1530. De-implementation Strategy to Reduce the Inappropriate Use of Urinary and Intravenous Catheters: the RICAT Study
Bart J. and Intravenous CATheters: the RICAT Study

1531. A CMV Vaccine Based on Non-Replicating Lymphocytic Choriomeningitis Virus Vectors Expressing gB and pp65 Is Safe and Immunogenic in Healthy Volunteers, Allowing for Development of a Phase II Clinical Trial in Living Donor Kidney Transplant Recipients
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Background. Cytomegalovirus (CMV) is a major pathogen in pregnancy and immuno compromised patients. Antiviral prophylaxis is limited by toxicities, recurrent infection, and antiviral resistance. A safe and protective CMV vaccine is highly desirable.

Methods. HB-101 is a CMV vaccine consisting of two nonreplicating lymphocytic choriomeningitis virus vectors, one expressing the human CMV antigen pp65 and the other a truncated, more antigenic isoform of the CMV fusion protein gB. The safety and immunogenicity of HB-101 were evaluated in a randomized, placebo-controlled, double-blind phase 1 dose-escalating trial (NCT02798692). Three dose cohorts (1: 2.6 x 10^8; 2: 2.6 x 10^9 and 3: 2.6 x 10^10 FU) of 18 subjects each were enrolled. On Day 0, Month 1, and Month 3, HB-101 or placebo was administered to 14 and 4 subjects, respectively. Immunogenicity studies included cellular responses against pp65, and humoral and cellular responses against gB and the LCMV vector.

Results. Injection site pain was the most frequently reported solicited adverse event (SAE). It affected 57.1% of HB-101 recipients in both cohorts 1 and 2 and 92.9% in cohort 3. Among the general SAE malaise, fatigue and generalized myalgia were most frequently reported. All SAE were generally mild to moderate and lasted <8 days. No serious adverse events and no abnormal lab tests were noted during the active phase of the study. HB-101-induced gB-specific IgG antibody responses at all doses, in a dose-dependent manner. All three dose levels also induced antibodies that neutralized HCMV infection in cultured human fibroblasts (MRC-5 cells), and resulted in a robust, boosterable and durable T-cell response by IFNγ ELISPOT for CMV gB and pp65. Polychromatic flow cytometry indicated induction of a high proportion of poly functional CMV-specific CD8 and CD4 T-cells. CD8 T-cells expressing IFNγ, IL2 and TNFα without CD107a were among the most prominent populations induced against CMV pp65.

Conclusion. HB-101 is a novel CMV vaccine with a good safety profile in healthy volunteers, eliciting strong humoral and cellular immune responses. We are starting a Phase 2 trial in kidney transplant candidates at higher risk for CMV infection. We plan to give multiple vaccinations prior to living donor kidney transplant, and will follow post-transplant for safety, immunogenicity, and efficacy.

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1532. Increased Risk of Bacterial, Fungal and Other Viral Infections During CMV Infection: Decreased Cytokine Production in Response to Toll-Like Receptor Ligands
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Background. In the solid-organ transplant (SOT) setting, CMV is an immuno modulatory virus that indirectly increases the risk for bacterial, fungal and viral infec tions. However, the pathogenesis of this phenomenon is poorly understood. The aim of our study was to determine whether inflammatory responses to different Toll-like receptor ligands are blunted during CMV infection in SOT patients.

Methods. CMV D+/R− SOT patients had blood drawn at the end of CMV prophylaxis and then weekly after onset of CMV viremia. PBMCs were extracted and incubated for 24 hours in the presence of bacterial (LPS, fungal (Zymosan (ZYM)), and viral (Resiquimod (R848)) ligands. Proinflammatory (IL1β), Th1 (IFNγ), Th2 (IL4), immunoregulatory (IL10), and chemotactic (MCP1) cytokines were measured in the supernatant by multiplex ELISA.

Results. Thirty-eight SOT patients were followed for at least 9 months. Patients who developed subsequent CMV infection had lower cytokines in response to bacterial, fungal and viral ligands (LPS, ZYM, and R848) at the end of prophylaxis compared with those with no CMV infection. These results were independent of immunosuppression and peripheral blood cell counts. Specifically, these trends were significantly different with respect to IFNγ, IL1β, and IL10 production in response to
LPS (P = 0.003, 0.003, and 0.039, respectively), R848 (P < 0.001, 0.039, and <0.001, respectively) and ZYM (P = 0.039, 0.003, and 0.003, respectively), as well as for MCP1 in response to R848 or ZYM (P = 0.039 for both). In the cohort with CMV infection, cytokine responses to TLR ligands were even lower during the acute CMV infection when compared with the end of prophylaxis, although this was significant only for IL10 production after R848 stimulation (P = 0.034). There was no influence of CMV viral load or duration of viremia on cytokine levels.

