Γ Ν Α "Γ ΓΕΝΝΗΜΑΤΑΣ"
ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ

ΠΝΕΥΜΟΝΙΚΗ ΥΠΕΡΤΑΣΗ

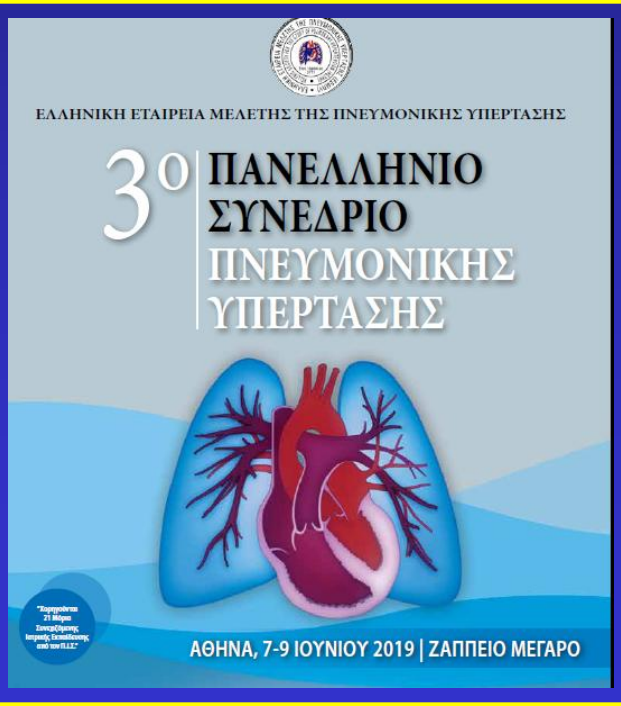
ΠΑΡΟΥΣΙΑΣΗ ΠΕΡΙΣΤΑΤΙΚΟΥ 4

Βασιλική Ματζαράκη
Καρδιολογική Κλινική
Γ.Ν.Α ΄΄Γ. Γεννηματάς΄΄

3ο Πανελλήνιο Συνέδριο
Πνευμονικής Υπέρτασης

Αθήνα - Ζάππειο Μέγαρο

7-9 Ιουνίου 2019



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ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ

Α. ΙΣΤΟΡΙΚΟ-ΔΙΑΓΝΩΣΗ

Γ Ν Α "Γ ΓΕΝΝΗΜΑΤΑΣ"
ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ

Κλινική περίπτωση

- Γυναίκα 71 ετών με ελεύθερο καρδιολογικό ιστορικό

- Παραπονείται για δύσπνοια προσπαθείας και εύκολη κόπωση το τελευταίο 1 -1½ έτος . Επιδείνωση συμπτωμάτων το τελευταίο εξάμηνο (WHO II-III).

- Τα συμπτώματα αυτά την έχουν οδηγήσει σε επανειλημμένες επισκέψεις σε καρδιολόγο.

- Α/Α,Παράγοντες Κινδύνου : -ΑΥ
  -Σακχαρώδης Διαβήτης
  -Δυσλιπιδαιμία
  -Οστεοπενία

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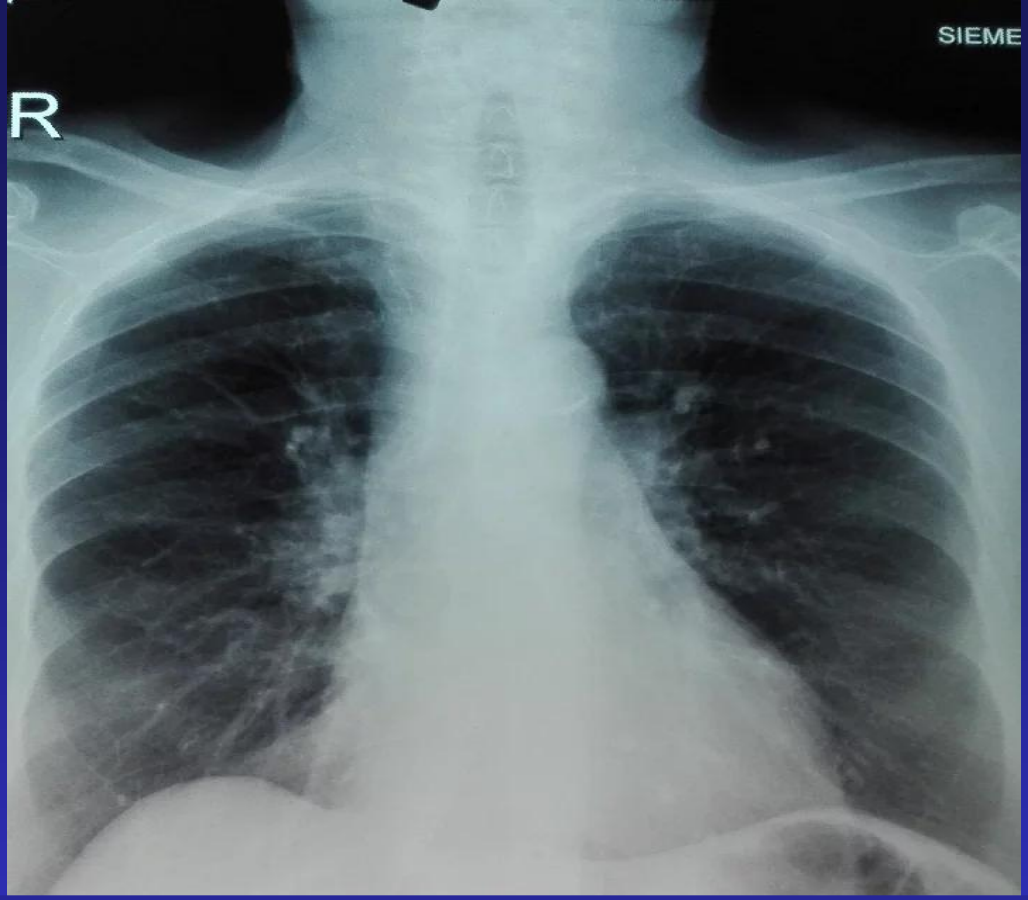
ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ

Φαρμακευτική αγωγή

- ✓ Νεμπιβολόλη 5 mg x 1
- ✓ Μανιδιπίνη 10 mg x 1
- ✓ Μετφορμίνη 850 mg x 1
- ✓ Ροσουβαστατίνη 5 mg x 1
- ✓ Ασβέστιο-D3

Γ Ν Α "Γ ΓΕΝΝΗΜΑΤΑΣ"
ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ



Ακτινογραφία θώρακος

Γ Ν Α "Γ ΓΕΝΝΗΜΑΤΑΣ"
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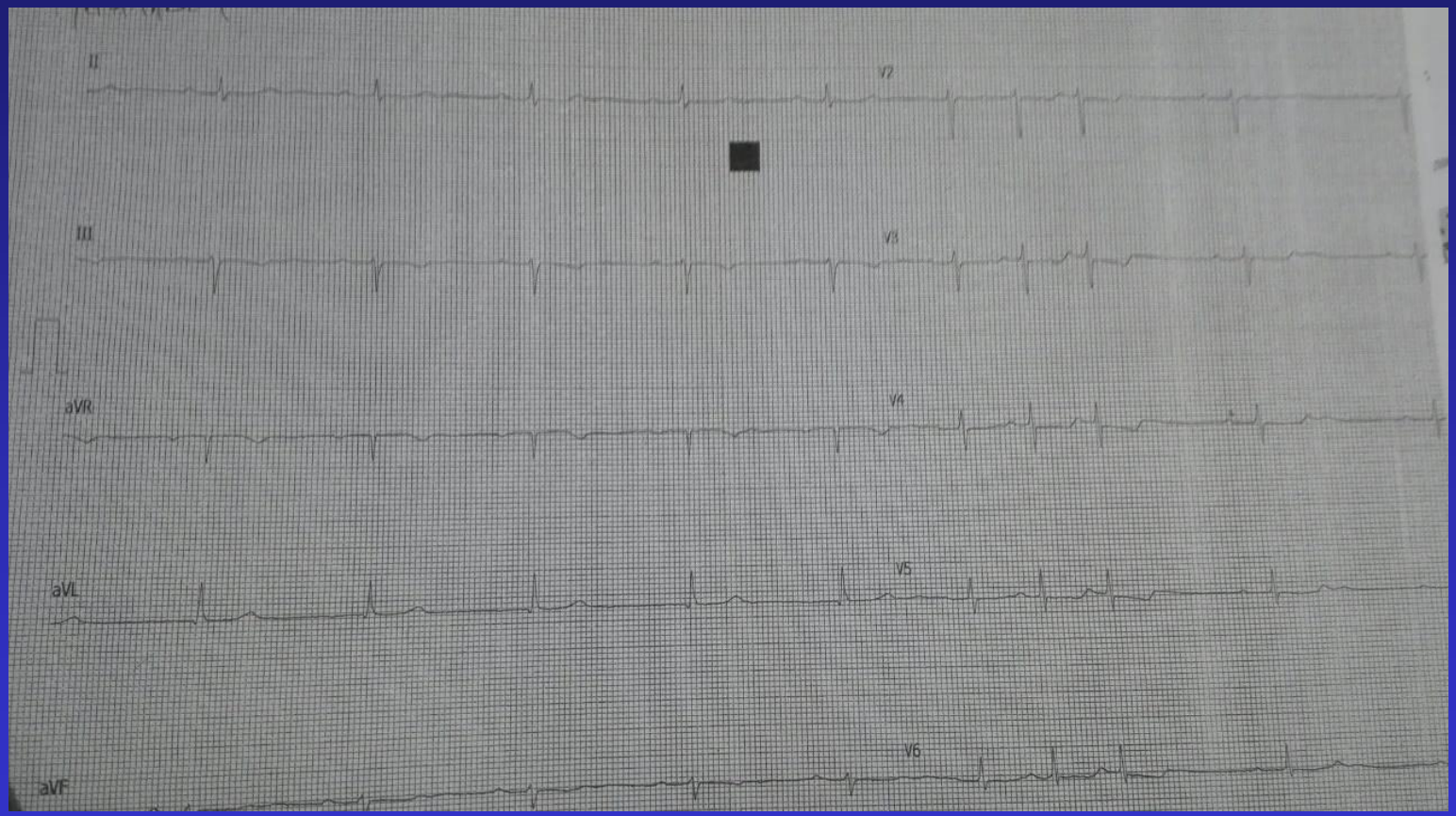
ΗΚΓ



Ειδικός καρδιολογικός έλεγχος

- Holter ρυθμού 24ώρου : nSR. 1820 PAC's /24ωρο με ριπές max 5 QRS

- Triplex καρδιάς : Καλή λειτουργικότητα αρ κοιλίας. Μέτριες ανεπάρκειες από τις κολποκοιλιακές βαλβίδες. Ενδείξεις πνευμονικής υπέρτασης.

