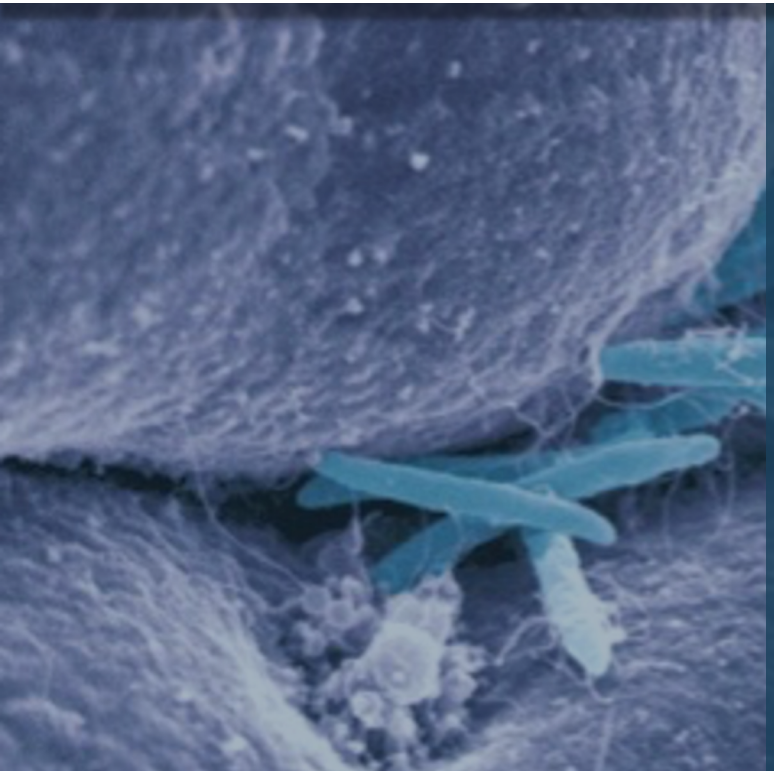
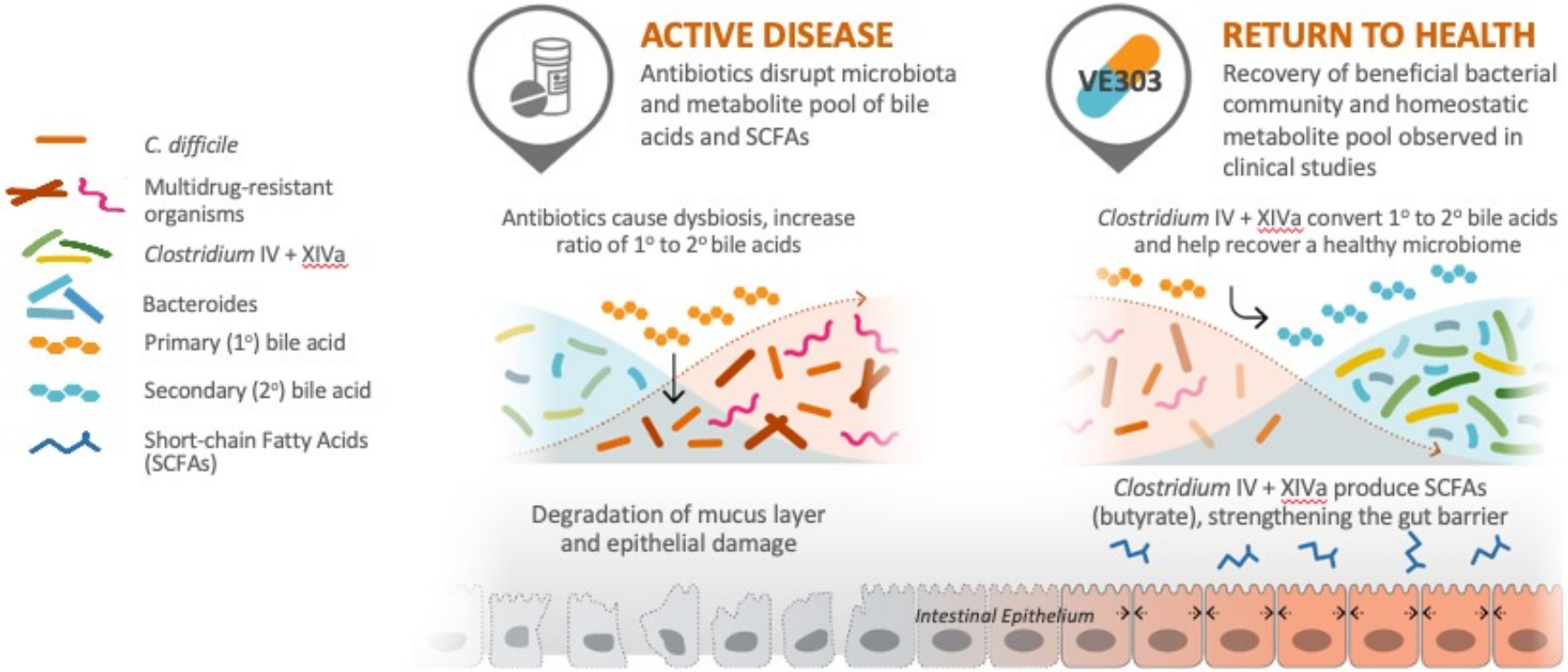
VEDANTA BIOSCIENCES



