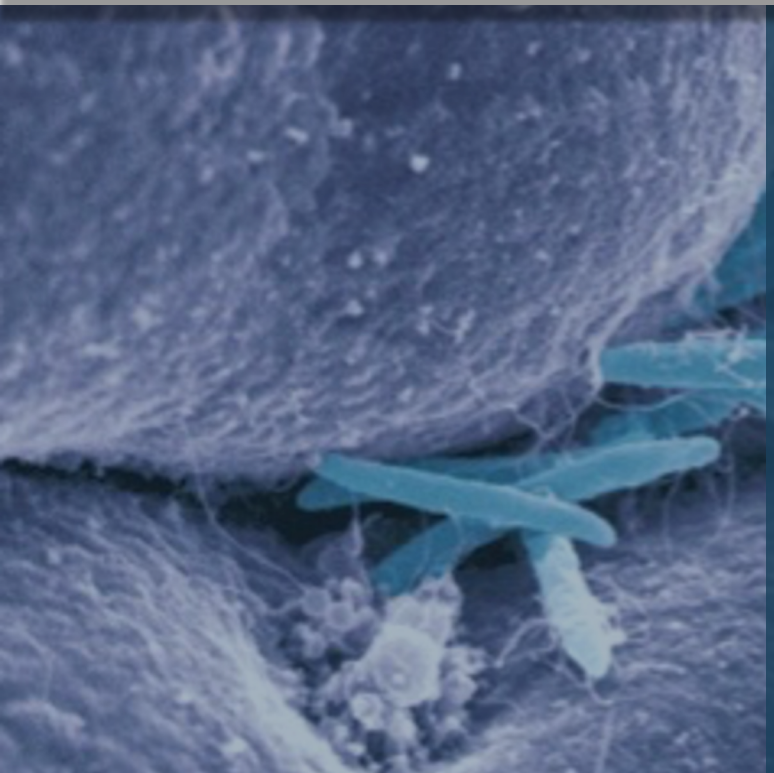
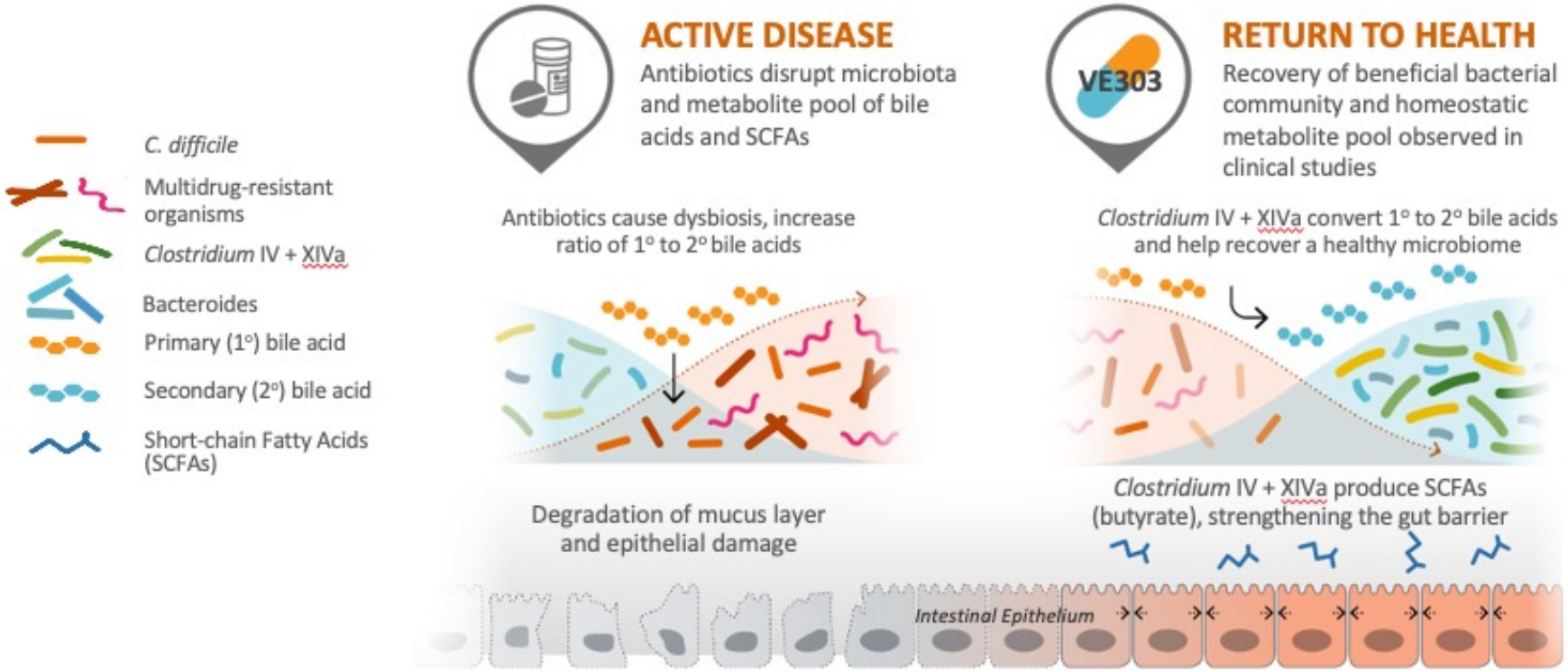