- Δοκιμασία Κόπωσης : μη διαγνωστική/κακή ανοχή στην κόπωση/ Stress echo: (-) για ισχαιμία

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ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ

Αντικειμενική Εξέταση

- Α.Π: 130 / 72 mmHg
- Σφύξεις : 68 b/min
- Σωματικό βάρος (ΣΒ): 58Kg
- Ύψος : 150 cm BSA: 1,53 cm2
- Αναπνοές : 13/min
- Καρδιά: S1 S2 ρ/ε
- Σφαγίτιδες : (-)
- Πνεύμονες: ΑΨ -> κφ
- Οιδήματα κάτω άκρων (-)

- Sat O_2 = 98%

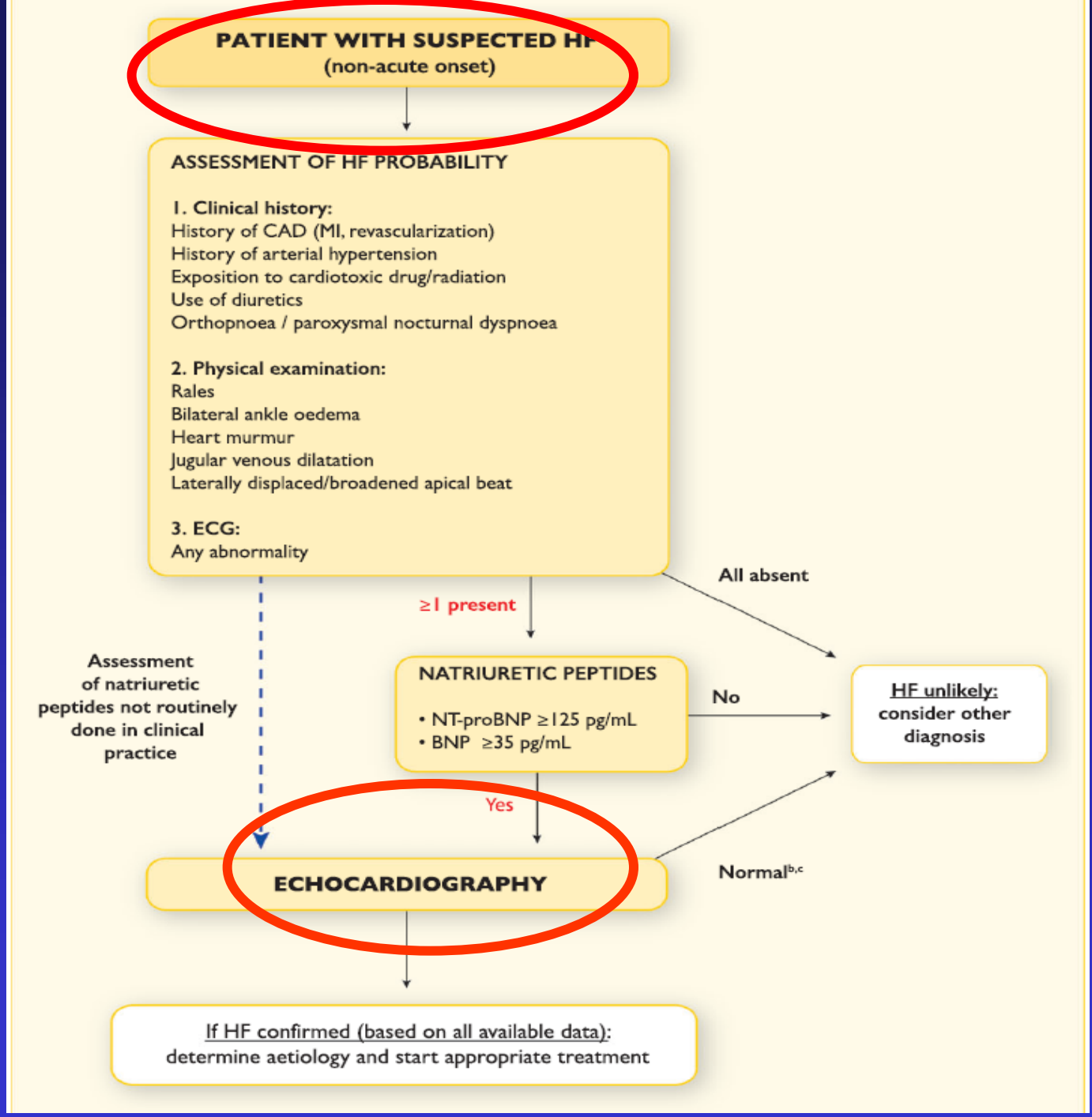
Βιοχημικός έλεγχος

Κρεατινίνη	1,0 mg/dl (57ml/min)
Ουρία	42 mg/dl
K	4,8 mEq/L
Na	141 mEq/L
hsTrop-I	1 pg/ml
BNP	375 pg/ml
SGOT/SGPT	18/12 U/L
HbA1C	6,4 U/L
TSH	1,6 ImU/ml
CRP	6,7 mg/L
Chol	168 mg/dl
LDL	92 mg/dl
HDL	43 mg/dl
TG	150 mg/dl

HCT :	38,0%
HGB :	12,1 g/dl F
MCV:	83.2 fl
MCH:	26.5 pg
WBC :	9300
NEU:	53%
LYM :	37%
PLT's:	316.000
Ddimers :	0,5 mg/L

UA :	6,7 mg/Dl
CPK :	62 IU/L

HFpEF / PAH ?


PATIENT WITH SUSPECTED HF
(non-acute onset)
ASSESSMENT OF HF PROBABILITY
1. Clinical history:
History of CAD (MI, revascularization)
History of arterial hypertension
Exposition to cardiotoxic drug/radiation
Use of diuretics
Orthopnoea / paroxysmal nocturnal dyspnoea
2. Physical examination:
Rales
Bilateral ankle oedema
Heart murmur
Jugular venous dilatation
Laterally displaced/broadened apical beat
3. ECG:
Any abnormality
All absent
≥1 present
Assessment of natriuretic peptides not routinely done in clinical practice
NATRIURETIC PEPTIDES
• NT-proBNP ≥125 pg/mL
• BNP ≥35 pg/mL
No
HF unlikely: consider other diagnosis
Yes
ECHOCARDIOGRAPHY
Normal[b,c]
If HF confirmed (based on all available data):
determine aetiology and start appropriate treatment

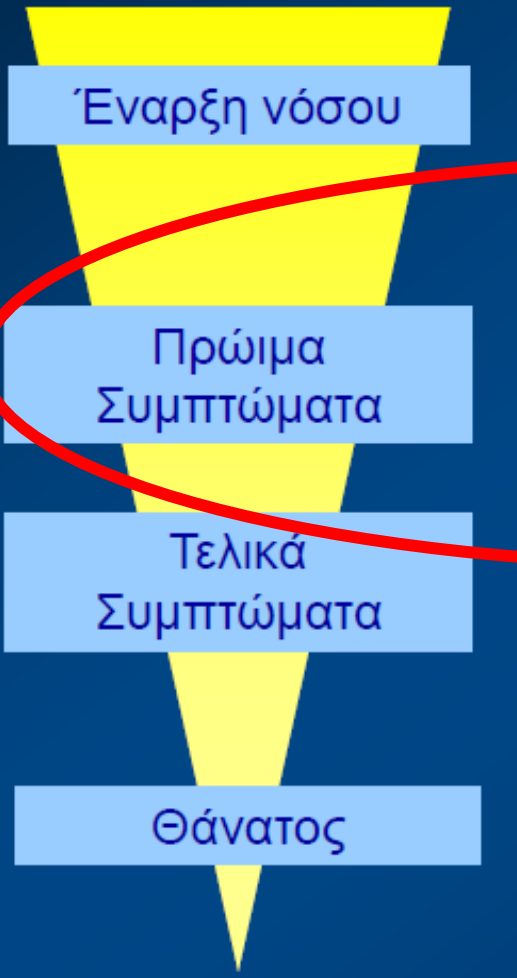
2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction

HF		HFrEF	HFmrEF	HFpEF
	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
	3	-	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).

ΠΑΥ: Κλινική Εικόνα



Κανένα αρχικό σύμπτωμα

Ετήσιος προληπτικός έλεγχος, αναγκαίος σε πληθυσμούς υψηλού κινδύνου

Προοδευτική δύσπνοια κοπώσεως, κόπωση, αίσθημα παλμών, θωρακικό άλγος, συγκοπτικό επεισόδιο, βήχας

Συμπτώματα δεξιάς καρδιακής ανεπάρκειας, Διάταση σφαγίτιδας, Οίδημα, Ηπατομεγαλία, Ασκίτης

Μέσος χρόνος επιβίωσης χωρίς θεραπεία 2.8 έτη[1]

[1] D'Alonzo et al. Ann Internal Med 1991;115:343
Harrison's Principles of Internal Medicine, 14th ed.

