EXPLORATORY CLINICAL STUDY OF SYNTHETIC RETINOID ON ALZHEIMER’S DISEASE LAUGHTED IN JAPAN

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Introduction:

- Tamibarotene is a synthetic retinoid which has a higher receptor selectivity and activity for the Retinoic Acid Receptor subtypes compared to the natural retinoid. It is approved in Japan for APL.
- Recently results are published showing the efficacy of retinoids to the AD animal models. Tamibarotene is also known to decrease amyloid-beta (Aβ) 42 deposition in APP mice, and increase TTR, VChT and ACh in the SAMP8 mice. In the behavioral models, tamibarotene showed improvement in reduced anxiety of SAMP8 mice, rat passive avoidance test, and in the scopolamine-induced memory deficit in rats.
- Tamibarotene as in other retinoids is known to moderate the immune system and reduce inflammatory cytokines and chemokines, which may control the excessive stimulation of astrocyte and microglia around the Aβ plaque.

- Furthermore, retinoids are known to have critical roles during the regeneration stage in the differentiation from neural stem cells (NSC). In spinal cord injured rats treated with tamibarotene showed better recovery compared to the control.
- Based on these evidences we have launched a clinical trial in Japan.

Aims: To evaluate the safety and efficacy of oral tamibarotene for mild to moderate Alzheimer’s Disease.

Methods:

- **Design**: placebo controlled double blind study.
- Patients: mid to moderate AD.

- Drug: Tamibarotene 4mg/day or Placebo for 24 weeks
- Primary Endpoint: MMSE, ADAS-cog, CIBIC-plus, ADCS-ADL

Results: The trial was approved by the institutional review board and started to enter patients. No serious adverse effects reported so far.