Diagnostic de l'endocardite: au-delà des critères de Duke ?

Résultats PHRC TEPvENDO

Xavier Duval
pour le groupe d'étude TEPvENDO

Déclaration de liens d'intérêt avec les industries de santé en rapport avec le thème de la présentation (loi du 04/03/2002) :

Intervenant : Duval Xavier

Titre: Résultats PHRC TEPvENDO

- L'orateur ne souhaite pas répondre ☐

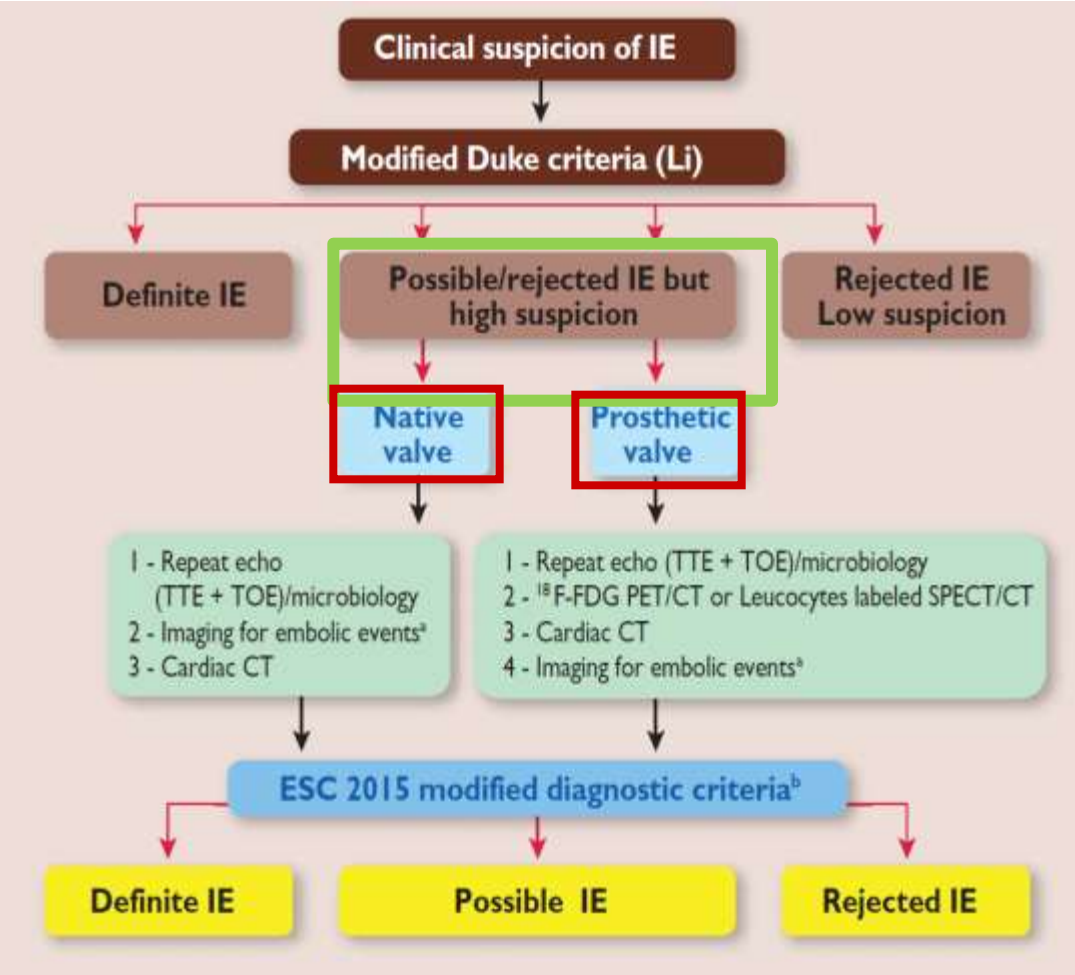
Consultant ou membre d'un conseil scientifique	☐ OUI	☑ NON
Conférencier ou auteur/rédacteur rémunéré d'articles ou documents	☐ OUI	☑ NON
Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès ou autres manifestations	☐ OUI	☑ NON
Investigateur principal d'une recherche ou d'une étude clinique	☑ OUI	☐ NON

Background

- **Difficult IE diagnosis**
- **Monocentric studies: 18^{F}-FDG PET/CT improves IE diagnosis**
- **ESC 2015 Recommendations**
  - Duke Classification as a diagnostic pathway
  - Integration of 18F-FDG PET/CT results in Duke classification