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Ηχοκαρδιογράφημα

- 12/10/2017

- ΚΕΑΚ: > 55 % (LVmassI=60g/m2 και RWT=0,33)
- LA d= 4,1 cm / LAVI= 34 ml/m2
- E/E'= 7 (E=0,9 m/s, E/A=1,4, E'=12&7) απροσδιόριστη διαστολική δυσλειτουργία

- Αορτική βαλβίδα : (1+/4+)
- Μιτροειδής : (1-2+/4+) με κεντρικό jet παλινδρόμησης

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

The next step comprises an advanced workup in case of initial evidence of HFpEF/HFmrEF and consists of objective demonstration of structural and/or functional alterations of the heart as the underlying cause for the clinical presentation. Key structural alterations are a left atrial volume index (LAVI) >34 mL/m^2 or a left ventricular mass index (LVMI) ≥115 g/m^2 for males and ≥95 g/m^2 for females.[65,67,72] Key functional alterations are an E/e' ≥13 and a mean e' septal and lateral wall <9 cm/s.[65,67,70,72,80–84] Other (indirect) echocardiographically derived measurements are longitudinal strain or tricuspid regurgitation velocity (TRV).[72,82] An overview

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ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ

Ηχοκαρδιογράφημα

- Τριγλώχινα : (2+/4+) - κεντρικό jet παλινδρόμησης και VC=0,33cm

- Vmax=3,3m/sec PPG=44 mmHg RVSP=44-49mmHg
- ΚΚΦ=1,7 cm με άριστη διακύμανση

- Πνευμονική βαλβίδα : PAEDP=8-13mmHg, meanPG=27/29 mmHg, AT=103 ms

- PA d= 25 mm
- RVWT= 0.6 cm

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 8A Echocardiographic probability of pulmonary hypertension in symptomatic patients with a suspicion of pulmonary hypertension

Peak tricuspid regurgitation velocity (m/s)	Presence of other echo 'PH signs'[a]	Echocardiographic probability of pulmonary hypertension
≤2.8 or not measurable	No	Low
≤2.8 or not measurable	Yes	Intermediate
2.9–3.4	No	
2.9–3.4	Yes	High
>3.4	Not required	

Table 8B Echocardiographic signs suggesting pulmonary hypertension used to assess the probability of pulmonary hypertension in addition to tricuspid regurgitation velocity measurement in *Table 8A*

A: The ventricles[a]	B: Pulmonary artery[a]	C: Inferior vena cava and right atrium[a]
Right ventricle/ left ventricle basal diameter ratio >1.0	Right ventricular outflow Doppler acceleration time <105 msec and/or midsystolic notching	Inferior cava diameter >21 mm with decreased inspiratory collapse (<50 % with a sniff or <20 % with quiet inspiration)
Flattening of the interventricular septum (left ventricular eccentricity index >1.1 in systole and/or diastole)	Early diastolic pulmonary regurgitation velocity >2.2 m/sec	Right atrial area (end-systole) >18 cm^2
	PA diameter >25 mm.	

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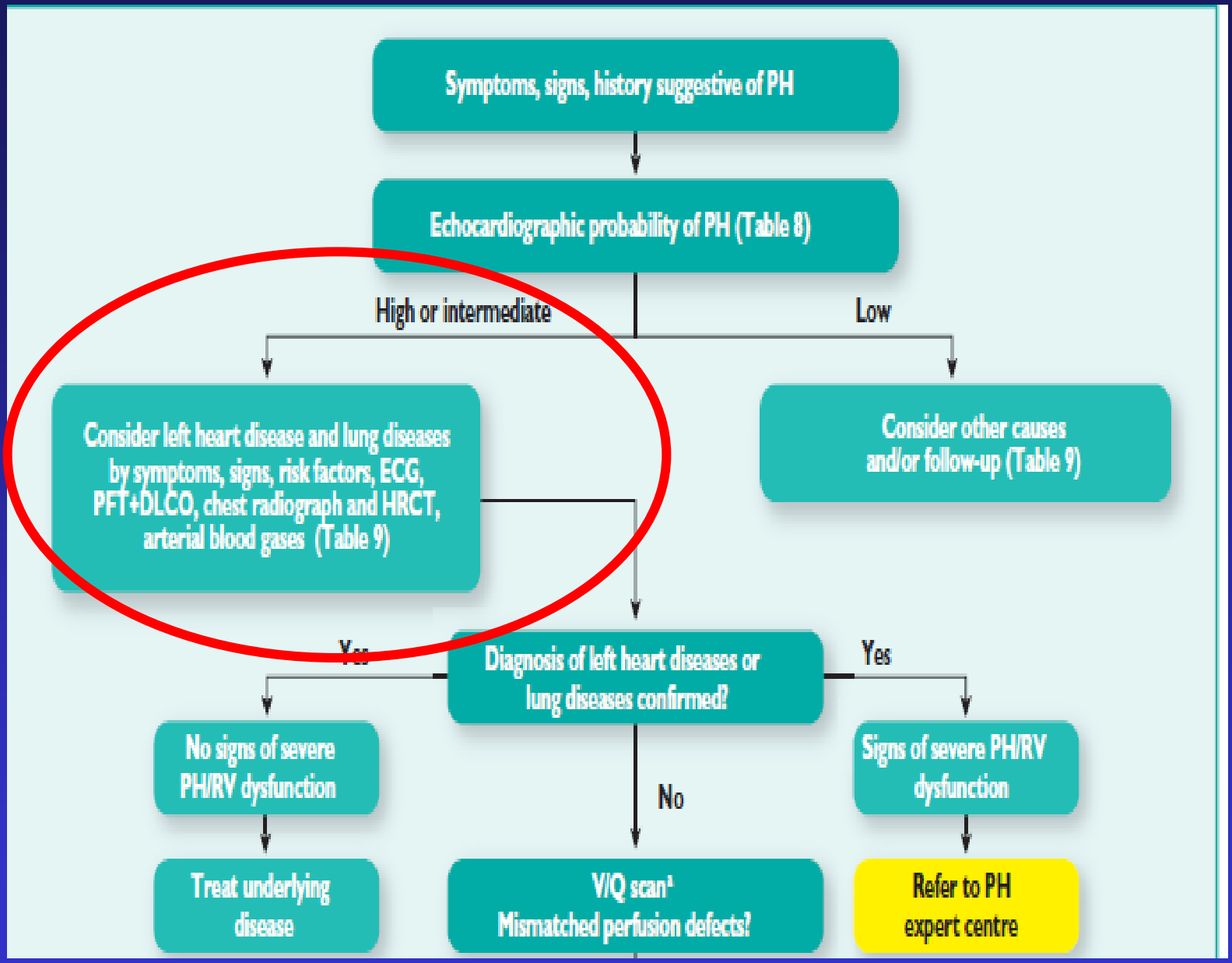
Symptoms, signs, history suggestive of PH
Echocardiographic probability of PH (Table 8)
High or intermediate
Low
Consider left heart disease and lung diseases by symptoms, signs, risk factors, ECG, PFT+DLCO, chest radiograph and HRCT, arterial blood gases (Table 9)
Consider other causes and/or follow-up (Table 9)
Yes
Diagnosis of left heart diseases or lung diseases confirmed?
Yes
No signs of severe PH/RV dysfunction
No
Signs of severe PH/RV dysfunction
Treat underlying disease
V/Q scan[3] Mismatched perfusion defects?
Refer to PH expert centre

ΣΠΙΡΟΜΕΤΡΗΣΗ 11/2017 ΕΙΔΙΚΟΣ ΣΥΝΤΕΛΕΣΤΗΣ ΔΙΑΧΥΣΗΣ DLCO	FEV1 =85% PRED FVC = 90 % PRED FEV1/FVC= 80,25% εφο
ΣΠΙΝΘΗΡΟΓΡΑΦΗΜΑ ΑΙΜΑΤΩΣΗΣ	αρνητικό για πνευμονική εμβολή και χρόνια θρομβοεμβολικη νόσο
HRCT ΘΩΡΑΚΟΣ	χωρίς παθολογικά ευρήματα εκ του πνευμονικού παρεγχύματος
ΠΟΛΥΣΩΜΑΤΟΓΡΑΦΙΚΗ ΜΕΛΕΤΗ ΥΠΝΟΥ	Δείκτης απνοιών/υποπνοιών/ώρα : 5.5 / hr
ΟΡΟΛΟΓΙΚΟΣ/ΑΝΟΣΟΛΟΓΙΚΟΣ/Η HIV	αρνητικός

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Αριστερός και Δεξιός καθετηριασμός 4/4/2018

ΣΒ(Kg)/Υ(cm)/ΕΣ(m2)	60/153/1.57
HR (bpm)	66
Hgb (g/dl)	11,7
Sa02 (%)	99
SPAO2 (%)	65
RAP (mean)	5
RVP (syst/diast)	45/8
PAP (syst/diast/mean)	45/15/27
PCWP (a/v/mean)	16/21/14
DPG (mmHg)	1
LVP (syst/diast)	146/23
AoP (syst/diast/mean)	143/60/93
CO (l/min) SV(ml/beat)	3.4/52
CI (l/min/m2)	2.2
PVR (Woods/dyn.s.cm-5)	3.8/306

Οξυμετρία
SO2

IVC: 69
RA : 62
RV : 64
PA : 65
PCW: 99
RadArt: 99

ΣΤΕΦΑΝΙΟΓΡΑΦΙΑ

χωρίς αιμοδυναμικά σημαντικές στενώσεις

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

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

Definition	Characteristics[a]	Clinical group(s)[b]
PH	PAPm ≥25 mmHg	All
Pre-capillary PH	PAPm ≥25 mmHg PAWP ≤15 mmHg	1. Pulmonary arterial hypertension 3. PH due to lung diseases 4. Chronic thromboembolic PH 5. PH with unclear and/or multifactorial mechanisms
Post-capillary PH	PAPm ≥25 mmHg PAWP >15 mmHg	2. PH due to left heart disease 5. PH with unclear and/or multifactorial mechanisms
Isolated post-capillary PH (Ipc-PH)	DPG <7 mmHg and/or PVR ≤3 WU[c]	
Combined post-capillary and pre-capillary PH (Cpc-PH)	DPG ≥7 mmHg and/or PVR >3 WU[c]	

Pulmonary hypertension due to left heart disease

Jean-Luc Vachiéry[1], Ryan J. Tedford[2], Stephan Rosenkranz[3], Massimiliano Palazzini[4], Irene Lang[5], Marco Guazzi[6], Gerry Coghlan[7], Irina Chazova[8] and Teresa De Marco[9]

TABLE 1 Pre-test probability of left heart disease (LHD) phenotype

Feature	High probability	Intermediate probability	Low probability
Age	>70 years	60–70 years	<60 years
Obesity, systemic hypertension, dyslipidaemia, glucose intolerance/diabetes	>2 factors	1–2 factors	None
Previous cardiac intervention#	Yes	No	No
Atrial fibrillation	Current	Paroxysmal	No
Structural LHD	Present	No	No
ECG	LBBB or LVH	Mild LVH	Normal or signs of RV strain
Echocardiography	LA dilation; grade >2 mitral flow	No LA dilation; grade <2 mitral flow	No LA dilation; *E*/*e*′ <13
CPET	Mildly elevated V'_E/V'_{CO_2} slope; EOV	Elevated V'_E/V'_{CO_2} slope *or* EOV	High V'_E/V'_{CO_2} slope; no EOV
Cardiac MRI	LA strain or LA/RA >1		No left heart abnormalities

Eur Respir J 2018;

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ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ

Αριστερός και Δεξιός καθετηριασμός 4/4/2018

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DPG (mmHg)	1
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CI (l/min/m2)	2.2
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Οξυμετρία
SO2

IVC: 69
RA : 62
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PCW: 99
RadArt: 99

Fluid challenge test
Έγχυση N/S 0,9% σε 5 min -> PCWP= 18mmHg

Pulmonary hypertension due to left heart disease

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- In patients with a PAWP 13–15 mmHg and high/intermediate probability of PH-HFpEF, provocative testing should be considered to uncover PH due to HFpEF. For technical reasons and reliability of pressure recording, a fluid challenge is preferred over exercise in the approach to differential diagnosis.
- PAWP >18 mmHg immediately after administration of 500 mL of saline over 5 min is considered abnormal.

