ΕΛΛΗΝΙΚΗ ΕΤΑΙΡΕΙΑ ΜΕΛΕΤΗΣ ΤΗΣ ΠΝΕΥΜΟΝΙΚΗΣ ΥΠΕΡΤΑΣΗΣ

3ο ΠΑΝΕΛΛΗΝΙΟ ΣΥΝΕΔΡΙΟ ΠΝΕΥΜΟΝΙΚΗΣ ΥΠΕΡΤΑΣΗΣ

Case Report
A patient with CTD-associated PAH

ΘΕΟΔΩΡΟΣ ΔΗΜΗΤΡΟΥΛΑΣ

ΕΠΙΚΟΥΡΟΣ ΚΑΘΗΓΗΤΗΣ ΡΕΥΜΑΤΟΛΟΓΙΑΣ ΑΠΘ

Declaration of interest

- None

- 49yo, male
  - Dyspnea on exertion (last 2 years)- WHO II
  - Fatigue

Background

- HEFpEF (since 2016)
- Arterial hypertension since 2013
- Obesity
- Raynaud's syndrome
- Mild photosensitivity
- Former smoker
- Alcohol intake

Bisoprolol 2,5mg 1x1

Aldactone 25 1x1

Clinical Examination

- Heart Sounds: S1, S2, Loud P2
- Lung Sounds: Clear
- Mild leg edema
- BP:135/75 mmHg
- HR: 98/min
- RR: 14/min
- SpO_2: 98% on air

- Echocardiography: Suspected PH

ECHO	
TAPSE (cm)	2,2
RA area (cm^2)	21.5
RVSP (mmHg)	72
P.Effusion (cm)	Mild

6MWD: 400m		
	Pre Exercise	Post Exercise
HR	89	95
Dyspnea (Borg Scale)	0	3
Fatigue (Borg Scale)	0	2
sO_2	98%	93%

LAB Tests (10/08/2018)			
Biochemical		**CBCC**	
Glucose (mg/dl)	106	WBC (K/µL)	5.04
Urea (mg/dl)	48	Ht (%)	30.9↓
Creatinine (mg/dl)	0,8	Hb (g/dL)	10.6↓
SGOT (U/lt)	23	PLT (K/µL)	217
SGPT (U/lt)	18	**Hormonal**	
K^+ (mmol/lt)	4.6	FT3 (pmol/Lt)	5
Na^+(mmol/lt)	135	FT4 (pmol/Lt)	20,9
NT-proBNP (pg/ml)	2131	TSH (mIU/mL)	4

Diagnostic approach

- Lung tests:
  - FEV1: 82%, FVC 76%, FEV1/FVC: 82%, TLC: 75%, **DLCO: 54%**
- **HRCT/pulmonary angiography**:
  - Normal findings from the lung parenchyma
  - Dilated main PA with no filling defects
  - **Lemphadenopathy**
- VQ Scan:
  - Normal Lung Ventilation and Perfusion scan
- MRI:
  - Pulmonary artery 35mm
  - Dilated RV, RV-EF 50%

RHC (8/2018)

Pressures (mmHg)	Sys	Dias	Mean	SVO_2 (%)
RA			4	
RV	65	3		
PA	55	30	41	64
PCWP			10	

Resistances	Woods
PVR	6,9
PVR Indexed	12.6

CI	L/min/m²
CI	2.4

Immunological	
ANA	1/640
dsDNA	(-)
Ro	(-)
La	(-)
Sm	76↑
Anti-RNP	>200↑↑↑
Anti-SCL 70	(-)
aCL IgG (U/ml)	(-)
aCL IgM (U/ml)	(-)
B2gpi(IgG)	(-)
B2GPI	(-)
LAC	(-)
C4 (mg/dl)	3,4↓ (16-38)
C3 (mg/dl)	26↓ (79-152)
RF (IU/ml)	90↑ (0-20)