ESC 2015

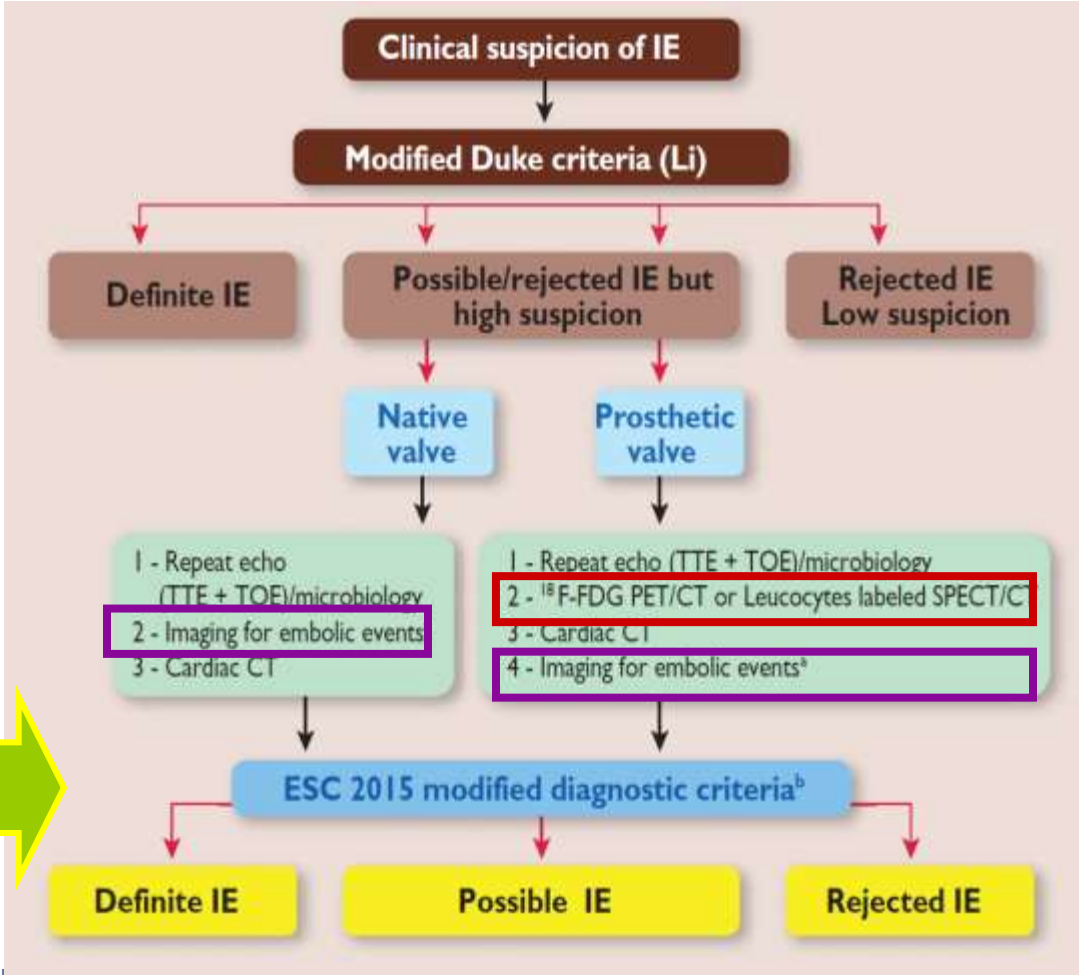
Diagnosis



Diagnosis

Imaging techniques

Nuclear imaging



To apply

ESC-2015 modified diagnostic criteria

Major criteria	
1. Blood cultues positive for IE a. Typical microorganisms consistent with IE from 2 separate blood cultures: • *Viridans streptococci, Streptococcus gallolyticus (Streptococcus bovis), HACEK group, Staphylococcus aureus;* or • Community-acquired enterococci, in the absence of a primary focus; or b. Microorganisms consistent with IE from persistently positive blood cultures: • ≥2 positive blood cultures of blood samples drawn >12 h apart; or • All of 3 or a majority of ≥4 separate cultures of blood (with first and last samples drawn ≥1 h apart); or c. Single positive blood culture for Coxiella burnetii or phase I IgG antibody titre >1:800	**2. Imaging positive for IE** a. Echocardiogram positive for IE: • Vegetation; • Abscess, pseudoaneurysm, intracardiac fistula; • Valvular perforation or aneurysm; • New partial dehiscence of prosthetic valve. b. Abnormal activity around the site of prosthetic valve implantation detected by ^{18}F-FDG PET/CT (only if the prosthesis was implanted for >3 months) or radiolabelled leukocytes SPECT/CT. c. Definite paravalvular lesions by cardiac CT.

More study is needed to define the utility of ^{18}F-fluoro-deoxyglucose positron emission tomography/CT in the diagnosis and management of IE.

American Heart Association®

ACC/AHA 2015

ESC-2015 modified diagnostic criteria

Major criteria

1. Blood cultues positive for IE

a. Typical microorganisms consistent with IE from 2 separate blood cultures:
- *Viridans streptococci, Streptococcus gallolyticus (Streptococcus bovis), HACEK group, Staphylococcus aureus;* or
- Community-acquired enterococci, in the absence of a primary focus; or

b. Microorganisms consistent with IE from persistently positive blood cultures:
- ≥2 positive blood cultures of blood samples drawn >12 h apart; or
- All of 3 or a majority of ≥4 separate cultures of blood (with first and last samples drawn ≥1 h apart); or

c. Single positive blood culture for Coxiella burnetii or phase I IgG antibody titre >1:800

2. Imaging positive for IE

a. Echocardiogram positive for IE:
- Vegetation;
- Abscess, pseudoaneurysm, intracardiac fistula;
- Valvular perforation or aneurysm;
- New partial dehiscence of prosthetic valve.

b. Abnormal activity around the site of prosthetic valve implantation detected by ^{18}F-FDG PET/CT (only if the prosthesis was implanted for >3 months) or radiolabelled leukocytes SPECT/CT.

c. Definite paravalvular lesions by cardiac CT.

Minor criteria

1. Predisposition such as predisposing heart condition, or injection drug use.
2. Fever defined as temperature >38°C.
3. Vascular phenomena (including those detected by imaging only) major arterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions.
4. Immunological phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor.
5. Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE.

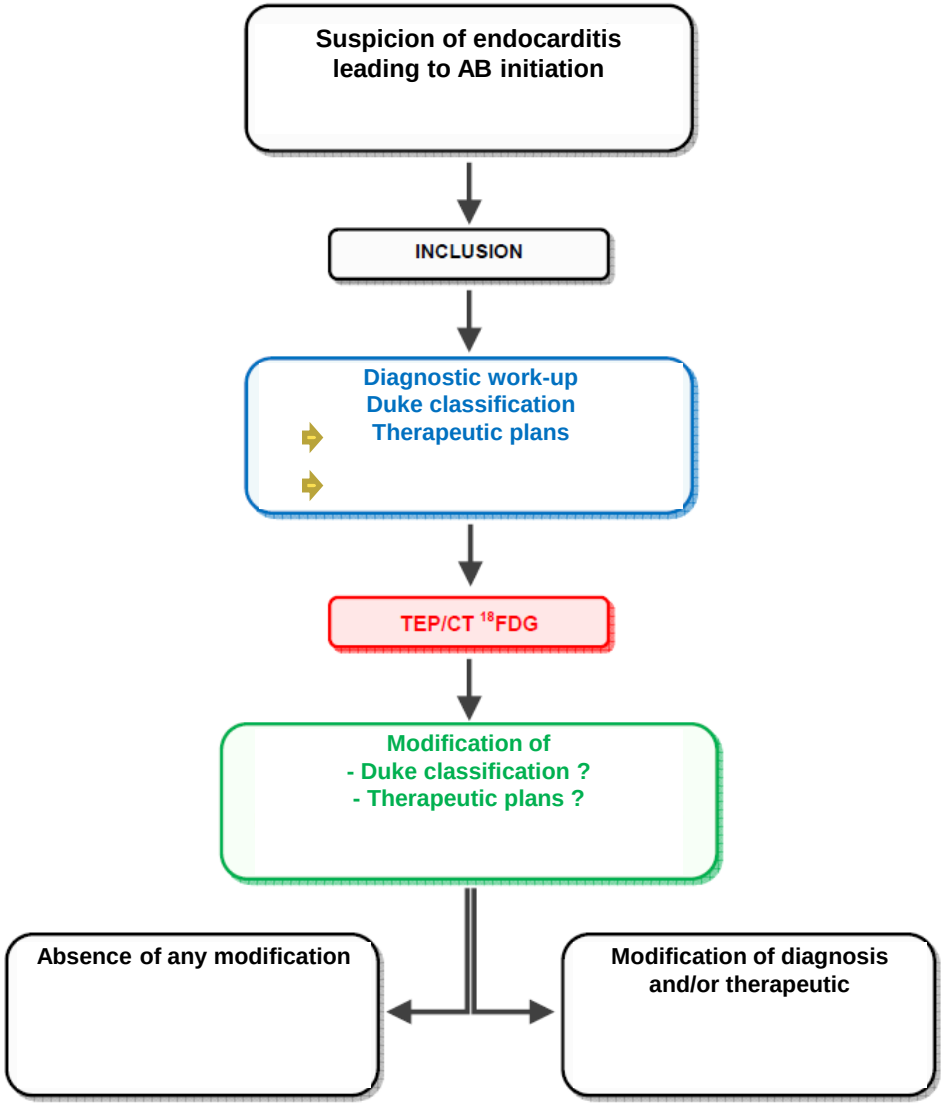
Background

- EI Difficultés diagnostic
- Monocentric studies: 18^{F}-FDG PET/CT improves IE diagnosis
- ESC 2015 Recommandations
  - Duke Classification as a diagnostic pathway
  - Integration of 18F-FDG PET/CT results in Duke classification
- **18^{F}-FDG PET/CT : False positif (93%) in patients with prosthetic valves without IE** (Mathieu C; Circ Cardiovasc Imaging 2017)

