LATE BREAKER ABSTRACTS

LB1. Regional Assessment and Containment of Candida auris Transmission in Post-Acute Care Settings—Orange County, California, 2019

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Thursday, October 3, 2019: 1:45 PM

Background. Patients in long-term acute care hospitals (LTACHs) and skilled nursing facilities with ventilator units (VSNFs) are at high risk for *Candida auris* colonization; among patients colonized with this emerging pathogen, 5%–10% develop invasive disease with >45% mortality. In September 2018, a California LTACH-affiliated laboratory began enhanced *C. auris* surveillance by classifying species of *Candida* isolated from routine urine specimens. In February 2019, the first known Southern California case was detected in an Orange County (OC) LTACH; the patient had not traveled outside the region, indicating local acquisition. We performed point prevalence surveys (PPS) and infection prevention (IP) assessments at all OC LTACHs and VSNF subacute units to identify patients colonized with *C. auris* and control transmission.

Methods. During March–August 2019, we conducted PPS at facilities by collecting composite axilla and groin swabs for *C. auris* polymerase chain reaction testing and reflex culture from all patients who assented. Facilities with ≥1 *C. auris*-colonized patient repeated a PPS every 2 weeks to assess for new transmission. Isolate relatedness was assessed by whole-genome sequencing (WGS). We evaluated hand hygiene (HH) adherence, access to alcohol-based hand rubs (ABHR), and cleaning of high-touch surfaces to guide IP recommendations.

Results. The first PPS at all OC LTACHs (n = 3) and adult VSNFs (n = 14) identified 45 *C. auris*-colonized patients in 3 (100%) LTACHs and 6 (43%) VSNFs; after repeated PPS, the total count reached 124. Most patients (70%) were at 2 facilities (Table 1). Three of 124 patients developed candidemia. To date, isolates from 48 patients have completed WGS; all were highly related (<11 single-nucleotide polymorphisms) in the African clade. Of 9 facilities with *C. auris*, 5 had HH adherence < 50%, 3 had limited ABHR, and at 2, <60% of assessed high-touch surfaces were clean. We recommended regular HH and cleaning audits, and increased ABHR.

Conclusion. Our investigation, prompted by enhanced surveillance, identified *C. auris* at 9 OC facilities. WGS indicated a single introduction and local transmission. Early detection, followed by rapid county-wide investigation and IP support, enabled containment efforts for *C. auris* in OC.

Table 1: Number of incident patients with *C. auris* colonization and prevalence of positive patients within each facility (LTACHS 1-3; VSNFs 1-6) after each completed point-prevalence survey (PPS 1-9) as of August 2, 2019— Orange County, California

	LTACH1	LTACH2	LTACH3	VSNF1	VSNF2	VSNF3	VSNF4	VSNF5	VSNF6	Total Incident Patients
	Number of incident patients | % prevalence of positive patients within each facility									
PPS 1	18|19%	5|12%	3|8%	12|48%	1|3%	2|6%	2|8%	1|2%	1|3%	45
PPS 2	9|26%	1|9%	0|5%	1|50%	2|12%	3|12%	0|8%	0|2%	0|3%	16
PPS 3	10|28%	1|5%	2|11%	3|64%	0|11%	0|13%	0|5%	2|5%	0|3%	18
PPS 4	15|43%	0|2%	2|13%	1|68%	1|14%	0|13%	0|5%	1|7%	-	20
PPS 5	3|39%	0|3%	3|22%	4|66%	2|24%	0|11%	-	-		12
PPS 6	6|37%	0|2%	0|14%	3|81%	0|23%	-				9
PPS 7	-	1|7%	-	1|77%	0|25%					2
PPS 8		0|4%		1|88%	-					1
PPS 9		-		1|86%						1
PPS 10				-						-
Total incident patients	61	8	10	27	6	5	2	4	1	124

LTACH= Long term acute care hospital; VSNF= Skilled nursing facility with ventilator units; PPS= Point prevalence survey

Disclosures. **All authors:** No reported disclosures.

