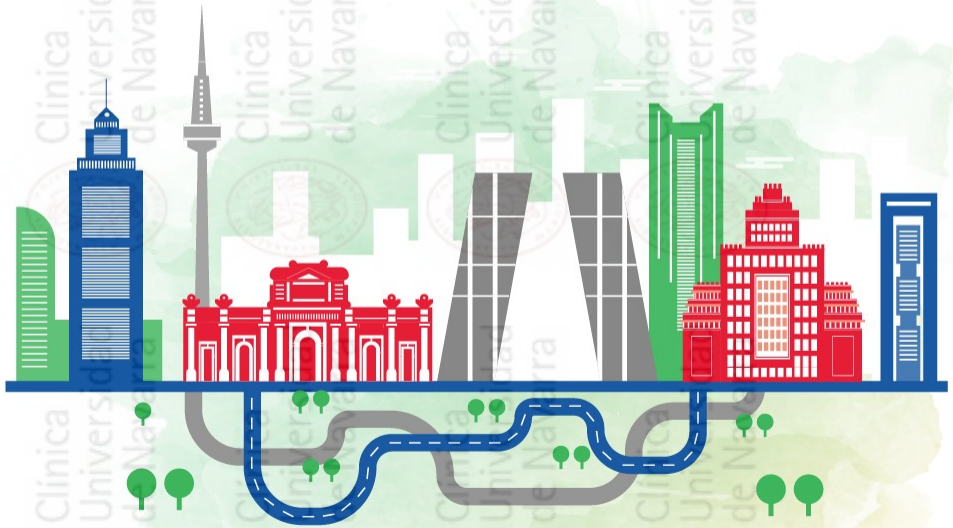
CURSO NACIONAL DE
NEURORRADIOLOGÍA

S.E.N.R
Sociedad Española de Neurorradiología

Radiología en la Patología Neurodegenerativa, Desmielinizante e Infecciosa del SNC

15 y 16 de febrero de 2024 | MADRID

Sede: CINESA. C/ Fuencarral 136



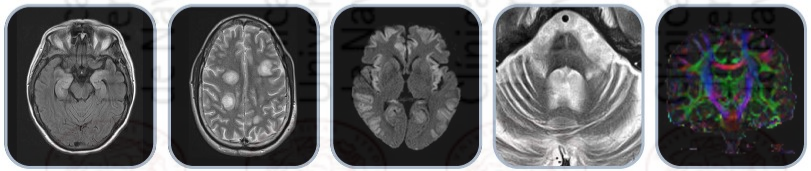
Biomarcadores PET en enfermedades neurodegenerativas

Javier ARBIZU

Clínica Universidad de Navarra

Pamplona/Madrid

jarbizu@unav.es



Clínica Universidad de Navarra

Estándares de la Imagen Molecular en Neurodegenerativas

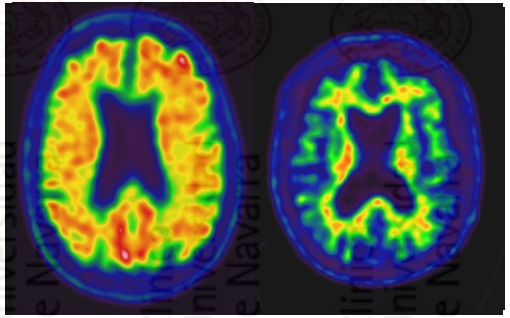
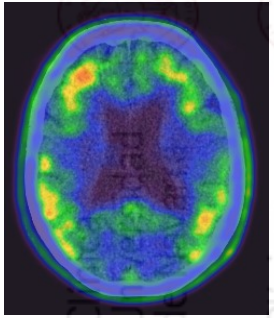
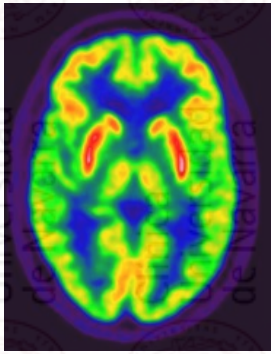


Imagen Amiloide

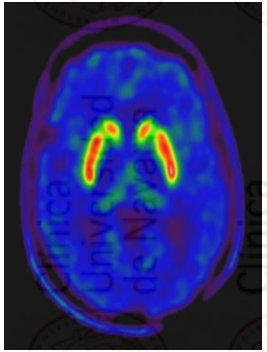
Imagen Tau





Actividad Sináptica & Neurodegeneración

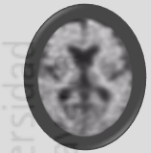
Imagen Dopaminérgica (vía nigro-estriatal)



Biomarcadores de la enfermedad de Alzheimer (EA)

Albert M, et al. Alzheimers Dement 2011; Dubois B, et al. Lancet Neurol 2014

Definición biológica de la EA

Perfiles A T N	Categoría de Biomarcador	
A-T-N-	Biomarcadores de EA normales	
A+T-N-	Fisiopatología Alzheimer	 **continuo patofisiológico de Alzheimer**
A+T-N+	Fisiopatología Alzheimer	
A+T+N-	Enfermedad Alzheimer	
A+T+N+	Alzheimers disease	
A-T+N-	No- patofisiología Alzheimer	
A-T-N+	No- patofisiología Alzheimer	
A-T+N+	No- patofisiología Alzheimer	

SÍNTOMAS CLÍNICOS

Biomarcadores de NEURODEGENERACIÓN (N)

