SF3PA
Société Francophone de Psychogériatrie et de Psychiatrie de la Personne Âgée

Réseau OMERIS

TRAITEMENTS MÉDICAMENTEUX DES MALADIES À CORPS DE LEWY

ÉTAT DES LIEUX DES PRATIQUES ACTUELLES

Dr Alexis LEPETIT
Psychiatre – Gériatre
Réseau OMERIS (CALUIRE-ET-CUIRE)
Team Neuroplasticity in Parkinson's disease, Institut des Sciences Cognitives (BRON)
Institut du Vieillissement, Hospices Civils de LYON

lundi 5 juin 2023

Vous sentir chez vous, c'est possible chez nous.

ISC Marc Jeannerod

HCL HOSPICES CIVILS DE LYON

L'INSTITUT DU VIEILLISSEMENT

LIENS ET CONFLITS D'INTERÊT

- Avec le sujet de cette communication
  - Acadia Pharmaceuticals
    - Investigateur associé protocole ACP-103-032
    - Investigateur associé protocole ACP-103-033

- Sans rapport avec le sujet de cette communication
  - Laboratoires Lundbeck
    - Investigateur principal protocole Memory
    - Symposium satellite (congrès SF3PA 2019 et 2023)
  - Biocodex
    - Frais de participation à une manifestation scientifique/congrès (congrès ECNP 2017)

PLAN

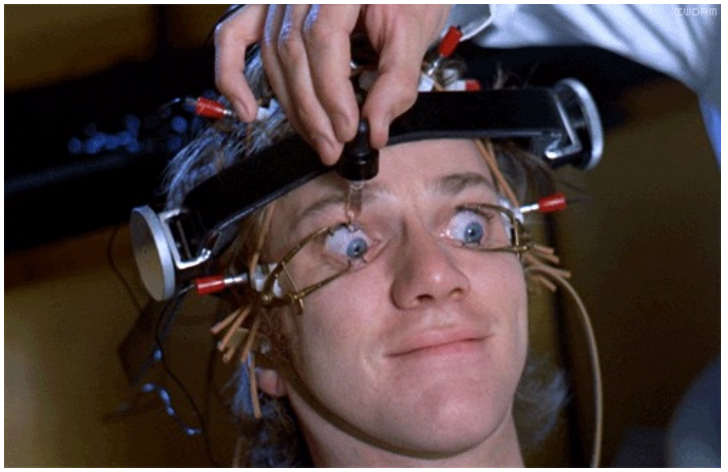
- Efficacité médicamenteuse
  - Symptômes moteurs
  - Troubles du sommeil paradoxal
  - Cognition
  - Symptômes psychocomportementaux
  - Nouvelles pistes thérapeutiques

- Take Home Message

PRÉAMBULE

HÉTÉROGÉNÉITÉ DE LA LITTÉRATURE SCIENTIFIQUE

- Maladie(s) à corps de LEWY (MCL)
  - Maladie de Parkinson idiopathique +/- trouble neurocognitif léger/majeur
  - Démence à corps de LEWY (DCL)



Efficacité des traitements médicamenteux

Symptômes moteurs et troubles du sommeil paradoxal

EFFICACITÉ DES TRAITEMENTS MÉDICAMENTEUX

VERNY & BLANC 2019

- Symptômes moteurs
  - L-Dopa
    - Efficacité supérieure dans la MPI que dans la DCL
    - Dose débutante: 50mg 1 à 2/J
    - Titration selon
      - Efficacité
      - Tolérance (symptômes psychotiques)
- TCSP
  - Mélatonine
    - 3 à 12 mg/j
    - Pas de RCT


Synthèse

Geriatr Psychol Neuropsychiatr Vieil 2019 ; 17 (2) : 189-97

Maladie à corps de Lewy avec troubles neurocognitifs majeurs : le traitement selon la médecine basée sur les preuves et en pratique

