Greek Pulmonary Hypertension Registry: Current data(II)

Medical therapy

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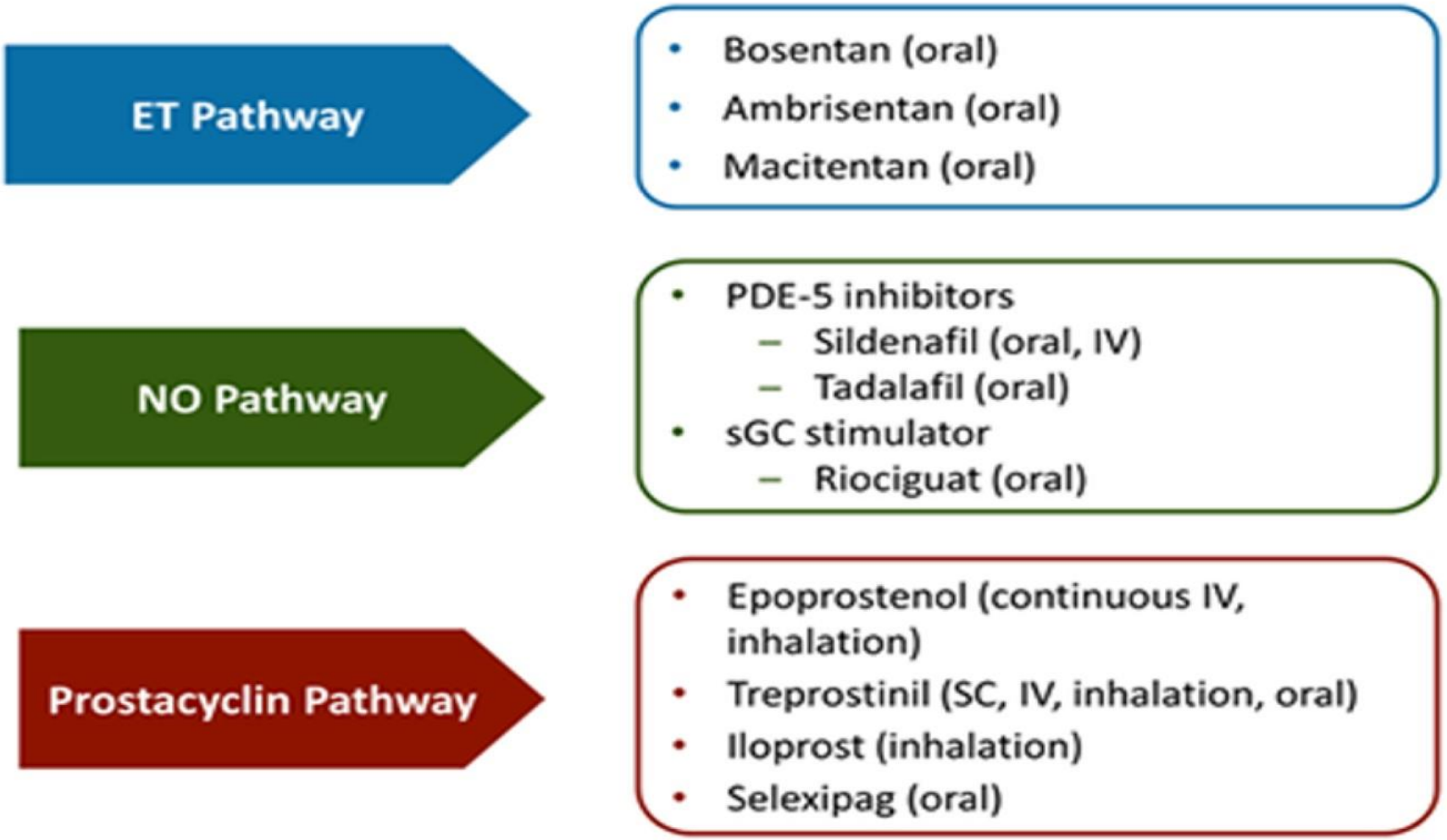
Cardiology Department, AHEPA University Hospital
On behalf of the Hellenic Society for the Study of Pulmonary Hypertension (HSSPH)

15 June 2018
Hellenic Congress of Pulmonary Hypertension

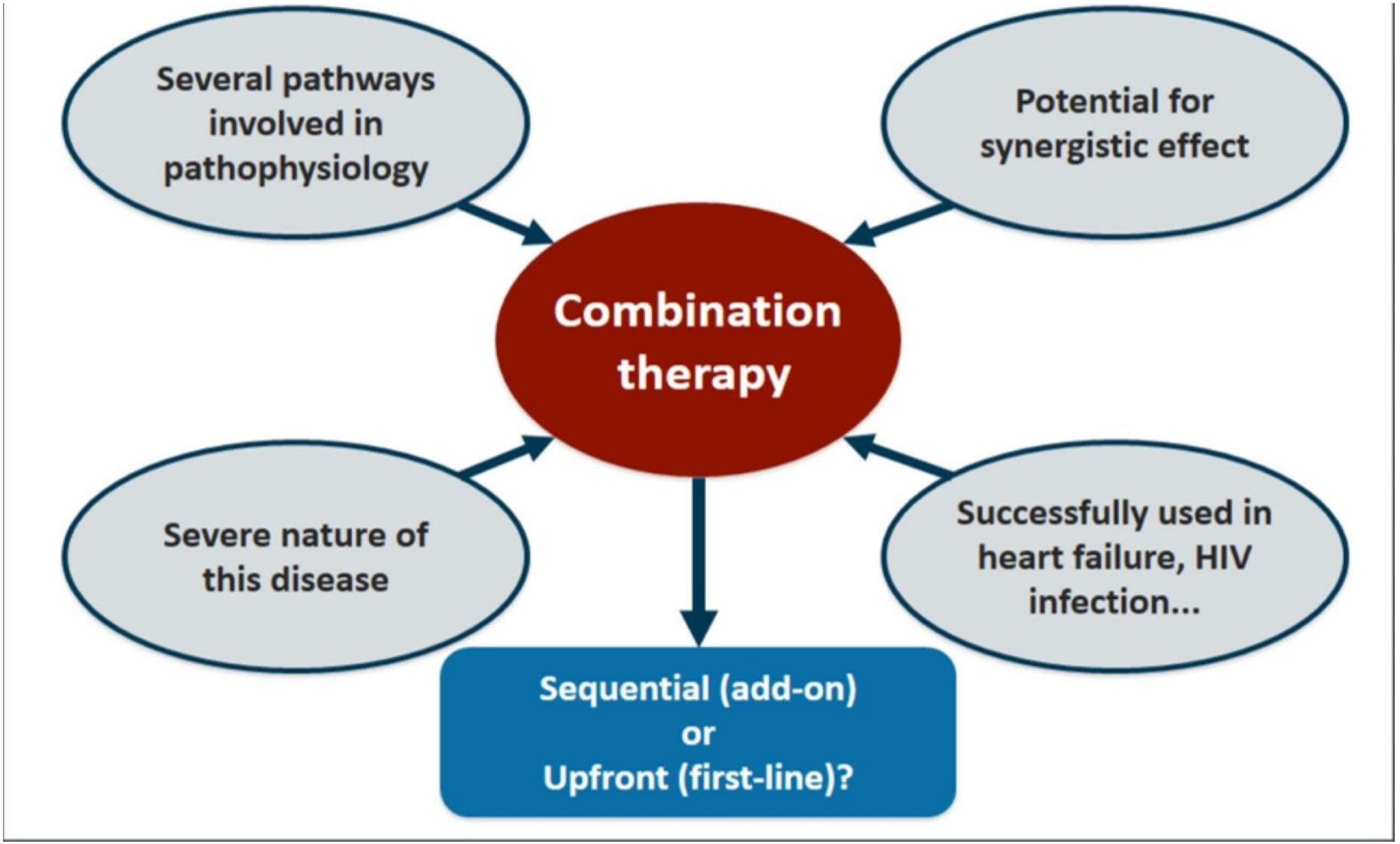
Pharmacotherapy in PAH (I)

Agents That Target Different Vasomotor Pathways in PAH



Galie N, et al. *J Am Coll Cardiol*. 2013;62(25 Suppl):D60-D72.
Humbert M, et al. *Thorax*. 2016;71:73-83.

Pharmacotherapy in PAH (II)



Greek Pulmonary Hypertension Registry

Non specific treatment in PH patients

Treatment	Total N=371	Group 1 N=232	Group 2 N=27	Group 3 N=24	Group 4 N=69	Group 5 N=19	P-value
Oxygen therapy, n (%)	85 (22.9)	50 (21.6)	2 (7.4)	11 **(45.8)**	20 (29)	1 (5.3)	**0.005**
Diuretics, n (%)	201 (54.2)	111 (47.8)	27 **(100)**	12 (50.0)	39 (56.5)	12 (63.2)	**0.0001**
Oral anticoagulant, n (%)	141 (38.0)	60 (25.9) **IPAH-HPAH** N=86 **41.8%**	8 (29.6)	6 (25.0)	56 **(81.1)**	12 (63.2)	**0.0001**

Greek PAHTool Registry

Greek Pulmonary Hypertension Registry

Non specific treatment in PH patients

Table 17 Recommendations for supportive therapy

Recommendations	Class[a]	Level[b]	Ref.[c]
Diuretic treatment is recommended in PAH patients with signs of RV failure and fluid retention	I	C	178
Continuous long-term O_2 therapy is recommended in PAH patients when arterial blood O_2 pressure is consistently <8 kPa (60 mmHg)[d]	I	C	179
Oral anticoagulant treatment may be considered in patients with IPAH, HPAH and PAH due to use of anorexigens	IIb	C	84,171, 175–177
Correction of anaemia and/or iron status may be considered in PAH patients	IIb	C	184
The use of angiotensin-converting enzyme inhibitors, angiotensin-2 receptor antagonists, beta-blockers and ivabradine is not recommended in patients with PAH unless required by co-morbidities (i.e. high blood pressure, coronary artery disease or left heart failure)	III	C	

HPAH = heritable pulmonary arterial hypertension; IPAH = idiopathic pulmonary arterial hypertension; O_2 = oxygen; PAH = pulmonary arterial hypertension; RV = right ventricular.

