ACTION

Pneumologi in azione nell'ipertensione arteriosa polmonare (PAH)

MILANO • 13 // 14 dicembre 2018

PALAZZO DELLE STELLINE

Migliorare l'outcome nell'ipertensione arteriosa polmonare: le nuove possibilità terapeutiche

Sergio Harari

Division of Pulmonary Disease,
Reference Centre for Rare pulmonary diseases
IRCCS MultiMedica San Giuseppe Hospital
Milan Italy

COI disclosure

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- Roche: investigator in trials, lectures, AB
- Actelion : investigator in trials, lectures, AB, grant for research
- Boehringer Ing. : investigator in trials, lectures, AB, grant for research

Task Force #6: Risk Stratification and Medical Therapy of Pulmonary Arterial Hypertension

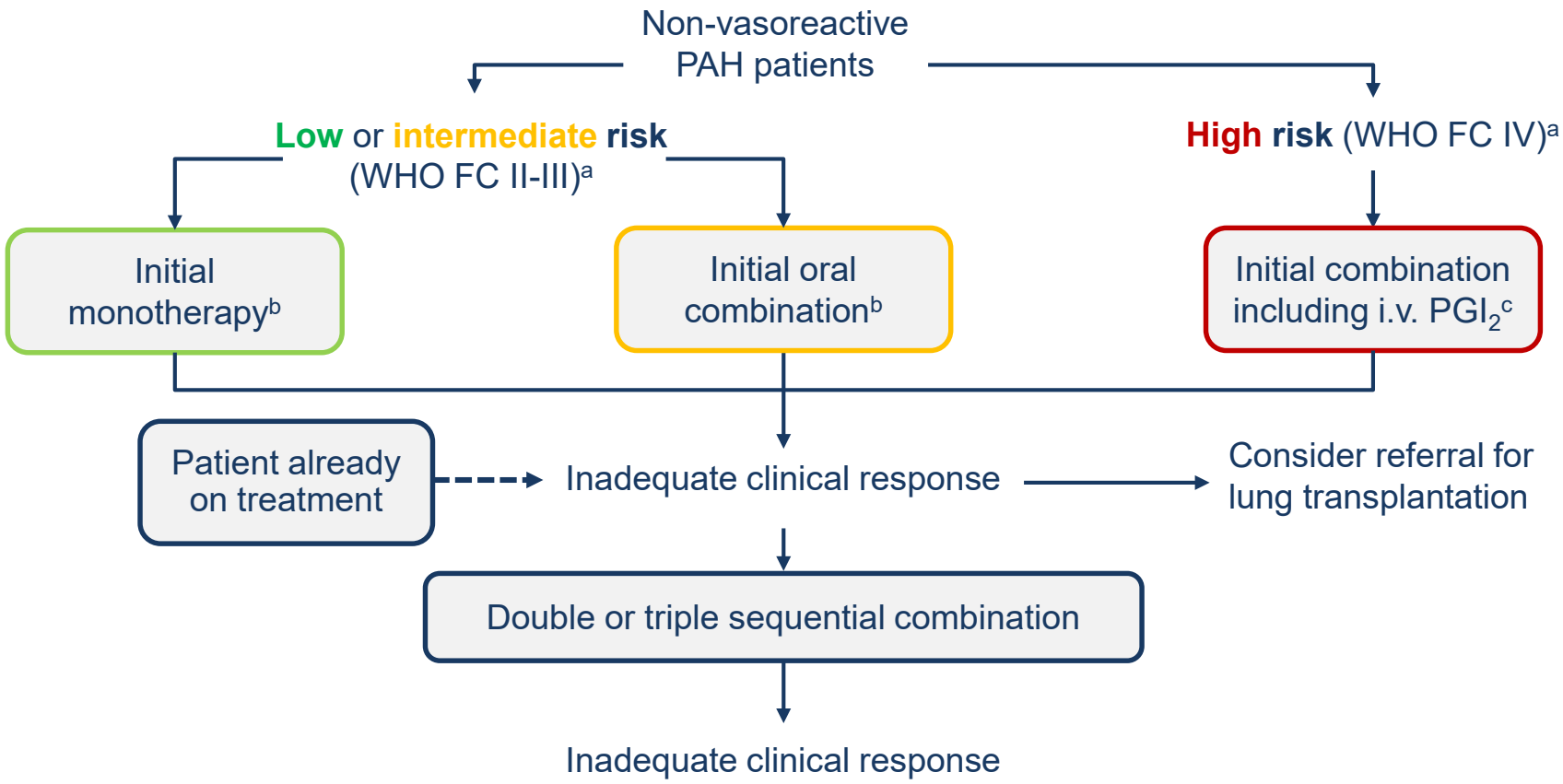
ACTION
Pneumologi in azione nell'ipertensione arteriosa polmonare (PAH)

6th WSPH Nice 2018

Nazzareno Galié (Bologna, Italy)
Vallerie V. McLaughlin (Ann Arbor MI, USA)

Richard N. Channick (Boston MA, USA)
Robert P. Frantz (Rochester MN, USA)
Ekkehard Grünig (Heidelberg, Germany)
Zhi Cheng Jing (Shanghai, China)
Olga Moiseeva (Saint Petersburg, Russia)
Ioana R. Preston (Boston MA, USA)
Zeenat Safdar (Houston TX, USA)
Yuchi Tamura (Tokyo, Japan)
Tomas Pulido (Mexico City, Mexico)

Risk assessment is fundamental for the determination of an optimal treatment strategy



[a] Some WHO-FC III patients may be considered high-risk;
[b] Initial combination with ambrisentan plus tadalafil has proven to be superior to initial monotherapy with ambrisentan or tadalafil in delaying clinical failure;
[c] Intravenous epoprostenol should be prioritized as it has reduced the 3 month rate for mortality in high-risk PAH patients also as monotherapy.

1. Galiè N, *et al. Eur Respir J* 2015; 46:903-75;
2. Galiè N, *et al. Eur Heart J* 2016; 37:67-119.

Risk Prediction Tools in PAH

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Risk equations or models currently available to predict outcomes in PAH

1. NIH registry equation[1]
2. French network equation[2,3]
3. PH Connection (PHC) equation[4,5]
4. Scottish composite score[6]
5. REVEAL equation[7] and risk score[8]
6. ESC/ERS risk stratification table[9]

1. D'Alonzo. *Ann Intern Med* 1991. 2. Humbert. *Circulation* 2010. 3. Humbert. *Eur Respir J* 2010. 4. Thenappan. *Eur Respir J* 2010. 5. Thenappan. *Chest* 2012. 6. Lee. *Eur Respir J* 2012. 7. Benza. *Circulation* 2010. 8. Benza. *Chest* 2012. 9. Galiè N, *Eur Heart J* 2016 & *Eur Respir J* 2015.

Recommendations for evaluation of PAH severity and response to therapy

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	Recommendations for evaluation of PAH severity and response to therapy	Class	Level
Risk Stratification	It is recommended to evaluate the severity of PAH patients with a panel of data derived from clinical assessment, exercise tests, biochemical markers and echocardiographic and hemodynamic evaluations	I	C
	It is recommended to perform regular follow-up assessments every 3 - 6 months in stable patients	I	C
Treatment goal	Achievement/maintenance of a low-risk profile is recommended as an adequate treatment response for patients with PAH	I	C
	Achievement/maintenance of an intermediate-risk profile should be considered an inadequate treatment response for most patients with PAH	IIa	C

1. Galiè N, *et al. Eur Respir J* 2015; 46:903-75;
2. Galiè N, *et al. Eur Heart J* 2016; 37:67-119.

Summary of four registries assessing risk scores

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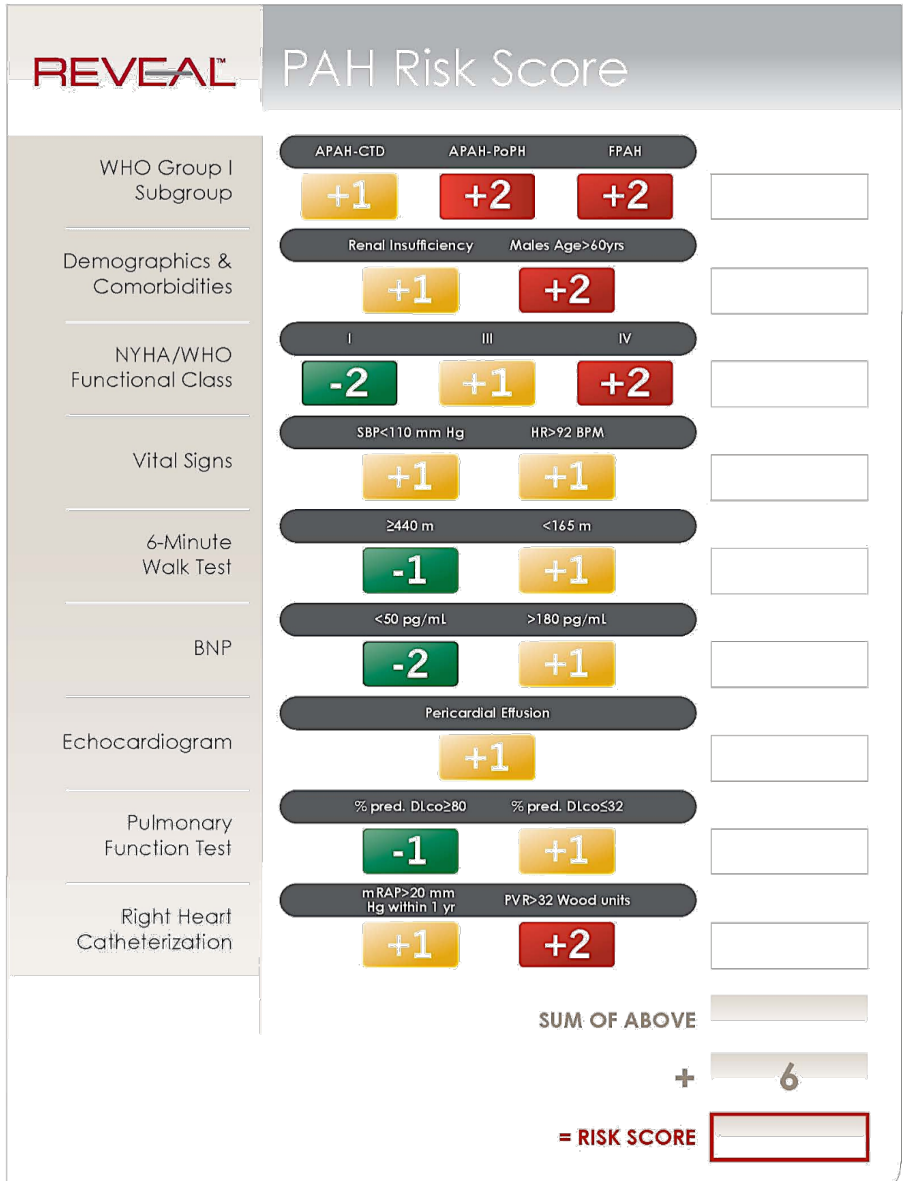
	REVEAL[1]	SPAHR[2]	COMPERA[3]	FPHN[4]
Required variables, *n*	12 - 14	8	8	4
Patients at baseline, *n*	2716	530	1588	1017
Patients at follow up, *n*	2529	383	1094	1017
Associated-PAH included	Yes	Yes	Yes	No
Definition of low-risk	≤ 6 REVEAL score	<1.5 Average score	< 1.5 Average score	3-4 of 4 low-risk criteria
1-year mortality by risk group (low/intermediate/high), %	≤2.6 / 7.0 / ≥10.7	1.0 / 7.0 / 26.0	2.8 / 9.9 / 21.2	1.0 / NA / 13.0-30.0

1. Benza RL, *et al. J Heart Lung Transplant*. 2015;34:356–61.
2. Kylhammar D, *et al. Eur Heart J* 2017; ehx257.
3. Hoeper MM, *et al. Eur Respir J* 2017; 50:1700740.
4. Boucly A, *et al. Eur Respir J* 2017; 50:1700889.

The REVEAL score



- **Score from 0 (low risk) to 22 (high risk)**
- **Estimated survival at 1 year**
- **Incident/prevalent cases**

Survival according to risk score at enrollment

Benza RL, et al. *Circulation* 2010. Benza RL, et al. *Chest* 2012.