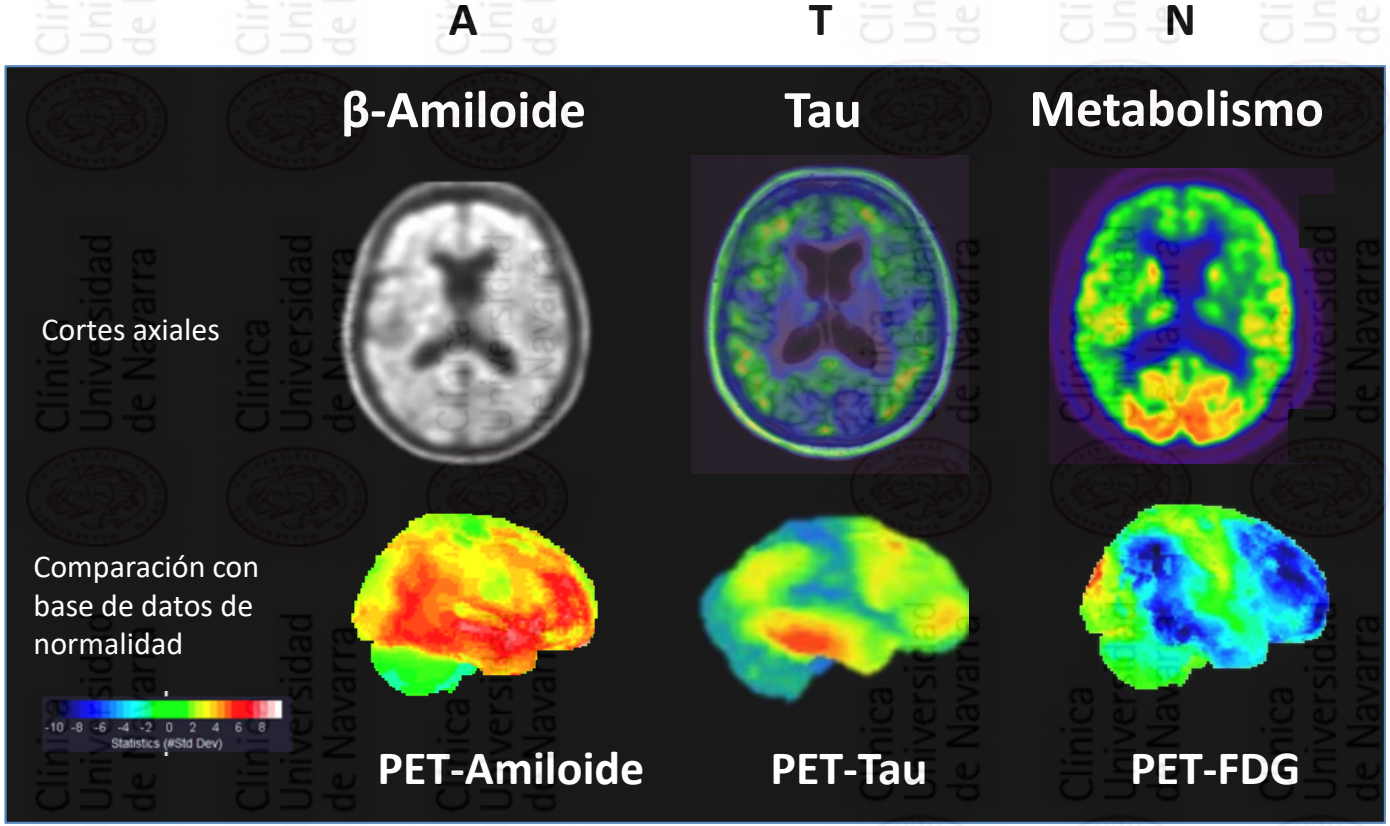
- Severidad
- Predecir evolución

NIA-AA Research Framework: Jack et al. 2018

NIA-AA Revised Clinical Criteria for Alzheimer's Disease

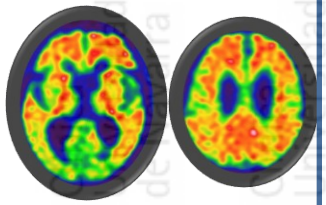
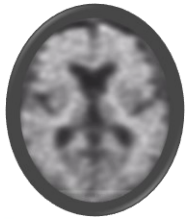
- **Symptoms are not necessary** to diagnose AD
- In living people the disease is **diagnosed by disease specific biomarkers**
- **Symptoms are a result** of the disease process, not its definition
- Clinical syndromes commonly seen with AD may also be caused by disorders other than AD and therefore **clinical presentation alone is not diagnostic of AD**
- The **same biology** (AD) may result in **different phenotypic presentations**

Biomarcadores PET en Enf. Alzheimer



PET Amiloide (A)

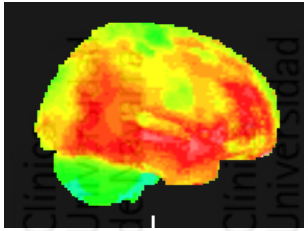
β Amiloide fibrilar (A)

[^{18}F]florbetapir	[^{18}F]flutemetamol	[^{18}F]florbetaben
		
Sensitivity 92% Specificity 100%	Sensitivity 91% Specificity 100%	Sensitivity 98% Specificity 89%

Clark et al. Lancet Neurology (2012); Salloway et al. A&D (2017);

Sabri et al. A&D (2015)

- **Contraindicaciones**: NO
- **Variabilidad inter-centros**: BAJA
- **Variabilidad individual**: BAJA
- **Detecta cambios evolución**: SI
- Informa sobre:
  - **Extensión**
  - **Localización**
  - **Efecto terapia anti-Amiloide**



Recomendaciones para la utilización de biomarcadores de imagen PET en el proceso diagnóstico de las enfermedades neurodegenerativas que cursan con demencia: consenso SEMNIM y SEN

Javier Arbizu

Ignasi Carrió

Puy Garrastachu

Guillermo García-Ribas

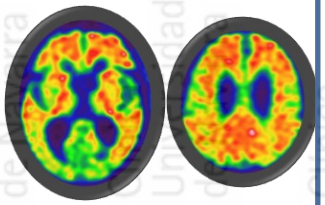
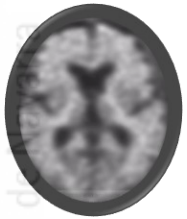
Pablo Martínez-Lage

José Luis Molinuevo

Arbizu et al, Rev Esp Med Nucl Imagen Mol, 2015

PET Amiloide (A)

β Amiloide fibrilar (A)

[18F]florbetapir	[18F]flutemetamol	[18F]florbetaben
		
Sensitivity 92% Specificity 100%	Sensitivity 91% Specificity 100%	Sensitivity 98% Specificity 89%

Clark et al. Lancet Neurology (2012); Salloway et al. A&D (2017);

Sabri et al. A&D (2015)

iDEAS
Imaging Dementia—Evidence For Amyloid Scanning

change in management in about 60% of patients

Rabinovici GD, et al. JAMA Neurol 2019

AMYPAD
Amyloid imaging to prevent Alzheimer's Disease

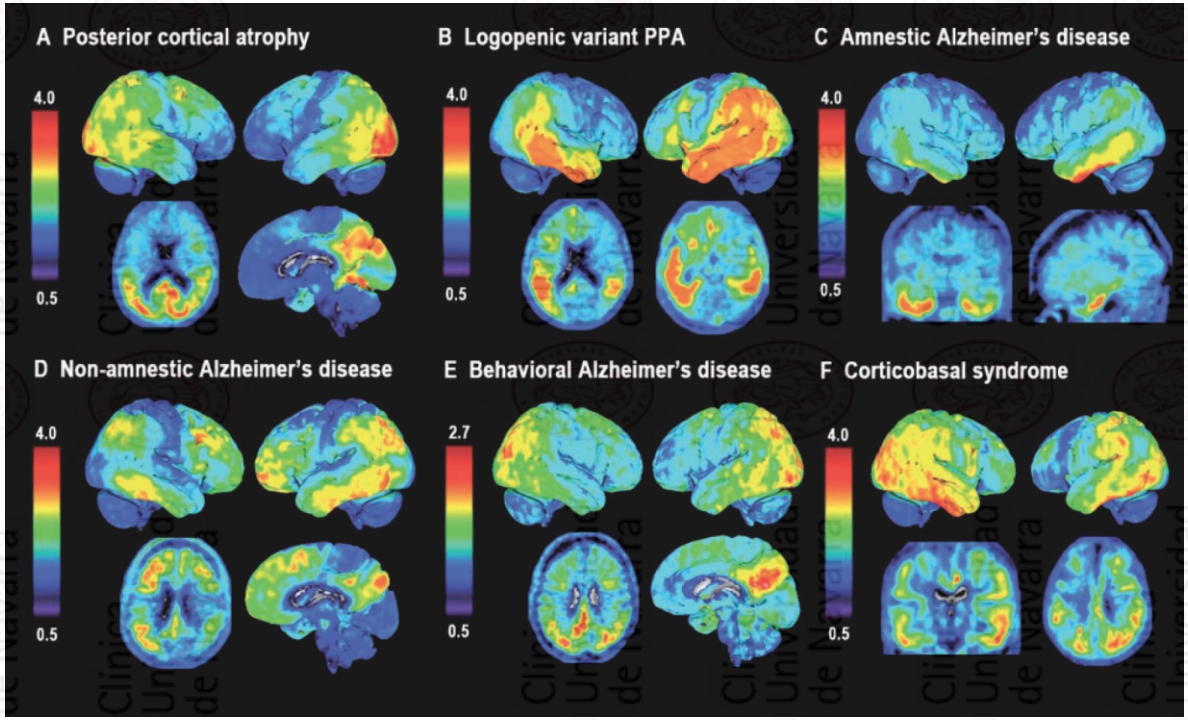
The Ducht ABIDE project

PETADDS
POSITRON EMISSION TOMOGRAPHY
ALZHEIMER DISEASE DIAGNOSIS SPAIN

PET Tau (T)

18F-Flortaucipir (T807, AV1451)

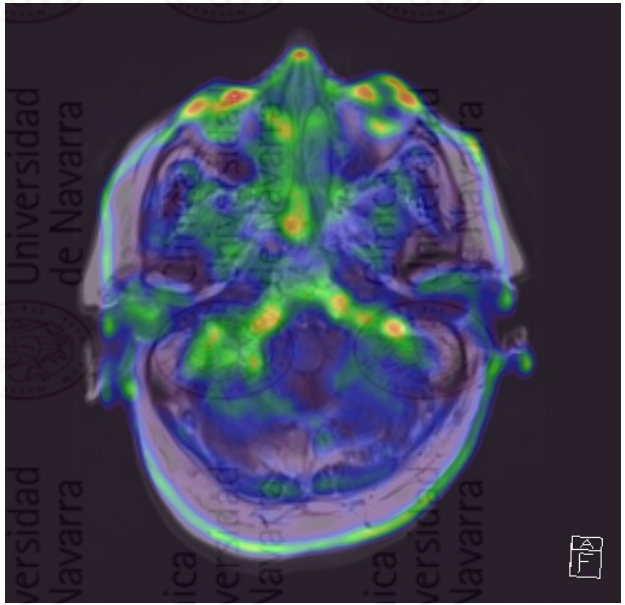
La distribución regional del Tau (no Aβ) coincide con el fenotipo clínico