[a]Class of recommendation.

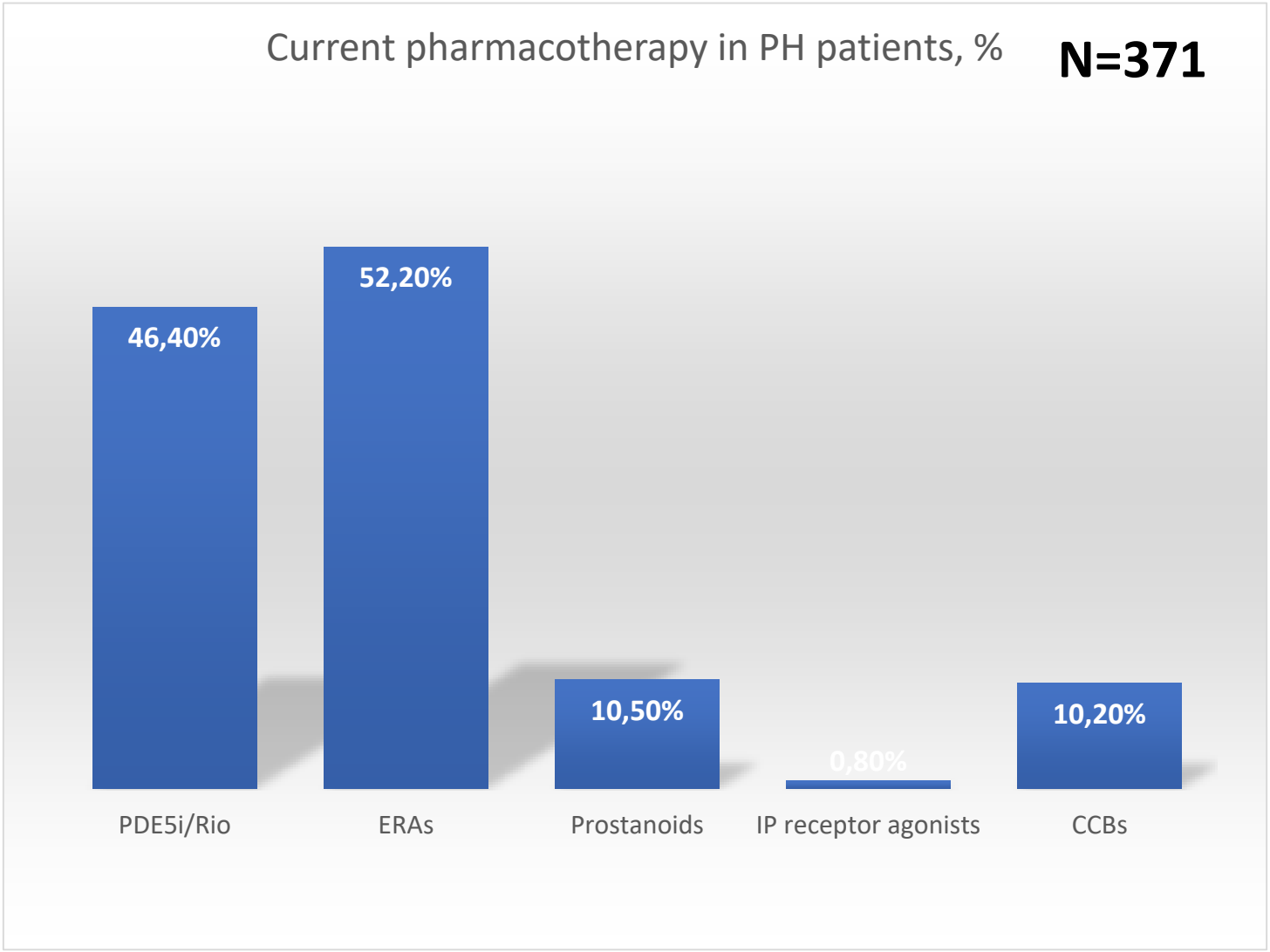
[b]Level of evidence.

[c]Reference(s) supporting recommendations.

[d]See also recommendations for PAH associated with congenital cardiac shunts.

Greek Pulmonary Hypertension Registry

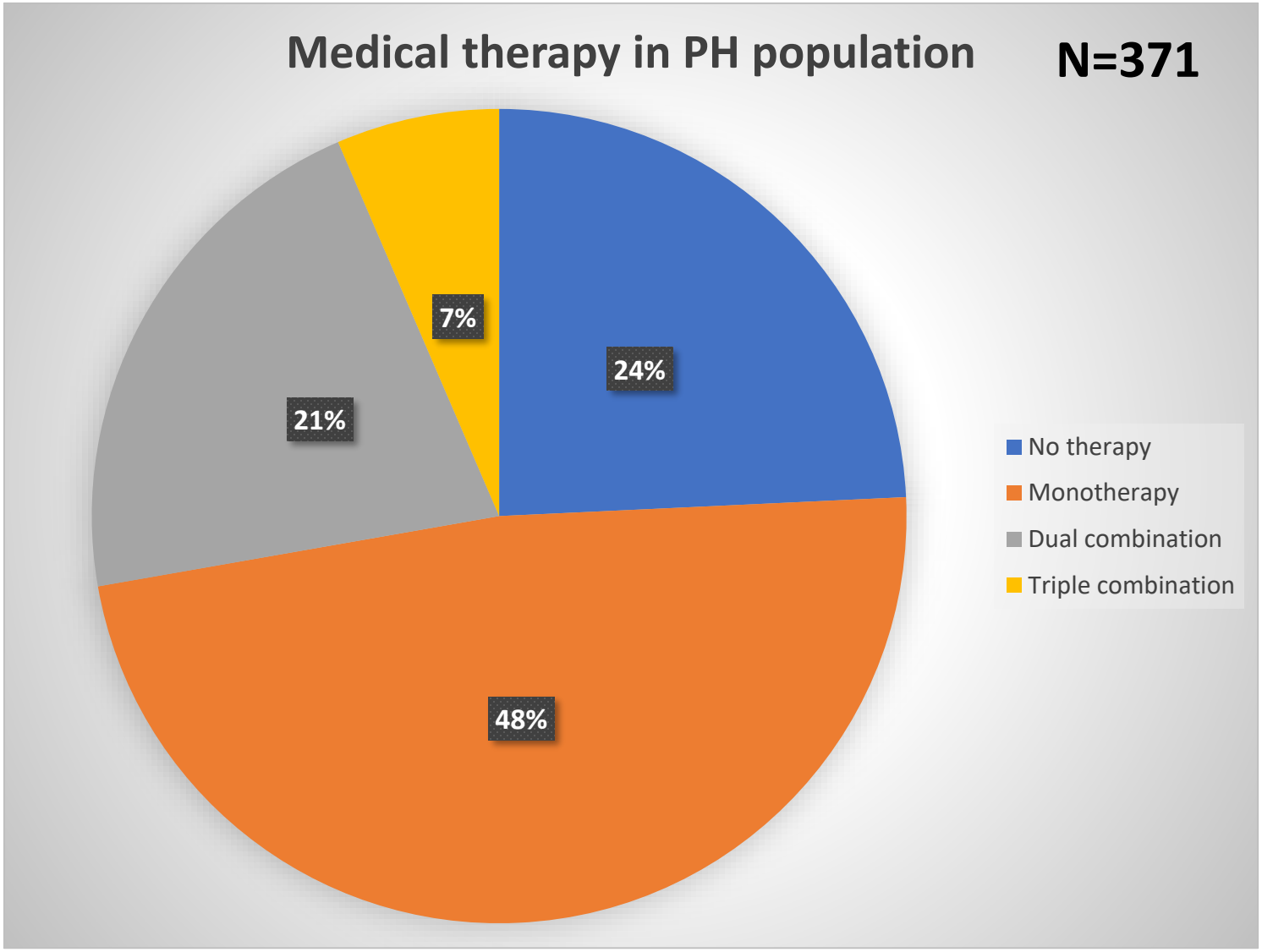
Medical therapy in PH patients (I)



Greek PAHTool Registry

Greek Pulmonary Hypertension Registry

Medical therapy in PH patients (II)



Greek PAHTool Registry

ORIGINAL ARTICLE

Pulmonary hypertension: Real-world data from a Portuguese expert referral centre

A. Gomes[a], C. Cruz[a], J. Rocha[a], M. Ricardo[a], M. Vicente[b], A. Melo[c], M. Santos[c,d], L. Carvalho[a,c], F. Gonçalves[a,c], A. Reis[c,*]

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[b] Department of Health Sciences, University of Aveiro, Aveiro, Portugal
[c] Pulmonary Vascular Disease Unit, Medicine Department, Centro Hospitalar do Porto Hospital de Santo António, Porto, Portugal
[d] Cardiology Service, Medicine Department, Centro Hospitalar do Porto – Hospital de Santo António, Porto, Portugal

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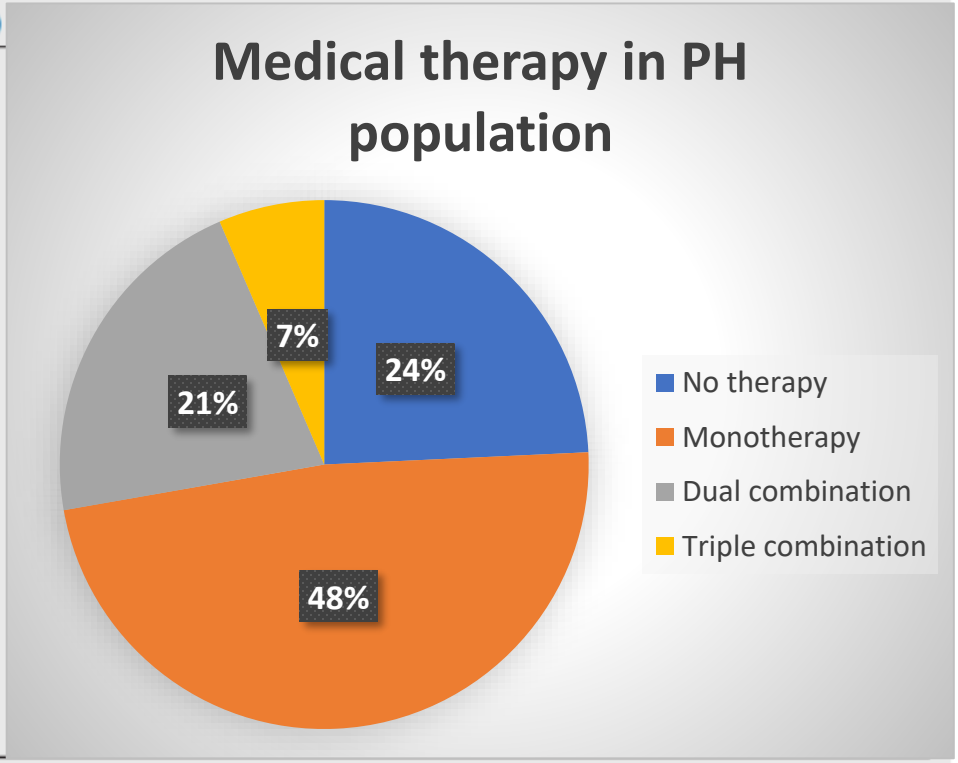
Table 2 Medical and surgical treatment at the last follow-up visit.

