








A scanning electron micrograph (SEM) showing a complex, porous biofilm structure. The biofilm is composed of numerous interconnected fibers and clusters of cells, creating a dense, three-dimensional network. The overall appearance is fibrous and textured, with some larger, more rounded structures interspersed within the network.

Defined Bacterial Consortia, a Novel Approach to Tackle Healthcare-Associated Infections

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Microbiota and Metabolic Alterations Characterize Colonization and Infection with *C. difficile* and MDRO

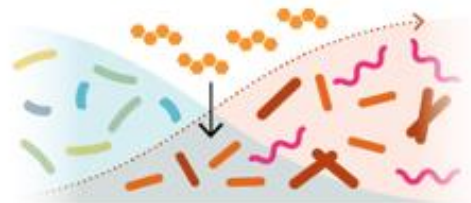
-  *C. difficile*
-  Multidrug-resistant organisms
-  *Clostridium* IV + *XIVa*
-  Bacteroides
-  Primary (1°) bile acid
-  Secondary (2°) bile acid
-  Short-chain Fatty Acids (SCFAs)



ACTIVE DISEASE

Antibiotics disrupt microbiota and metabolite pool of bile acids and SCFAs

Antibiotics cause dysbiosis, increase ratio of 1° to 2° bile acids



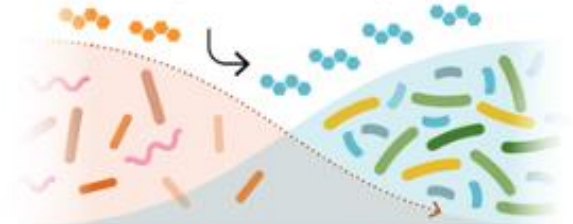
Degradation of mucus layer and epithelial damage



RETURN TO HEALTH

Recovery of beneficial bacterial community and homeostatic metabolite pool observed in clinical studies

Clostridium IV + *XIVa* convert 1° to 2° bile acids and help recover a healthy microbiome

