NAPA Advisory Council Meeting

Research on ADRD: Lewy Body Dementia

Jennifer G. Goldman, MD, MS
Adjunct Professor of Neurology,
Barrow Neurological Institute
JPG Enterprises LLC

1

Disclosures

- Grants/research support: Acadia, American Parkinson's Disease Association, Lewy Body Dementia Association, Michael J. Fox Foundation, Parkinson's Foundation
- Honoraria: International Parkinson Disease and Movement Disorders Society, Lewy Body Dementia Association, Parkinson's Foundation, Parkinson Study Group
- Consultant or advisory board: Curasen, EIP Pharma (DSMB member), GE healthcare, KeifeRx, Neuropath, Roche, SAGE

- Off-label medication use will be mentioned

- I serve as Chair of the Lewy Body Dementia Association (LBDA) Scientific Advisory Council and Industry Advisory Council and as Secretary-Elect of the International Parkinson and Movement Disorder Society.

2

Lewy Body Dementia (LBD) - Outline

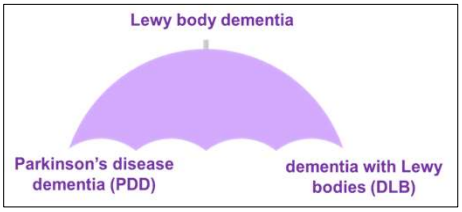
- Terminology
- Epidemiology
- Impact
- Biomarkers, pathology, genetics
- ADRD Research recommendations for LBD
- Resources and Programs
- Considerations for Governmental Agencies

3

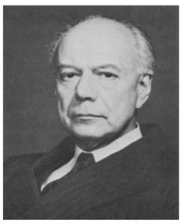
LBD - Terminology

- Lewy body dementia = CLINICAL
  - Parkinson's disease with dementia (PDD)
  - Dementia with Lewy bodies (DLB)

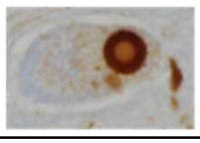
- Lewy body disease = PATHOLOGY
  - Pathologic diagnosis with Lewy bodies and neuronal loss
  - Multiple types - brainstem predominant, transitional (limbic), and diffuse (neocortical) forms

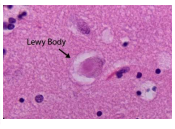


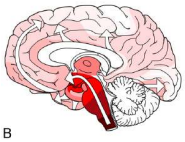
Lewy 1934 , immigration file
National Archives Philadelphia



Lewy 1949
(Brown JR. 'The early years of the American Academy of Neurology'. Neurology 1974;24:1)







B

4

LBD - Epidemiology

- Dementia with Lewy Bodies (DLB) – 2nd most frequent neurodegenerative dementia after AD
  - Affects 1.4M in US
  - Incidence - 3.8% of new dementia diagnosis
  - Prevalence - 4.2% of dementia diagnosis in community settings and 7.5% of diagnoses in secondary care
  - Represents 4-30% of dementia cases in population- and clinic-based studies
- PD dementia (PDD)
  - Incidence – 95.3-112.5/1000 patient-years, ~10% of a PD population developing dementia per year
  - Point prevalence – 30% with cumulative prevalence of 75-80%

Bach et al., 2011; Savica et al., 2018; Willis et al., 2022

5

LBD - Impact

Delayed or misdiagnosis
- On average, takes 18 months and 3 doctors to receive correct diagnosis

Increased disability and decreased quality of life
- Neuropsychiatric symptoms, cognitive fluctuations, motor features, and other symptoms
- "Like having both Alzheimer's and Parkinson's disease"

High economic burden

Marked caregiver stress and burden

Management challenges – limited medications, side effects, no disease-modifying agents

Frazer et al., 2023; Desai et al., 2022; Espinosa et al., 2020; LBDA

6

Diagnosis and management of dementia with Lewy bodies

Fourth consensus report of the DLB Consortium

OPEN

McKeith et al., 2017

- Core features
  - Dementia, sufficient to interfere with normal functions or daily activities
  - Fluctuating cognition
  - Recurrent visual hallucinations
  - REM sleep behavior disorder, which may precede cognitive decline
  - Parkinsonism motor features
- Supportive clinical features
  - *Severe sensitivity to antipsychotics, postural instability, repeated falls, syncope or episodes of unresponsiveness, autonomic dysfunction, hypersomnia, hyposmia, hallucinations, delusions, apathy, anxiety, depression*
- Biomarkers
  - *Indicative (dopamine transporter uptake scan, MIBG, sleep study)*
  - *Supportive (related to imaging, EEG)*

