

Differences in Cardiac Nuclear Imaging Results With ^{99m}Tc-DPD, ^{99m}Tc-PYP, and ^{99m}Tc-HMDP Bone Radiotracers in Patients With Left Ventricular Hypertrophy of Unknown Etiology Screened for Transthyretin Amyloid Cardiomyopathy in the TTRACK Study

Francisco Javier Haro del Moral¹, Pablo Garcia-Pavia¹, Carmen Munteanu², Denis Keohane², Pablo Mallaina², Thibaud Damy³, Emmanuel Itti³

¹Hospital Universitario Puerta de Hierro Majadahonda University Hospital, Madrid, Spain; ²Pfizer Inc, New York, NY, USA; ³Assistance Publique-Hôpitaux de Paris, Henri Mondor University Hospital, Créteil, France

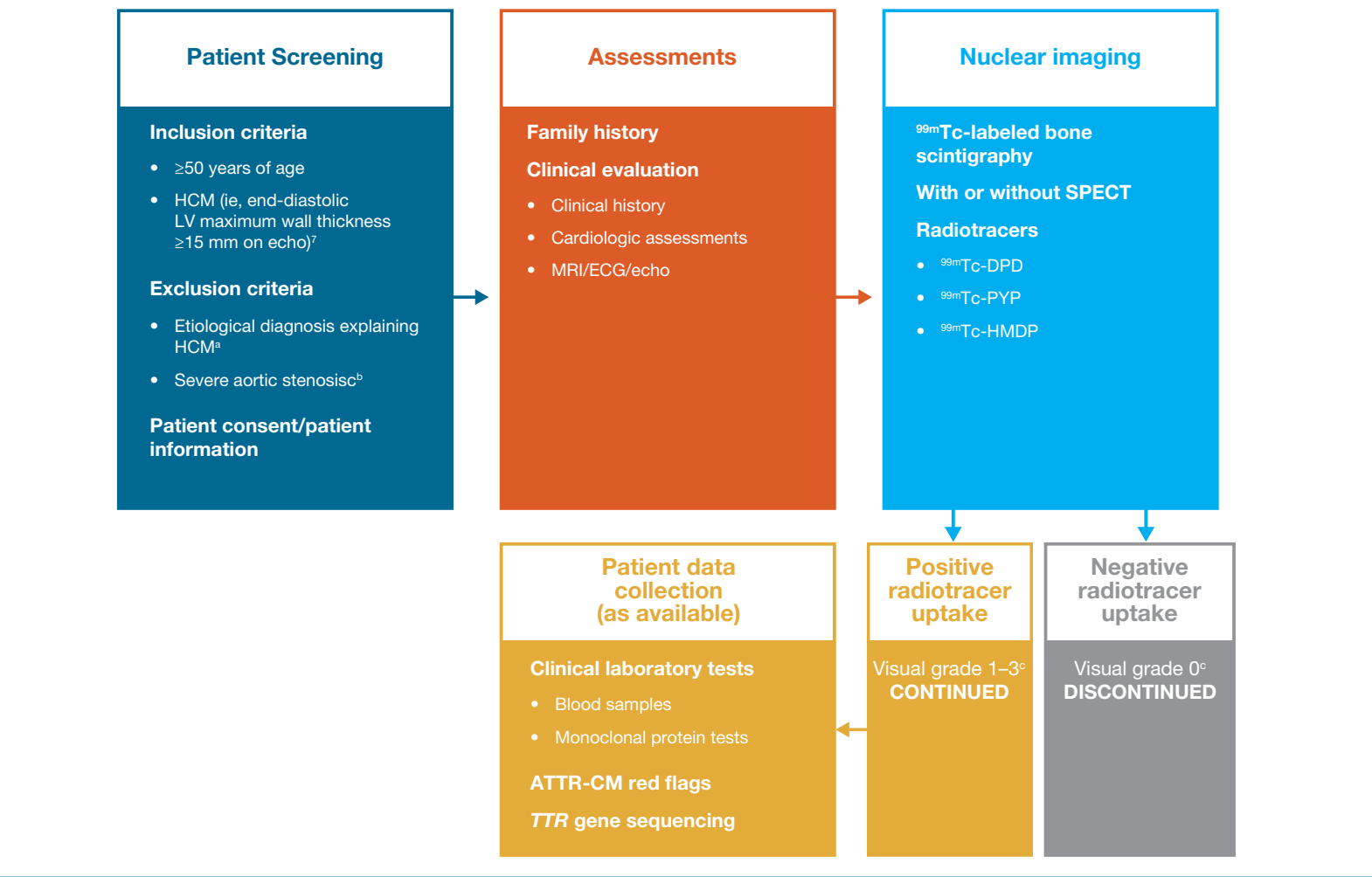
INTRODUCTION

- Transthyretin amyloid cardiomyopathy (ATTR-CM) is a progressive, fatal disease characterized by a broad spectrum of signs/symptoms that may overlap with other cardiac conditions.¹⁻³
 - Increased left ventricular (LV) wall thickness, a common finding in ATTR-CM, may be mistaken for hypertrophic cardiomyopathy (HCM) in some patients with undiagnosed cardiac amyloid disease.³
- The prognosis associated with untreated ATTR-CM is generally poor, with a reported median survival of:
 - 2.6 years for variant ATTR-CM (V122I)⁴ and
 - 3.6 years for wild-type ATTR-CM.⁵
- Diagnosis of ATTR-CM is often delayed due to the heterogeneous presentation of ATTR-CM and low awareness of “red flags” that should prompt suspicion.³
- Technetium (Tc)-labeled cardiac scintigraphy and single photon emission computed tomography (SPECT) are recommended for the non-invasive diagnosis of ATTR-CM, in tandem with monoclonal protein testing, to help facilitate early diagnosis.^{3,6}
- Although nuclear imaging is increasingly considered a cornerstone of ATTR-CM diagnosis, little information is available on variability in imaging techniques used to detect the disease in clinical practice.
- In this analysis, we explored differences among the radiotracers used for cardiac nuclear imaging in older adults with hypertrophic cardiomyopathy (HCM) screened for ATTR-CM in the TTRACK study.

METHODS

- Study design: Multicenter, noninterventional, cross-sectional, epidemiologic study (NCT03842163) (**Figure 1**).

Figure 1: TTRACK study flow



^a Genetic HCM, Fabry disease, sarcoidosis, any type of amyloidosis.
^b Aortic valve area <1.0 cm².