Δοκιμασία αγγειοδραστικότητας

- Ακολούθησε iv στάγδην έγχυση adenosine με αρχική δόση 50 μg/kg/min και ανά 2 min αύξηση κατά 50 mg/kg/min μέχρι τελική δόση 350 μg/kg/min. Δεν παρατηρήθηκε αξιόλογη μείωση της mPAP.
- **ΣΥΜΠΕΡΑΣΜΑ**

✓ Προτριχοειδική πνευμονική υπέρταση

✓ Απουσία ανταπόκρισης στην iv χορήγηση αδενοσίνης

1. Pulmonary arterial hypertension

- 1.1 Idiopathic
- 1.2 Heritable
  - 1.2.1 BMPR2 mutation
  - 1.2.2 Other mutations
- 1.3 Drugs and toxins induced
- 1.4 Associated with:
  - 1.4.1 Connective tissue disease
  - 1.4.2 Human immunodeficiency virus (HIV) infection
  - 1.4.3 Portal hypertension
  - 1.4.4 Congenital heart disease (Table 6)
  - 1.4.5 Schistosomiasis

1'. Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis

- 1'.1 Idiopathic
- 1'.2 Heritable
  - 1'.2.1 EIF2AK4 mutation
  - 1'.2.2 Other mutations
- 1'.3 Drugs, toxins and radiation induced
- 1'.4 Associated with:
  - 1'.4.1 Connective tissue disease
  - 1'.4.2 HIV infection

1''. Persistent pulmonary hypertension of the newborn

2. Pulmonary hypertension due to left heart disease

- 2.1 Left ventricular systolic dysfunction
- 2.2 Left ventricular diastolic dysfunction
- 2.3 Valvular disease
- 2.4 Congenital / acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies
- 2.5 Congenital /acquired pulmonary veins stenosis

3. Pulmonary hypertension due to lung diseases and/or hypoxia

- 3.1 Chronic obstructive pulmonary disease
- 3.2 Interstitial lung disease
- 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
- 3.4 Sleep-disordered breathing
- 3.5 Alveolar hypoventilation disorders
- 3.6 Chronic exposure to high altitude
- 3.7 Developmental lung diseases (Web Table III)

4. Chronic thromboembolic pulmonary hypertension and other pulmonary artery obstructions

- 4.1 Chronic thromboembolic pulmonary hypertension
- 4.2 Other pulmonary artery obstructions
  - 4.2.1 Angiosarcoma
  - 4.2.2 Other intravascular tumors
  - 4.2.3 Arteritis
  - 4.2.4 Congenital pulmonary arteries stenoses
  - 4.2.5 Parasites (hydatidosis)

5. Pulmonary hypertension with unclear and/or multifactorial mechanisms

- 5.1 Haematological disorders: chronic haemolytic anaemia, myeloproliferative disorders, splenectomy
- 5.2 Systemic disorders, sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
- 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
- 5.4 Others: pulmonary tumoral thrombotic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

ΠΡΟΓΝΩΣΤΙΚΟΙ ΠΑΡΑΓΟΝΤΕΣ	
ΚΛΙΝΙΚΑ ΣΗΜΕΙΑ ΔΚΑ	(-)
ΕΠΙΔΕΙΝΩΣΗ ΣΥΜΠΤΩΜΑΤΩΝ	ΑΡΓΗ
ΣΥΓΚΟΠΗ	(-)
WHO FUNCTIONAL CLASS	II-III
ΣΥΓΠΟΠΤΙΚΑ ΕΠΕΙΣΟΔΙΑ	(-)
ΚΑΡΔΙΟΑΝΑΠΝΕΥΣΤΙΚΗ ΚΟΠΩΣΗ 6MWT	- 390 m
BNP	375 pg/ml
ΗΧΟΚΑΡΔΙΟΓΡΑΦΙΚΟΣ ΕΛΕΓΧΟΣ	RA<18cm2 χωρίς περικαρδιακή συλλογή
ΑΙΜΟΔΥΝΑΜΙΚΟΙ ΔΕΙΚΤΕΣ	RAP : 5 mmHg CI:2.2ml/m2

Table 13 Risk assessment in pulmonary arterial hypertension

Determinants of prognosis[a] (estimated 1-year mortality)	Low risk <5%	Intermediate risk 5–10%	High risk >10%
Clinical signs of right heart failure	Absent	Absent	Present
Progression of symptoms	No	Slow	Rapid
Syncope	No	Occasional syncope[b]	Repeated syncope[c]
WHO functional class	I, II	III	IV
6MWD	>440 m	165–440 m	<165 m
Cardiopulmonary exercise testing	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 <11 ml/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
Imaging (echocardiography, CMR imaging)	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
Haemodynamics	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%

Γ Ν Α "Γ ΓΕΝΝΗΜΑΤΑΣ"
ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ

Β. ΘΕΡΑΠΕΙΑ

Γ Ν Α "Γ ΓΕΝΝΗΜΑΤΑΣ"
ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ

Management of Pulmonary Arterial Hypertension

Vallerie V. McLaughlin, MD,* Sanjiv J. Shah, MD,† Rogerio Souza, MD,‡ Marc Humbert, MD, PhD§

- Modified NYHA functional class (World Health Organization functional class): I or II
- Echocardiography/CMR: normal or near-normal RV size and function
- Hemodynamics: normal indexes of RV function (right atrial pressure <8 mm Hg and cardiac index >2.5 to 3.0 l/min/m^2)
- 6MWD >380 to 440 m
- Cardiopulmonary exercise testing: peak oxygen uptake >15 ml/min/kg and ventilatory equivalents for CO_2 <45 l/min
- BNP level: "normal" (determined by local laboratory cutoff values)

J Am Coll Cardiol 2015;65:1976–97)

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

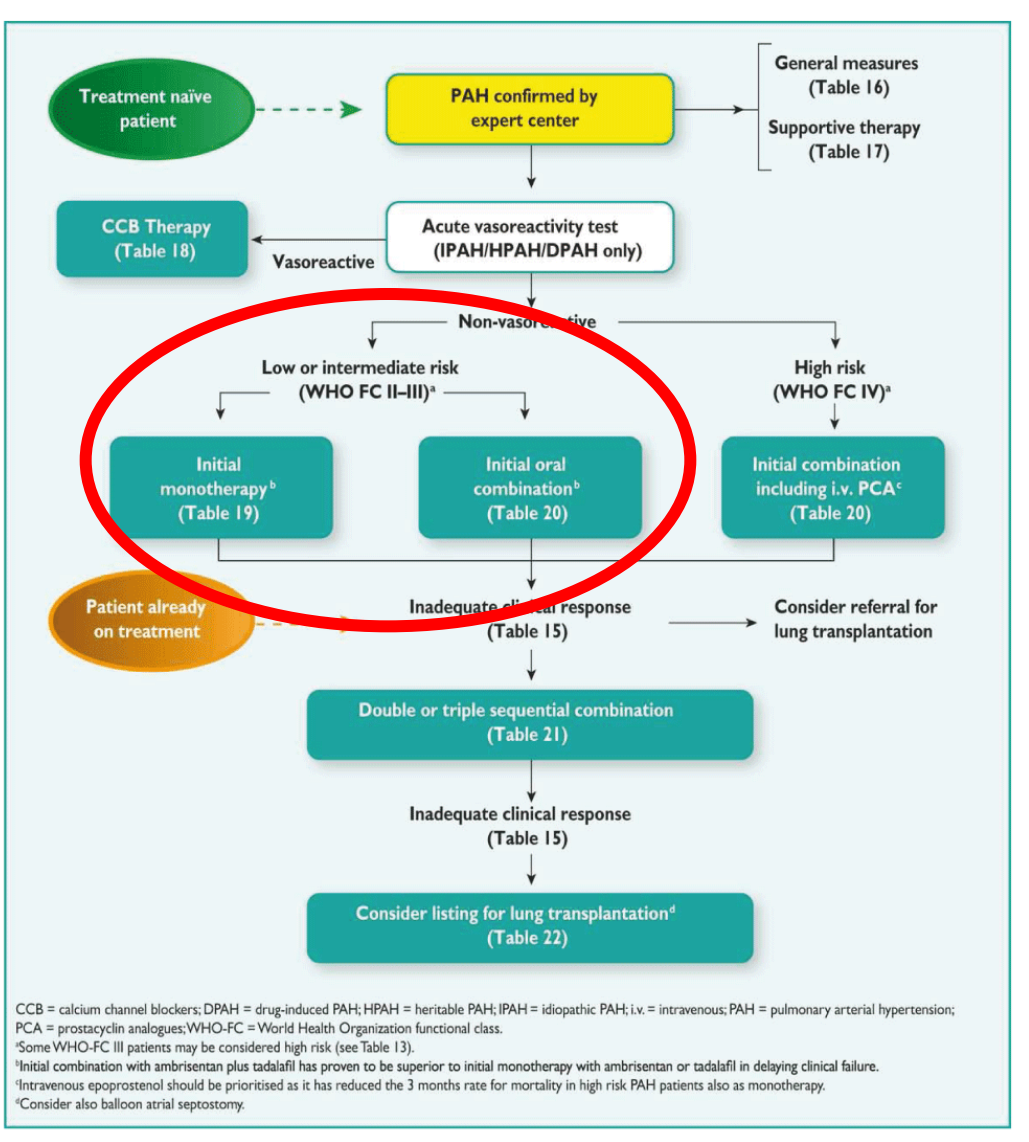
The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)

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

Table 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

Treatment algorithm from the 2015 European Society of Cardiology/European Respiratory Society



CCB = calcium channel blockers; DPAH = drug-induced PAH; HPAH = heritable PAH; IPAH = idiopathic PAH; i.v. = intravenous; PAH = pulmonary arterial hypertension; PCA = prostacyclin analogues; WHO-FC = World Health Organization functional class.

