Relapse Risk after Discontinuation of Risperidone in Alzheimer’s Disease

NEJM Oct. 18, 2012

Goal: Establish risk of recurrence of symptoms in pts with AD who have had a positive response to risperidone for treatment of psychosis or agitation.

Methods:

Phase A: Pt’s with AD received open-label risperidone for 16 weeks

Phase B: Positive responders to risperidone were randomized to 3 regimens

Group 1. Continued risperidone for 32 wks

Group 2. Risperidone for 16 wks, then switched to placebo for 16 wks

Group 3. Placebo for 32 wks

Inclusion criteria: AD pts living in community, assisted-living or nursing home. Age 50-95, NPI >4 on psychosis or agitation scale, MMSE 5-26 (community) or MMSE 2-26 (NH)

Outcome Measures:

Phase A: Positive response to risperidone if 30% reduction in baseline score on NPI and score of 1 or 2 on CGI-C

Phase B: Relapse if NPI increase of 30% or 5 point increase on CGI-C

Secondary Outcome Measures: EPS severity (Simpson-Angus Scale), Tardive dyskinesia (AIMS), General somatic symptoms (Treatment Emergent Symptoms Scale TESS), Cognition (MMSE and ADAS-Cog), Physical function (Physical Self-Maintenance Scale)

Results:

Phase A: 112/180 had a positive response, 110 randomized

Phase B: First 16 wks: 60% on placebo relapsed vs 33% on risperidone ), p=0.004

Second 16 wks: 48% on placebo relapsed vs 15% on risperidone, p=0.02

No significant differences in rates of adverse events amongst the different treatment groups.