Efficacité des traitements médicamenteux

Cognition

COGNITION MCL

MATSUNAGA ET AL. 2016

RESEARCH ARTICLE

Cholinesterase Inhibitors for Lewy Body Disorders: A Meta-Analysis

Shinji Matsunaga, Taro Kishi, Ichiro Yasue, Nakao Iwata

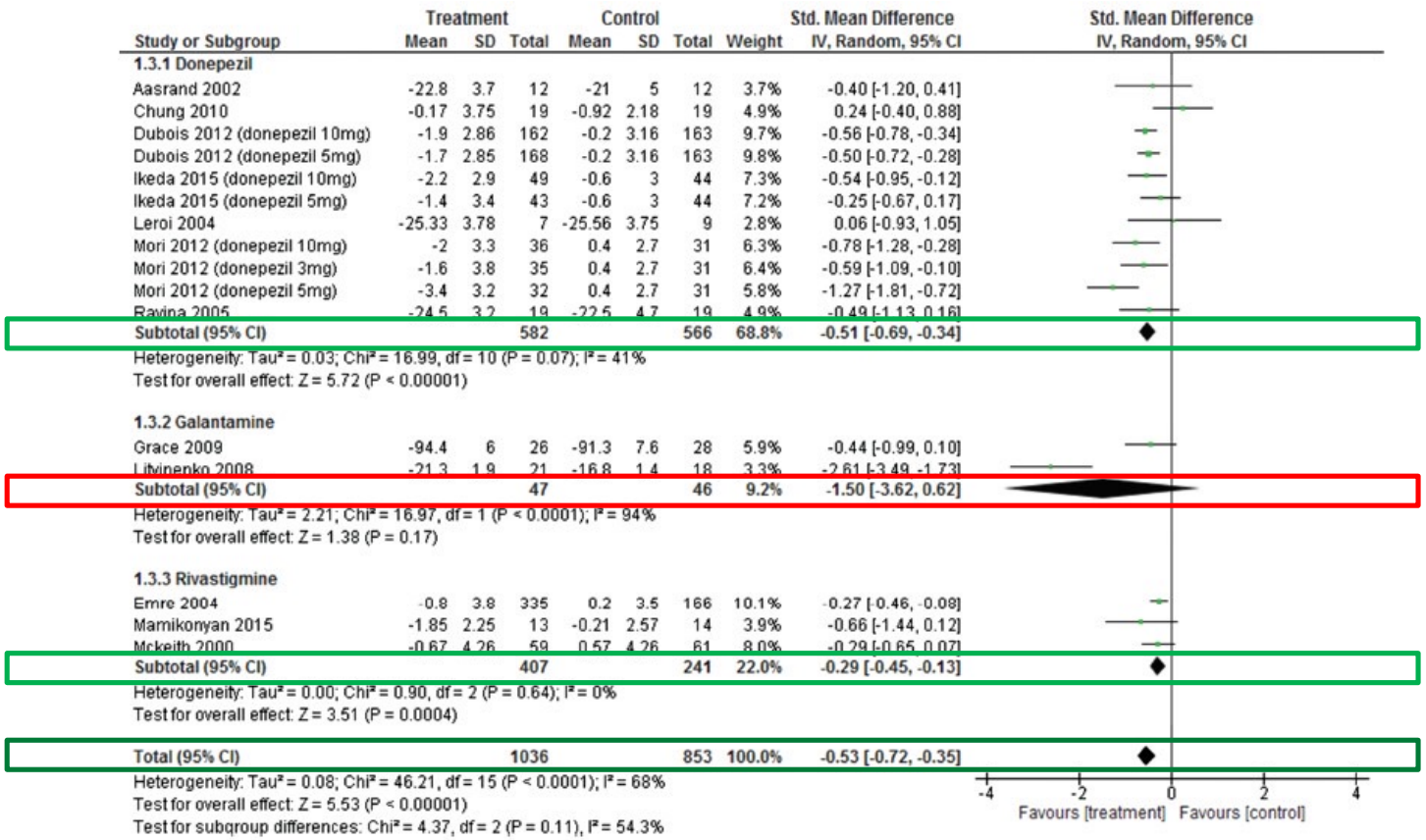


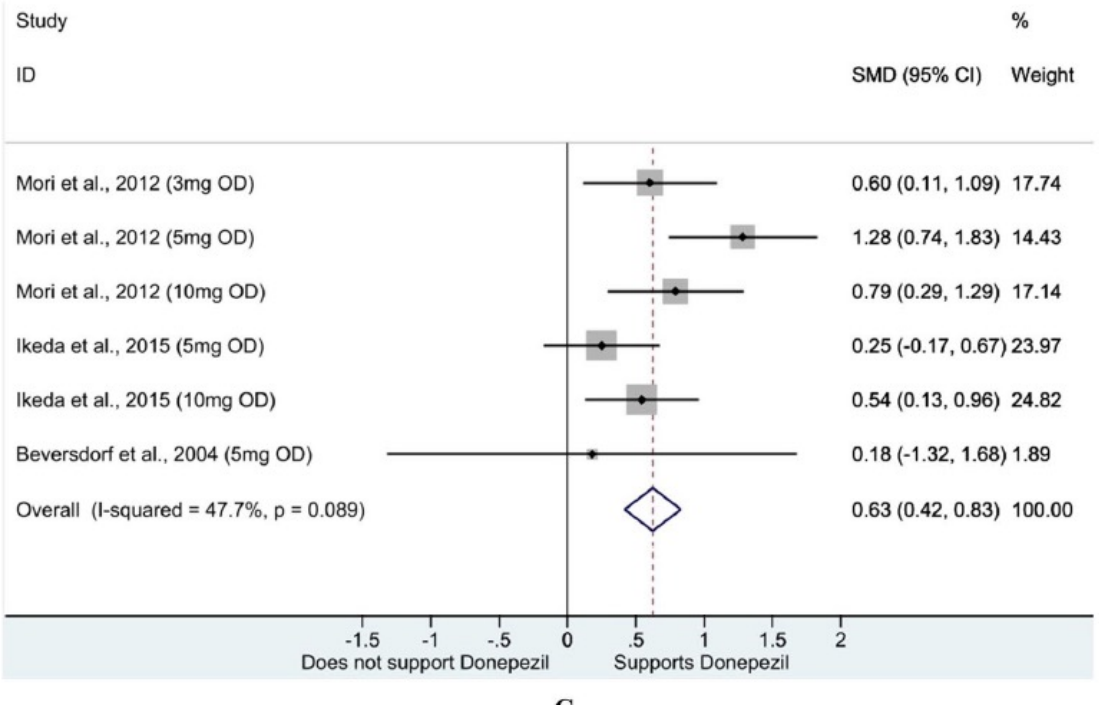
Figure 3. Forest plot of cognitive function (16 comparisons, n = 1889).