Movement Disorders
Vol. 22, No. 12, 2007, pp. 1689-1707
© 2007 Movement Disorder Society

Clinical Diagnostic Criteria for Dementia Associated with Parkinson's Disease

Emre et al., 2007

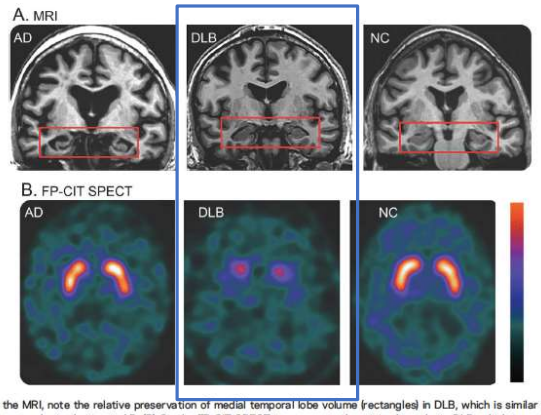
Murat Emre, MD,[1]* Dag Aarsland, MD,[2,3] Richard Brown, PhD,[4] David J. Burn, MD,[5] Charles Duyckaerts, MD,[6] Yoshikino Mizuno, MD,[7,8] Gerald Anthony Broe, MD,[9,10] Jeffrey Cummings, MD,[11] Dennis W. Dickson, MD,[12] Serge Gauthier, MD,[13] Jennifer Goldman, MD,[14] Christopher Goetz, MD,[14] Amos Korczyn, MD,[15] Andrew Lees, MD,[16] Richard Levy, MD, PhD,[17] Irene Litvan, MD,[18] Ian McKeith, MD,[19] Warren Olanow, MD,[20] Werner Poewe, MD,[21] Niall Quinn, MD,[22] Christina Sampaio, MD, PhD,[23] Eduardo Tolosa, MD,[24] and Bruno Dubois, MD[25]

- Core features
  - Dementia syndrome, insidious onset, slow progression in context of PD
  - Impairment in > 1 cognitive domain
  - Decline from pre-morbid level
  - Deficits severe enough to impair daily life (independent of motor symptoms)
- Associated clinical features
  - *Cognitive:* attention, executive function, visuospatial, memory, language
  - *Behavioral:* apathy, mood, psychosis, excessive sleepiness

7

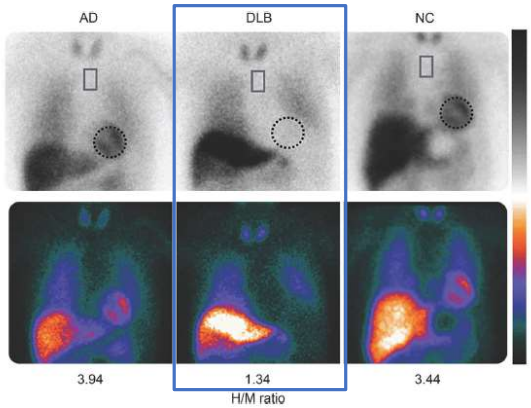
Biomarkers in DLB criteria: AD vs. DLB vs. NC

Figure 1 Coronal T1-weighted MRI and ^{123}Iodine FP-CIT SPECT images in Alzheimer disease (AD), dementia with Lewy bodies (DLB), and normal controls (NC)



(A) On the MRI, note the relative preservation of medial temporal lobe volume (rectangles) in DLB, which is similar to NC, whereas atrophy is obvious in AD. (B) On the FP-CIT SPECT images, note the minimal uptake in DLB, which is restricted to the caudate (period or full-stop appearance) compared to the robust uptake in the caudate and putamen in AD and NC (comma appearance). Reproduced with permission from Dr. Val Lowe, Mayo Clinic, Rochester, MN.

Figure 2 ^{123}Iodine-metaiodobenzylguanidine myocardial imaging in patients with Alzheimer disease (AD), dementia with Lewy bodies (DLB), and age-matched normal controls (NC)



Images taken 3 hours after injection are shown in 2 color scales, and typical regions of interest are shown on the heart (dotted circle) and upper mediastinum (rectangle). Heart-to-mediastinum (H/M) ratios are standardized to the values comparable to a medium-energy general-purpose collimator condition.[+12] Reproduced with permission from Dr. Kenichi Nakajima, Department of Nuclear Medicine, Kanazawa University.