Defined Bacterial Consortia, a Novel Approach to Tackle Healthcare-Associated Infections

Silvia Caballero, Director Infectious Diseases
Vedanta Biosciences

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



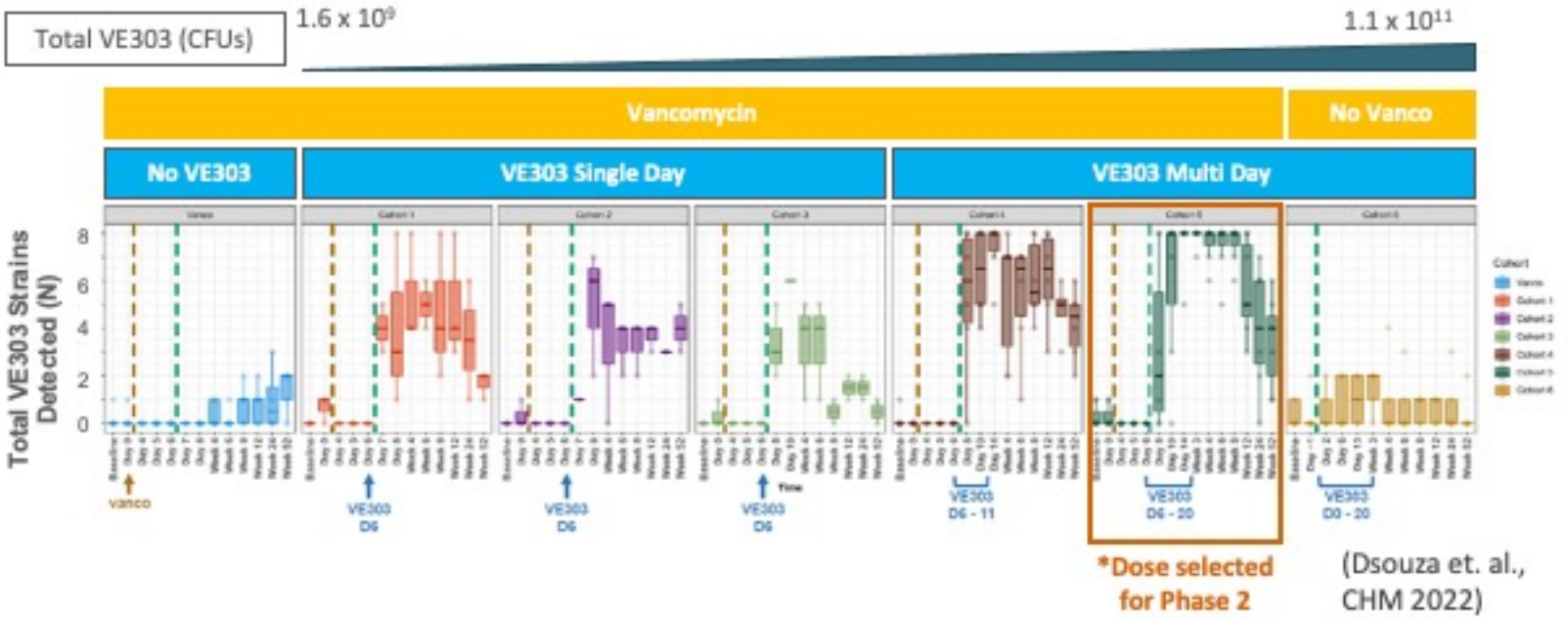
VEDANTA BIOSCIENCES

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).