[a]Some WHO-FC III patients may be considered high risk (see Table 13).

[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 prioritised as it has reduced the 3 months rate for mortality in high risk PAH patients also as monotherapy.

[d]Consider also balloon atrial septostomy.

Tsai H, Sung YK and de Jesus Perez V. Recent advances in the management of pulmonary arterial hypertension [version 1]. F1000Research 2016, 5:2755 (doi: 10.12688/f1000research.9739.1)

Table 20 Recommendations for efficacy of initial drug combination therapy for pulmonary arterial hypertension (group 1) according to World Health Organization functional class. Sequence is by rating

Measure/ treatment	Class[a]-Level[b]						Ref.[c]
	WHO-FC II		WHO-FC III		WHO-FC IV		
Ambrisentan + tadalafil[d]	I	B	I	B	IIb	C	247
Other ERA + PDE-5i	IIa	C	IIa	C	IIb	C	-
Bosentan + sildenafil + i.v. epoprostenol	-	-	IIa	C	IIa	C	246
Bosentan + i.v. epoprostenol	-	-	IIa	C	IIa	C	198, 245
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	-

ΘΕΡΑΠΕΙΑ 1η

15/4/2018

- Lasix 40 mg x1

- Ambrisentan 5mg x1

+

- Tadalafil 20 mg x1

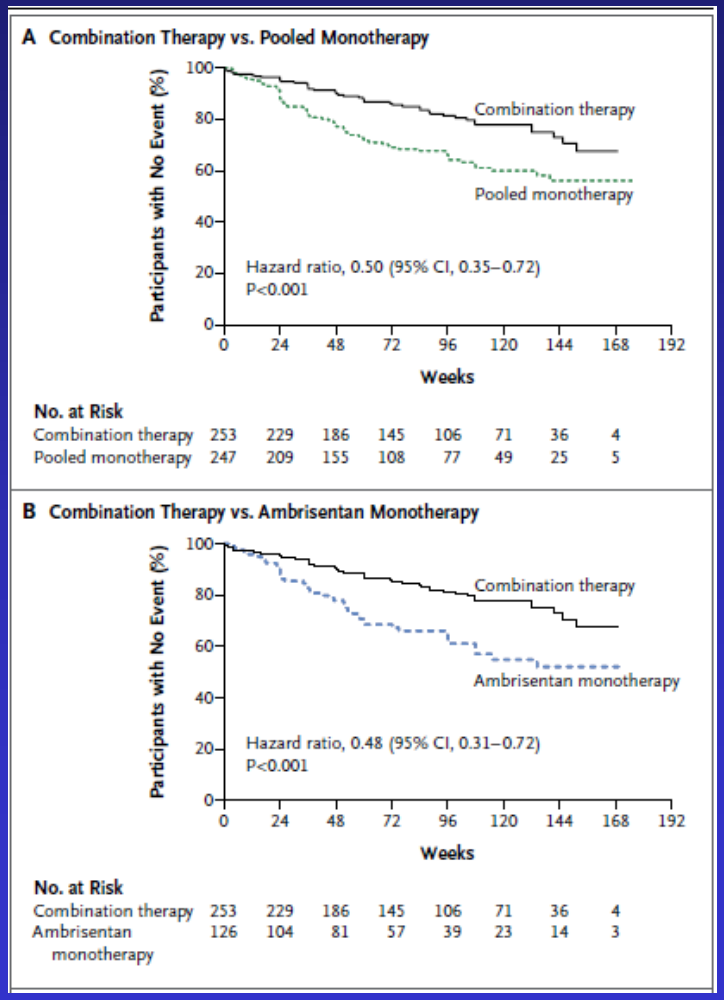
(2weekslater)

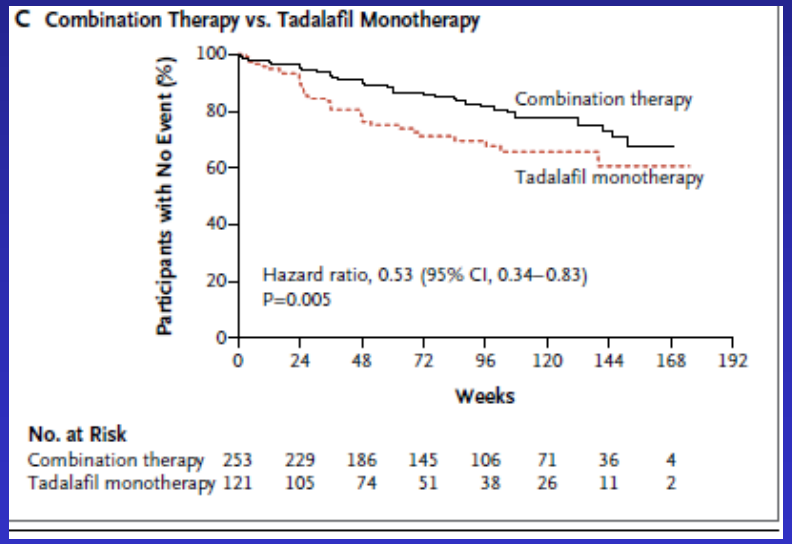
ORIGINAL ARTICLE

Initial Use of Ambrisentan plus Tadalafil in Pulmonary Arterial Hypertension

N. Galiè, J.A. Barberà, A.E. Frost, H.-A. Ghofrani, M.M. Hoeper, V.V. McLaughlin, A.J. Peacock, G. Simonneau, J.-L. Vachiery, E. Grünig, R.J. Oudiz, A. Vonk-Noordegraaf, R.J. White, C. Blair, H. Gillies, K.L. Miller, J.H.N. Harris, J. Langley, and L.J. Rubin, for the AMBITION Investigators*