McKeith et al., 2017

8

LBD - Pathology

Alpha-synuclein (ASYN) in Lewy bodies and neurites

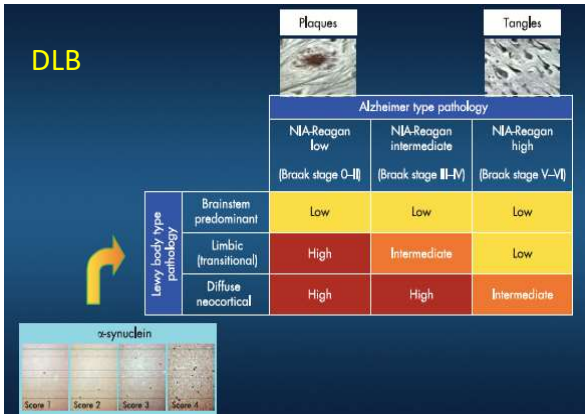
- Brainstem
- Limbic and neocortical regions

Amyloid-beta plaques and tau

Mixed or co-pathologies

- ~2/3rd of DLB with AD path and ~1/3rd of PDD with AD path
- Cerebrovascular
- TDP-43 or limbic-predominant age-related TDP-43 (LATE)

May influence clinical phenotype and progression



McKeith 2007; Ferreira et al., 2020; Toledo et al., 2022; Jellinger et al., 2023

9

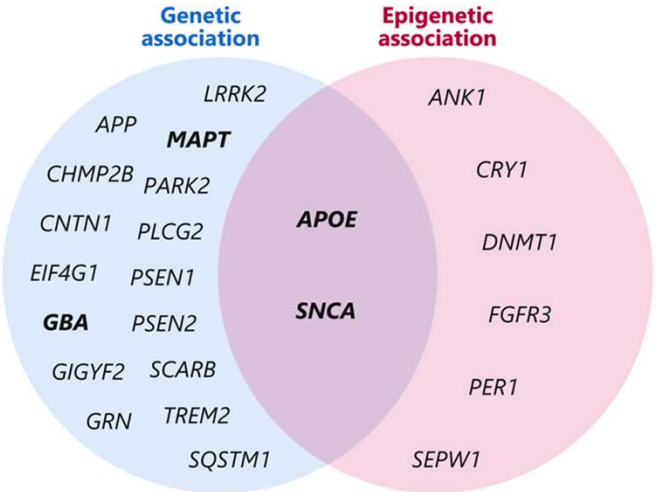
LBD – Genetics

Systematic review of genetic association studies in people with Lewy body dementia 2020

Hazel Sanghvi[1] | Ricky Singh[1] | Hamilton Morrin[1] | Anto P. Rajkumar[2,3]

Epigenetic regulation in the pathophysiology of Lewy body dementia 2020

Leonidas Chouliaras[a,*], Gautham S. Kumar[a], Alan J. Thomas[b], Katie Lunnon[c], Patrick F. Chinnery[d], John T. O'Brien[a]



10

2022 NAPA ADRD Summit – Research Recommendations for LBD

- Recommendation 1 – Priority 1. Prepare for and initiate clinical trials that aim to alleviate or slow the course of LBD symptoms, and delay or prevent the onset of disease. (1-7 years)
- Recommendation 2 – Priority 2. Develop and refine neuroimaging biomarkers that track progression, assist in differential diagnosis, provide therapeutic target engagement, and relate to pathology. (2-7 years)
- Recommendation 3 – Priority 3. Develop and refine biomarkers for diagnosis, prediction, and prognosis utilizing biofluids, tissues, and digital and electrophysiological methods. (2-7 years)
- Recommendation 4 – Priority 4. Expand existing and develop new longitudinal LBD study cohorts, including diverse populations, from pre-symptomatic disease to autopsy to support diagnostic, epidemiologic, and therapeutic studies. (1-7 years)
- Recommendation 5 – Priority 1. Delineate genetic loci and their functions contributing to the onset and progression of LBDs using genetic, transcriptomic, epigenetic, and environmental characterization analyses. (1-7 years)
- Recommendation 6 – Priority 2. Enhance and standardize the techniques for neuropathologic characterization of LBD and the use of LBD pathology cohorts including more diverse cohorts. (2-7 years)
- Recommendation 7 – Priority 3. Develop models to understand the pathophysiology and normal molecular and cellular functions of α-synuclein to support drug discovery. (5-7 years)
- Recommendation 8 – Priority 4. Identify mechanisms of selective vulnerability, disease heterogeneity, disease spread/propagation, and interaction with other age-related pathologies as therapeutic targets. (5-7 years)

