L'Hypertension Artérielle Pulmonaire (HTAP) en 2026

Xavier JAIS
Service de Pneumologie
Centre coordonnateur CRMR PulmoTension
Hôpital Bicêtre

Conflits d’intérêts

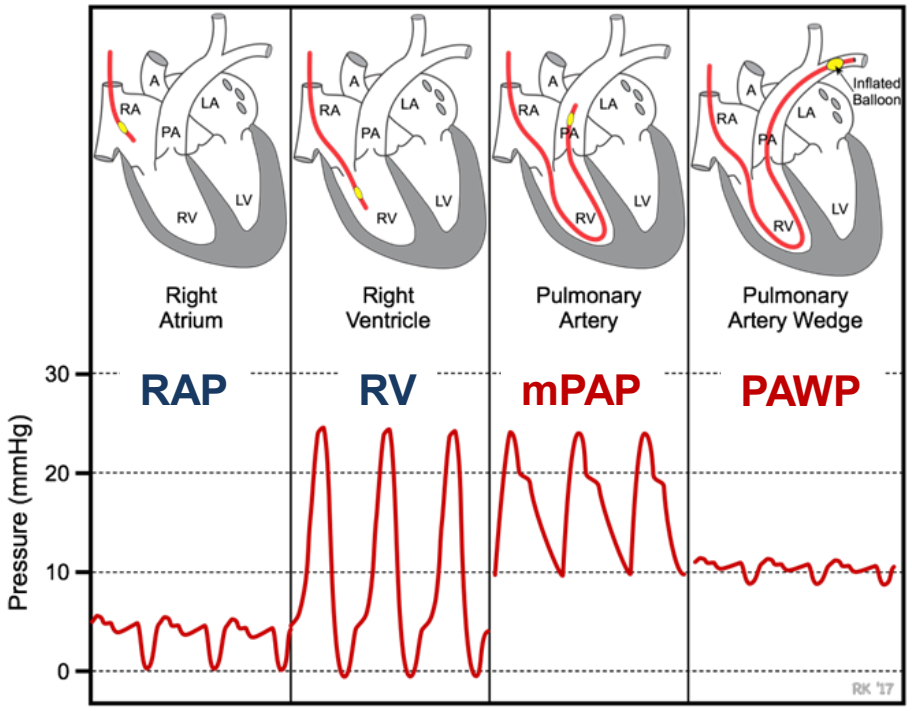
J'ai actuellement, ou j'ai eu au cours des trois dernières années, une affiliation ou des intérêts financiers ou intérêts de tout ordre avec une société commerciale ou je reçois une rémunération ou des redevances ou des octrois de recherche d'une société commerciale :

Type de relations financières :	**Laboratoires pharmaceutiques** :
Grant/Research Support:	Janssen, MSD
Consulting Fees/Honoraria	Janssen, MSD
Major Stock Shareholder/Equity:	None
Royalty Income:	None
Ownership/Founder:	None
Intellectual Property Rights:	None
Other Financial Benefit:	None

Définition de l'hypertension pulmonaire

Guidelines 2022

ESC ERS



PVR = (mPAP – PAWP) / cardiac output

Definition	Haemodynamic characteristics
PH	**mPAP >20 mmHg**
Pre-capillary PH	mPAP >20 mmHg **PAWP ≤15 mmHg** **PVR >2 WU**
Isolated post-capillary PH	mPAP >20 mmHg **PAWP >15 mmHg** **PVR ≤2 WU**
Combined post- and pre-capillary PH	mPAP >20 mmHg **PAWP >15 mmHg** **PVR >2 WU**
Exercise PH	mPAP/CO slope between rest and exercise >3 mmHg/L/min

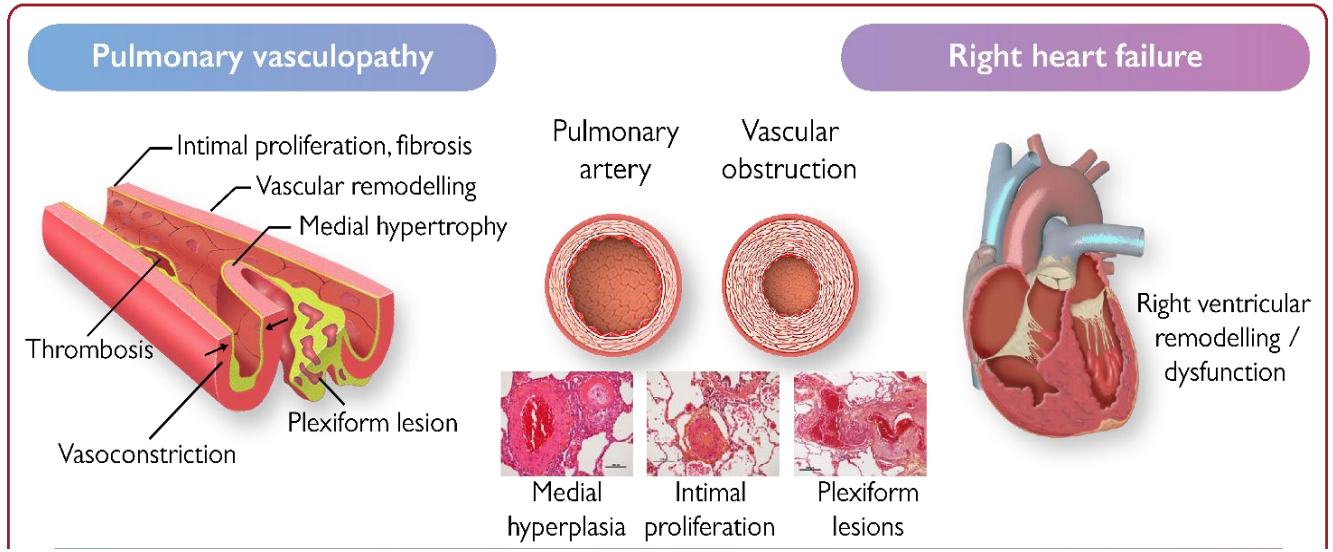
Humbert M *et al. Eur Heart J* 2022; Humbert M, *et al. Eur Respir J* 2023.

HTAP (PAH) : De quoi parle-t-on ?

GROUPE 1: HTAP (PAH)

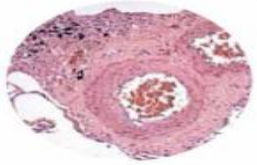
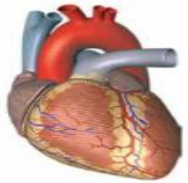
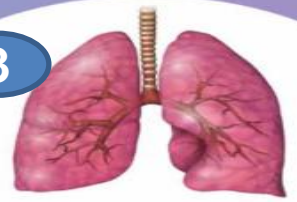
- 1.1 Idiopathique
- 1.2 Héritable
- 1.3 Associée à la prise de toxiques ou médicaments
- 1.4 Associée à:
  - 1.4.1 Connectivite
  - 1.4.2 Infection VIH
  - 1.4.3 Hypertension portale
  - 1.4.4 Cardiopathie congénitale
  - 1.4.5 Schistosomiase
- 1.5 HTAP avec signes d'atteinte veinulaire et/ou capillaire (maladie veino-occlusive pulmonaire)

- Pathologie(s) rare(s)
- Hypertension pulmonaire précapillaire
- Remodelage vasculaire pulmonaire marqué
- Dysfonction endothéliale = cible essentielle des thérapeutiques actuelles



Humbert M *et al. Eur Heart J* 2022; Humbert M, *et al. Eur Respir J* 2023.

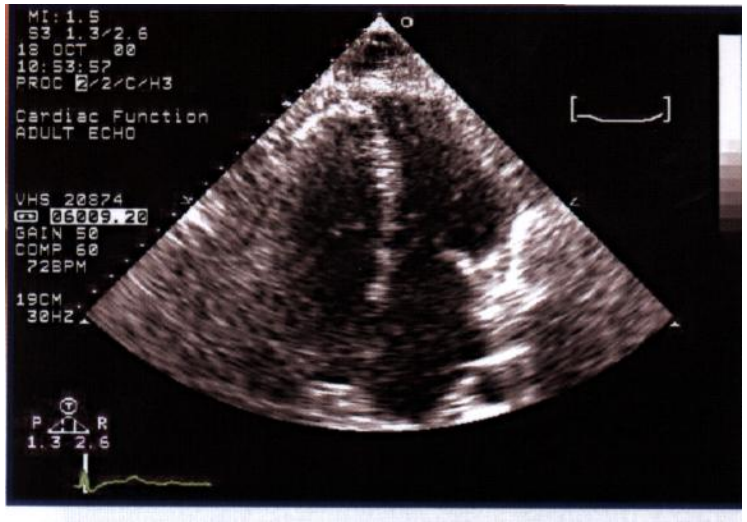
Classification clinique des hypertensions pulmonaires

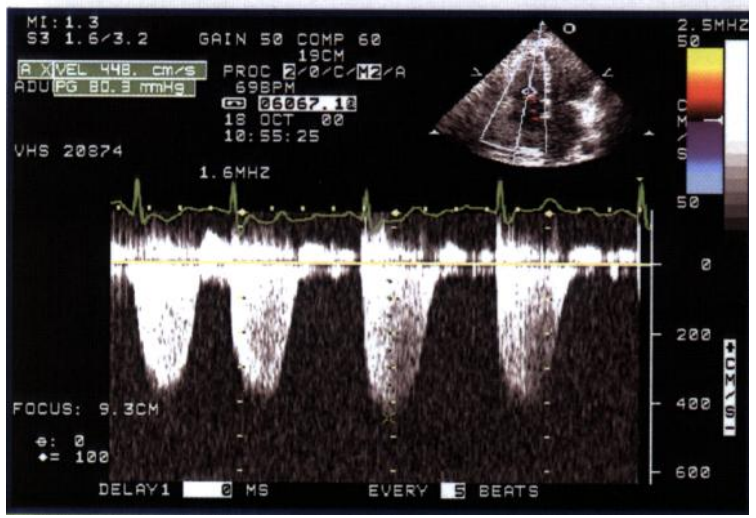
	1	2	3	4	5
	Pulmonary arterial hypertension (PAH)	PH associated with left heart disease	PH associated with lung disease	PH associated with pulmonary artery obstructions	PH with unclear and/or multifactorial mechanisms
					