2015 ESC/ERS Guidelines – Risk stratification in PAH

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Pneumologi in azione nell'ipertensione arteriosa polmonare (PAH)

	Determinants of prognosis	Estimated 1-year mortality		
		Low risk < 5%	Intermediate risk 5-10%	High risk > 10%
Clinical Evaluation	Clinical signs of right heart failure	Absent	Absent	Present
	Progression of symptoms	No	Slow	Rapid
	Syncope	No	Occasional syncope	Repeated syncope
	FC	I, II	III	IV
Exercise Capacity	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 - 44.9	Peak VO_2 < 11ml/min/kg (< 35% pred.) VE/VCO_2 slope ≥ 45
	NT-proBNP plasma levels	BNP < 50 ng/l NT-proBNP < 300 ng/l	BNP 50–300 ng/l NT-proBNP 300–1400 ng/l	BNP > 300 ng/l NT-proBNP > 1400 ng/l
Right Ventricular Function	Imaging (echo, CMR)	RA area < 18 cm^2 No pericardial effusion	RA area 18–26 cm^2 No or minimal pericardial effusion	RA area > 26 cm^2 Pericardial effusion
	Hemodynamics	RAP < 8 mmHg CI ≥ 2.5 l/min/m^2 SvO_2 > 65%	RAP 8–14 mmHg CI 2.0–2.4 l/min/m^2 SvO_2 60–65%	RAP > 14 mmHg CI < 2.0 l/min/m^2 SvO_2 < 60%

Galiè N, *et al. Eur Respir J* 2015; 46:903-75;
Galiè N, *et al. Eur Heart J* 2016; 37:67-119.

2015 ESC/ERS Guidelines – Risk stratification in PAH

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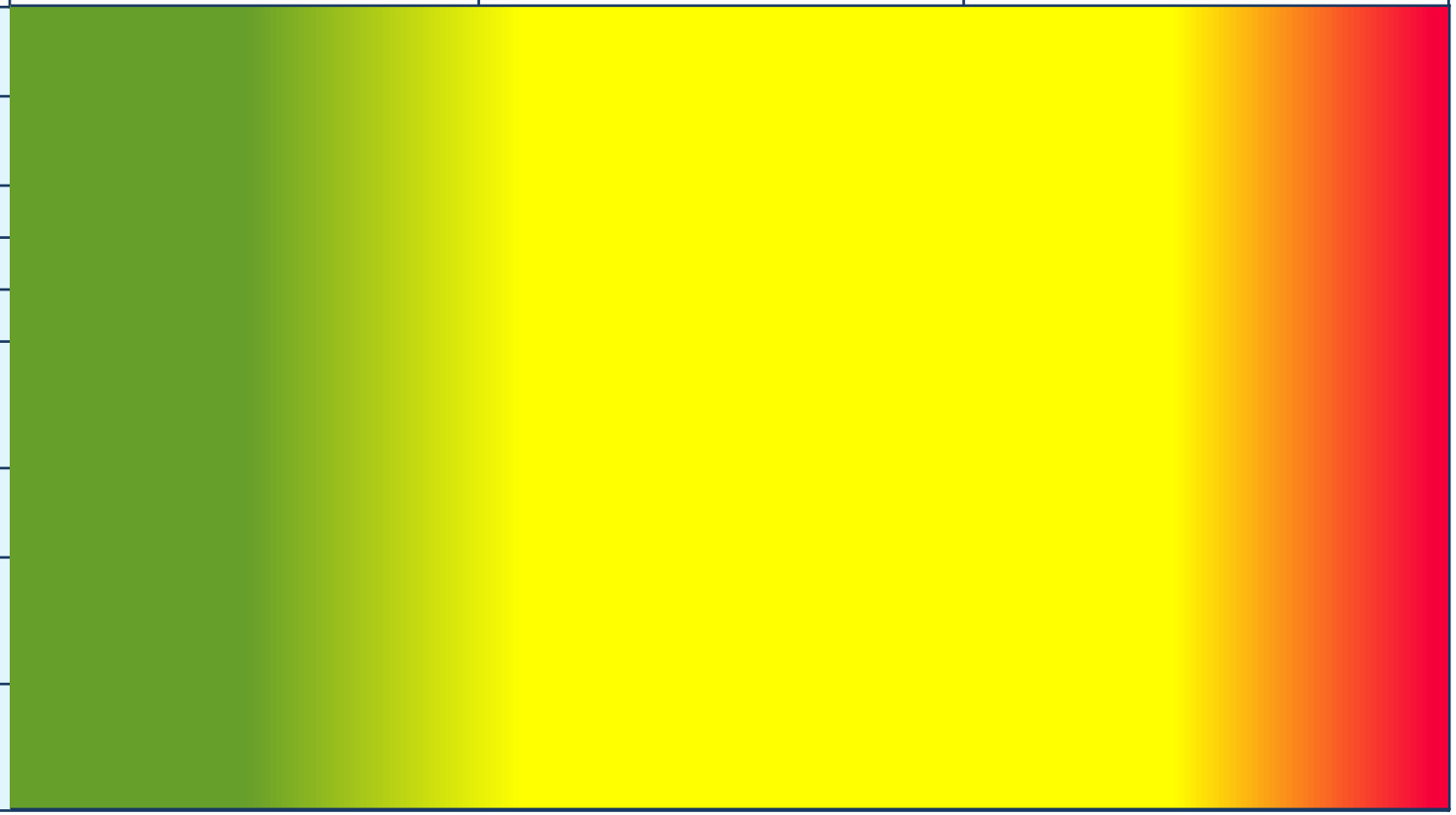
Clinical Evaluation	Clinical signs of right heart failure			
	Progression of symptoms			
	Syncope			
	FC			
Exercise Capacity	6MWD			
	CPET			
	NT-proBNP plasma levels			
Right Ventricular Function	Imaging (echo, CMR)			
	Hemodynamics			

Slide courtesy of Nazzareno Galiè

Galiè N, *et al. Eur Respir J* 2015; 46:903-75;
Galiè N, *et al. Eur Heart J* 2016; 37:67-119.

Validation of ESC/ERS risk stratification for PAH

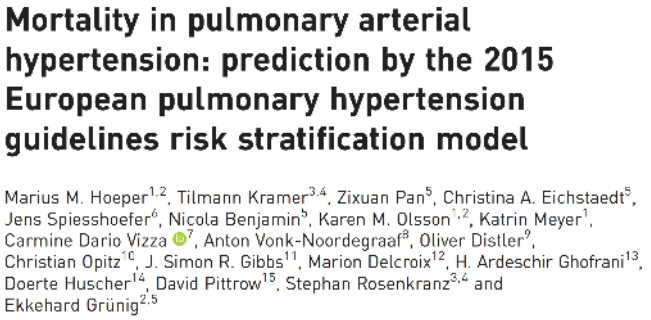
ACTION
Pneumologi in azione nell'ipertensione arteriosa polmonare (PAH)


European Heart Journal (2017) 0, 1–7
doi:10.1093/eurheartj/ehx257

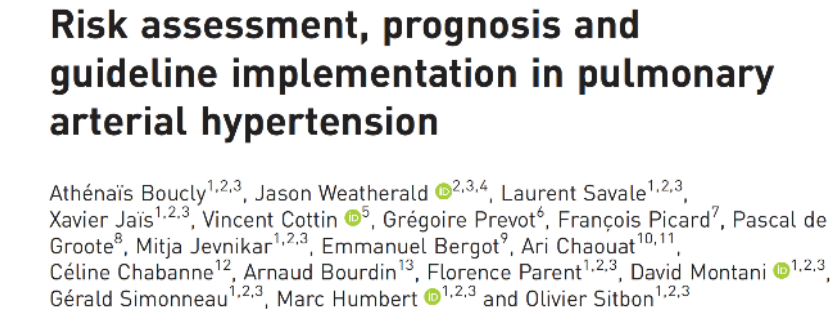
CLINICAL RESEARCH
Pulmonary circulation

A comprehensive risk stratification at early follow-up determines prognosis in pulmonary arterial hypertension

David Kylhammar[1]*, Barbro Kjellström[2], Clara Hjalmarsson[3], Kjell Jansson[4], Magnus Nisell[5], Stefan Söderberg[6], Gerhard Wikström[7], and Göran Rådegran[1], on behalf of SveFPH and SPAHR


Mortality in pulmonary arterial hypertension: prediction by the 2015 European pulmonary hypertension guidelines risk stratification model

Marius M. Hoeper[1,2], Tilmann Kramer[3,4], Zixuan Pan[5], Christina A. Eichstaedt[5], Jens Spiesshoefer[6], Nicola Benjamin[5], Karen M. Olsson[1,2], Katrin Meyer[1], Carmine Dario Vizza[7], Anton Vonk-Noordegraaf[8], Oliver Distler[9], Christian Opitz[10], J. Simon R. Gibbs[11], Marion Delcroix[12], H. Ardeschir Ghofrani[13], Doerte Huscher[14], David Pittrow[15], Stephan Rosenkranz[3,4] and Ekkehard Grünig[2,5]


Risk assessment, prognosis and guideline implementation in pulmonary arterial hypertension

Athénaïs Boucly[1,2,3], Jason Weatherald[2,3,4], Laurent Savale[1,2,3], Xavier Jaïs[1,2,3], Vincent Cottin[5], Grégoire Prevot[6], François Picard[7], Pascal de Groote[8], Mitja Jevnikar[1,2,3], Emmanuel Bergot[9], Ari Chaouat[10,11], Céline Chabanne[12], Arnaud Bourdin[13], Florence Parent[1,2,3], David Montani[1,2,3], Gérald Simonneau[1,2,3], Marc Humbert[1,2,3] and Olivier Sitbon[1,2,3]

Kylhammar (8 variables)	Hoeper (6 variables)	Boucly (4 or 3 variables)
n = 530 PAH (2008-2016)	*n* = 1588 PAH (2009-2016)	*n* = 1017 IPAH (2006-2016)
WHO 6MWD BNP RA area Pericardial effusion RAP CI SvO_2	WHO 6MWD BNP RAP CI SvO_2	WHO 6MWD RAP CI WHO 6MWD BNP
Sum of grades (1 low-3 high) /number available variables	Sum of grades (1 low-3 high) /number available variables	Number of low risk variables

Kylhammar D, *et al. Eur Heart J* 2017; ehx257; Hoeper MM, *et al. Eur Respir J* 2017; 50:1700740; Boucly A, *et al. Eur Respir J* 2017; 50:1700889.

Validation of ESC/ERS risk stratification in large registries

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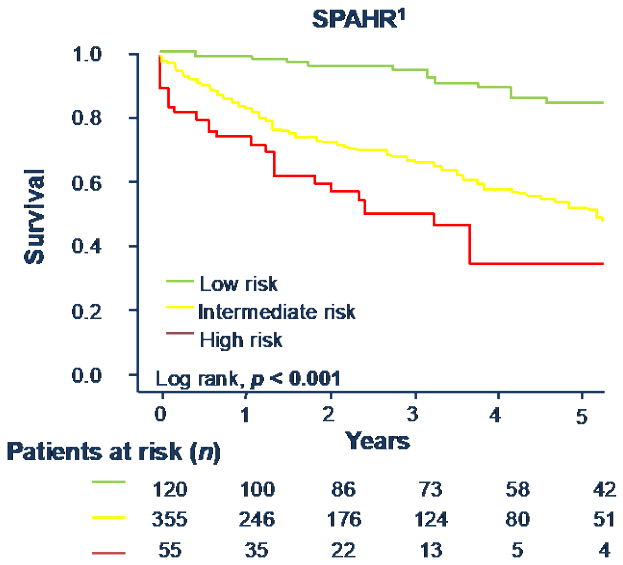
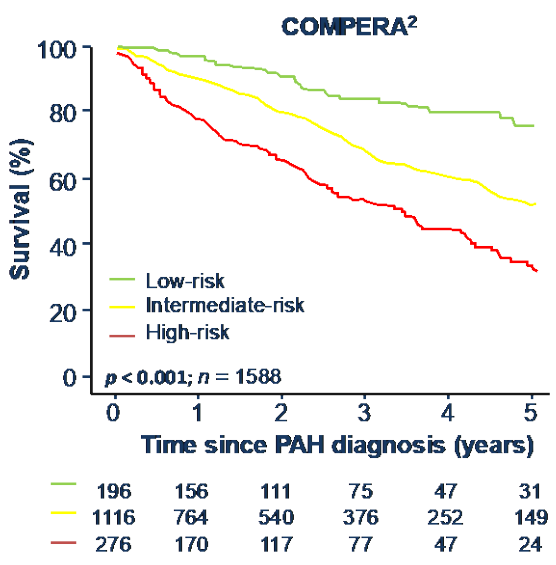
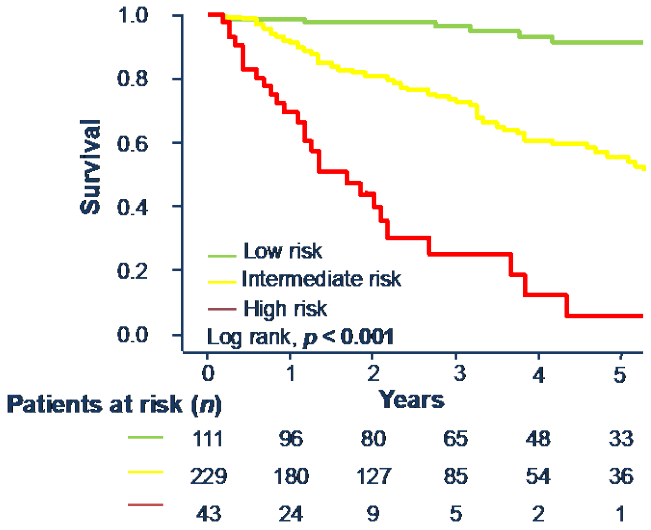
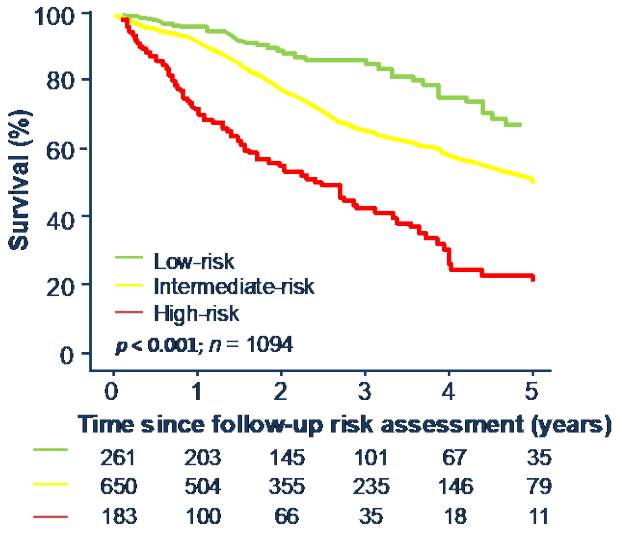
Baseline

