

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.
- ZnSO₄ was well tolerated and no grade 3 / 4 adverse events were observed.
- We observed a decline in total bilirubin C_{max} and AUC₀₋₂₄ both after single and multiple ZnSO₄ 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_{trough}, C_{max} and AUC₀₋₂₄ after single and multiple dose of ZnSO₄, 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 ZnSO₄ led to a moderate decrease in total bilirubin C_{max} 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 ZnSo₄ supplementation could represent a useful tool in the management of atazanavir related HBR.