	• Idiopathic/heritable • Associated conditions	• IpcPH • CpcPH	• Non-severe PH • Severe PH	• CTEPH • Other pulmonary obstructions	• Haematologic disorders • Systemic disorders
Prevalence	Rare	Very common	Common	Rare	Rare
Therapeutic strategies	**Medical therapy** • PAH drugs • CCB in responders **Lung transplantation**	**IpcPH:** • Treatment of LHD[a] **CpcPH:** • Treatment of LHD[a] • Potentially: PAH drugs (trials)	**PH-lung disease:** • Optimized care of underlying lung disease **Severe PH:** • Potentially: PAH drugs (trials)	**Surgical therapy:** • PEA **Interventional:** • BPA **Medical therapy:** • PH drugs	**Optimized treatment of underlying disease** • Potentially: PAH drugs (trials)

Humbert M *et al. Eur Heart J* 2022; Humbert M, *et al. Eur Respir J* 2023.

L'échocardiographie cardiaque : examen de dépistage de référence en cas de suspicion d'HTP

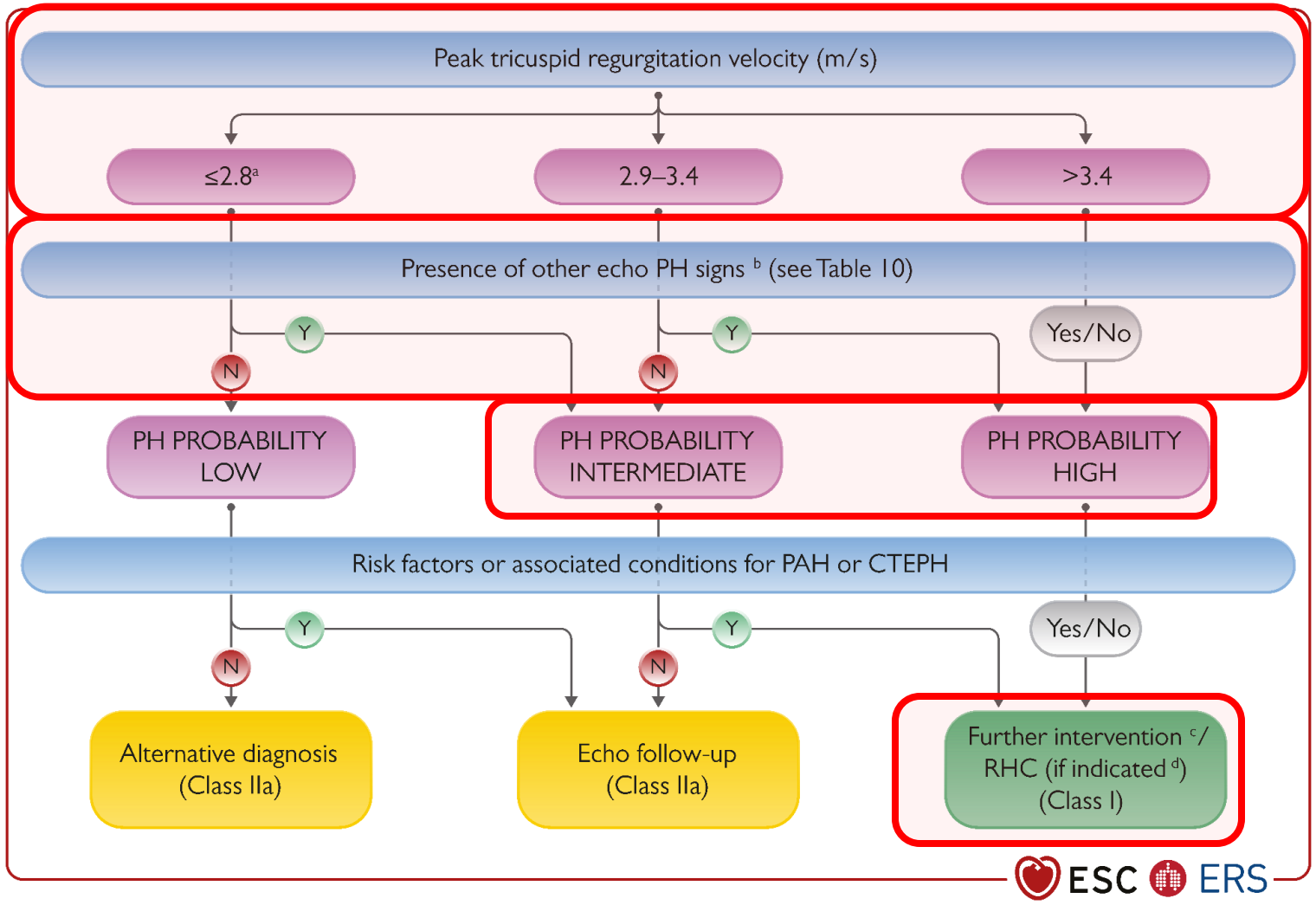
Recommendations	Class	Level
Echocardiography		
Echocardiography is recommended as **the first-line**, non-invasive, diagnostic **investigation in suspected PH**	**I**	**B**
It is recommended **to assign an echocardiographic probability of PH**, based on an abnormal TRV and the presence of other echocardiographic signs suggestive of PH	**I**	**B**





Humbert M *et al. Eur Heart J* 2022; Humbert M, *et al. Eur Respir J* 2023.

Probabilité échographique d'HTP



TRV ++
(≤ 2.8 m/s, 2.9 – 3.4, > 3.4 m/s)

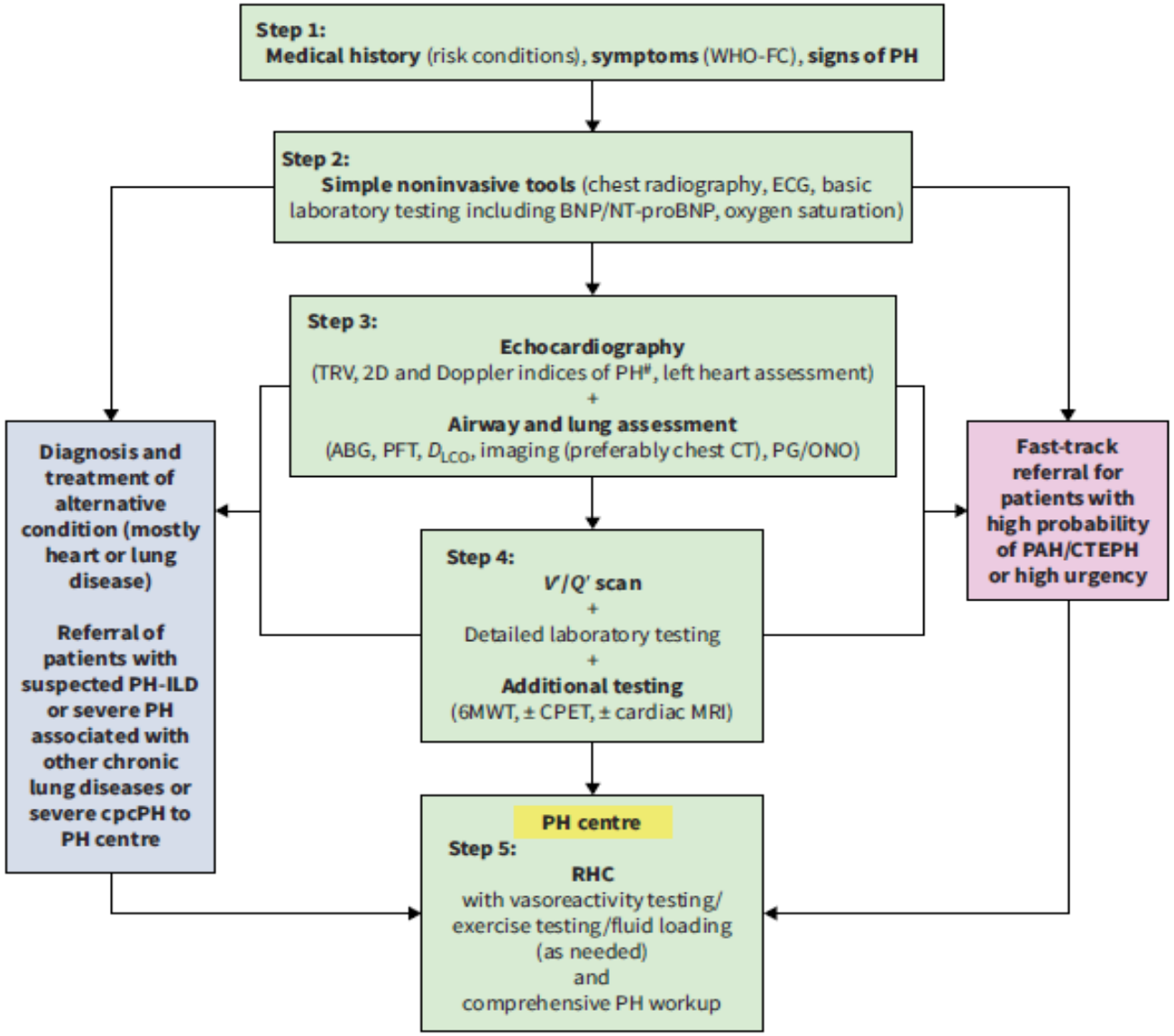
Presence of other echo PH signs

A: The ventricles	B: Pulmonary artery	C: Inferior vena cava and RA
RV/LV basal diameter/area ratio >1.0	RVOT AT <105 ms and/or mid-systolic notching	IVC diameter >21 mm with decreased inspiratory collapse (<50% with a sniff or <20% with quiet inspiration)
Flattening of the interventricular septum (LVEI >1.1 in systole and/ or diastole)	Early diastolic pulmonary regurgitation velocity >2.2 m/s	RA area (end-systole) >18 cm^2
TAPSE/sPAP ratio <0.55 mm/mmHg	PA diameter >AR diameter PA diameter >25 mm	

AR, aortic root; IVC, inferior vena cava; LV, left ventricle; LVEI, left ventricle eccentricity index; PA, pulmonary artery; RA, right atrium; RV, right ventricle; RVOT AT, right ventricular outflow tract acceleration time; sPAP, systolic pulmonary arterial pressure; TAPSE, tricuspid annular plane systolic excursion; TRV, tricuspid regurgitation velocity. [a]Signs contributing to assessing the probability of PH in addition to TRV (see Figure 5). Signs from at least two categories (A/B/C) must be present to alter the level of echocardiographic probability of PH.

