# Summary of report A3384-001

**Trial Title:** A double-blind, randomized, placebo-controlled, study to demonstrate the efficacy and safety of 250 mg or 1 g A3384 administered orally twice daily for two weeks to patients with Bile Acid Malabsorption (BAM)/Bile Acid Diarrhea

**EudraCT No:** 2013-002924-17

**Trial Design** This was a Phase II double-blind, randomized, placebo-controlled, multi-center, study of the efficacy and safety of twice daily oral 250 mg or 1 g doses of A3384 for two weeks in up to 19 patients diagnosed with BAM/BAD. The study was designed to assess "the reduction in average number of BMs during the second week of treatment" compared to baseline period 2 between two dose levels of A3384 and placebo.
The study consisted of 5 clinic visits where at visit 3 patients were randomized in a 1:1:1 ratio to receive one of two dose levels of A3384 or placebo, administered orally.

**Efficacy assessments**
The primary efficacy criterion was assessed based upon patients' recordings, through the paper diary, of the date and time of each BM during treatment week 2 or the last 7 days of reporting. Secondary efficacy criteria was assessed based upon patients' recordings, through the paper diary during treatment week 2 or the last 7 days of reporting:

- Stool consistency using the Bristol Stool Form Scale (BSFS)
- Abdominal discomfort using rating scales
- Bloating using rating scales
- Severity of diarrhea using rating scale
- Degree of global symptom relief using rating scales

**Safety assessments**
The primary safety criterion was the incidence of treatment-emergent SAEs, based upon information from patient reports, including the description, incidence, and severity of an SAE.
Secondary safety criteria was assessed based upon information in patients' diary reports.

- Occurrence of treatment-emergent AEs including severity and relatedness to study drug
- Physical examinations at screening and at visits 4 and 5
- Concomitant medication at all visits
- Vital sign measurements at all clinic visits
- Laboratory test results (including hematology, clinical chemistry and urinalysis) at all visits

**Results:** This study was prematurely stopped due to results received from the final clinical report from study A4250-001 where A3384 was evaluated in combination with A4250 in healthy volunteers. From study A4250-001 it has been concluded that the colonic release cholestyramine formulation A3384 did not have any major impact on BA modulation or on GI events.

In this study (A3384-001) both doses of A3384, 1 g and 250 mg were well tolerated when administered twice daily during a period of 14-17 days. During the study, one SAE was reported as severe in nature and was judged to be not related to the study drug and was classified as post study event. Of the 14 AEs reported by nine patients in the study most AEs were mild in nature and AEs were most prevalent in the placebo group. Vital signs indicated no clinically significant abnormalities and there were no apparent differences between the placebo group and the two doses of A3384.

The primary efficacy comparison of the primary efficacy endpoint in this study (A3384-001) was not met. However, the important secondary parameters evaluating stool function (diarrhea and stool consistency) showed statistically significant reductions in diarrhea and statistically significant improvements in stool consistency for patients receiving both doses of A3384, compared to placebo. A statistically significant difference was found for the change in serum levels of total BAs from visit 2, when patients were on conventional resin therapy, to visit 4 for the 250 mg group compared to placebo.