FOCUS DONEPEZIL COGNITION DCL

WATTS ET AL. 2023

Systematic review of pharmacological interventions for people with Lewy body dementia

Katrina E. Watts, Nicholas J. Storr, Phoebe G. Barr & Anto P. Rajkumar



COGNITION MPI

SEPPI ET AL. 2019

MDS COMMISSIONED REVIEW

CME **Update on Treatments for Nonmotor Symptoms of Parkinson's Disease—An Evidence-Based Medicine Review**

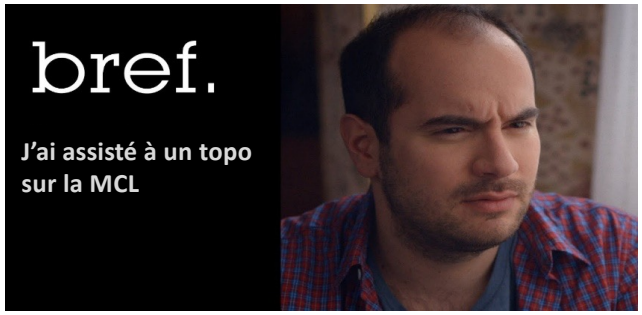
Klaus Seppi, MD,[1]* K. Ray Chaudhuri, MD,[2] Miguel Coelho, MD,[3] Susan H. Fox, MRCP (UK), PhD,[4] Regina Katzenschlager, MD,[5] Santiago Perez Lloret, MD,[6] Daniel Weintraub, MD,[7,8] Cristina Sampaio, MD, PhD,[9,10] and the collaborators of the Parkinson's Disease Update on Non-Motor Symptoms Study Group on behalf of the Movement Disorders Society Evidence-Based Medicine Committee

TABLE 5. Interventions to treat dementia and nondementia cognitive impairment in PD

Intervention				
Drug class/intervention strategy	Drug/intervention	Efficacy	Safety	Practice implications
Dementia				
Acetylcholinesterase inhibitors	**Donepezil**	Insufficient evidence	Acceptable risk without specialized monitoring[a]	*Possibly useful*[b]
	Rivastigmine	Efficacious	Acceptable risk without specialized monitoring[a]	Clinically useful
	Galantamine	Insufficient evidence	Acceptable risk without specialized monitoring[a]	*Possibly useful*[c]
N-methyl-D-aspartate (NMDA) antagonists	Memantine	Insufficient evidence	Acceptable risk without specialized monitoring	Investigational
Nondementia cognitive impairment				
Acetylcholinesterase inhibitors	**Rivastigmine**	*Insufficient evidence*	*Acceptable risk without specialized monitoring*[d]	*Investigational*
Monoamine oxidase B (MAO-B) inhibitors	**Rasagiline**	*Insufficient evidence*	*Acceptable risk without specialized monitoring*	*Investigational*
Nonpharmacological Interventions	**Transcranial direct-current stimulation (T-DCS)**	*Insufficient evidence*	*Insufficient evidence*	*Investigational*
	Cognitive rehabilitation	*Insufficient evidence*	*Insufficient evidence*	*Investigational*

