**Proposed Mechanism of Action of Montelukast**

- **Leukotrienes** are small lipidic mediators of inflammation.
- They function through binding to the leukotriene receptors GPR17 and CysLT1, present in different cell types of the brain.
- Harmful effects associated with leukotrienes include:
  - Disturbed neurotransmission
  - Inhibited neurogenesis
  - Disrupted blood brain barrier
  - Enhanced neuroinflammation
  - Induced neurodegeneration
  - Disrupted myelin and axons

**Phase I Clinical Study: Plasma and CSF Concentrations**

Montelukast-Film in comparison to Montelukast-Tablet (Single) at 10 mg in 8 healthy subjects.

**Phase II Clinical Study:**

- Based on Phase 1 clinical results, IntelGenx Corp. has initiated a Phase 2a Montelukast VersaFilm™ proof of concept (POC) clinical trial in Alzheimer’s patients, following clearance of the Clinical Trial Application by Health Canada.
- The Phase 2a Montelukast VersaFilm™ clinical trial (NCT03402503) is a randomized, double-blind, placebo controlled POC study that will enroll approximately 70 subjects with mild to moderate Alzheimer’s Disease across 8 Canadian research sites.

**Primary Study objective:**

- To evaluate whether 26 weeks of treatment with 10 mg montelukast administered once a day is superior to placebo, assessed at Week 26 using the global Neuropsychological Test Battery (NTB) composite score. This composite of indications, based on an equally weighted average of standardized change from baseline scores on the IRTL, IRTL-Delay, One Back Test, One Card Learning Test, Verbal Fluency Test Category Fluency Test, Identification Test and Detection Test.

**Secondary study objectives:**

- Evaluate whether 26 weeks of treatment with montelukast improved the following:
  - Mini Mental State Examination (MMSE) score
  - Alzheimer’s Disease Cooperative study - Clinical Global Impression of Change (ADCS-CGIC) score
  - Alzheimer’s Disease Cooperative study – Activities of Daily Living (ADCS-ADL3)
  - Behavioural disturbances measured by neuropsychiatric inventory (NPI)
  - Bladder Incontinence
- Evaluate whether 6 and 12 weeks of treatment with montelukast is superior to placebo, assessed using the global NTB composite scores as compared to change from baseline

**Conclusions:**

- Montelukast-Oral Films exhibit increased bioavailability compared to the Montelukast tablet.
- Montelukast accumulates in the CSF.
- Given the inherent attributes of Montelukast VersaFilm, this might be a novel effective therapeutic and treatment modality as part of the armamentarium against Alzheimer’s Disease.