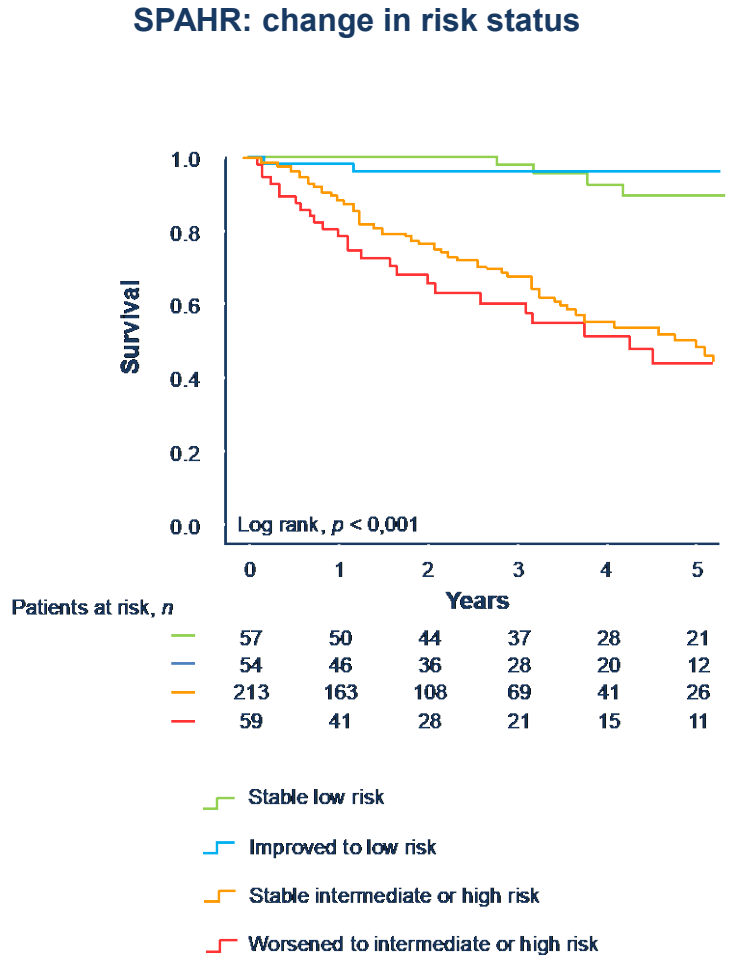
Follow-up







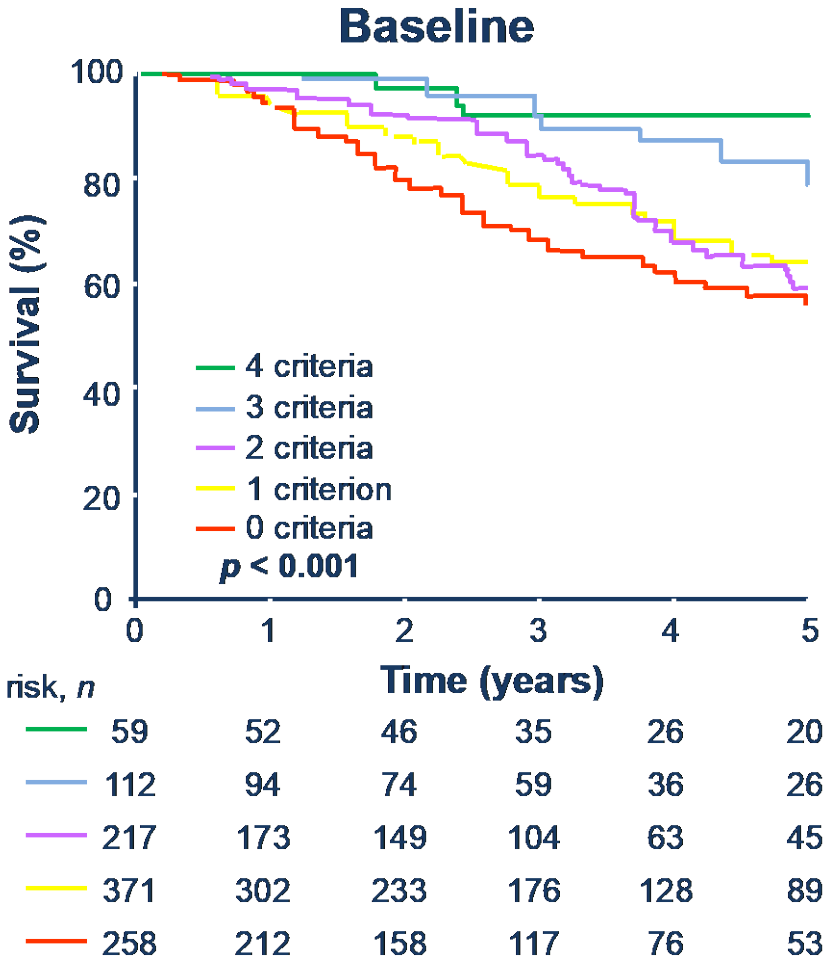


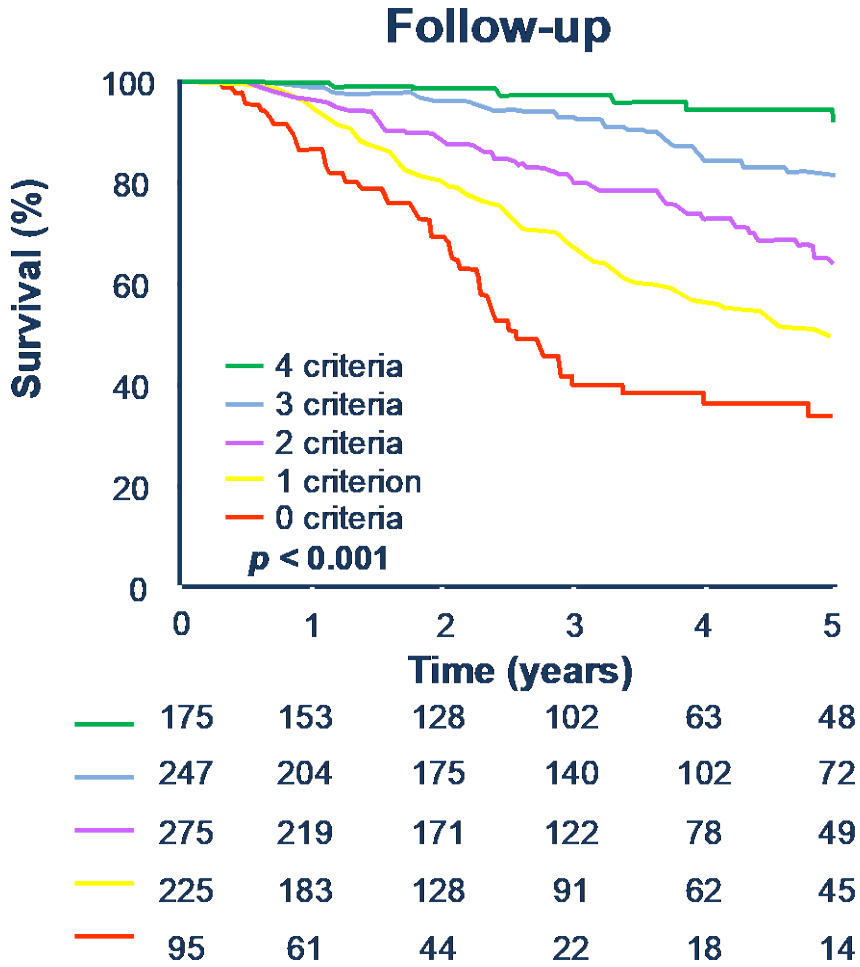


1. Kylhammar D, *et al. Eur Heart J* 2017; Epub ahead of print;
2. Hoeper MM, *et al. Eur Respir J* 2017; 50:1700740.

Achievement of multiple low risk criteria is associated with improved long-term outcomes

Low-risk criteria:
NYHA FC I-II
6MWD >440 m
RAP <8 mmHg
CI >2.5 L/min/m^2

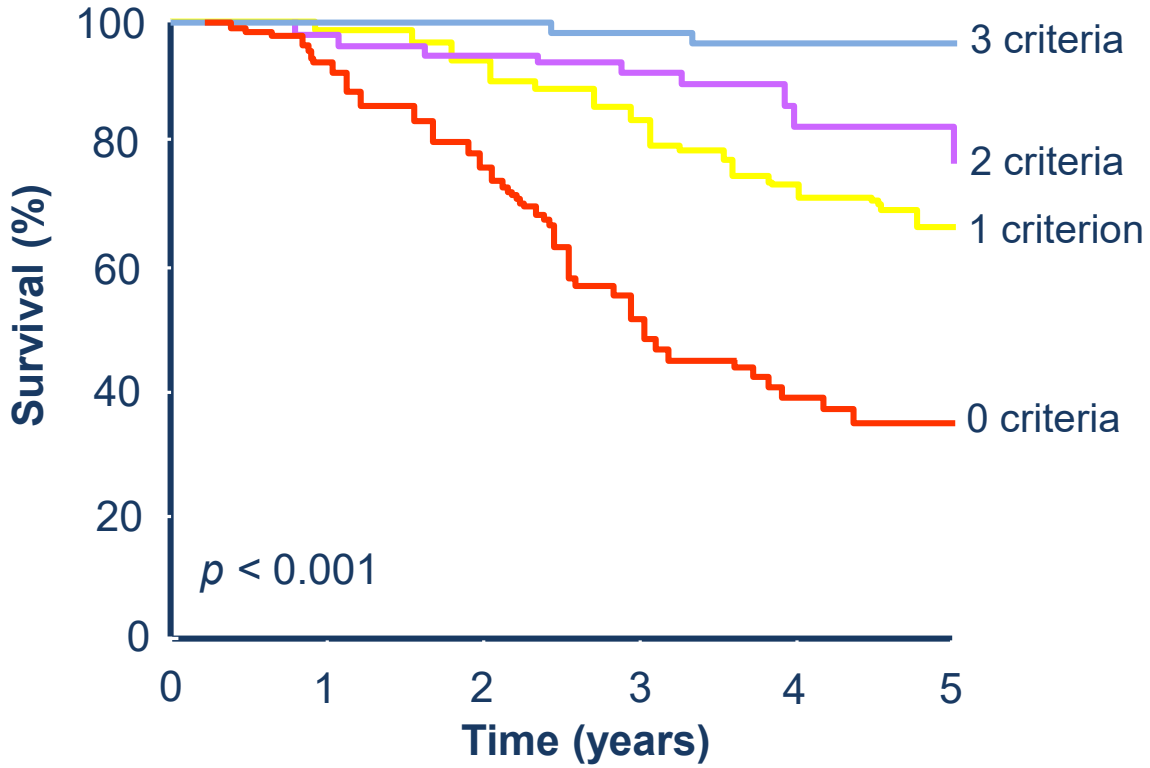




Incident patients enrolled in the French registry

Boucly A., *et al. Eur Respir J* 2017; 50: 1700889.