VEDANTA BIOSCIENCES

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



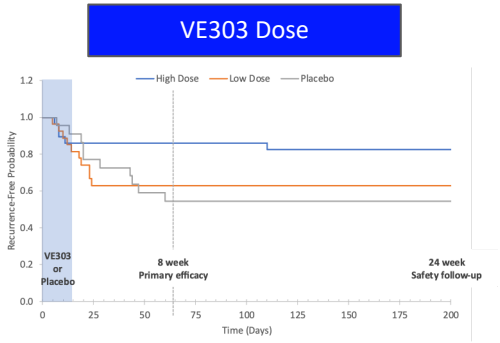
- Antibiotics are necessary to create a niche for VE303 colonization
- More robust colonization with multiple-day dosing after Abx
- Recovery of beneficial bacteria, Secondary Bile Acids and SCFAs with VE303

VEDANTA BIOSCIENCES

CARB-X Combating Antibiotic-Resistant Bacteria

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



VEDANTA BIOSCIENCES

BARDA

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

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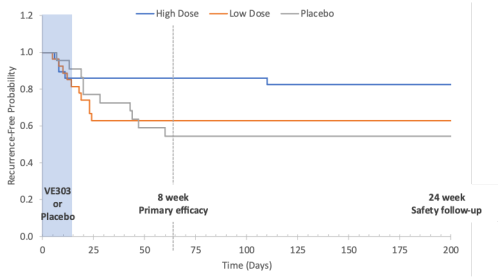
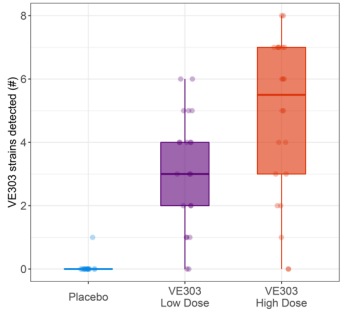
VE303 Dose



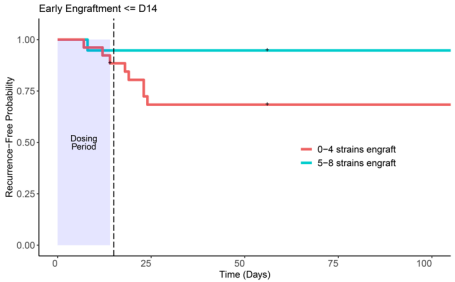
VE303 dosing led to effective, dose-dependent strain colonization

VE303 Detection



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

Strain Engraftment



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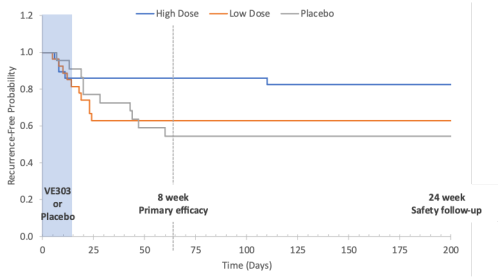
VE303 Dose



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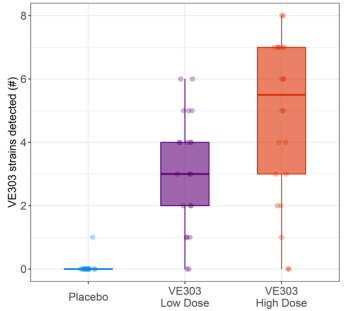