EN BREF

COGNITION ET IACE



- MCL
  - Efficacité Donepezil et Rivastigmine
- DCL
  - Efficacité Donepezil

Efficacité des traitements médicamenteux

Symptômes psychocomportementaux

SPCD MCL

MATSUNAGA ET AL. 2016

RESEARCH ARTICLE

Cholinesterase Inhibitors for Lewy Body Disorders: A Meta-Analysis

Shinji Matsunaga, Taro Kishi, Ichiro Yasue, Nakao Iwata

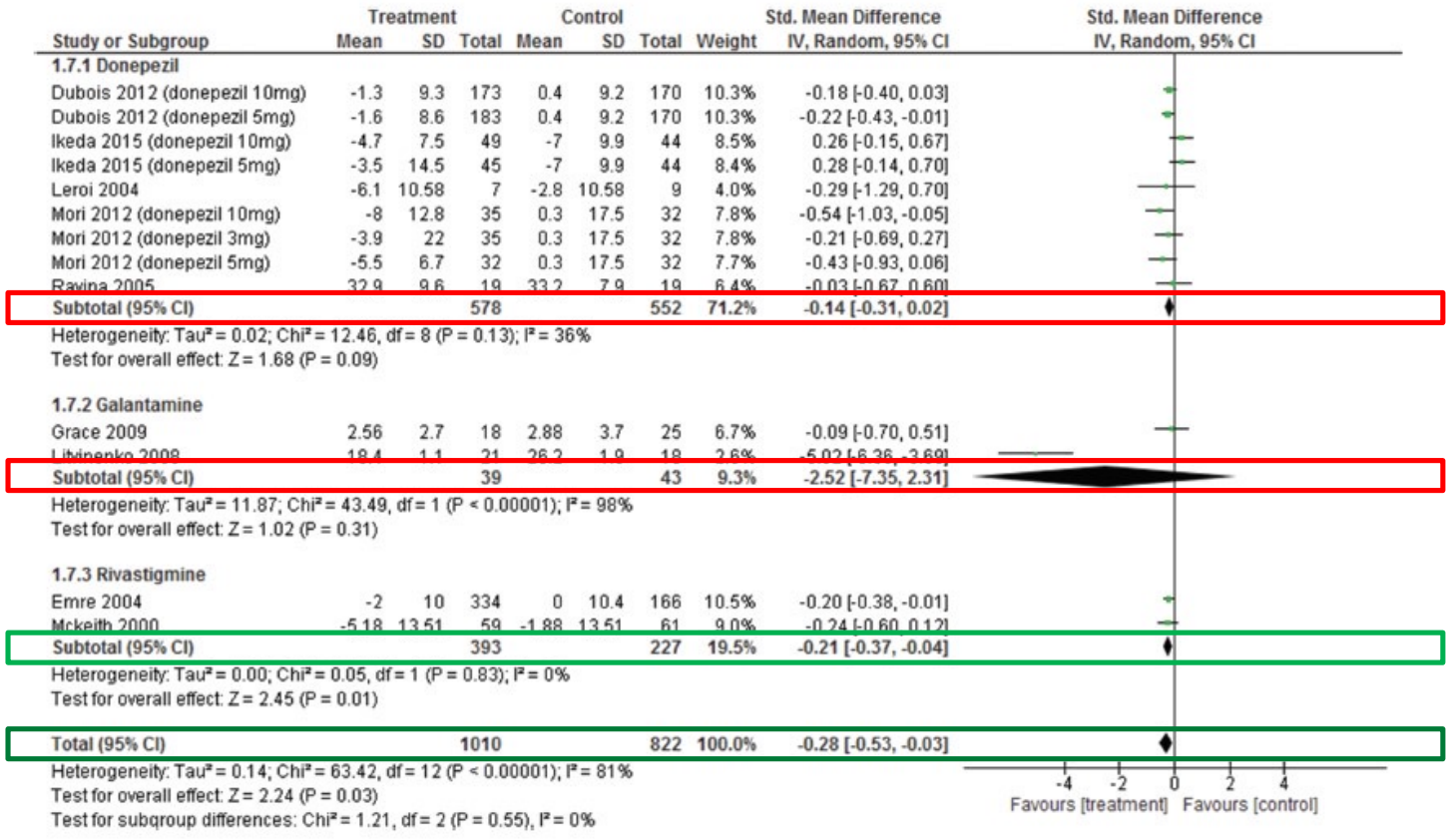


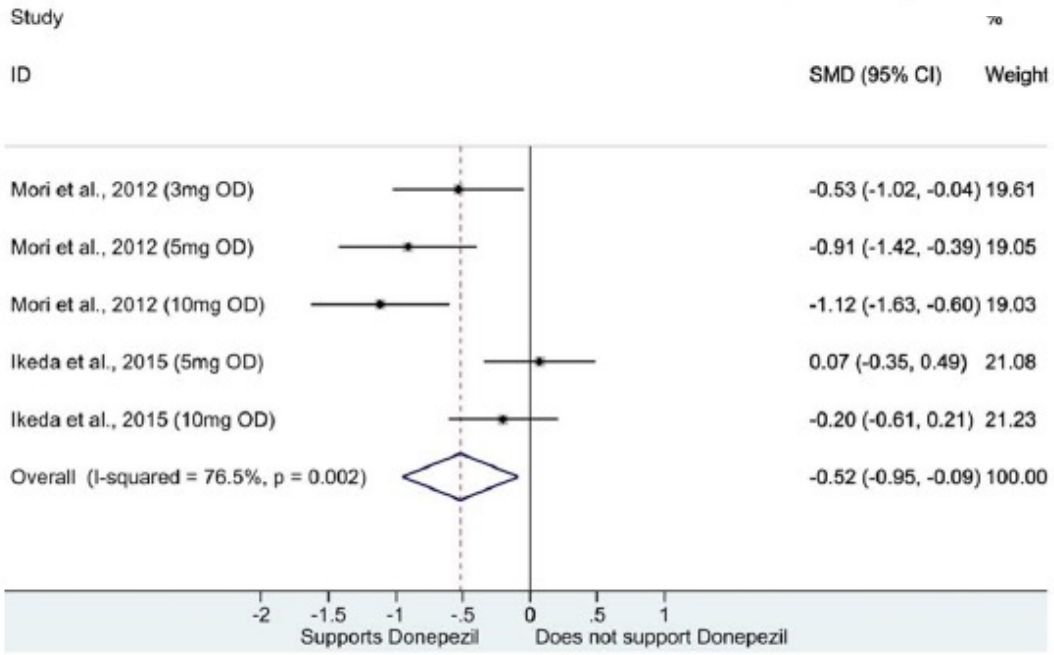
Figure 5. Forest plot of behavioral disturbance (13 comparisons, n = 1832).