TEPvENDO protocol

- **Prospective multicenter protocol**
- **Systematic 18^{F}-FDG PET/CT within 7 days**
- **Quantification of the impact of systematic FDG-PET**
  - on diagnosis
  - on therapeutic plans
- **Inclusion of consecutive adults with high suspicion of IE leading to the initiation of IE antibiotic treatment**
- **Written informed consent**

TEPvENDO study design



Interobserver variability

- Harmonization strategy conducted before study onset
- 17 clinical cases of IE suspected pts (PET images)
- Read by 8 nuclear medicine specialists originating from 8 different hospitals
- Interpretation: IE probable, doubtful, excluded

Interobserver variability

- **Harmonization strategy conducted before study onset**
- **17 clinical cases of IE suspected pts (PET images)**
- **Read by 8 nuclear medicine specialists originating from 8 different hospitals**
- **Interpretation: IE probable, doubtful, excluded**
- **Agreement among the 8 readers:**
  - **3/17** clinical cases: **total agreement**
  - **14/17** clinical cases: **disagreement**
    - Minor (excluded versus doubtful or doubtful versus definite)
      n=4
    - Major (at least 2 readers with extreme disagreement (excluded versus definite)
      n=10

Training session

Results

- **Inclusion of 140 pts (March 2015 to Sept 2016)**
  - **70 pts** with native valves
  - **70 pts** with ≥ 1 prosthetic valve
- **Mean age: 65 years (± 15); 74% male**
- **History of IE in 26 pts (19%)**
- **Blood culture**
  - positive in 113 pts (81%)
  - fulfilled Major duke criteria definition in 94 pts (67%)
- **Echocardiography:**
  - Major duke criteria in 87 pts (62%)

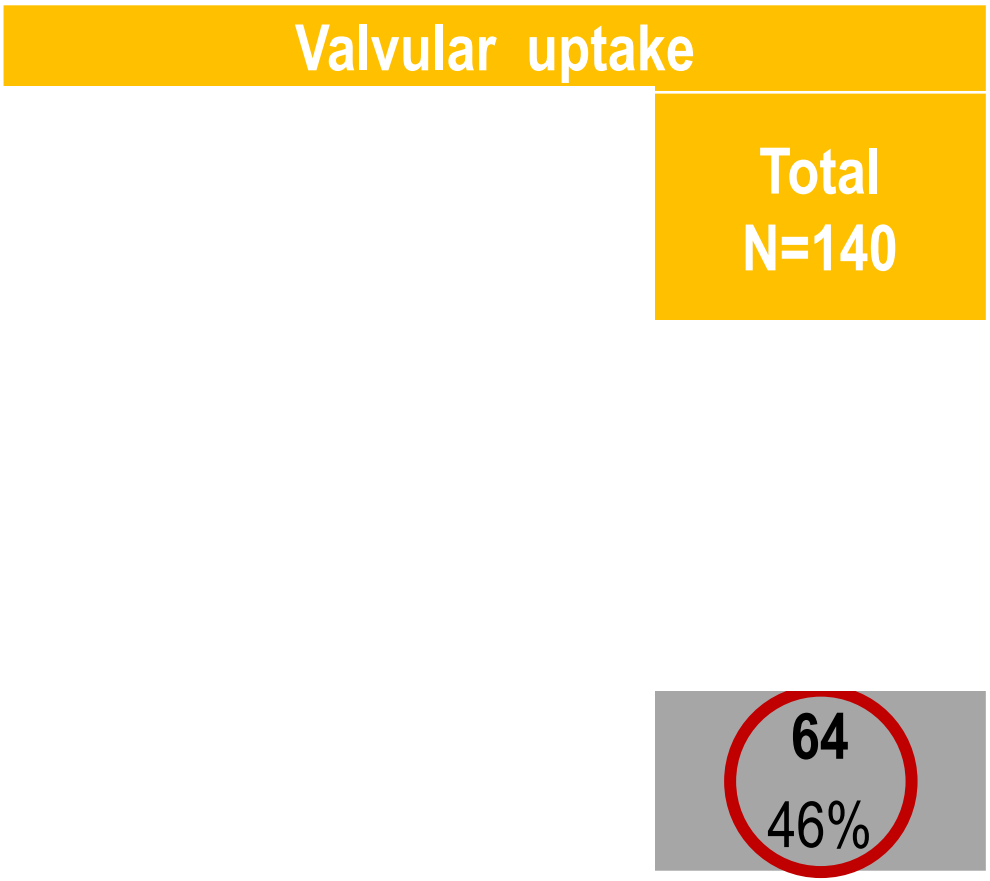
Results

- **Duke classification before FDG-TEP**
  - **Definite IE N= 80 pts (57%)**
    - Prosthetic valve pts 34 pts **(49%)**
    - Native valve pts 46 pts **(66%)**
  - Possible IE N= 56 pts (40%)
    - Prosthetic valve pts 33 pts (47%)
    - Native valve pts 23 pts (33%)

FDG-TEP results

- **Cardiac uptake**

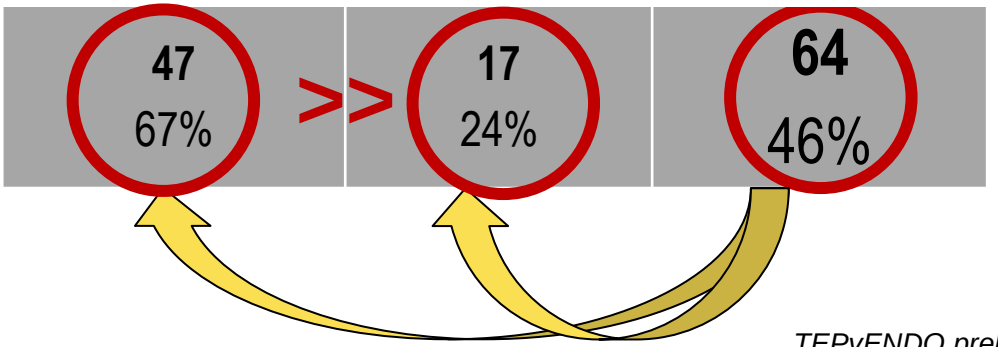
Cardiac valve uptake (N=140 pts)