Humbert M *et al. Eur Heart J* 2022; Humbert M, *et al. Eur Respir J* 2023.

Approche diagnostique



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1.5 HTAP avec signes d'atteinte veinulaire et/ou capillaire (maladie veino-occlusive pulmonaire)

- Bilan biologique minimum
  - Bilan hépatique
  - Recherche d'AAN
  - Sérologie VIH
- Imagerie
  - Echographie abdominale + Doppler portal

Kovacs G, *et al. Eur Respir J* 2024.

Le cathétérisme cardiaque droit est obligatoire pour confirmer et classer l'hypertension pulmonaire

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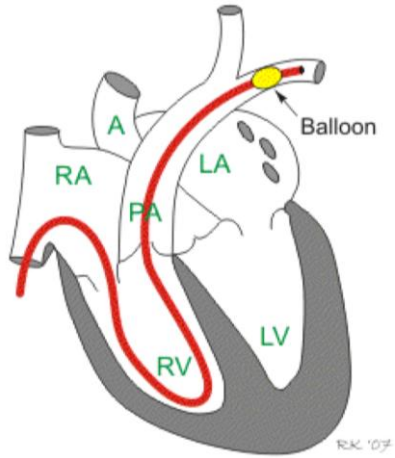
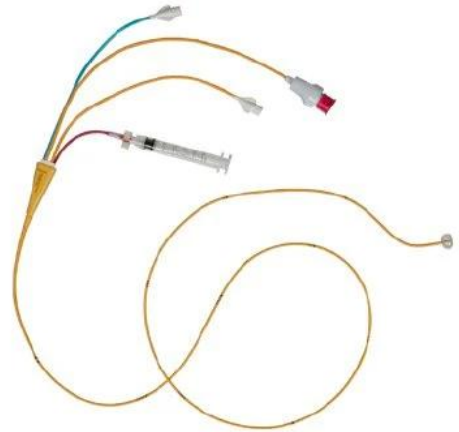
Recommendations	Class	Level
Right heart catheterization (RHC)		
RHC is recommended **to confirm the diagnosis of PH** (especially PAH or CTEPH), and to support treatment decisions	**I**	**B**
In patients with suspected or known PH, it is recommended to perform RHC **in experienced centres**	**I**	**C**
It is recommended that RHC comprises a complete set of haemodynamics, and is performed following **standardized protocols**	**I**	**C**





Humbert M *et al. Eur Heart J* 2022; Humbert M, *et al. Eur Respir J* 2023.

Mesures générales

General measures throughout the course of the disease (ReCo Table 5) (Class I)

Anticoagulation is **not generally recommended** in patients with PAH but may be considered on an individual basis	IIb	C

Supervised exercise training
Psychological support
Immunisation against SARS-CoV-2, influenza, *Streptococcus pneumoniae* and consider vaccination against RSV
Diuretic treatment in patients with fluid retention
Continuous LTOT when arterial blood oxygen pressure is consistently <8 kPa (60 mmHg)
Correction of iron status in patients with iron-deficiency anaemia
Advise against pregnancy
Clear contraceptive advice
Pre-transplant counselling

Humbert M *et al. Eur Heart J* 2022; Humbert M, *et al. Eur Respir J* 2023; Chin KM, *et al. Eur Respir J* 2024.

Stratification du risque au diagnostic (modèle à 3 strates)

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Recommendations	Class	Level
For risk stratification **at the time of diagnosis**, the use of a **three-strata model** (low, intermediate, and high risk) is recommended, taking into account all available data including haemodynamics	I	B

Determinants of prognosis (estimated 1-year mortality)	Low risk <5%	Intermediate risk 5–20%	High risk >20%
Signs of right heart failure	Absent	Absent	Present
Progression of symptoms and clinical manifestations	No	Slow	Rapid
Syncope	No	Occasional syncope	Repeated syncope
WHO-FC	I, II	III	IV
6MWD	>440 m	165–440 m	<165 m
CPET	Peak VO_2 >15 mL/min/kg (>65% pred.) VE/VCO_2 slope <36	Peak VO_2 11–15 mL/min/kg (35–65% pred.) VE/VCO_2 slope 36–44	Peak VO_2 <11 mL/min/kg (<35% pred.) VE/VCO_2 slope >44
BNP or NT-proBNP	BNP <50 ng/L NT-proBNP <300 ng/L	BNP 50–800 ng/L NT-proBNP 300–1100 ng/L	BNP >800 ng/L NT-proBNP >1100 ng/L
Echocardiography	RA area <18 cm^2 TAPSE/sPAP >0.32 mm/mmHg No pericardial effusion	RA area 18–26 cm^2 TAPSE/sPAP 0.19–0.32 mm/mmHg Minimal pericardial effusion	RA area >26 cm^2 TAPSE/sPAP <0.19 mm/mmHg Moderate or large pericardial effusion
cMRI	RVEF >54% SVI >40 mL/m^2 RVESVI <42 mL/m^2	RVEF 37–54% SVI 26–40 mL/m^2 RVESVI 42–54 mL/m^2	RVEF <37% SVI <26 mL/m^2 RVESVI >54 mL/m^2
Haemodynamics	RAP <8 mmHg CI ≥2.5 L/min/m^2 SVI >38 mL/m^2 SvO_2 >65%	RAP 8–14 mmHg CI 2.0–2.4 L/min/m^2 SVI 31–38 mL/m^2 SvO_2 60–65%	RAP >14 mmHg CI <2.0 L/min/m^2 SVI <31 mL/m^2 SvO_2 <60%

ESC/ERS risk calculation

SPAHR/COMPERA 1.0

Parameters		
Low risk 1 point	Intermediate risk 2 points	High risk 3 points

Overall risk = sum of the points / n of parameters

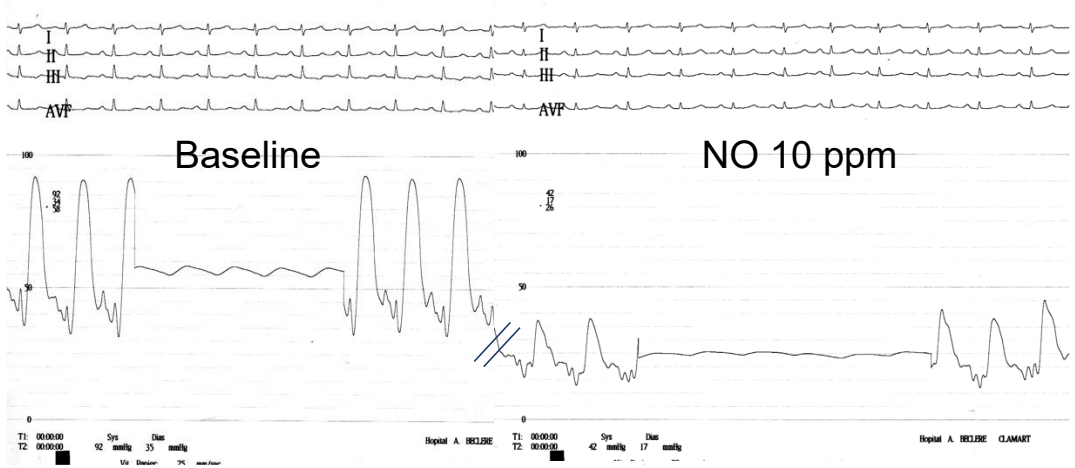
1.0–1.49=	Low risk
1.5–2.49=	Intermediate risk
≥2.5=	High risk

Humbert M *et al. Eur Heart J* 2022; Humbert M, *et al. Eur Respir J* 2023.

Test de vasoréactivité et traitement par inhibiteur calcique chez les patients présentant un diagnostic présumé d'HTAP idiopathique, héritable ou associée à la prise de toxiques ou médicaments

Compound	Route	Half-life	Dosage	Duration
Nitric oxide	inh	15–30 s	10–20 p.p.m.	5–10 min
Iloprost	inh	30 min	5–10 µg	10–15 min
Epoprostenol	i.v.	3 min	2–12 ng/kg/min	10 min

Positive vasoareactivity test
≥ 10 mmHg mPAP drop from baseline to ≤ 40 mmHg,
Without decrease in CO/CI



mPAP = 58 mm Hg

mPAP = 25 mm Hg

Therapy for Group 1 PAH Vasodilator Responder (IPAH, HPAH, DT-PAH)[a]

↓

CCB Monotherapy[b,c]

↓

Follow-up Risk Reassessment at 3-4 months And Repeated Frequently[d]

Low Risk[e]	**Not Low RIsk**
Continue CCB Alone	**PAH Therapy Based on Risk Assessment[f]**

Multicentre Study of Vasodilator Responders

- Confirms
  - A low response rate: 10% (184 / 1904)
  - A good overall 5-year survival (87%)
- Excellent survival in “Long-term responders” (low-risk, still on CCB at 1 year): 54%

Humbert M *et al. Eur Heart J* 2022; Humbert M, *et al. Eur Respir J* 2023; Chin KM, *et al. Eur Respir J* 2024; Gerhardt F, *et al. Circulation* 2024.