11

Recommendation 1 – Priority 1. Prepare for and initiate clinical trials that aim to alleviate or slow the course of LBD symptoms, and delay or prevent the onset of disease. (1-7 years)

www. clinicaltrials.gov

NCT Number	Study Title	Study Status	Conditions	Interventions	Sponsor
NCT06098612	PET Imaging Evaluation of [11C]SY08	RECRUITING	PD, MSA, DLB, HC	DRUG: C11-SY08	MGH
NCT05869669	RewinD-LB - Clinical Study of Neflamapimod in Patients With Dementia With Lewy Bodies	RECRUITING	DLB	DRUG: Neflamapimod|DRUG: Placebo	EIP Pharma Inc
NCT05590637	Comparing Antipsychotic Medications in LBD Over Time	RECRUITING	PD Psychosis, DLB	DRUG: Pimavanserin|DRUG: Quetiapine	UTH-San Antonio
NCT05225415	Study to Evaluate the Safety, Tolerability and Efficacy of CT1812 in Subjects With Mild to Moderate Dementia With Lewy Bodies	RECRUITING	DLB	DRUG: CT1812	Cognition Therapeutics
NCT04739423	A Study of CST-103 Co-administered With CST-107 in Subjects With Neurodegenerative Disorders	ACTIVE_ NOT_RECRUITING	MCI, LBD, PD RBD, PDD	DRUG: CST-103, CST-107, matching placebo	CuraSen Therapeutics, Inc.
NCT04831281	ATH-1017 Treatment in Subjects With Parkinson's Disease Dementia or Dementia With Lewy Bodies (SHAPE Trial)	ACTIVE_ NOT_RECRUITING	PDD, DLB	DRUG: ATH-1017|DRUG: Placebo	Athira Pharma
NCT06120049	[18F]-MFBG Versus [123I]-MIBG and [18F]-PE2I in PD vs. MSA and DBL vs. AD	NOT_YET_ RECRUITING	PD, DLB, MSA, AD	DIAGNOSTIC_TEST: [18F]-MFBG PET, [123I]-MIBG SPECT CT|DIAGNOSTIC_TEST: [18F]-MFBG PET dosimetry scans	prof. dr. Koen Van Laere
NCT05428475	Implementation and Evaluation of Improved Access to Medical Imaging for Geriatric Patients of The Royal Ottawa Hospital	NOT_YET_ RECRUITING	Dementia|Cognitive Impairment|DLB	DIAGNOSTIC_TEST: [18F]FDG-PET Scan	Tim Lau
NCT04760860	Terazosin for Dementia With Lewy Bodies	NOT_YET_ RECRUITING	DLB	DRUG: Terazosin Hydrochloride|OTHER: Placebo	Qiang Zhang

12

Dementia with Lewy Bodies Drug Therapies in Clinical Trials: Systematic Review up to 2022

Metabolism/Bioenergetics
Neurotransmitter receptors
Multitarget
Oxidative stress
Proteostasis/Proteinopathies
Synaptic plasticity/Neuroprotection
Grow factors
Unknown

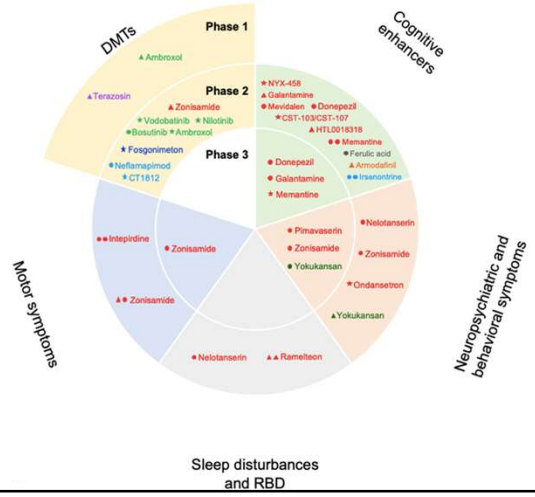


Table 1 General characteristics of clinical trials in DLB as of September 27, 2022

Clinical trial phase	Number of clinical trials	Status			Classification		Repurposed agents
		Completed	Active[a]	Other status	DMT	Symptomatic	
Phase3	7 (17.5%)	6 (86%)	1 (14%)	0	0	7 (100%)	7 (100%)
Phase 2	31 (77.5%)	15 (48.4%)	8 (25.8%)	8[b] (25.8%)	8 (25.8%)	23 (74.2%)	16 (51.6%)
Phase 1	2 (5%)	0	0	2[c] (100%)	2 (100%)	0	2 (100%)
Total	40	21 (52.5%)	9 (22.5%)	10 (27%)	10 (25%)	30 (75%)	25 (65%)