Number of non-invasive low-risk criteria at follow-up is also associated with prognosis



Patients at risk, *n* (*n* = 603)

3 criteria	115	97	81	63	38	26
2 criteria	145	116	95	72	36	21
1 criterion	175	136	101	62	38	24
0 criteria	168	117	76	39	23	11

Non-invasive measurements were WHO/NYHA FC, 6MWD and either BNP or NT-proBNP

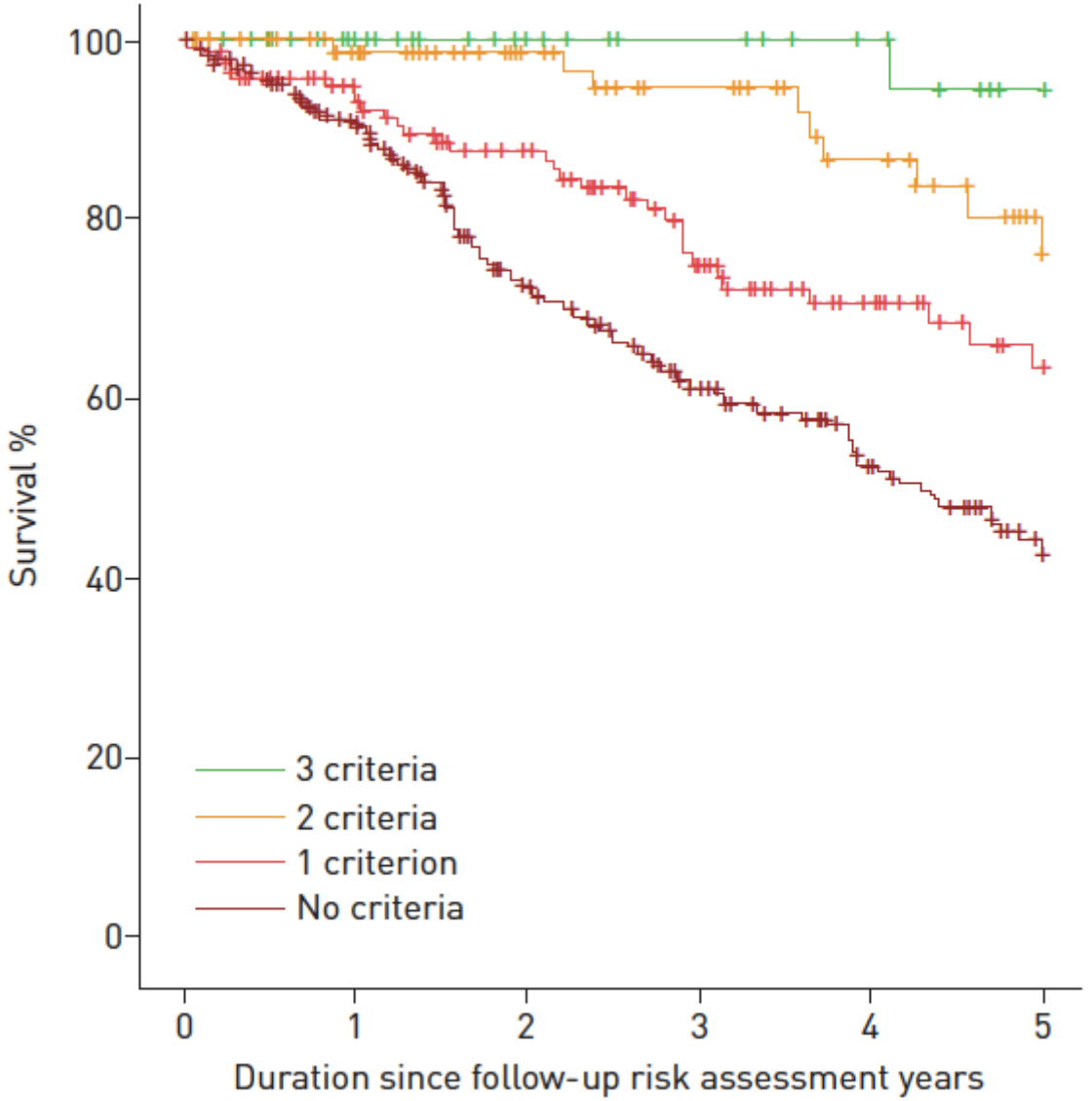
Non-invasive low-risk criteria:
NYHA FC I-II
6MWD >440 m
BNP <50 ng/L or NT-proBNP <300 ng/L

Patients with all 3 non-invasive low-risk criteria had a 2-, 3- and 5-year survival of 100%, 99% and 97%, respectively

Boucly A., *et al. Eur Respir J* 2017; 50: 1700889.

Validation of the french methodology in COMPERA

- 579 idiopathic PAH
- 1st f-up (median 4.6 months)
- 3 non invasive criteria:
  - NYHA FC I-II
  - 6MWD > 440m
  - BNP < 50 ng/L or NT-proBNP < 300 ng/mL



Hoeper M, *et al. Eur Respir J* 2018; 51: 1702606.

Limitations of Risk Assessment

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- Data derived from retrospective and prospective observational registries
- Data collection was not standardized in all published registries
- Significant missing data and patients lost to follow-up (SPAHR & COMPERA)
- Other important prognostic features, e.g. imaging, Echo, and CPET, were not collected systematically
- Intermediate risk patients is the largest group

Proposal of a simplified risk assessment in pulmonary arterial hypertension

Risk Criteria	Determinants of Prognosis[a] (estimated 1-year mortality)	Low Risk Variables (<5%)	Intermediate Risk Variables (5-10%)	High Risk Variables (>10%)
A.	WHO functional class	I, II	III	IV
B.	6MWD	> 440 m	165–440 m	< 165 m
C.	NT-proBNP/BNP plasma levels or RAP	BNP < 50 ng/l NT-proBNP < 300 ng/l or RAP < 8 mmHg	BNP 50–300 ng/l NT-proBNP 300–1400 ng/l or RAP 8–14 mmHg	BNP > 300 ng/l NT-proBNP > 1400 ng/l or RAP > 14 mmHg
D.	CI or SvO_2	CI ≥ 2.5 l/min/m^2 or SvO_2 > 65%	CI 2.0–2.4 l/min/m^2 or SvO_2 60–65%	CI < 2.0 l/min/m^2 or SvO_2 < 60%
Individual Risk Category Definition		Low Risk Definition	Intermediate Risk Definition	High Risk Definition
		At least 3 low risk criteria and no high risk criteria	Definitions of low or high risk not fulfilled	At least 2 high risk criteria including CI or SvO2

Slide courtesy of Nazzareno Galiè

WSPH 2018, in revision.

Risk stratification at baseline and follow-up

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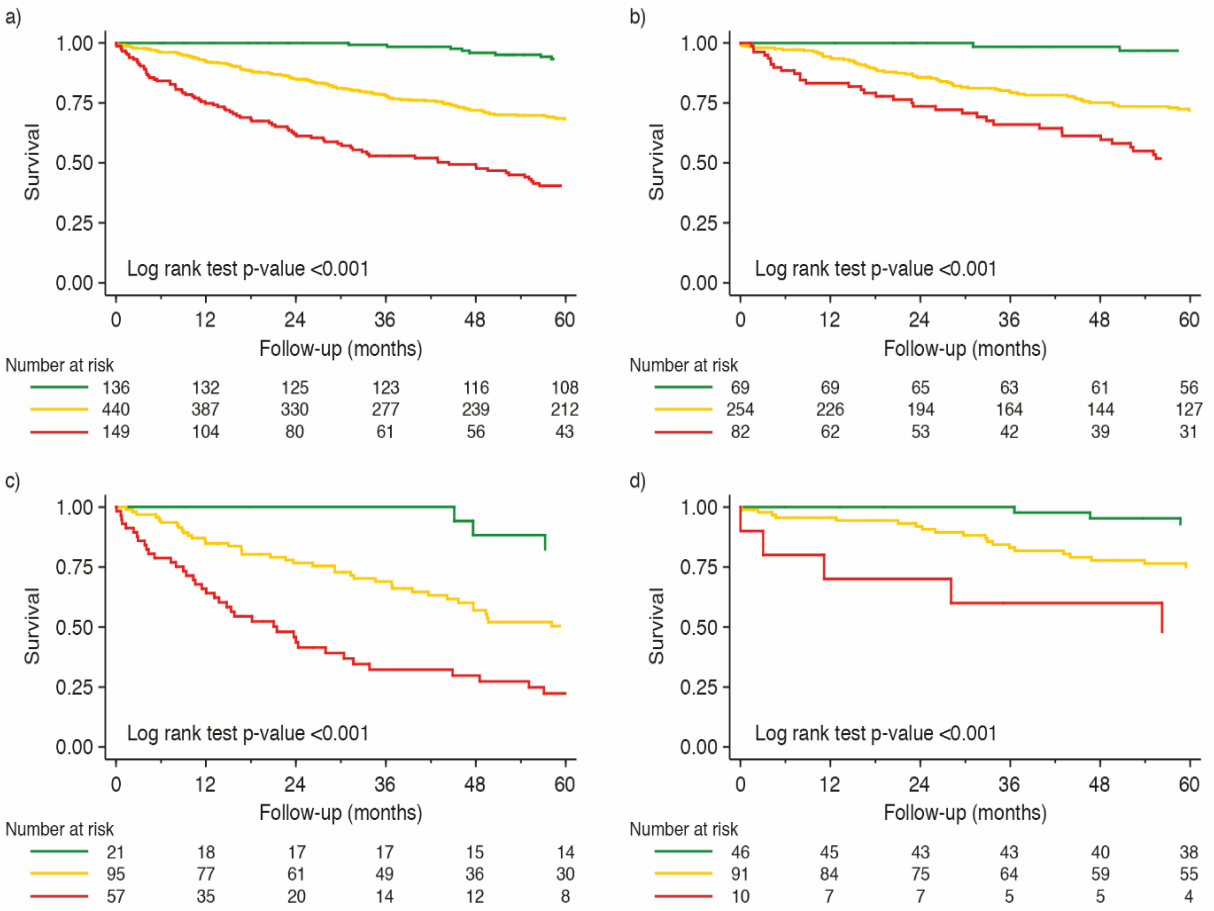
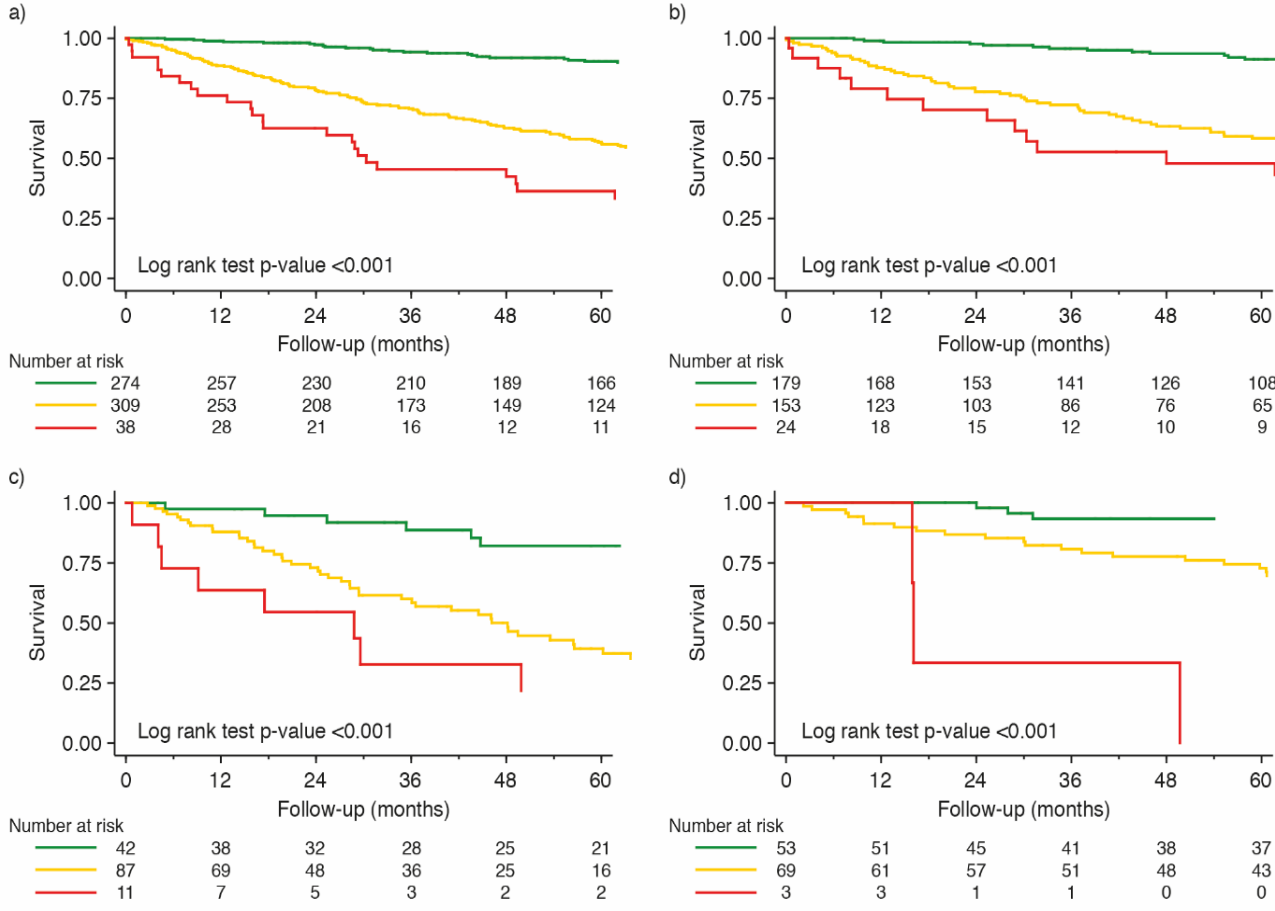
BASELINE EVALUATION



TREATMENT RESPONSE



Slide courtesy of Nazzareno Galiè

Dardi F, *et al.*. ESC 2018.