TEPvENDO preliminary results

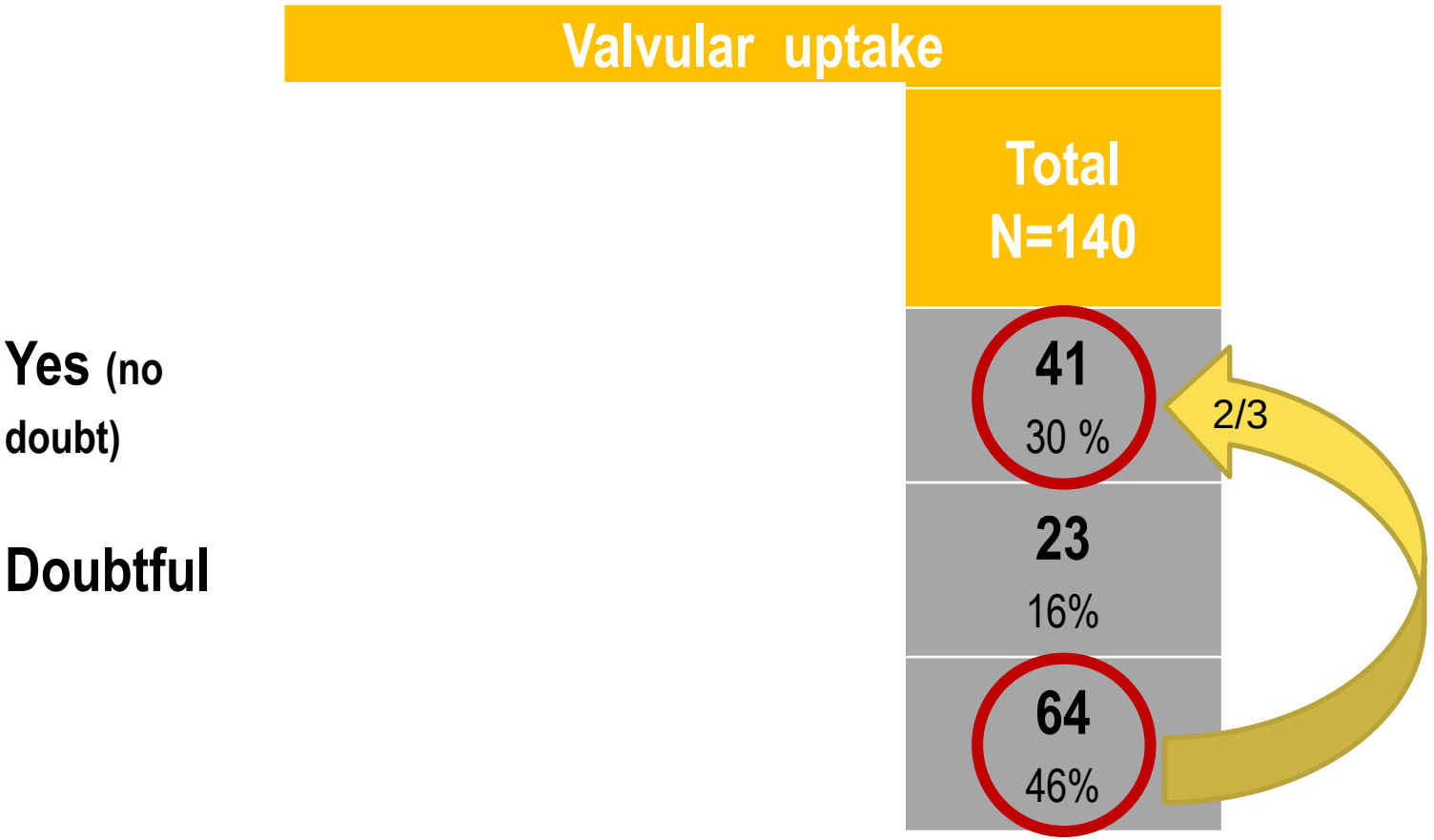
Cardiac valve uptake (N=140 pts)

Valvular uptake		
Prosthetic valve pts N=70 	Native valve pts N=70	Total N=140



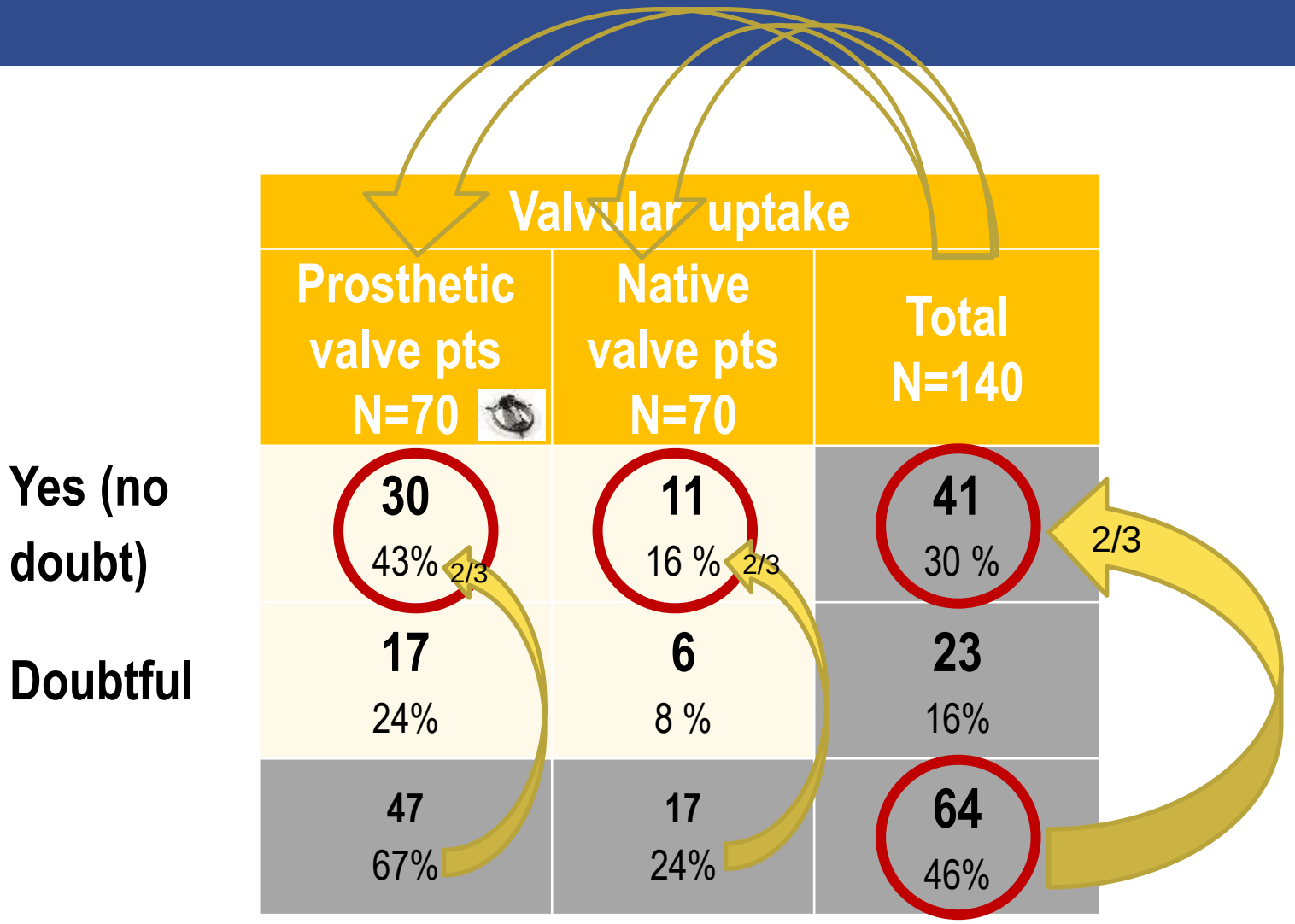
TEPvENDO preliminary results

Cardiac valve uptake (n=140 pts)