^c Visual grade 0 / 1 / 2 / 3 = no / low / moderate / high radiotracer uptake.
^{99m}Tc-DPD=99mTc-3-diphosphono-1,2-propanodicarboxylic acid; ^{99m}Tc-PYP=99mTc-pyrophosphate; ^{99m}Tc-HMDP=99mTc-hydroxymethylene diphosphonate;
ATTR-CM=transthyretin amyloid cardiomyopathy; HCM=hypertrophic cardiomyopathy; LV=left ventricular; ECG=electrocardiogram; echo=echocardiogram;
SPECT=single photon emission computed tomography; TTR=transthyretin

- Sites: 20 centers in 11 countries across 3 continents (Australia, Austria, France, Italy, Portugal, Romania, Slovakia, Slovenia, South Korea, Spain, and United Kingdom).
- Study period: July 2018 to October 2022.
- Main eligibility criteria:
 - Age ≥50 years.
 - HCM based on the 2014 ESC guidelines (end-diastolic LV maximum wall thickness ≥15 mm on echocardiogram [echo])⁷ in the absence of a previously identified cause.
- Nuclear image review and grading:
 - A nuclear medicine expert at each center and a centralized independent expert reviewer graded radiotracer cardiac uptake on each image.
 - A second central reader reviewed images with initially discrepant grades; final grades were decided by a consensus of 2 of 3 readers.
 - Nuclear image grading was based on cardiac vs bone radiotracer uptake following the Perugini system (**Table 1**).⁸

Table 1: Visual grading system for cardiac uptake of bisphosphonate radiotracers⁸

Level of cardiac uptake	Cardiac vs bone uptake	Visual grade
No cardiac uptake	—	0
Low	Less	1
Moderate	Equal	2
High	Greater	3

- Prevalence analyses: Descriptive statistics
 - Perugini grades 0–3 for cardiac uptake on bone scintigraphy based on the radiotracer used.
 - Cardiac amyloidosis and ATTR-CM based on the radiotracer used for scintigraphy.
- Concordance analyses: Rates calculated for scintigraphy vs SPECT images for all and individual radiotracers.
 - Concordance in image grading: Measured using Cohen’s kappa (κ) coefficients (95% CI).
 - Coefficient interpretation: <0 = discordance; 0–0.2 = very light concordance; 0.2–0.4 = light concordance; 0.4–0.6 = moderate concordance; 0.6–0.8 = strong concordance; and 0.8–1.0 = very strong concordance.
 - Clinical relevance: Non-clinically relevant = differences in readings between grades 0 and 1 or grades 2 and 3; clinically relevant = differences in readings between grades 0 or 1 vs 2 or 3.