Recommendations for evaluation of PAH severity and response to therapy

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Pneumologi in azione nell'ipertensione arteriosa polmonare (PAH)

6th WSPH Nice 2018

Risk Stratification

Treatment goal

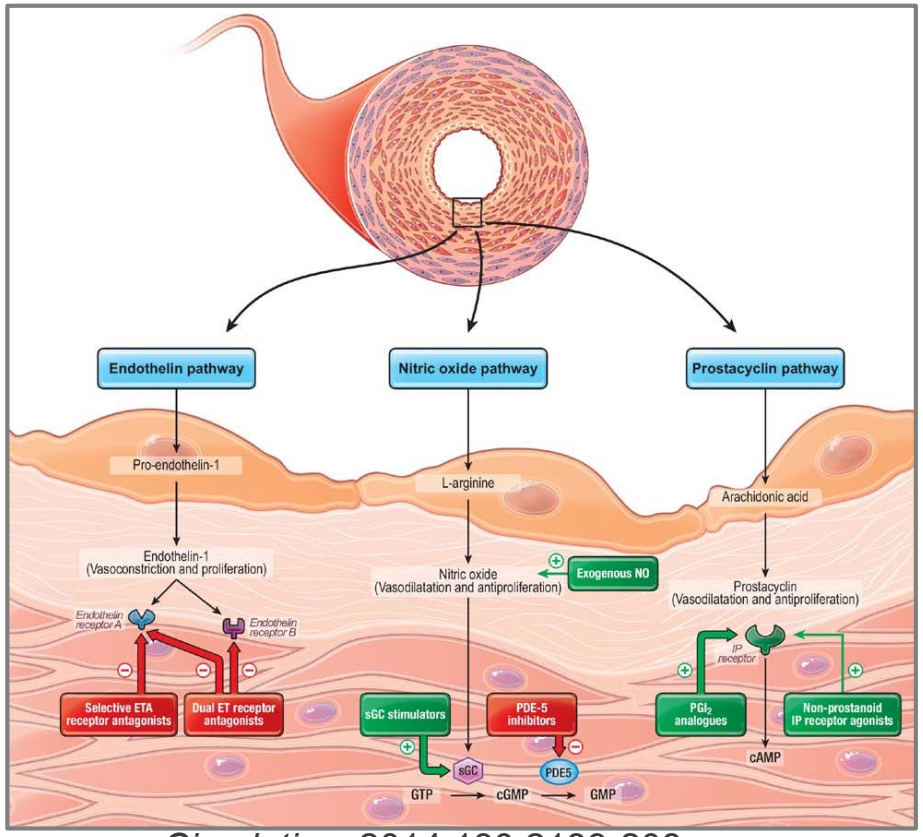
Recommendations for evaluation of PAH severity and response to therapy	Class	Level
It is recommended to evaluate the severity of PAH patients with a panel of data derived from clinical assessment, exercise tests, biochemical markers and echocardiographic and hemodynamic evaluations	I	C > B
It is recommended to perform regular follow-up assessments every 3 - 6 months in stable patients	I	C > B
Achievement/maintenance of a low-risk profile is recommended as an adequate treatment response for patients with PAH	I	C > B
Achievement/maintenance of an intermediate-risk profile should be considered an inadequate treatment response for most patients with PAH	IIa	C > B

1. Galiè N, *et al. Eur Respir J* 2015; 46:903-75;
2. Galiè N, *et al. Eur Heart J* 2016; 37:67-119.

Current PAH-targeted medications:
Targeting 3 major pathways of endothelial dysfunction

Advances in Therapeutic Interventions for Patients With Pulmonary Arterial Hypertension

Marc Humbert, MD, PhD; Edmund M.T. Lau, MD, PhD; David Montani, MD, PhD; Xavier Jaïs, MD; Oliver Sitbon, MD, PhD; Gérald Simonneau, MD



Circulation. 2014;130:2189-208.

Endothelin pathway

Endothelin receptor antagonists (ERAs)
- Ambrisentan
- Bosentan
- Macitentan

NO–cGMP pathway

PDE5 inhibitors
- Sildenafil
- Tadalafil

sGC stimulators
Riociguat

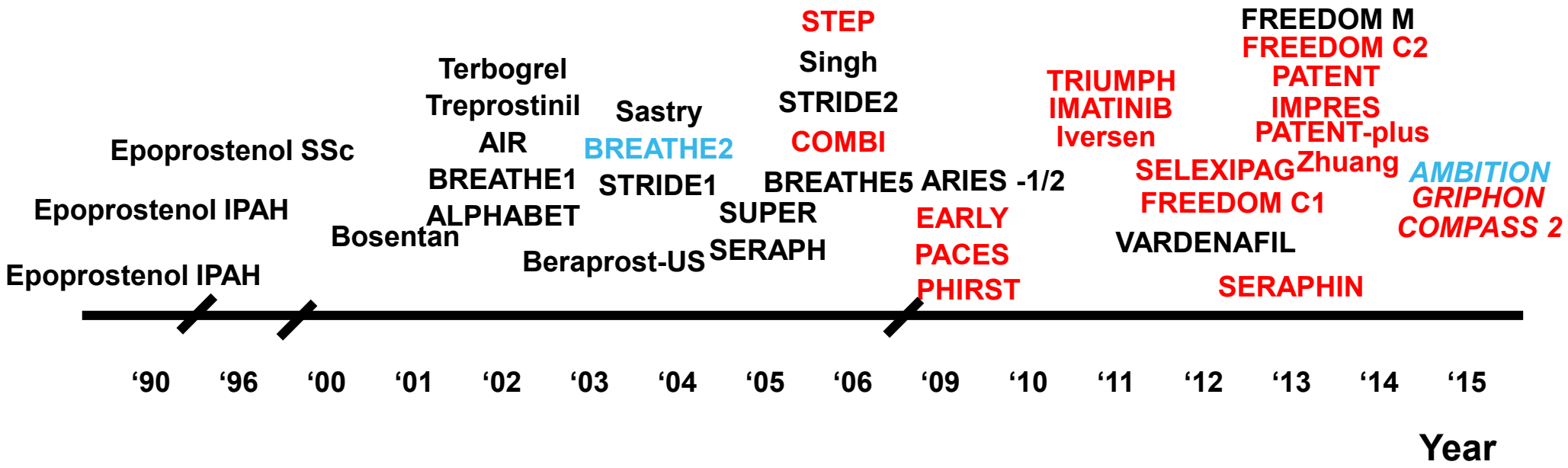
Prostacyclin pathway

Prostanoids
- Epoprostenol iv
- Iloprost inhaled, iv
- Treprostinil sc, iv, (inhaled, oral)*
- (Beraprost)**

Non prostanoids IP receptor agonist
Selexipag (oral)

*Only approved in the US; **Only approved in Japan and South Korea

Time-course of completed and published RCTs in PAH (41): Therapy Strategy



RCTs on monotherapy vs placebo or vs monotherapy (21)

RCTs on monotherapy and/or sequential combination vs placebo (18)

RCTs on initial combination vs monotherapy (2)

Modified from Galiè N, *et al. Eur Heart J* 2010;31:2080-6.

Meta-analyses comparison on all-cause mortality

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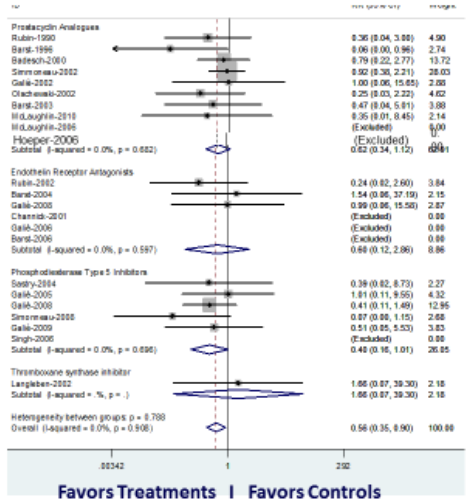
MONOTHERAPY

Pulmonary arterial hypertension: from the kingdom of the near-dead to multiple clinical trial meta-analyses