TEPvENDO preliminary results

Cardiac valve uptake (n=140 pts)

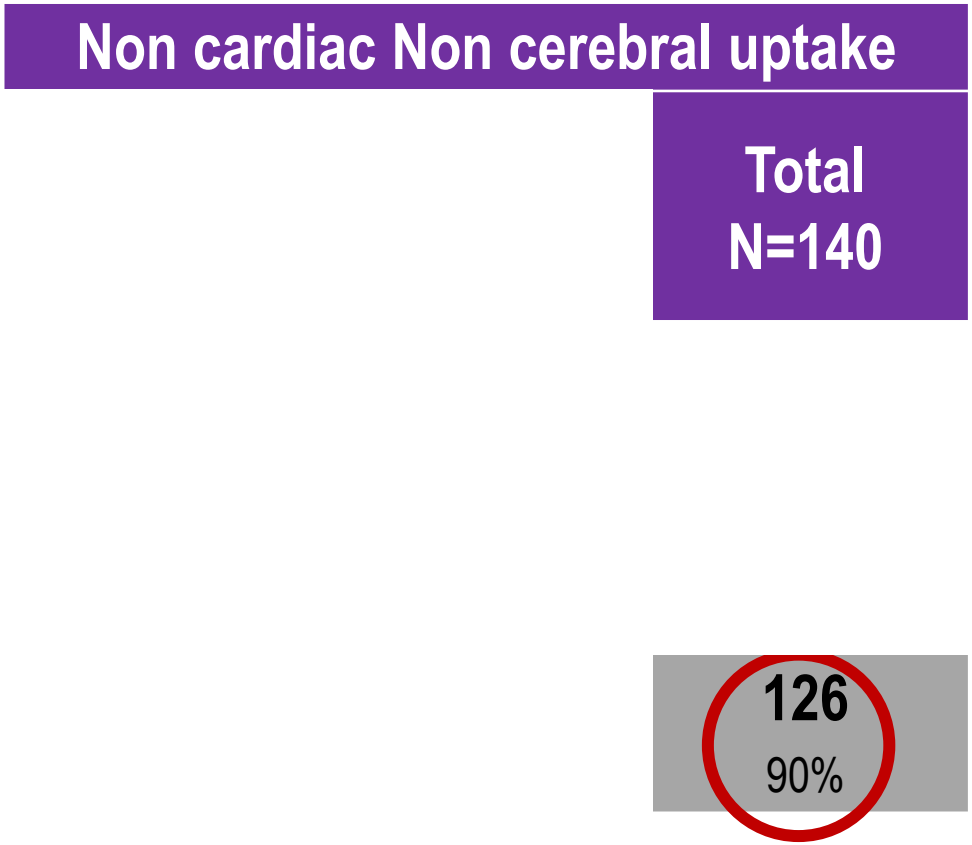


TEPvENDO preliminary results

FDG-TEP results

- **Extra Cardiac uptake**
  - Extra cerebral

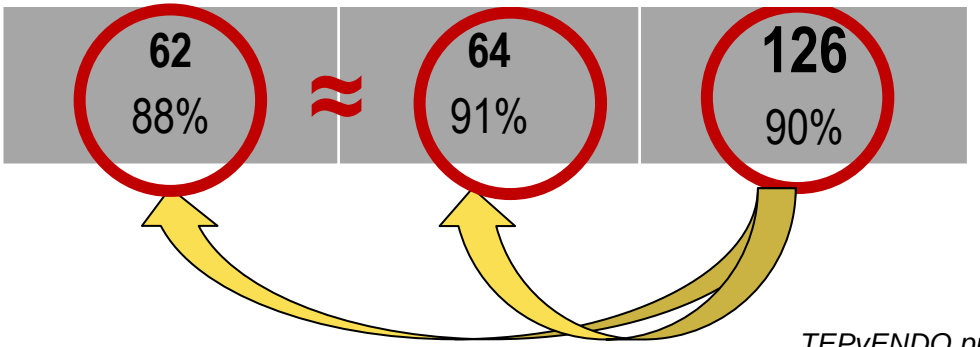
Non cardiac Non cerebral uptake (N=140 pts)



TEPvENDO preliminary results

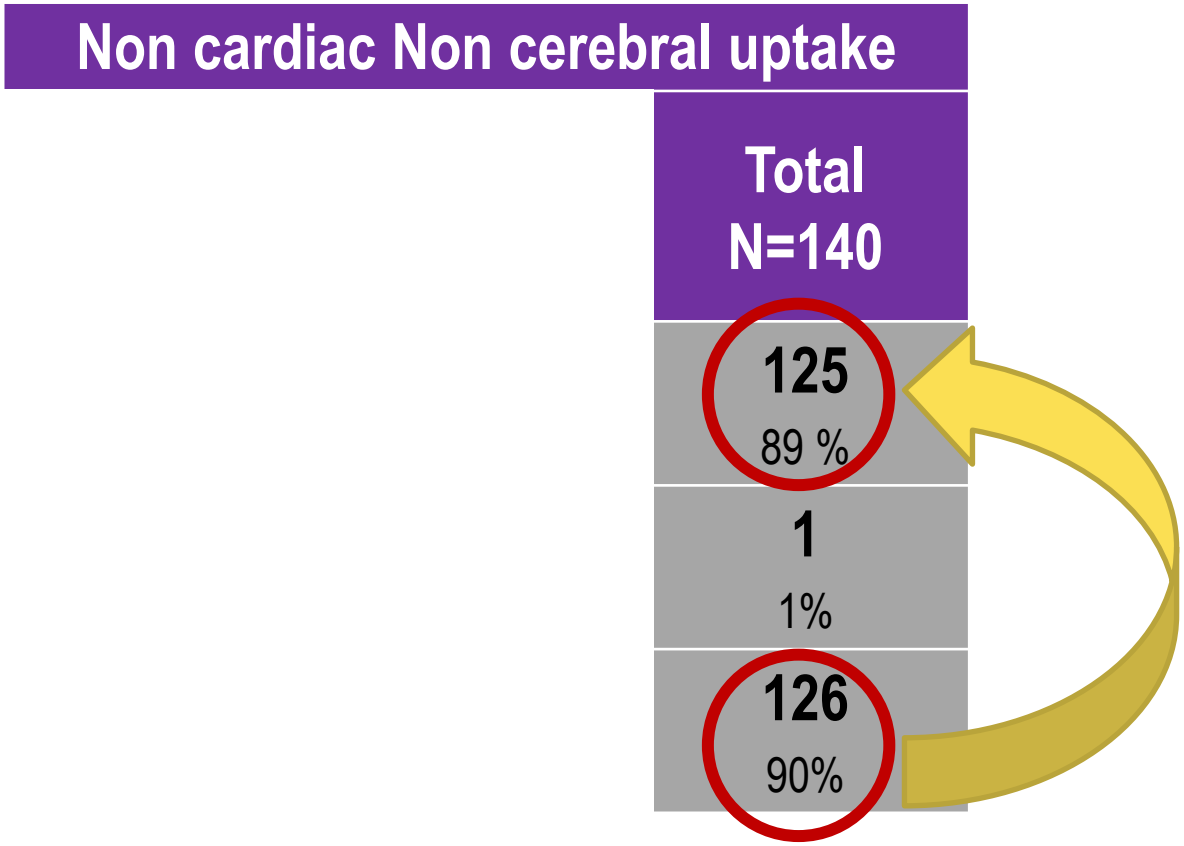
Non cardiac Non cerebral uptake (N=140 pts)