FOCUS DONEPEZIL SYMPTÔMES PSYCHOTIQUES DCL

WATTS ET AL. 2023

Systematic review of pharmacological interventions for people with Lewy body dementia

Katrina E. Watts, Nicholas J. Storr, Phoebe G. Barr & Anto P. Rajkumar



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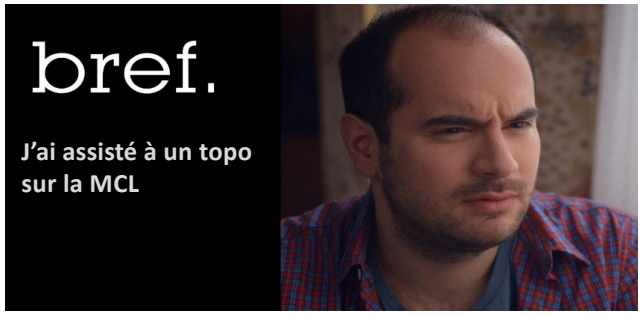
SPCD ET IACE



- MCL
  - Efficacité des IACE: Rivastigmine
- DCL
  - Niveau de preuve limité
  - Donepezil uniquement sur les symptômes psychotiques ?

APARTÉ: HABITUDES DE PRESCRIPTION

WEINTRAUB ET AL. JAMA NEUROLOGY 2011

ORIGINAL CONTRIBUTION

Patterns and Trends in Antipsychotic Prescribing for Parkinson Disease Psychosis

Daniel Weintraub, MD; Peijun Chen, MD, PhD, MPH; Rosalinda V. Ignacio, MS; Eugenia Mamikonyan, MS; Helen C. Kales, MD

Table 2. Antipsychotic Prescribing in Patients With Psychosis by Parkinson Disease and Dementia Status (FY2008)

AP Prescribing	PD Group, No. (%) (n=2597)		Non-PD Dementia Group, No. (%) (n=6907)	Test of Significance
	With Dementia (n=793)[a]	Without Dementia (n=1804)		
Any AP use	451 (56.9)	847 (47.0)	3350 (48.5)	χ^2_2=23.35, P<.001[b,c]
Any typical AP	35 (4.4)	69 (3.8)	500 (7.2)	χ^2_2=33.50, P<.001[c]
High-potency AP	32 (4.0)	56 (3.1)	456 (6.6)	χ^2_2=37.00, P<.001[c]
Any atypical AP	437 (55.1)	814 (45.1)	3110 (45.0)	χ^2_2=29.63, P<.001[b,c]
Quetiapine	306 (38.6)	550 (30.5)	1522 (22.0)	χ^2_2=139.35, P<.001[b,c]
Risperidone	81 (10.2)	143 (7.9)	1282 (18.6)	χ^2_2=141.88, P<.001[c]
Aripiprazole	41 (5.2)	116 (6.4)	273 (4.0)	χ^2_2=21.16, P<.001
Olanzapine	56 (7.1)	93 (5.2)	458 (6.6)	χ^2_2=5.87, P=.05
Ziprasidone	18 (2.3)	31 (1.7)	100 (1.4)	χ^2_2=3.44, P=.18
Clozapine	5 (0.6)	18 (1.0)	4 (0.1)	χ^2_2=48.27, P<.001[c]

SYMPTÔMES PSYCHOTIQUES MPI

SEPPI ET AL. 2019

MDS COMMISSIONED REVIEW

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TABLE 6. Interventions to treat psychosis in PD

Drug	Efficacy	Safety[a]	Practice implications
Clozapine	Efficacious	Acceptable risk with specialized monitoring	Clinically useful
Olanzapine	*Not efficacious*	Unacceptable risk	*Not useful*
Quetiapine	Insufficient evidence	Acceptable risk without specialized monitoring	*Possibly useful*[b]
Pimavanserin	*Efficacious*	*Acceptable risk without specialized monitoring*[c]	*Clinically useful*

