**OBSERVATIONS**

- Vortioxetine, a novel antidepressant with a multimodal mechanism of action, was approved for the treatment of adults with major depressive disorder (MDD) by the US Food and Drug Administration (FDA, 30th September 2013).
- An extension of a recently published network meta-analysis (Llorca 2014) compared the efficacy and tolerability of vortioxetine with seven commonly used antidepressants marketed in the US including branded (levomilnacipran, vilazodone, desvenlafaxine and generic duloxetine, escitalopram, sertraline, venlafaxine) antidepressants.

**METHODS**

- Data from 54 double-blind, short-term placebo-controlled registration studies examining efficacy and tolerability in treating MDD were included in a systematic literature review (N = 16,812 patients). The focus on pivotal trials was needed to make comparability of these agents feasible.
- Six additional studies were included for this extension in Llorca 2014: one vortioxetine study and 5 pivotal trials for levomilnacipran in a systematic literature review (N = 18,312 patients). The focus on pivotal trials was needed to make comparability of these agents feasible.
- Only experimental drug and placebo arms were included in primary analyses to ensure treatment comparability (no possible previous exposure to the treatment). If an active reference was included in an individual trial, it was not included in the present analysis so that the potential for patient selection bias would be minimized. This strategy is in line with the conclusions from the European Medicines Agency (EMA) as described in the EPAR of vortioxetine.
- Dose ranges, according to the Summary of Product Characteristics or the EPAR of vortioxetine. Conclusions from the European Medicines Agency (EMA) as described in the EPAR of vortioxetine.
- Indirect comparison analysis via placebo: meta-regression, an extension (levomilnacipran, vilazodone, desvenlafaxine) and generic (duloxetine, escitalopram, sertraline).
- No external funding was provided for this research, which is presented at the ISPOR 20th Annual International Meeting, May 16–20, 2015, Philadelphia, PA, USA.

- Direct comparisons vs. placebo using meta-analysis
- Direct comparisons vs. placebo using meta-regression
- Indirect comparisons of similar clinical studies.

- The weighted mean incidence of withdrawal due to any AE was lowest for escitalopram (8.6%), followed by vortioxetine (26.2%). All other weighted mean incidence proportions are shown in Table 4.
- For desvenlafaxine, venlafaxine and sertraline, rates were over 10% and approached 18% for sertraline.

**RESULTS**

- Efficacy: Direct Comparisons vs. Placebo Using Meta-Analyses
- For vortioxetine, all direct comparisons in efficacy in treating MDD relative to placebo were in terms of statistical significance (p<0.05) and clinical relevance (SMD>0.2) (see Figure 2).

**CONCLUSIONS**

- A methodological strength of this meta-analysis, which was based on 54 pivotal placebo-controlled studies, is that all data came from trials of comparable design and clinical relevance (SMD≥0.2). This makes the comparability of the evidence discussed here feasible. The corresponding methodology is explained in the introduction section of this paper.
- No statistically significant differences were observed. For example, no treatment difference between vortioxetine and active comparators exceeded the 0.2 value on SMD.

**REFERENCES**

1. Llorca et al. Relative efficacy and tolerability of vortioxetine versus selected antidepressants by indirect comparisons of similar clinical studies.
3. Citrome L. Levomilnacipran for major depressive disorder: a systematic review of the efficacy and safety profile for this newly approved antidepressant—what is the number needed to treat, number needed to harm and likelihood to be helped or harmed?