[a]Recruiting, Active/not recruiting
[b]Withdrawn = 3, pending = 2, not recruiting = 2, terminated = 1
[c]Not yet recruiting = 2

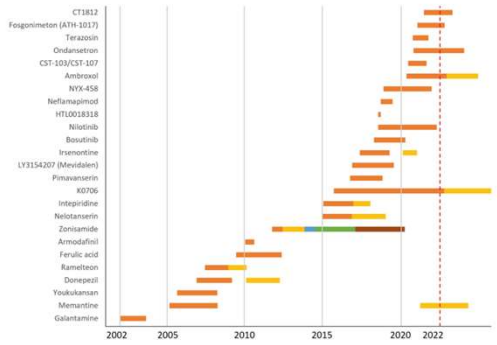


Fig. 2 Evolution of clinical trials for DLB, showing all the agents investigated in DLB clinical trials from 2002 to 2022. *Each color* represents one clinical trial

Abdelnour et al., 2023

13

Outcome Measures for Dementia With Lewy Body Clinical Trials

A Review

Bhavana Patel, DO, David J. Irwin, MD,† Daniel Kaufer, MD,‡ Bradley F. Boeve, MD,§ Angela Taylor, BMus,‖¶ and Melissa J. Armstrong, MD, MSc**

Clinical outcome measures in dementia with Lewy bodies trials: critique and recommendations

Federico Rodriguez-Porcel[1*], Kathryn A. Wyman-Chick[2], Carla Abdelnour Ruiz[3], Jon B. Toledo[4], Daniel Ferreira[5,6], Prabitha Urwyler[7], Rimona S. Weil[8], Joseph Kane[9], Andrea Pilotto[10], Arvid Rongve[11,12], Bradley Boeve[13], John-Paul Taylor[14], Ian McKeith[14], Dag Aarsland[15] and Simon J. G. Lewis[16] on behalf of the Lewy Body Dementias Clinical Trials Workgroup from the Lewy Body Dementias Professional Interest Area - Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment (ISTAART)+

STUDY PROTOCOL

Developing a core outcome set (COS) for Dementia with Lewy bodies (DLB) [version 1; peer review: 1 approved, 2 approved with reservations]

Emilia Grycuk[1], Emily Eichenholtz[2], Dag Aarsland[3], Sara Betzhold[4], Gillian Daly[2], Ann-Kristin Folkerts[5], Elke Kalbe[5], Joseph PM Kane[6], Irina Kinchin[7], Ian Saldanha[8], Valerie Smith[9], John-Paul Taylor[10], Rachel Thompson[11,12], Iracema Leroi[13]

TABLE 1. Cognitive Scales Used as Primary or Secondary Outcomes in DLB Clinical Trials

	Primary Outcome		Secondary Outcome	
	Frequency	References	Frequency	References
MMSE	6	10,13,14,17,26,41	18	15,18,25,27,30,32,40,43,45,48–50, 53,55,57,63,64,66
COGDRAS	3	12,27,49	2	18,32
Verbal Fluency	2	10,45	0	NA
COWAT or COWA	1	54	4	24,27,43,57
MoCA	1	63	3	47,65,67
Clinician's Assessment of Fluctuations scale	1	45	3	25,47,65
ADAS-Cog (memory)	0	NA	6	11,24,43,47,49,65
Trail Making test (executive)	0	NA	5	24,27,45,47,65
Stroop test	0	NA	3	24,27,45
Benton Judgement of Line Orientation (visuospatial)	0	NA	2	24,45
Clock drawing 10 point (executive)	0	NA	2	24,25
Digit span forward/backward	0	NA	2	43,57
Cognitive Fluctuation Inventory	0	NA	2	15,63
One day fluctuation assessment	0	NA	2	25,57

ADAS-Cog indicates Alzheimer's Disease Assessment Scale-Cognitive Subscale; COGDRAS, Cognitive drug research computerized cognitive assessment system; COWAT or COWA, Controlled oral word association test measure of verbal fluency; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment.