PSYCHOSE PARKINSONIENNE

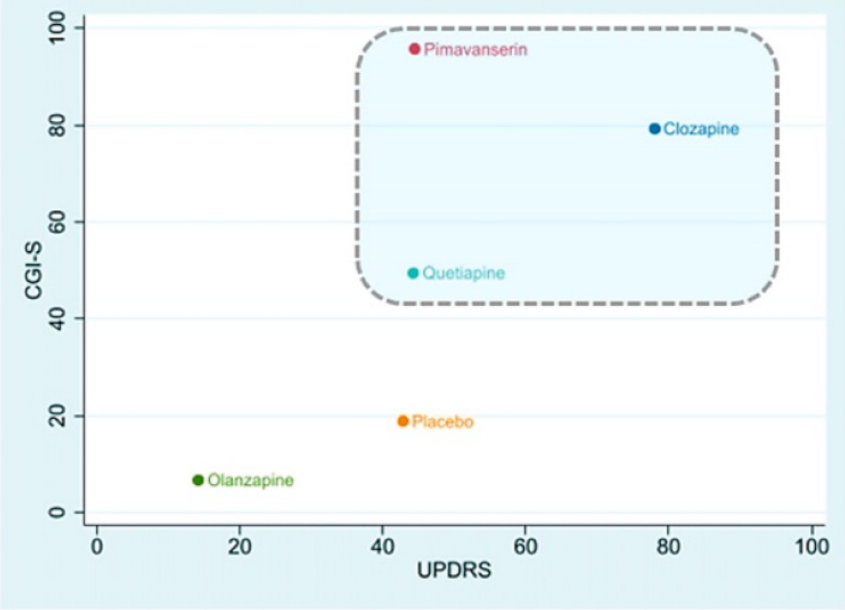
YUNUSA ET AL. 2023

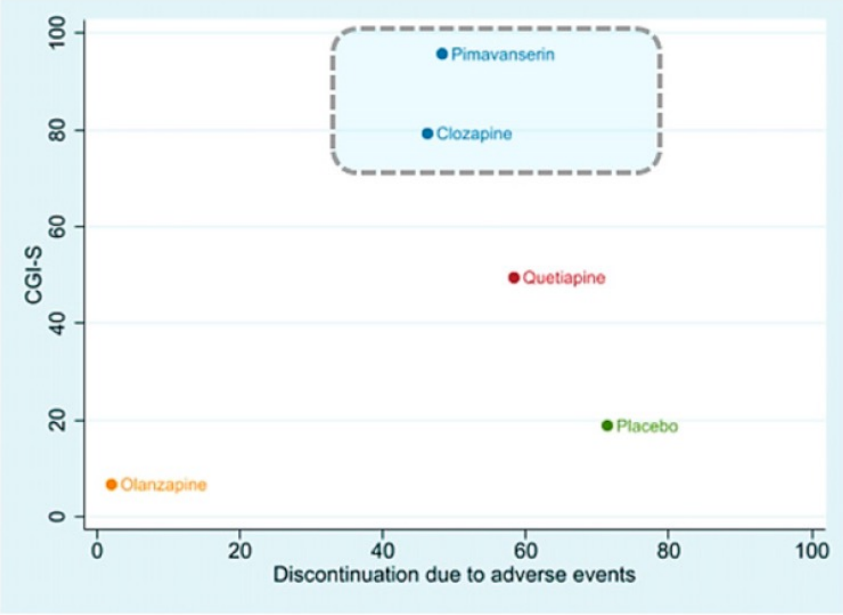
Original Research Article

Journal of Geriatric Psychiatry and Neurology
2023, Vol. 0(0) 1–16

DOI: 10.1177/08919887231154933
journals.sagepub.com/home/jgp
SAGE

Comparative Efficacy, Safety, and Acceptability of Pimavanserin and Other Atypical Antipsychotics for Parkinson's Disease Psychosis: Systematic Review and Network Meta-Analysis





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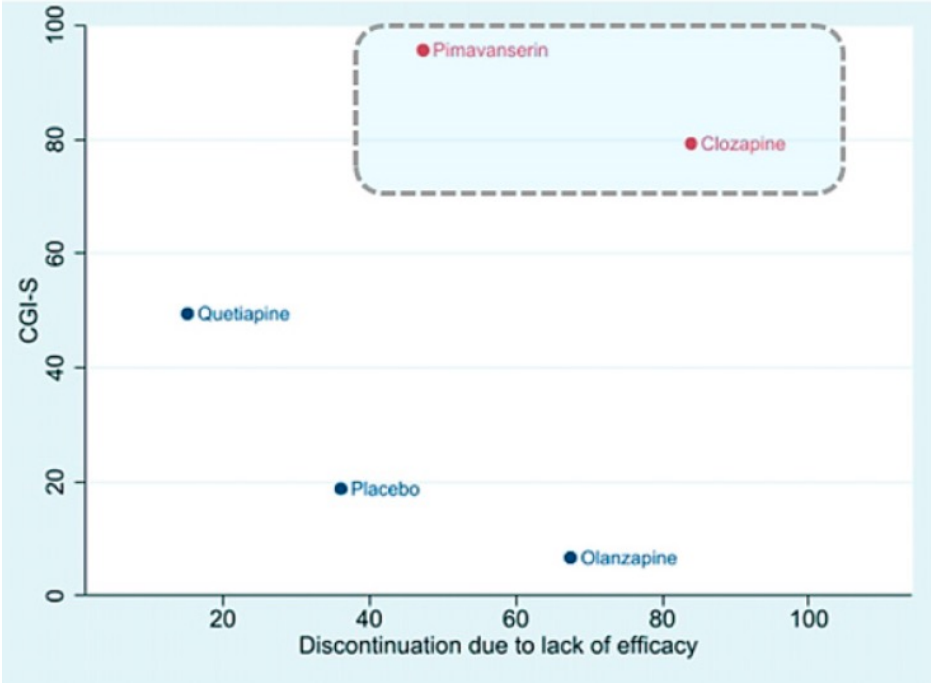


