Dementia-Related Psychosis in Long-Term Care: Identification and Management

Nearly 50 million people worldwide live with dementia, and of those, up to 90% will experience Behavioral and Psychological Symptoms of Dementia (BPSD), including psychosis, during their disease progression. Psychotic symptoms of dementia include hallucinations, delusions, and delusional misidentifications. These symptoms decrease patients’ quality of life and are often distressing for patients and caregivers. Management of psychosis in dementia can be challenging and requires a comprehensive pharmacologic and non-pharmacologic approach. Pharmacologic management is complicated by a lack of approved medications for this indication and marked by low efficacy and high risk of adverse effects for the agents normally employed. This educational activity will educate pharmacists and nurses on the types and causes of dementia-related psychosis (DRP) and how to recognize DRP in the older adult population. This activity will educate pharmacists and nurses on the proper use of treatments for DRP, with a focus on the long-term care setting. This activity will also include discussion on emerging treatments for DRP, as this remains an area of high need. Clinical data about agents currently being studied for DRP will be presented and discussed to give learners the most up-to-date view of the treatment landscape.

Learning Objectives

**Pharmacist**
1. Differentiate between types and causes of dementia-related psychosis (DRP).
2. Compare and contrast treatments for DRP, including non-pharmacological and current pharmacological treatments.
3. Examine clinical data for agents being studied for the treatment of DRP.

**Nurse**
1. Differentiate between types and causes of dementia-related psychosis (DRP).
2. Compare and contrast treatments for DRP, including non-pharmacological and current pharmacological treatments.
3. Examine clinical data for agents being studied for the treatment of DRP.
Accreditation
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CE hours provided by PharmCon meet the ANCC criteria for formally approved continuing education hours. The ACPE is listed by the AANP as an acceptable, accredited continuing education organization for applicants seeking renewal through continuing education credit.

Target Audience
Pharmacists, Nurses

Universal Activity Number
Pharmacist: 0798-0000-21-029-L01-P
Nurse: 0798-0000-21-029-L01-N

Credit Hours
1.0 Hour

Activity Type
Application-Based

CE Broker Tracking Number
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Activity Release Date
May 18, 2021

Activity Offline Date
May 18, 2024

ACPE Expiration Date
May 18, 2024

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Consult full prescribing information on any drugs or devices discussed.

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- Tammie Lee Demler declares no existence of a financial interest in any amount related to the content of this activity.

- Advisory Board members and other individuals, not previously disclosed, who may review, propose recommendations, and/or edit the content of PharmCon CE activities declare no existence of a financial interest in any amount related to the content of this activity.
Nearly 50 million people worldwide live with dementia, and of those, up to 90% will experience Behavioral and Psychological Symptoms of Dementia (BPSD), including psychosis, during their disease progression.

Psychotic symptoms of dementia include hallucinations, delusions, and delusional misidentifications. These symptoms decrease patients’ quality of life and are often distressing for patients and caregivers.

Management of psychosis in dementia can be challenging and requires a comprehensive pharmacologic and non-pharmacologic approach. Pharmacologic management is complicated by a lack of approved medications for this indication and marked by low efficacy and high risk of adverse effects for the agents normally employed.

This educational activity will educate pharmacists and nurses on the types and causes of dementia-related psychosis (DRP) and how to recognize DRP in the older adult population.

This activity will educate pharmacists and nurses on the proper use of treatments for DRP, with a focus on the long-term care setting. This activity will also include discussion on emerging treatments for DRP, as this remains an area of high need.

Clinical data about agents currently being studied for DRP will be presented and discussed to give learners the most up-to-date view of the treatment landscape.
Learning Objectives

At the conclusion of this activity, participants should be better able to:

• Differentiate between types and causes of dementia-related psychosis (DRP)
• Compare and contrast treatments for DRP, including non-pharmacological and current pharmacological treatments
• Examine clinical data for agents being studied for the treatment of DRP.

Meet Our Patient

• JT is a 75-year-old male who developed Parkinson’s disease (PD) approximately 15 years ago, with motor difficulties which started with tremors roughly 5 years after his diagnosis.
• Although JT did not have a significant medical history prior to his PD diagnosis, he struggled with metabolic risks that included elevated blood glucose, pre-hypertension and high cholesterol.
Meet Our Patient

Because he was also considered moderately obese, JT’s medical physician had repeatedly educated him on the need to lose weight and focus on lifestyle factors to improve his health.