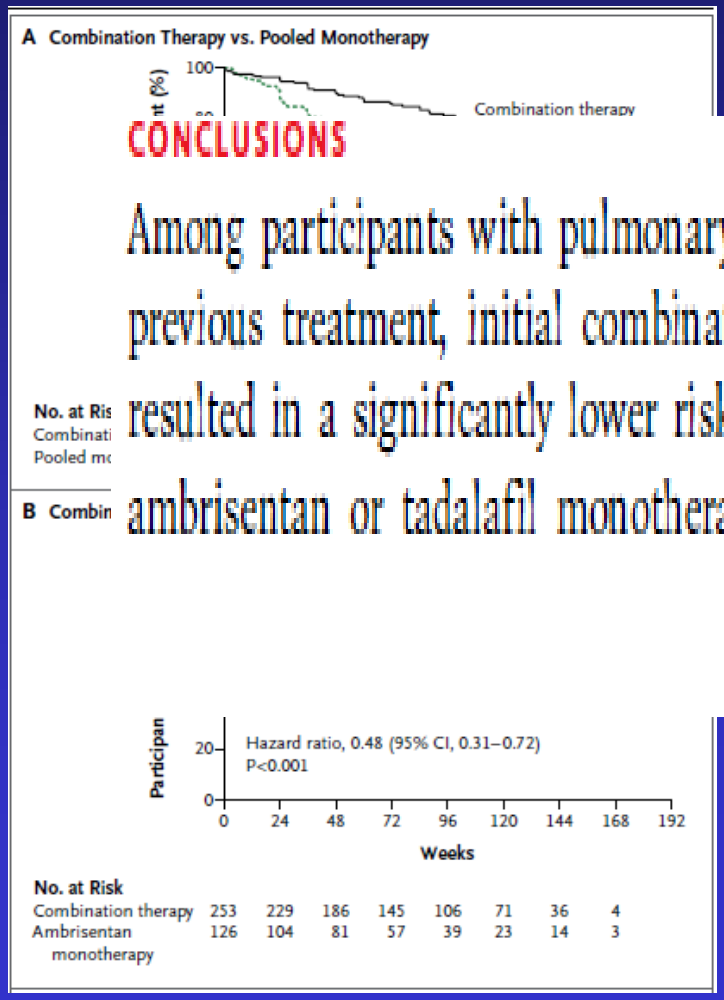
AMBITION study





N ENGL J MED 373;9 NEJM.ORG AUGUST 27, 2015

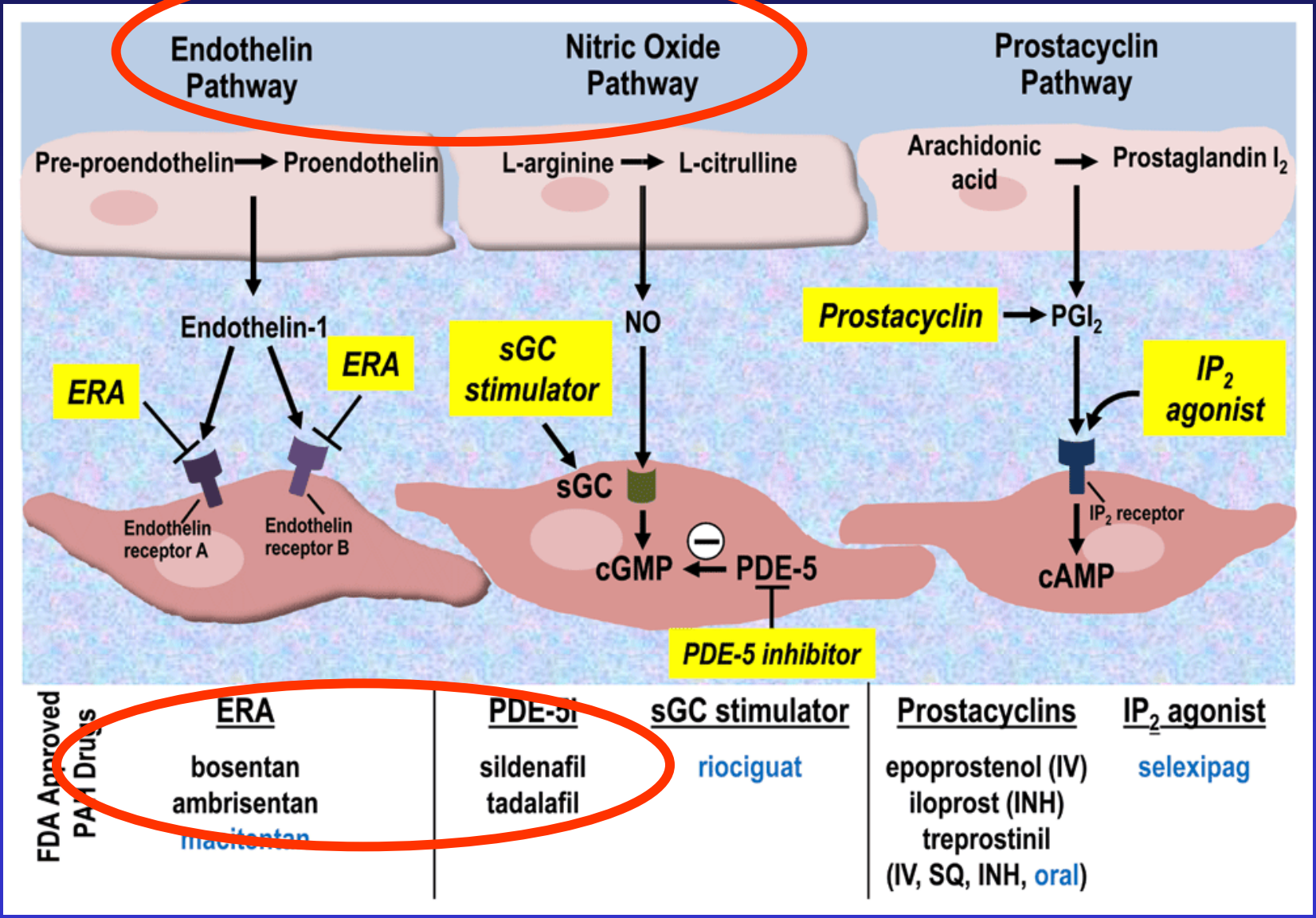
AMBITION study



CONCLUSIONS

Among participants with pulmonary arterial hypertension who had not received previous treatment, initial combination therapy with ambrisentan and tadalafil resulted in a significantly lower risk of clinical-failure events than the risk with ambrisentan or tadalafil monotherapy.

Figure 1. Pathways targeted in current therapies for pulmonary arterial hypertension.



Tsai H, Sung YK and de Jesus Perez V. Recent advances in the management of pulmonary arterial hypertension [version 1]. F1000Research 2016, 5:2755 (doi: 10.12688/f1000research.9739.1)

2 ΕΒΔΟΜΑΔΕΣ ΑΡΓΟΤΕΡΑ…

30/4/2018

- …και με την έναρξη **Tadalafil** ….η ασθενής έρχεται στο νοσοκομείο με

- **Οίδημα λάρυγγα**

(βράγχος φωνής/δύσπνοια)

- **Οίδημα προσώπου**

ΘΕΡΑΠΕΙΑ 2η

20/5/2018

- (3 εβδομάδες)-> Τιτλοποίηση **ambrisentan στα 10 mg …**

20/6/2018 **+**

- 1 μήνα μετά -> προσθήκη **Sildenafil** 20 mg x 3

Updated Treatment Algorithm of Pulmonary Arterial Hypertension

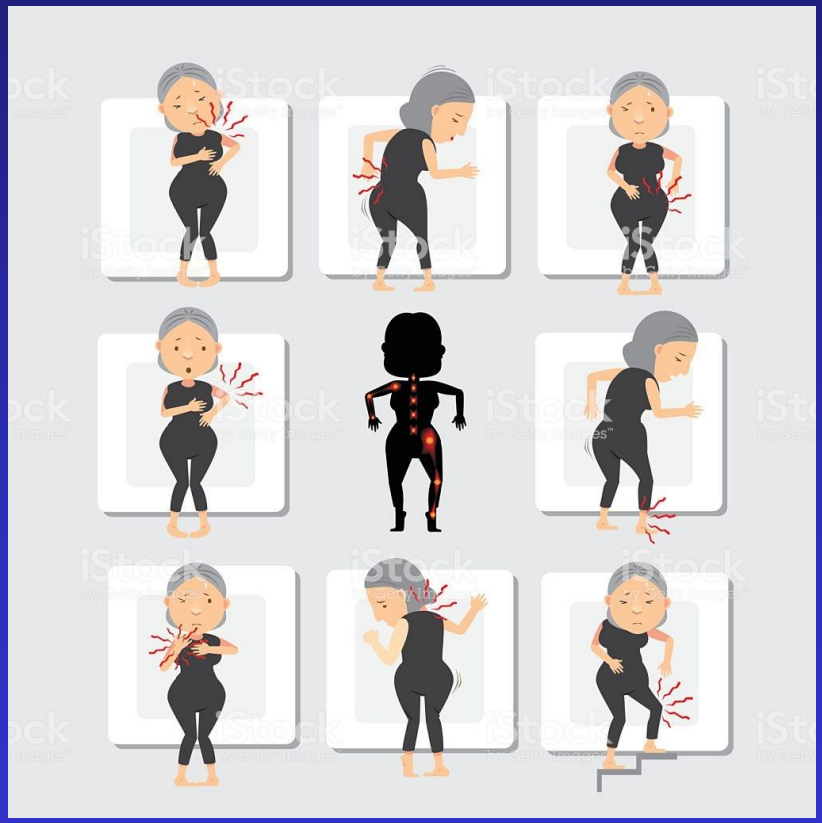
Table 4 Characteristics of Randomized Controlled Trials With Pulmonary Arterial Hypertension Drugs Interfering With the Nitric Oxide Pathway (See Text for References)

Drug(s) Tested	Study	Background	Primary Endpoint	Outcome (Secondary Endpoint)	Duration (weeks)	No. of Patients
Soluble Guanylate Cyclase Stimulators						
Riociguat*	PATENT	No bosentan or prostanoids	6MWD	TTCW	12	443
Phosphodiesterase Type-5 Inhibitors						
Sildenafil	SUPER-1	No	6MWD	TTCW (NS)	12	277
	Sastry	No	TT	—	12	22
	Singh	No	6MWD	—	6	20
	PACES	Epoprostenol	6MWD	TTCW	16	264
	Iversen	Bosentan	6MWD	—	12	20
Tadalafil	PHIRST	No or bosentan (54%)	6MWD	TTCW	16	405
Vardenafil†	EVALUATION	No	6MWD	TTCW	12	66

J Am Coll Cardiol 2013;62:D60–72)

ΓΝΑ "ΓΕΝΝΗΜΑΤΑΣ"
ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ

10/8/2018



- **διακοπή sildenafil**

Λόγω εμμένουσας μυαλγίας-αρθραλγίας παρά την καθημερινή χρήση κοινών αναλγητικών

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 14 Suggested assessment and timing for the follow-up of patients with pulmonary arterial hypertension

	At baseline	Every 3–6 months[a]	Every 6–12 months[a]	3–6 months after changes in therapy[a]	In case of clinical worsening
Medical assessment and determination of functional class	+	+	+	+	+
ECG	+	+	+	+	+
6MWT/Borg dyspnoea score	+	+	+	+	+
CPET	+		+		+[a]
Echo	+		+	+	+
Basic lab[b]	+	+	+	+	+
Extended lab[c]	+		+		+
Blood gas analysis[d]	+		+	+	+
Right heart catheterization	+		+[f]	+[a]	+[a]

Βιοχημικός έλεγχος

Κρεατινίνη	1,1 mg/dl	-> 0,95
Ουρία	43 mg/dl	-> 39
BNP	375 pg/ml	-> 175
SGOT/SGPT	18/12 U/L	-> 13/9
HbA1C	6,4 U/L	-> 5,9
Chol	168 mg/dl	-> 134
LDL	92 mg/dl	-> 80
HDL	43 mg/dl	
HCT	38 %	-> 32,8
HGB	12,1	-> 9,5

- 10/2019

Γ Ν Α "Γ ΓΕΝΝΗΜΑΤΑΣ"
ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ

Βιοχημικός έλεγχος

Κρεατινίνη	1,1 mg/dl	->	0,95
Ουρία	43 mg/dl	->	39
BNP	375 pg/ml	->	75
SGOT/SGPT	18/12 U/L	->	13/9
HbA1C	6,4 U/L	->	5,9
Chol	168 mg/dl	->	134
LDL	92 mg/dl	->	80
HDL	43 mg/dl		
HCT	38 %	->	32,8
HGB	12,1	->	9,5
Φερριτίνη	**8**		

ΚΛΙΝΙΚΑ ΣΗΜΕΙΑ ΔΚΑ	(-)
ΕΠΙΔΕΙΝΩΣΗ ΣΥΜΠΤΩΜΑΤΩΝ	ΑΡΓΗ
ΣΥΓΚΟΠΗ	(-)
WHO FUNCTIONAL CLASS	II-III
ΣΥΓΠΟΠΤΙΚΑ ΕΠΕΙΣΟΔΙΑ	(-)
ΚΑΡΔΙΟΑΝΑΠΝΕΥΣΤΙΚΗ ΚΟΠΩΣΗ 6MWT	- 415 m (+25m)
BNP	75 pg/ml (από 375)
ΗΧΟΚΑΡΔΙΟΓΡΑΦΙΚΟΣ ΕΛΕΓΧΟΣ	RA<18cm2 χωρίς περικαρδιακή συλλογή
	TRVmax= 2,8m/sec από 3,3 m/sec PPG= 31 mmHg RVSP= 31-36 mmHg

