1718. Rezafungin Clinical Safety and Efficacy in Patients With Candidemia and/or Invasive Candidiasis in the Randomized, Double-Blind, Multicenter, Phase 2 STRIVE Study

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Background. STRIVE was conducted to assess the safety and efficacy of rezafungin (RZF), a novel echinocandin with pharmacokinetics allowing once weekly dosing and high, front-loaded plasma drug exposure, and to help determine dosing for a Phase 3 study.

Methods. Adults (≥18 years) with mycologically confirmed candidemia and/or invasive candidiasis (IC) were randomized (1:1:1) to receive RZF IV for up to 4 weeks dosed at either 400 mg weekly (Group 1) or 400 mg on week 1 and 200 mg weekly thereafter (Group 2), or standard of care (SOC; daily caspofungin [CSP] with optional criteria-defined oral stepdown after ≥3 days of IV therapy; Group 3). Safety and efficacy were evaluated by treatment-emergent adverse events (TEAEs) and overall success at day 14 (1° endpoint; clinical cure + mycological success), investigator assessment of clinical cure, mycological success (in subjects with candidemia only), overall success in IC subjects only, and mortality. Outcomes at day 5 were also assessed.

Results. The rate of TEAEs was 88.6% in Group 1, 94.4% in Group 2, and 81.8% in Group 3. Severe AEs occurred in 37.1%, 27.8%, and 39.4% of the groups, respectively. There were no concerning trends in System Organ Class groups, specific AEs, or laboratory abnormalities. The most common *Candida* species isolated was *C. albicans* (*n* = 45), followed by *C. glabrata* (*n* = 17), *C. tropicalis* (*n* = 15), and *C. parapsilosis* (*n* = 13). A high number of indeterminate responses due to missing data points in Group 1 led to analyses including and excluding the indeterminate responses. Overall, clinical, and mycological response rates at day 14 are shown in Table 1. Overall response at day 5 (Table 2) was highest in the RZF 400 mg/200 mg group, followed by the RZF 400 mg/400 mg and SOC groups. The overall mortality rate was 15.2% in Group 1, 9.7% in Group 2, and 17.9% in Group 3.

Conclusion. RZF demonstrated safety and efficacy comparable to CSP in the treatment of candidemia/IC. There were no concerning trends in AEs. The efficacy rates were similar among all 3 treatment groups, trending higher with the RZF 400 mg/200 mg regimen on most efficacy outcomes, although the sample size is small and confirmation of these findings is required in a larger Phase 3 clinical trial. These findings support further clinical study of RZF in Phase 3.

Table 1: Overall, Clinical, and Microbiological Responses at Day 14, Including and Excluding Indeterminate Responses (mITT Population)

	Group 1: RZF 400mg once weekly	Group 2: RZF 400mg Wk1/ 200mg once weekly	Group 3: CSP 70 mg D1/ 50 mg once daily
	n (%)		
Overall Success (D14)	19/33 (57.6)	22/31 (71.0)	18/28 (64.3)
- Failure	7 (21.2)	6 (19.4)	8 (28.6)
- Indeterminate[a]	7 (21.2)	3 (9.7)	2 (7.1)
	Excluding Indeterminate Response[a]		
Overall Success (D14)	19/26 (73.1)	22/28 (78.6)	18/26 (69.2)
- Failure	7 (26.9)	6 (21.4)	8 (30.8)
Clinical Cure (D14) by PI Assessment[b]	25/33 (75.8)	24/31 (77.4)	20/28 (71.4)
- Failure	7 (21.2)	4 (12.9)	8 (28.6)
- Indeterminate[a]	1 (3.0)	3 (9.7)	0
Clinical Cure (D14) by PI Assessment[b]	Excluding Indeterminate Response[a]		
	25/32 (78.1)	24/28 (85.7)	20/28 (71.4)
- Failure	7 (21.9)	4 (14.3)	8 (28.6)
Mycological Success (D14)[c]	21/30 (70.0)	17/26 (65.4)	18/25 (72.0)
- Failure	6 (20.0)	6 (23.1)	6 (24.0)
- Indeterminate[a]	3 (10.0)	3 (11.5)	1 (4.0)
	Excluding Indeterminate Response[a]		
Mycological Success (D14)[c]	21/27 (77.8)	17/23 (73.9)	18/24 (75.0)
- Failure	6 (22.2)	6 (26.1)	6 (25.0)
Overall Success in IC (D14)	1/3 (33.3)	5/5 (100.0)	1/3 (33.3)
- Failure	1 (33.3)	0	2 (66.7)
- Indeterminate[a]	1 (33.3)	0	0

[a]Indeterminate response indicates inability to assess outcome due to missing data point(s).
[b]Outcome that most closely approximates the primary outcome in prior candidemia/IC clinical trials.
[c]In patients with candidemia only.

