Galidesivir, a Direct-Acting Antiviral Drug, Abrogates Viremia in Rhesus Macaques Challenged with Zika Virus

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Accessibility
Table 3. Multivariate analysis of 30-day infection-related mortality

<table>
<thead>
<tr>
<th>OR</th>
<th>p value</th>
<th>95% CI</th>
</tr>
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<tr>
<td>5.908</td>
<td>0.031</td>
<td>1.176–29.67</td>
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<tr>
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<td>0.281</td>
<td>0.403–22.89</td>
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Disclosures. All authors: No reported disclosures.

1779. Prevalence of and Factors Associated with Cladribine Diffuse Co-infection Among Patients with Candidiasis, United States, 2014–2016
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Session: 216. The Fungus Among-us – Clinical Advances
Saturday, October 7, 2017: 8:30 AM

Background. Candidemia and Cladribine diffuse infection (CDI) are two common healthcare-associated infections (HAIs) and share risk factors such as antibiotic use and prolonged hospitalization. CDI and CDI treatment disrupt gut microbial diversity, allowing Candida overgrowth and translocation to the bloodstream. We describe CDI co-infection among patients with candidemia.

Methods. Population-based surveillance for candidemia was conducted through CDC's Emerging Infections Program during 2014–2016. A case of candidemia was defined as a blood culture positive for Candida species collected from a surveillance area resident. Demographic and medical information, including occurrence of CDI, was collected. We defined co-infection as CDI within 90 days of candidemia and performed bivariable analysis to assess factors associated with co-infection.

Results. Among 2129 cases of candidemia, 190 (9%) had CDI co-infection; 116 (6%) had CDI following candidemia (median: 8 days). The median age of those with CDI-candidemia co-infection was 61 years and 100 (53%) were male. Compared with candidemia alone, the odds of CDI co-infection were greater for male, black race (OR 1.41, 95% CI 1.05–1.90), those with diabetes (OR 1.68, 1.24–2.27), pancreatitis (OR 1.91, 1.01–3.61), or solid organ transplant (OR 4.15, 2.09–8.22). Those with co-infection had higher odds of certain healthcare exposures: hemodialysis (OR 2.27, 1.57–3.28), hospital stay in the past 90 days (OR 1.78, 1.20–2.66), and central venous catheter (CVC) at the time of candidemia (OR 1.71, 1.19–2.46). There were no significant differences in 30-day mortality or in type of Candida species, although C. parapsilosis was less common in the co-infection group (8% vs. 13%).

Conclusion. Nearly one in ten patients with candidemia also had CDI co-infection. Black race, certain underlying conditions, hemodialysis, previous hospitalization, ICU stay, and the presence of a CVC were associated with co-infection. Clinicians should be vigilant for co-infection of CDI and candidemia, particularly in situations with associated risk factors.

Disclosures. W. Schaffner, Pfizer: Scientific Advisor, Consulting fee; Merck: Scientific Advisor, Consulting fee; Novavax: Consultant, Consulting fee; Dynavax: Consultant, Consulting fee; Sanofi-pasteur: Consultant, Consulting fee; GSK: Consultant, Consulting fee; Seqirus: Consultant, Consulting fee

1780. Routine Cryptococcal Antigen Screening in Solid Organ Transplant Recipients: Is it Time to Save Lives and Money?
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Background. Cryptococcosis affects 1 in 270 solid organ transplant (SOT) recipients with high mortality. In HIV-infected patients, cryptococcal antigen (CRAG) is detectable in blood weeks to months before symptomatic infection and screening is recommended. No screening guidelines exist for SOT recipients.

Methods. We performed a cost-effectiveness analysis of CRAG screening amongst SOT recipients. We estimated costs of screening from Medicare reimbursement of $16.49 for CPT 87899 (Infectious agent antigen detection by immunoassay). We determined the number at risk from a large cohort of 42,634 adult SOT recipients from ICD-9 CM billing data from HCUP State Inpatient Databases of Florida (2006–2012), New York (2006–2011), and California (2004–2010). Cost of screening was compared with the cost of inpatient hospitalization.