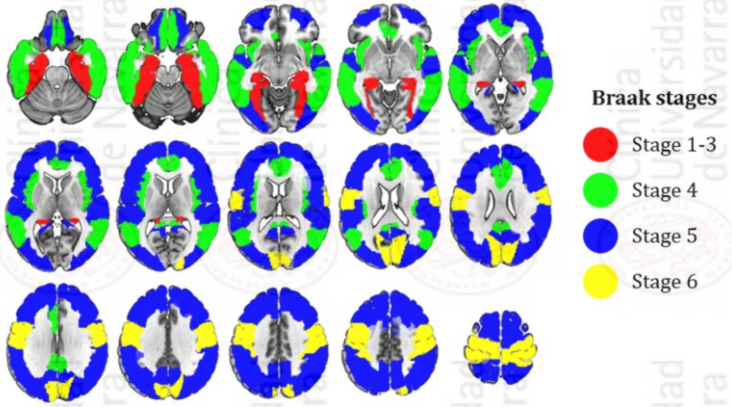


Ossenkoppele et al., Brain, 2016

PET-Tau (T)

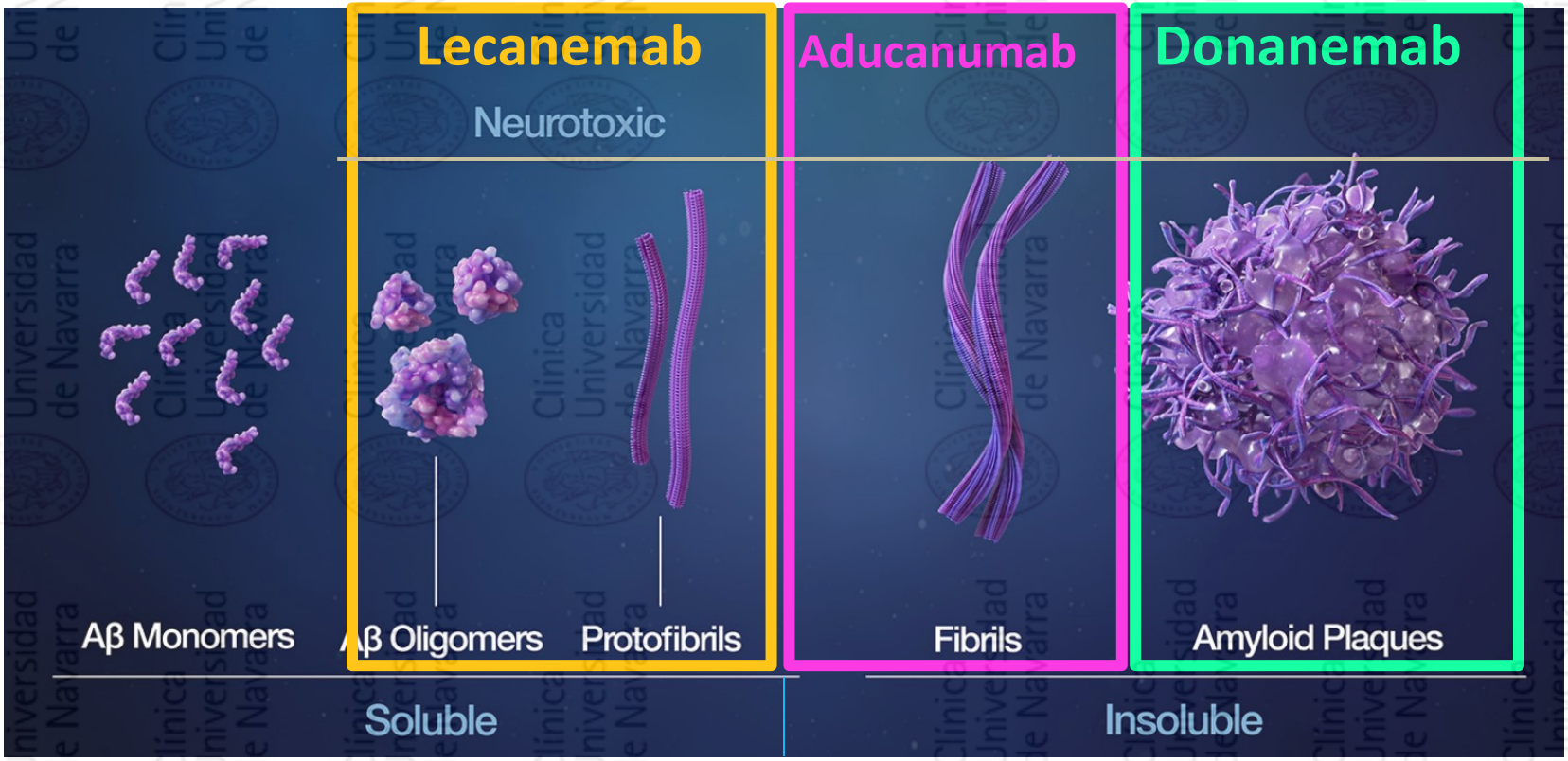
PET-Tau
(18F-GTP1)





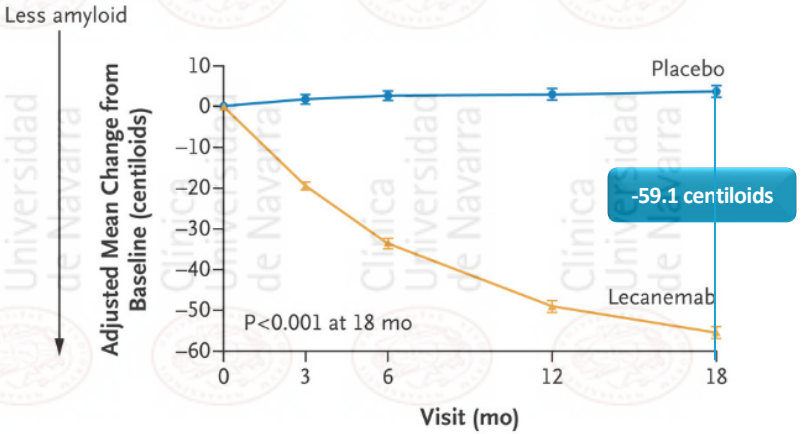
Schward A, et al. Alzheimers Dement (Amst). 2018; 10: 221–231.