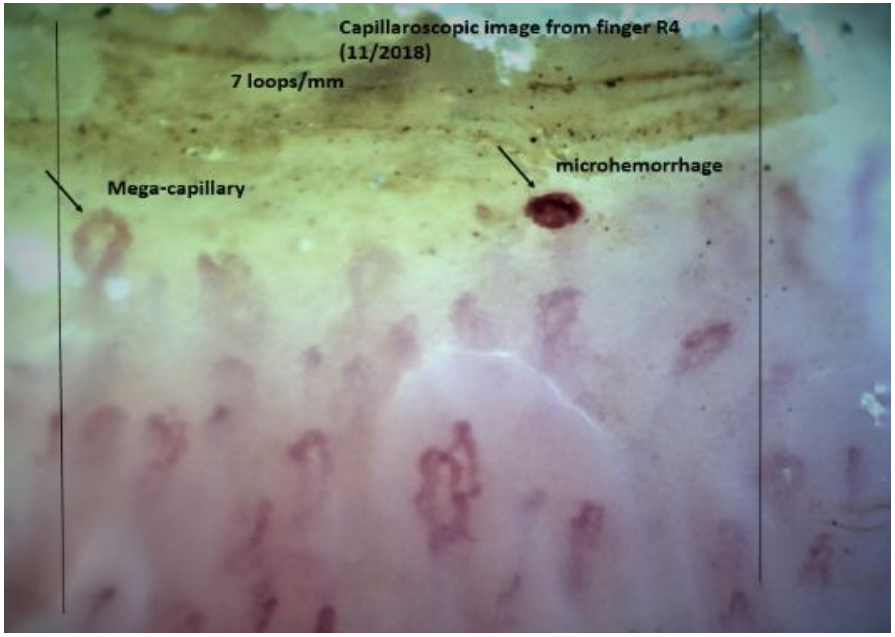
Rheumatologic Consultation

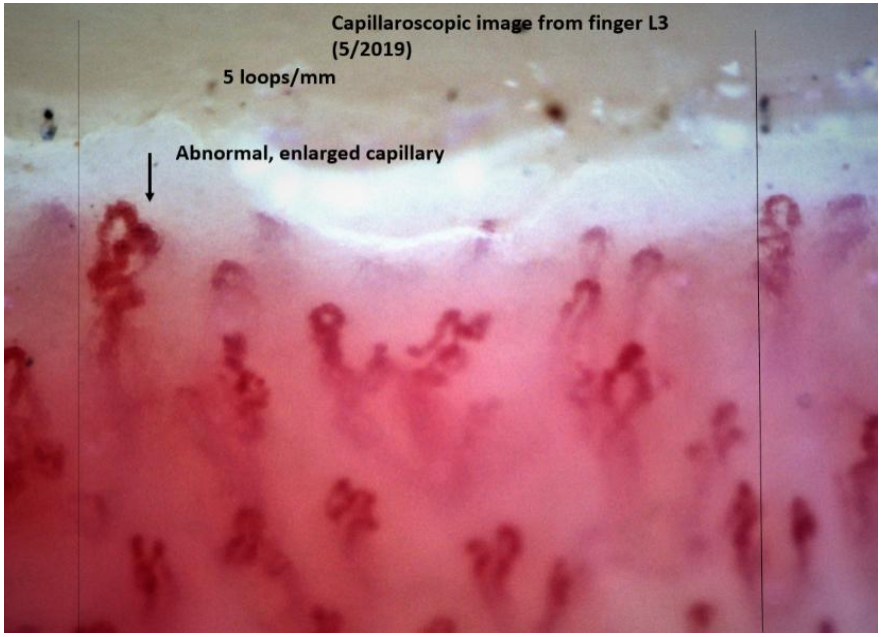
Συστηματικός Ερυθηματώδης Λύκος

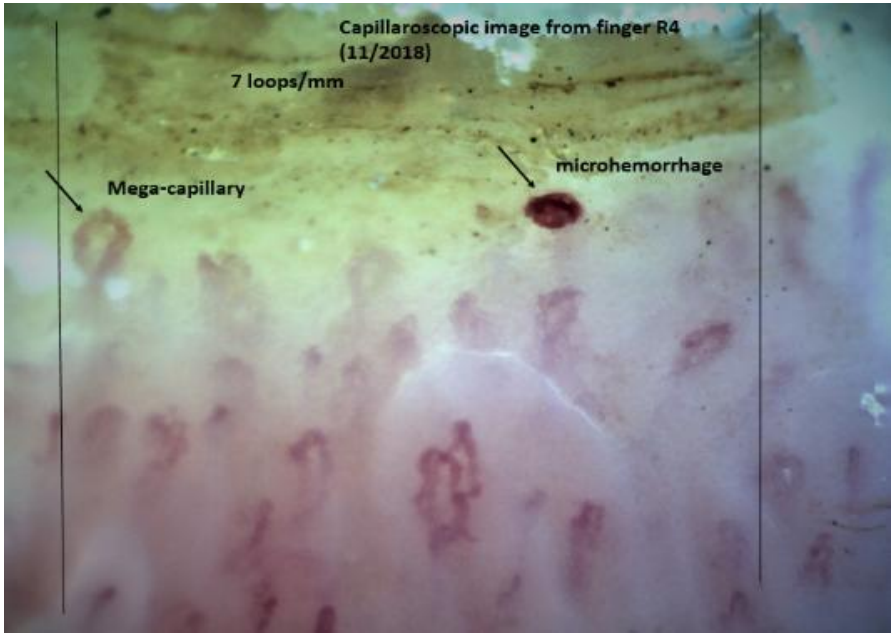
HB (g/L)	9,5↓
WBC	7,2 (54/30/8)
PLT/μl	220000
ΤΚΕ (mm/h)	85↑
CRP (mg/l)	0,5
Γ. ούρων	0-1 πυοσφαίρια 0-1 ερυθρά

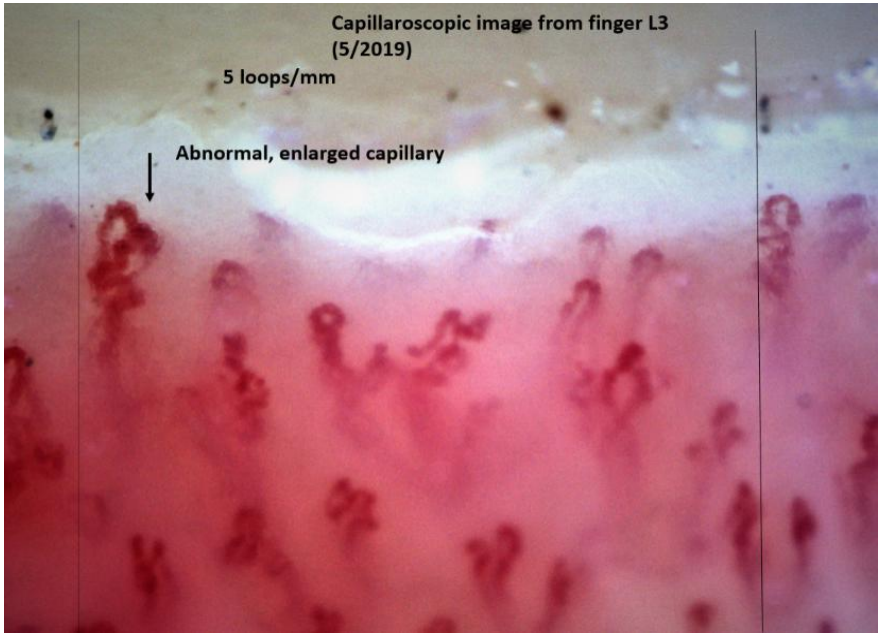
Άμεση Coombs: +++
Λεύκωμα ούρων 24ώρου: 240mg
Hepatis screen (-)
HIV (-)

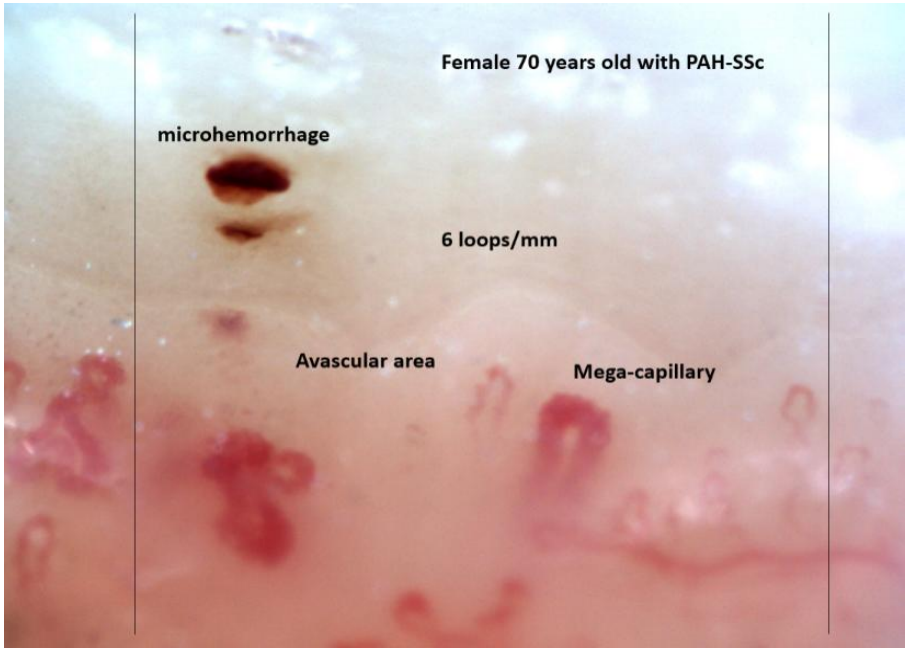
IgA: 386
IgG: 2130 ↑
IgM: 386
Ηλεκτροφόρηση: κφ
Ανοσοκαθήλωση: κφ

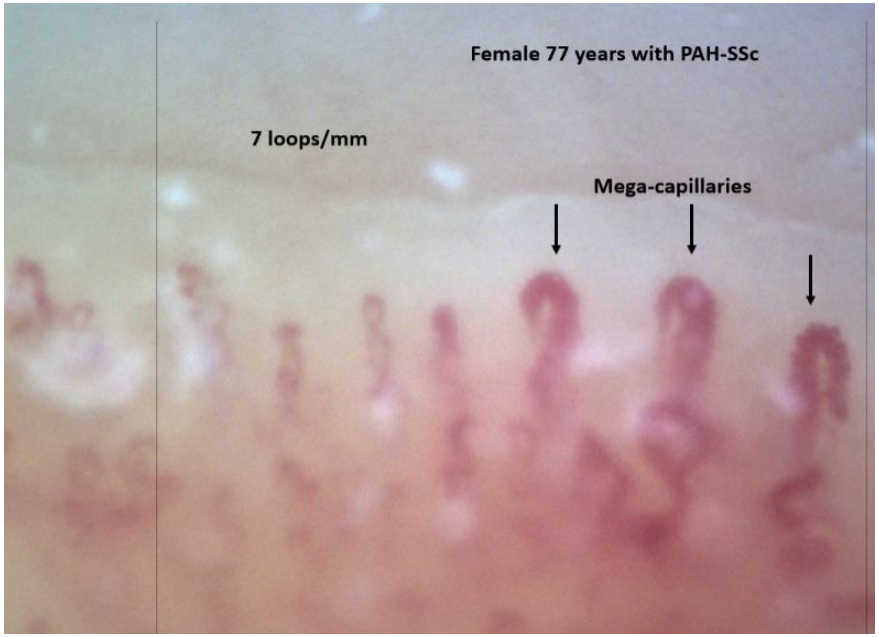

Capillaroscopic image from finger R4
(11/2018)
7 loops/mm
microhemorrhage
Mega-capillary