All Cause Mortality

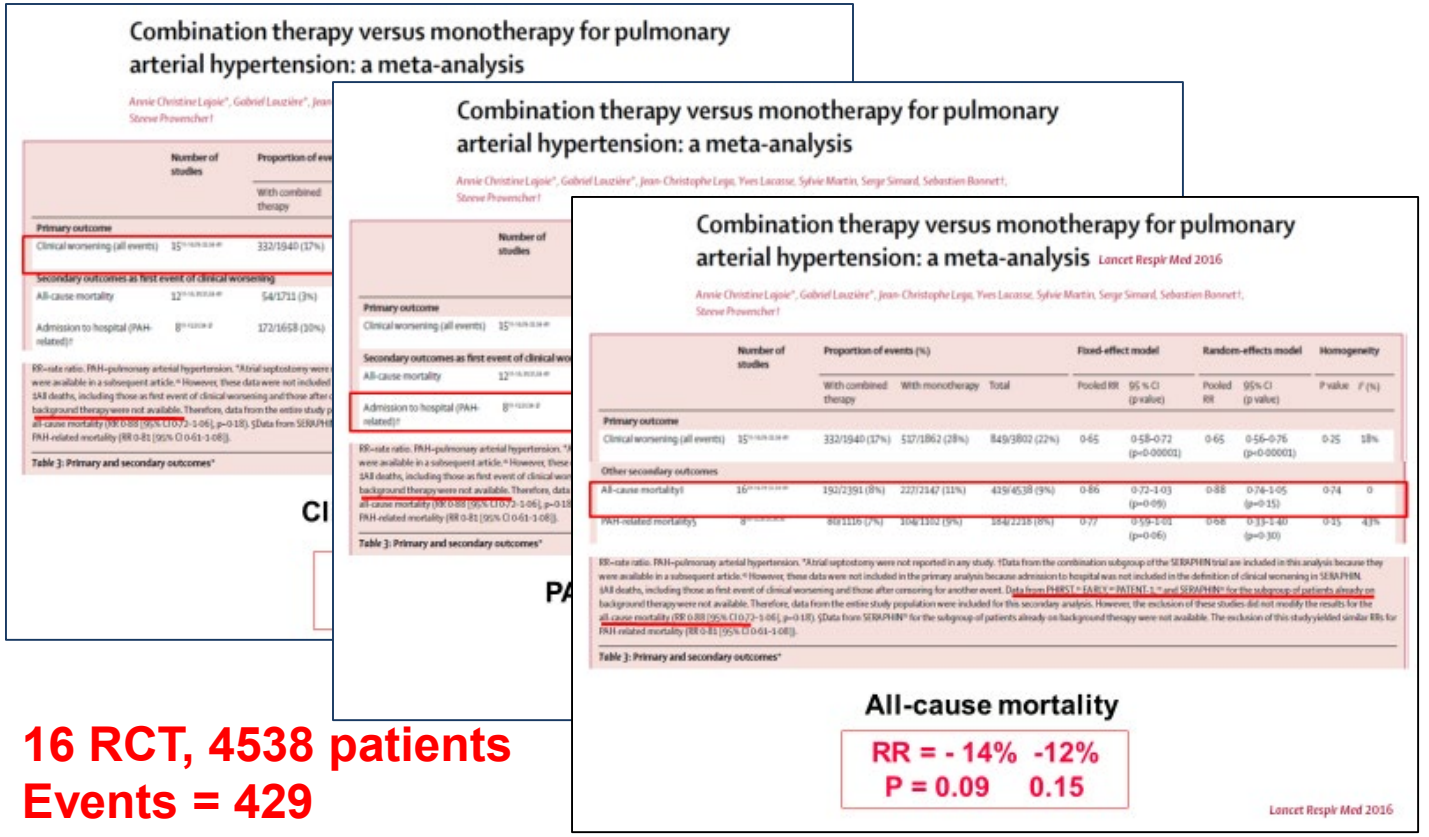
RR = - 44%
P = 0.016



N.Galiè, M.Palazzini, A.Manes, Eur Heart J 2010

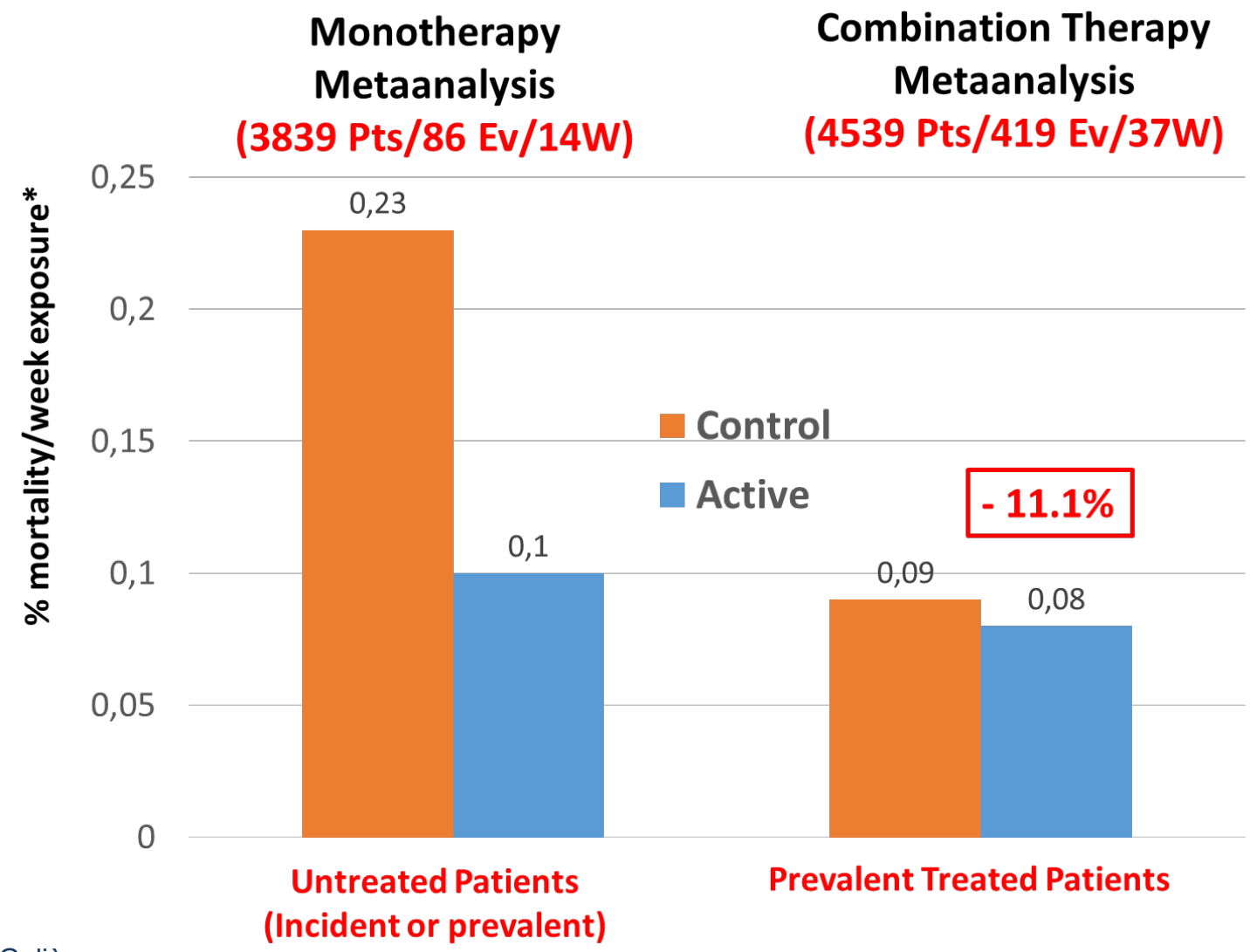
25 RCTs, 3839 patients
Events = 86
Average Mortality = 2.5%
Average Exposure Period = 14.2 weeks

SEQUENTIAL COMBINATION



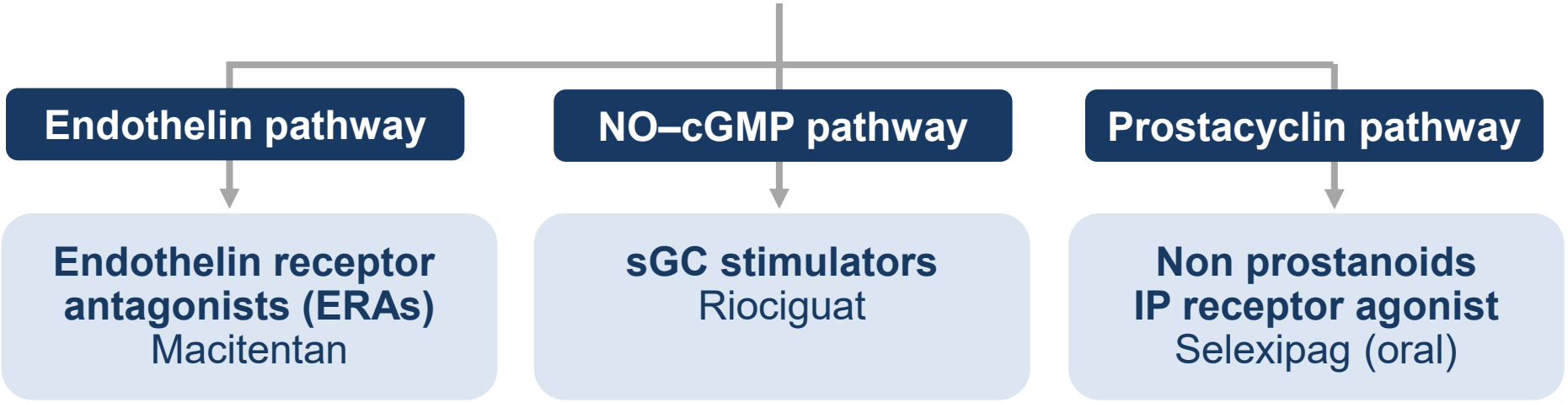
16 RCT, 4538 patients
Events = 429
Average Mortality = 9%
Average Exposure Period = 36.9 weeks

Meta-analyses comparison on all-cause mortality



Slide courtesy of Nazzareno Galiè

Combination therapy: New endpoints/ New strategies



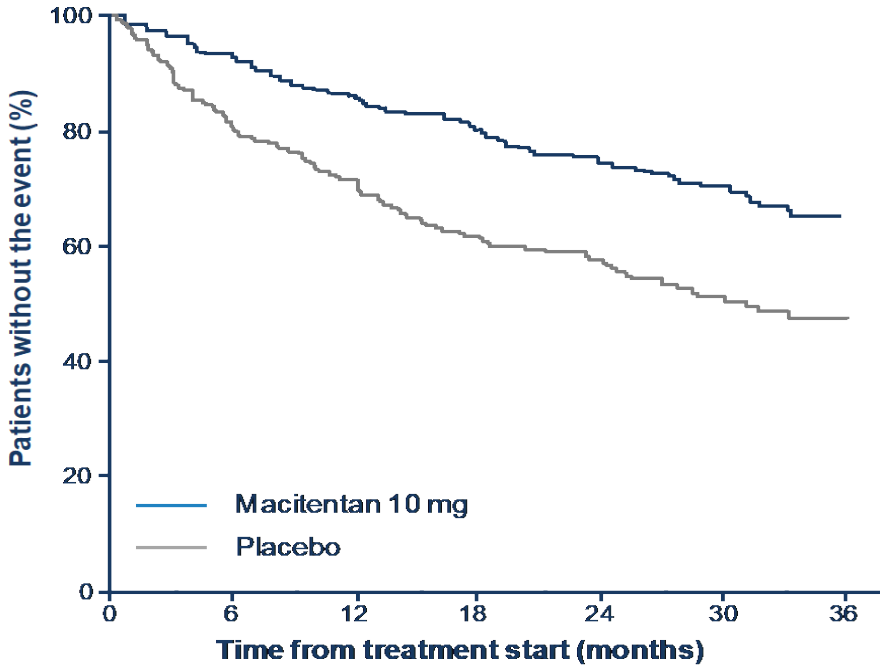
Drug tested	Study	Background	N	Duration (weeks)	Primary endpoint
Bosentan	COMPASS-2[1]	Sildenafil	334	92	Time to first occurrence of death or morbidity event **(NEG)**
Macitentan	SERAPHIN[2]	None (36%), PDE5i (61%) or oral/inhaled prostanoids	742	≈ 100	Time to first occurrence of death or morbidity event **(POS)**
Selexipag	GRIPHON[3]	None (21%),ERA (13%), PDE5i (32%) or both (34%)	1156	≈ 70	Time to first occurrence of death or morbidity event **(POS)**
Ambrisentan + tadalafil	AMBITION[4]	None (incident cases)	500	≈ 74	Time to first occurrence of clinical failure event **(POS)**

1. McLaughlin VV, *et al*. *Eur Respir J* 2015. 2. Pulido T, et al. *N Engl J Med* 2013. 3. Sitbon O, et al. *N Engl J Med* 2015. 4. Galié N, et al. *N Engl J Med* 2015.

SERAPHIN & GRIPHON: macitentan and selexipag reduced the risk of the primary outcome composite of death or morbidity due to PAH

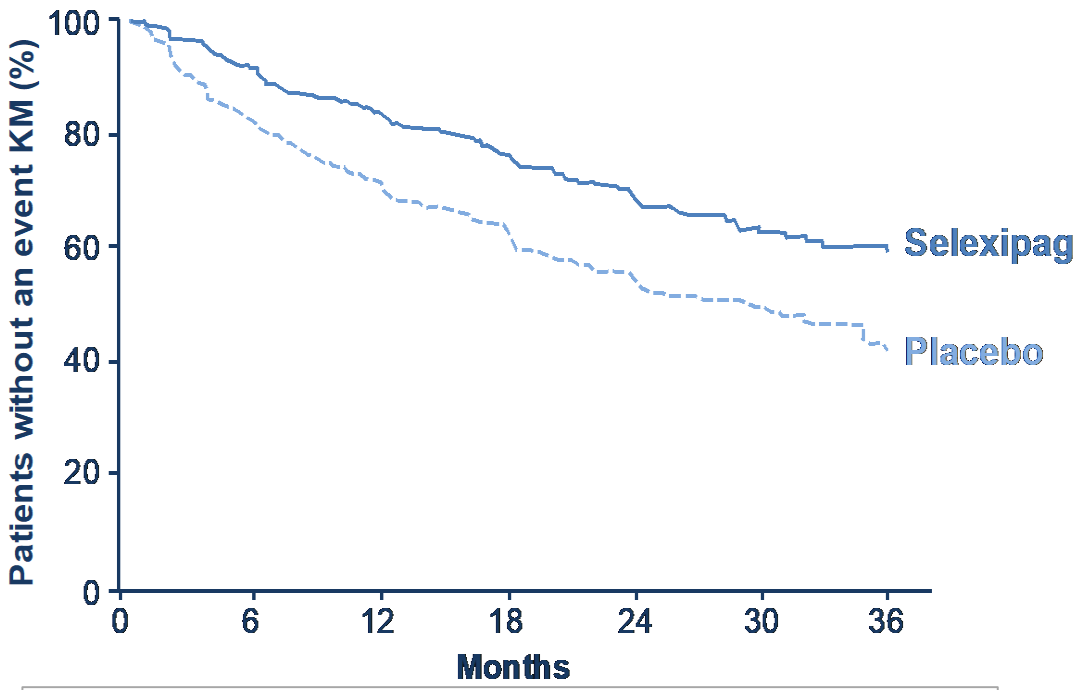
ACTION
Pneumologi in azione nell'ipertensione arteriosa polmonare (PAH)

SERAPHIN[1]



Risk reduction of primary endpoint event vs placebo
Macitentan 10 mg: 45% (< 0.001)

