Background. Numerous microbiota-based therapies are being evaluated for prevention of C. difficile infection (rCDI), a public health threat with high recurrence rates among patients with current standard of care. RBX2660, a standardized microbiota-based drug, was efficacious for preventing rCDI in a double-blinded Phase 2b clinical study (PUNCH CD 2). Herein we report the durability of RBX2660 beyond the initial primary clinical end-point of a subsequent Phase 2 open-label study, demonstrating rCDI prevention at 6 months post-treatment.

Methods. This prospective, multi-center, open-label Phase 2 study enrolled subjects who had experienced either ≥2 recurrences of CDI following standard-of-care antibiotic therapy or ≥2 episodes of severe CDI requiring hospitalization. Participants received up to two doses of RBX2660 delivered via enema with doses 7 days apart. The primary endpoint of the open-label clinical study was defined as efficacy as absence of CDI at 8 weeks from the last dose. Safety follow-ups and durability assessments occurred via telephone at 3, 6, 12, and 24 months. The study is ongoing, and not all subjects have completed their assessments.

Results. This study included 149 RBX2660-treated subjects and 110 historical control subjects from 31 and 4 centers, respectively, in the United States and Canada. At 8-weeks post-treatment, RBX2660’s efficacy in preventing rCDI (79.9%; 119/149) was higher than CDI-free rates in the historical control group (51.8%. 57/110; P < 0.001). Of the 119 subjects who were determined to be treatment success at 8 weeks, 117 have data through 6 months, of which 8 were exited for non-CDI reasons. Of those 109 subjects through the 6-month follow-up, (2.8%) had a new CDI beyond 8 weeks after enema. The 6-month long-term CDI-free rate was 97.2% (106/109) (median follow-up: 82 days; mean: 177 days).

Conclusion. RBX2660, a microbiota-based drug, was efficacious for the prevention of recurrent CDI with long-term durability at 6 months post-treatment; a result consistent with 6-month rCDI prevention reported for the Phase 2b PUNCH CD2 trial. Long-term follow-up of RBX2660 and 24 months is ongoing.

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Table. Protocol-specified nephropathy and renal AEs

| AEs | Protocol-specified nephropathy | Renal AEs |
|-----|-----------------------------|----------|
| n/m | % (95% CI) | n/m | % (95% CI) |
| Stage 1 | 3/29 | 10.3 (9.3%–11.4%) | 7/16 | 43.8 (35.7%–52.1%) |
| Stage 2 | 1/29 | 3.4 (0.6%–10.3%) | 7/16 | 43.8 (35.7%–52.1%) |
| Stage 3 | 0/29 | 0 | 5/16 | 31.3 (21.5%–41.5%) |
| Injury | 1/29 | 3.4 | 2/16 | 12.5 (2.8%–22.2%) |

Conclusion. IMI/REL demonstrates a more favorable renal safety profile compared with CST-based therapy, as demonstrated by a lower incidence of treatment-emergent nephropathy and AKI with IMI/REL across several different analyses.
same-strain relapse and new-strain reinfection of CDI. We used WGS of paired C. difficile samples from patients with CDI recurrence in the EXTEND study to assess EPFX and SV in relation to relapse and reinfection.

**Methods.** Patients aged 260 years with CDI were randomized (1:1) to receive either EPFX (fidaxomycin 200 mg tablets, twice daily on Days 1–5 and once daily on alternate days on Days 7–25) or SV (125 mg capsules, four times daily on Days 1–10). Paired stool samples were collected from all patients at screening and from patients with recurrence after test-of-cure (TOC). Recurrence was defined as diarrhoea occurring to a greater extent than the frequency recorded at TOC, and confirmed positive for C. difficile toxin A/B and requiring further CDI therapy. C. difficile isolates from paired samples underwent WGS and single nucleotide variant (SNV) difference analysis. Paired samples with ≤2 SNV differences were considered relapses, paired samples with >10 SNV differences were considered reinfection, and those with >2 but ≤10 SNV differences without evidence of a new strain were considered indeterminate.

**Results.** At Day 90, 11/177 (6%) patients in the EPFX arm and 34/179 (19%) patients in the SV arm had CDI recurrence. Of these, samples from 7/111 EPFX- and 19/54 SV-treated patients were available for paired WGS analysis. SNV analysis showed that most CDI recurrences were new-strain reinfections (table).

**Conclusion.** Most recurrences were reinfections, but small sample sizes limited definitive conclusions.

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**Table. SNV analysis**

| Treatment arm | EPFX | SV | Total |
|---------------|------|----|-------|
| Patients with CDI recurrence (n/N) | 11/177 | 34/179 | 45/356 |
| Test-positive (n/N%) | 7 (13.6) | 19 (22.5) | 26 (57.8) |
| Relapse (≤2 SNV) | 1 (2.2) | 3 (6.7) | 4 (8.9) |
| Reinfection (>10 SNV) | 5 (11.1) | 15 (33.3) | 20 (44.4) |
| Indeterminate (>2 but ≤10 SNV) | 1 (2.2) | 2 (2.2) | 2 (4.4) |
| No available SNV results | 15 (33.3) | 19 (42.2) | |

*Calculated over total number of patients with CDI recurrence in both treatment arms*

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1953. Comparative Effectiveness of High- vs. Standard-Dose Influenza Vaccine on Hospitalization for Acute Myocardial Infarction in Nursing-Home Residents: A Post-hoc Analysis From a Large Cluster-Randomized Trial

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**Conclusion.** High-dose flu vaccine reduces the risk of hospitalization for ACE in long-term care residents by 8% relative to standard-dose vaccine.

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1954. A Randomized Study to Evaluate the Shedding and Immunogenicity of H1N1 Strains in Trivalent and Quadrivalent Formulations of FluMist in Children 2-17 Years of Age

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**Registration:** NCT01815268.

**Funding:** sanofi pasteur.

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**Conclusion.** High-dose flu vaccine reduces the risk of hospitalization for ACE in long-term care residents by 8% relative to standard-dose vaccine.