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



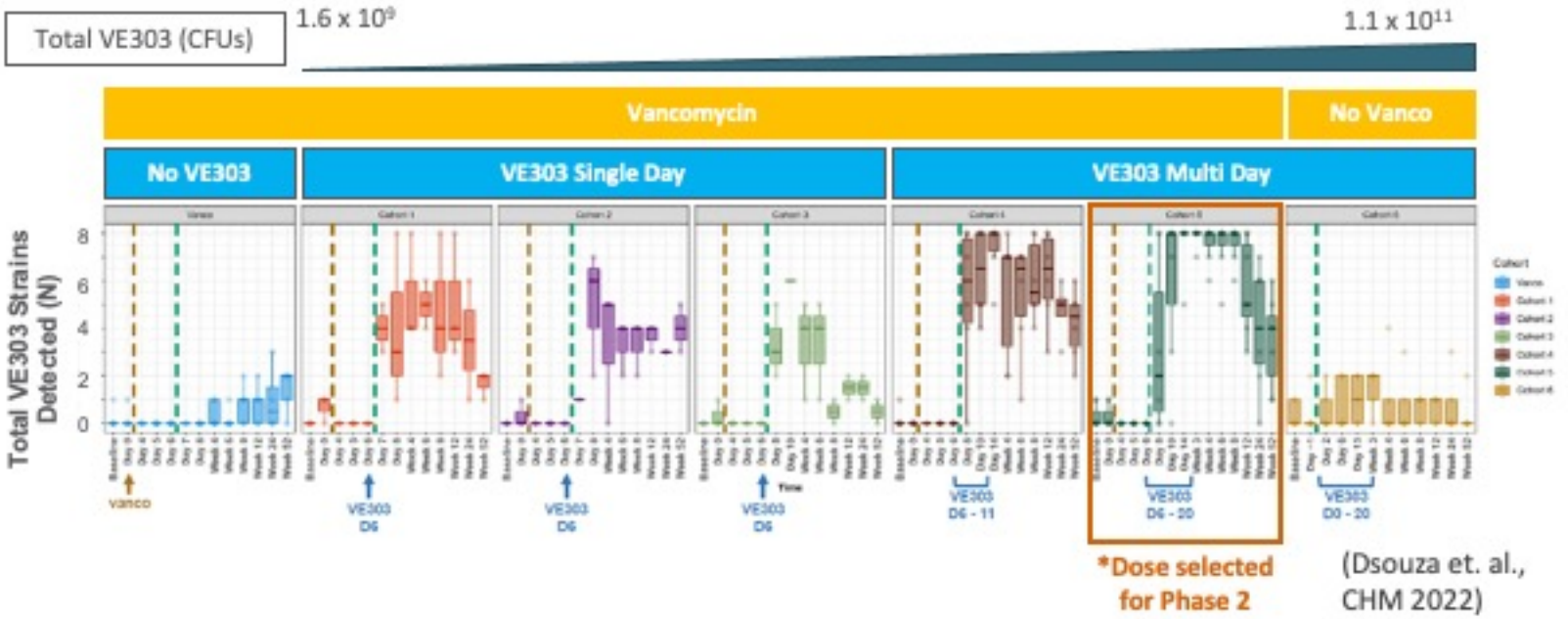
VEDANTA BIOSCIENCES

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*



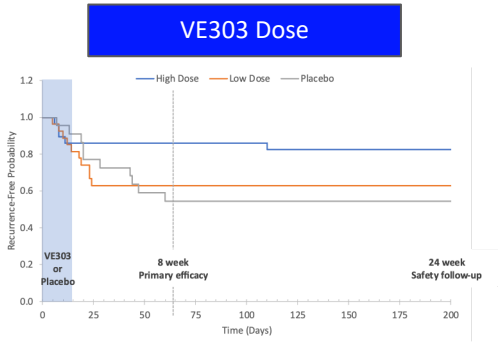
- Antibiotics are necessary to create a niche for VE303 colonization
- More robust colonization with multiple-day dosing after Abx
- Recovery of beneficial bacteria, Secondary Bile Acids and SCFAs with VE303

VEDANTA BIOSCIENCES

CARB-X Combating Antibiotic-Resistant Bacteria

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

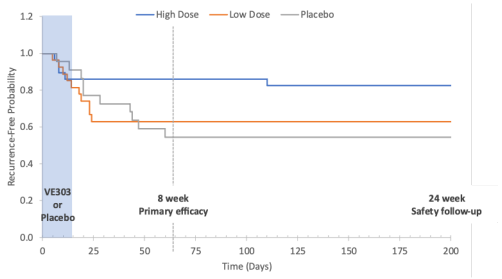
VE303 high dose prevented recurrence in subjects at high risk of rCDI