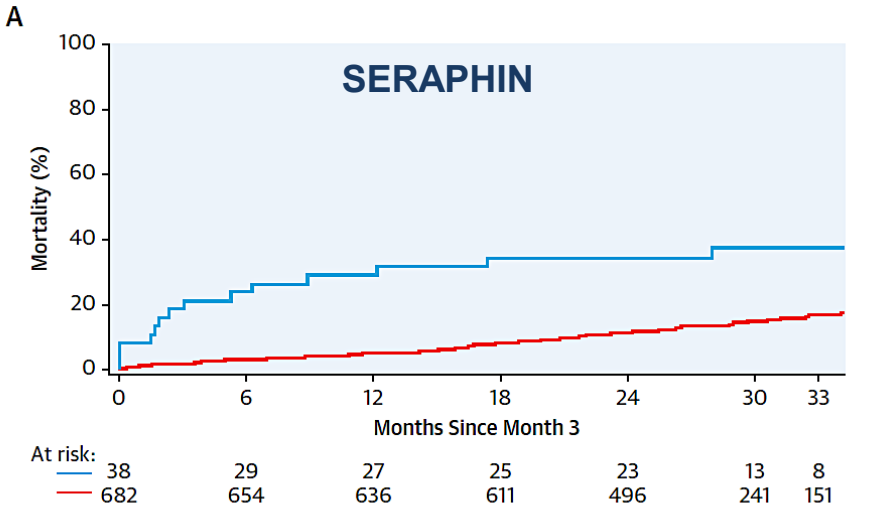
GRIPHON[2]

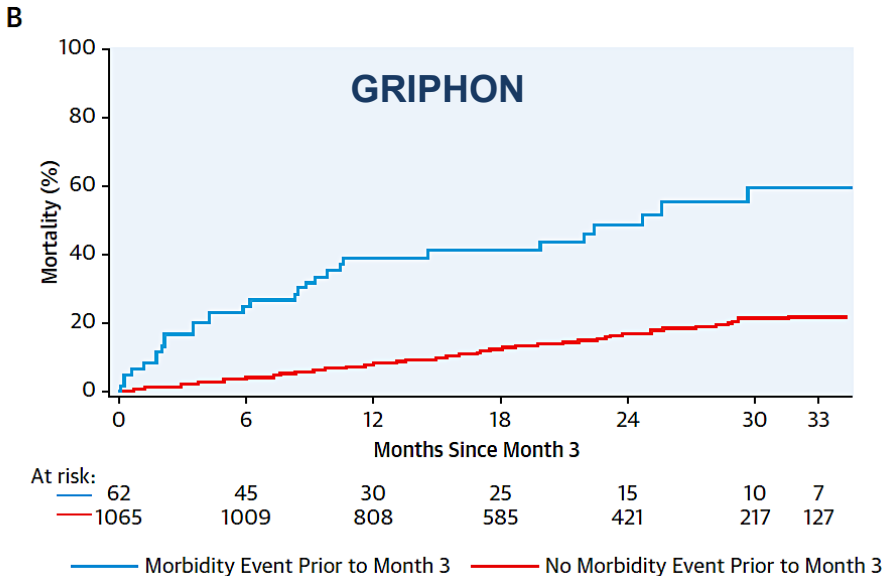


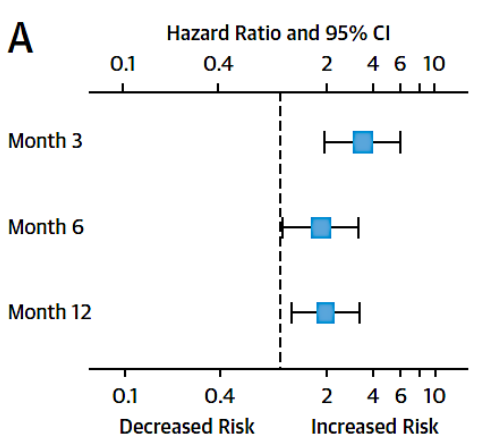
Risk reduction of primary endpoint event vs placebo
Selexipag: 40% (p < 0.0001)

1. Pulido T, *et al. N Engl J Med* 2013; 369:809-18.
2. Sitbon O, et al. *N Engl J Med* 2015;373:2522-33.

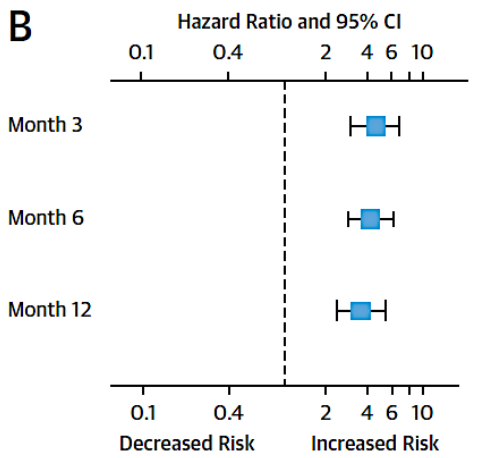
SERAPHIN & GRIPHON Landmark analysis: Morbidity events were prognostic for mortality







			Prior Morbidity Event		No Prior Morbidity Event	
	HR	95% CI	Patients	Events	Patients	Events
Month 3	3.39	1.94-5.92	38	15	682	98
Month 6	1.84	1.02-3.29	63	14	635	81
Month 12	1.98	1.17-3.35	106	20	565	57



			Prior Morbidity Event		No Prior Morbidity Event	
	HR	95% CI	Patients	Events	Patients	Events
Month 3	4.48	2.98-6.73	62	30	1065	160
Month 6	4.10	2.86-5.87	106	42	983	120
Month 12	3.52	2.34-5.31	147	37	817	72

McLaughlin VV, *et al. J Am Coll Cardiol* 2018;71:752-63.

Initial combination therapy: What is the evidence?

ACTION
Pneumologi in azione nell'ipertensione arteriosa polmonare (PAH)

Measure/ treatment	Class[a]-Level[b]					
	WHO-FC II		WHO-FC III		WHO-FC IV	
Ambrisentan + tadalafil[d]	I	B	I	B	IIb	C
Other ERA + PDE-5i	IIa	C	IIa	C	IIb	C
Bosentan + sildenafil + i.v. epoprostenol	-	-	IIa	C	IIa	C
Bosentan + i.v. epoprostenol	-	-	IIa	C	IIa	C
Other ERA or PDE-5i + s.c. treprostinil			IIb	C	IIb	C
Other ERA or PDE-5i + other i.v. prostacyclin analogues			IIb	C	IIb	C

AMBITION: Galiè N, *et al. N Engl J Med* 2015;273:834:44.

Sitbon O, *et al. Eur Respir J* 2016;47:1727-36.

Sitbon O, *et al. Eur Respir J.* 2014;43:1691–7.

BREATHE-2: Humbert M, *et al. Eur Respir J.* 2004;24:353-9.

Kemp K, *et al. J Heart Lung Transplant* 2012;31:150–8.

TRITON study (macitentan, tadalafil, ± selexipag) ongoing

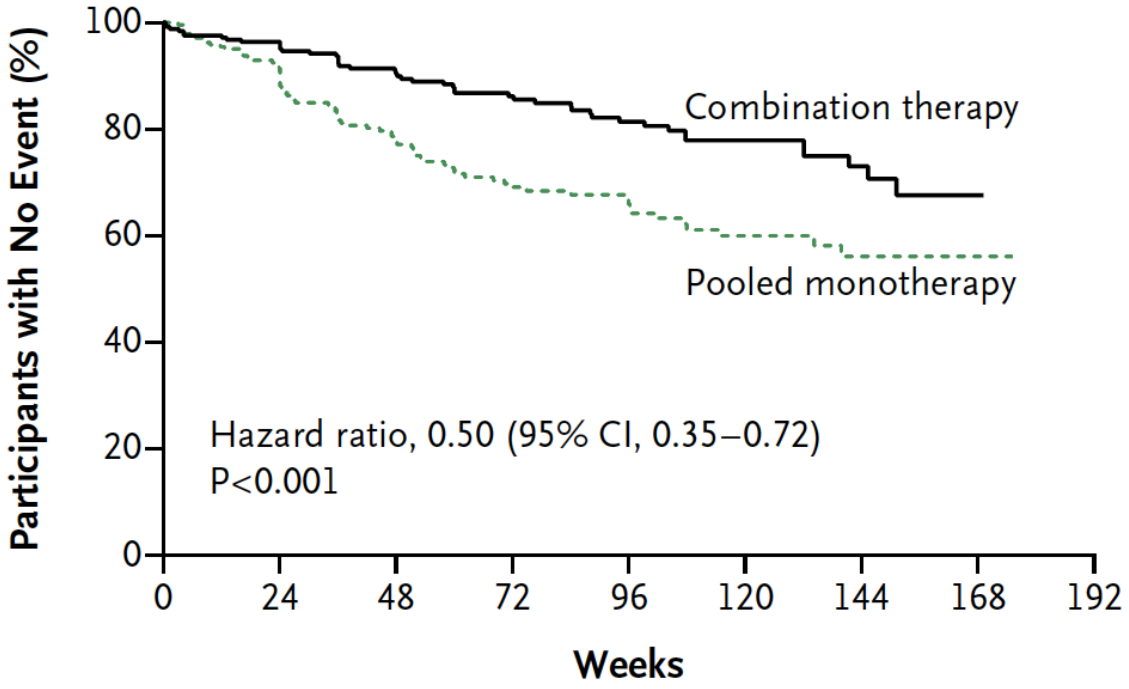
RCTs

Galiè N, Humbert M, *et al. Eur Respir J* 2015;46:903–75; *Eur Heart J* 2016;37:67–119.

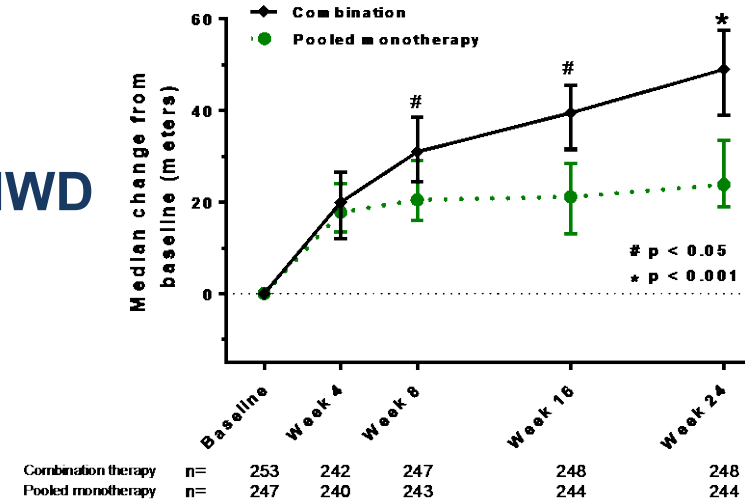
AMBITION: Initial combo of ambrisentan AND tadalafil is superior to monotherapy with ambrisentan OR tadalafil

ACTION
Pneumologi in azione nell'ipertensione arteriosa polmonare (PAH)

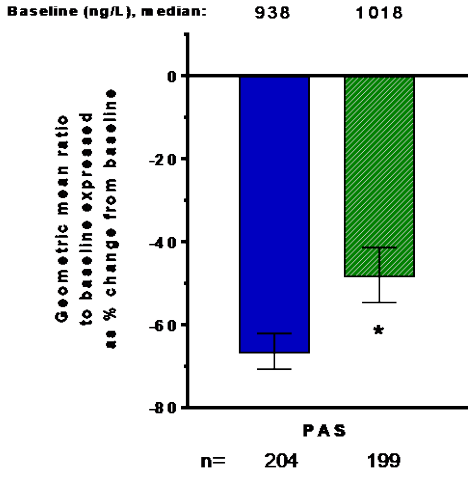
- N=500 treatment-naïve patients with PAH (31% FC II)
- **Primary endpoint**: Time to the first occurrence of a composite endpoint of death, hospitalization for PAH worsening, disease progression, or unsatisfactory long-term clinical response



6MWD



NT-ProBNP



Hospitalisation for PAH worsening was the main component of the primary endpoint

Galiè N, et al. N Engl J Med 2015;273:834:44.