Table 4 Selected functional, quality of life, caregiver burden and global impression outcomes

Outcome	Type of measure	Rater	Reliability	Responsiveness	MCID	Used in DLB trials
ADCS-ADL	ADLs	Informant	+	+	2 points	Yes [44–46]
DAD	ADLs	Informant	+	+	NE	Yes [40, 47]
UPDRS-II	ADLs	Informant Subject	NE	NE	NE	Yes [48, 49]
SEADL	ADLS	Informant	NE	NE	NE	No
QOL-AD	QoL	Subject	+	+	NE	Yes [32]
PDQ-39	QoL	Subject	+/−	NE	NE	No
ZBI	CB	Informant	+/−	+	13 points	Yes [43, 45, 47, 50–53]
RSS	CB	Informant	+	NE	NE	No
CIBIC+	IoC	Clinician/Informant	+/−	+	NE	Yes [43, 54–58]
CGI	IoC	Clinician	+/−	+	NE	Yes [54, 59, 60]
ADCS-CGIC	IoC	Clinician	+/−	+	1 point	Yes [44, 45, 61, 62]

+, good/adequate; +/−, acceptable; −, performance is questionable/mediocre. *ADLs* activities of daily living, *CB* caregiver burden, *IoC* impression of change, *MCID* minimal clinically important difference, *NE* not evaluated, *QoL* quality of life, *ADCS-ADL* Alzheimer's Disease Cooperative Study—Activities of Daily Living Scale, *DAD* Disability Assessment for Dementia, *UPDRS-II* Unified Parkinson's Disease Rating Scale Part II, *SEADL* Schwab and England Activities of Daily Living, *QOL-AD* Quality of Life in Alzheimer's Disease Scale, *PDQ-39* 39-Item Parkinson's Disease Questionnaire, *ZBI* Zarit Burden Interview, *RSS* Relative Stress Scale, *CIBIC+* Clinician's Interview-Based Impression of Change Scale, *CGI* Clinical Global Impression Scale, *ADCS-CGI* Alzheimer's Disease Cooperative Study–Clinician's Global Impression of Change

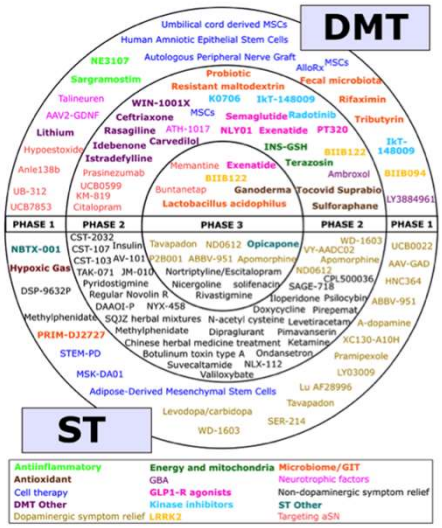
Patel et al., 2022; Rodriguez-Porcel et al., 2022; Grycuk et al., 2022; Sabbagh et al., 2022

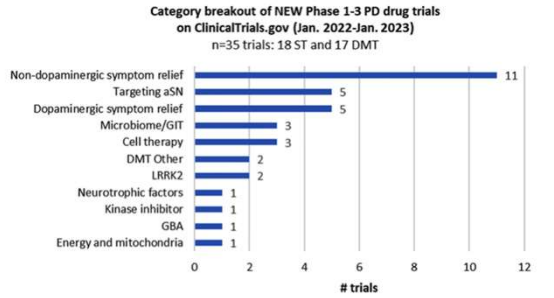
14

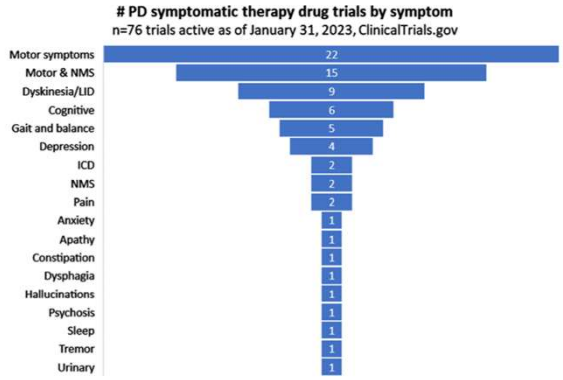
Parkinson's Disease Drug Therapies in the Clinical Trial Pipeline: 2023 Update

Jrl PD 2023

Kevin McFarthing[a], Susan Buff[b], Gary Rafaloff[c], Brian Fiske[d], Leah Mursaleen[e], Rosie Fuest[e], Richard K. Wyse[e] and Simon R.W. Stott[e,*]







15

Recommendation 2 – Priority 2. Develop and refine neuroimaging biomarkers that track progression, assist in differential diagnosis, provide therapeutic target engagement, and relate to pathology. (2-7 years)

- Structural MRI
  - Preserved medial temporal lobe
- Diffusion tensor imaging
- Susceptibility-weighted imaging
- Functional MRI
- Nuclear medicine / metabolic imaging (PET, SPECT)
  - Decreased glucose metabolism and perfusion in parietotemporal and occipital areas
  - Cingulate island sign
  - Reduced dopamine transporter uptake (DaT scan)
  - Amyloid-beta deposition variable

