

## Clinical Trial Summary – SSAT043

**Name of Sponsor:** Chelsea and Westminster Hospital NHS Foundation Trust.

**EudraCT Number:** 2011-001913-14

**Title of Study:** A randomized crossover study of the effects of zinc sulphate supplementation on atazanavir/ritonavir-associated hyperbilirubinemia.

**Phase of Development:** Phase IV – Pilot Study

**Principal Investigator/ Chief Investigator:** Dr Marta Boffito

### Objectives:

#### Primary

To assess the change in unconjugated hyperbilirubinaemia following acute and chronic administration of zinc sulphate during atazanavir/ritonavir therapy.

#### Secondary

To assess the safety and tolerability of zinc sulphate supplement when given concomitantly with atazanavir/ritonavir

To assess atazanavir plasma exposure in the presence of zinc and relationship between the latter and hyperbilirubin during zinc intake.

To investigate the association between genetic

### Summary of results:

- 16 male patients completed the study maintaining virologic suppression throughout.
- ZnSO<sub>4</sub> was well tolerated and no grade 3 / 4 adverse events were observed.
- We observed a decline in total bilirubin C<sub>max</sub> and AUC<sub>0-24</sub> both after single and multiple ZnSO<sub>4</sub> intake compared to reference phase (Table 1).
- No significant changes in conjugated bilirubin were observed, indicating that the changes were secondary to declines in the unconjugated fraction.
- Atazanavir pharmacokinetic parameters and GMR (90% CI) for C<sub>trough</sub>, C<sub>max</sub> and AUC<sub>0-24</sub> after single and multiple dose of ZnSO<sub>4</sub>, are illustrated in Table 3.
- All individuals with the exception of one (whose levels were low throughout the study) maintained atazanavir concentration above the suggested MEC of 150 ng/mL.

### Conclusions:

- The intake of ZnSO<sub>4</sub> led to a moderate decrease in total bilirubin C<sub>max</sub> and overall exposure.

- However, a decrease in atazanavir concentrations was also observed. In this short term study, it did not affect virological response.
- Further data are required to understand whether ZnSo<sub>4</sub> supplementation could represent a useful tool in the management of atazanavir related HBR.