Capillaroscopic image from finger L3
(5/2019)
5 loops/mm
Abnormal, enlarged capillary

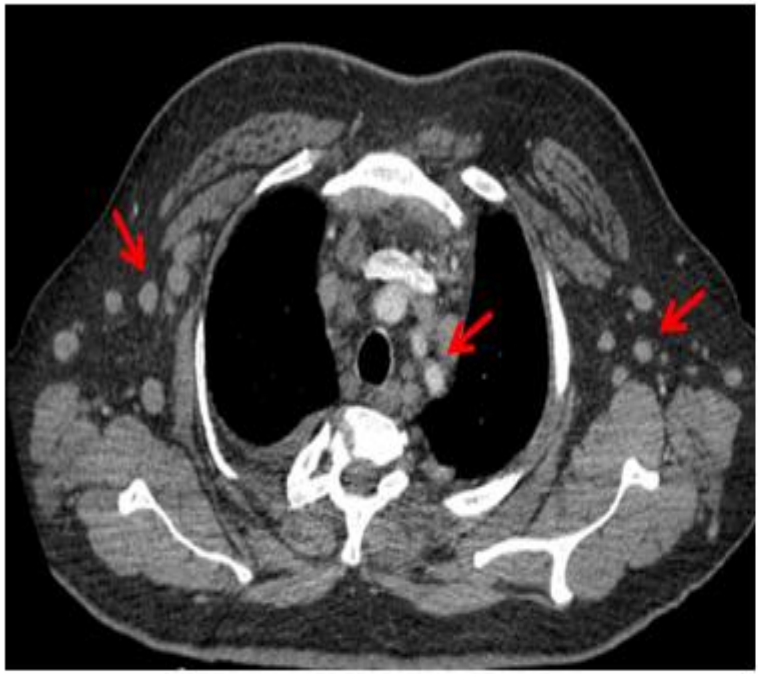


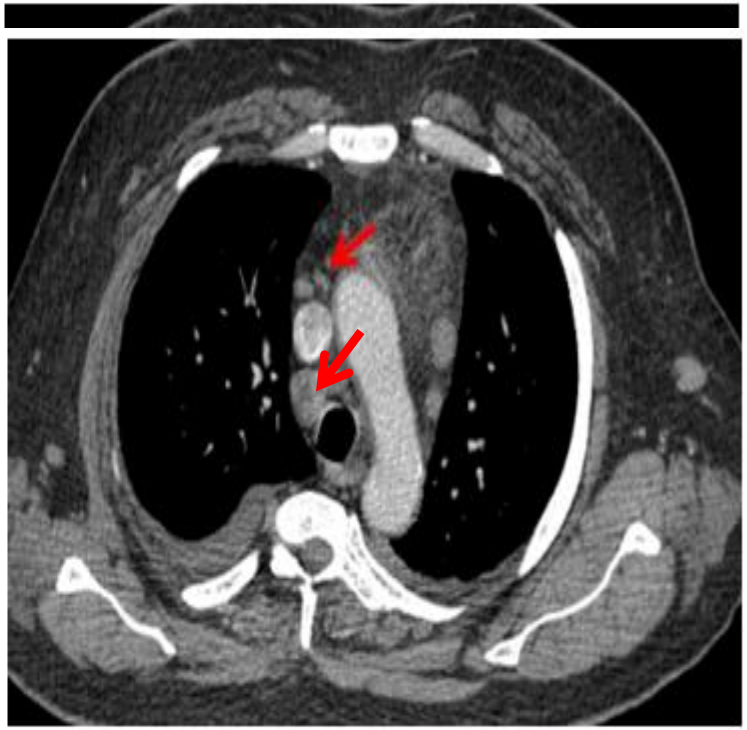


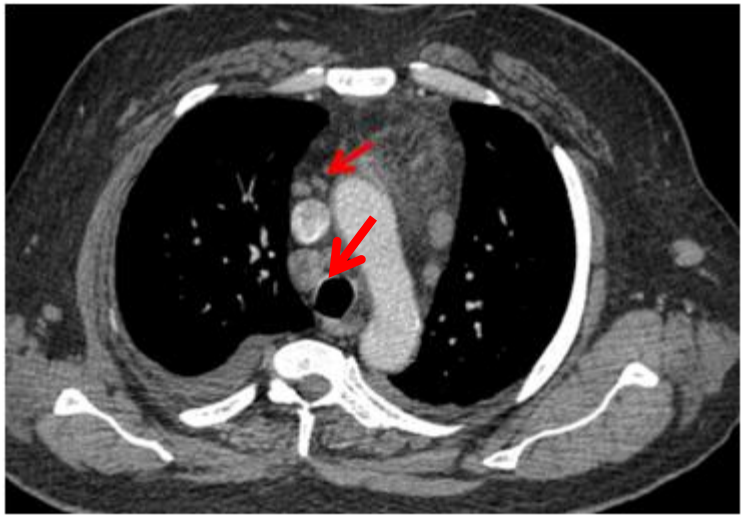


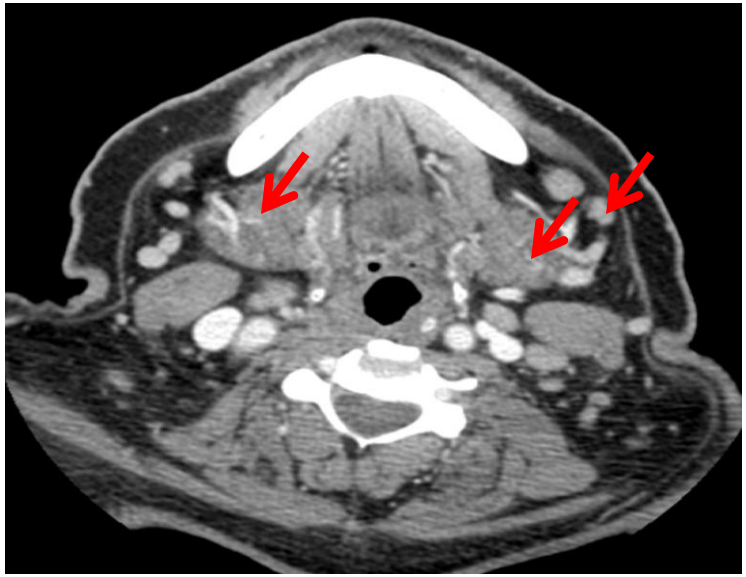


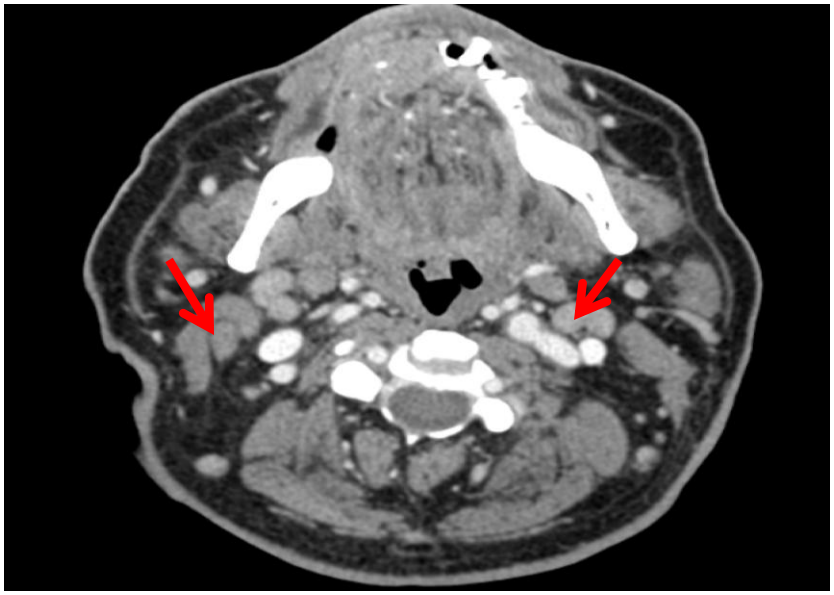
Δ/Δ Αρβανιτάκη Αλεξάνδρα

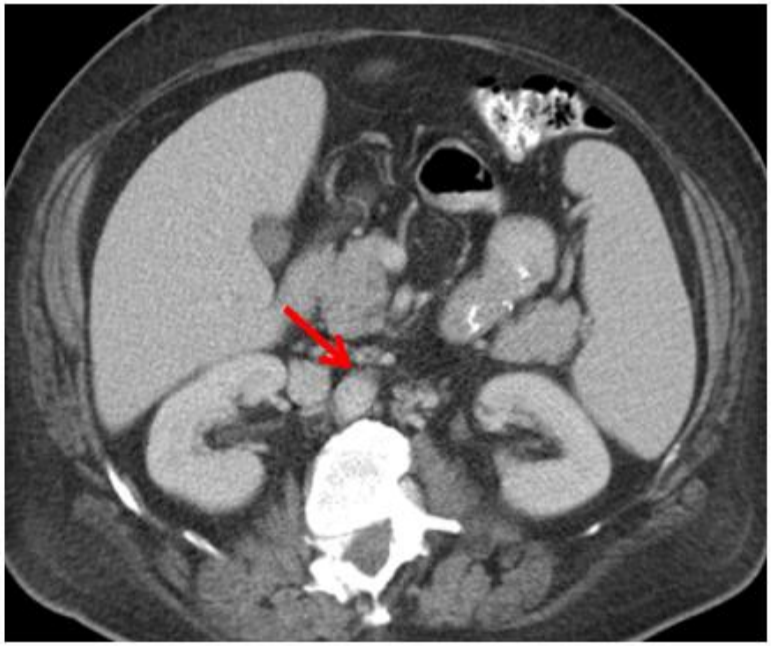


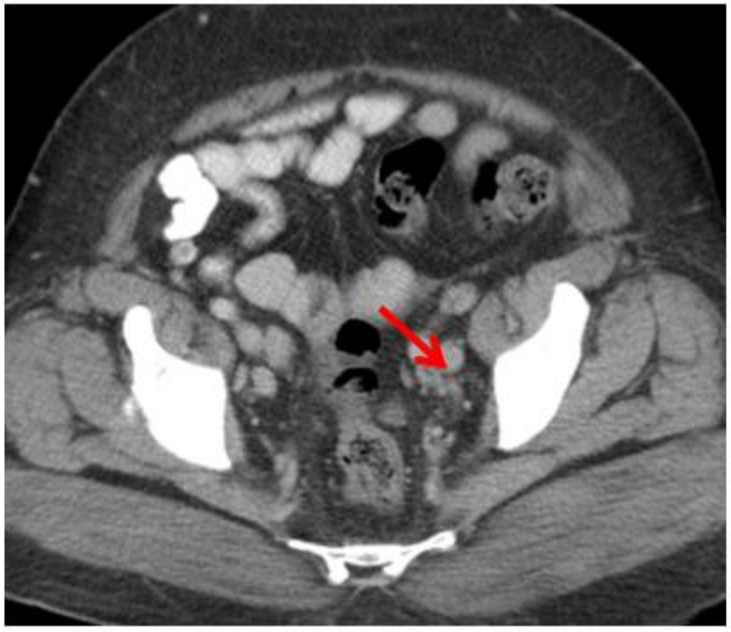