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

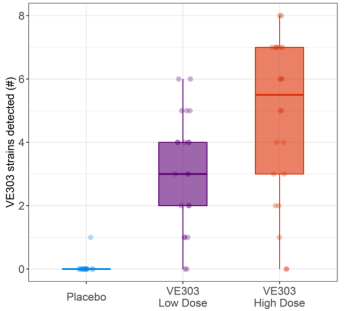
VE303 high dose prevented recurrence in subjects at high risk of rCDI

VE303 Dose



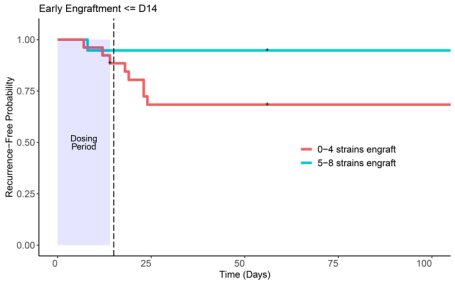
VE303 dosing led to effective, dose-dependent strain colonization

VE303 Detection



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

Strain Engraftment



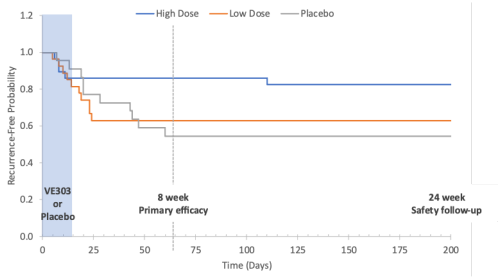
VEDANTA BIOSCIENCES

BARDA

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

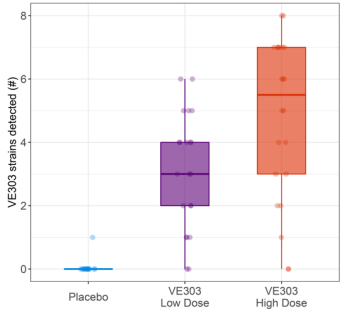
VE303 high dose prevented recurrence in subjects at high risk of rCDI

