treatment decisions & drug development Deimante Hoppenot
11:30-11:50	How to include underrepresented patients into cardiovascular clinical trials Cati Brown-Johnson

Addressing sex differences in treatment decisions & drug development

Deimante Hoppenot

- Women are more likely to develop PAH, but men are more likely to die from the disease
- While sex hormones seem implicated, they seem not suitable as treatment targets
- Some gender differences exist in therapeutic efficacy, but this area is underexplored
- Gender differences are not accounted for in therapeutic guidelines

Patient perspective

Next steps?

- Discover treatments designed for each sex
- Include sex as a key factor in all clinical trials and treatment guidelines

How to include underrepresented patients into cardiovascular clinical trials

Cati Brown-Johnson

- Systemic racism and historic mistrust lead to underrepresentation of minorities in clinical trials
- Community engagement, registries and social media use may take away some barriers during recruitment
- Use of some of these strategies were not developed for or tested in rare diseases
- New barriers may arise due to barriers to access to standard of care drugs

How to include underrepresented patients into cardiovascular clinical trials

Cati Brown-Johnson

How Patient Associations Can Support Inclusion in Clinical Trials

- ✔ Trusted voice with broad social media reach
- ✔ Accessible websites & clear communication
- ✔ Seen as reliable by patients
- ✔ Willing partners in outreach & education

💬 *"Engaging patient associations means engaging more patients – especially those we often miss."*

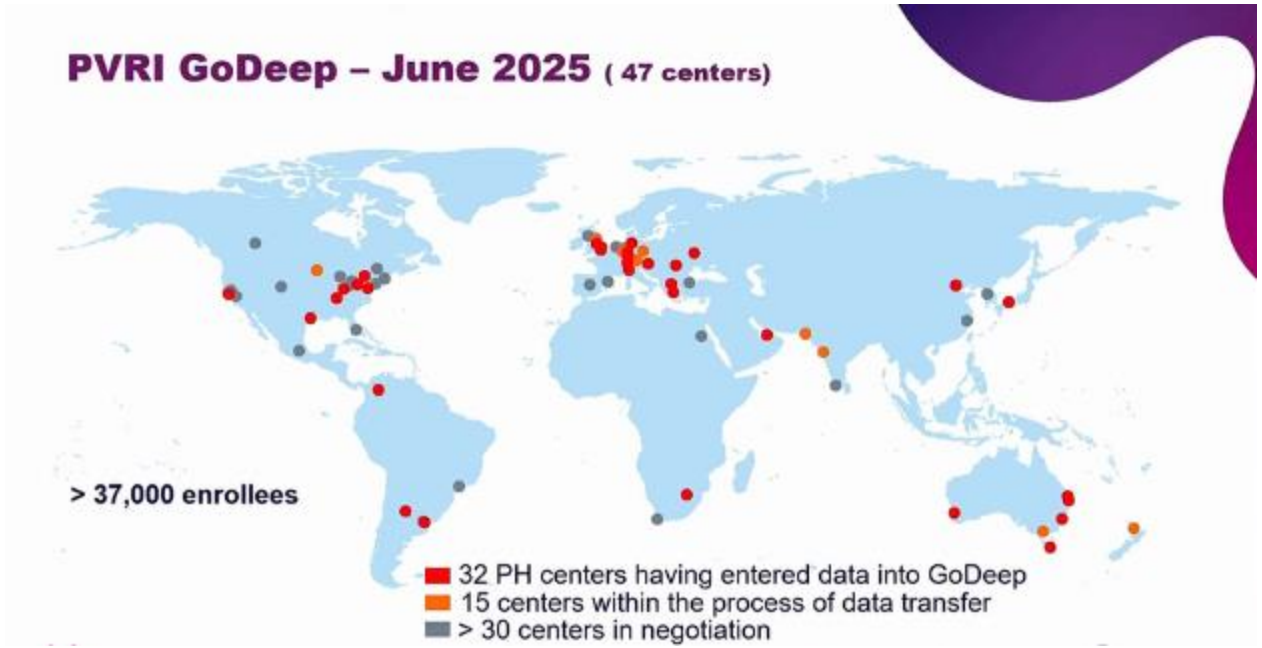
SESSION 4: Global aspects of drug development & availability

Moderators: Anton Vonk-Noordegraaf, Deimante Hoppenot

12:00-12:15	**Using the GoDeep Registry to prioritise & facilitate global drug trials** Werner Seeger
12:15-12:40	**Pro/con debate: It is Big Pharma's responsibility to prioritise drug availability over drug discovery** Pro: Anna Hemnes / Con: Ardeschir Ghofrani

