Figure. Time (days) to death post-transplant in a cohort of adult solid organ transplant recipients, stratified according to the presence or absence of coccidiomycosis.

Table. Multivariable risk factors for death in 20,602 SOT recipients.

| HR(95% CI for death) | Age (years) | Coccidiomycosis | Renal transplant | Lung transplant | Liver transplant | Heart transplant | Others (pancreas, intestine, multigang) | Transplant failure/ejection | Diabetes | Renal failure |
|----------------------|-------------|-----------------|-----------------|----------------|-----------------|-----------------|---------------------------------------|---------------------------|---------|-------------|
|                      | 18–60       | 1.00            | 1.00            | 1.00           | 1.00            | 1.00            | 1.00                                  |                           |         | 1.31(1.14–1.50) |
|                      | 41–50       | 1.37(1.16–1.62) | 1.55(1.32–1.81) | 2.23(1.94–2.67) | 3.52(3.02–4.47) | 3.10(2.02–4.28) | 3.00                                  |                           |         |              |
|                      | 51–60       | 1.17(1.32–1.81) | 2.23(1.94–2.67) | 3.52(3.02–4.47) | 3.10(2.02–4.28) | 3.00                                  |                         |                           |         |              |
|                      | 61–70       | 1.00            | 1.00            | 1.00           | 1.00            | 1.00            | 1.00                                  |                           |         |              |
|                      | >70         | 1.00            | 1.00            | 1.00           | 1.00            | 1.00            | 1.00                                  |                           |         |              |

Disclosures. All authors: No reported disclosures.

154. Posaconazole-Induced Hypertension and Hypokalemia: Mechanistic Evaluation

George R. Thompson, MD; Diana Chang, MD; Rebecca Wittenberg, PharmD; Ian Mchardy, PhD and Alison Semrad, MD

Background. Recent studies have shown the new posaconazole delayed-release tablets have superior bioavailability compared with the liquid suspension formulation. As higher serum posaconazole concentrations have been associated with improved clinical responses, this formulation has been a welcome addition to available treatment options. However, higher serum and tissue levels are likely to reveal sequelae of posaconazole-mediated inhibition of 11β-HSD2, and cortisol/cortisone ratios were observed in both patients. The TTKG in both patients was inappropriately elevated.

Results. Posaconazole-induced disruption of the steroid biosynthesis pathway in patients has not previously been described, but has been suggested by in vitro studies. Our patients’ laboratory results show clinically significant inhibition of 11β-hydroxysteroid dehydrogenase enzyme type 2 (11β-HSD2) as evidenced by: the elevated 11β-deoxycorticisol (with subsequent suppression of renin and aldosterone), the highly elevated cortisol/cortisone ratio, and the inappropriately elevated TTKG in the setting of hypokalemia. The normal deoxycorticosterone confirms normal function of 11β-hydroxylase and the observed effects in our patients are thus downstream from this enzyme.

Conclusion. Our findings support in vitro predictions and highlight the clinical sequelae of posaconazole-mediated inhibition of 11β-HSD2. Additional studies are necessary to determine the frequency of posaconazole-induced apparent mineralocorticoid excess syndrome and whether other azole antifungals can be associated with this phenomenon.

Disclosures. All authors: No reported disclosures.

155. Detection of (1,3)-β-D-Glucan in Cerebrospinal Fluid in Histoplasma Meningitis

Therin Myint, MBBS; Karen Bloch, MD, MPH, FIDSA; Luke Raymond-Guillen, MD and I. Joseph Wheat, MD, FIDSA

Background. Central nervous system (CNS) histoplasmosis is a life-threatening condition, and represents a diagnostic and therapeutic challenge. Although CSF (1,3)-β-D-glucan (CSF BDG) is available as a biologic marker for diagnosis of fungal meningitis, there are limited data on its use for diagnosis of Histoplasma meningitis. We evaluated CSF BDG detection using the Fungitell assay in patients with CNS histoplasmosis and controls.

Methods. Patients were classified as cases if there was CNS inflammation (CSF white blood cells >5.0/mm3) plus laboratory confirmation of H. capsulatum CNS samples or from extra-CNS sites with no alternative etiology for CSF pleocytosis. Controls were patients with histoplasmosis but no evidence of CNS involvement, an alternative diagnosis, or other fungal meningitis.