Results. Among 42,634 adult SOT recipients, 158 (0.37%) developed cryptococcosis at a median time of 15.5 months (range 0.1–80) after transplant. During the 43 month follow-up, there was approximately 2.5% annual mortality. The estimated costs for CRAG screening could detect 75% of asymptomatic cryptococcal antigenemia prior to symptomatic disease requiring prolonged hospitalization, it would be approximately cost neutral ($11.5 million), and even cost saving if above 80% of hospitalizations are averted. Alternatively stated, for every one hospitalization avoided, 4245 persons could be CRAG screened for similar cost and likely better outcome.

Conclusion. Assuming the ability of routine screening to identify 75% of patients who would develop invasive cryptococcosis; CRAG screening every 3 months among SOT recipients likely would be at least cost neutral to the healthcare system. Antecedent duration of cryptococcal antigenemia prior to symptomatic disease in Non-HIV/SOT cohorts should inform optimal screening intervals should be further studied. Prospective SOT cohorts should validate this approach to save lives in a cost-effective manner.

Disclosures. All authors: No reported disclosures.

1781. Galidesivir, a Direct-Acting Antiviral Drug, Abrogates Viremia in Rhesus Macaques Challenged with Zika Virus
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Session: 217. Zika - A to Z
Saturday, October 7, 2017: 8:30 AM

Background. Zika virus (ZIKV) was first isolated from a sentinel rhesus monkey in 1947. ZIKV infection in humans is associated with serious neurological and reproductive complications. No antiviral or protective vaccine is yet available. Galidesivir an adenosine analog is a potent viral RNA-dependent RNA polymerase inhibitor with demonstrated broad-spectrum antiviral activity.

Methods. We have conducted four pre-clinical studies in rhesus macaques to assess the antiviral efficacy and dosing strategies of galidesivir against ZIKV infection. Collectively, we have evaluated 170 rhesus macaques by intramuscular route at 10x1 TCID50 of a Puerto Rican ZIKV isolate. We have evaluated galidesivir therapy administered via IM injection as early as 90 minutes and up to 72 hours after subcutaneous (SC) ZIKV challenge, and as late as 5 days after intravaginal (IVAG) challenge. In these studies, we evaluated the efficacy of a range of loading and maintenance doses of galidesivir. The highest dose evaluated has been a loading dose of 100mg/kg BID followed by a maintenance dose of 25mg/kg BID for nine days. We followed multiple endpoints, including ZIKV RNA levels in plasma, urine, saliva, and cerebrospinal fluid. Immune activation, complete blood counts, chemistries and galidesivir pharmacokinetics were also monitored.

Results. Galidesivir was well-tolerated in all studies. All untreated controls developed high-level plasma viremia, and had readily detectable ZIKV RNA in CSF, saliva and vaginal fluids. Animals challenged with ZIKV at 70 hours after SC ZIKV challenge that did not develop plasma viremia and were either negative or had significantly reduced ZIKV RNA in bodily fluids. Animals treated with galidesivir later (up to 72 hours) were partially protected; they had detectable plasma ZIKV RNA, but the onset was delayed compared to magnitude significantly reduced compared with controls. Animals infected with IVAG were protected by galidesivir treatment up until day 5 after infection, with no blood viremia and significant reductions in ZIKV RNA in the CSF as compared with controls.

Conclusion. Galidesivir dosing in rhesus macaques was well-tolerated and offered significant protection against ZIKV infection. These results warrant continued study and clinical evaluation.


1782. Outcomes of women with laboratory evidence of Zika infection in pregnancy
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Session: 217. Zika - A to Z
Saturday, October 7, 2017: 8:30 AM

Background. Zika virus (ZIKV) infection in pregnancy is a global health concern. With onset of local transmission, obstetricians in Miami-Dade County, FL,