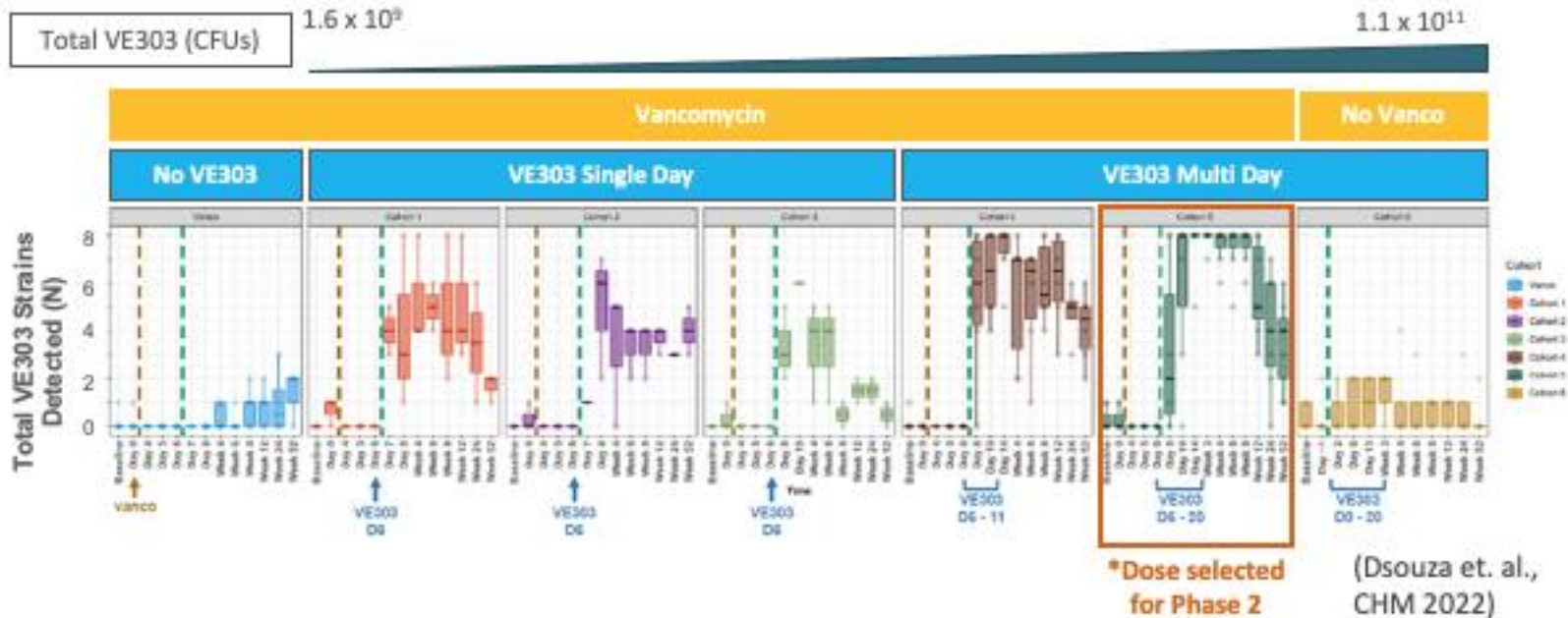


Clostridium IV + *XIVa* produce SCFAs (butyrate), strengthening the gut barrier

VE303 : An Investigational Defined Bacterial Consortium Against *C. difficile* Infection (CDI)

- Defined composition of 8 nonpathogenic, nontoxigenic strains of bacteria isolated initially from the stool of healthy donors.
 - Designed to eliminate risk of pathogen transfer associated with FMT
- VE303 strains showed
 - *In-vitro* and *in-vivo* suppression of *C. difficile*
 - *In-vitro* SCFA production and *in-silico* encoding of 1° to 2° BA conversion
- Isolates manufactured from clonal cell banks under GMP conditions; Consistent composition and quality attributes.
- Stable lyophilized drug product amenable to at-home storage and dosing.
- Durable strain colonization following oral dose administration (Dsouza et. al., CHM 2022).

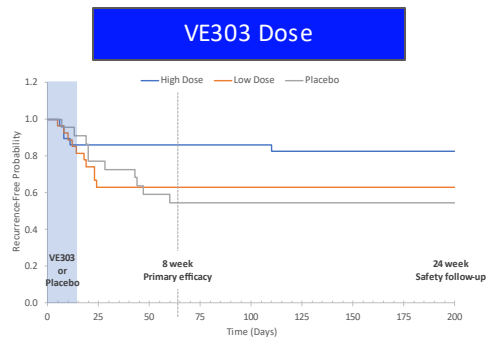
Phase 1 Study Established Recommended Phase 2 Dose and Described Pharmacokinetics (PK) and Pharmacodynamics (PD) in Healthy Volunteers: *Important Considerations for Clinical Trial Design*



- Antibiotics are necessary to create a niche for VE303 colonization
- More robust colonization with multiple-day dosing after Abx
- Recovery of beneficial bacteria, Secondary Bile Acids and SCFAs with VE303

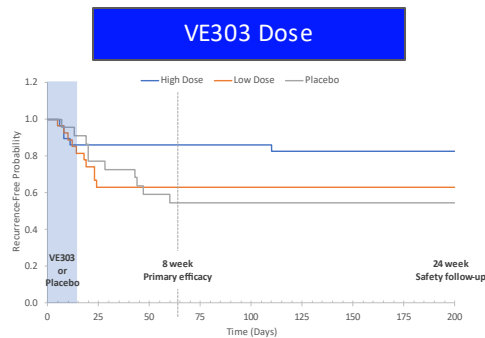
Phase 2 CONSORTIUM Study: Colonization Data Provide Rationale for Superior Activity Observed with High Dose

VE303 high dose prevented recurrence in subjects at high risk of rCDI

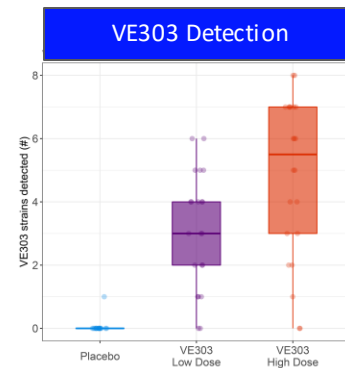


Phase 2 CONSORTIUM Study: Colonization Data Provide Rationale for Superior Activity Observed with High Dose

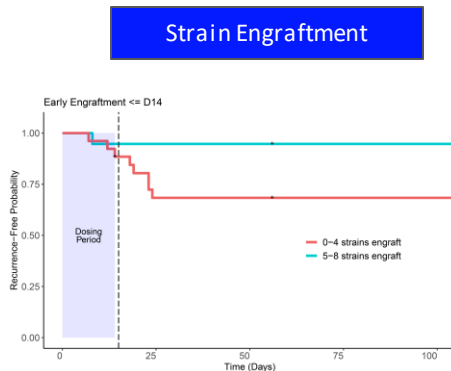
VE303 high dose prevented recurrence in subjects at high risk of rCDI