McKeith et al., 2017; Mavroudis et al., 2019

16

Recommendation 3 – Priority 3. Develop and refine biomarkers for diagnosis, prediction, and prognosis utilizing biofluids, tissues, and digital and electrophysiological methods. (2-7 years)

Seed amplification assay for the detection of pathologic alpha-synuclein aggregates in cerebrospinal fluid

Luis Concha-Marambio, Sandra Pritzkow, Mohammad Shahnawaz, Carly M. Farris & Claudio Soto

Nature Protocols **18**, 1179–1196 (2023) | Cite this article

Assessment of heterogeneity among participants in the Parkinson's Progression Markers Initiative cohort using α-synuclein seed amplification: a cross-sectional study

Andrew Siderowf, Luis Concha-Marambio*, David-Erick Lafontant, Carly M Farris, Yihua Ma, Paula A Urenia, Hieu Nguyen, Roy N Alcalay, Lana M Chahine, Tatiana Foroud, Douglas Galasko, Karl Kieburtz, Kalpana Merchant, Brit Mollenhauer, Kathleen L Poston, John Seibyl, Tanya Simuni, Caroline M Tanner, Daniel Weintraub, Aleksandar Videnovic, Seung Ho Choi, Ryan Kurth, Chelsea Caspell-Garcia, Christopher S Coffey, Mark Frasier, Luis M A Oliveira, Samantha J Hutten, Todd Sherer, Kenneth Marek, Claudio Soto, on behalf of the Parkinson's Progression Markers Initiative†*

Clinical effects of Lewy body pathology in cognitively impaired individuals

Received: 21 January 2023
Accepted: 8 June 2023
Published online: 18 July 2023

Corinne Quadalti[1,2], Sebastian Palmqvist[2,3,7], Sara Hall[2,3], Marcello Rossi[1], Angela Mammana[1], Shorena Janelidze[2,7], Sofia Dellavalle[1], Niklas Mattsson-Carlgren[2,4,5], Simone Baiardi[1,6], Erik Stomrud[2,3], Oskar Hansson[2,3,7] & Piero Parchi[1,6,7]

- Synuclein seeding assay (SAA) measured in CSF
- Assay detected Parkinson's (PD) with high sensitivity and specificity
- Differentiate PD from atypical parkinsonian syndromes (MSA)
- In the BioFINDER study, CSF was studied in 883 memory clinic patients (MCI or dementia)
  - SAA found to be positive in 23%, with only 21% fulfilling clinical criteria for LBD (PDD or DLB) at baseline
  - Among those who were SAA+, 48% had AD pathology
  - Presence of SAA, but not amyloid or tau, was associated with hallucinations, worse attention/executive, visuospatial and motor function as well as faster cognitive decline

Scott et al., 2022; Bellomo et al., 2022; Concha-Marambio et al., 2023; Quadatli et al., 2023

17

Implications for prodromal cohorts

Assessment of heterogeneity among participants in the Parkinson's Progression Markers Initiative cohort using α-synuclein seed amplification: a cross-sectional study

Andrew Siderowf, Luis Concha-Marambio*, David-Erick Lafontant, Carly M Farris, Yihua Ma, Paula A Urenia, Hieu Nguyen, Roy N Alcalay, Lana M Chahine, Tatiana Foroud, Douglas Galasko, Karl Kieburtz, Kalpana Merchant, Brit Mollenhauer, Kathleen L Poston, John Seibyl, Tanya Simuni, Caroline M Tanner, Daniel Weintraub, Aleksandar Videnovic, Seung Ho Choi, Ryan Kurth, Chelsea Caspell-Garcia, Christopher S Coffey, Mark Frasier, Luis M A Oliveira, Samantha J Hutten, Todd Sherer, Kenneth Marek, Claudio Soto, on behalf of the Parkinson's Progression Markers Initiative†*

2023

- Among prodromal and at-risk groups, 44 (86%) of 51 of participants with RBD or hyposmia had positive α-synuclein SAA (16/18 with hyposmia, 28/33 with RBD).