RESULTS

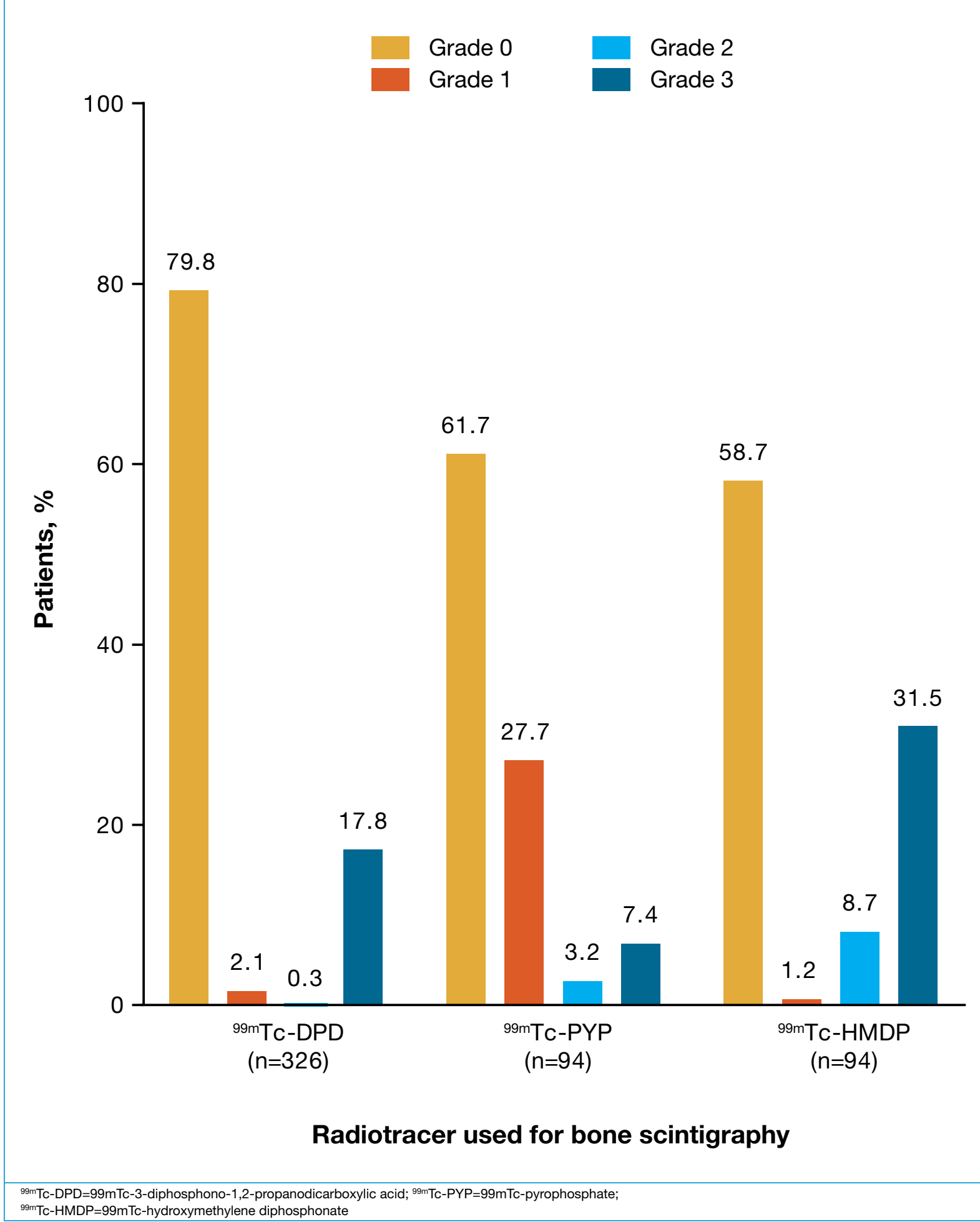
Patient Disposition

- Among 766 patients who satisfied eligibility criteria and had nuclear imaging data:
 - 691 (90.2%) underwent scintigraphy alone and
 - 75 (9.8%) underwent both scintigraphy and SPECT.
- ^{99m}Tc-DPD, PYP, and HMDP radiotracer-labeled scintigraphy was used in 42.6%, 12.3%, and 45.2% of patients, respectively.

