CESSATION VERSUS CONTINUATION OF 12 MONTHS GALANTAMINE THERAPY IN PATIENTS WITH ALZHEIMER DISEASE: A RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED WITHDRAWAL TRIAL

B. Schaeuble¹, U. Richarz², M. Adami³, M. Gaudig⁴, A. Jacobs⁵, E. Scarpini⁶

¹EMEA Medical Affairs, Janssen Cilag GmbH, Neuss, Germany, ²Janssen, Pharmaceutical Companies of Johnson & Johnson, Baar, Switzerland, ³Janssen, Pharmaceutical Companies of Johnson & Johnson, Milan, Italy, ⁴Janssen, Pharmaceutical Companies of Johnson & Johnson, High Wycombe, ⁵Dianthus Medical Ltd., Lodon, UK, ⁶University of Milan, Dept. of Neurological Sciences, Milan, Italy

Introduction: Galantamine improves cognition, activities of daily living, and behavioural symptoms in patients with AD.

Aim: To assess whether continuation of treatment with galantamine beyond 12 months results in delayed cognitive deterioration.

Methods: 12 months multicenter open label (OL) followed by a 24 months double blind (DB), randomized withdrawal study. Subjects with probable AD and a MMSE between 11-24 were included and eligible to enter DB if cognitive decline of < 4 points on ADAS-cog/11 at OL endpoint was recorded. Galantamine was titrated to 16mg/day. Assessments included ADAS-cog/11, DAD, CIBI-Plus, safety parameters. Patients were withdrawn if the ADAS-cog/11 deteriorated by 4 or more points. The differences between Galantamine and placebo in time to dropout for any reason and dropout for lack of efficacy were estimated using the Cox proportional hazard model.

Results: 176 / 254 subjects completed the OL phase. 139 patients entered DB and were randomized to Gal (76 patients) or PLC (63 patients). 47.4% GAL and 31.7% PLC subjects completed DB. PLC patients were more likely than GAL patients to discontinue prematurely for any reason (hazard ratio [HR] 1.76, 95% CI 1.10-2.81, P = 0.02), or lack of efficacy (HR 1.80, 95% CI 1.02-3.18, P = 0.04). No unusual AE occurred during OL or DB. Reported serious AEs were unrelated to treatment.

Conclusions: Patients who responded to 12 months of galantamine treatment benefited from continued drug therapy for up to 36 months. Treatment was generally safe and well tolerated.