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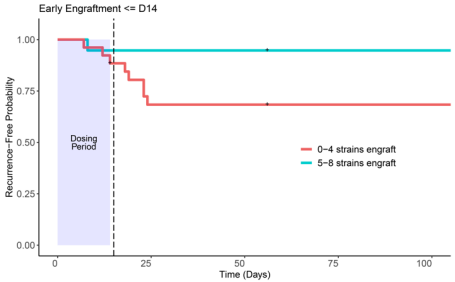
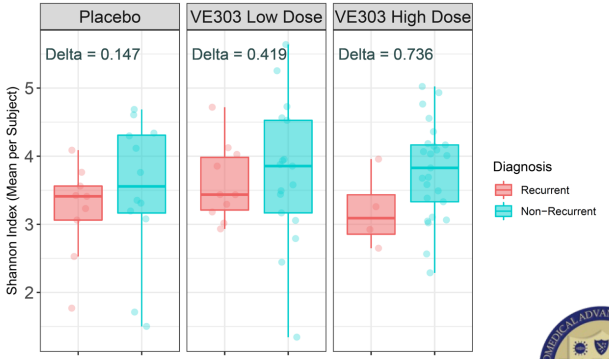


Higher VE303 dosing was associated with faster host microbiome recovery, which correlates with clinical cure

Diversity



VEDANTA BIOSCIENCES

Unpublished Data

BARDA

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*

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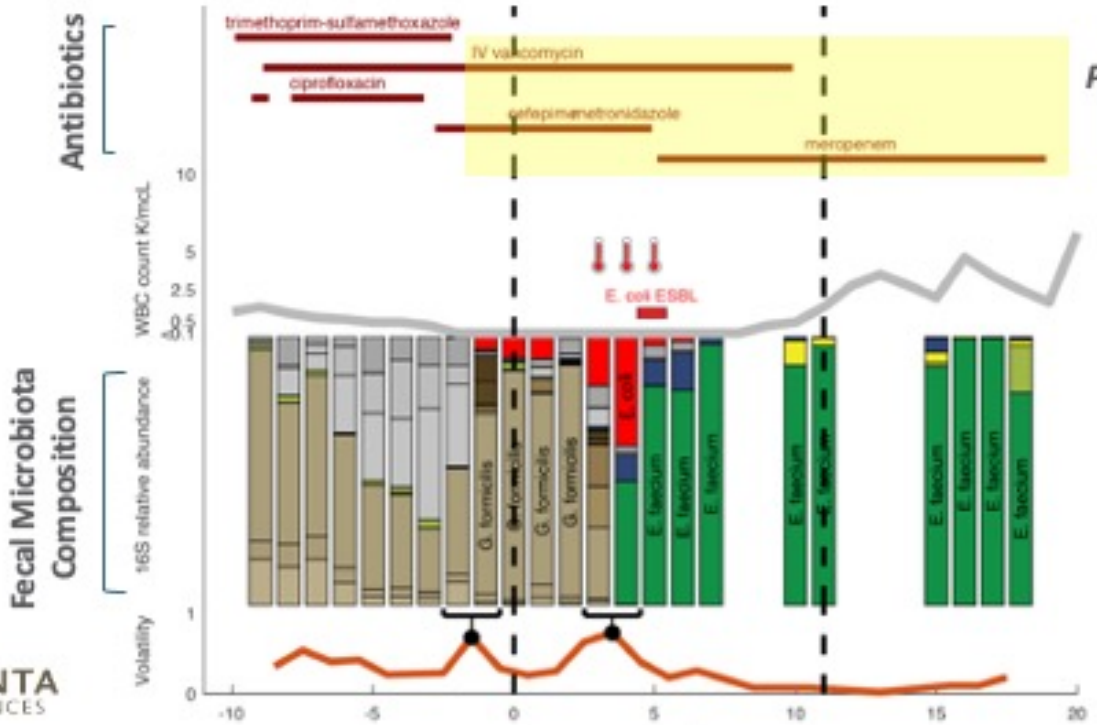
CARB-X
Combating Antibiotic-Resistant Bacteria

MDRO Colonization Frequently Precedes MDRO Infection in High-Risk Patient Populations Highlighting the Need for Surveillance

- **Intestinal MDRO colonization increases infection risk by ≥10-fold** in susceptible individuals (e.g., HSCT, SOT, ICU).