JT’s wife reported a change in JT’s memory just before his PD tremor became noticeable and what she described as interrupted “thinking” and disorientation that also was accompanied by some moodiness and lack of motivation. At that time, these symptoms were dismissed as potential neurologic effects of the PD.

Years later, as these behavioral and memory symptoms worsened, a CT scan determined JT likely experienced a small unnoticed stroke that resulted in vascular dementia years later. JT’s wife had also noticed recently that he started describing seeing black cats running around the house, even though they had no pets.

He also began exhibiting paranoia and asking her where she had “been” even though she had not left the house and had been caring for him all day. He became more aggressive, and she admitted to feeling afraid for her safety and reluctantly agreed with family and friends to admit JT to a long-term care facility for treatment.

Objective #1

Differentiate between types and causes of dementia-related psychosis (DRP)
Dementia Overview

• Dementia is a general term that describes loss of problem solving and thinking capabilities (including memory)
• Affects mostly older adults and is not a “normal” part of aging
• Estimated 5 million adults with dementia in 2014 and projected to be ~14 million by 2060
• Normal aging may include some age-related memory changes that may show as:
  • Occasionally misplacing car keys
  • Struggling to find a word but remembering it later
  • Forgetting the name of an acquaintance
  • Forgetting the most recent events
• Changes associated with normal aging can occur but allow knowledge and experiences built over one’s lifetime, including old memories and language to stay intact.

Dementia Overview

• Memory changes that are not normal and may be signs of dementia:
  • Getting lost in a familiar part of town
  • Forgetting old memories
  • Using unusual or incorrect words to refer to familiar objects
  • Forgetting the name of a close family member or friend
  • Not being able to complete tasks independently
Different Causes of Dementia

What increases the risk for dementia?

• **Age:** the strongest known risk factor for dementia is increasing age, with most cases affecting those of 65 years and older

• **Family history:** those who have parents or siblings with dementia are more likely to develop dementia themselves

• **Race/ethnicity:** older black individuals are twice more likely and Hispanic individuals are reported to be 1.5 times more likely to have dementia than white individuals

• **Poor heart health:** high blood pressure, high cholesterol, and smoking increase the risk of dementia if not managed properly

• **Traumatic brain injury:** head injuries can increase the risk of dementia, especially if they are severe or occur repeatedly


Different Types of Dementia

• DSM-5 is the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders

• Dementia, amnestic, and cognitive disorders included as neurocognitive disorders (NCDs)

• NCDs are considered either mild or major and cover a wide array of diagnoses

• Behavioral and psychological symptoms of dementia (BPSD) occur in approximately 90%

• BPSD lead to increased caregiver burden and early unnecessary institutionalization.

• Most patients with dementia will experience one or more BPSDs
Different Types of Dementia

**Alzheimer’s disease (AD)**
- Most common cause of dementia, accounting for 60%-80% of cases
- First-degree relative with AD increases the risk of developing it by 10%-30%

**Vascular dementia (VD)**
- About 10% of dementia cases are linked to VD
- Diabetes, high blood pressure and high cholesterol are also risk factors.
- Symptoms vary depending on the area and size of the brain impacted. The disease progresses with symptoms worsening with additional strokes

**Dementia with Lewy bodies (DLB)**
- In addition to memory loss, movement or balance problems and altered alertness including daytime sleepiness, confusion, or staring spells. Accounts for up to 7% of dementia cases
- Commonly experience trouble sleeping at night or may experience visual hallucinations

**Frontotemporal dementia (FTD)**
- Often leads to changes in personality and behavior because of the part of the brain it affects. There may also be problems with language skills like speaking or understanding.

**Mixed dementia**
- It is estimated that 50% of the NCD population has mixed dementia (both an AD and VD presentation). Disease progression may be faster than with one kind of dementia.

**Reversible causes**
- People who have dementia may have a reversible underlying cause such as side effect of medication, increased pressure in the brain, vitamin deficiency, and thyroid hormone imbalance.