VE303 dosing led to effective, dose-dependent strain colonization

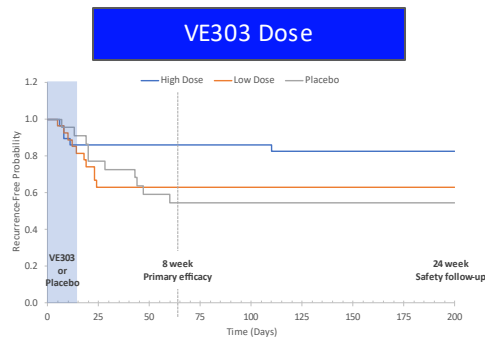


Subjects with high vs low VE303 strain engraftment had higher recurrence-free probability

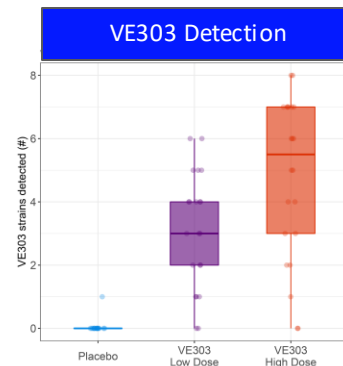


Phase 2 CONSORTIUM Study: Colonization Data Provide Rationale for Superior Activity Observed with High Dose

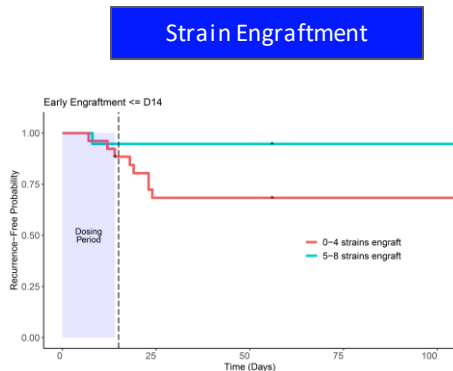
VE303 high dose prevented recurrence in subjects at high risk of rCDI



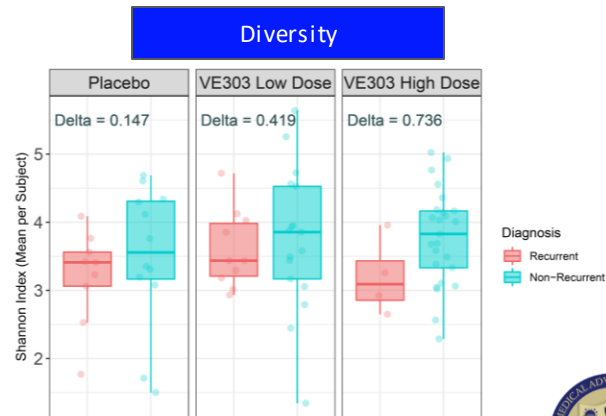
VE303 dosing led to effective, dose-dependent strain colonization



Subjects with high vs low VE303 strain engraftment had higher recurrence-free probability



Higher VE303 dosing was associated with faster host microbiome recovery, which correlates with clinical cure



VE707 – A Defined Bacterial Consortium for Decolonization of MDR Enterobacteriaceae as an Infection Prevention Strategy



CDC, 2019 AR Threats Report

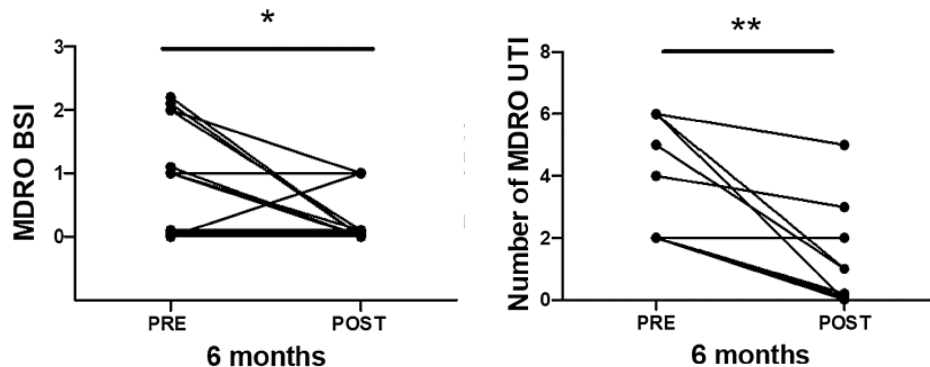
- **MDR *E.coli* and *K. pneumoniae* represent ~40% of all MDRO colonization cases with 17-65% colonized patients developing infections, compared to 0.5-11% in non-colonized cohorts.**
- **Clinical proof of concept for CRE and ESBL decolonization established with other sub-optimal modalities.**
 - **Selective Digestive Decontamination (SDD): ~80% reduction in infections** following successful decolonization in “at risk” patients. *Caveat: Emergence of antibiotic-resistant strains*
 - **Fecal microbiota transplantation (FMT): 33-90% efficacy** at treating persistent colonization with prevention of infection. *Caveat: Donor variability, number of FMT doses*