Treatment	Overall (n = 101)
Single targeted treatment	
Patients under monotherapy only	43 (42.6)
PDE-5I	5 (5.0)
ERA	38 (37.6)
Combination treatment	
Patients under combination therapy	49 (48.5)
Dual combination therapy	30 (29.7)
Triple combination therapy	19 (18.8)
PDE-5I + Prostanoids	0 (0.0)
Prostanoids + ERA	9 (8.9)
PDE-5I + ERA	21 (20.8)
PDE-5I + Prostanoids + ERA	19 (18.8)
Surgical treatment	
Pulmonary endarterectomy	11 (10.9)
Conventional treatment	
Conventional therapy only	9 (8.9)
Conventional plus targeted therapy	92 (91.1)

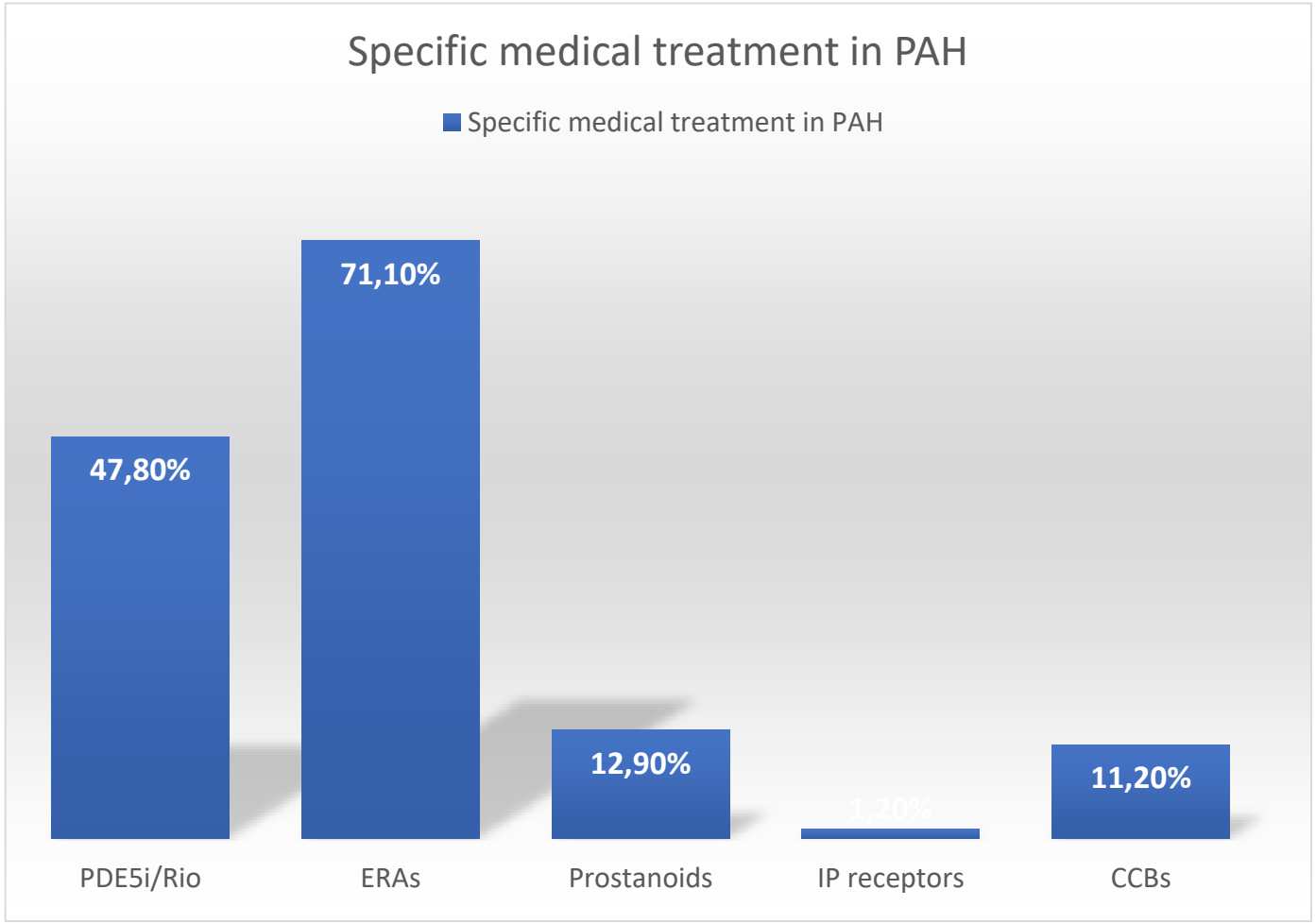


Results are presented as absolute frequency (percentage).
IPAH: idiopathic pulmonary arterial hypertension; HPAH: heritable pulmonary arterial hypertension; CTD: connective tissue disease; CHD: congenital heart disease; CTEPH: chronic thromboembolic pulmonary hypertension; PDE-5I: phosphodiesterase-5 inhibitors; ERA: endothelin-1 receptor antagonists; NA: not applicable.

Greek Pulmonary Hypertension Registry

Medical therapy in PAH (Group 1) patients (I)