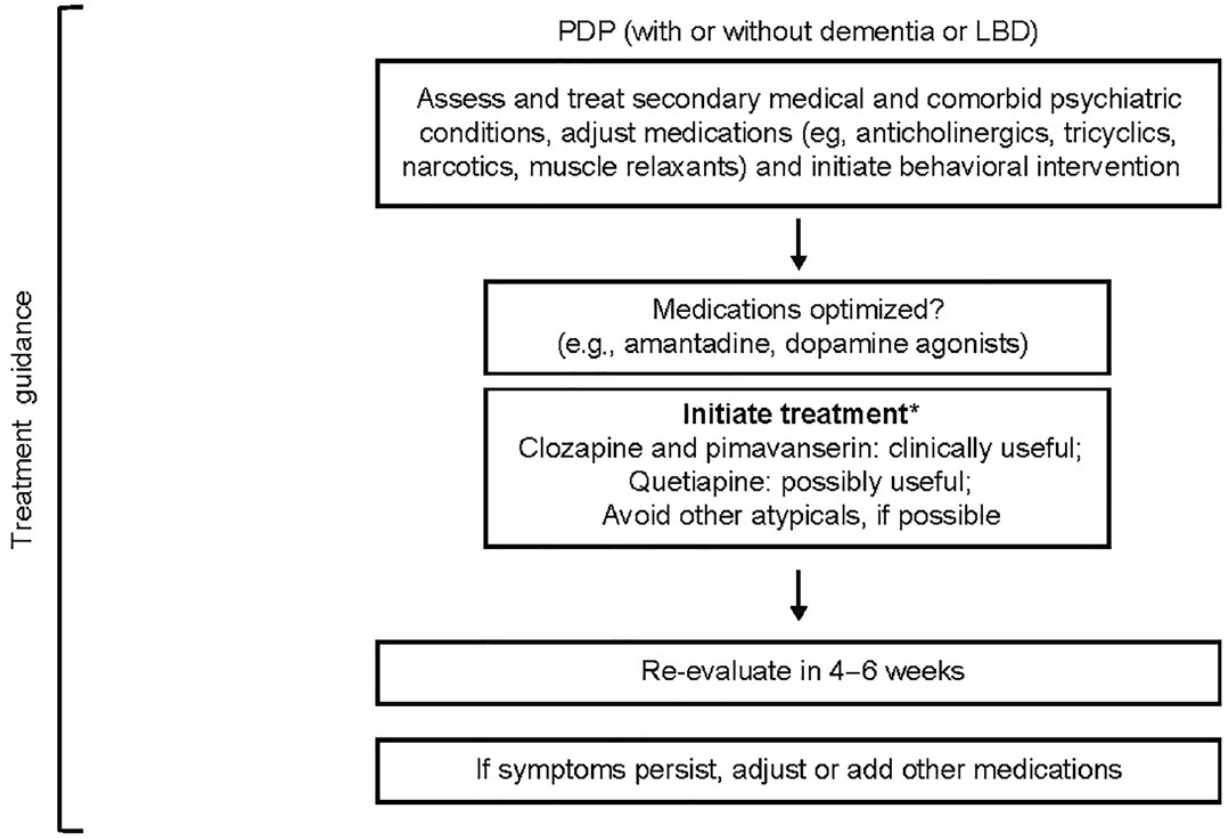
EN PRATIQUE

PAHWA ET AL. 2022

ORIGINAL RESEARCH

Screening, Diagnosis, and Management of Parkinson's Disease Psychosis: Recommendations From an Expert Panel

Rajesh Pahwa · Stuart H. Isaacson · Gary W. Small · Yasar Torres-Yaghi · Fernando Pagan · Marwan Sabbagh



EN PRATIQUE

SWANN & O'BRIEN 2018


REVIEW

International Psychogeriatrics: page 1 of 22 © International Psychogeriatric Association 2018
doi:10.1017/S1041610218001400

Management of visual hallucinations in dementia and Parkinson's disease

Peter Swann[1] and John T. O'Brien[2]

- Limitation de la iatrogénie
  - Iatrogénie des traitements antiparkinsoniens
  - Stratégie hiérarchisée d'arrêt
    - Anticholinergiques
    - Selegiline
    - Amantadine
    - Agonistes dopaminergiques
    - Inhibiteurs de la COMT
    - Levodopa
  - Décroissance progressive pour prévenir un syndrome confusionnel
  - Balance entre signes moteurs et les symptômes psychotiques

EN PRATIQUE

BURGETT ET AL. 2019

- Titration en IACE
- Réduction de l'APA

Case report

Acute treatment of psychotic symptoms in a newly diagnosed Lewy body dementia patient with an accelerated titration schedule of rivastigmine and de-escalation of antipsychotics