La dysfonction endothéliale est la cible actuelle des traitements de l'HTAP

The big three!

Antagonistes des recepteurs de l'endothéline (ERA)

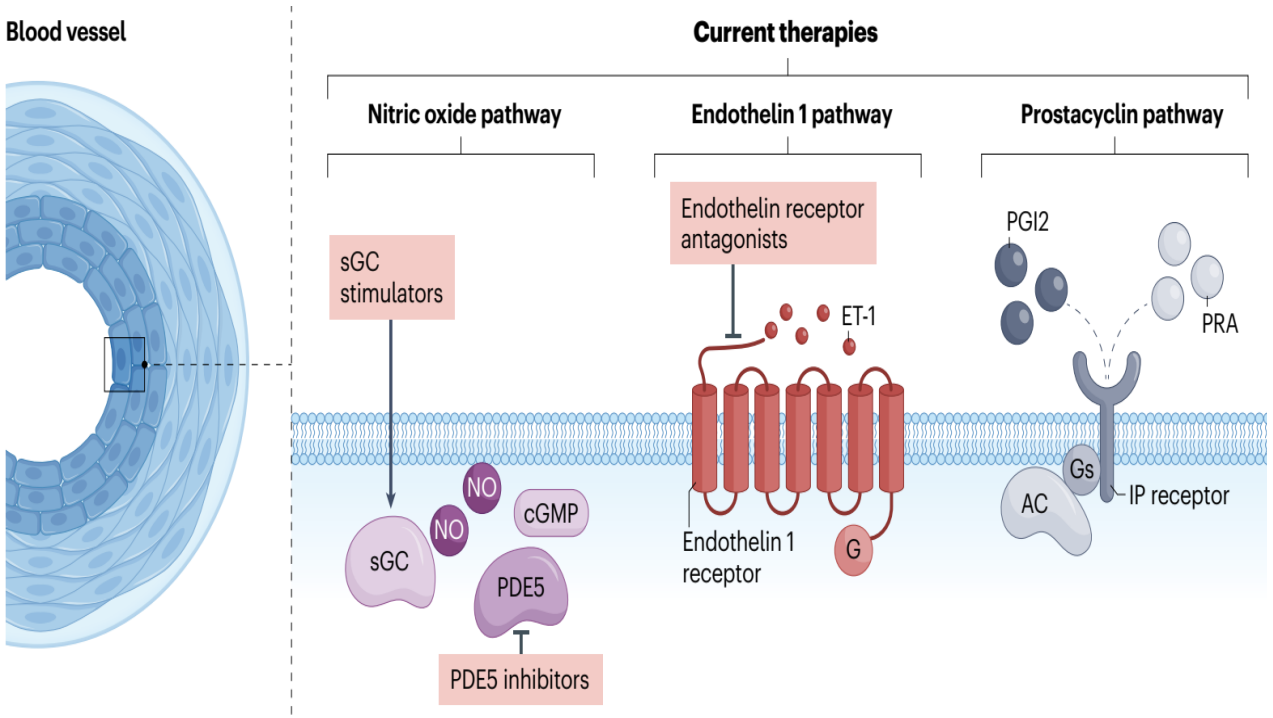
Ambrisentan
Bosentan

Inhibiteurs de la PDE5 (PDE5i)

Sildenafil
Tadalafil

Stimulateur de la GCs (sGCs)

Riociguat



Prostacyclines (iv/sc PCA)

Epoprostenol (i.v.)
Treprostinil (s.c., i.v.)

Agonistes des recepteurs de la prostacycline (PRA)

Selexipag (oral)

Mocumbi A, *et al. Nat Rev Dis Primers* 2024.

Algorithme de traitement: impact des comorbidités sur le choix du traitement initial

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Presence of comorbidities
Risk assessment

→ **Management strategy / Initial therapy**

General measures throughout the course of the disease (ReCo Table 5) (Class I)

Patients WITHOUT cardiopulmonary comorbidities

Risk (3 strata) (Table 16)

- Low or intermediate → Initial ERA + PDE5i therapy (Class I)
- High → Initial ERA + PDE5i and i.v./s.c. PCA[a] (Class IIa)

Regular follow-up assessment (Table 17)

Patients WITH cardiopulmonary comorbidities All risk categories

Initial oral monotherapy with PDE5i or ERA (Class IIa)

Regular follow-up assessment and individualized therapy

Focuses first on comorbidity status

Patient with cardiopulmonary comorbidities [a] All risk categories

Initial oral monotherapy with PDE5i or ERA (Class IIa)

Regular follow-up assessment and individualized therapy

Humbert M *et al. Eur Heart J* 2022; Humbert M, *et al. Eur Respir J* 2023.

Algorithme de traitement: impact des comorbidités CV dans le traitement initial

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2022 ESC/ERS PH guidelines

Patient with cardiopulmonary comorbidities [a]
All risk categories

↓

Initial oral monotherapy with PDE5i or ERA (Class IIa)

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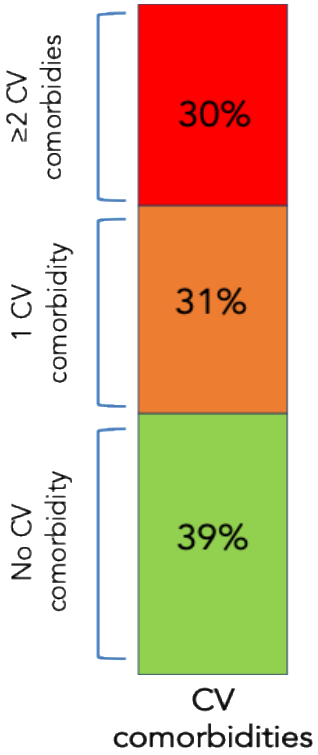
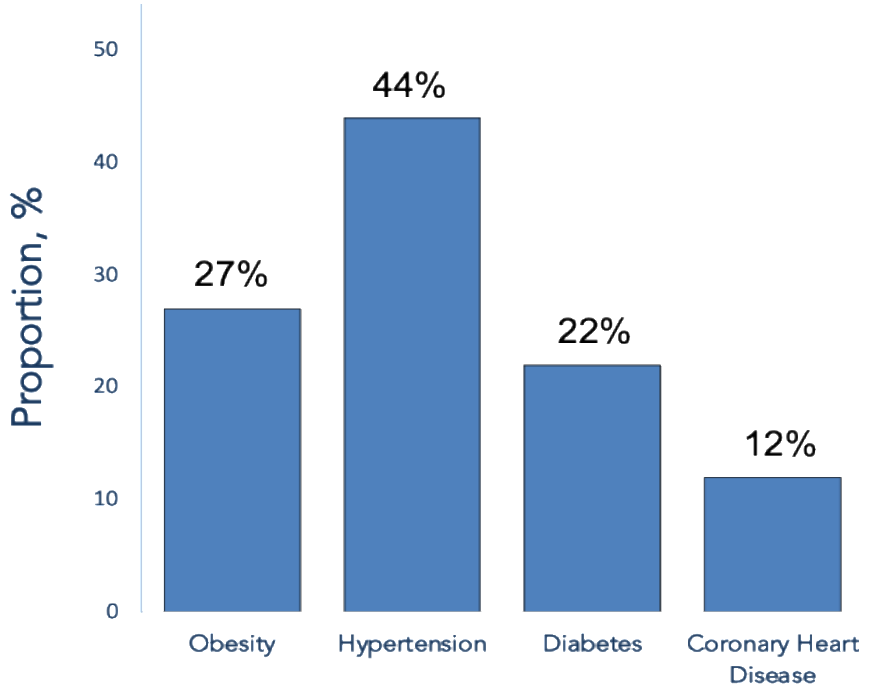
Regular follow-up assessment and individualized therapy

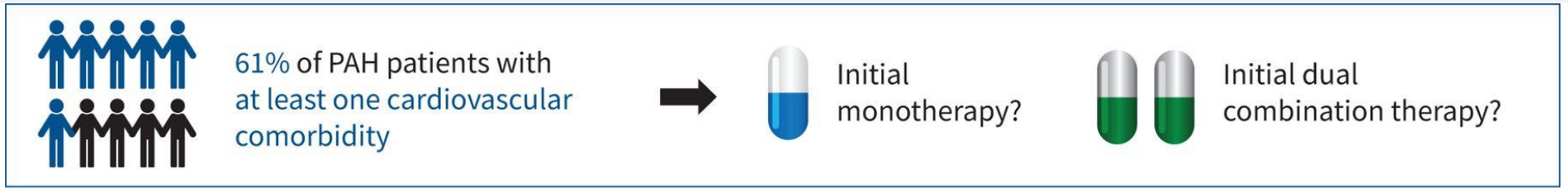
Proportion of PAH patients with CV comorbidities