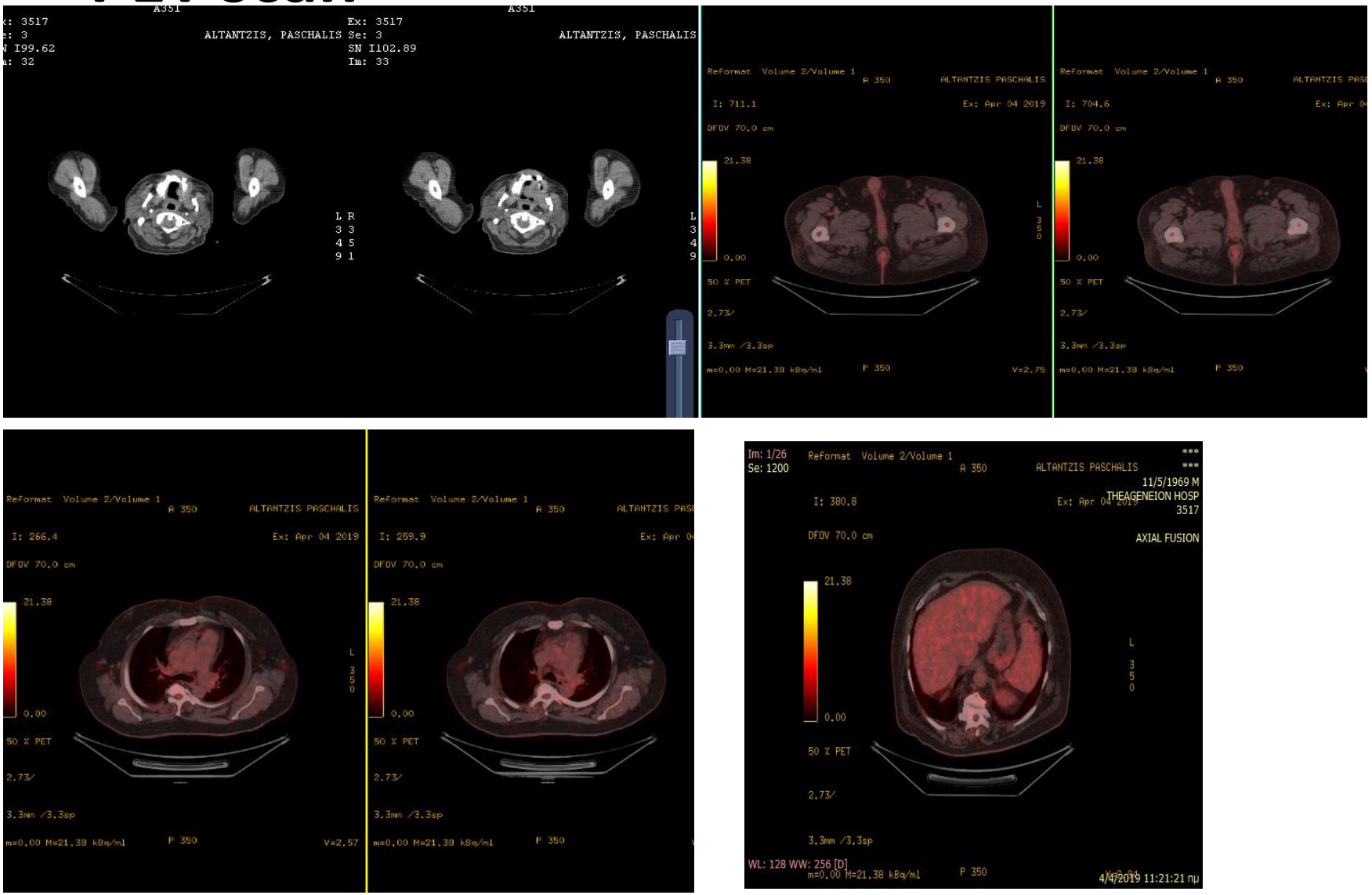








PET scan



Χαμηλού βαθμού μεταβολική δραστηριότητα σε μικρού οριακού μεγέθους λεμφαδένες (αντιδραστικής αιτιολογίας στα πλαίσια ΣΕΛ)

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RESEARCH ARTICLE Open Access

Incidence and survival impact of pulmonary arterial hypertension among patients with systemic lupus erythematosus: a nationwide cohort study