**Other causes:** traumatic brain injury, HIV infection, prion disease (e.g., mad cow disease), Parkinson’s disease, or Huntington’s disease

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### Symptom Clusters of Dementia

<table>
<thead>
<tr>
<th>Symptom</th>
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Fauth EB, Gibbons A. Which behavioral and psychological symptoms of dementia are the most problematic? Variability by prevalence, intensity, distress ratings, and associations with caregiver depressive symptoms. Int J Geriatr Psychiatry. 2013;
Differentiate Between Types and Causes of Dementia-Related Psychosis (DRP)

- Progression of BPSD and DRP is highly individualized and differs based on the type of dementia
- According to Li and colleagues, consider the possibility of early-onset AD in middle-aged or elderly patients whose first symptoms are the behavioral and psychological symptoms of dementia
- Patients with early-onset AD that exhibits first as psychotic symptoms usually lack obvious cognitive impairment, so they may be misdiagnosed with late-onset schizophrenia
- To distinguish early-onset AD from late-onset schizophrenia, clinicians should evaluate cognitive function, perform MRI and PET


Differentiate Between Types and Causes of Dementia-Related Psychosis (DRP)

- The prevalence of hallucinations and delusions in dementia is generally progressive and often may double over the course of the illness
- Brandt and colleagues conducted a quantitative online survey which was patient reported (completed by patients with dementia-related psychosis) or care partner reported (by care partners of patients with dementia-related psychosis)
- Subjects were recruited through direct outreach by the advocacy groups UsAgainstAlzheimer’s and the Lewy Body Dementia Association
- In total, 26 patients and 186 care partners participated in the quantitative online survey

Brandt, et al. Dementia-Related Psychosis Symptoms and Impact from the Patient and Care Partner (Caregiver) Perspective: An Observational, Prospective Study to Describe the Patient Experience 47164_Dementia-Related Psychosis Symptoms and Impact from the Patient and Care Partner_7.8.20a_0.pdf (usagainstalzheimers.org); accessed January 12, 2010
Differentiate Between Types and Causes of Dementia-Related Psychosis (DRP)

• The dementia-related psychosis symptoms most frequently reported in patients:

<table>
<thead>
<tr>
<th>Experienced by the patient</th>
<th>Reported by caregivers</th>
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<tbody>
<tr>
<td>visual hallucinations (88.5%)</td>
<td>paranoid delusions (75.8%)</td>
</tr>
<tr>
<td>auditory hallucinations (53.8%)</td>
<td>visual hallucinations (75.3%)</td>
</tr>
<tr>
<td>distortion of senses (53.8%)</td>
<td>lack of trust for loved ones (52.2%)</td>
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• Visual hallucinations were reported to occur in roughly 50% of patients at least weekly

* Brandt, et al Dementia-Related Psychosis Symptoms and Impact from the Patient and Care Partner (Caregiver) Perspective: An Observational, Prospective Study to Describe the Patient Experience 47164, Dementia-Related Psychosis Symptoms and Impact from the Patient and Care Partner. 7/8/20a.0.pdf (usagainstalzheimers.org) accessed January 12, 2020

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Figure 1. Qualitative Interviews: Symptom Occurrence and Impacts* (N=16)

*Patient-reported and care partner-reported data are combined.

Brandt, et al Dementia-Related Psychosis Symptoms and Impact from the Patient and Care Partner (Caregiver) Perspective: An Observational, Prospective Study to Describe the Patient Experience 47164, Dementia-Related Psychosis Symptoms and Impact from the Patient and Care Partner. 7/8/20a.0.pdf (usagainstalzheimers.org) accessed January 12, 2021
Differentiate Between Types and Causes of Dementia-Related Psychosis (DRP)

Visual hallucinations were most impactful in the patient self-report group and paranoid delusions were most impactful for care partner report group with most common impacts reported as determining what is real and not real, anxiety and effects on relationships

Brandt, et al Dementia-Related Psychosis Symptoms and Impact from the Patient and Care Partner (Caregiver) Perspective: An Observational, Prospective Study to Describe the Patient Experience 47164_Dementia-Related Psychosis Symptoms and Impact from the Patient and Care Partner_7.8.20a_0.pdf (usagainstalzheimers.org) accessed January 12, 2021