MDRO Eradication from the Intestine is NOT Required for Infection Prevention

Disease Prevention Not Decolonization: A Model for Fecal Microbiota Transplantation in Patients Colonized With Multidrug-resistant Organisms

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Horace R. T. Williams,^{1,3} Eimear T. Brannigan,² Siddharth Mookerjee,²
Giovanni Satta,² Mark Gilchrist,² Neill Duncan,⁵ Richard Corbett,⁵ Andrew J. Innes,⁶
Jiri Pavlu,⁸ Mark R. Thursz,^{1,3} Frances Davies,² and Julian R. Marchesi^{1,7}

CID, 2020



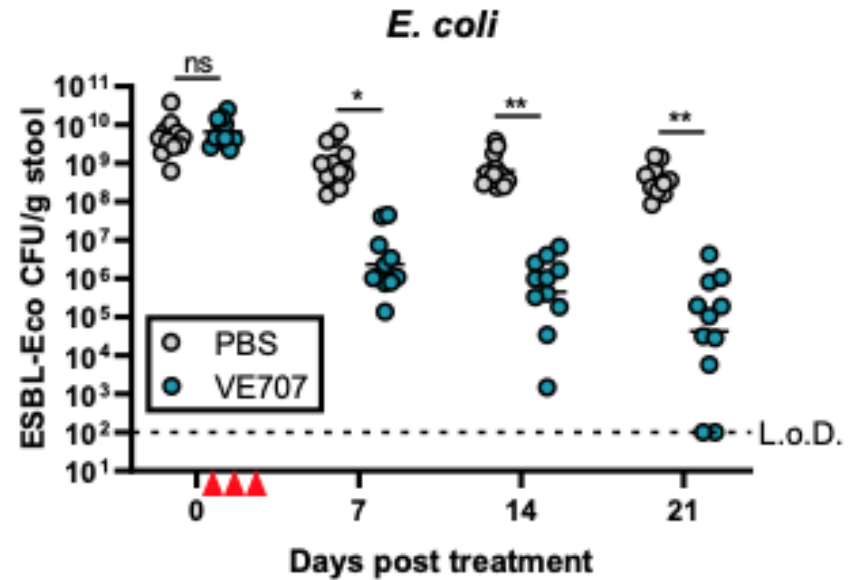
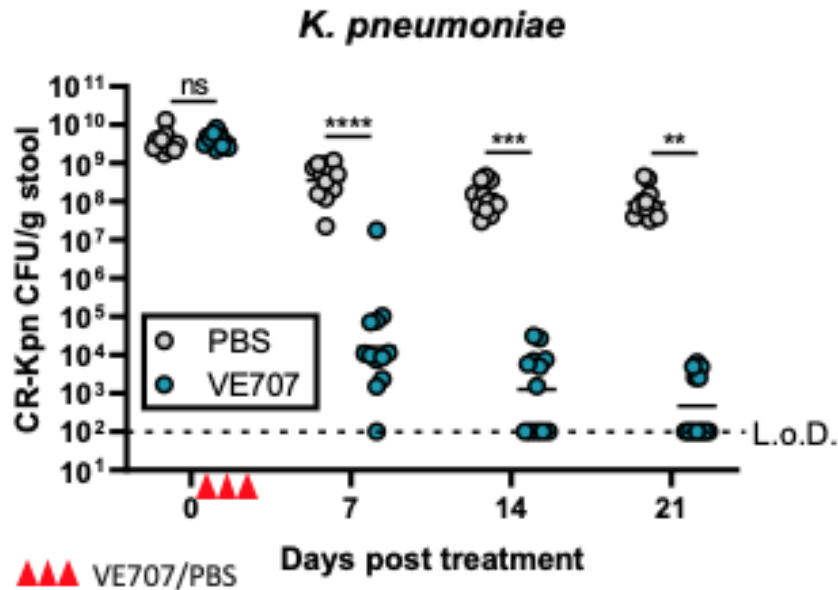
Decolonization efficacy: 41%

**Other factors important
for infection prevention**

- Carriage reduction
- Microbiota restoration
- Epithelial Barrier integrity

VE707 Candidate is Highly Efficacious at Decolonizing MDR *K. pneumoniae* and *E. coli* in Mice

- 60 unique defined bacterial consortia were tested *in vivo*. VE707 reduced MDR Kpn and Eco titers by ≥ 3 -logs compared to untreated mice.



Microbiome Restoration as a New Paradigm for Infection Control