Rebecca Nicole Burgett,[1] Thomas Michael Farley,[1,2] Lori Ann Beireis[3]

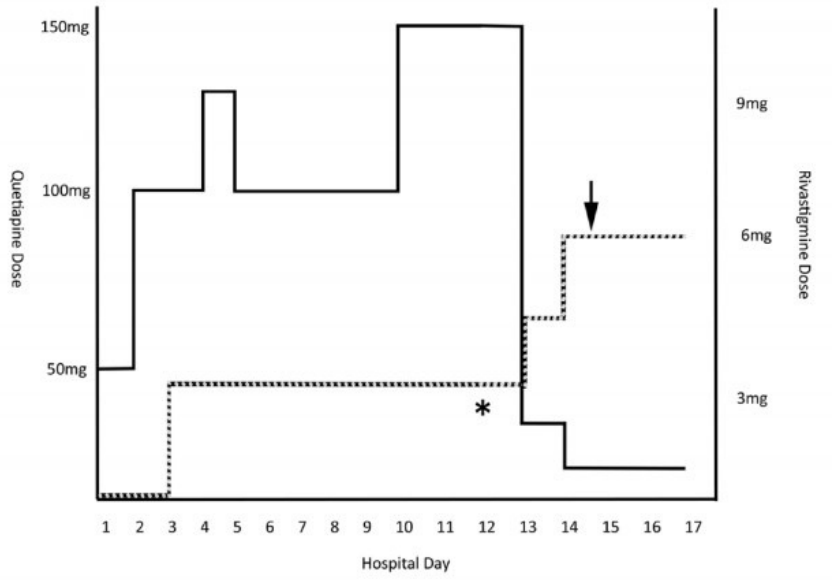


Figure 1 Daily doses for quetiapine (solid line) and rivastigmine (dashed line) over the hospitalisation. Aggressive behaviour is noted with an asterisk (*) and marked clinical improvement in agitation and mental status is indicated with an arrow (↓).

Nouvelles pistes médicamenteuses

TRAITEMENTS ABANDONNÉS

VELAYUDHAN ET AL. 2017

New Therapeutic Strategies for Lewy Body Dementias

Latha Velayudhan[1] · Dominic Ffytche[1] · Clive Ballard[1,2] · Dag Aarsland[1]

- Antagonistes/agonistes inverses 5-HT
  - Intepirdine (antagoniste 5-HT6)
    - Résultats négatifs
  - Nelotanserine (agoniste inverse 5-HT2C)
    - Résultats négatifs sur les troubles du sommeil paradoxal
    - Résultats non publiés sur les hallucinations

TRAITEMENT EN COURS D'INVESTIGATION

KWAN & HUOT 2022

An overview of the active clinical trials for Parkinson's disease psychosis

Cynthia Kwan[1] & Philippe Huot*[,1,2,3]

Table 1. Drugs under investigation for the treatment of Parkinson's disease psychosis.

Drug	Mechanism of action	PDP as an end point	Phase of testing	Trial identifier/status	Status
Apomorphine	Dopamine agonist	Primary	II	NCT02702076	Unknown
AZD0328	Alpha-7 nicotinic agonist	Secondary	II	NCT04810104	Active, not recruiting
Cannabis	Cannabinoid agonist	Primary	Case-only observational	NCT05106504	Active, recruiting
Carvedilol	Adrenoceptor antagonist	Other	II, open label	NCT03775096	Active, recruiting
DAAOI-P	D-amino acid oxidase inhibitor	Secondary	II	NCT04470037	Active, recruiting
ENT-01	Alpha-synuclein inhibitor	Secondary	I, open label	NCT03938922	Active, not recruiting
Nelotanserin	5-HT_{2A} inverse agonist	Secondary	II	NCT02640729	Completed, no results posted
NYX-458	NMDA modulator	Primary	II	NCT04148391	Active, recruiting
Ondansetron	5-HT_3 antagonist	Primary	II	NCT04167813	Active, recruiting
Saracatinib	Src and Bcr-Abl kinase inhibitor	Secondary	I	NCT03661125	Unknown
SEP-363856	5-HT_{1A} and trace amine-associated receptor agonist	Primary	II	NCT02969369	Completed, no results posted

Drugs are listed in alphabetical order.
5-HT_{1A}: Serotonin type $_{1A}$ receptor; 5-HT_{2A}: Serotonin type 2A receptor; 5-HT_3: Serotonin type 3 receptor; NMDA: *N*-methyl-D-aspartate; PDP: Parkinson's disease psychosis.

Take Home Message

TAKE HOME MESSAGE

LES TRAITEMENTS MÉDICAMENTEUX DES MCL

- Cognition
  - Il reste une place pour les IACE (donepezil et rivastigmine)
- Symptômes psychotiques
  - IACE ?
  - Clozapine
  - Pimavanserine

SF3PA

Société Francophone de Psychogériatrie et de Psychiatrie de la Personne Âgée

Merci de votre attention

ISC Marc Jeannerod

HCL HOSPICES CIVILS DE LYON

L'INSTITUT DU VIEILLISSEMENT