Symptom Clusters of Dementia

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Symptom Clusters of Dementia

• Recommendation against using sleep promoting medications, including melatonin, for older adults with Irregular Sleep-Wake Rhythm Disorder (ISWRD) and a comorbid diagnosis of dementia

• The authors concluded that withdrawn behaviors observed in patients during melatonin administration, may be related to supraphysiologic serum concentrations

• 2.5 mg dose administered during the study that led to sleepiness and dysphoria which was misinterpreted as mood change


Objective #2

Compare and contrast treatments for DRP, including non-pharmacological and current pharmacological treatments
Compare and Contrast Treatments for DRP, Including Non-Pharmacological and Current Pharmacological Treatments: Psychosocial Interventions

The Association recommends training and education for both professional and family caregivers on psychosocial interventions that might include:

• Review medications, especially new medications
• Promote routine activity
• Separate the person from what seems to be upsetting them
• Assess for the presence of pain, constipation, or other physical problem
• Travel with them to where they are in time
• Don’t disagree; respect the person’s thoughts even if incorrect. Avoid finger-pointing, scolding, or threatening

Compare and Contrast Treatments for DRP: When Considering Pharmacological Treatment Interventions

• Only after initiating non-pharmacologic alternatives as first-line therapy for control
• Identify and remove triggers for BPSD
• Assess severity and consequences of BPSD with less severe behaviors (limited harm) with more severe or “high risk” behaviors
• Determine overall risk to self or others and risks and benefits with and without medication
• Consider pharmacotherapy as a short-term intervention that must be regularly reevaluated for appropriate time of cessation or need for continuation


Compare and Contrast Treatments for DRP: When Considering Pharmacological Treatment Interventions

• In recent years, several pharmacological and psychosocial approaches have proven inadequate
• **Medication with benefits when risks are managed:** antipsychotics, AChEIs, NMDA antagonist, and antidepressants
• **Medication with a risk greater than potential benefit:** benzodiazepines, AED mood stabilizers associated with high probability of adverse effects and low probability of meaningful clinical improvement

Compare and Contrast Treatments for DRP, Including Non-Pharmacological and Current Pharmacological Treatments: Antipsychotics

- **Target symptoms**: severe agitation, aggression and psychosis
- **Benefits**: small to moderate efficacy with onset generally observed within the first 1 to 2 weeks of use (however sedating effects are usually reported upon immediate administration)
- In 2005, the US Food & Drug Administration warned that the use of antipsychotics for psychosis or agitation increased the risk of death by 1.6–1.7 times in older people.
- Recent guidance from the American Psychiatric Association: nonemergency antipsychotic medication should only be used for the treatment of dangerous, and/or distressing symptoms
- The doses of antipsychotics that appear to be efficacious and tolerated in older AD patients with agitation are much lower than those used for psychosis in younger patients


**Risks** in addition to the increased risk of mortality:
- Extrapyramidal side effects (EPS)
- Metabolic consequences
- Risk of thromboembolism
- Potential increased cognitive decline
- Risk of falls

- Still off-label in US for DRP.
- Risperidone is indicated for the short-term treatment (6–12 weeks) of persistent aggression in AD in some countries outside the US.
- Efficacy data reported also for SGAs: olanzapine (Zyprexa), quetiapine (Seroquel), aripiprazole (Abilify) and the FGA haloperidol (Haldol) though the latter is not recommended first line
- Brexpiprazole in AD patients with agitation
- Pimavanserin for dementia related psychosis

**SGA**: second generation antipsychotic  
**FGA**: first generation antipsychotic
**Compare and Contrast Treatments for DRP, Including Non-Pharmacological and Current Pharmacological Treatments: Acetylcholinesterase Inhibitors (AChEIs)**

- **Medication:** donepezil (Aricept), galantamine (Razadyne), rivastigmine (Exelon)
- **Target symptoms:** depression, dysphoria and anxiety
- **Benefits:** small improvements in BPSD, evidence of slowed cognitive decline (disease progression remains inevitable).
- **Risks in addition to GI complaints:**
  - Anorexia and weight loss
  - Bradycardia
  - Risk of falls


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**Compare and Contrast Treatments for DRP, Including Non-Pharmacological and Current Pharmacological Treatments: NMDA Antagonist Memantine**