VE303 Dose



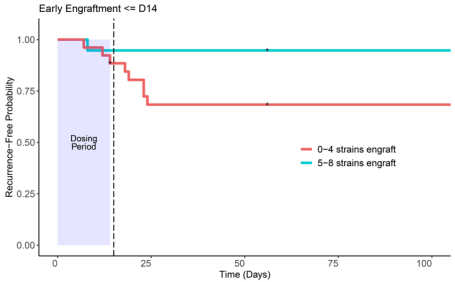
VE303 dosing led to effective, dose-dependent strain colonization

VE303 Detection



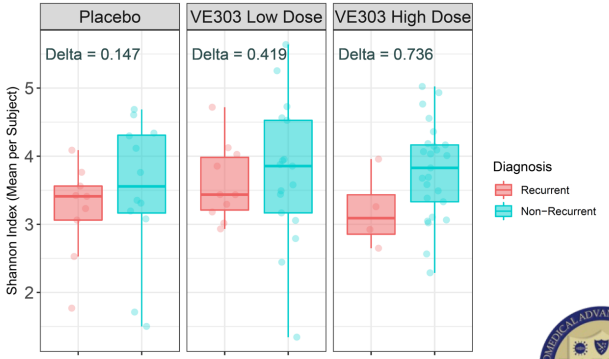
Subjects with high vs low VE303 strain engraftment had higher recurrence-free probability

Strain Engraftment



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

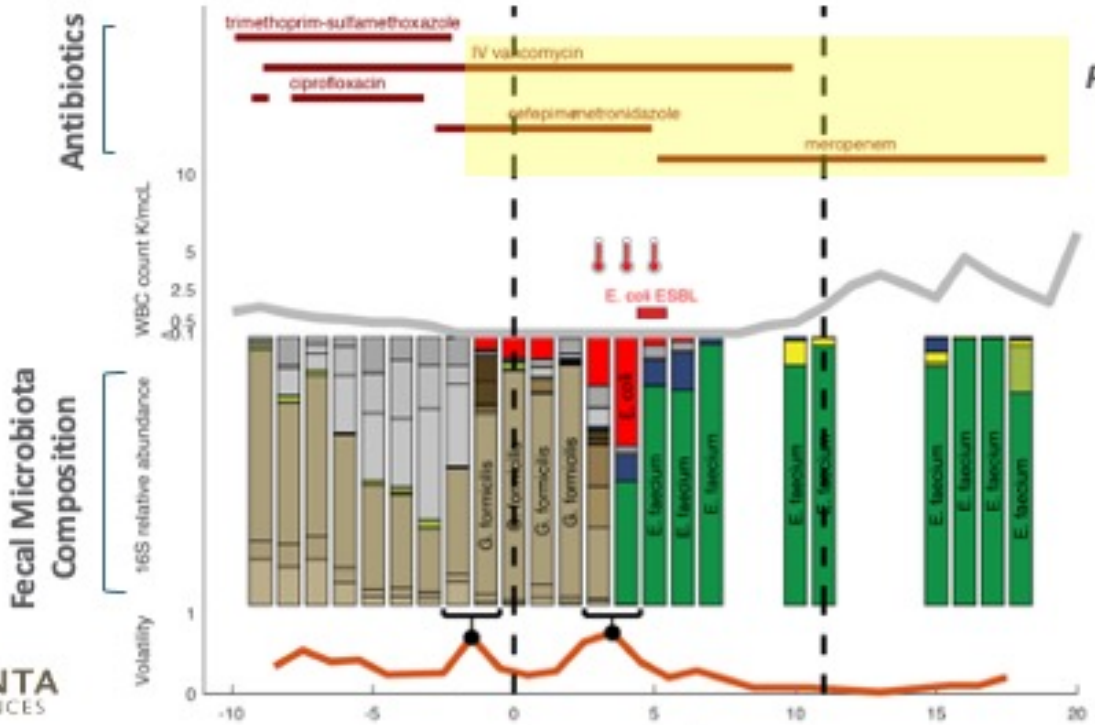
- **MDR *E.coli* and *K. pneumoniae* represent ~40% of all MDRO colonization cases with 17-65% colonized patients developing infections**, compared to 0.5-11% in non-colonized cohorts.
- **Clinical proof of concept for CRE and ESBL decolonization established** with other sub-optimal modalities.
  - Selective 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*