Table 2: Overall Responses at Day 5, Including and Excluding Indeterminate Responses (mITT Population)

	Group 1: RZF 400mg once weekly	Group 2: RZF 400mg Wk1/ 200mg once weekly	Group 3: CSP 70 mg D1/ 50 mg once daily
	n (%)		
Overall Success (D5)	19/33 (57.6)	21/31 (67.7)	15/28 (53.6)
- Failure	10 (30.3)	8 (25.8)	12 (42.9)
- Indeterminate[a]	4 (12.1)	2 (6.5)	1 (3.6)
	Excluding Indeterminate Response[a]		
Overall Success (D5)	19/29 (65.5)	21/29 (72.4)	15/27 (55.6)
- Failure	10 (34.5)	8 (27.6)	12 (44.4)

[a]Indeterminate response indicates inability to assess outcome due to missing data point(s).

Disclosures. **G. R. Thompson**, Cidara: Investigator, Research support. Mayne: Investigator, Research support. Astellas: Consultant and Investigator, Consulting fee and Research support. Scynexis: Investigator, Research support. Vical: Consultant, Consulting fee. **A. Soriano**, Cidara Therapeutics, Inc.: Investigator, Research grant. **L. Ostrosky-Zeichner**, Cidara Therapeutics: Grant Investigator, Research grant. **K. Mena**, Cidara Therapeutics: Employee, Salary. **L. Navalta**, Cidara Therapeutics, Inc.: Employee, Salary. **T. Sandison**, Cidara Therapeutics: Employee, Salary. **P. Pappas**, Cidara Therapeutics: Consultant and Grant Investigator, Research grant. IMMY: Consultant and Grant Investigator, Research grant. Scynexis: Consultant and Grant Investigator, Research grant. Gilead: Grant Investigator, Research grant.

1719. Pharmacokinetics (PK) of Oritavancin in Children: The ORKIDS Trial

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Background. Oritavancin (ORI) is a lipoglycopeptide antibiotic approved in adults as a single 1,200 mg intravenous (IV) dose for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by Gram-positive organisms, including methicillin-resistant *Staphylococcus aureus*. The objective in children is to achieve a PK profile that is similar to that attained in adults. PK and safety data from the first 3 age-specified cohorts are presented.

Methods. The ORKIDS trial is a Phase 1 open-label, sequential, dose-finding study evaluating the PK, safety and tolerability of a single-dose 15 mg/kg (max 1,200 mg) IV infusion of oritavancin in children under 18 years. The first 3 age cohorts (12 to <18 years, 6 to <12 years, 2 to < 6 years) with 8 subjects in each cohort have completed the study. Subjects were required to have a suspected or confirmed Gram-positive bacterial infection for which they received standard-of-care antibiotic therapy. Following a single dose of ORI, PK samples were obtained at 3, 4, 9, 24, 48, 72, and 336 hours after the start of the 3-hour infusion. Plasma concentrations were analyzed by noncompartmental Methods. Subjects were evaluated for safety through Day 60. An independent data safety monitoring board evaluated the safety and PK data of each cohort prior to dosing the subsequent cohort.

Results. PK in children compared with adult data from the SOLO Phase 3 ABSSSI studies (Table 1).

Table 1: Mean PK Parameters from Cohorts 1–3 and Adults

	Cohort 1, 12 to <18 years (*n* = 8)	Cohort 2, 6 to <12 years (*n* = 8)	Cohort 3, 2 to <6 years (*n* = 8)	Range from Pooled Adult SOLO Trials
Cmax (µg/mL)	127	136	84	106–170
AUC0-inf (h µg/mL)	4,014	3,709	1,963	1,999–3,600

Conclusion. In subjects 6 to <18 years, a single 15 mg/kg dose of ORI appears to be well tolerated and provides a PK profile similar to a single 1,200 mg dose in adults. Mean $AUC_{0\text{-}inf}$ of 1,963 h µg/mL in subjects 2 to <6 years is lower than the targeted exposure range in adults. A higher dose of ORI is currently being studied in this cohort.