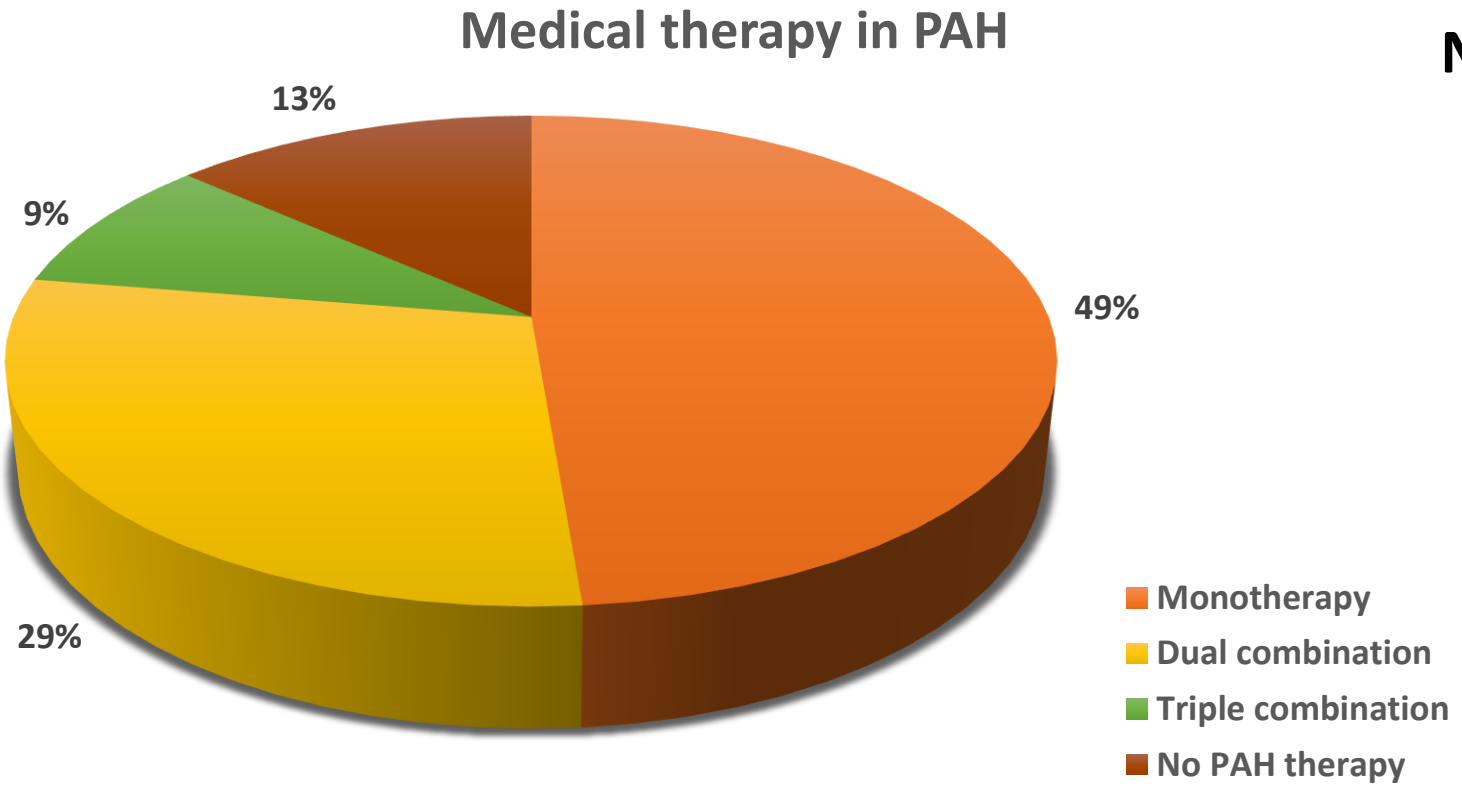
N=232



Greek PAHTool Registry

Greek Pulmonary Hypertension Registry

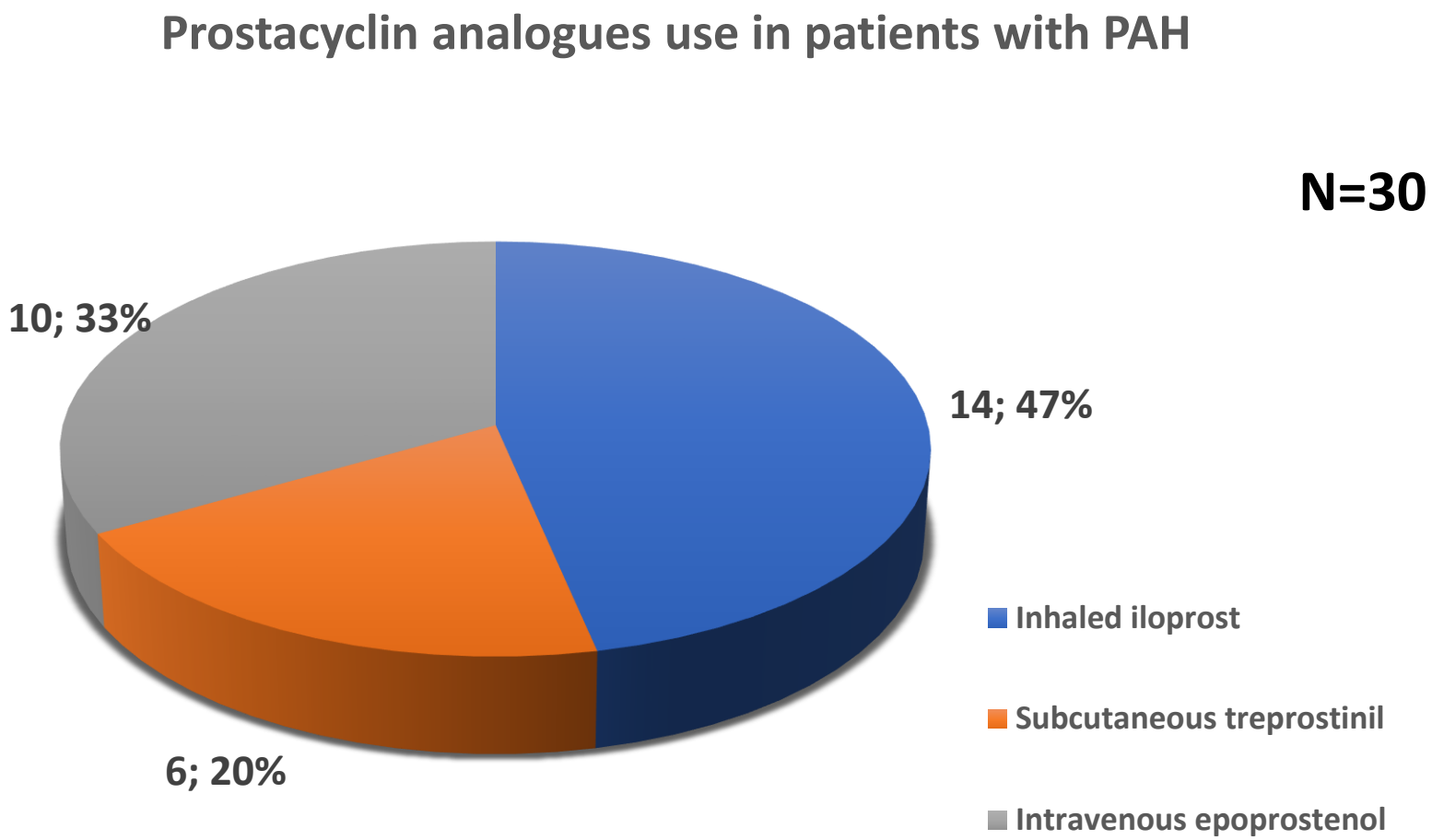
Medical therapy in PAH (Group 1) patients (II)



Dual combination	PAH (N=68), n (%)
PDE5i/Rio + ERA	57 (84)
PDE5i/Rio + Prostacyclin analogue	8 (11.7)
ERA+ Prostacyclin analogue	3 (3.7)

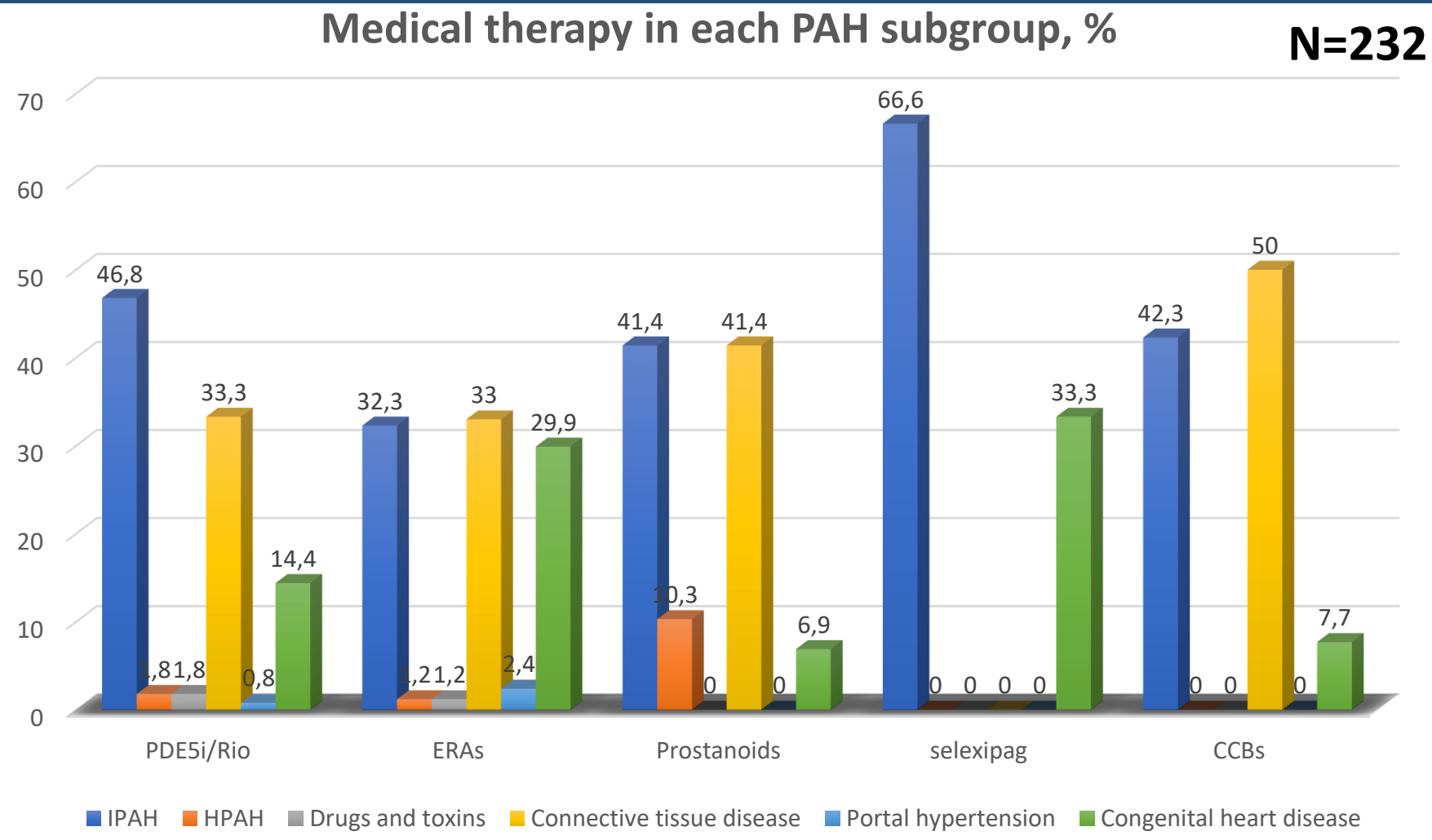
Greek Pulmonary Hypertension Registry

Medical therapy in PAH (Group 1) patients (III)



Greek Pulmonary Hypertension Registry

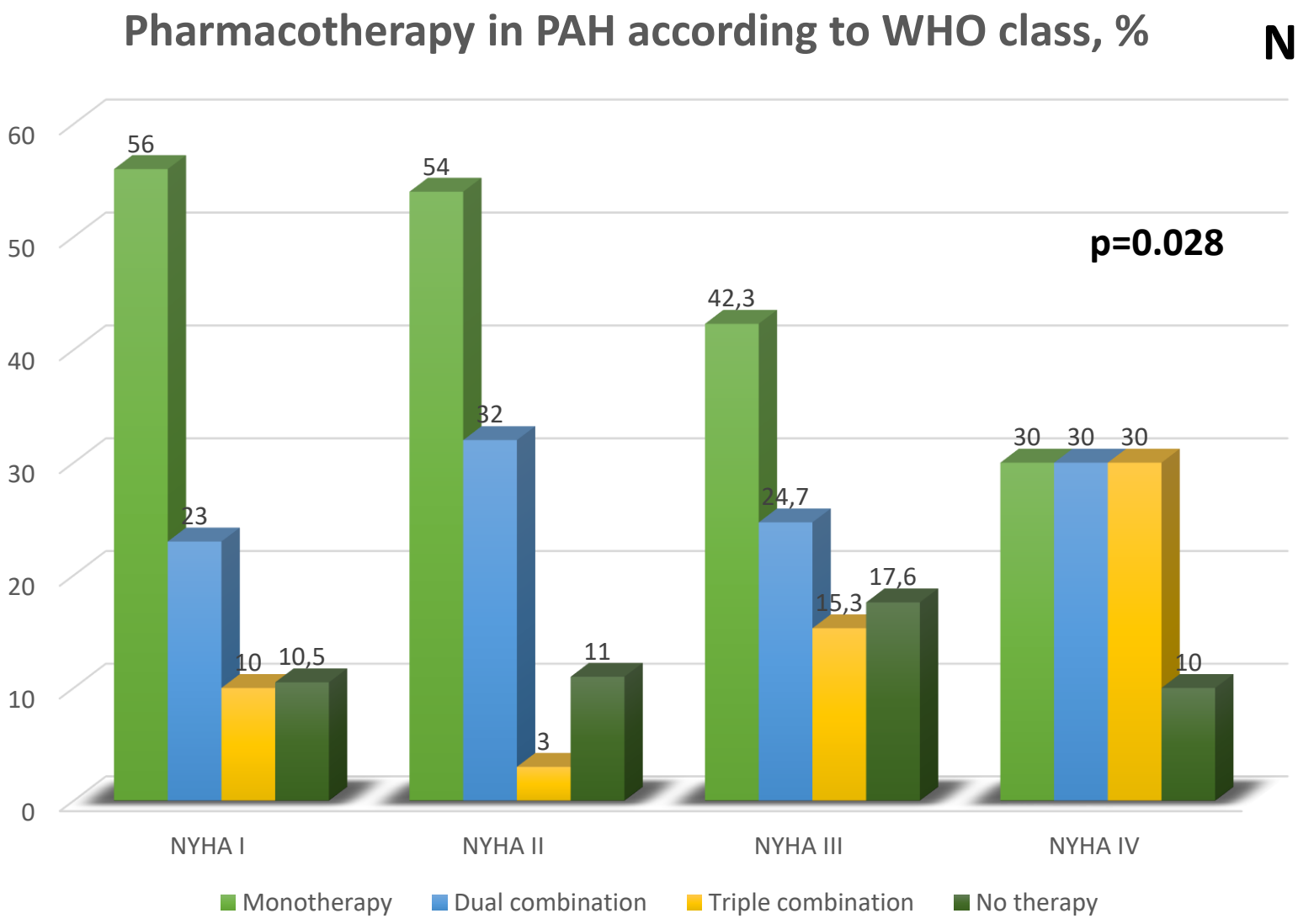
Medical therapy in PAH (Group 1) patients (IV)