Terapia anti-β Amiloide



Fármacos anti-Amiloide: eliminación efectiva de β-Amiloide cerebral

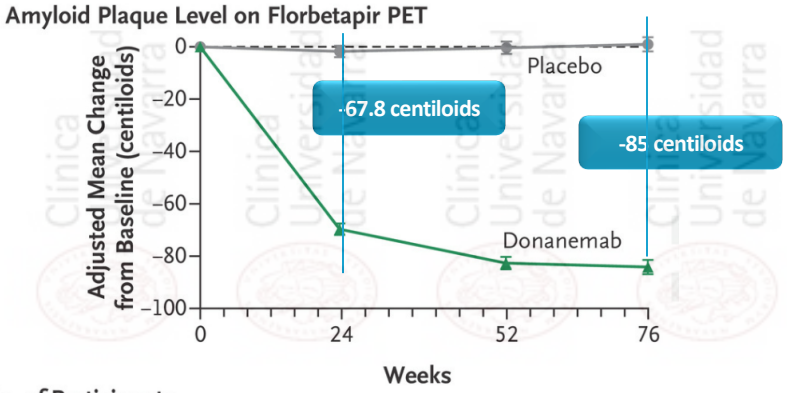
Lecanemab



No. of Participants

Lecanemab	354	296	275	276	210
Placebo	344	303	286	259	205

Donanemab

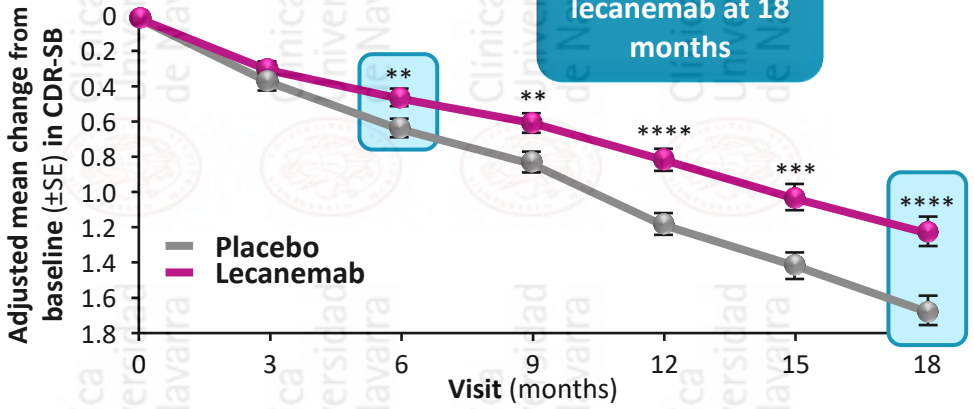


No. of Participants

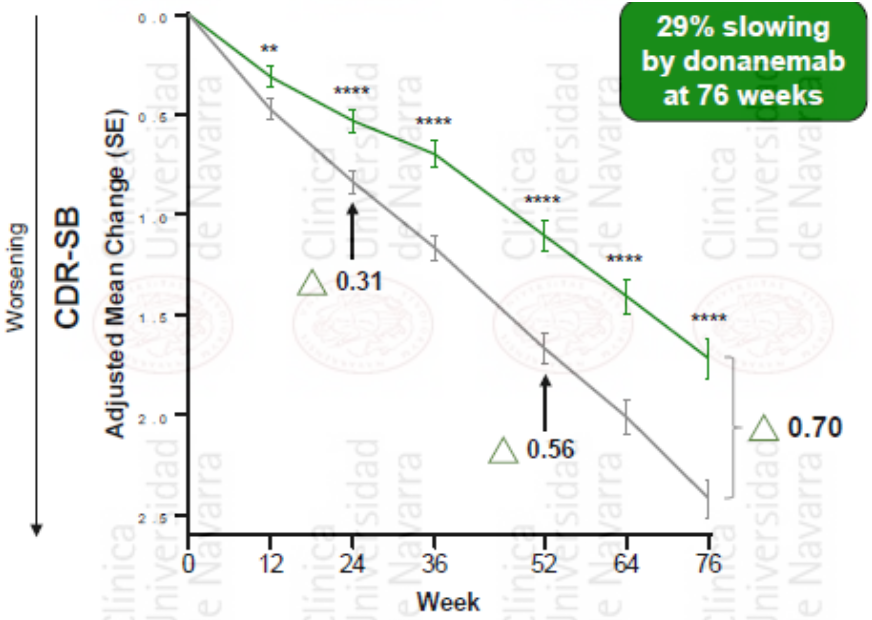
Donanemab	121	115	92	90
Placebo	112	111	91	91

Fármacos anti-Amiloide: disminución efectiva de la progresión de la EA

Lecanemab

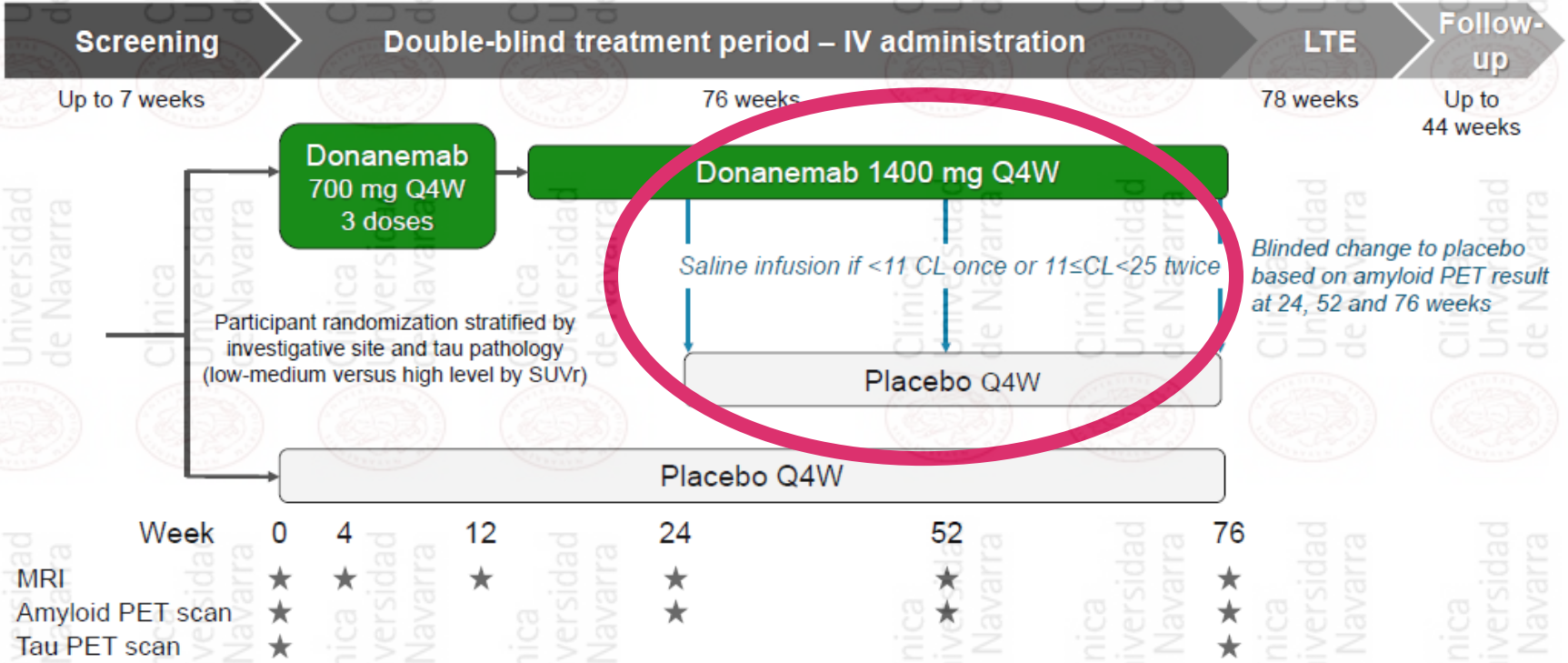


Donanemab



TRAILBLAZER-ALZ 2 study design

Donanemab



October 13, 2023

NCA - Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease (CAG-00431R) - Decision Memo

