DAV132, an Adsorbent-Based Product, Protects the Gut Microbiome and Prevents Clostridium difficile Infections During Moxifloxacin Treatments

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Session: 129. All Things Microbiome
Friday, October 9, 2015: 12:30 PM

Background. During antibiotic treatments, antibiotics reach the colon and alter the microbiome, resulting in emergence and dissemination of resistant bacteria, antibiotic-associated diarrhea (AAD) and occurrence of *Clostridium difficile* (Cd) infections (CDI). We developed an oral adsorbent-based product, DAV132, to be co-administered with antibiotics in order to prevent these effects. We report here the results of protection of the microbiome in human volunteers treated with oral moxifloxacin (MOX), and protection against CDI in vitro in a human gut model (HGM) and in vivo in experimental hamsters.

Methods. Four groups (MOX [400 mg OD for 5 days], MOX + DAV132 [7.5 g TID for 7 days], DAV132, or control) of healthy volunteers (n = 44) were included in a randomized clinical trial. Feces were collected at screening, daily from D1 to D9 and at D12, D16, D23, D30, D37 and plasma PK assayed at D1and5. Metagenomic analyses were done by shotgun sequencing at screening, D3, D6, D9, D16 and D37. The effect of DAV132 on MOX was also assessed in a HGM inoculated with Cd spores (ribotype 027, MOX MIC 32 mg/L); bacterial counts, toxin production and MOX concentrations were measured over time. MOX dosed hamsters were inoculated with 10^4 spores of a non-epidemic Cd (TcdA + , TcdB + , cdtB−) and treated ±DAV132. Mortality and Cd counts were assessed over time.

Results. In humans, DAV132 was well tolerated and decreased free fecal MOX by > 99% compared to MOX alone: ratio of mean $\text{LogAUC}_{\text{D1-D16}} = 0.0093$ (95% CI 0.0061-0.0144), $p = 0.03 \times 10^{-16}$; MOX plasma PK was not changed significantly. Alterations of the fecal microbiome observed with MOX were prevented. In the HGM, DAV protected the microbiota and prevented Cd overgrowth and toxin production. Hamsters were fully protected by DAV against MOX-induced CDI (dose dependent), with decreased free fecal MOX and Cd counts.

Conclusion. DAV132 protects humans against fecal microbiome disruption after oral MOX treatment, without altering its plasma PK. In vitro results in HGM and in vivo results in hamsters suggest that DAV132 should be protective against antibiotic-induced CDI. These results warrant further clinical development of DAV132 to protect the intestinal microbiota, and so prevent AAD and CDI, in patients receiving oral or parenteral antibiotics.

Disclosures. **J. De Gunzburg**, Da Volterra: Board Member, Consultant and Shareholder, Consulting fee; **A. Ducher**, Da Volterra: Employee, Salary; **E. Ruppé**, Da Volterra: Consultant, Consulting fee; **C. Chilton**, Da Volterra: Collaborator, Research grant; **E. Chachaty**, Da Volterra: Consultant, Consulting fee; **S. Sayah-Jeanne**, Da Volterra: Employee, Salary; **W. Weiss**, Da Volterra: Research Contractor, Research grant; **M. Wilcox**, Da Volterra: Consultant, Grant Investigator and Scientific Advisor, Consulting fee and Research grant; **F. Mentré**, Da Volterra: Consultant, Consulting fee; **A. Andremont**, Da Volterra: Scientific Advisor, Consulting fee