Using the GoDeep Registry to prioritise & facilitate global drug trials

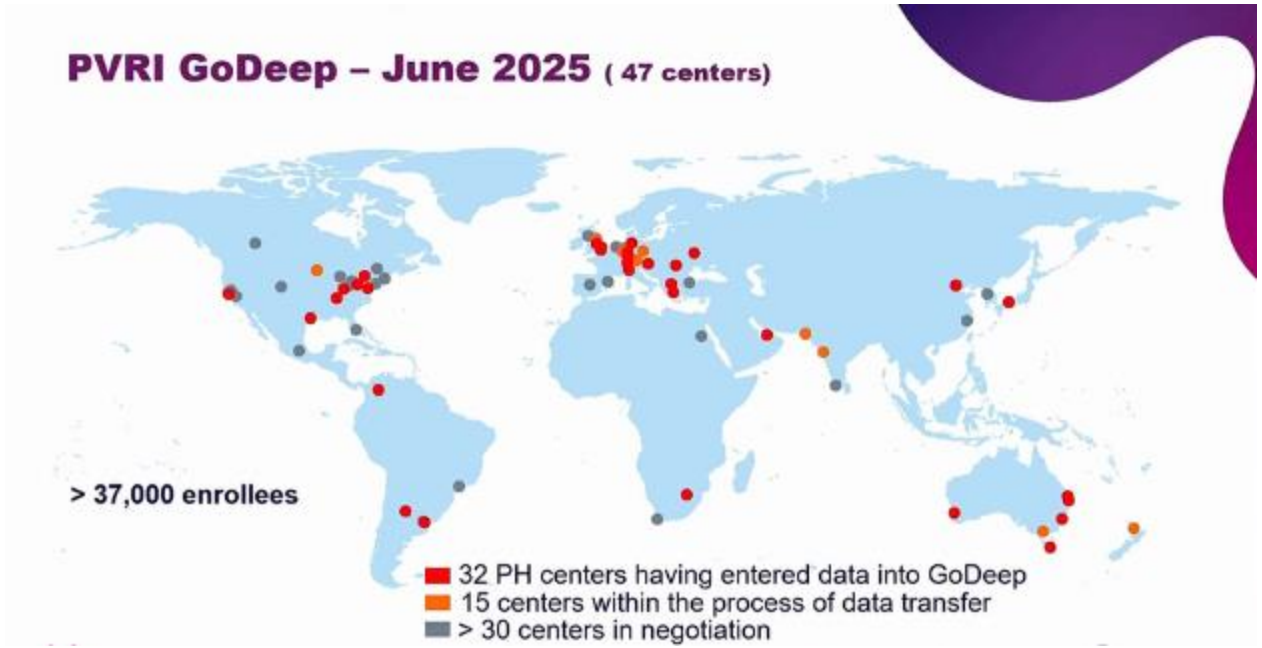
Werner Seeger



- Define subgroups of interest
- Inform on recruitment strategies
- Perform registry based clinical trial
- Validation of novel biomarkers for enrichment and or efficacy assessment
- Cost efficacy estimations

Using the GoDeep Registry to prioritise & facilitate global drug trials

Werner Seeger

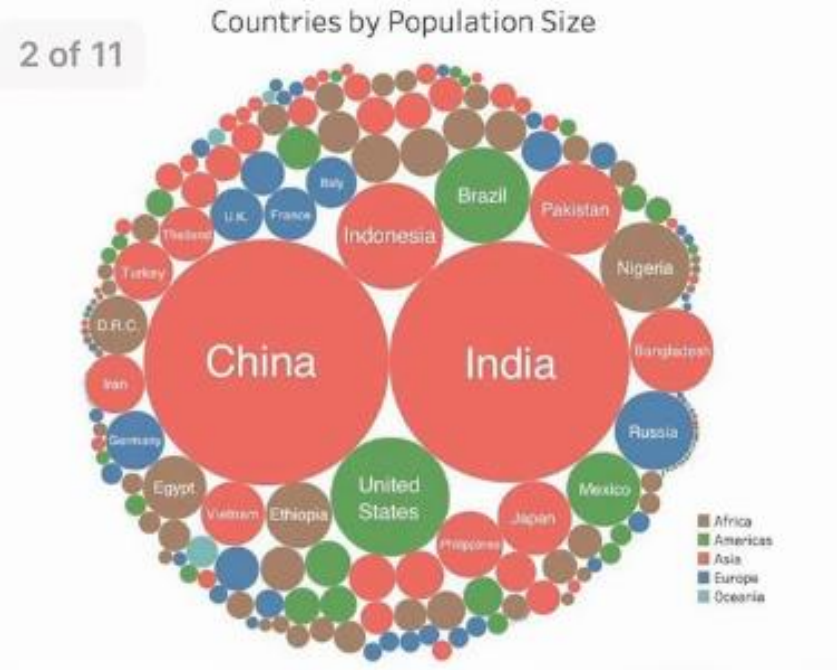


Why the registry matters for future treatments

- Help researchers decide who should or shouldn’t take part in a trial.
- Make sure trials include enough people to show whether a treatment works
- Test if new digital tools (like wearables or apps) can track disease activity