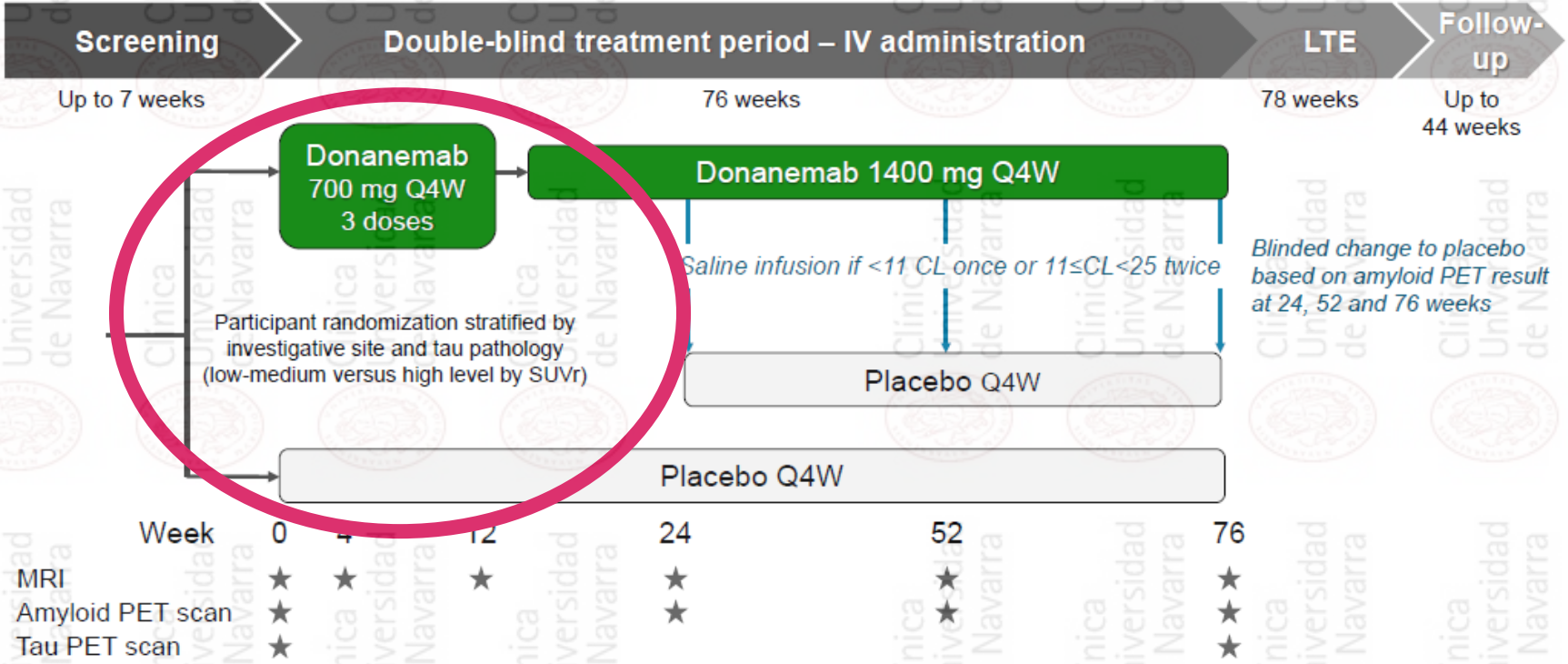
Decision Summary

CMS is **removing the national coverage determination (NCD) at § 220.6.20,** and **permitting Medicare coverage determinations for PET beta amyloid imaging to be made by the Medicare Administrative Contractors (MACs)** under § 1862(a)(1)(A) of the Social Security Act (the Act).

Elimina la limitación actual de 1 PET en la vida del paciente, abriendo la puerta a esta importante herramienta para utilizarlo más ampliamente

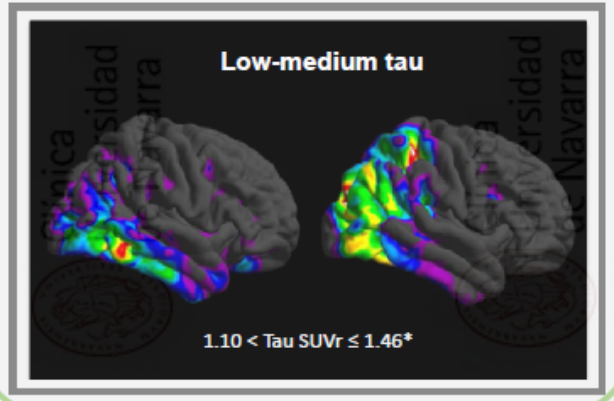
TRAILBLAZER-ALZ 2 study design

Donanemab

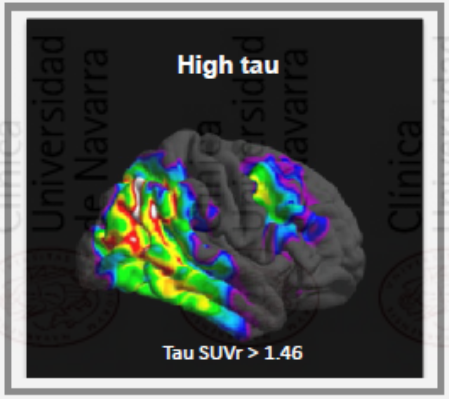


Donanemab: inclusión de pacientes basado en patología Tau

Study Powered to Test
Low-medium Tau Population
(same as TRAILBLAZER-ALZ Phase 2)



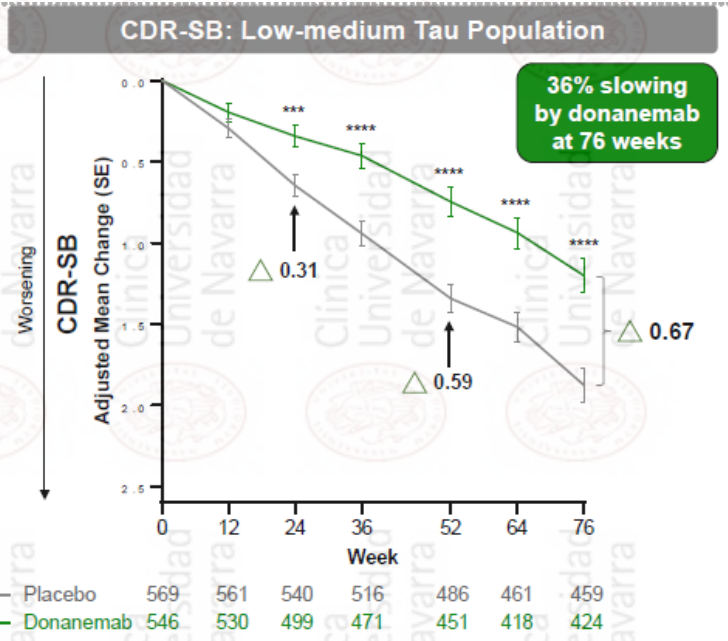
Study allowed enrollment of high tau participants so efficacy could be tested in combined population (low-medium plus high tau)

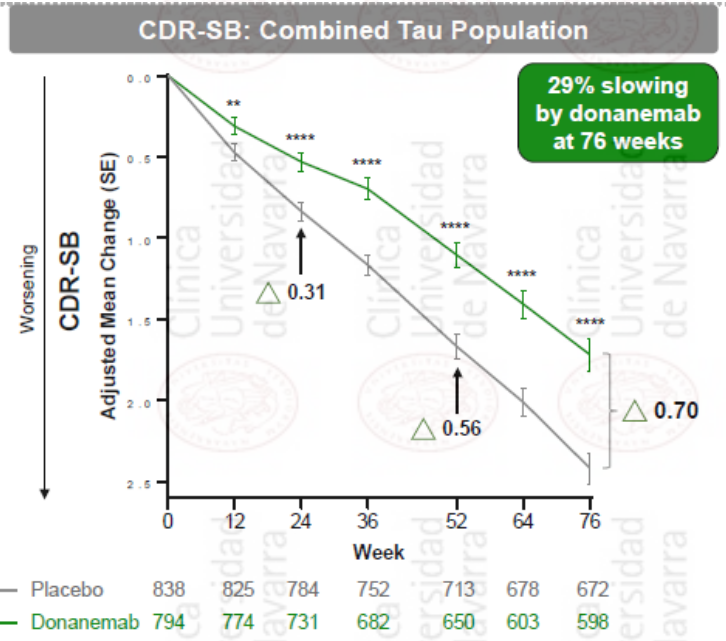


Sims et al. JAMA (2023)

Impacto de PET Tau basal en la respuesta terapéutica

Donanemab





Sims et al. JAMA 2023

PET FDG (N)

EAN GUIDELINES/CME ARTICLE

European Association of Nuclear Medicine and European Academy of Neurology recommendations for the use of brain ^{18}F-fluorodeoxyglucose positron emission tomography in neurodegenerative cognitive impairment and dementia: Delphi consensus

F. Nobili[a,1], J. Arbizu[b,1], F. Bouwman[c,2], A. Drzezga[d,1], F. Agosta[e,2], P. Nestor[f,2], Z. Walker[g,1], M. Boccardi[h], for the EANM-EAN Task Force for the Prescription of FDG-PET for Dementing Neurodegenerative Disorders[†]