Chen et al. Arthritis Research & Therapy (2019) 21:82

15783 SLE patients, 336 (2,13%) identified with PAH

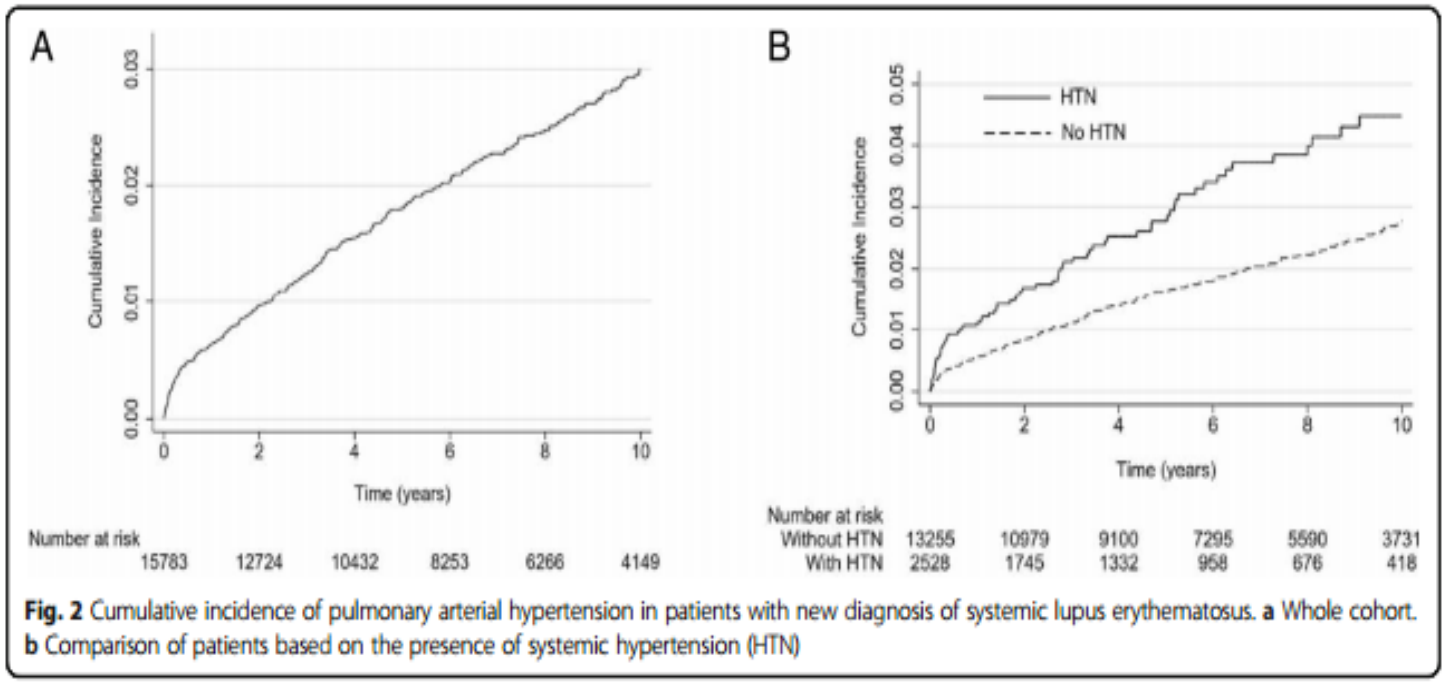

Fig. 2 Cumulative incidence of pulmonary arterial hypertension in patients with new diagnosis of systemic lupus erythematosus. **a** Whole cohort. **b** Comparison of patients based on the presence of systemic hypertension (HTN)

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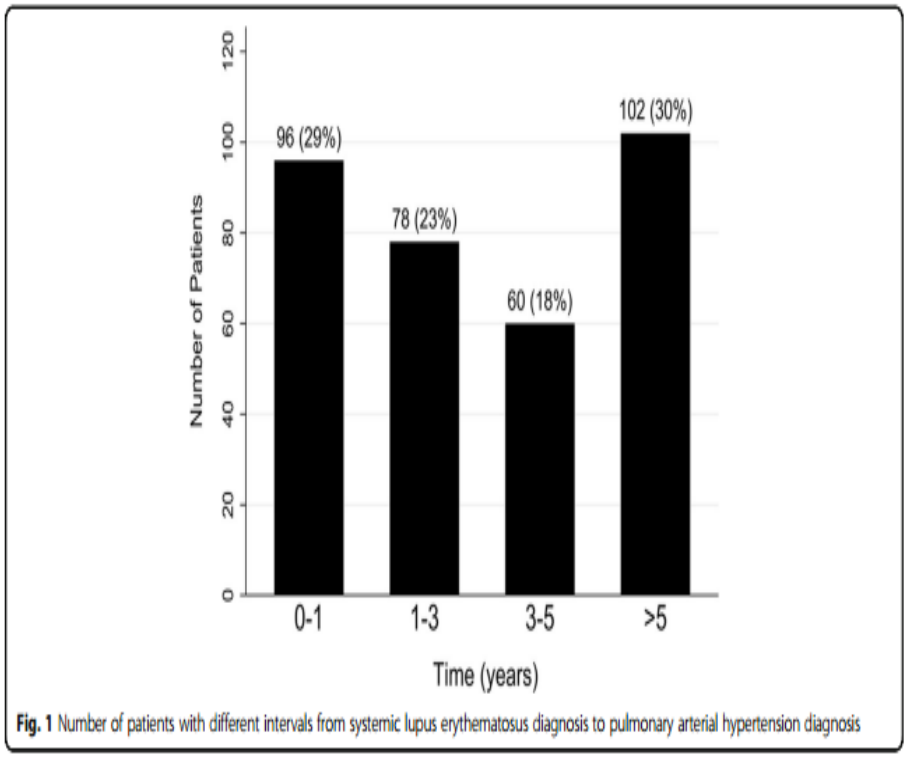


Fig. 1 Number of patients with different intervals from systemic lupus erythematosus diagnosis to pulmonary arterial hypertension diagnosis