- N-methyl-D-aspartate (NMDA antagonist) Memantine (Namenda) approved for the treatment of AD, has some effects on behavior as measured by the Neuropsychiatric Inventory (NPI)
- **Target symptoms:** agitation, aggression and delusions
- **Benefits:** Small improvements in BPSD and slowed cognitive decline (progression continues)
- **Risks:** minimal adverse effects reported but include:
  - Headache
  - Dizziness
  - Constipation
- Reduced agitation and irritability were seen with the add-on of memantine to AChEI
- Dementia drugs should not be considered as primary therapy for agitation in AD; however, they should not be discontinued unless there is clear evidence that their introduction may have caused the episode

Compare and Contrast Treatments for DRP, Including Non-Pharmacological and Current Pharmacological Treatments: Antidepressants

- **Medication:** selective serotonin reuptake inhibitors (SSRI) - sertraline (Zoloft), citalopram (Celexa) and escitalopram (Lexapro)
- **Target symptoms:** agitation, depression and irritability
- **Benefits:** tolerability reported to be better than antipsychotics, and can have similar efficacy for target symptoms
- **Risks in addition to GI complaints:**
  - Hyponatremia
  - Increased bleeding potential
  - Possible bone loss
  - Tremor/akathisia
  - Cognitive decline


Compare and Contrast Treatments for DRP, Including Non-Pharmacological and Current Pharmacological Treatments: Regulations and Recommendations

- Regulatory expectations
- Gradual dose reductions
- Chemical restraint and ethical considerations
Compare and Contrast Treatments for DRP, Including Non-Pharmacological and Current Pharmacological Treatments: Regulations and Recommendations

- November 28, 2017, CMS announced several regulatory changes for skilled nursing facilities
- The definition of a psychotropic medication now includes:
  - Any drug that affects brain activities associated with mental processes and behavior
  - These drugs include antipsychotics, antidepressants, antianxiety medications, hypnics, as well as medication classes that may affect brain activity which are now included on expanded list
- **This expanded list** of psychotropic medications includes central nervous system agents, mood stabilizers, anticonvulsants, muscle relaxants, anticholinergic medications, antihistamines, N-methyl-D-aspartate receptor modulators, and over-the-counter natural or herbal products.

Compare and Contrast Treatments for DRP, Including Non-Pharmacological and Current Pharmacological Treatments: Regulations and Recommendations

- **F-Tags**
- The Centers for Medicare & Medicaid Services (CMS) establishes requirements and provides interpretive guidelines for the survey process to ensure optimal patient safety

**Federal Regulatory Groups for Long Term Care**

*Substandard Quality of Care = one or more deficiencies with s/s levels of F, H, I, J, K, or L in Red

** Tag to be cited by Federal Surveyors Only

<table>
<thead>
<tr>
<th>F-Tag</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>F-756</td>
<td>Gradual Dose reductions (F-758)</td>
</tr>
<tr>
<td>F-758</td>
<td>Psychotropic medication is given only when necessary to treat a specific diagnosis and documented condition</td>
</tr>
<tr>
<td></td>
<td>Gradual dose reductions must be implemented for residents unless contraindicated</td>
</tr>
<tr>
<td></td>
<td>Limiting PRN antipsychotic orders to 14 days and not entering a new order without evaluating the resident</td>
</tr>
<tr>
<td></td>
<td>Limiting PRN psychotropic orders (excludes antipsychotics) to 14 days unless longer timeframe is deemed appropriate and documented by the attending physician</td>
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<tr>
<td></td>
<td>Residents who use psychotropic medications receive gradual dose reductions and behavioral interventions, unless clinically contraindicated, in an effort to discontinue these medications</td>
</tr>
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Compare and Contrast Treatments for DRP, Including Non-Pharmacological and Current Pharmacological Treatments: Regulations and Recommendations

**Continued use of these medications is permitted provided:**

- When a resident is experiencing an acute medical problem or psychiatric emergency that poses an immediate risk to self or others
- Use should only be initiated/used in the presence of active clinical symptoms and after nonpharmacological interventions and least restrictive measures have been attempted

It was anticipated that with these expanded rules, many SNFs would be encouraged to discontinue orders for standing PRN antipsychotic medications.