HSCT: hematopoietic stem cell transplant
SOT: Solid organ transplant

Morjaria S et al., Infect Immun. 2019

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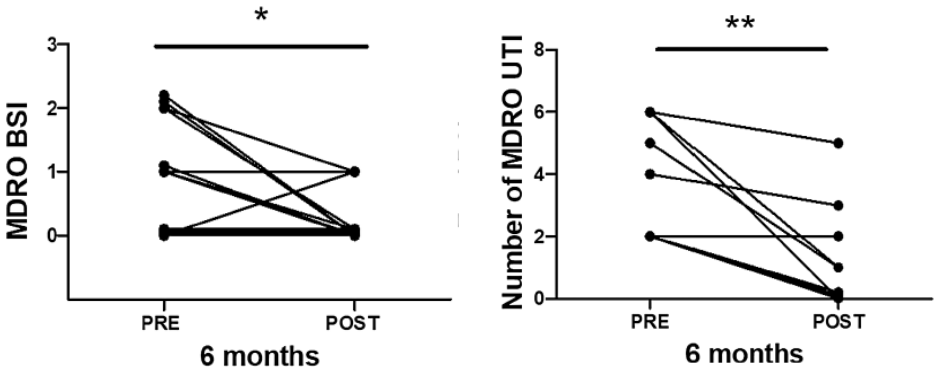
MDRO Eradication from the Intestine is NOT Required for Infection Prevention

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

Rohma Ghani,[1,2] Benjamin H. Mullish,[1,3,a,©] Julie A. K. McDonald,[1,4] Anan Ghazy,[2] 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] Jiří Pavlů,[6] 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

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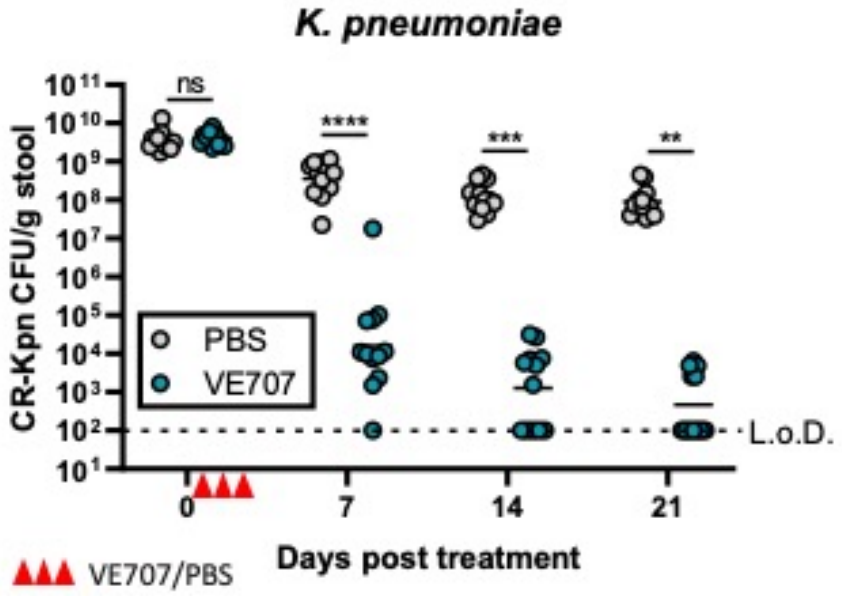
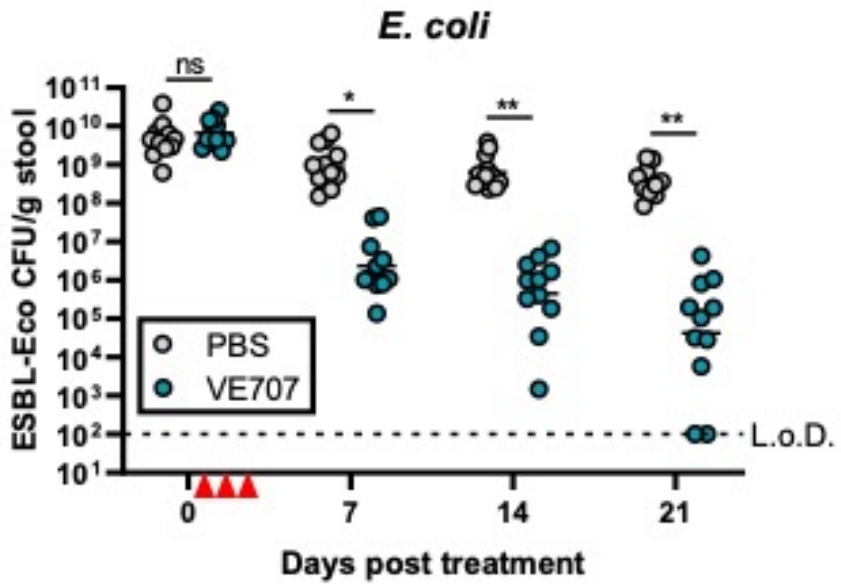
VE707 Candidate is Highly Efficacious at Decolonizing MDR *K. pneumoniae* and *E.coli* in Mice