Greek PAHTool Registry

Greek Pulmonary Hypertension Registry

Medical therapy in PAH (Group 1) patients (V)



Eur Respir Rev 2012; 21: 123, 8–18
DOI: 10.1183/09059180.00008211
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EUROPEAN RESPIRATORY UPDATE

REVEAL: a contemporary US hypertension registry

M.D. McGoon* and D.P. Miller#

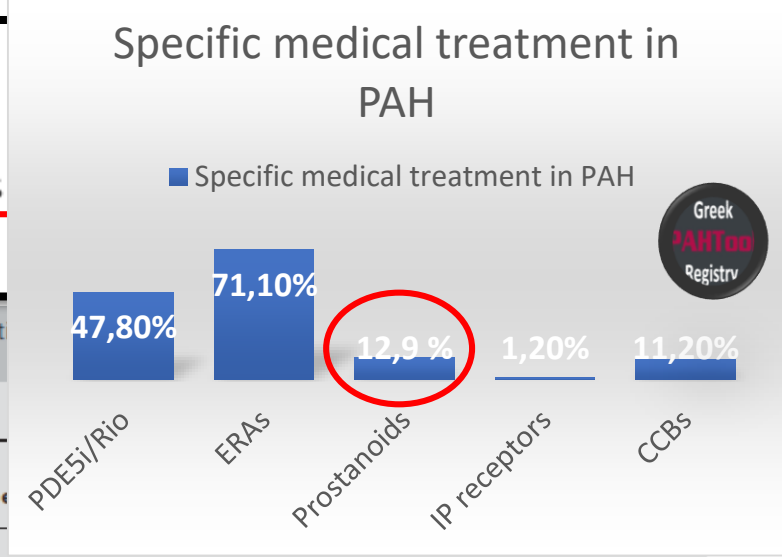

TABLE 2 Pulmonary arterial hypertension-specific medications among pat… the REVEAL registry at enrolment

	ERA#	PDE-5 inhibitor¶			
Overall use§	1147 (47.0)	1194 (49.0)	480 (19.7)	237 (9.7)	307 (12.6)
Monotherapy	452 (18.5)	417 (17.1)	188 (7.7)	23 (0.9)	84 (3.4)
Combination with one oral therapy+	291 (11.9)	290 (11.9)	243 (10.0)	138 (5.7)	148 (6.1)
Combination with one prostacyclin analogue	224 (9.2)	305 (12.5)	2 (0.1)	3 (0.1)	5 (0.2)
Combination with >1 other therapy	180 (7.4)	182 (7.5)	47 (1.9)	73 (3.0)	70 (2.9)
NYHA/WHO functional class I/II					
Overall use	468 (47.1)	474 (47.7)	187 (18.8)	71 (7.1)	111 (11.2)
Monotherapy	216 (21.7)	187 (18.8)	83 (8.4)	4 (0.4)	26 (2.6)
Combination with one oral therapy+	110 (11.1)	109 (11.0)	85 (8.6)	41 (4.1)	60 (6.0)
Combination with one prostacyclin analogue	76 (7.6)	110 (11.1)			
Combination with >1 other therapy	66 (6.6)	686 (6.8)	19 (1.9)	26 (2.6)	25 (2.5)
NYHA/WHO functional class III					
Overall use	525 (47.7)	567 (51.5)	218 (19.8)	130 (11.8)	161 (14.6)
Monotherapy	181 (16.4)	177 (16.1)	80 (7.3)	16 (1.5)	43 (3.9)
Combination with one oral therapy+	147 (13.4)	147 (13.4)	117 (10.6)	78 (7.1)	79 (7.2)
Combination with one prostacyclin analogue	114 (10.4)	160 (14.5)	2 (0.2)	2 (0.2)	4 (0.4)
Combination with >1 other therapy	83 (7.5)	83 (7.5)	19 (1.7)	34 (3.1)	35 (3.2)
NYHA/WHO functional class IV					
Overall use	55 (44.4)	61 (49.2)	44 (35.5)	14 (11.3)	15 (12.1)
Monotherapy	5 (4.0)	14 (11.3)	17 (13.7)	2 (16)	5 (4.0)
Combination with one oral therapy+	16 (12.9)	16 (12.9)	21 (16.9)	8 (6.5)	4 (3.2)
Combination with one prostacyclin analogue	18 (14.5)	15 (12.1)			
Combination with >1 other therapy	16 (12.9)	16 (12.9)	6 (4.8)	4 (3.2)	6 (4.8)

42%

37%

58%

Data are presented as n (%). Combinations with one oral therapy, with one prostacyclin analogue, and with more than one oral therapy are mutually exclusive and exclude calcium channel blockers. Blinded clinical trial patients are excluded from this presentation (n=87). ERA: endothelin receptor antagonist; PDE-5: phosphodiesterase type-5; NYHA/WHO: New York Heart Association/World Health Organization. #: 953 on bosentan, 106 on sitaxsentan and 89 on ambrisentan; ¶: 1,147 on sildenafil and 47 on tadalafil; +: treprostinil use includes 159 on intravenous, 112 on subcutaneous, 28 on inhaled and nine on oral treprostinil; §: n=2,435; f: oral therapy is defined as bosentan, sildenafil, ambrisentan, sitaxsentan and tadalafil. Reproduced from [15] with permission from the publisher.

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Current epoprostenol use in patients with severe idiopathic, heritable or anorexigen-associated pulmonary arterial hypertension: Data from the French pulmonary hypertension registry

Emmanuel Bergot [a,*,1], Olivier Sitbon [b,c,d,1], Vincent Cottin [e,1], Grégoire Prévot [f,1], Matthieu Canuet [g,1], Arnaud Bourdin [h,1], Pascal de Groote [i,1], Laurence Rottat [c,1], Virginie Gressin [j,1], Xavier Jaïs [b,c,d,1], Marc Humbert [b,c,d,1], Gérald Simonneau [b,c,d,1]

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[c] APHP, Centre de Référence de l'Hypertension Pulmonaire Sévère, Le Kremlin-Bicêtre, France
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[f] Hôpital Larrey, Centre de compétences de l'Hypertension Pulmonaire, Toulouse, France
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[i] Hôpital Cardiologique de Lille, Centre de compétences de l'Hypertension Pulmonaire, Lille, France
[j] Actelion Pharmaceuticals France, Paris, France

2006-2010

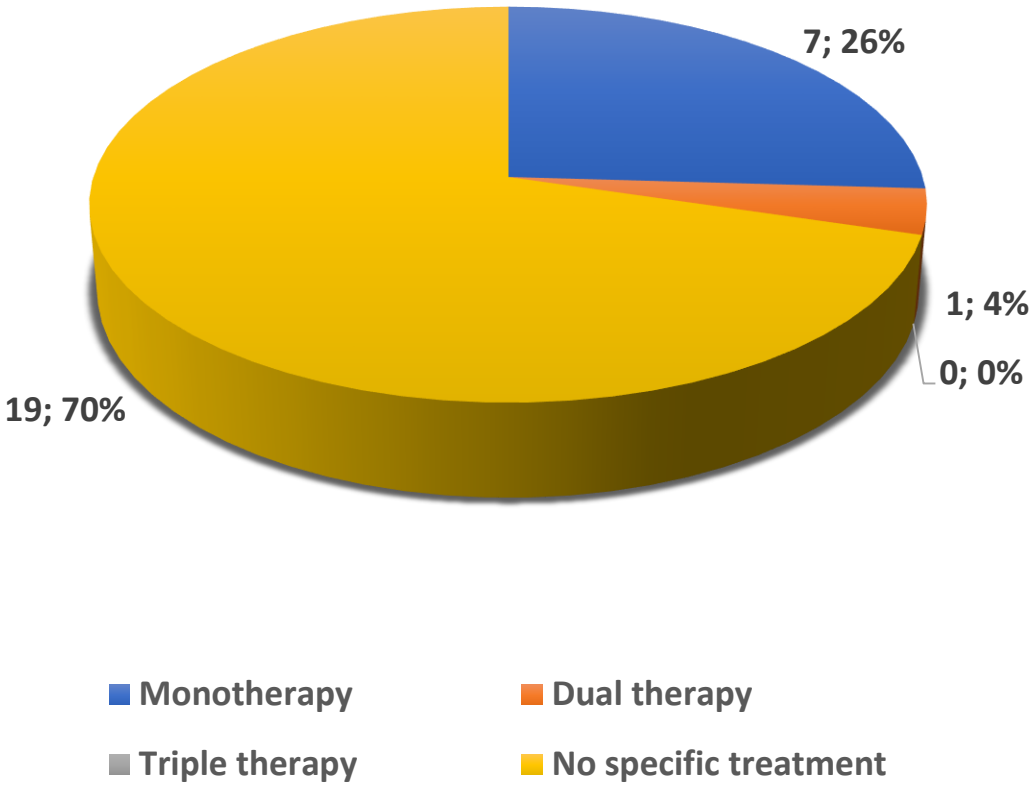
Table 1
Characteristics of IHA-PAH patients at epoprostenol initiation.