LTC facilities establish processes and a plan going forward that not only ensures compliance with these rules but that also (and most importantly) residents are receiving the care and treatments that they need.

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When antipsychotic discontinuation is advisable and may not result in decompensation

- If no benefit seen at 4 weeks, taper and discontinue
- If response is noted, consider continuation for up to 6 months, then trial taper
- Ruths et al. found no difference in scale scores 30 days after patients were tapered off (85% of those patients remained symptom free)
- Ballard et al. reported no significant changes after taper and discontinuation
- Devanand et al. however did report relapse and worsening when patients were tapered and discontinued when compared to those who remained on risperidone

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Objective #3
Examine clinical data for agents being studied for the treatment of DRP

Examine Clinical Data for Agents Being Studied for the Treatment of DRP

• The dysfunction of the serotonin (5-HT$_{2A}$) receptor has been associated with onset of psychosis and aggression in AD
• Pimavanserin (Nuplazid) is a selective 5-HT$_{2A}$ inverse agonist (phase III clinical trials)
• Other second-generation antipsychotics (SGAs) that also act 5-HT$_{2A}$ antagonists
  lumateperone (Caplyta) and brexpiprazole (Rexulti) also advanced to phase III clinical trials for dementia related psychosis and agitation
• Brexpiprazole was reported to significantly reduce agitation; lumateperone trial was terminated due to lack of efficacy
• Pimavanserin has been a target of ongoing FDA review for potential expansion of indication to include DRP

Clinical Data for Agents Being Studied for Treatment of DRP


<table>
<thead>
<tr>
<th>Phase of trial</th>
<th>Duration</th>
<th>Subjects</th>
<th>Dose</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase II</td>
<td>12 weeks</td>
<td>N=181 AD</td>
<td>34 mg once daily</td>
<td>Large treatment effects in AD patients with more severe psychosis at baseline (NPI-NH-PS ≥12)</td>
</tr>
<tr>
<td>Phase III</td>
<td>38 weeks</td>
<td>N=360 DRP</td>
<td>20 mg or 34 mg once daily on their open-label phase</td>
<td>A long-term relapse prevention study of pimavanserin for the treatment of hallucinations and delusions associated with DRP</td>
</tr>
<tr>
<td>Clinical trial: NCT03325556</td>
<td>12 weeks Open-label + 26 weeks Double-blind period</td>
<td></td>
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</tbody>
</table>

* clinicaltrials.gov/ct2/show/NCT03325556
* Relapse Prevention Study of Pimavanserin in Dementia-related Psychosis - Full Text View - ClinicalTrials.gov accessed February 15, 2021

Examine Clinical Data for Agents Being Studied for the Treatment of DRP

International Delphi consensus published 2019

- Expert panel comprised of 11 international members with clinical and research expertise in BPSD management
- Consensus outcomes showed a clear preference for an escalating approach to the management of BPSD commencing with the identification of underlying causes
- Based on relevant results observed in the phase II and phase III clinical trials and evidence of efficacy and tolerability of this drug in PDP patients with cognitive impairment
- Regarding future treatments for psychosis, the greatest priority was placed on pimavanserin

Examine Clinical Data for Agents Being Studied for the Treatment of DRP

- New drug candidates target a different pathology than that known to cause dementia-related psychosis but are associated with a favorable pharmacologic profile and benefit
- These include agonists of M1/M4, CB1 and mGluR2
- Future pharmacotherapy of dementia-related psychosis, agitation and aggression will depend on outcomes of phase III trials and future approvals of novel agents or old agents “drafted” for new use
- Researchers now suggest that avoiding antagonism of the H1, M1 & alpha-2 adrenoceptors to reduce the risk of stroke, excessive sedation, cardiotoxicity and additional worsening memory impairments