Disclosures. **J. Bradley**, Melinta Therapeutics: Investigator, Research support. **A. Arrieta**, Melinta Therapeutics: Investigator, Research support. **P. Bokesch**, Melinta Therapeutics: Consultant, Consulting fee. **K. Fusaro**, Melinta Therapeutics: Employee, Salary. **D. C. Griffith**, Melinta Therapeutics: Consultant, Consulting fee. **J. S. Loutit**, Melinta Therapeutics: Consultant, Consulting fee.

1720. Regional Differences in Trends of Hospitalizations Associated With Tick-Borne Diseases in the United States, 2009–2014

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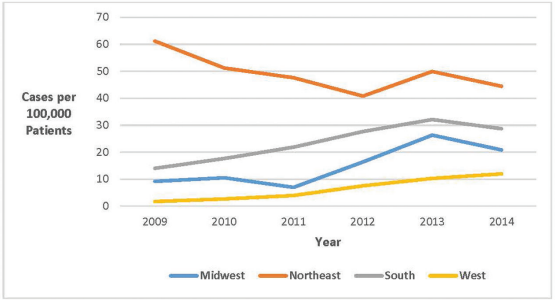
Background. Tick-borne diseases are increasing in incidence in the United States; however, limited data exist on regional trends of associated hospitalizations. Using a nationally distributed dataset of US hospital-based medical records, we aimed to assess trends in incidence of hospitalizations from tick-borne disease by geographic region.

Methods. Data were examined from 156 US hospitals from 2009 to 2014 to identify hospitalizations with tick-borne disease. Cases were described and Poisson regression used to estimate the annual percent change (APC) and associated 95% confidence intervals (CI) in incidence by region over time.

Results. Overall, 2,543 hospitalized patients with tick-borne disease were identified (average annual incidence = 28.4 cases/100,000 hospitalized persons), including 1,613 (63%) with Lyme disease, 379 (15%) tick-borne fever, 293 (12%) ehrlichiosis, 93 (4%) babesiosis, 43 (2%) rickettsiosis, and 122 (4%) multiple tick-related diagnoses. Tick-borne diseases varied significantly by region, with Lyme disease more frequent in those residing in the Northeast (68%) than the South (57%) or West (42%) and tick-borne fever more common in the West (28%) vs. the South (18%), Midwest (14%), and Northeast (13%) ($P < 0.0001$). Significant increases in tick-borne disease hospitalizations were identified across nearly all US regions, ranging from 15% per year in the South (95% CI=8–24%) to 45% per year in the West (34–58%), with the exception of the Northeast, where incidence declined by 6% per year (0.04–11%). Lyme disease hospitalizations showed similar trends, with the greatest increase in the South (APC = 53%, 95% CI = 33–76%) and a decrease in the Northeast (APC = 13%; 3%–23%). Hospitalizations with tick-borne fever increased in the Midwest (APC = 49%; 8–206%) and Northeast (APC = 18%; 4–34%); with ehrlichiosisincreased in the West (APC = 231%; 75–306%); and with babesiosis increased in the South (APC = 50%; 12–201%) and the Midwest (APC = 21%; 5–39%).

Conclusion. Incidence of hospitalizations from tick-borne disease is increasing throughout much of the nation, except in the Northeast where decreases in Lyme disease were observed. While hospitalizations with tick-borne diseases remain rare, the increases noted are substantial and may reflect rising incidence of these diseases within the represented states.

Figure 1. Regional trends in incidence of hospitalizations associated with a tick-borne disease diagnosis in the United States from 2009-2014.



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

1721. An Outbreak of Botulism Associated With Nacho Cheese Sauce From a Gas Station in California

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Background. Foodborne botulism is rare with 0–6 cases reported annually in California. During April 24–28, 2017, 4 hospitalized patients with suspect foodborne botulism were reported to the California Department of Public Health (CDPH) from 2 adjacent California counties. In collaboration with local public and environmental health, CDPH conducted an investigation to determine the magnitude of the outbreak, identify potential sources, and implement control measures.