ΘΕΡΑΠΕΙΑ 3η

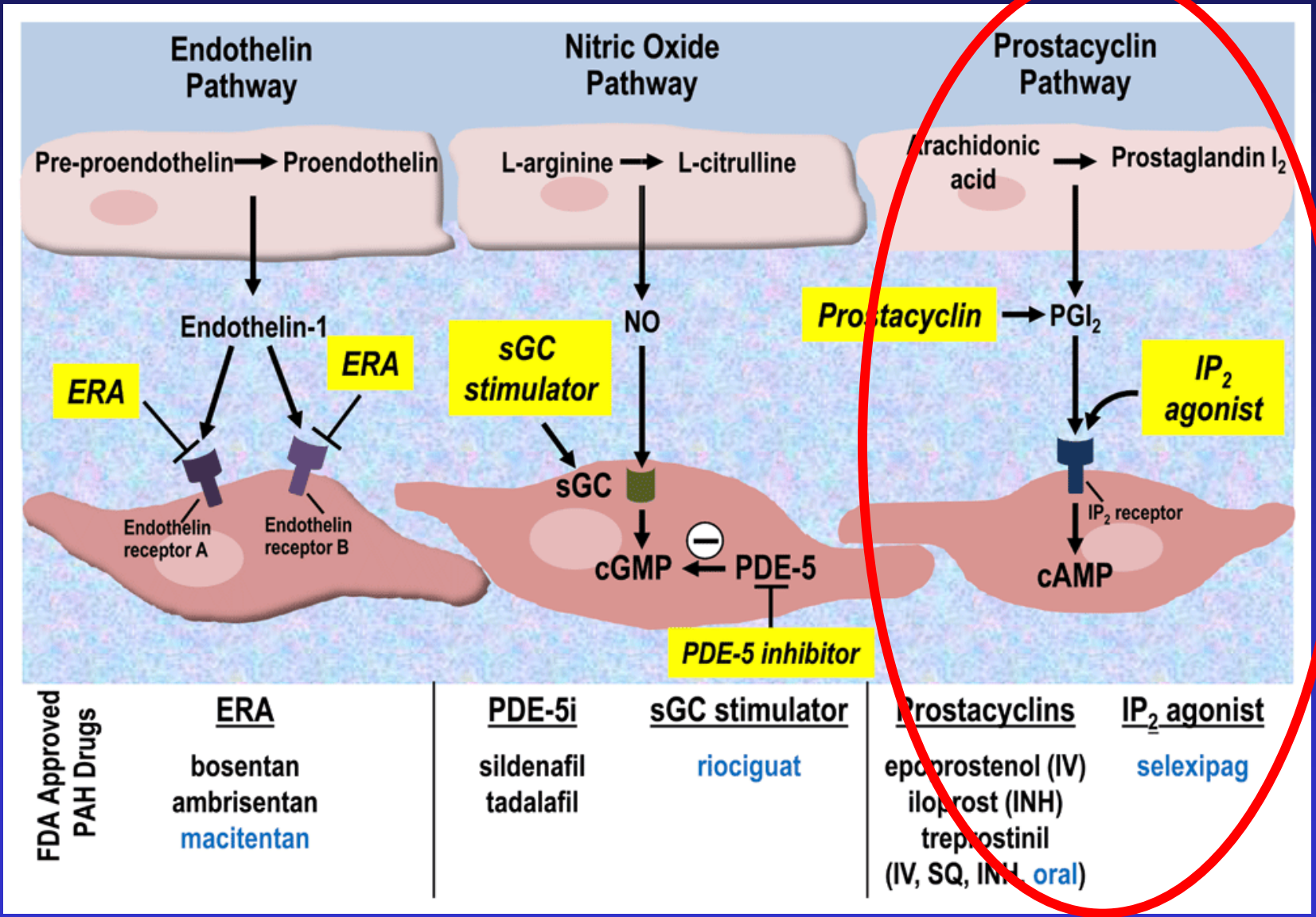
19/11/2018

- Ambrisentan 10mg x1

+

- selexipag 200 mg x2

Figure 1. Pathways targeted in current therapies for pulmonary arterial hypertension.



Tsai H, Sung YK and de Jesus Perez V. Recent advances in the management of pulmonary arterial hypertension [version 1]. F1000Research 2016, 5:2755 (doi: 10.12688/f1000research.9739.1)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Selexipag for the Treatment of Pulmonary Arterial Hypertension

Olivier Sitbon, M.D., Richard Channick, M.D., Kelly M. Chin, M.D., Aline Frey, Pharm.D., Sean Gaine, M.D., Nazzareno Galiè, M.D., Hossein-Ardeschir Ghofrani, M.D., Marius M. Hoeper, M.D., Irene M. Lang, M.D., Ralph Preiss, M.D., Lewis J. Rubin, M.D., Lilla Di Scala, Ph.D., Victor Tapson, M.D., Igor Adzerikho, M.D., Jinming Liu, M.D., Olga Moiseeva, M.D., Xiaofeng Zeng, M.D., Gérald Simonneau, M.D., and Vallerie V. McLaughlin, M.D., for the GRIPHON Investigators*

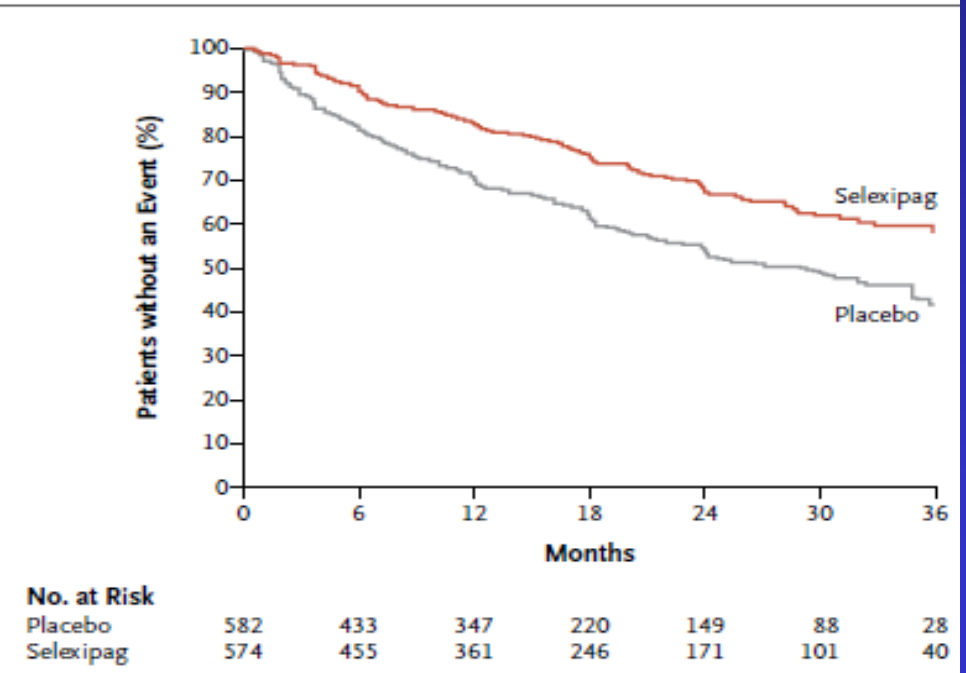


Figure 2. Primary Composite End Point.

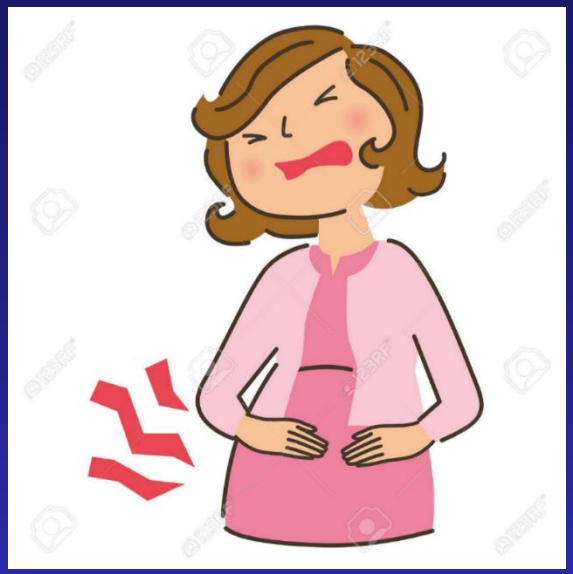
Shown are Kaplan–Meier curves for the primary composite end point of

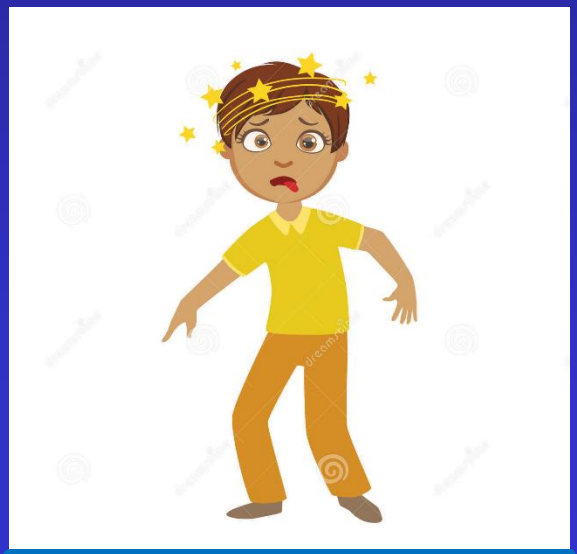
CONCLUSIONS

Among patients with pulmonary arterial hypertension, the risk of the primary composite end point of death or a complication related to pulmonary arterial hypertension was significantly lower with selexipag than with placebo. There was no significant difference in mortality between the two study groups. (Funded by Actelion Pharmaceuticals; GRIPHON ClinicalTrials.gov number, NCT01106014.)