Non cardiac Non cerebral uptake		
Prosthetic valve pts N=70	Native valve pts N=70	Total N=140



TEPvENDO preliminary results

Non cardiac Non cerebral uptake (N=140 pts)



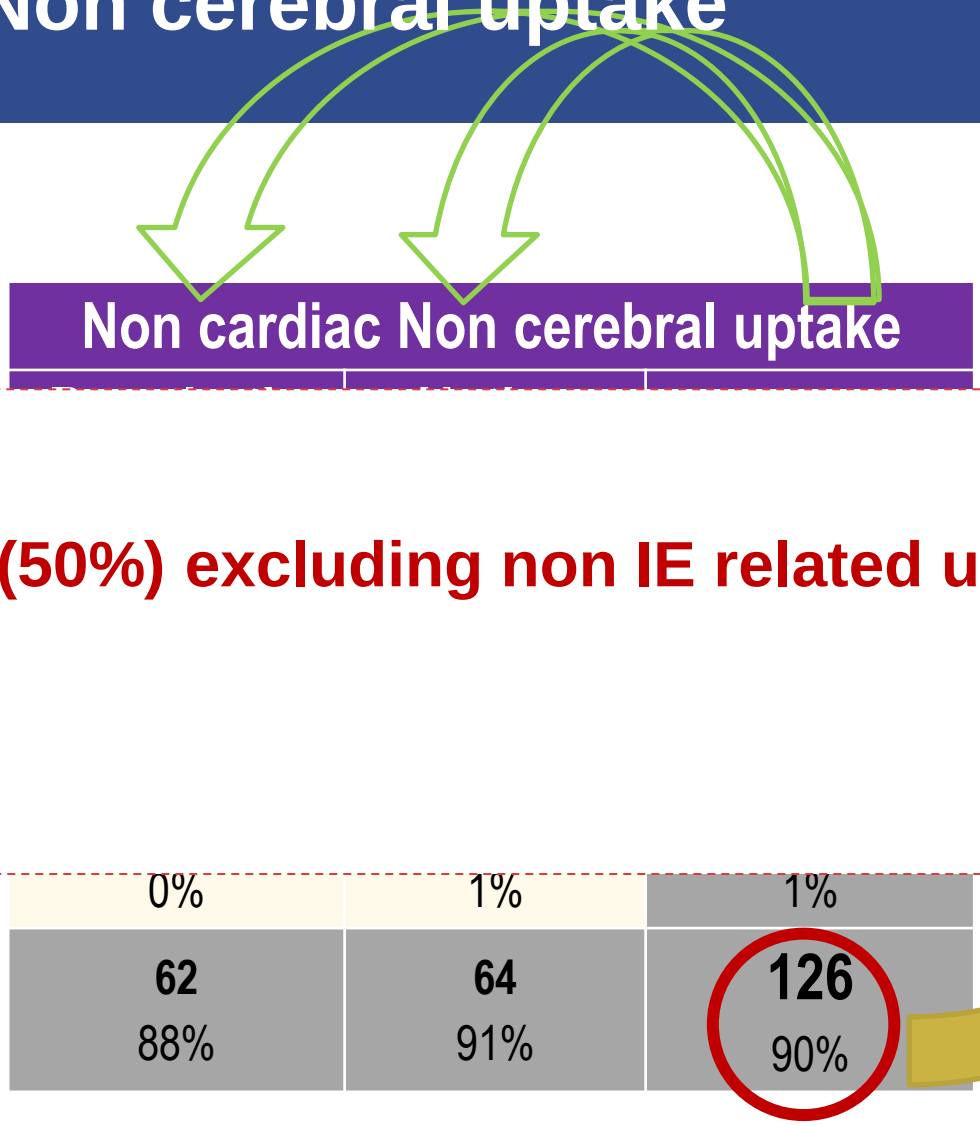
TEPvENDO preliminary results

Non cardiac Non cerebral uptake

Non cardiac Non cerebral uptake	Prosthetic valve pts N=70	Native valve pts N=70	Total N=140
Yes	62 88%	≈ 63 90 %	125 89 %
Doubtful	0 0%	1 1%	1 1%
	62 88%	64 91%	126 90%

TEPvENDO preliminary results

Non cardiac Non cerebral uptake

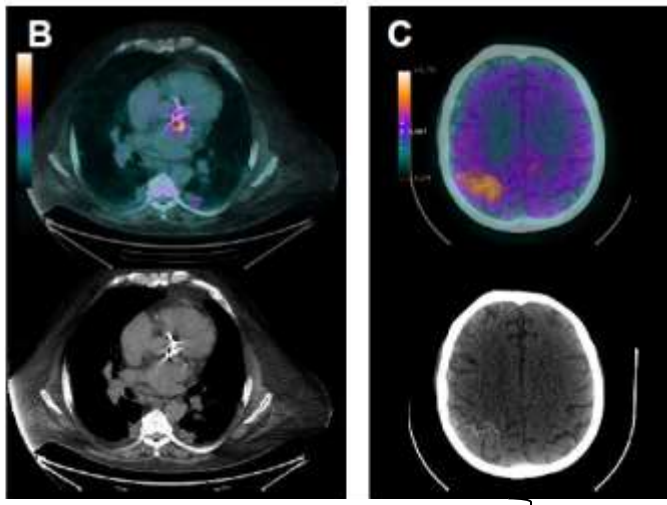


69 patients (50%) excluding non IE related uptake

TEPvENDO preliminary results

FDG-TEP results

- **Extra Cardiac uptake**
  - Extra cerebral
  - **Cerebral performed in 137/140 pts**



- Cerebral uptake — n=6 pts (4%)
- Reduced uptake (ischemic stroke) — n= 6 pts (4%)