	Treatment-naïve patients (n = 43)			Non-naïve (n = 35)	All patients (n = 78)
	Epoprostenol monotherapy (n = 17)	Combination (n = 26)	All naïve (n = 43)		
Demographics					
Female gender, %	64.7	69.2	67.4	54.3	62.0
Age, years	50 ± 16	39 ± 14	43 ± 16*	54 ± 16*	48 ± 17
Time from symptoms to enrolment, months, median [Q1–Q3]	13 [5–20] (n = 17)	13 [9–17] (n = 25)	13 [5–20] (n = 42)	10 [5–34] (n = 31)	12 [5–22] (n = 73)
Time from enrolment to epoprostenol initiation, months, median [Q1–Q3]	0 [0–0]	0 [0–0]	0 [0–0]*	7 [4–16]*	1 [0–6]
Functional capacity					
NYHA class, % II/III/IV	12: 29: 59 (n = 17)	0: 46: 54 (n = 26)	5: 39: 56 (n = 43)	12: 55: 33 (n = 33)	8: 46: 46 (n = 76)
6MWD, m	165 ± 154 (n = 15)	278 ± 170 (n = 24)	235 ± 171 (n = 39)	257 ± 197 (n = 28)	244 ± 182 (n = 67)
Hemodynamics					
RAP, mm Hg	10.7 ± 4.5 (n = 13)	11.1 ± 5.2 (n = 25)	11.0 ± 4.9 (n = 38)	11.1 ± 4.5 (n = 27)	11.0 ± 4.7 (n = 65)
mPAP, mm Hg	58.5 ± 16.5 (n = 17)	64.7 ± 15.9 (n = 26)	62.2 ± 16.2* (n = 43)	53.7 ± 9.5* (n = 30)	58.7 ± 14.4 (n = 73)
PAOP, mm Hg	8.0 ± 2.9 (n = 15)	7.8 ± 3.3 (n = 25)	7.9 ± 3.1* (n = 40)	9.7 ± 4.3* (n = 30)	8.6 ± 3.8 (n = 70)
Cardiac index, $L \cdot min^{-1} \cdot m^{-2}$	1.9 ± 0.5 (n = 17)	1.7 ± 0.3 (n = 26)	1.8 ± 0.4 (n = 43)	2.0 ± 0.6 (n = 30)	1.9 ± 0.5 (n = 73)
PVR, $dyn \cdot s \cdot cm^{-5}$	1236 ± 433 (n = 15)	1540 ± 645 (n = 25)	1426 ± 591* (n = 40)	1035 ± 444* (n = 30)	1258 ± 564 (n = 70)

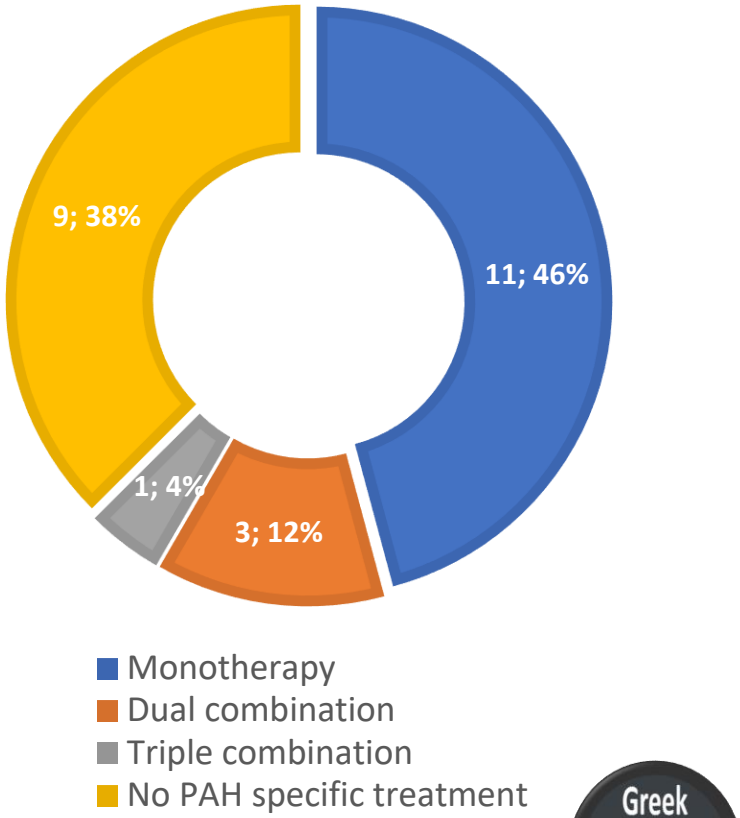
Greek Pulmonary Hypertension Registry

Medical therapy in Group 2 and Group 3 PH

PH-LHD off label treatment with PAH specific drugs N=27



OFF-LABEL SPECIFIC PAH TREATMENT IN PH DUE TO LUNG DISEASE N=24



Greek PAHTool Registry

Medical therapy in Group 2 and Group 3 PH

Recommendations

European Heart Journal doi:10.1093/eurheartj/ehv317

ESC/ERS GUIDELINES

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)

Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT)

Table 31 Management of pulmonary hypertension in left heart disease

Recommendations	Class[a]	Level[b]	Ref.[c]
Optimization of the treatment of the underlying condition is recommended before considering assessment of PH-LHD (i.e. treating structural heart disease)	I	B	396
It is recommended to identify other causes of PH (i.e. COPD, sleep apnoea syndrome, PE, CTEPH) and to treat them when appropriate before considering assessment of PH-LHD	I	C	396
It is recommended to perform invasive assessment of PH in patients on optimized volume status	I	C	
Patients with PH-LHD and a severe pre-capillary component as indicated by a high DPG and/or high PVR should be referred to an expert PH centre for a complete diagnostic workup and an individual treatment decision	IIa	C	
The importance and role of vasoreactivity testing is not established in PH-LHD, except in patients who are candidates for heart transplantation and/or LV assist device implantation	III	C	396
The use of PAH-approved therapies is not recommended in PH-LHD	III	C	396

COPD = chronic obstructive pulmonary disease; CTEPH = chronic thromboembolic pulmonary hypertension; DPG = diastolic pressure gradient; LHD = left heart disease; LV = left ventricular; PE = pulmonary embolism; PH = pulmonary hypertension; PVR = pulmonary vascular resistance.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

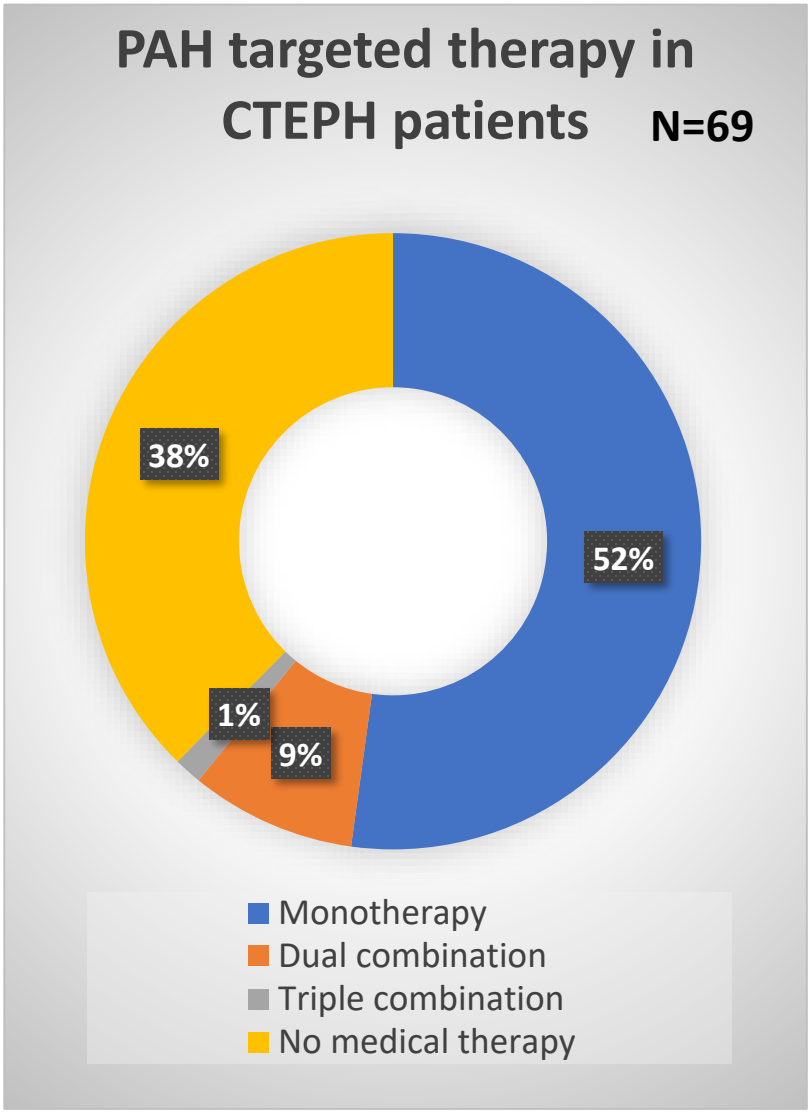
Table 33 Recommendations for pulmonary hypertension due to lung diseases