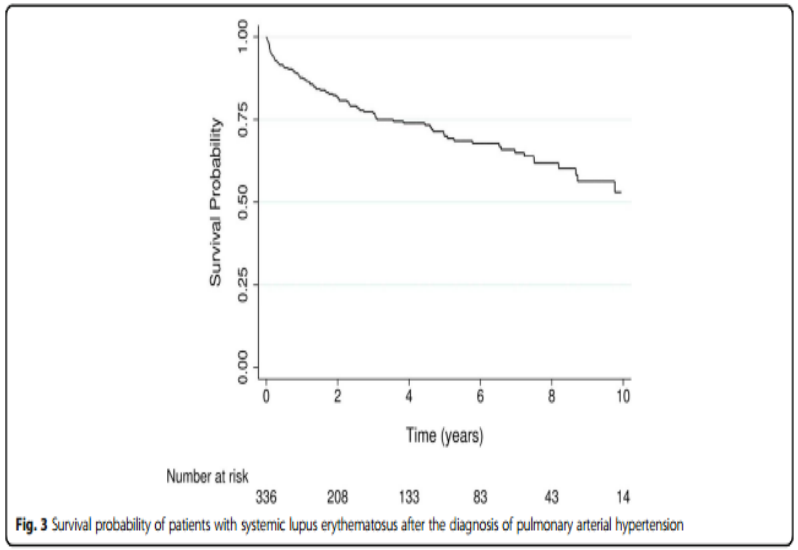


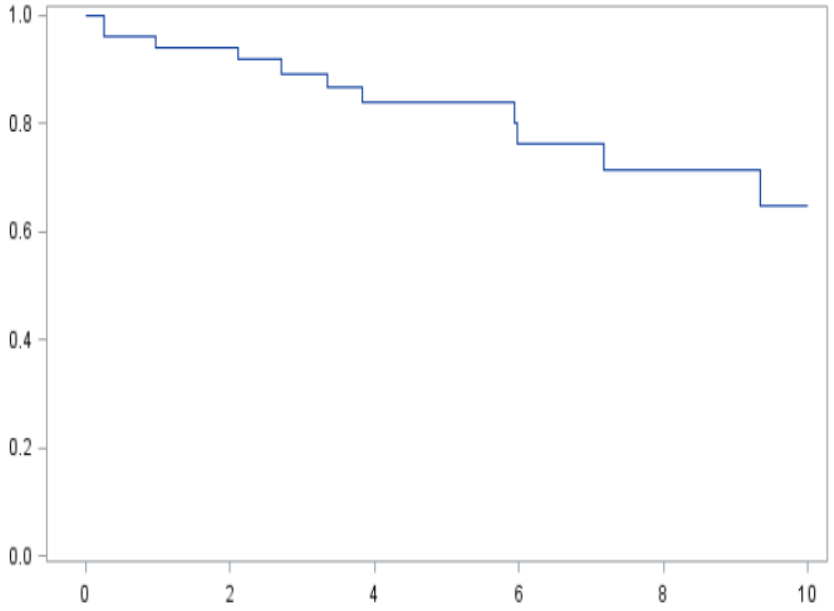
Fig. 3 Survival probability of patients with systemic lupus erythematosus after the diagnosis of pulmonary arterial hypertension

The survival rates at 3 and 5 years after the diagnosis of PAH were 76.8% and 70.1%, respectively

Chest. 2018 Jan;153(1):143-151. doi: 10.1016/j.chest.2017.08.014. Epub 2017 Aug 26.

Pulmonary Arterial Hypertension Associated With Systemic Lupus Erythematosus: Results From the French Pulmonary Hypertension Registry.

Hachulla E[1], Jais X[2], Cinquetti G[3], Clerson P[4], Rottat L[2], Launay D[5], Cottin V[6], Habib G[7], Prevot G[8], Chabanne C[9], Foïs E[10], Amoura Z[11], Mouthon L[12], Le Guern V[12], Montani D[2], Simonneau G[2], Humbert M[2], Sobanski V[5], Sitbon O[2]; French Collaborators Recruiting Members(*).



Three and five-year overall survival rates were 89.4% and 83.9%

Years	0	1	2	3	4	5	6	7	8	9	10
N at risk	51	47	44	35	30	27	20	17	14	13	10

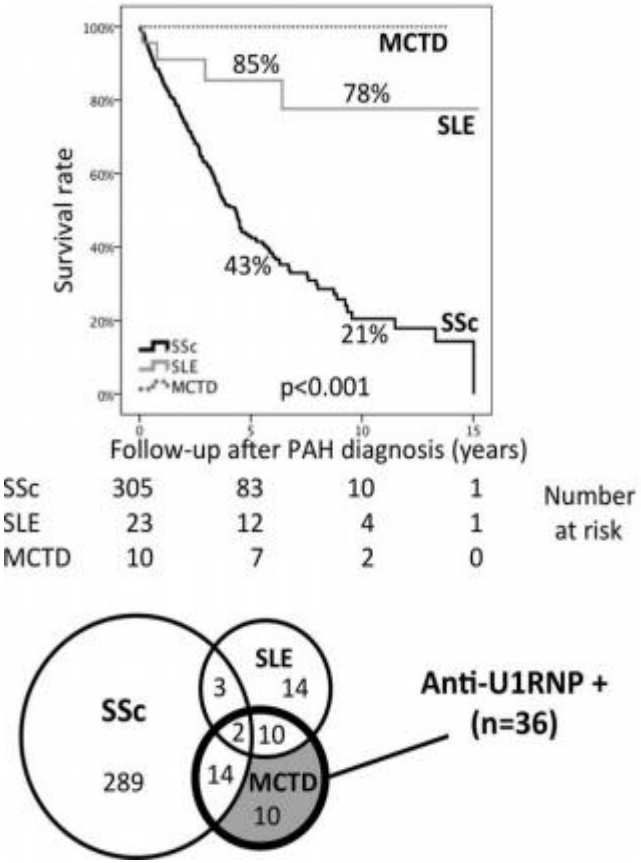
	HR	95% CI	p
Lupus nephritis	12.71	[2.07;60.52]	0.001
Cardiac involvement*	1.92	[0.49;7.46]	0.35
IgG anticardiolipin antibodies	1.48	[0.43;5.01]	0.53
Anti-U1-RNP antibodies**	-	-	0.04
Anti-SSA antibodies	0.34	[0.08;1.44]	0.14
Anti-SSB antibodies***	-	-	0.17
NYHA III-IV	0.80	[0.25;2.93]	0.80
6-min walk distance (by 10 m)	0.97	[0.90;1.05]	0.47
DLCO (% of predicted)	0.98	[0.92;1.03]	0.36
mPAP (mmHg)	1.02	[0.98;1.07]	0.36
PVR (by 80 dyn.sec.cm-5)	1.23	[1.08;1.41]	0.002
Treatment with hydroxychloroquine	0.31	[0.09;1.11]	0.07

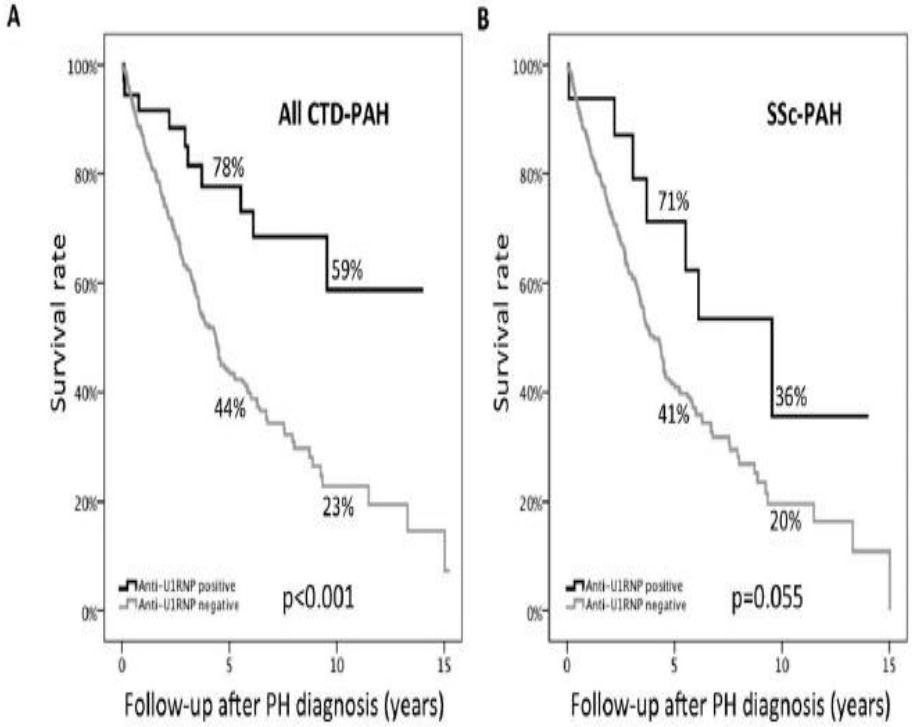
Arthritis & Rheumatology
AN OFFICIAL JOURNAL OF THE AMERICAN COLLEGE OF RHEUMATOLOGY

Characteristics and Survival of Anti–U1 RNP Antibody–Positive Patients With Connective Tissue Disease–Associated Pulmonary Arterial Hypertension

Vincent Sobanski,[1] Jonathan Giovannelli,[2] Bernadette M. Lynch,[3] Benjamin E. Schreiber,[3] Svetlana I. Nihtyanova,[3] Jennifer Harvey,[3] Clive E. Handler,[3] Christopher P. Denton,[3] and John G. Coghlan[3]