VEDANTA BIOSCIENCES

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

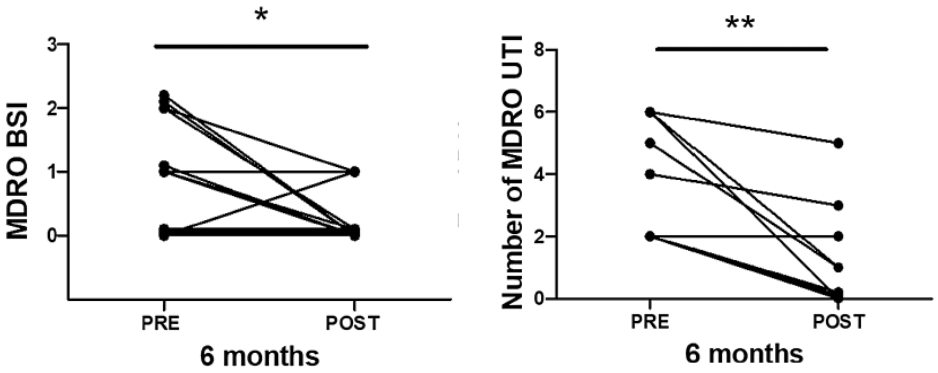
VEDANTA BIOSCIENCES

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%

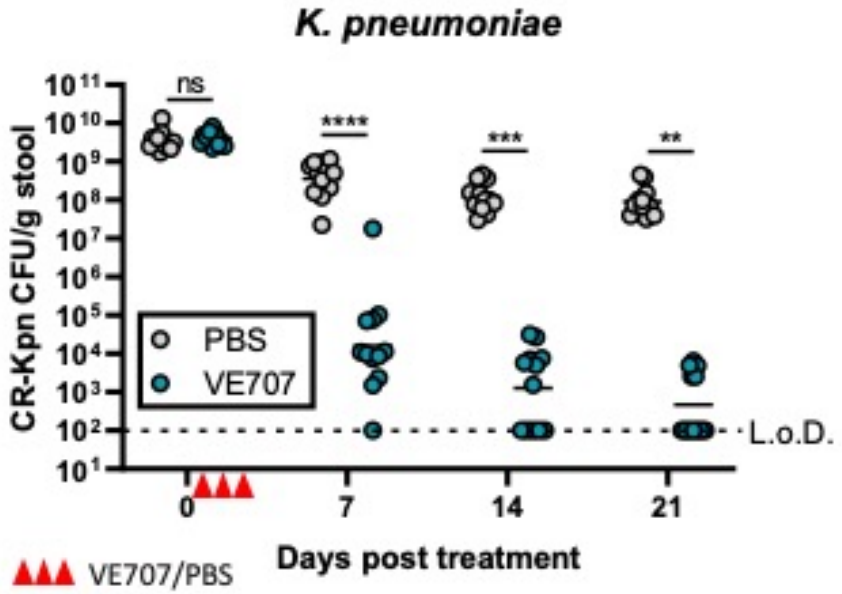
Other factors important for infection prevention

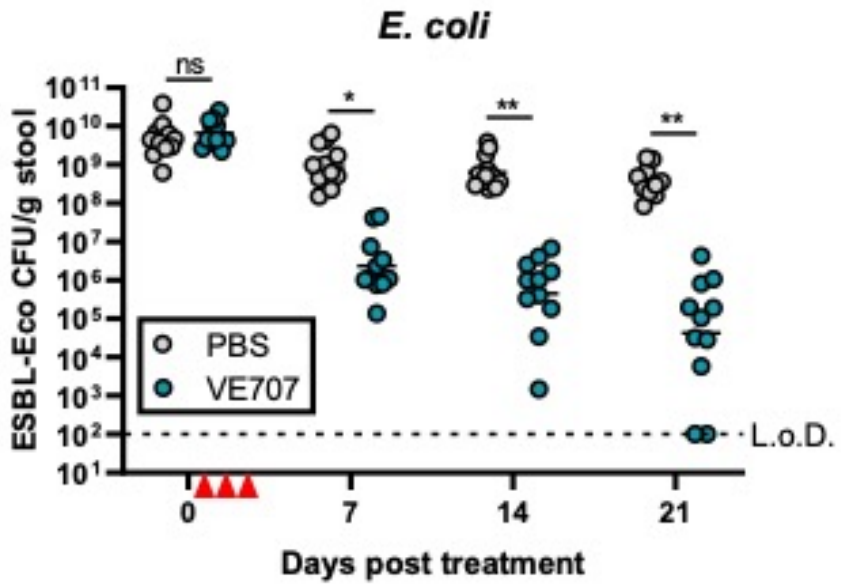
- Carriage reduction
- Microbiota restoration
- Epithelial Barrier integrity