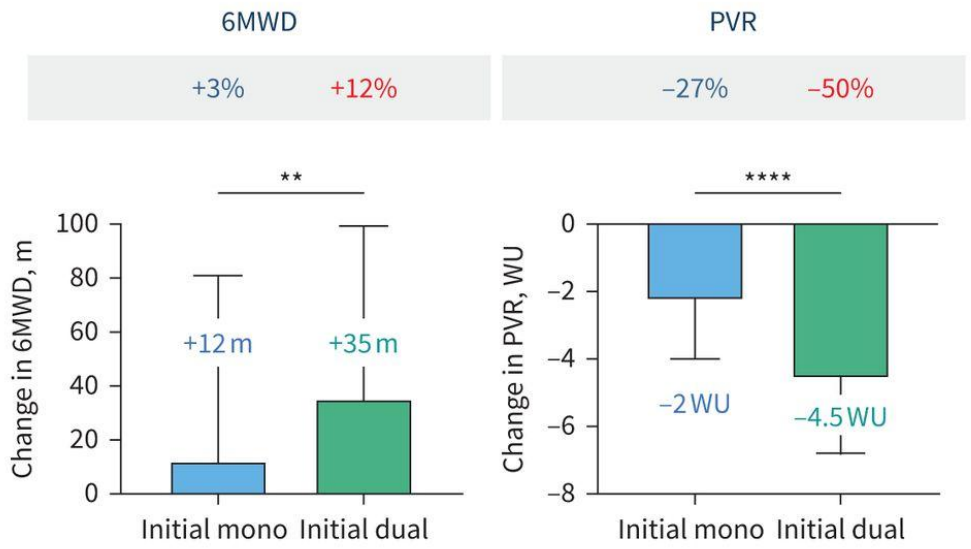


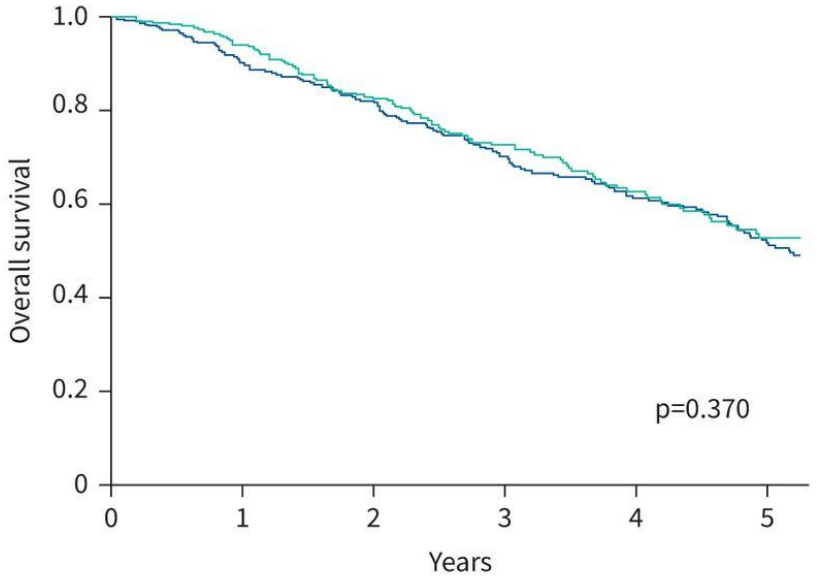


Humbert M *et al. Eur Heart J* 2022; Humbert M, *et al. Eur Respir J* 2023; Boucly A, *et al. Eur Respir J* 2025.

Le traitement combiné d'emblée est supérieur à la monothérapie chez les patients avec comorbidités cardiovasculaires







Initial monotherapy
24% treatment discontinuation

Initial dual combination therapy
23% treatment discontinuation

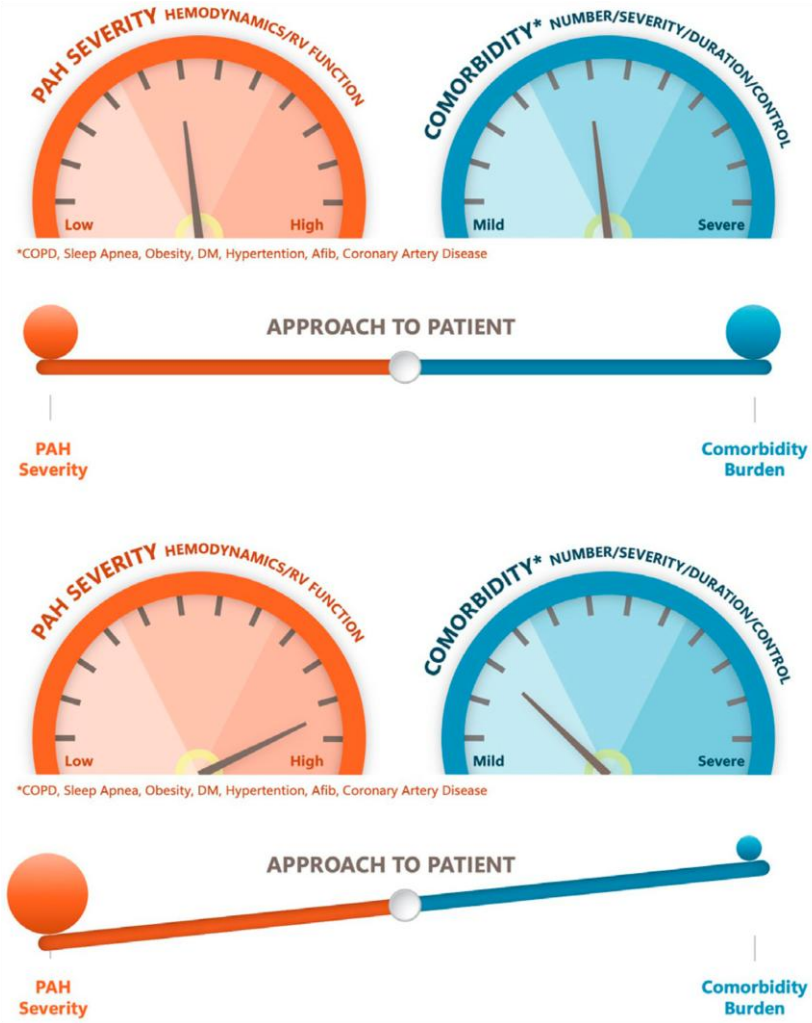
Initial dual combination therapy led to larger improvements at first follow-up than initial monotherapy without changes in long-term survival or treatment discontinuation

Boucly A, *et al. Eur Respir J* 2025.

Une approche centrée sur le patient est nécessaire chez les patients avec comorbidités

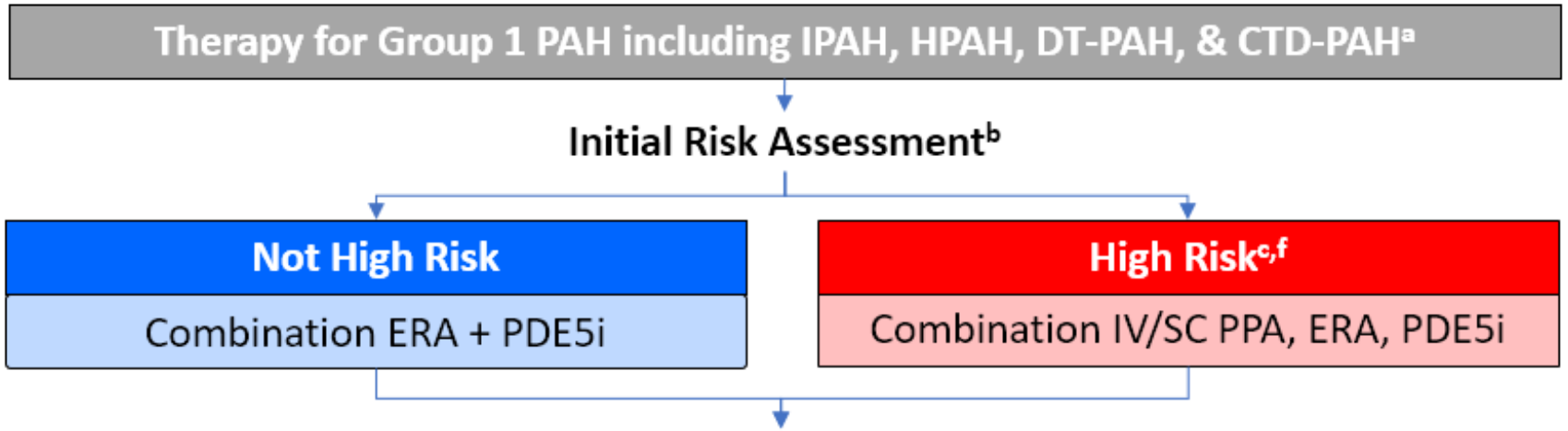
Evaluation des patients atteints d'HTAP avec comorbidités