ΓΝΑ "ΓΕΝΝΗΜΑΤΑΣ"
ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ

11/02/2019





stop

- **selexipag**

λόγω γαστρεντερικών διαταραχών και

Αστάθειας-ιλίγγου

Γαστροσκόπηση (3/2019):
ήπια γαστρίτιδα

ΘΕΡΑΠΕΙΑ 4η

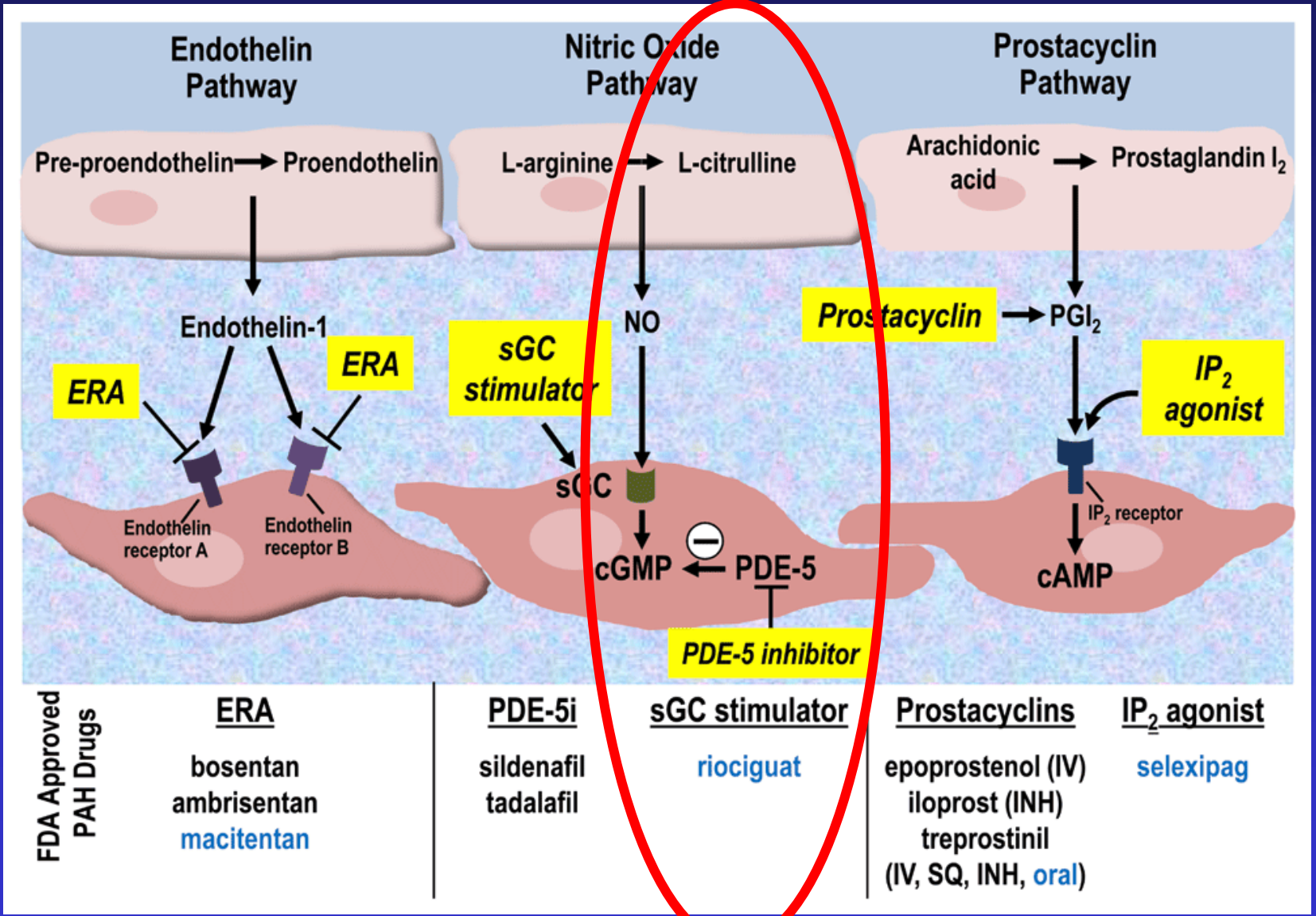
4/5/2019

- Ambrisentan 10mg x1

+

- riociguat 0,5 mg x2

Figure 1. Pathways targeted in current therapies for pulmonary arterial hypertension.



Tsai H, Sung YK and de Jesus Perez V. Recent advances in the management of pulmonary arterial hypertension [version 1]. F1000Research 2016, 5:2755 (doi: 10.12688/f1000research.9739.1)

4/5/2018

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Riociguat for the Treatment of Pulmonary Arterial Hypertension

Hossein-Ardeschir Ghofrani, M.D., Nazzareno Galiè, M.D., Friedrich Grimminger, M.D., Ekkehard Grünig, M.D., Marc Humbert, M.D., Zhi-Cheng Jing, M.D., Anne M. Keogh, M.D., David Langleben, M.D., Michael Ochan Kilama, M.D., Arno Fritsch, Ph.D., Dieter Neuser, M.D., and Lewis J. Rubin, M.D., for the PATENT-1 Study Group*

- Ambrisentan 10mg x1

+

- riociguat 0,5 mg x2

CONCLUSIONS

Riociguat significantly improved exercise capacity and secondary efficacy end points in patients with pulmonary arterial hypertension. (; PATENT-1 and PATENT-2 ClinicalTrials.gov numbers, NCT00810693 and NCT00863681, respectively.)

4/5/2018

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Riociguat for the Treatment of Pulmonary Arterial Hypertension

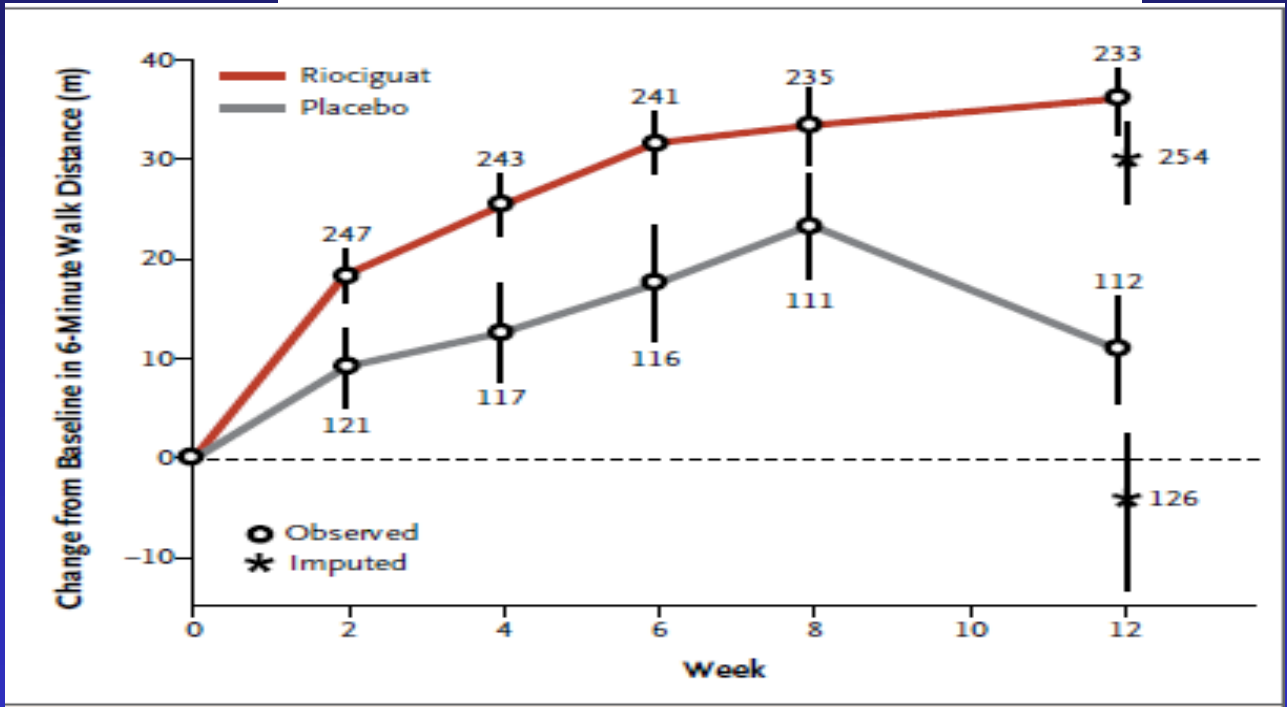


Figure 2. Mean Change from Baseline in the 6-Minute Walk Distance.

CONCLUSIONS

Riociguat significantly improved exercise capacity and secondary efficacy end points in patients with pulmonary arterial hypertension. (; PATENT-1 and PATENT-2 ClinicalTrials.gov numbers, NCT00810693 and NCT00863681, respectively.)

2/06/2019

οριστική διακοπή

- **riociguat**

λόγω γαστρεντερικών διαταραχών (κοιλιακό άλγος-δυσπεψία-μετεωρισμός-δυσφορία)

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 15 Recommendations for evaluation of the severity of pulmonary arterial hypertension and clinical response to therapy

Recommendations	Class[a]	Level[b]	Ref.[c]
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 haemodynamic evaluations (*Tables 13* and *14*)	I	C	96,97, 99
It is recommended to perform regular follow-up assessments every 3–6 months in stable patients (*Table 14*)	I	C	98
Achievement/maintenance of a low-risk profile (*Table 13*) is recommended as an adequate treatment response for patients with PAH	I	C	96–99
Achievement/maintenance of an intermediate-risk profile (*Table 13*) should be considered an inadequate treatment response for most patients with PAH	IIa	C	96–99

ΓΝΑ "ΓΕΝΝΗΜΑΤΑΣ"
ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ

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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 19 Recommendations for efficacy of drug monotherapy for pulmonary arterial hypertension (group 1) according to World Health Organization functional class. The sequence is by pharmacological group, by rating and by alphabetical order

Measure/treatment			Class[a]-Level[b]						Ref.[c]
			WHO-FC II		WHO-FC III		WHO-FC IV		
Calcium channel blockers			I	C[d]	I	C[d]	-	-	84,85
Endothelin receptor antagonists	Ambrisentan		I	A	I	A	IIb	C	194
	Bosentan		I	A	I	A	IIb	C	196–200
	Macitentan[e]		I	B	I	B	IIb	C	201
Phosphodiesterase type 5 inhibitors	Sildenafil		I	A	I	A	IIb	C	205–208
	Tadalafil		I	B	I	B	IIb	C	211
	Vardenafil[g]		IIb	B	IIb	B	IIb	C	212
Guanylate cyclase stimulators	Riociguat		I	B	I	B	IIb	C	214
Prostacyclin analogues	Epoprostenol	Intravenous[e]	-	-	I	A	I	A	220–222
	Iloprost	Inhaled	-	-	I	B	IIb	C	229–231
		Intravenous[g]	-	-	IIa	C	IIb	C	232
	Treprostinil	Subcutaneous	-	-	I	B	IIb	C	233
		Inhaled[g]	-	-	I	B	IIb	C	237
		Intravenous[f]	-	-	IIa	C	IIb	C	234
		Oral[g]	-	-	IIb	B	-	-	238–240
	Beraprost[g]		-	-	IIb	B	-	-	218
IP receptor agonists	Selexipag (oral)[g]		I	B	I	B	-	-	241,248

Γ. Και τώρα ???