Initial dual oral combination in PAH: *A matter of drugs or a question of strategy?*

ACTION
Pneumologi in azione nell'ipertensione arteriosa polmonare (PAH)

	AMBITION–BONSAI* Ambrisentan + tadalafil (n=19)[1]	Joint–INTENTION# Bosentan + sildenafil (n=23)[2]	French Network Cohort ERA + PDE5i (n=97)[3]	OPTIMA Macitentan + tadalafil (n=16)[4]
Δ RAP (%)	-17	- 36	-29	-10
Δ mPAP (%)	-33	- 21	-16 (-10 mmHg)	-22 (-10 mmHg)
Δ CI (%)	+56	+63	+46 (+1 L/min/m^2)	+45 (+1 L/min/m^2)
Δ PVR (%)	-61	-60	-45 (from 12.7 WU)	-54 (from 10 WU)
Δ 6MWD (%)	+25	+ 42	+22 (+71 m)	+8 (+27 m)

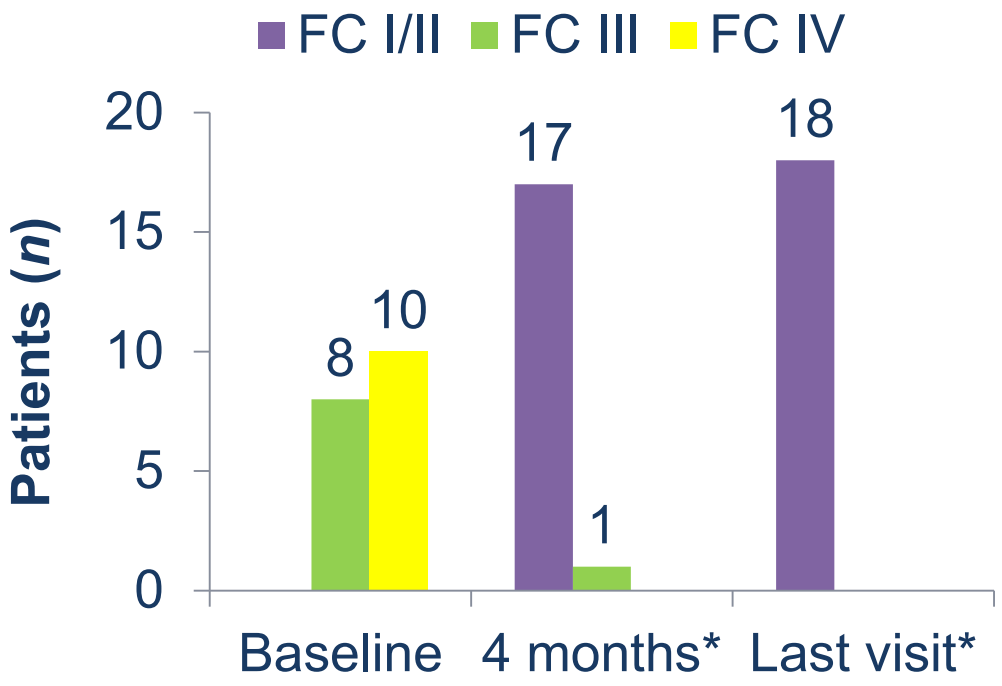
*BONSAI: BOlogNa Sub-study on hAemodynamIcs
#Joint Bologna and Calgary study on INiTial bosENTan plus sIldenafil in pulmonary arterial hypertension.

1. Bachetti C *et al. Am J Respir Crit Care Med* 2015;191:A479.
2. Palazzini M *et al. Am J Respir Crit Care Med* 2016;193:A6317.
3. Sitbon O *et al. Eur Respir J* 2016;47:1727–36.
4. Sitbon O *et al.* Presented as poster at ATS conference 2017.

Initial triple combination therapy in severe PAH: Treatment benefit on FC and hemodynamics

ACTION
Pneumologi in azione nell'ipertensione arteriosa polmonare (PAH)

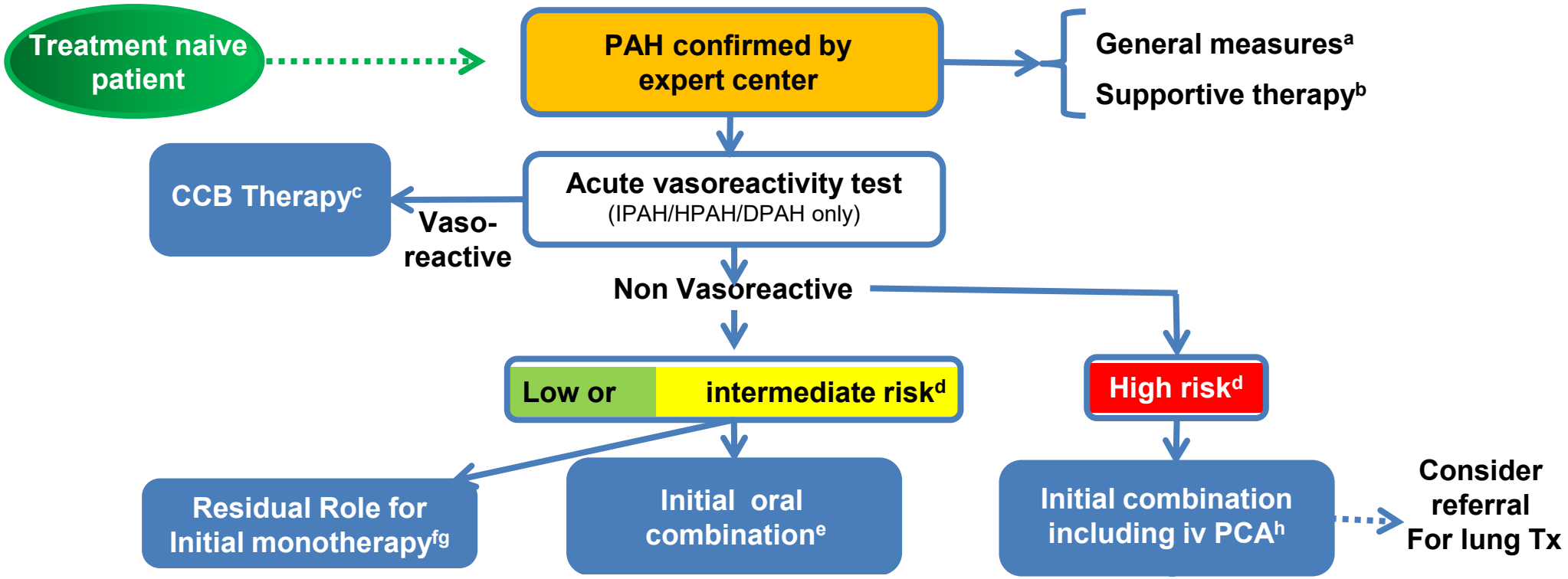
Prospective, observational analysis of idiopathic or heritable PAH patients (*n* = 19) treated with triple initial combination therapy (epoprostenol, bosentan and sildenafil)



	Baseline	4-month	Last visit (32 ± 19 months)
RAP (mmHg)	11.9 ± 5.2	4.9 ± 4.9*	5.2 ± 3.5*
mPAP (mmHg)	65.8 ± 13.7	45.7 ± 14.0*	44.4 ± 13.4*
CI (l/min/m^2)	1.66 ± 0.35	3.49 ± 0.69*	3.64 ± 0.65*
PVR (d.s.cm^{-5})	1718 ± 627	564 ± 260*	492 ± 209*
SvO_2 (%)	51.0 ± 8.5	69.7 ± 5.2*	72.2 ± 4.0*

*$p < 0.01$ versus baseline

Sitbon O, *et al. Eur Respir J.* 2014;43:1691–7.



ACTION
Pneumologi in azione nell'ipertensione arteriosa polmonare (PAH)

6th WSPH Nice 2018

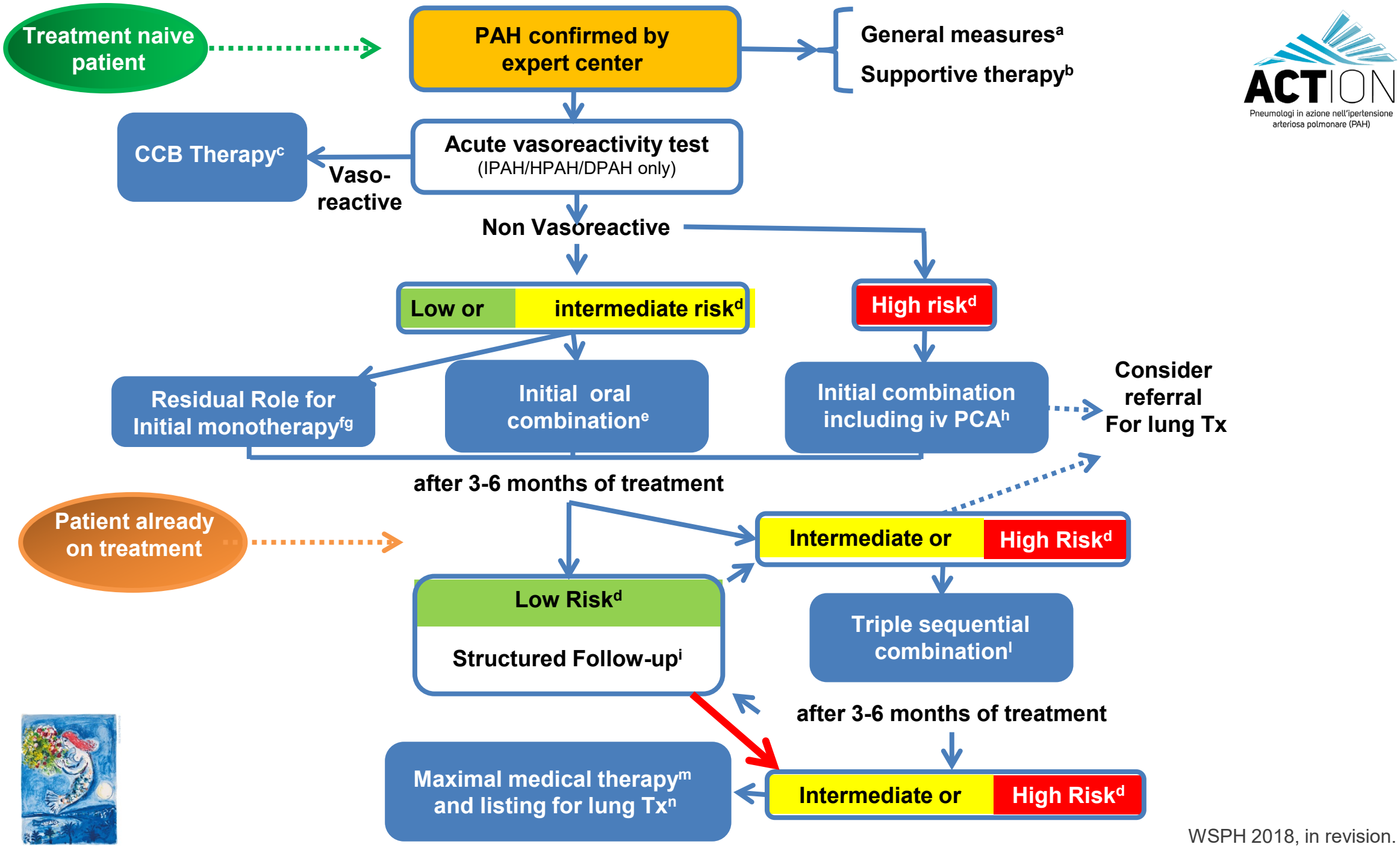
WSPH 2018, in revision.

Residual role for monotherapy

ACTION
Pneumologi in azione nell'ipertensione arteriosa polmonare (PAH)

- I/H/D PAH patients **responders to acute vasoreactivity tests** and with near-normalization of symptoms, exercise capacity, PAP and PVR on highest tolerated doses of CCBs
- **Long-term treated historical PAH patients with monotherapy** (> 5-10 years) stable with low risk profile
- **PAH patients > 75 yo with multiple risk factors for HFpEF** (high blood pressure, diabetes mellitus, coronary artery disease, atrial fibrillation, obesity)
- PAH patients with suspicion or high probability of **PVOD/PCH**
- Patients with PAH associated with **HIV** or **portal hypertension** or **uncorrected CHD** as they were not included in RCTs of initial combination therapy
- PAH patients with **very mild disease** (e.g. FC I, PVR < 4 WU, mPAP < 30 mmHg, normal RV)
- **Combination therapy unavailable** or contraindicated (e.g. severe liver disease)

WSPH 2018, in revision.



ACTION
Pneumologi in azione nell'ipertensione arteriosa polmonare (PAH)

6th WSPH Nice 2018

WSPH 2018, in revision.

Conclusions

ACTION
Pneumologi in azione nell'ipertensione arteriosa polmonare (PAH)

- Multiparametric evalution is essential to evaluate prognosis and optimal therapeutic strategy
- Low risk cathegory need a clear definition and could be a tstatus to attend and mantain
- Intensive follow up is necessary for all pts to adapte and ev. Increase (combination) therapy
- Double therapy is now the most appropriate therapy for the vast majority of intermediate risk pts
- For more severe pts a parenteral PC associated to 2 oral drugs is recommended