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Lecanemab, Donanemab, and Emerging Disease-Modifying Therapies for Alzheimer Disease: Clinical Evidence and Primary Care Implications in Canada

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Abstract

Introduction: Alzheimer's disease is a progressive neurodegenerative disorder with current treatment limited to symptomatic relief and no alteration in disease progression. Advances in the DMTs (Disease-modifying-therapies) may alter the progression if used in early phase of the disease.

Objective: To review and summarize the current evidence on advancements in DMTs in AD; review their regulatory status in Canada; Examine risk vs. benefit and explore implications for Family Physicians.

Methods: Narrative review of recent randomized controlled trials. regulatory status and submissions, and Canadian policy documents up to mid-2025. Sources include PubMed, clinical trial registries, Health Canada Notices, Alzheimer's Society of Canada materials.

Results: Monoclonal antibodies such as lecanemab and donanemab show reduction in amyloid plaque and slowing of cognitive and functional decline (modest) in early AD (mild cognitive impairment or mild dementia). In contrast, Aducanumab while initially promising ended up showing mixed results and due to inconsistent clinical outcomes, it is not approved by Health Canada at present. Tau-targeting and anti-inflammatory agents are under investigation but have not yet demonstrated definitive benefit. Key risks include amyloid-related imaging abnormalities (ARIA), infusion reactions, cost, and lack of data for long term safety. Canadian health system challenges include lack of access to biomarker testing and imaging, Lack of healthcare specialists, and reimbursement frameworks.

Conclusion: Using DMTs in the early phases of AD offers significant promise in altering disease progression. However, Family Physicians needs to thoroughly evaluate the risk to benefit ratio, ensure careful patient selection, and work in close collaboration with specialists. Furthermore, ensuring the healthcare system is ready— with access to proper testing facilities, coverage models, and support systems—is essential for the safe and equitable implementation of these therapies.

Key points

Monoclonal antibodies (lecanemab, donanemab) are the most advanced DMTs in AD at present with evidence that shows slight slowing in clinical decline in early AD patients.

Risks associated to the treatment like ARIA etc. requires biomarker confirmation which is not readily available throughout Canada yet.

Family Physicians and Canadian Healthcare System play a crucial role in selection of patient, their monitoring, treatment coverage and testing.

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Keywords: Alzheimer Disease; Disease-Modifying-Therapy; Monoclonal Antibodies; Primary Care; Canada

1. Introduction

When it comes to Dementia, Alzheimer disease remains one of the most common causes in Canada. Treatments available currently pharmacologically includes Cholinesterase inhibitors like donepezil, rivastigmine, galantamine and memantine providing symptomatic relief with no alteration to underlying disease process. 1,2 Studies shows that amyloid-B deposition and Tau pathology begins to manifest years prior to any cognitive symptoms. 3 Family physicians are often the first point of contact and are essential for early phase detection, referral and patient selection for the emerging DMTs and their safety monitoring.

2. Review of Emerging Disease-Modifying Therapies

2.1. Monoclonal antibodies Targeting Amyloid

Per The EMERGE and ENGAGE trials: Aducanumab has reported amyloid clearance along with slight effect on progression of decline in EMERGE but not in ENGAGE. Due to lack of certain results and some safety concerns (like ARIA), Aducanumab is currently not approved in Canada for AD.4

Lecanemab, on the other hand for early AD patients with mild cognitive impairment or mild dementia per the CLARITY-AD trial showed reduction in amyloid and produced significant preservation of cognitive and functional abilities vs placebo. 5

For Donanemab, recent Phase 3 trials i.e., TRAILBLAZER-ALZ suggest benefits in early disease, for participants with lower tax burden; though imaging and safety monitoring are key.6

2.2. Other Agents Under Investigation

Tau-targeted therapies: Agents studied with aim to stop accumulation of Tau protein and its spread are still in development phase and currently shows mixed results, and blood-brain barrier penetration. Timing and patient selection being other major issues.7

Anti-inflammatory/immunomodulatory therapeutics: Considering that neuroinflammation contributes directly to worsening of the AD patients, there are trials being conducted targeting the microglial activation or cytokine pathways but at present none of them have shown promising data.8

BACE inhibitors: Studied to see its effects (reduction) on amyloid production multiple trials were carried out and later discontinued due to adverse effects like cognitive worsening which was counterproductive and due to insufficient clinical benefit.9

2.3. Regulatory Status in Canada

As of mid-2025, Lecanemab is under review by Health Canada for approval for early phase AD. 10

Donanemab remains investigational and due to mixed trial results and controversy associated to Aducanumab, its Canadian application was withdrawn. 11

Trials demonstrating benefit (lecanemab, donanemab) shows clinically meaningful slowing of disease progression particularly when treatment is initiated early. Long-term data about safety and effectiveness in diverse, real-world populations are lacking.

2.4. Risks, Monitoring, and Safety

- Amyloid-related imaging abnormalities (ARIA): Both ARIA-edema and ARIA-hemorrhage occur and the therapy requires baseline MRI screening and periodic follow-up imaging.12
- Infusion reactions and logistics (e.g., frequent infusions, limited access to infusion centers).
- Cost, and access to biomarker testing or imaging remains significant issues till date.

2.5. Implications for Family Physicians

- Patient selection & timing is crucial with thorough monitoring for family physicians.
- Best suited for patients in earliest clinical stages of AD with mild cognitive implications and dementia with confirmed amyloid pathology via PET scan or CSF biomarkers.
- Family physicians should screen for subtle cognitive changes, conduct diagnostic evaluation and/or refer to memory clinics.
- Collaborate with specialists (neurology, geriatrics) for diagnostic confirmation, imaging, treating adverse events.
- Set up monitoring schedule: cognitive and functional assessments (e.g., every 6-12 month); MRI scans per protocol.

3. Challenges, Barriers, and System factors

- Insufficient date for the efficacy and safety of the therapies in real world.
- Limited availability of biomarker testing, specialist services alongside, high cost of therapy and monitoring.
- Local availability of imaging (MRI, PET), biomarker labs, and specialist capacity are not always readily available.
- Reimbursement status; costs may be high for drug, imaging, clinic visits.
- Advocate for equitable access (rural, underserved populations).
- Health System, Policy, Ethical Considerations
- Infrastructure: Access to imaging and biomarker services is non-consistent through the country; costly PET or CSF testing only available in certain centres.
- Policy: Health Canada approvals are necessary but insufficient; payer coverage and public reimbursement policies will influence access.

4. Conclusion

Family physicians in Canada should stay up to date on approvals and emerging evidence. Be prepared to identify early-stage AD and refer for biomarker confirmation, followed by collaboration with specialists for initiation and monitoring. Emerging DMTs represent a promising shift in AD management, but implementing them safely, ethically, and equitably will require careful planning and coordination. Primary care will have a key role in ensuring patients derive benefit without undue harm.

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