Pro/con debate: It is Big Pharma's responsibility to prioritise drug availability over drug discovery

Pro: Anna Hemnes / Con: Ardeschir Ghofrani



How to promote drug availability

Regulatory approaches:

- Reduce barriers to market entry
- Reduce "evergreening" for patents that facilitate prolonged drug exclusivity
- Consider reciprocal generic drug approvals across countries

Price reduction approaches:

- Facilitate legal use of generic drugs,
- Facilitate government negotiation of prices with producers
- Withdraw ineffective drugs in specific patients
- Precision medicine approaches to avoid polypharmacy

National Academics of Sciences, Engineering and Medicine, 2017

Pro/con debate: It is Big Pharma's responsibility to prioritise drug availability over drug discovery

Pro: Anna Hemnes / Con: Ardeschir Ghofrani

From Patients: We Support the Final Conclusion

- Innovation and access must go hand in hand
- We need new treatments—and we need to reach them
- Discovery gives hope, access turns it into reality

💬 *"Patients don't choose between innovation and access. We need both—always."*

SESSION 5: Innovations in trial design

Moderators: Athénaïs Boucly, Frances Varian

14:00-14:20	How to use risk scores (enrichment, endpoints) Athénaïs Boucly
14:20-14:40	How to use imaging endpoints reflecting the pulmonary circulation & RV David Kiely
14:40-15:10	n=1 trials & randomised withdrawal studies Martin Wilkins
15:50-16:10	Novel statistical approaches: Bayesian statistics, use of win ratio Alex Rothman
16:10-16:30	Practical & ethical aspects around OLE studies Harm Jan Bogaard
16:30-16:50	Climate impact of drug development Frances Varian

How to use imaging endpoints reflecting the pulmonay circulation & RV

Patients vision on:

Use of cMRI

- Backed by meta-analysis: 2,000+ patients, strong outcome prediction
- Non-invasive and safer than catheterisation
- Helps track disease progression and treatment effect
- Aligns with patient comfort and quality of care

Innovations like **AI-enhanced imaging** and **multi-modal techniques** (e.g., CT, implantable devices)

- offer detailed patient profiling and quicker, cost-effective measurements.

Practical and ethical aspects around OLE (Open Label Extension) studies

Open-Label Extension (OLE) Studies – A Key Priority for Patients

✅ Continuing treatment after a trial is essential for patients
✅ Major motivation to participate in studies
⚠️ Without this, fewer patients may join future trials
⚠️ OLE studies can lead to bias and reduce trial enrollment
💡 Alternative models must *still ensure* treatment access for responders

Climate impact of drug development

Reducing the Climate Impact of Clinical Trials

🌍 Digitization & remote trials = 20–30% fewer emissions

👩‍⚕️ Improves patient experience & retention

✅ Sustainable innovation benefits everyone

SESSION 6: Novel drug & device therapies

Moderators: Frances de Man, Jurjan Aman

08:30-08:55	**Antibody based inhibition of Endothelin signalling** Zhi-Cheng Jing
08:55-09:20	**Elafin** Roham Zamanian (virtual)
09:20-09:45	**Mosliciguat** Ardeschir Ghofrani
09:45-10:10	**New drugs to modify TGF- receptor signalling** Paul Yu
10:10-10:40	Refreshment break
10:40-11:05	**Seralutinib** Pilar Escribano Subías
11:05-11:30	**Aria Device** Marc Pritzker
11:30-11:55	**Pulmonary artery denervation** Alex Rothman

Seralutinib and Mosliciguat

Seralutinib

- Inhaled
- Phase 3:Prosera: PAH
- Start inclusion PH -ILD
- disease-modifying therapy?

Mosliciguat

- Inhaled, 1 x p day
- Phase 2 trial PH-ILD is coming

Take home messages

- The availability of Sotatercept will change many aspects of drug development, from development to new treatment algorithms, trial design, use of endpoints, choice of biomarkers, etc

- Call to action to address gender differences, barriers to trial participation, global disparities in drug availability, patient participation in drug development

- Personal disclosure> Small meetings are nice, Amsterdam is great!