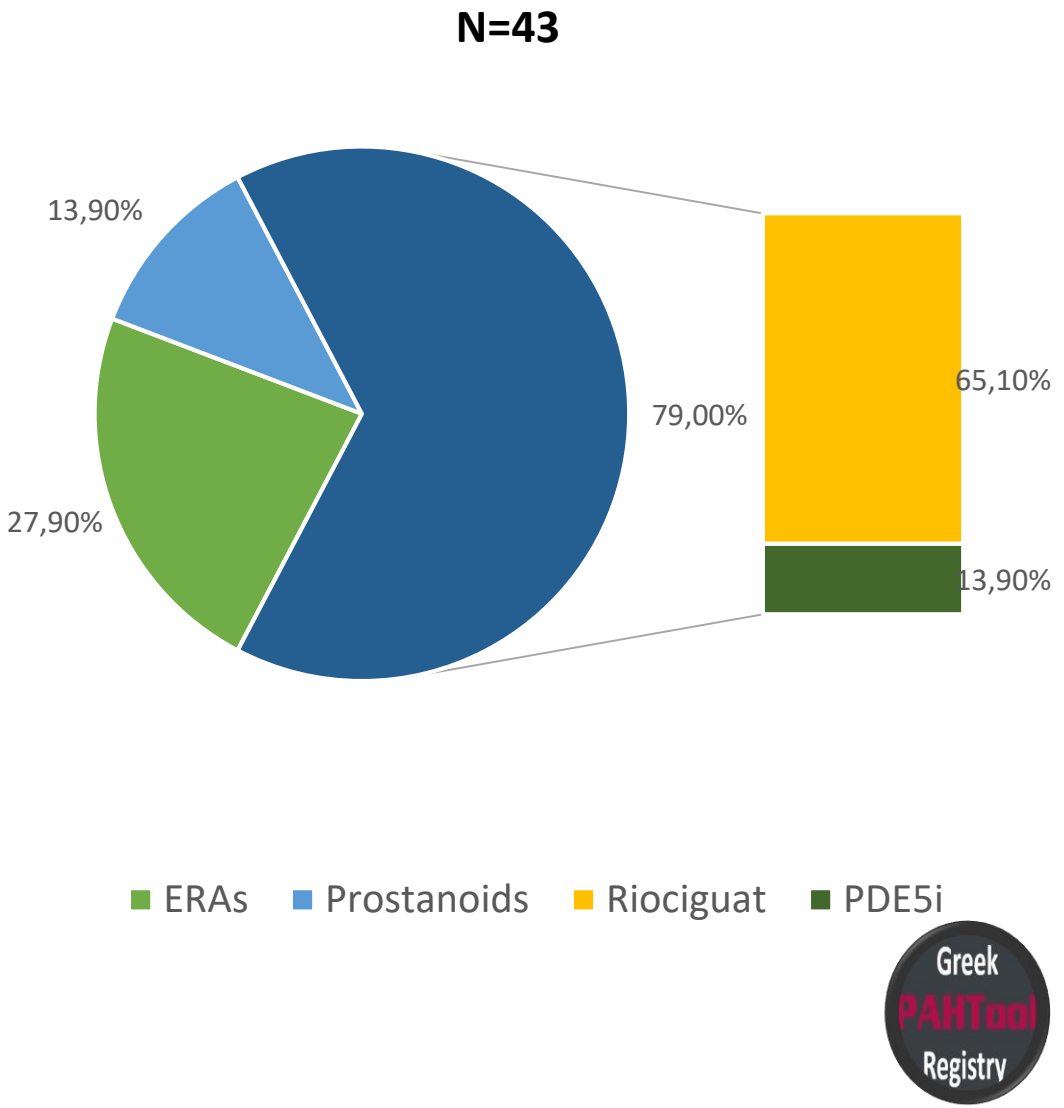
Recommendations	Class[a]	Level[b]	Ref.[c]
Echocardiography is recommended for the non-invasive diagnostic assessment of suspected PH in patients with lung disease	I	C	403, 405
Referral to an expert centre is recommended[d] in patients with echocardiographic signs of severe PH and/or severe right ventricular dysfunction	I	C	
The optimal treatment of the underlying lung disease, including long-term O_2 therapy in patients with chronic hypoxaemia, is recommended in patients with PH due to lung diseases	I	C	169
Referral to PH expert center should be considered for patients with signs of severe PH/severe RV failure for individual-based treatment	IIa	C	
RHC is not recommended for suspected PH in patients with lung disease, unless therapeutic consequences are to be expected (e.g. lung transplantation, alternative diagnoses such as PAH or CTEPH, potential enrolment in a clinical trial)	III	C	169
The use of drugs approved for PAH is not recommended in patients with PH due to lung diseases	III	C	411–416

CTEPH = chronic thromboembolic pulmonary hypertension; PAH = pulmonary arterial hypertension; PH = pulmonary hypertension; RHC = right heart catheterization.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.
[d]This recommendation does not apply to patients with end-stage lung disease who are not considered candidates for lung transplantation.

Greek Pulmonary Hypertension Registry

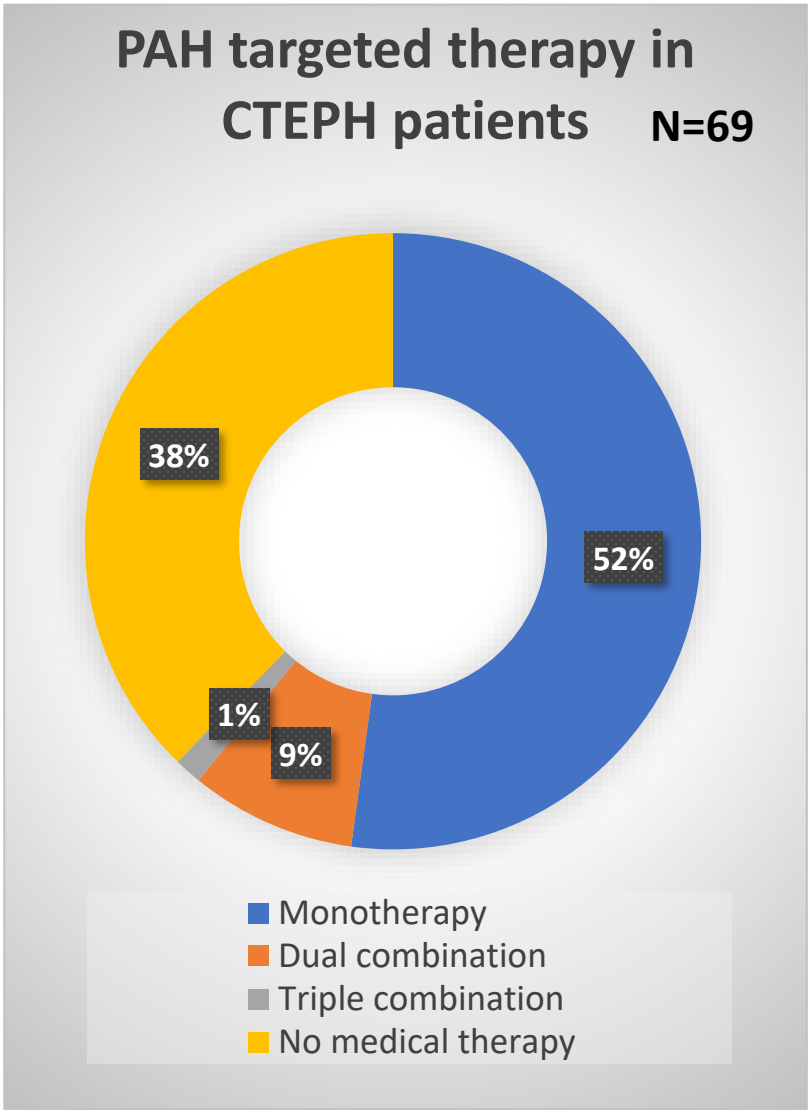
Medical therapy in Group 4 PH





Greek Pulmonary Hypertension Registry

Medical therapy in Group 4 PH



Circulation

American Heart Association

Chronic Thromboembolic Pulmonary Hypertension (CTEPH): Results From an International Prospective Registry

Joanna Pepke-Zaba, Marion Delcroix, Irene Lang, Eckhard Mayer, Pavel Jansa, David Ambroz, Carmen Treacy, Andrea M. D'Armini, Marco Morsolini, Repke Snijder, Paul Bresser, Adam Torbicki, Bent Kristensen, Jerzy Lewczuk, Iveta Simkova, Joan A. Barberà, Marc de Perrot, Marius M. Hoeper, Sean Gaine, Rudolf Speich, Miguel A. Gomez-Sanchez, Gabor Kovacs, Abdul Monem Hamid, Xavier Jaïs and Gérald Simonneau

Circulation. 2011;124:1973-1981; originally published online October 3, 2011;
doi: 10.1161/CIRCULATIONAHA.110.015008
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539

Table 6. PAH-Targeted Therapy Initiated at Diagnosis

	All Patients (n=679)	Operable Patients* (n=427)	Nonoperable Patients* (n=247)	*P* (Exploratory)
PAH-targeted therapy, % (n)	37.9 (676)	28.3 (427)	53.8 (247)	<0.0001
Phosphodiesterase type V inhibitor, %	17.5	16.2	19.4	0.2923
Endothelin receptor antagonist, %	21.7	12.2	37.7	<0.0001
Prostacyclin analogue, %	2.7	1.6	4.5	0.0443
Combination therapies, %	4.0	1.6	7.7	0.0002