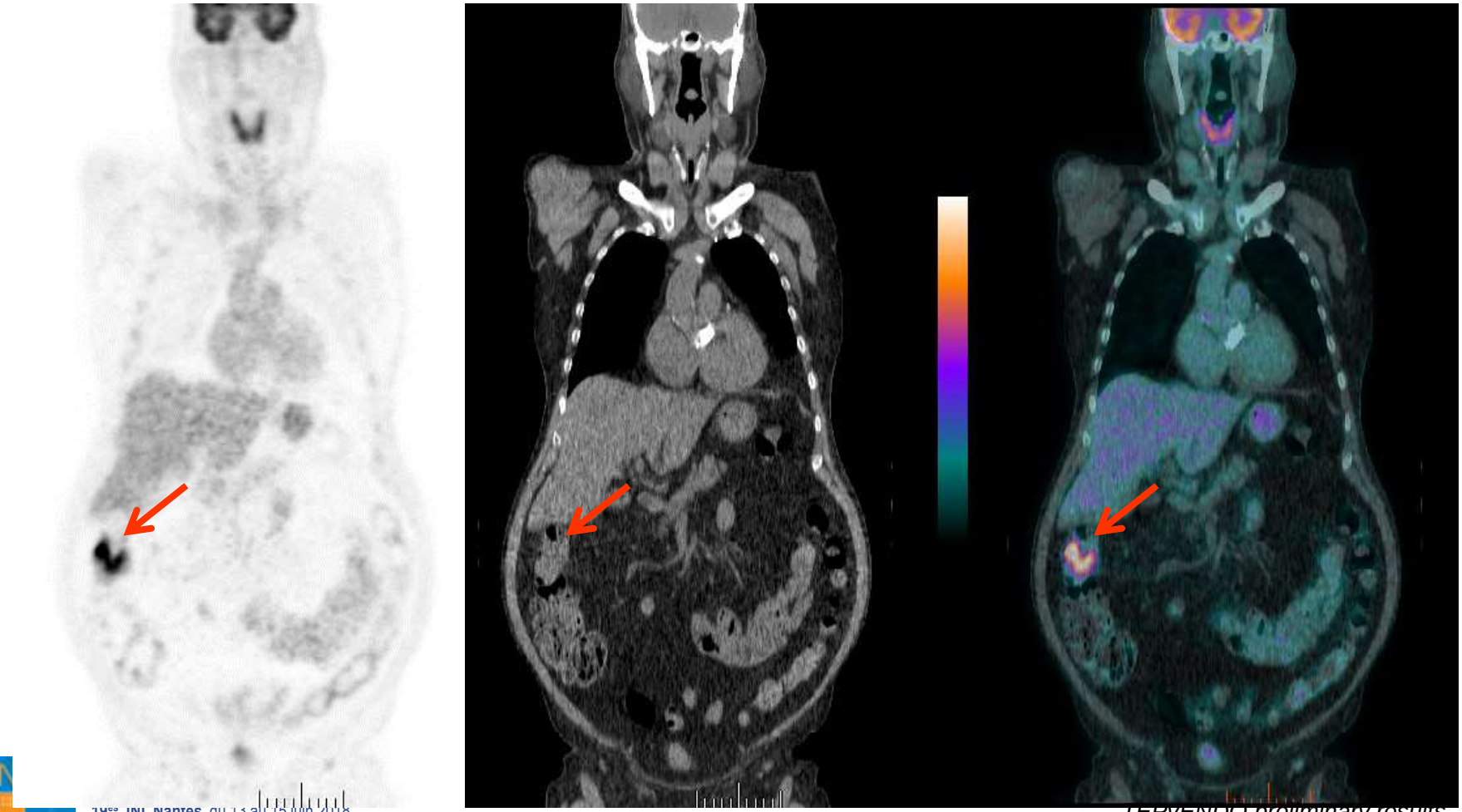
8%

FDG-TEP results

- **Extra Cardiac uptake**
  - Extra cerebral
  - Cerebral
  - **Portal of entry**
    - **detection** **n=12 (9%)** **(8 PV / 4 NV)**
    - **validation** **n=21 (15%)** **(7 PV / 14 NV)**

[18F]FDG PET/CT Portal of entry

- Recurrent chills, fever, and positive blood cultures (*E. faecalis*)
- Suspicion of aortic prosthetic valve infection



TEPVENDO preliminary results

Diagnostic IMPACT

TEPvENDO preliminary results

Diagnostic IMPACT

- **Modification of ≥ 1 Duke criteria** **n=43 (31%)**
  (26 PV / 17 NV)

TEPvENDO preliminary results

Diagnostic IMPACT

- **Modification of ≥ 1 Duke criteria** **n=43 (31%)**
  (26 PV / 17 NV)

- **Among the 43 pts with negative Echocardiography, 25 had cardiac uptake 58%**

TEPvENDO preliminary results

Diagnostic IMPACT

- **Modification of ≥ 1 Duke criteria** **n=43 (31%)**
  (26 PV / 17 NV)

- **Among the 43 pts with negative Echocardiography, 25 had cardiac uptake 58%**

- **Modification of Duke classification** **n=21 (15%)**
  (17 PV / 4 NV)

- **Affirmation of the cardiac infection localisation n= 54 (38,6%)**
  (43 PV / 11 NV)

TEPvENDO preliminary results

Cardiac localisation
Echocardiography vs FDG TEP

	Echo +	Echo -	Total
FDG TEP +	39	25	64
FDG TEP -	23	18	41
Total	62	43	105

Sensitivity **0.63 (0.50, 0.75)**
Specificity **0.42 (0.27, 0.58)**

Excluding doubtfull FDG TEP results

TEPvENDO preliminary results

Results

- **Duke classification before FDG-TEP**
  - **Definite IE N= 80 pts (57%)**
    - Prosthetic valve pts 34 pts **(49%)**
    - Native valve pts 46 pts **(66%)**

- **Duke classification after FDG-TEP**
  - **Definite IE N= 95 pts (68%)**

TEPvENDO preliminary results

Prosthetic valve patients N=70
Modification of Duke classification

		Total
BEFORE FDG TEP	Definite	34 49%
	Possible	33 47%
	Excluded	3 4%
	Total	70 100%

TEPvENDO preliminary results

Prosthetic valve patients N=70
Modification of Duke classification

		AFTER FDG TEP			
		Definite	Possible	Excluded	Total
BEFORE FDG TEP	Definite	33 47%	1 1%	0	34 49%
	Possible	13 19%	19 27%	1 %	33 47%
	Excluded	0	2 3%	1 1%	3 4%
	Total	46 66%	22 31%	2 3%	70 100%

+ 12
17%

TEPvENDO preliminary results

Prosthetic valve patients N=70
Modification of Duke classification

		AFTER FDG TEP			
		Definite	Possible	Excluded	Total
BEFORE FDG TEP	Definite	33 47%	1 1%	0	34 49%
	Possible	13 19%	19 27%	1 1%	33 47%
	Excluded	0	2 3%	1 1%	3 4%
	Total	46 66%	22 31%	2 3%	70 100%

+ 12

Final diagnosis			
Definite	Possible	Excluded	Total
47 %	17 %	6	70

Prosthetic valve patients N=70
Modification of Duke classification

		AFTER FDG TEP			
		Definite	Possible	Excluded	Total
BEFORE FDG TEP	Definite	33 47%	1 1%	0	34 49%
	Possible	13 19%	19 27%	1 1%	33 47%
	Excluded	0	2 3%	1 1%	3 4%
	Total	46 66%	22 31%	2 3%	70 100%