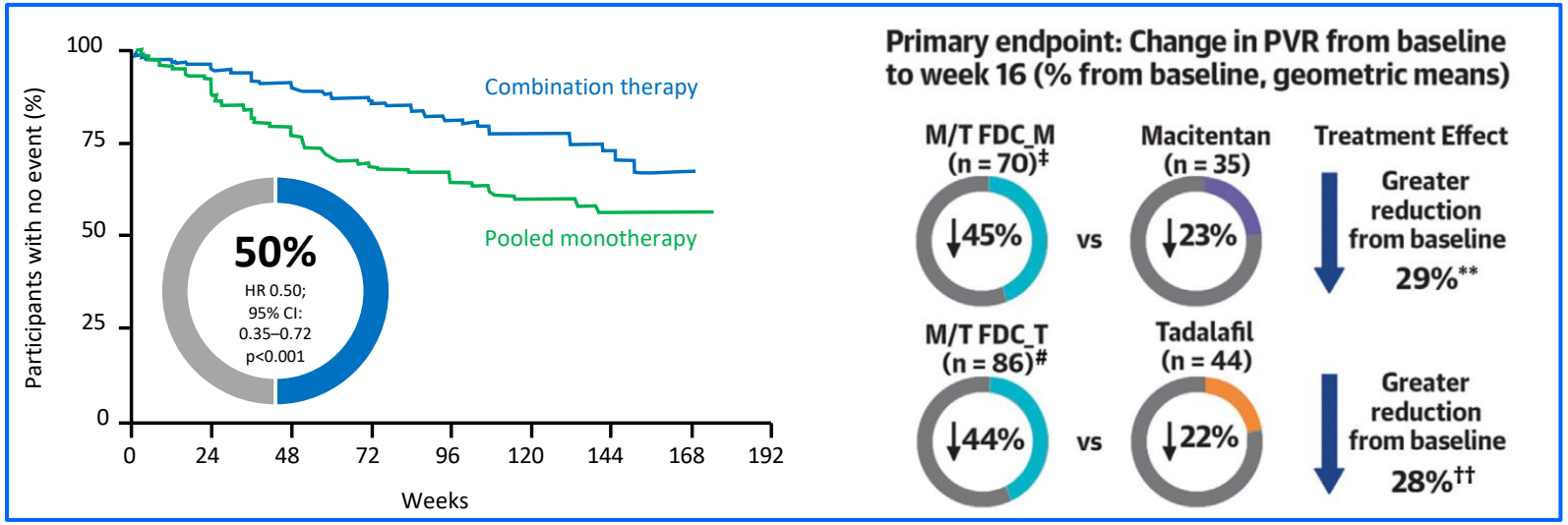
- Apprécier la sévérité de l'HTAP au regard du poids des comorbidités (obésité, HTA non contrôlée, FA, diabète, coronaropathie…)
- Optimiser précocement la prise en charge des comorbidités en tenant compte de la sévérité de l'HTAP



Sahay S *et al. Am J Respir Crit Care Med.* 2024.

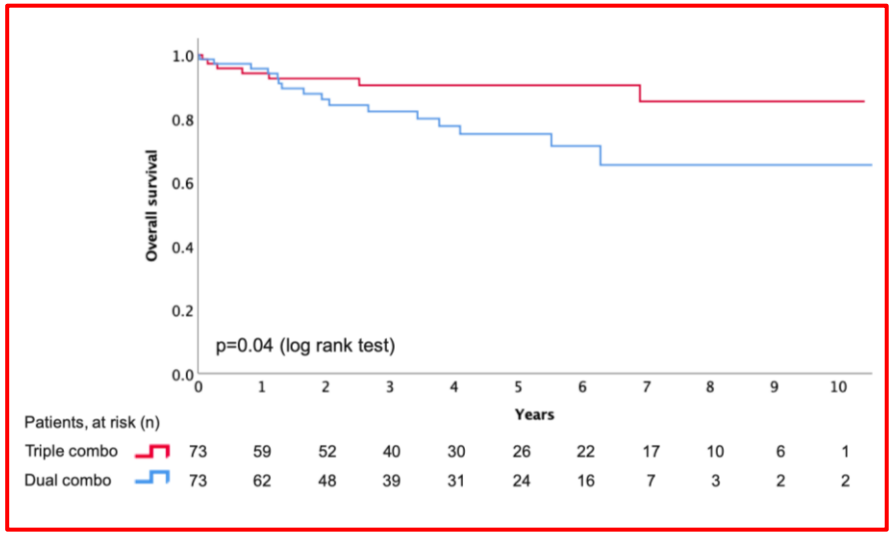
Proposition d'algorithme actualisé: choix du traitement initial fondé sur 2 niveaux de risque uniquement





Galiè N, *et al. N Engl J Med* 2015.

Grünig E, *et al. J Am Coll Cardiol* 2024.

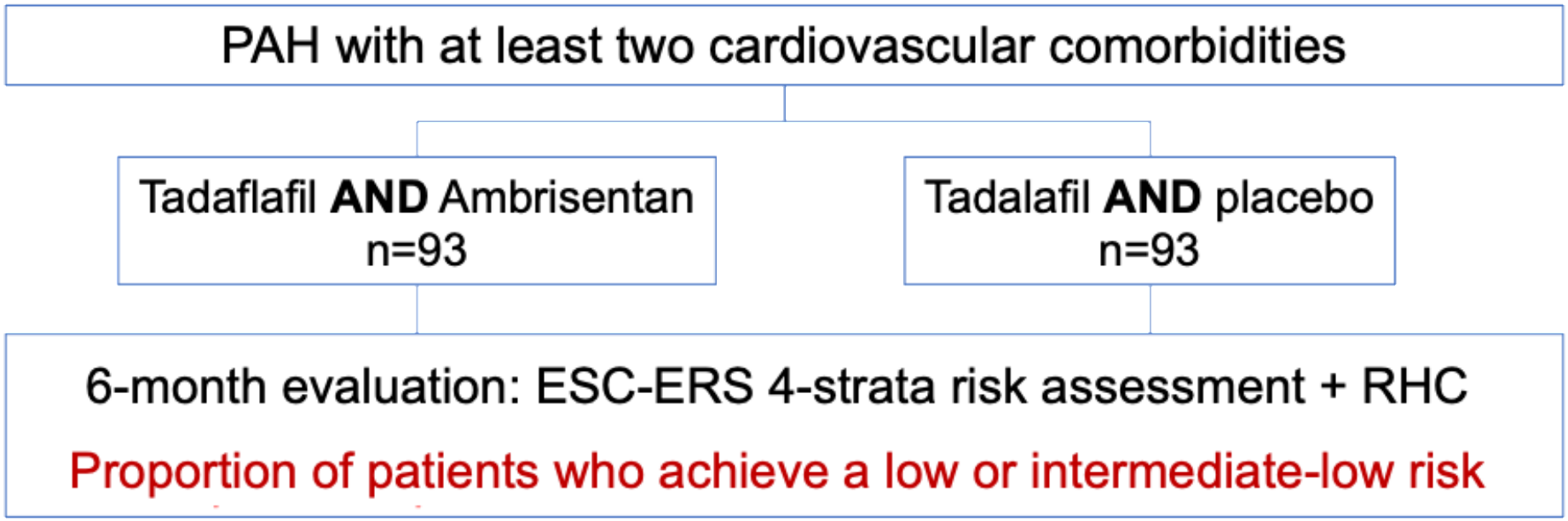


Boucly A, *et al. Am J Respir Crit Care Med* 2021.

Chin KM, *et al. Eur Respir J* 2024.

Etude ‘COMMODITIES’ réalisée au sein du reseau français de l’HTP

Main Objective: To analyse the effect of the initial treatment strategy (**tadalafil and ambrisentan *vs.* tadalafil and placebo**) on disease control assessed at 6-months in treatment-naïve patients with newly diagnosed PAH and cardiovascular comorbidities



Stratification du risque au cours du suivi (modèle à 4 strates)

Guidelines 2022

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Recommendation	Class	Level
For risk stratification **during follow-up**, the use of a **four-strata model** (low, intermediate-low, intermediate-high, and high risk) based on WHO-FC, 6MWD, and BNP/NT-proBNP is recommended, with additional variables taken into account as necessary	I	B

Determinants of prognosis	Low risk	Intermediate-low risk	Intermediate-high risk	High risk
Points assigned	1	2	3	4
WHO-FC	I or II	-	III	IV
6MWD, m	>440	320–440	165–319	<165
BNP or NT-proBNP, ng/L	<50 <300	50–199 300–649	200–800 650–1100	>800 >1100

Recommendation	Class	Level
Achieving and maintaining a **low-risk profile** on optimized medical therapy is recommended as a **treatment goal** in patients with PAH	I	B

Humbert M *et al. Eur Heart J* 2022; Humbert M, *et al. Eur Respir J* 2023.

Ajustements thérapeutiques au cours du suivi

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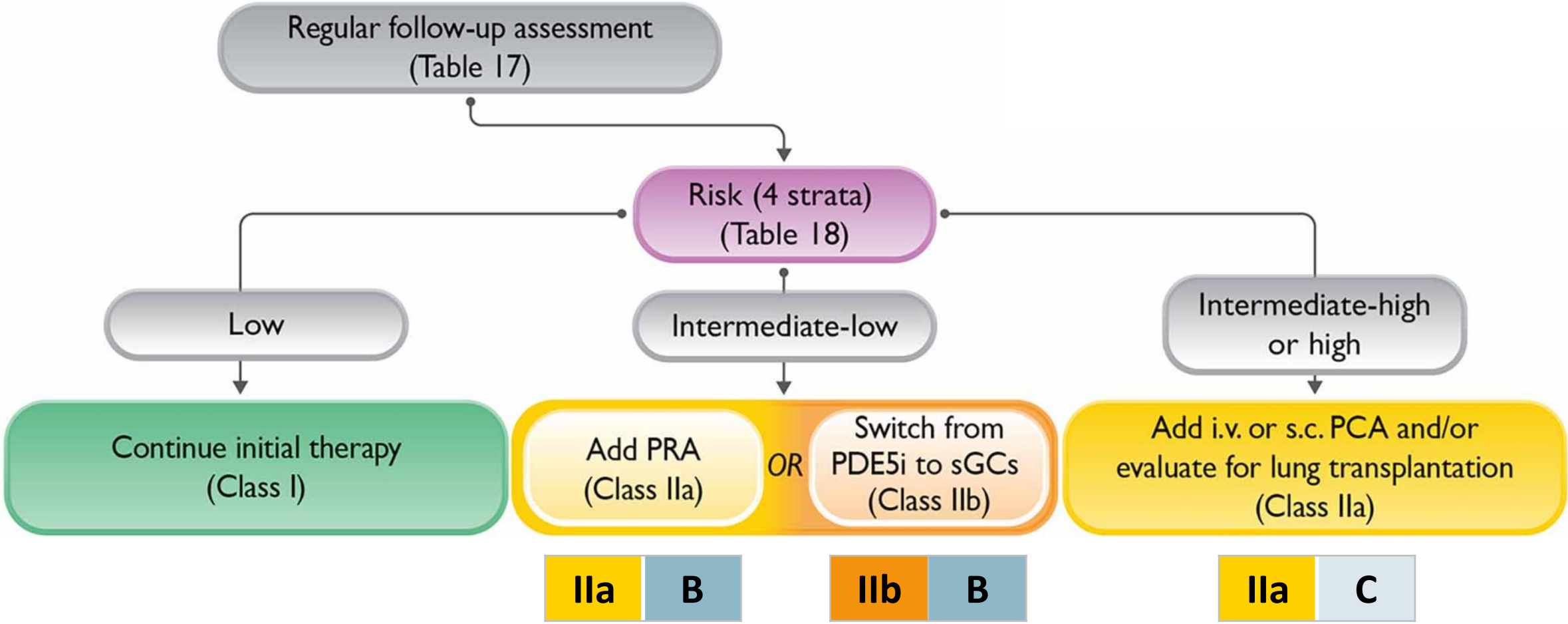


Humbert M *et al. Eur Heart J* 2022; Humbert M, *et al. Eur Respir J* 2023.