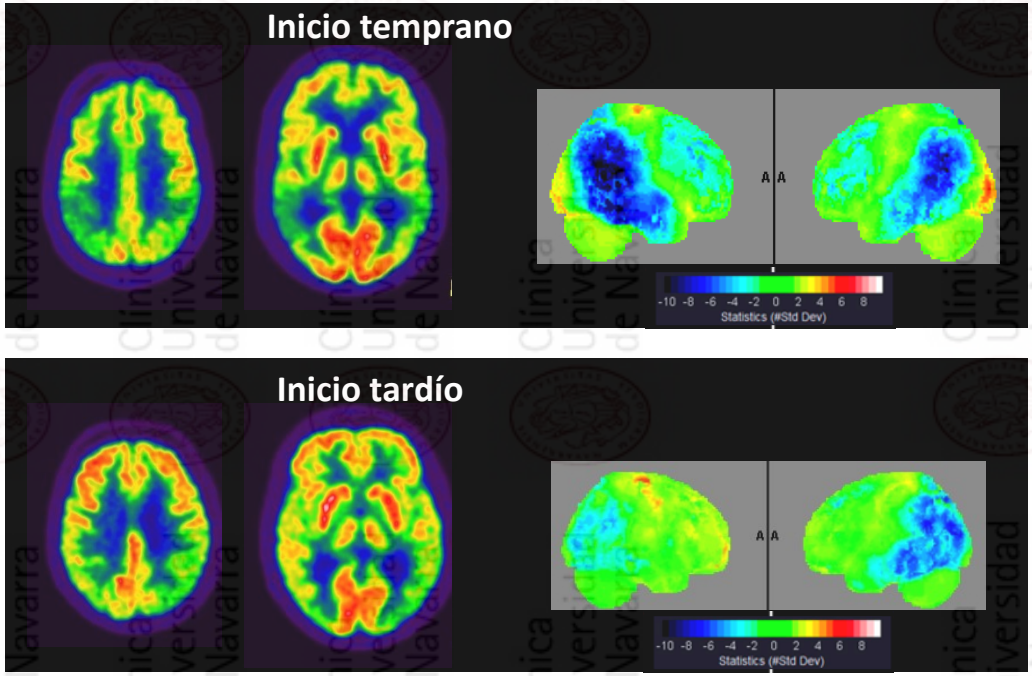
EANM-EAN Task Force for the Prescription of FDG-PET for Dementing Neurodegenerative Disorders

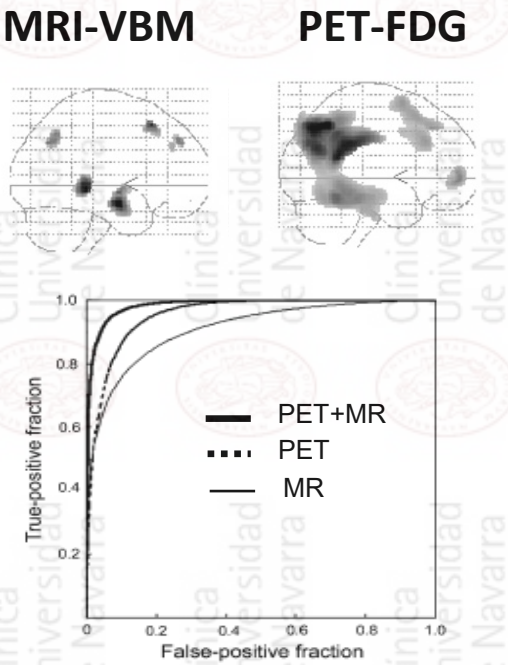
Assessment of accuracy studies which investigated the utility of brain PET in AD and other neurodegenerative diseases by means of FDG in supporting the diagnosis

Nobili F, et al. Eur J Neurol 2018

PET FDG (N)

DCL por EA: patrón característico



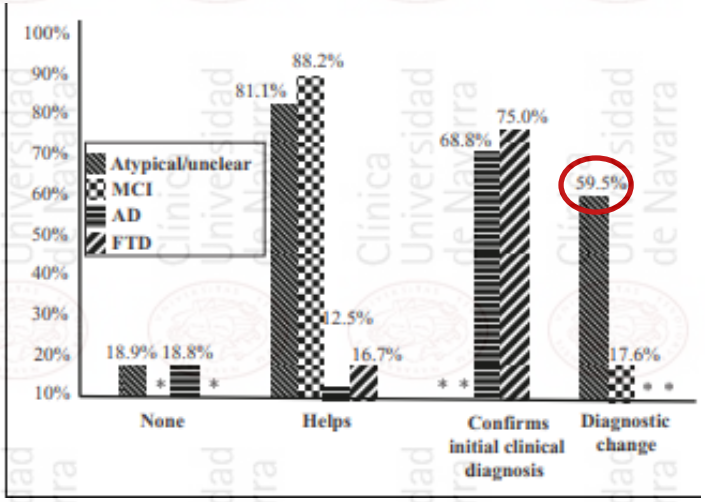


Matsunari et al. J Nucl Med 2007; Yuan Y, et al. Am J Neuroradiol 2009; Arbizu J, et al. Eur J Nucl Med Mol Imaging. 2018

PET FDG (N)

EA Atípica: impacto clínico

Cambio Diagnóstico



Ayuda a la toma de decisiones

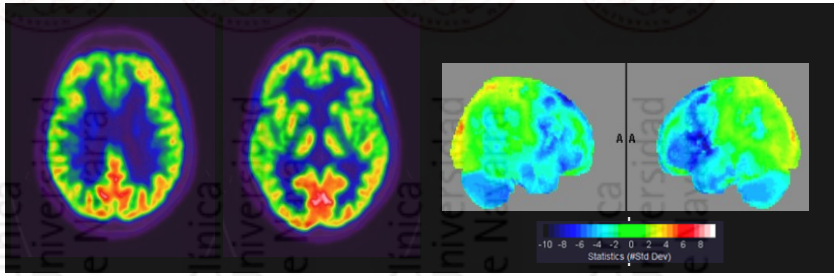
desde 13.8% a 38.3%

Laforce RJ, et al. Am J Alzheimer's Dis Other Demen. 2010

PET FDG (N)

Espectro FTLD

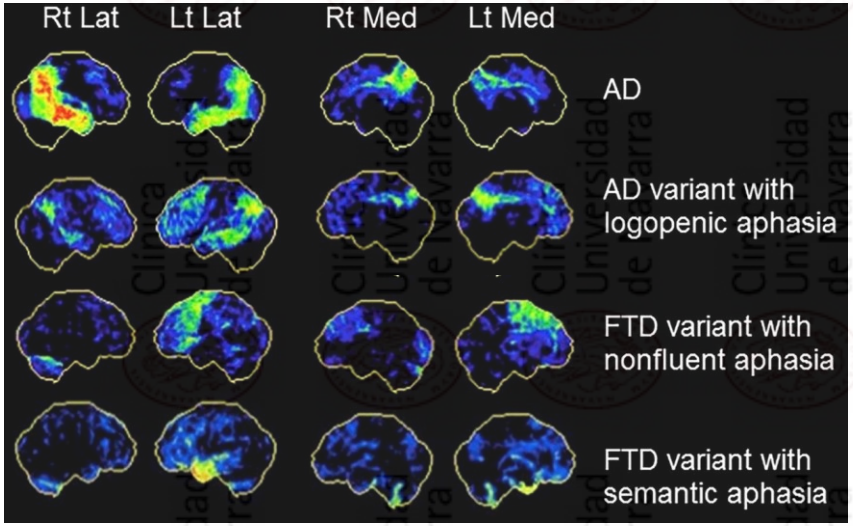
Variante del Comportamiento FTD (bvFTD)