+ 12
17%

Classification downgraded in 2 pts

TEPvENDO preliminary results

Prosthetic valve patients N=70
Modification of Duke classification

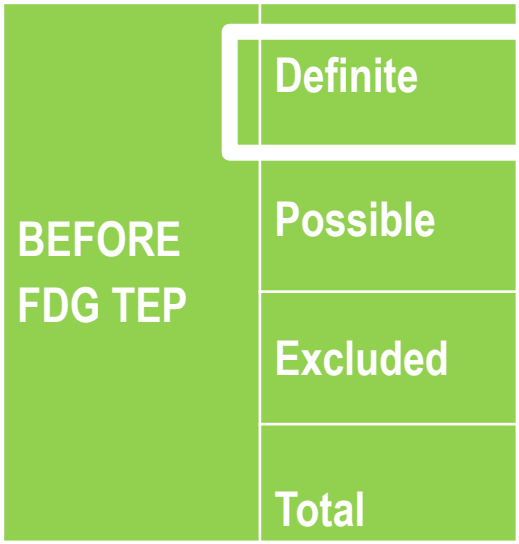
		AFTER FDG TEP			
		Definite	Possible	Excluded	Total
	Excluded		3%	1%	4%
	Total	**46** 66%	**22** 31%	**2** 3%	**70** 100%

NRI = 14 pts /70 pts = 20%

Classification downgraded in 2 pts

TEPvENDO preliminary results

Native valve patients N=70
Modification of Duke classification



	Total
Definite	46 66%
Possible	23 33%
Excluded	1 1%
Total	70 100%

TEPvENDO preliminary results

Native valve patients N=70
Modification of Duke classification

		AFTER FDG TEP			
		Definite	Possible	Excluded	Total
BEFORE FDG TEP	Definite	46 66%	0	0	46 66%
	Possible	3 4%	19 27%	1 1%	23 33%
	Excluded	0	0	1 1%	1 1%
	Total	49 70%	19 27%	2 3%	70 100%

+ 3
4%

TEPvENDO preliminary results

Native valve patients N=70
Modification of Duke classification

		AFTER FDG TEP			
		Definite	Possible	Excluded	Total
BEFORE FDG TEP	Definite	46 66%	0	0	46 66%
	Possible	3 4%	19 27%	1 1%	23 33%
	Excluded	0	0	1 1%	1 1%
	Total	49 70%	19 27%	2 3%	70 100%

+ 3
4%

Final diagnosis			
Definite	Possible	Excluded	Total
48	9	13	70

Native valve patients N=70
Modification of Duke classification

		AFTER FDG TEP			
		Definite	Possible	Excluded	Total
BEFORE FDG TEP	Definite	46 66%	0	0	46 66%
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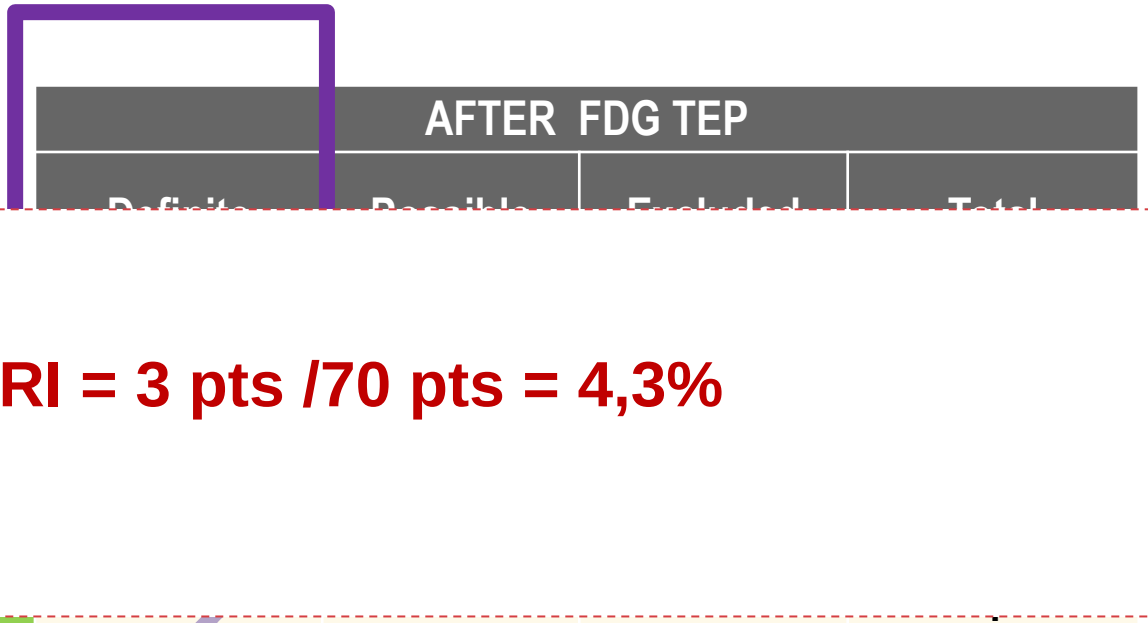
	Total	49 70%	19 27%	2 3%	70 100%

+ 3

Classification down-graded in 1 pts

TEPvENDO preliminary results

Native valve patients N=70
Modification of Duke classification



		AFTER FDG TEP			
		Definite	Possible	Excluded	Total
BEFORE FDG TEP	Excluded			1%	1%
	Total	**49** 70%	**19** 27%	**2** 3%	**70** 100%

NRI = 3 pts /70 pts = 4,3%

Classification down-graded in 1 pts

TEPvENDO preliminary results

Therapeutic IMPACT

- **Therapeutic modifications** **n= 37 (26%)**

  (CI 95% 19.12% - 37.74%)

  – Prosthetic valve pts **n=15/70** **(21%)**

  – Native valve pts **n=22/70** **(31%)** (p=0,17)

Conclusions

- Frequent valvular uptake — 67% (PV) -> 24% (NV)
  but 1/3 of doubtful uptake
- Frequent extra cardiac uptake — 46% (PV) -> 53%
- Portal of entry revealed in 10%
- Cerebral localization detected in 8%
- Net reclassification improvement — 20 % (PV) -> 4% (NV)
- Therapeutic impact — 21% (PV) -> 31% (NV)

Conclusions

- **First multicentric study**
- **First comparison of impact in PV and NV patients**
- **High rate of doubtful results**
- **Need for**
  - Standardization of FDG TEP interpretation
  - Cautious application of ESC-2015 Duke classification
- **Improvement of patients prognosis remained to be established**

TEPvENDO Study group:

Principal investigator: DUVAL Xavier.

Steering Committee: HOEN Bruno, IUNG Bernard, ROUZET Francois, TUBIANA Sarah.

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Coordination and statistical analyses: ESPOSITO-FARESE Marina, LAOUENAN Cedric, MAKLOUF Sonia , PREVAULT Margot, ROGIER Ophelie.

Sponsor: DRCI APHP

Funding: French ministry of health

Clin Trial. Gov identification number: NCT02287792