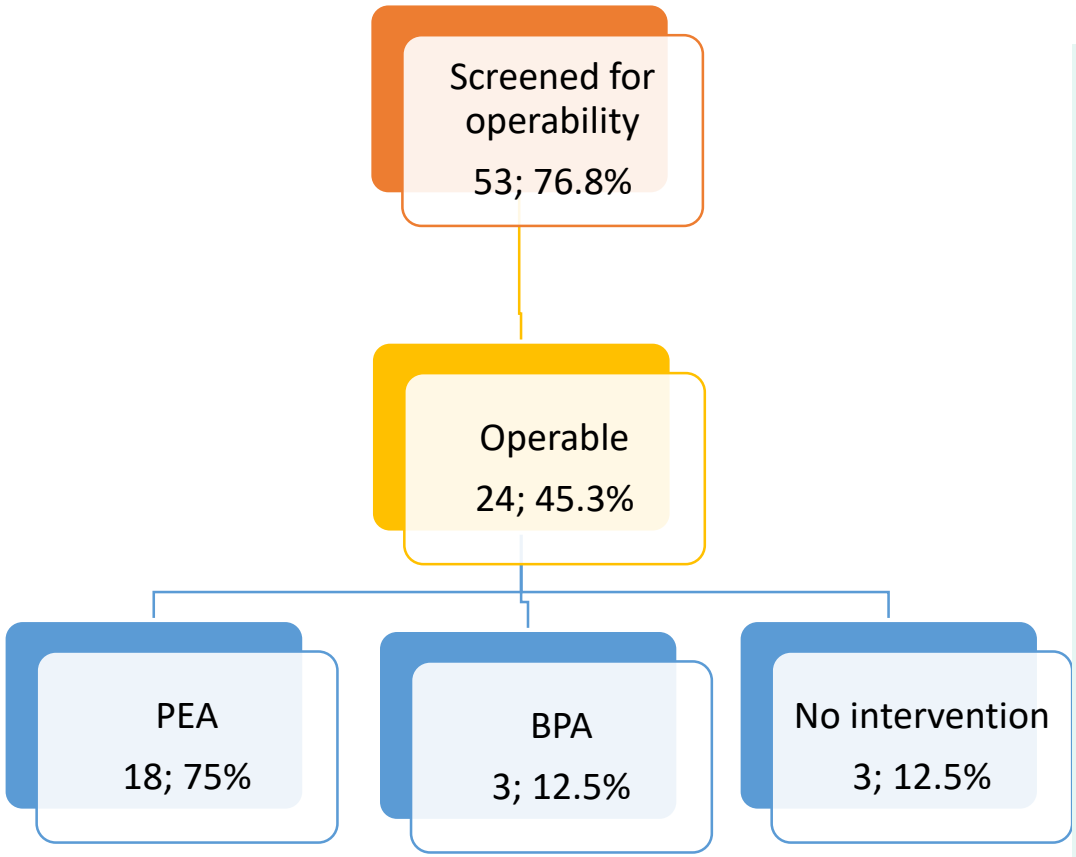
P values from Fisher exact test. (n): patients with assessment. PAH indicates pulmonary arterial hypertension.

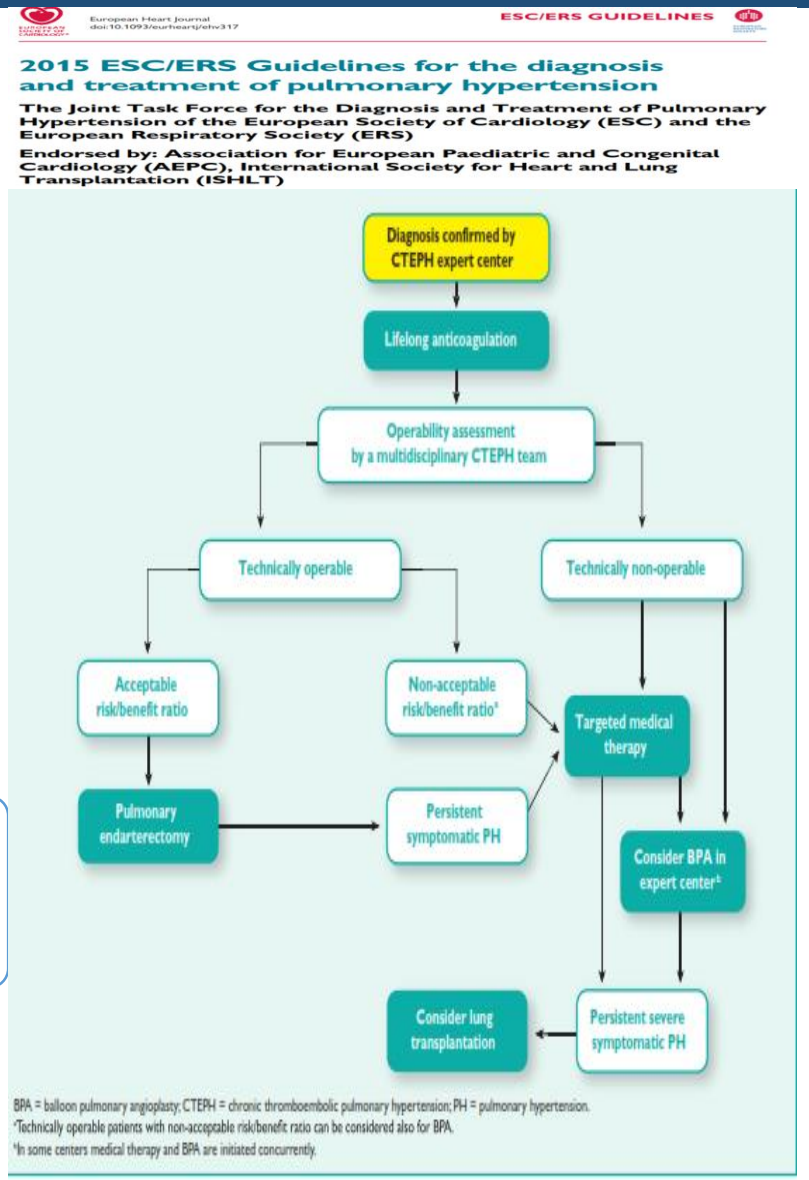
*Five patients had no data on operability.

Greek PAHTool Registry

Greek Pulmonary Hypertension Registry

Interventional therapies in Group 4 PH

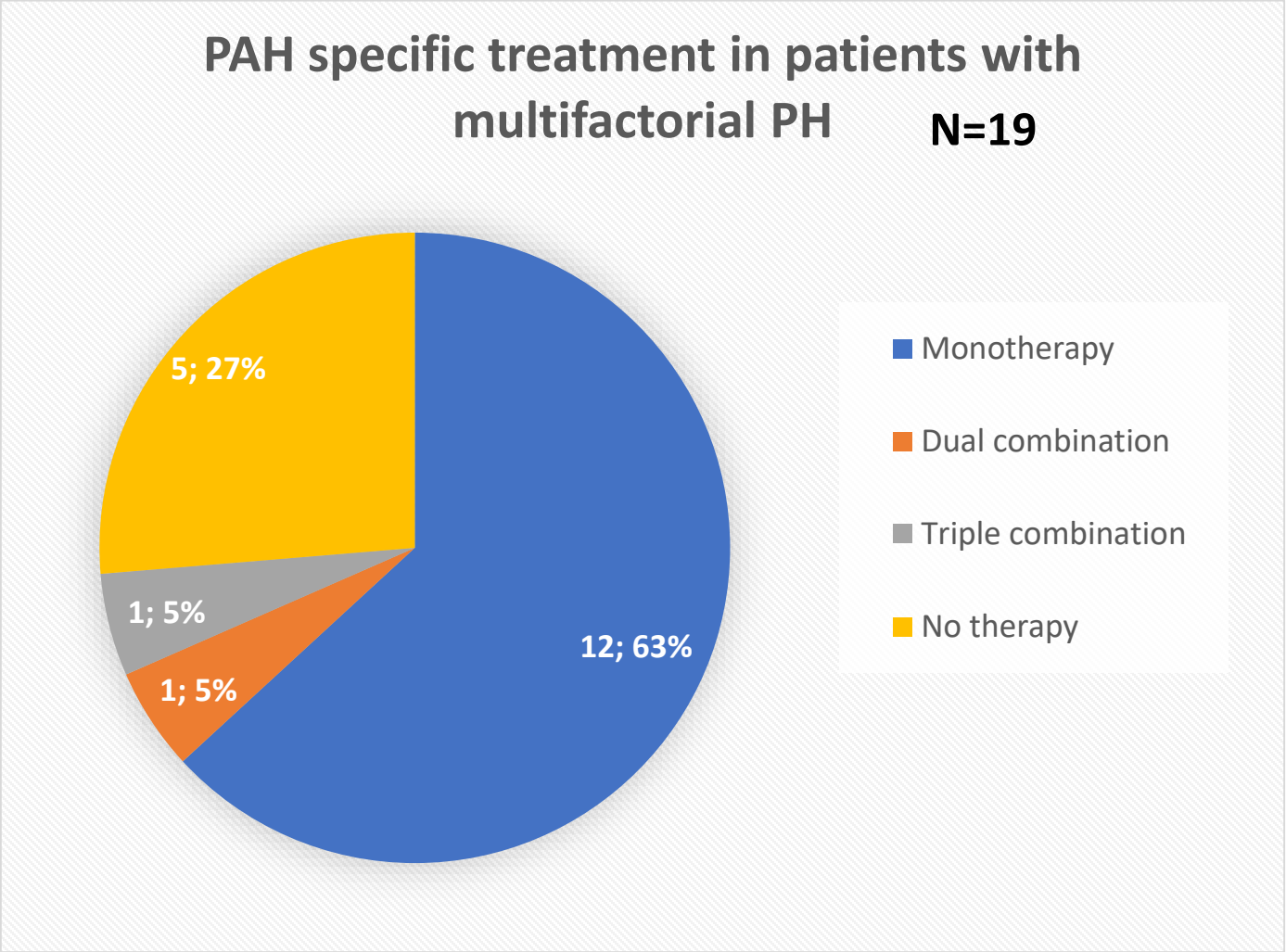




Greek PAHTool Registry

Greek Pulmonary Hypertension Registry

Medical therapy in Group 5 PH



Greek Pulmonary Hypertension Registry
Conclusion and future perspectives

Current data on pharmacotherapy in **PAH patients** present **several differences** compared with **foreign registries**.

- The majority of patients have mild symptoms on exertion (WHO II).
- Half of PAH patients receive monotherapy.
- About 40% receive a combination therapy, while the most frequent combination is a PDE5i with an ERA.
- Prostanoids are used less compared with other registries.

- In **CTEPH** population more effort should be made regarding operability assessment.
- An expert center in endarterectomy should be established in Greece

- More effort should be made regarding data collection and follow up of patients.
- Cooperation between physicians and expert centers is essential.