Traitements de l'HTAP en 2026: de 3 à 4 voies thérapeutiques

Antagonistes des recepteurs de l'endothéline

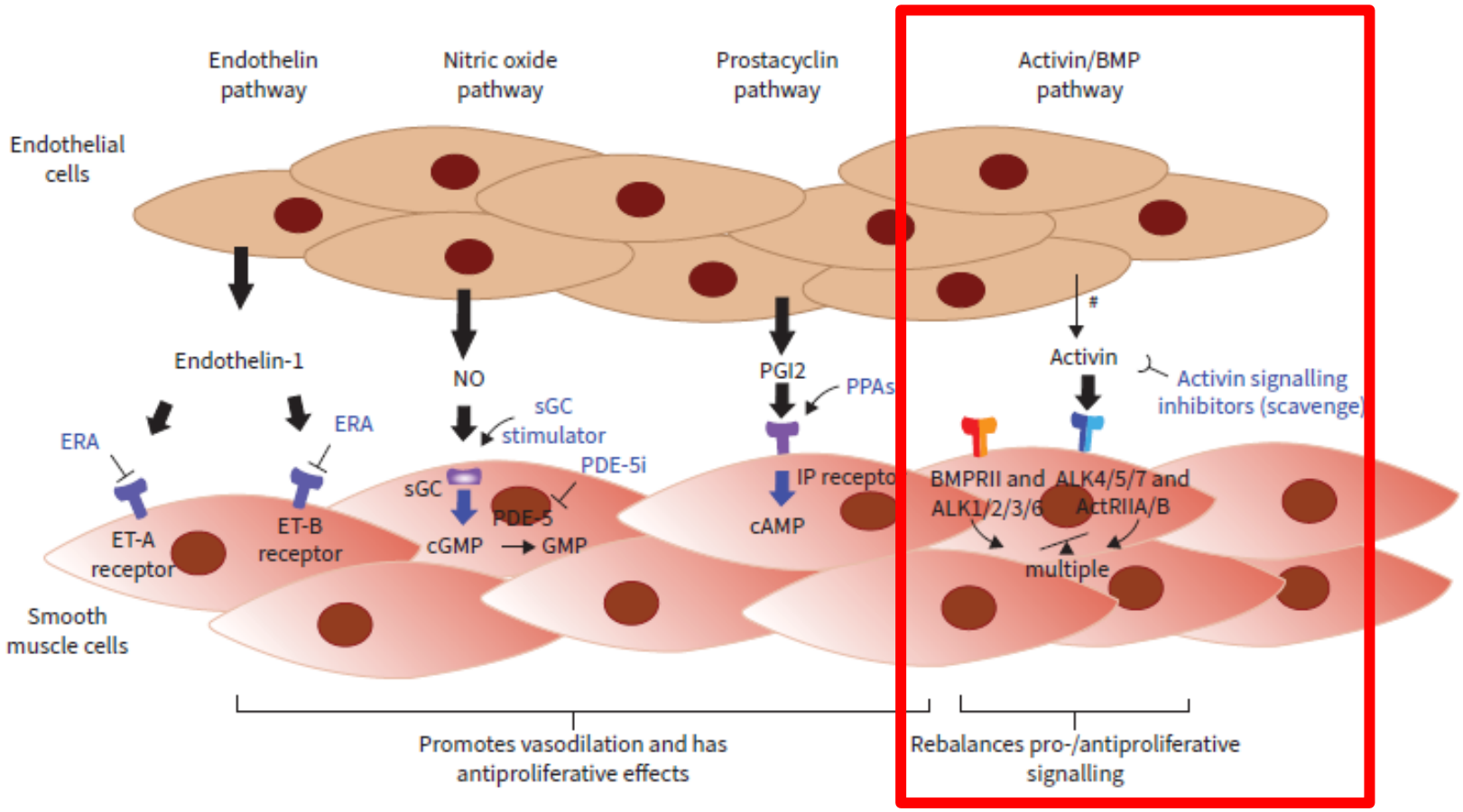
Ambrisentan
Bosentan

Inhibiteurs de la PDE5

Sildenafil
Tadalafil

Stimulateur de la GCs

Riociguat



Prostacyclines

Epoprostenol (i.v.)
Treprostinil (s.c., i.v.)

Agonistes des recepteurs de la prostacycline

Selexipag (oral)

Inhibiteur de la signalisation de l'activine

Sotatercept (s.c)

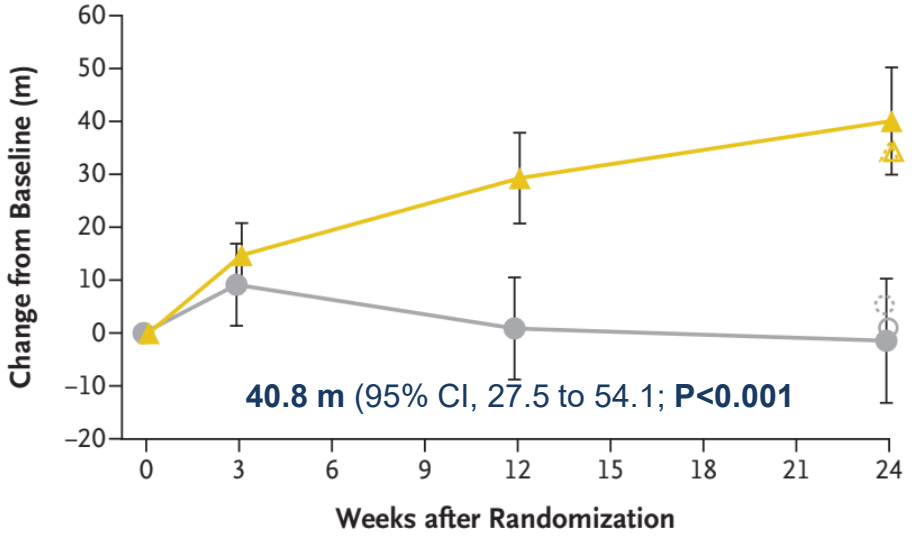
Chin KM, *et al*. *Eur Respir J* 2024.

L’ajout du sotatercept améliore des critères d’évaluation majeurs chez des patients recevant déjà un traitement de l’HTAP

STELLAR

323 pts with FC II-III PAH, stable **on background therapy (triple 61%, parenteral PGI_2 40%)**

