DAV131, an oral adsorbent-based product, exerts a dose-dependent protection of hamsters against Clostridium difficile-induced antibiotic-associated diarrhea (AAD)

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ABSTRACT

Objective: Antibiotic treatments greatly impact gut microbiota which can result in potentially severe, sometimes lethal Clostridium difficile infection (CDI). Prevention strategies would be highly welcomed. DAV131, a new adsorbent-based product, significantly reduces the level of residual antibiotics reaching the colon in several animal models. Here, we report on an escalating dose study of the protective effect of DAV131 in a mouse model of C. difficile infection.

Methods: Male Syrian hamsters were administered 30 mg/kg moxifloxacin subcutaneously once per day for 5 days, and infected orally with a mix of C. difficile 630 and DAV131. Groups of 10 animals were orally administered 100, 300, 600 or 900 mg/kg DAV131 twice per day starting on day 0 and continuing until day 5. C. difficile counts were determined using a barrier and viable C. difficile counts were separately determined using a barrier and standard plates.

Results: Animal administered moxifloxacin showed rapid mortality upon ingestion of C. difficile, with 50% survival at day 4, 50% at day 5, 30% at day 6, and 5% at day 7. Animals that received 100 mg/kg DAV131 had protection, while those that received 300 mg/kg DAV131 showed a 50% reduction in survival. All animals that received both C. difficile spores and 300 mg/kg DAV131 showed similar survival rates to those that received C. difficile spores only.

Conclusion: DAV131 is a protective agent for all doses tested, and it could be a potential strategy for the prevention of CDI in humans (name code DAV131) are under way.

INTRODUCTION

Treatment by most antibiotics can lead to CDI by perturbing the colonic commensal flora, thereby allowing colonization of the intestine by C. difficile. Amongst antibiotics, clindamycin, cephalosporins and fluoroquinolones are considered as the principal risk factors (1, 2). CDI is not only a major public health problem, but also a grave economic burden. The prediction of C. difficile episodes and CDI relapses would therefore be a major need for prophylactic treatment with improved quality of life for patients, and a decrease of public health costs.

DA Volterra (Paris, France) has been developing a novel adsorbent-based product, which limits the adverse effect of antibiotics on the gut microbiota by adsorbing unwanted antibiotic residues in the lower intestine before they can reach the colon and perturb the host’s gut microbiota. In this work, we assessed the protective effect of the moxifloxacin-induced hamster Clostridium difficile Associated Disease (CDAAD) model on the incidence of C. difficile infection and other related outcomes (3, 4). Here, we report the results of a dose-dependent study of the protective effect of DAV131.

RESULTS: Preventive effect of DAV131 on the induction of C. difficile infection by moxifloxacin treatment

Fig 1: Evolution of body weight

Fig 2: Survival of hamsters following inoculation of C. difficile spores

Fig 3: Viable C. difficile counts on Day 4

Fig 4: Evolution of viable C. difficile counts

Fig 5: Mean fecal moxifloxacin concentrations

Fig 6: Evolution of body weight

Fig 7: Viable C. difficile counts on Day 4

Fig 8: Mean fecal moxifloxacin concentrations

CONCLUSION

The results of this study confirm that, when co-administered with moxifloxacin, DAV131 can prevent the gut colonization and infection by C. difficile in addition, our study supports the dose-dependency of this protective effect on animal survival, as well as on fecal concentrations of moxifloxacin.

In conclusion, we confirm that DAV131 represents an excellent pharmacological strategy to protect against CDI, if applied concomitantly with the causative antibiotic treatment.

The development of this promising strategy for the prevention of CDI in humans (with code name DAV132) is ongoing. The first trial in healthy volunteers of DAV132 is presented in poster P024 at ECCMID 2014.

REFERENCES

1. Miossec C et al., ECCMID 2014, Poster 2A13, ECCMID 2014


5. DAV131, an oral adsorbent-based product, exerts a dose-dependent protection of hamsters against Clostridium difficile-induced antibiotic-associated diarrhea (AAD)