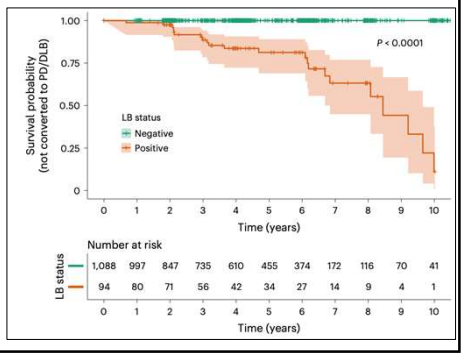
Cognitive effects of Lewy body pathology in clinically unimpaired individuals

Received: 21 January 2023
Accepted: 8 June 2023
Published online: 18 July 2023

Sebastian Palmqvist[2,3,8], Marcello Rossi[2,3], Sara Hall[2,3], Corinne Quadalti[2], Niklas Mattsson-Carlgren[3,4,5], Sofia Dellavalle[2], Pontus Tideman[3,5], Joana B. Pereira[1], Maria H. Nilsson[3,6], Angela Mammana[2], Shorena Janelidze[3,7], Simone Baiardi[3,7], Erik Stomrud[2,3], Piero Parchi[3,7,8] & Oskar Hansson[3,5,8]

2023

- Examined CSF SAA in 1182 cognitively unimpaired
- Found 8% LB+, 26% Abeta+ (13% also LB+), and 16% tau+
- LB+ status associated with conversion to PD/DLB



18

Recommendation 4 – Priority 4. Expand existing and develop new longitudinal LBD study cohorts, including diverse populations, from pre-symptomatic disease to autopsy to support diagnostic, epidemiologic, and therapeutic studies. (1-7 years)

- Pre-symptomatic and early stage disease
- North American Prodromal Synucleinopathy (NAPS)
  - REM Sleep Behavior Disorder (RBD)
- Parkinson's Progression Marker Initiative (PPMI)
  - De novo PD
  - RBD, hyposmia, imagine with dopamine transporter deficit, genetic risk variants
- Prodromal DLB cohorts

NAPS CONSORTIUM
For REM Sleep Behavior Disorder

Parkinson's Progression Markers Initiative

19

Global cohorts & research initiatives for DLB

Name Website *Country*	Year establishe
EUROPE	
European DLB Consortium (E-DLB) www.e-dlb.com *Multinational*	2016
PDWAVES www.pdwaves.eu *Multinational*	2014
Italian DLB consortium** *Italy*	2016
UK-ENLIST** *United Kingdom*	2019
NORTH AMERICA***	
Comprehensive Assessment of Neurodegeneration and Dementia (COMPASS-ND) www.ccna-ccnv.ca *Canada*	2017
DLB Consortium (DLBC) https://pdbp.ninds.nih.gov/index.php/Dementia-with-Lewy-Bod *USA*	2017
Alzheimer's Dementia Care (ADC) program https://naccdata.org/ *USA*	1985
Longitudinal Imaging Biomarkers of Disease Progression in DLB *USA*	2018
SOUTH AMERICA[c]	
Multi-partner consortium to expand dementia research in Latin America (ReDLat) *Multinational*	2019
Brazilian Biobank for Aging Studies *Brazil*	2004
DLB Consortium (COL-DLB) *Colombia*	2019
ASIA[c]	
Tianjin Dementia Institute *China*	2016
Dementia collaborative research network (PKU-DCRN) *China*	2006
The Innovation Center for Neurological Disorders (CMU-ICND) *China*	2019
Dementia with Lewy Bodies Society Japan (DLBSJ) *Japan*	2007
AUSTRALIA[c]	
ForeFront DLB *Australia*	2017
Lewy body study *Australia*	2018

D'Antonio et al., 2021

20

LBD – Key resources and programs

NIH National Institute on Aging

NIH National Institute of Neurological Disorders and Stroke

LBD global community

LBDA LEWY BODY DEMENTIA ASSOCIATION

The Lewy Body Society
Shining a light on Lewy body dementia

LEWY BODY DEMENTIA AUSTRALASIA

LEWY BODY IRELAND

LEWY BODY ESPAÑA

A2MCL
Association des Aidants et Malades à Corps de Lewy

Lewy.ca

LEWY BODY DEMENTIA RESOURCE CENTER
BRINGING AWARENESS, SUPPORTING WITH

Lewy.be

ALIBA

21

LBD – Considerations for government agencies

Clinical considerations

- Support efforts for improving diagnoses, access to care and specialists, coverage for tests for diagnosis, etc
- Assist patients and families to reduce disability and disease burden and enhance quality of life through a variety of care models and treatment options across all disease stages
- Identify early / prodromal stages and follow longitudinally

Research

- Advance clinical trials for symptomatic therapies and disease-modifying agents, including study design, outcome measures
- Address specific symptoms, e.g., cognitive fluctuations
- Further research on biomarkers, genetics, mechanisms, and models

22