- parte de los criterios diagnósticos
- Incorporado a la rutina clínica

K. Rascovsky et al. Brain 2011

Afasia Progresiva Primaria

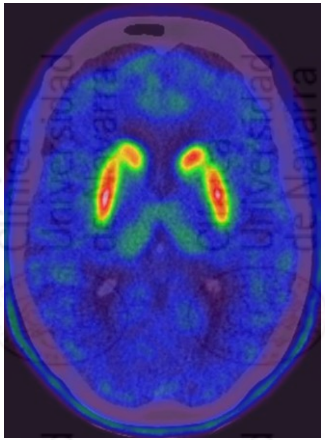


Taswell et al. J Nucl Med 2015

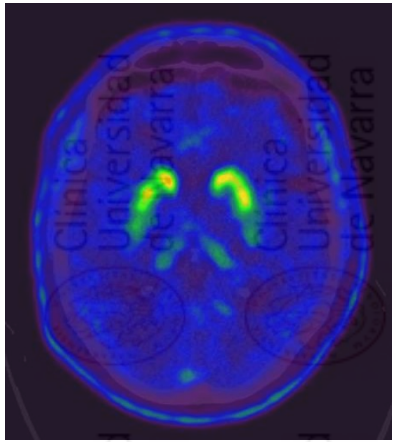
PET FDG (N)

Demencia con Cuerpos de Lewy: Función Dopaminérgica Presináptica

PET-^{18}F-FDOPA

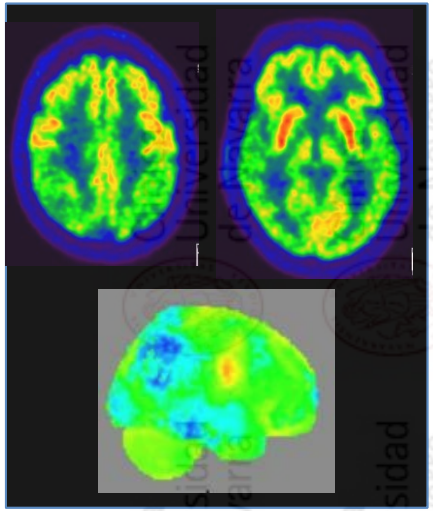


E. Alzheimer

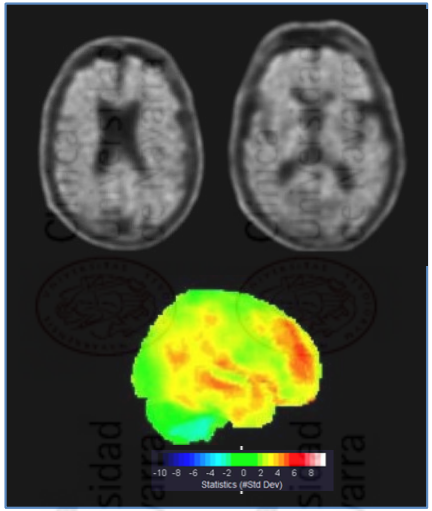


Demencia con Cuerpos de Lewy

PET-^{18}F-FDG



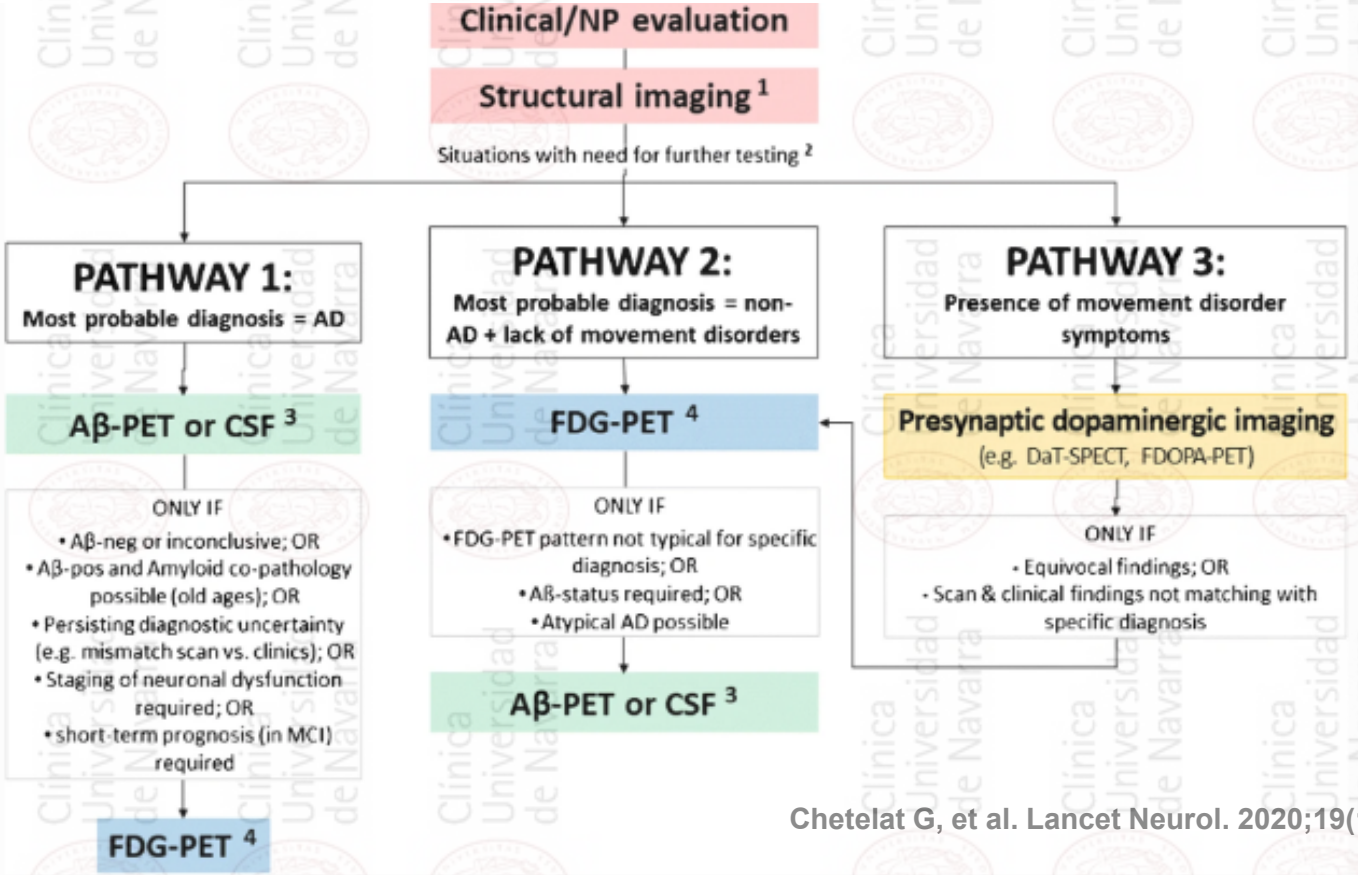
PET-Amiloide



Demencia con Cuerpos de Lewy

McKeith, et al. Neurology 2017

Evaluación Diagnóstica: combinación de biomarcadores según la situación clínica



Chetelat G, et al. Lancet Neurol. 2020;19(11):951-962

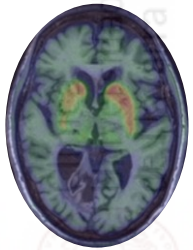
Diagnóstico diferencial del Parkinsonismo de origen incierto

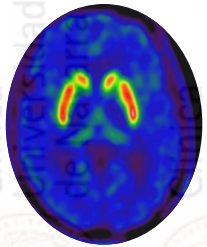
Secundario

Tumor

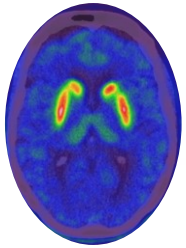
Vascular

Fármaco-inducido





Temblor Esencial



Neurodegenerativo

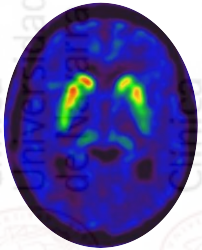
EP

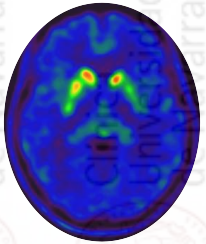
PSP

DCB

AMS-P

AMS-C





Brooks DJ. J Nucl Med. 2010;
Arbizu J, et al. Rev Esp Med Nucl Med. 2014

Diagnóstico Clínico PSP:

The Movement Disorder Society Criteria 2017

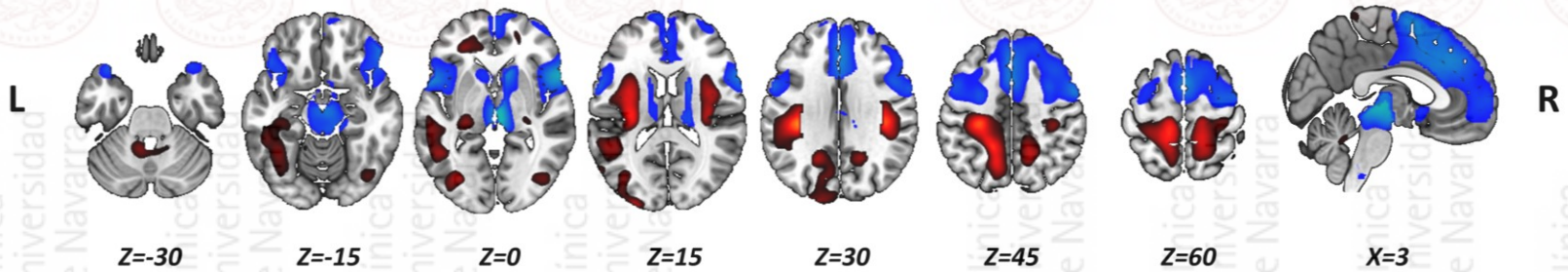
Level of diagnostic certainty	definition
Definite PSP	**Neuropathological** exam
Probable PSP	Highly specific **Clinical features**
Possible PSP	**Clinical features** that increase sensitivity * **Biomarkers** to increase diagnostic specificity
Suggestive PSP	**Subtle early signs** * **Biomarkers** that help an earlier diagnosis

Höglinger. *Mov Disord* 2017; Whitwell. *Mov Disord* 2017

FDG PET

Clínica Universidad de Navarra

PSP vs Control



PATRÓN PET FDG en PSP

-SSM/ PCA (PSP-RP): **Scaled Subprofile Model & Principal Component Analysis**

detección de regiones cerebrales que muestran interrelación en base a su consumo metabólico (redes neuronales)

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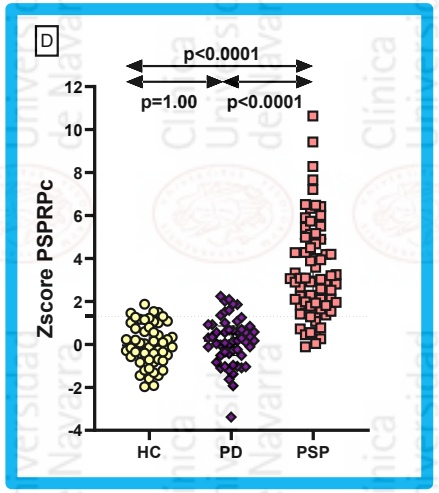
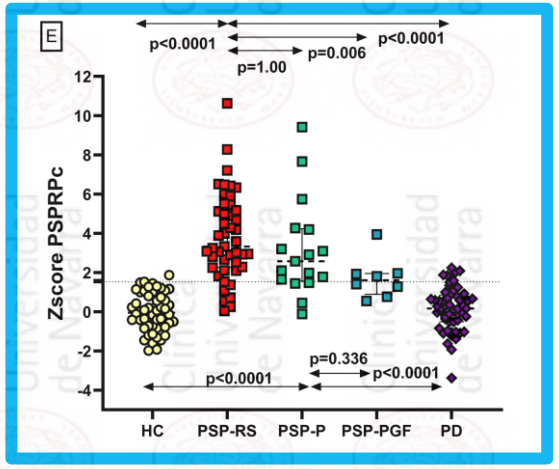
FDG PET

Patrón PSP: Validación

	Validación interna	Validación externa	
	PSP vs HC		PSP vs PD
Sensibilidad (%)	100	80.4	80.4
Especificidad (%)	100	96.9	90.7
Valor Predictivo Positivo (%)	100	97.6	89.1
Valor Predictivo Negativo (%)	100	75.6	83.1
Área Bajo de la Curva	1	0.945	0.910
Punto de corte (Z-score)	>1.3	>1.53	>1.59





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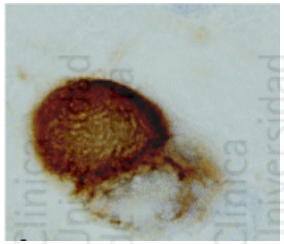
Parálisis Supranuclear Progresiva (PSP)

Fisiopatología

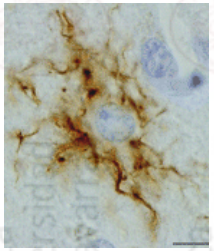
Tau hiperfosforilada 4R: Neuronas y Glía

Neuronas mesencéfalo y subcorticales:
inclusiones tau

Neocortex:
ovillos neuronales y gliales



globose neuronal tau tangle



tufted astrocytes

Irwin, *Parkinsonism Relat Disord*. 2016

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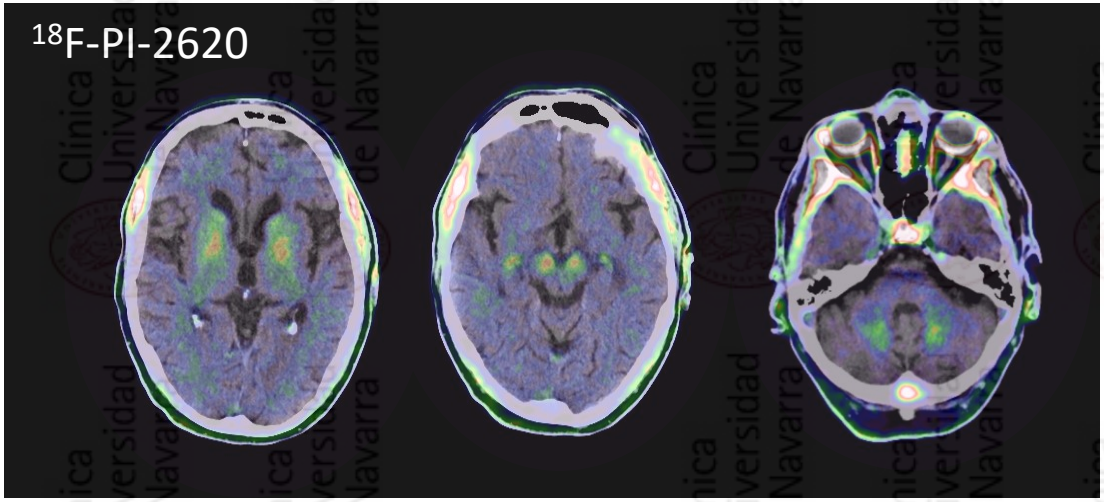
VALORACIÓN DEL DEPÓSITO CEREBRAL DE TAU 4R MEDIANTE PET CEREBRAL CON 18F-PI2620 EN PARÁLISIS SUPRANUCLEAR PROGRESIVA RESPECTO A CONTROLES SIN TAUPATÍA NEURODEGENERATIVA 4R:



Conclusiones

Biomarcadores de imagen molecular: papel decisivo en el diagnóstico de las enf. neurodegenerativas

PET-Amiloide (A)

- Biomarcador de EA; extension y distribución de la patología EA evolutivamente
- Importante en el manejo terapéutico de la EA

PET-Tau (T)

- Biomarcador de EA: correlación regional con el fenotipo clínico: diagnóstico diferencial
- Tau precede a la neurodegeneración: más sensible para predecir la conversion de SCD y MCI a demencia EA

PET-FDG (N)

- Facilita el diagnóstico diferencial
- Predicción de la evolución a corto plazo a demencia y estadificación del proceso neurodegenerativo

PET y SPECT actividad Dopaminérgica

- Define el origen neurodegenerativo del parkinsonismo

Biomarcadores PET en Neurodegenerativas

¡Gracias!

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