Methods. A case was defined as clinical botulism in a visitor to or resident of Sacramento County with illness onset during April 20 to May 5, 2017. Case-patients or their proxies were interviewed. Patient specimens and suspect food items were tested for the presence of botulinum toxin and toxin-producing *Clostridium botulinum*; *C. botulinum* isolates underwent whole genome sequencing (WGS) at the CDPH laboratory.

Results. In April–May 2017, a total of 10 patients were hospitalized with laboratory-confirmed botulism. Median age was 34 years (range 16–57); 7 were male, and 8 were Latino. All patients required intensive care, 7 required ventilator support, and 1 died. Nine patients confirmed visiting Gas Station A in the week before illness onset; 8 reported consuming nacho cheese sauce served from a dispenser there. Inspection of Gas Station A on May 5 indicated that the cheese in the dispenser had a best by date of April 11; the dispenser was removed that day, before all patients were identified. The remaining pouch of nacho cheese sauce was laboratory confirmed to have botulinum toxin type A and toxin-producing *C. botulinum*. *C. botulinum* isolates from 3 patients clustered with the cheese isolate by WGS.

Conclusion. Contaminated nacho cheese sauce served at a local gas station was the source of the largest outbreak of foodborne botulism reported to date in California. No other botulism cases associated with this commercial cheese sauce were identified elsewhere in the United States; although the mechanism of contamination is unclear, the cheese was likely contaminated locally. Intensive public health investigation and intervention, before all cases were identified and *C. botulinum* toxin was detected in the product, likely prevented additional cases and possible deaths

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

1722. The Changing Epidemiology of Candidemia in the United States: Injection Drug Use as an Emerging Risk Factor for Candidemia

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Background. Known risk factors for candidemia include diabetes, malignancy, antibiotics, total parenteral nutrition (TPN), prolonged hospitalization, abdominal surgery, and central venous catheters. Injection drug use (IDU) is not a common risk factor. We used data from CDC Emerging Infections Program's candidemia surveillance to assess prevalence of IDU among candidemia cases and compare IDU and non-IDU cases.

Methods. Active, population-based candidemia surveillance was conducted in 45 counties in 9 states during January–December 2017. Data from 2014 to 2016 were available from 4 states and were used to look for trends. A case was defined as blood culture with *Candida* in a surveillance area resident. We collected clinical information, including IDU in the past 12 months. Differences between IDU and non-IDU cases were tested using logistic regression.

Results. Of 1,018 candidemia cases in 2017, 123 (12%) occurred in the context of recent IDU (1% in Minnesota and 27% in New Mexico) (Figure 1). In the 4 states with pre-2017 data, the proportion of IDU cases increased from 7% in 2014 to 15% in 2017, with the proportion in Tennessee nearly tripling from 7% to 18% (Figure 2). IDU cases were younger than non-IDU cases (median 34 vs. 62 years, $P < 0.001$). Compared with non-IDU cases, IDU cases were less likely to have diabetes (16% vs. 35%; OR 0.4, CI 0.2–0.6), malignancies (7% vs. 30%; OR 0.2, CI 0.1–0.3), abdominal surgery (6% vs. 19%; OR 0.3, CI 0.1–0.6), receive TPN (6% vs. 27%; OR 0.2, CI 0.1–0.4) and were more likely to have hepatitis C (96% vs. 47%; OR 16.1, CI 10.4–24.9), be homeless (13% vs. 1%; OR 17.8, CI 7.1–44.6), and have polymicrobial blood cultures (33% vs. 17%; OR 2.4, CI 1.6–3.6). Median time from admission to candidemia was 0.5 vs. 3 days and in-hospital mortality was 7% vs. 28% for IDU and non-IDU cases, respectively.

Conclusion. In 2017, 1 in 8 candidemia cases had a history of IDU, including a quarter of cases in some sites. The proportion of such cases increased since 2014. IDU cases lacked many of the typical risk factors for candidemia, suggesting that IDU may be an independent risk factor. Given the growing opioid epidemic, further study is necessary to elucidate how people who inject drugs acquire candidemia and design effective interventions for prevention.

Figure 1. Candidemia cases associated with injection drug use by site, Emerging Infections Program, 2017