<table>
<thead>
<tr>
<th>Receptor Agonists</th>
<th>Clinical Trial Phase</th>
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<tbody>
<tr>
<td>CB1</td>
<td>Naboline completed phase II/III clinical trials after demonstrating efficacy in reducing aggression in patients with dementia</td>
</tr>
<tr>
<td>mGluR2</td>
<td>LY2979165-advanced to phase II clinical trials to evaluate safety and efficacy in the treatment of dementia and psychosis and agitation/aggression</td>
</tr>
<tr>
<td>NMDA (indirect)</td>
<td>SND-51-advanced to phase II clinical trials to evaluate safety and efficacy in the treatment of dementia and psychosis</td>
</tr>
<tr>
<td>M4</td>
<td>HTL0016878-advanced to phase I clinical trials</td>
</tr>
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Examine Clinical Data for Agents Being Studied for the Treatment of DRP

Other pipeline agents under review; more traditional pathways

**Dementia related aggression**

- 5-HT₁A/5-HT₁B receptor agonists (eltoprazine) – completed phase II
- Centrally acting alpha-1 adrenergic antagonist (prazosin) – currently in phase II studies
- SERT inhibitors: including SSRIs citalopram and escitalopram

**Nocturnal agitation**

- Mirtazapine (phase III) and gabapentin (phase IV)

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**Key Takeaways**

**Early Detection, Better Care**

- Recent studies suggest that identifying mild neurocognitive disorder as early as possible may allow interventions to be more effective
- Early intervention efforts may enable the use of treatments that are not effective at more severe levels of impairment and may prevent or slow progression
- Efforts focusing on prevention: healthy heart, healthy brain
- Long term care facility providers should utilize resources such as consultant pharmacists and medical and nursing directors to not only meet regulations, but to also develop and implement a process to make sure patients have access to appropriate medications, especially those with less potential for adverse events. The Beers criteria can also be used as a guide to assist with this selection process.

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DSM-5 Fact Sheets (psychiatry.org) accessed February 15, 2021
JT’s wife admits to feeling afraid and very concerned about her husband’s recent hallucinations and delusions and would like help from their physician. Because these symptoms were initially attributed to vascular dementia, the worsening dementia could possibly now also be psychosis associated with his Parkinson’s Disease.

JT’s physician recommends considering pimavanserin as a medication intervention and provides her with information about the medication. Concerned about the FDA boxed warning which warned about use for dementia related psychosis, they inquire with you, their pharmacist about your opinion in moving ahead with this therapy.

Thoughts and considerations for your consultation:

1. The FDA boxed warning must be evaluated for benefits of use of the antipsychotic versus leaving the patient without symptom relief. Here, the patient is potentially at risk of harm to self and possibly staff caring for him.
2. Guidelines advising LTC facilities on appropriate use of medications in their residents will ensure appropriate use of psychotropic agents, including this antipsychotic.
3. Pimavanserin (Nuplazid) is an excellent choice for this patient, given his PD diagnosis and the concomitant impact of the vascular dementia contributing to his psychosis. This antipsychotic agent will not worsen his abnormal movements from his PD and will mitigate his psychotic symptoms.
Thank You

References

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- Fauth EB, Gibbons A. Which behavioral and psychological symptoms of dementia are the most problematic? Variability by prevalence, intensity, distress ratings, and associations with caregiver depressive symptoms. Int J Geriatr Psychiatry. 2013;
References

Clinical Trials:

- A Phase 3, 12-week, Multicenter, Randomized, Double-blind, Placebo-controlled Trial to Evaluate the Efficacy, Safety, and Tolerability of 2 Fixed Doses of Brexpiprazole in the Treatment of Alzheimer’s Agitation - Full Text View - ClinicalTrials.gov
- Safety and Tolerability Study of Flexible Dosing of Brexpiprazole in the Treatment of Subjects With Agitation Associated With Dementia of the Alzheimer’s Type - Full Text View - ClinicalTrials.gov
- Brexpiprazole for the Long-term Treatment of Patients With Agitation Associated With Dementia of the Alzheimer’s Type - Full Text View - ClinicalTrials.gov
- A 12-week Extension Trial to Evaluate the Safety and Tolerability of Brexpiprazole in the Treatment of Subjects With Agitation Associated With Dementia of the Alzheimer’s Type - Full Text View - ClinicalTrials.gov
- Brexpiprazole for the Treatment of Patients With Agitation Associated With Dementia of the Alzheimer’s Type - Full Text View - ClinicalTrials.gov
- Relapse Prevention Study of Pimavanserin in Dementia-related Psychosis - Full Text View - ClinicalTrials.gov