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





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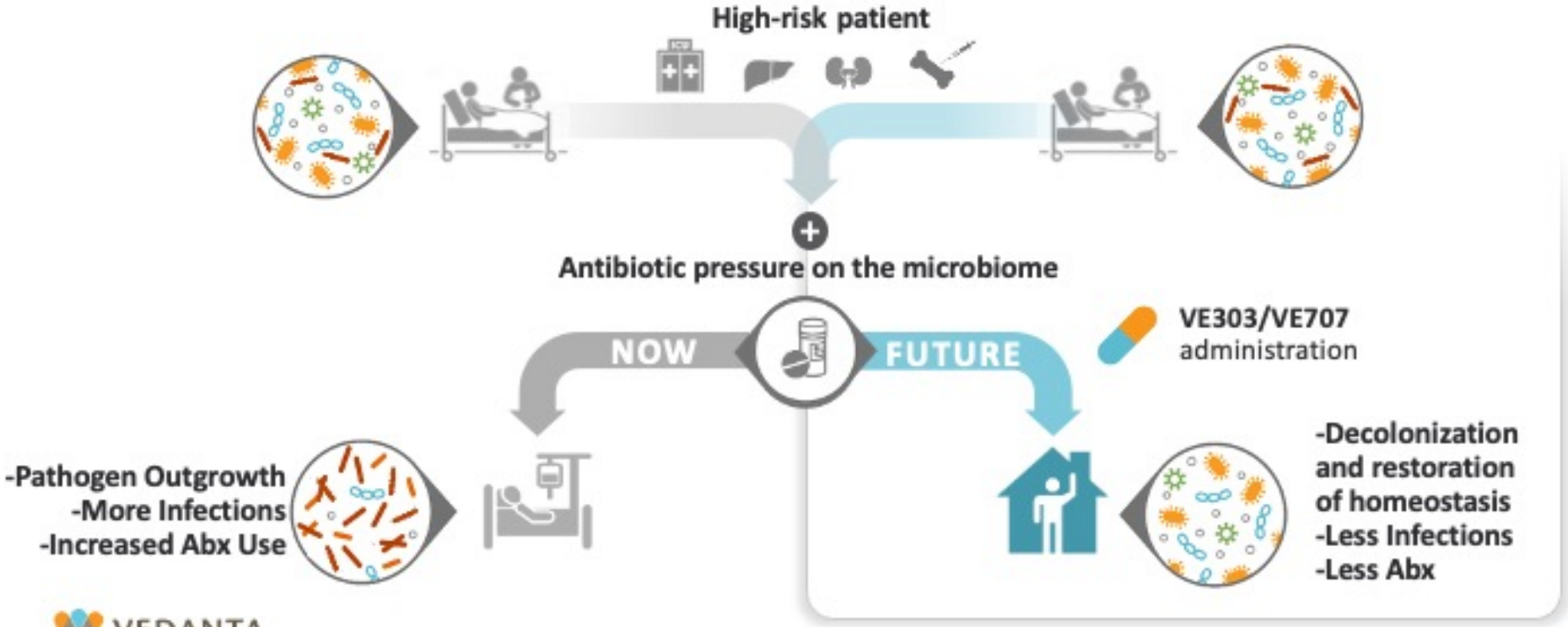
L.o.D., limit of detection
Unpublished Data

Microbiome Restoration as a New Paradigm for Infection Control



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