Radiotracer-Related Differences

- The proportion of patients with combined grades 0 and 1 cardiac uptake was higher with ^{99m}Tc-PYP (89.4%) than ^{99m}Tc-DPD (81.9%) or ^{99m}Tc-HMDP (59.9%) (**Figure 2**).

Figure 2: Prevalence of Perugini grades on bone scintigraphy by radiotracer used



Concordance

- In 75 patients who underwent both types of nuclear imaging, nearly perfect agreement was observed between grading for scintigraphy vs SPECT (κ coefficient, 0.93 [95% CI 0.86–1.00]; **Table 2**).
- Discrepant grades were only seen with ^{99m}Tc-PYP radiotracer-labeled images (3/75 [4%]; κ coefficient, 0.55 [95% CI 0.15–0.96]).
 - None of these differences were considered clinically relevant.

Table 2: Concordance of Perugini grades assigned for scintigraphy vs SPECT images by radiotracer (n=75)

Grade for scintigraphy	Grade for SPECT			
	Grade 0	Grade 1	Grade 2	Grade 3
All radiotracers				
n	43	8	16	8
Grade 0	43 (100)	3 (37.5)	0	0
Grade 1	0	5 (62.5)	0	0
Grade 2	0	0	16 (100)	0
Grade 3	0	0	0	8 (100)
Concordance, κ (95% CI)				
^{99m} Tc-DPD-labeled				
n	27	2	3	5
Grade 0	27 (100)	0	0	0
Grade 1	0	2 (100)	0	0
Grade 2	0	0	3 (100)	0
Grade 3	0	0	0	5 (100)
Concordance, κ (95% CI)				
^{99m} Tc-PYP-labeled				
n	4	6	0	1
Grade 0	4 (100)	3 (50)	0	0
Grade 1	0	3 (50)	0	0
Grade 2	0	0	0	0
Grade 3	0	0	0	1 (100)
Concordance, κ (95% CI)				
^{99m} Tc-HMDP-labeled				
n	12	0	13	2
Grade 0	12 (100)	0	0	0
Grade 1	0	0	0	0
Grade 2	0	0	13 (100)	0
Grade 3	0	0	0	2 (100)
Concordance, κ (95% CI)				
Coefficient interpretation: <0=discordance; 0–0.2=very light concordance; 0.2–0.4=light concordance; 0.4–0.6=moderate concordance; 0.6–0.8=strong concordance; and 0.8–1.0=very strong concordance.				
99mTc-DPD=99mTc-3-diphosphono-1,2-propanodicarboxylic acid; 99mTc-PYP=99mTc-pyrophosphate; 99mTc-HMDP=99mTc-hydroxymethylene diphosphonate; SPECT=single photon emission computed tomography				

CONCLUSIONS

- In this real-world study, differences were found among the specific radiotracers used, but their clinical relevance is unclear.
- A high level of concordance was seen in nuclear image grading by scintigraphy vs SPECT.
- Additional information is needed on the sensitivity of the different radiotracers used for ATTR-CM diagnosis.

REFERENCES

- Garcia-Pavia P, et al. Eur J Heart Fail 2021;23:895-905. 2. Damy T, et al. Eur Heart J 2016;37:1826-34. 3. Kittleson MM, et al. J Am Coll Cardiol 2023;81:1076-126. 4. Lane T, et al. Circulation 2019;140:16-26. 5. Grogan M, et al. Am Coll Cardiol 2016;68:1014-20. 6. Garcia-Pavia P, et al. Eur J Heart Fail 2021;23:512-26. 7. Elliott P, et al. Eur Heart J 2014;35:2733-79. 8. Perugini E, et al. J Am Coll Cardiol 2005;46:1076-84.

DISCLOSURES

FJHM: Pfizer. **PGP:** Consultant or speaker's bureau for Alexion, Alnylam, AstraZeneca, ATTRalus, Bridgebio, General Electric, Intellia, Ionis, Neurimmune, Novo Nordisk, and Pfizer. **TD:** Alnylam, GlaxoSmithKline, Pfizer, and Prothena. **El:** Janssen-Cilag and Pfizer. **CM, DK,** and **PM:** Employees of Pfizer and hold stock/stock options.

ACKNOWLEDGMENTS

This study was supported by Pfizer. Editorial assistance was provided by Donna McGuire of Engage Scientific Solutions and was funded by Pfizer.

Electronic Poster
Please scan this Quick Response (QR) code with your smartphone app to view an electronic version of this poster. If you do not have access to a smartphone, please access the poster via the following link:
<https://scientificpubs.congressposter.com/p/xpvnvdlloeujlh>