VEDANTA BIOSCIENCES

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.

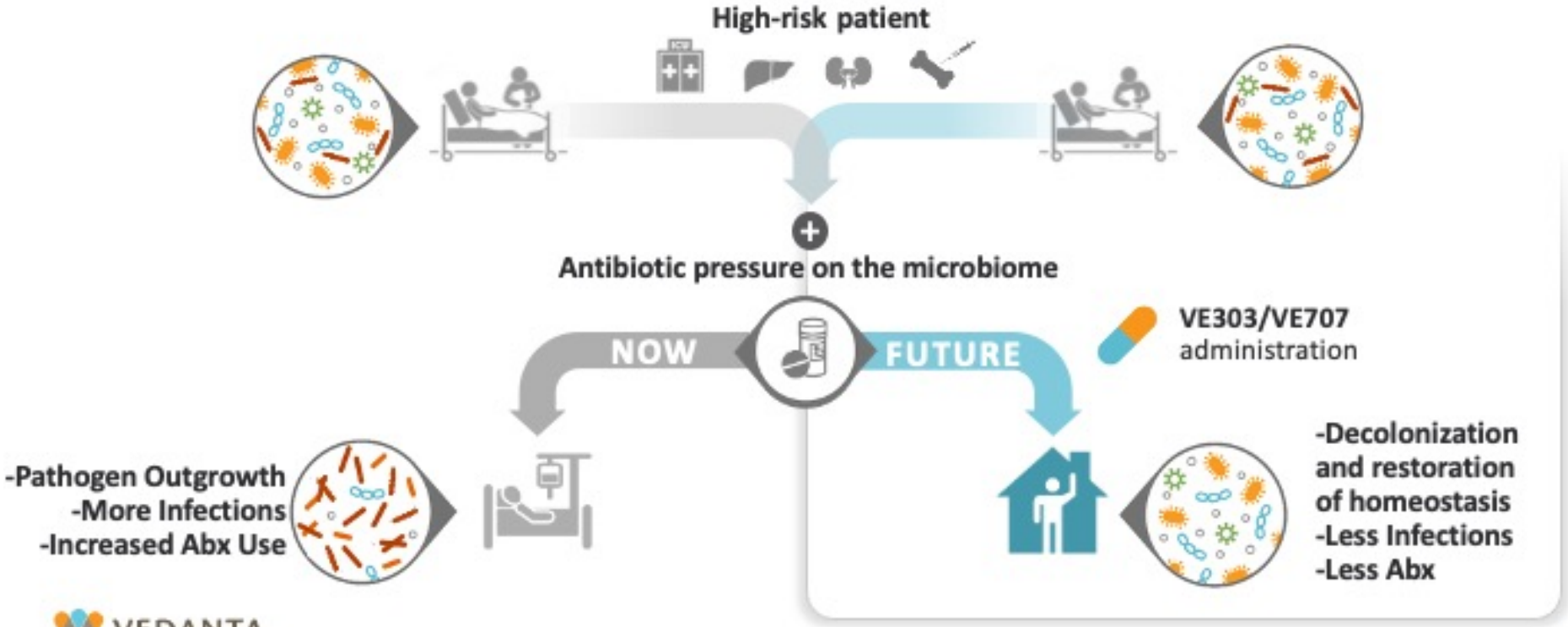




VEDANTA BIOSCIENCES

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

Microbiome Restoration as a New Paradigm for Infection Control



VEDANTA BIOSCIENCES