Conclusion. Response to non-CMV antigens during CMV infection was blunted supporting the clinical observation in transplant recipients that CMV infection increases susceptibility to bacterial, fungal, and other viral infections. However, inherited differences in patients that are neither directly related to CMV nor to their net level of immunosuppression also contribute to this increased susceptibility, as cytokine levels at the end of prophylaxis were lower among patients with compared with those without subsequent CMV infection.

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1534. Prevalence and Outcome of Neutropenic Enterocolitis Among Pediatric Acute Myeloid Leukemia Patients: A Developing Country Experience
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Background. Neutrophilic enterocolitis (NEC) is a life-threatening disease with substantial morbidity and mortality, seen primarily in patients with hematologic malignancies. The frequency of NEC has increased with the widespread use of chemotherapy regimens. Enterocolitis can result from severe immunosuppression and may occur with or without classical clinical symptoms. NEC cannot reasonably be ruled out. Though rare, fungal infection should be suspected specially in cases with worsening signs of typhlitis despite broad antimicrobial coverage.

Methods. We retrospectively reviewed all adults hospitalized at our institution with neutropenic fever from January 2006 to December 2016 and had CT abdomen for source identification. Demographic, clinical, imaging, and outcome data were abstracted and analyzed using descriptive statistics.

Results. Overall, 156 patients (61.5% males) met the study criteria. The most common underlying hematologic malignancies were leukemia in 83 (53.2%) and malignant lymphoma 46 (29.5%). Others included multiple myeloma, myelodysplasia, and benign hematologic malignancies. The most common presenting symptoms, besides fever, at the time of CT abdomen were chills (33.5%), abdominal pain (23.9%), nausea (23.2%), diarrhea (20.6%), cough (19.5%), shortness of breath (12.3%), and skin rash (18.4%). Initial CT abdomen was positive in 45 (28.8%). Repeat CT abdomen was obtained in 22 (14.3%) for persistent fevers and had positive findings for infection source in 85.7%. Sources of infection identified on CT abdomen were involving gastrointestinal tract (46.7%), hepatobiliary system (24.4%), urinary tract (21.1%) and peritoneum (7.8%). In terms of microbiology, a causative organism was identified in blood in 53 (34.9%), urine in 15 (9.9%), stool in 15 (9.9%), and respiratory secretions in 8 (5.3%). Causative pathogens included Gram-positive bacteria in 30 (62.5%), Gram-negative bacteria in 23 (47.9%) and Anaerobes in 5 (10.4%) cultures. CT abdomen finding resulted in antimicrobial changes in 75 (59.5%) of patients and procedural intervention in 14 patients (9.3%).

Conclusion. While routine use of CT abdomen for evaluation of neutropenic fevers is low yield, CT findings can help identify a source of infection, necessitating change in antimicrobial therapy or procedural intervention, in patients with abdominal symptoms or persistent fever despite broad-spectrum antimicrobial therapy.

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1536. Donor-Derived Mycobacterium tuberculosis Infection After Solid-Organ Transplantation: A Comprehensive Review
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Background. Donor-derived Mycobacterium tuberculosis (DDTB) has occasionally been reported after solid-organ transplantation (SOT).

Methods. To characterize DDTB, MEDLINE OVID, and EMBASE were reviewed from inception to December 31, 2016 using key words donor-derived infection, tuberculosis and solid-organ transplant.

Results. A total of 36 cases of proven (17), probable (8) and possible (11) DDTB were identified among 16 lung, 13 kidney, six liver, and one heart recipient. Most patients were male (21/35, 60%); median age was 48 (range 23–68) years. Median time to DDTB was 2.7 (0.2–29) months after SOT. Donor residence in TB-endemic area (13/28, 46.4%) was common. Fever was the most frequent symptom (20/36, 56.5%). DDTB was classified as pulmonary (36%), extra-pulmonary (28%) or disseminated (36%), with common involvement of the allograft (31/36, 86%). Diagnosis was made by smear (21/36, 58.3%) or culture (21/36, 58.3%) or histopathology (13/36, 36.1%), or ZYME (0.001, 0.003, and 0.039, respectively), as well as for MCP1 in response to R848 or ZYM (0.039 for both). In the cohort with CMV infection, cytokine responses to TLR ligands were even lower during the acute CMV infection when compared with the end of prophylaxis, although this was significant only for IL10 production after R848 stimulation (P = 0.034). There was no influence of CMV viral load or duration of viremia on cytokine levels.

Conclusion. The diagnosis of typhlitis was based on clinical features, supported by radiologic evidence in almost half of the study group. Surgical intervention should be reserved for specific complications or where another surgical pathologic condition cannot reasonably be ruled out. Though rare, fungal infection should be suspected specially in cases with worsening signs of typhlitis despite broad antimicrobial coverage.

Disclosures. All authors: No reported disclosures.