February 2016, pp 484–493



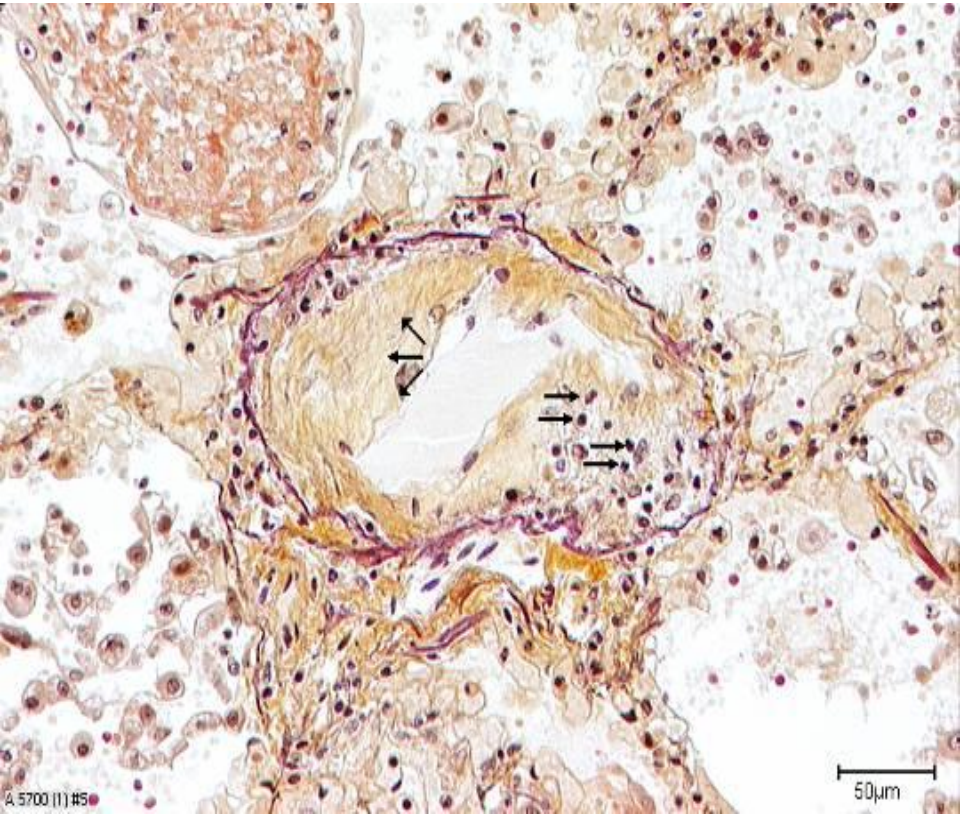


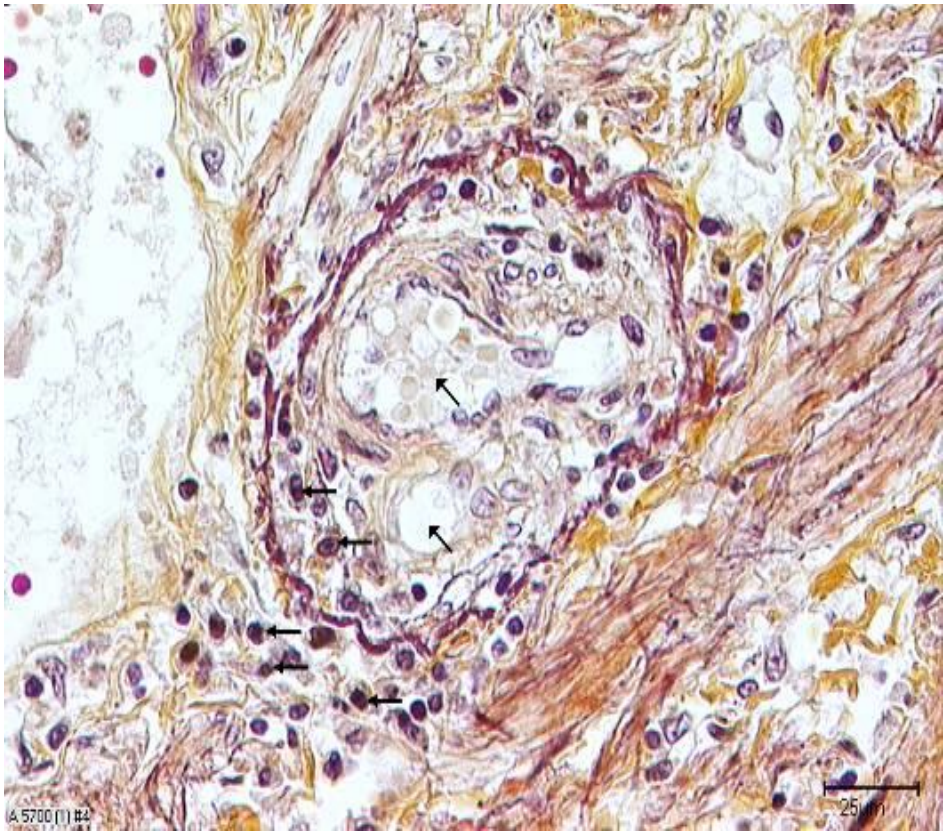
Anti-U1RNP		Number at risk		
- Positive	36	18	6	0
- Negative	302	84	10	1

Anti-U1RNP		Number at risk		
- Positive	16	8	2	0
- Negative	289	75	8	1

SLE-PAH

- ***Μεγαλύτερη συμμετοχή φλεγμονωδών κυττάρων***
- ***Ανοσοσυμπλέγματα***
- ***Παραγωγή κυτοκινών***





ΜΕΓΑΛΥΤΕΡΗ ΣΥΜΜΕΤΟΧΗ ΤΗΣ ΑΥΤΟΑΝΟΣΙΑΣ ΣΤΗΝ ΑΝΑΔΙΑΜΟΡΦΩΣΗ ΤΟΥ ΠΝΕΥΜΟΝΙΚΟΥ ΑΓΓΕΙΑΚΟΥ ΔΕΝΤΡΟΥ

RHEUMATOLOGY

Pulmonary arterial hypertension in systemic lupus erythematosus may benefit by addition of immunosuppression to vasodilator therapy: an observational study

2015 Sep;54(9):1673-9

Sirisha Kommireddy[1], Srinivas Bhyravavajhala[2], Kishorebabu Kurimeti[1], Srinivasa Chennareddy[1], Suresh Kanchinadham[1], Irlapati Rajendra Vara Prasad[1] and Liza Rajasekhar[1]

24 SLE patients received CYC for various reasons (nephritis, severe lung ,CNS involvement etc)

TABLE 5 Comparison of baseline clinical and haemodynamic characteristics between responders and non-responders

	Responders ($n = 11$)	Non-responders ($n = 13$)	P-value
Age, mean (S.D.), years	27.18 (9.62)	23.84 (6.42)	0.19
Duration of SLE, median (range), months	60 (1–144)	18 (4–168)	0.11
Duration of PAH in months, median (range)	3 (0–36)	1 (0–12)	0.23
NYHA functional class			
Classes III and IV	9	4	
Classes I and II	1	5	
Asymptomatic	1	4	
Right ventricular systolic pressure, mean (S.D.), mmHg	64.45 (16.90)	52.46 (22.41)	0.38
SLEDAI before immunosuppression, mean (S.D.)	14.43 (7.21)	14.73 (9.87)	0.94

NYHA: New York Heart Association; PAH: pulmonary arterial hypertension.