Open Forum Infectious Diseases® 2019;6(S2):S993–1002

DOI: 10.1093/ofid/ofz415

LB2. TORC1 Inhibition with RTB101 as a Potential Pan-Antiviral Immunotherapy to Decrease the Incidence of Respiratory Tract Infections Due to Multiple Respiratory Viruses in Older Adults

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Session: 83. Late Breaker Oral Abstract Session 1
Thursday, October 3, 2019: 1:55 PM

Background. Respiratory tract infections (RTIs) are a leading cause of hospitalization and death in people age ≥65 years. RTIs are caused by multiple viruses, most of which lack effective treatments. An immunotherapy that enhances pan-antiviral innate immunity may reduce RTI incidence in older adults. Inhibition of targets downstream of target of rapamycin complex 1 (TORC1) was reported to upregulate pan-antiviral gene expression and protect mice from a viral RTI (York AG *et al.* Cell 2015). We evaluated whether TORC1 inhibition increased antiviral gene expression and decreased RTI incidence in older adults.

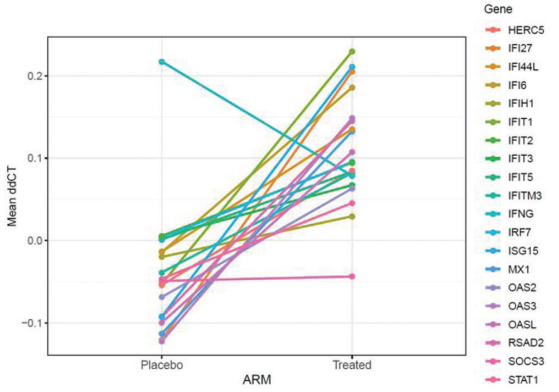
Methods. A randomized, double-blind, placebo, controlled study was conducted to determine whether the TORC1 inhibitor RTB101 alone or in combination with the TORC1 inhibitor everolimus reduced the incidence of laboratory-confirmed RTIs. The study enrolled 652 older adults at increased risk of RTI-related morbidity and mortality (defined as age ≥85 years, or age ≥65 years with asthma, COPD, type 2 diabetes mellitus, or current smokers). Subjects were treated for 16 weeks during winter cold and flu season with oral RTB101 5 mg or 10 mg once daily (QD), RTB101 10 mg twice daily, RTB101 10 mg + everolimus 0.1 mg QD, or matched placebo. The primary endpoint was the percentage of subjects with ≥1 laboratory-confirmed RTI through Week 16.

Results. RTB101 was well tolerated. In the intent-to-treat analysis, RTB101 10 mg QD was observed to: reduce the percentage of subjects with laboratory-confirmed RTIs by 30.6% compared with placebo (P = 0.025); reduce the incidence of RTIs caused by multiple different viruses; and upregulate interferon-stimulated pan-antiviral gene expression in whole blood (P = 0.00001 vs. placebo, Figure 1). Furthermore, RTB101 10 mg QD was observed to reduce the time to alleviation of moderate to severe RTI symptoms by 5 days, and to reduce the rate of all-cause hospitalization (rate ratio 0.439, 90% CI 0.196–0.983, P = 0.047).

Conclusion. RTB101 10 mg QD was associated with a significant reduction in laboratory-confirmed RTIs due to multiple viral pathogens that lack effective medicines for treatment or prevention. RTB101 was observed to upregulate interferon-stimulated pan-antiviral gene expression, which may underlie the reduction in RTI incidence.

Figure 1: Treatment with RTB101 10mg QD was observed to increase expression of multiple interferon-stimulated pan-antiviral genes relative to placebo.

A



B

Interferon-stimulated genes (ISGs) (N =20)	Placebo (N[%])	RTB101 10mg QD (N[%])	P-value
Number of ISGs that were upregulated (mean ddCT ≤0)	5 (25%)	19 (95%)	0.00001
Number of ISGs that were not upregulated (mean ddCT >0)	15 (75%)	1 (5%)	-

Note: Quantitative RT-PCR was performed to assess the change in expression levels of 20 interferon-stimulated genes (ISGs) in blood samples collected at the Week 16 and Baseline study visits. All subjects in the placebo and RTB101 10 mg QD treatment arms with a valid dCT value for at least one gene at both time points were included in the analysis (N = 292). The ddCT is the change in normalized gene expression at Week 16 compared to Baseline. **Panel A** shows the mean ddCT for each gene in the placebo as compared to the 10mg RTB101 QD treatment groups. **Panel B** reports the number of ISGs whose expression was upregulated at Week 16 as compared to Baseline in each of the placebo and RTB101 10 mg QD treatment arms. P value was determined using a Fisher's Exact Test comparing mean ddCT (Week 16 compared to Baseline) as a binary variable for each gene. Abbreviations: CT = Cycle threshold, dCT = delta-CT, ddCT = delta-delta-CT.

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