Primary endpoint (6MWD) met

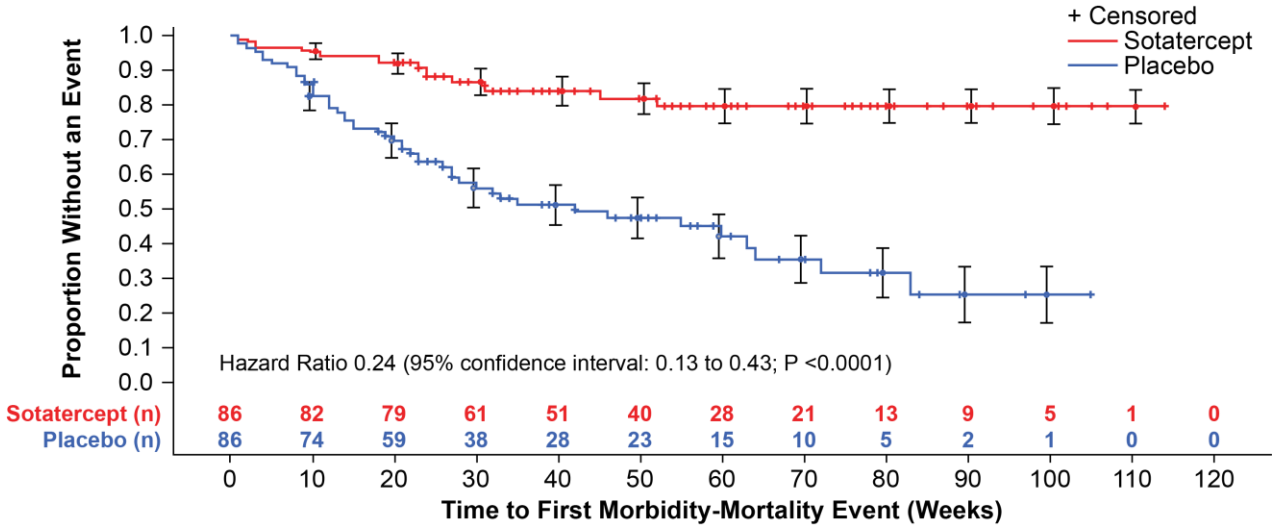


No. at Risk				
Sotatercept	163	157	154	157
Placebo	160	154	151	147

ZENITH

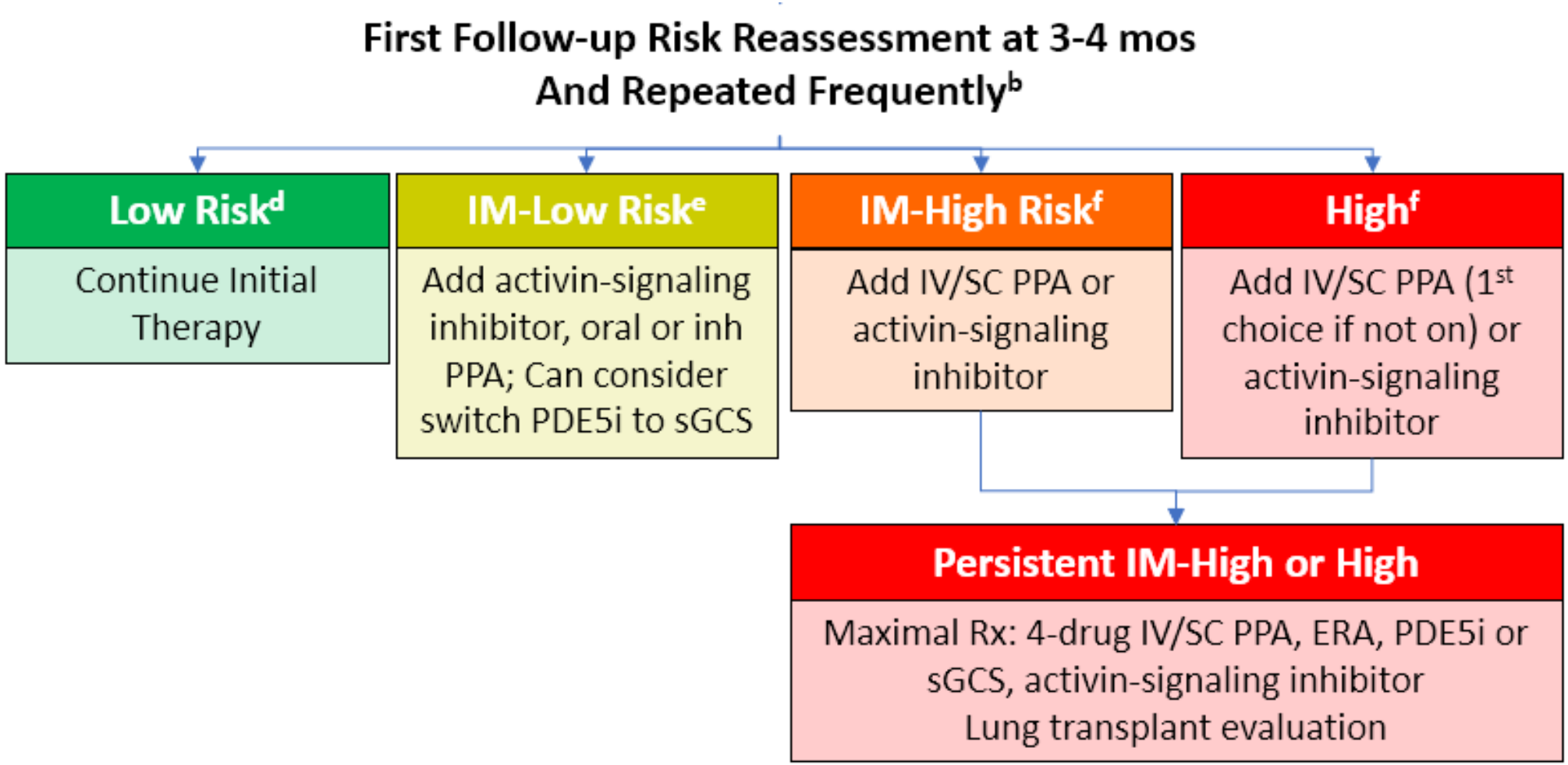
172 pts with severe PAH (FC III-IV, REVEAL risk score ≥9), **on background therapy (triple 72%, parenteral PGI_2 59%)**

Primary endpoint (time to first event of death, lung transplant, or PAH worsening-related hospitalization) met



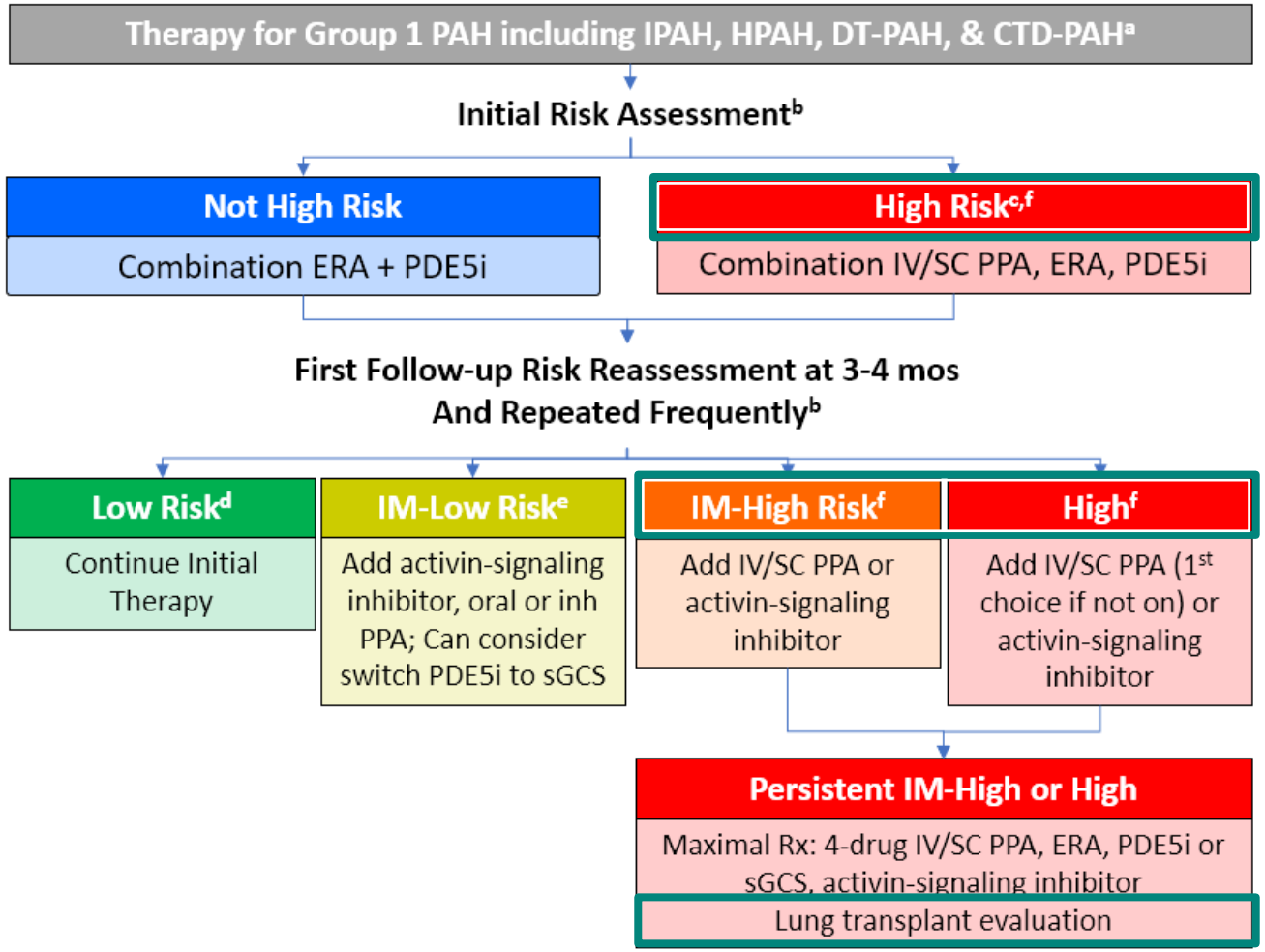
Hoeper MM, *et al. N Engl J Med* 2023; Humbert M, *et al. N Engl J Med* 2025.

Proposition d'algorithme actualisé: choix du traitement au cours du suivi



Chin KM, *et al*. *Eur Respir J* 2024.

Proposition d'algorithme actualisé: place de la transplantation pulmonaire



Transplant referral should be considered for **selected high-risk patients** at diagnosis

Transplant referral should be considered for **intermediate-high** and **high-risk** patients at first or subsequent follow-up.

Lung transplant evaluation for patients at **persistent intermediate-high** or **high-risk on maximal therapy**

Chin KM, *et al*. *Eur Respir J* 2024.

Take-Home Messages

- L’échographie cardiaque reste l’examen de référence pour le dépistage d’une HTP.
- Le diagnostic d’HTP est hémodynamique et repose sur le cathétérisme cardiaque droit (PAPm >20 mmHg).
- L’HTAP regroupe des pathologies caractérisées par une HTP précapillaire (PAPm >20 mmHg, PAPO ≤ 15 mmHg, RVP > 2 UW) associée à un remodelage vasculaire pulmonaire marqué.
- L'algorithme thérapeutique repose sur l'évaluation du risque, la prise en compte des comorbidités et les objectifs du traitement.
- Le traitement combiné d’emblée et, le cas échéant, l'intensification thérapeutique au cours du suivi constituent le standard actuel de prise en charge.
- Le sotatercept ouvre une 4ème voie thérapeutique et représente une avancée importante dans le traitement de l’HTAP.