Prognosis

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 ≥45
NT-proBNP plasma levels	BNP <50 ng/l NT-proBNP <300 ng/ml	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%

European Heart Journal
doi:10.1093/eurheartj/ehv317

Treatment

- **Ambrisentan 5 mg 1x1**
- **Tadalafil 20mg 2x1**
- Furosemide 40mg 1/2x2
- Plaquenil 1*2
- IV methylprednisolone 500mg x 3
- **Έναρξη κυκλοφωσφαμίδης iv**
- Prezolon 5mg 3*1

Follow-Up

	1st Visit	M 6	M 9
WHO	II	II	I
6MWD	400	485	500
NT-proBNP	2131	1606	830
RHC mRAP (mmHg) mPAP (mmHg) PCWP (mmHg) PVR (Woods) CI (L/min/m²) SVO_2 (%) Hb (g/dL)	 **4** 41 10 6,7 **2,4** **64** 10,8		 **9** 39 10 3,6 **4,2** **73** 12,3
ECHO TAPSE (cm) RA area (cm²) RVSP (mmHg) P.Effusion (cm)	 2,2 21.5 72 Mild	 2,2 21.5 67 Mild	

HB (g/L)	9,5↓	11,9
WBC	7,2(54/30/8)	4,93
PLT/µl	220000	230000
TKE	85↑	25
CRP (mg/l)	0,5	0,8

Month 9

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
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WHO functional class	I, II	III	IV
6MWD	>440 m	165–440 m	<165 m
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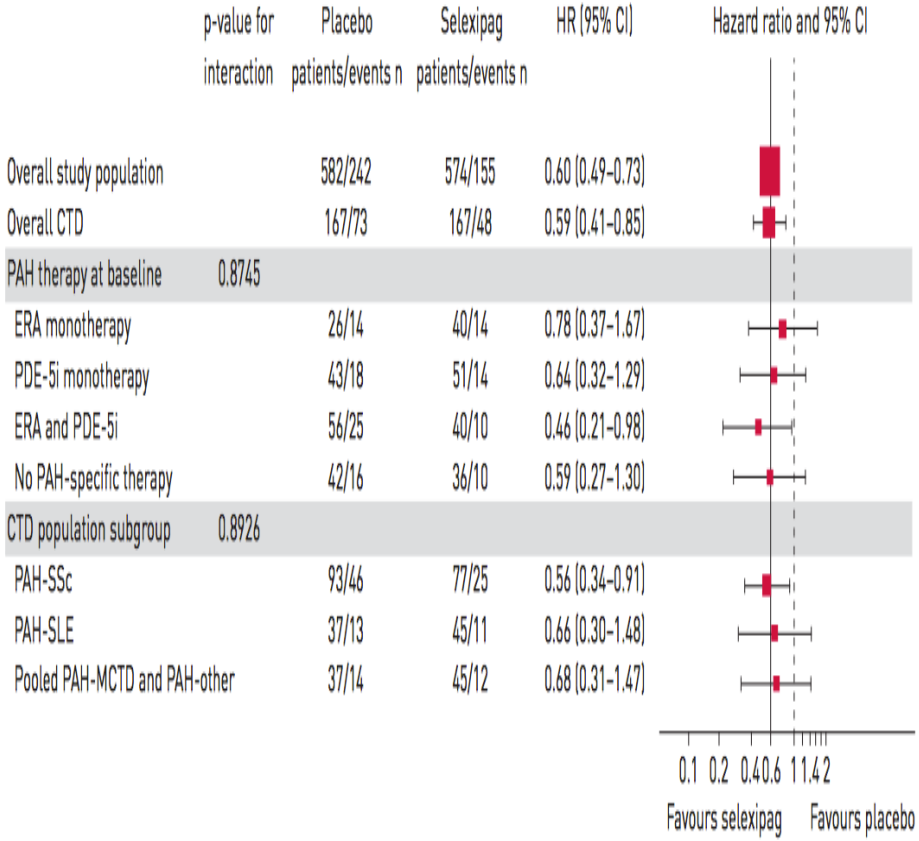
NT-proBNP plasma levels	BNP <50 ng/l NT-proBNP <300 ng/ml	BNP 50–300 ng/l NT-proBNP 300–1400 ng/l	BNP >300 ng/l NT-proBNP >1400 ng/l
Imaging (echocardiography, CMR imaging)	RA area <18 cm^2 No pericardial effusion	RA area 18–26 cm^2 No or minimal, pericardial effusion	RA area >26 cm^2 Pericardial effusion
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%

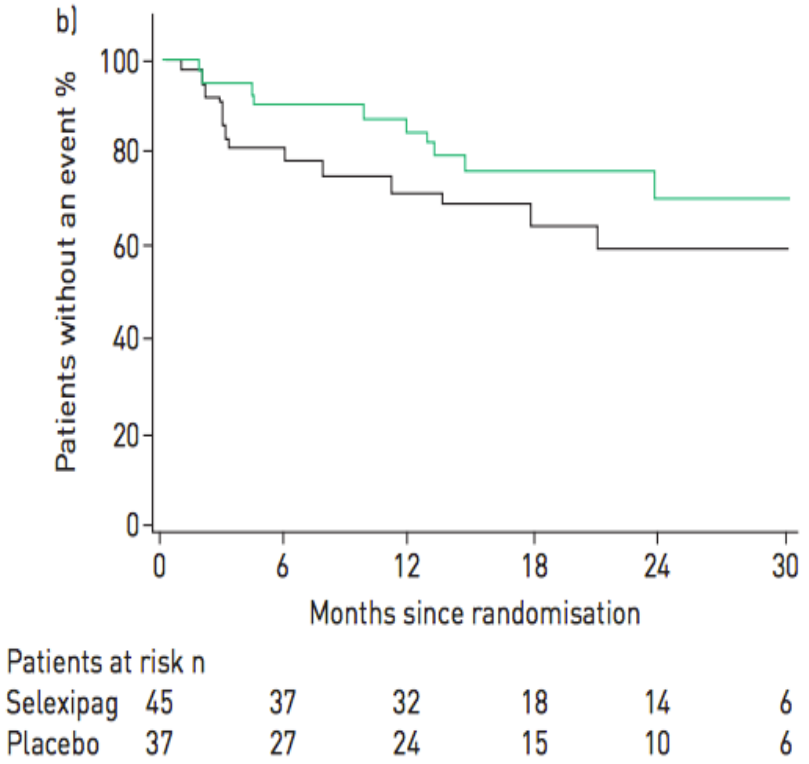
European Heart Journal
doi:10.1093/eurheartj/ehv317

Eur Respir J. 2017 Aug 17;50(2). pii: 1602493. doi: 10.1183/13993003.02493-2016. Print 2017 Aug.

Selexipag for the treatment of connective tissue disease-associated pulmonary arterial hypertension.

Gaine S[1], Chin K[2], Coghlan G[3], Channick R[4], Di Scala L[5], Galiè N[6], Ghofrani HA[7,8,9], Lang IM[10], McLaughlin V[11], Preiss R[5], Rubin LJ[12], Simonneau G[13,14,15], Sitbon O[13,14,15], Tapson VF[16], Hoeper MM[17].





Treatment

- Ambrisentan 5mg 1x1
- Tadalafil 20mg 2x1
- **Selexipag 200mg bid**

- Plaquenil 1*2
- Prezolon 5mg 2*1

  Azathioprine 50 1*3

ΣΥΜΠΕΡΑΣΜΑΤΑ

- Η ΡΑΗ σε ασθενείς με ΣΕΛ αποτελεί μία ιδιαίτερη κατηγορία ασθενών με CTD-PAH που αναγνωρίζεται τα τελευταία χρόνια
- Η συμμετοχή της αυτοανοσίας πιθανόν να είναι μεγαλύτερη στους ασθενείς αυτούς σε σχέση με τη SSc-PAH
- Η ανοσοκατασταλτική αγωγή σε συνδυασμό με τα αγγειοδιασταλτικά έχει θέση στην αντιμετώπιση της ΡΑΗ στους ασθενείς με ΣΕΛ αλλά είναι επιτακτική η ανάγκη συλλογής δεδομένων κυρίως από μεγάλες προοπτικές μελέτες κα βάσεις δεδομένων.


Спасибо
Gracias
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Dziękuję
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Diolch
Thank
You
Merci
Ngiyabonga
Tack
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Danke
Grazie
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