Results. In total, 47 cases and 153 controls were evaluated (Table 1). Forty-nine percent of patients with CNS histoplasmosis and 43.8% of controls were immunocompromised. CSF BDG was positive in 25 (53.2%) cases using a level of ≥80 pg/ml, the median CSF BDG level was 140.5 pg/ml (range from <31 to 500 pg/ml). The detection of CSF BDG level ≥80 pg/ml was not associated with positive CSF Histoplasma antigen (P = 0.28) or positive CSF Histoplasma culture (P = 0.56). The sensitivity for detection of CSF BDG was 53.2% and the specificity was 87.3%, compared with 78.7% (P = 0.009) and 96.4% (P = 0.003), respectively, for detection of antigen. CSF BDG was positive in 20 of 153 (13.1%) patients in the control group. Seven of 11 (63.6%) other CNS fungal meningitis cases (five Cryptococcus, two Aspergillus, two Blastomyces, one Candida, and one suspected fungal meningitis) had CSF BDG ≥80 pg/ml.

Conclusion. A positive CSF BDG supports the diagnosis of fungal meningitis but cannot distinguish among the different etiologies. The sensitivity and specificity of detection of CSF BDG was lower than that of antigen detection.

Table 1: Characteristic of the study patients

| Parameter | Number of patients | Positive BDG (%) | Controls* | Controls* (%) | P-value |
|-----------|--------------------|------------------|-----------|--------------|---------|
| Immunosuppressed | 23/47 (48.9%) | 67/153 (43.8%) | 0.54 |
| CSF BDG > 80 pg/ml | 29/47 (61.7%) | 80/153 (52.1%) | <0.0001 |
| CSF Histoplasma antigen positive | 37/47 (78.7%) | 5/143 (3.5%) | <0.0001 |
| CSF culture positive | 9/44 (20.5%) | 11/117 (9.4%) | 0.058 |

*aControl included five Cryptococcus, two Aspergillus, two Blastomyces, one Candida, and one suspected fungal meningitis. bP-value = 0.009; cP-value = 0.003.

Disclosures. No reported disclosures.

156. Real-World Experience of Voriconazole Prophylaxis in Allogeneic Hematopoietic Cell Transplant Recipients: A Single-Center Study

Shuk-Ying Chan, MRCP(UK), FHCP, HFHAM (Medicine); Dionysios Neofytos, MD, MPH; Rachel M. Hughes, BS; Yao-Ting Huang, PhD, MPH; Miguel Angel Parejas, MD, PhD and Genoveva Papanicolaou, MD, PhD

Background. Recent experience of voriconazole prophylaxis for invasive fungal infections in neutropenic patients receiving hematopoietic cell transplantation (HCT) is limited. Voriconazole is a broad-spectrum triazole antifungal agent, which has demonstrated activity against many common opportunistic fungal pathogens. Voriconazole prophylaxis is recommended in the allogeneic HCT setting. We sought to describe (i) adherence to AF guidelines and (ii) reasons for premature voriconazole discontinuation (DIC).

Methods. Retrospective review of 215 adult allo-HCT recipients from September 2014 – December 31, 2015 at our center. Per standards of care (SOC), patients received micafungin from Day 2 post-allo-HCT, then switched to VCZ by Day 7 unless there was clinical evidence of fungal infection. VCZ prophylaxis was continued until Day 100 post-allo-HCT or until day 28 post-engraftment, whichever occurred later. We evaluated adherence to AF guidelines and DIC reasons.

Results. In total, 215 patients were included in the study. Among the 189 patients who received Voriconazole prophylaxis, adherence to the AF guidelines was achieved in 149 (78.9%) patients. Reasons for premature discontinuation of Voriconazole are shown in Table 1. The most common reason for DIC was unexplained increase in liver enzymes (44 cases, 23.4%). The incidence of DIC was 24% in patients with adherence to AF guidelines and 2% in patients with non-adherence (P = 0.0001).

Conclusion. Voriconazole prophylaxis for allogeneic HCT recipients is well tolerated, and adherence to AF guidelines is associated with lower risk of DIC. Further studies are needed to determine the optimal duration of Voriconazole prophylaxis in the allogeneic HCT setting.

Table 1: Reasons for Voriconazole Prophylaxis Discontinuation

| Reason for DIC | Number of Patients |
|---------------|--------------------|
| Unexplained increase in liver enzymes | 44 (23.4%) |
| Other | 41 (21.7%) |

Disclosures. No reported disclosures.
for high-risk patients. AFP modification, D/C and treatment emergent adverse events (TEAE) regardless of causality were captured through D100. Standard definitions were used for invasive fungal infections (IFI).

**Results.** Of 215 patients, 42 had contraindications to VCZ at baseline. Of 173 patients included in the analysis, 65 (37.6%) received ex vivo T-cell depleted (TCD) peripheral blood (PB), 15% cord and 47.4% conventional PB or marrow allografts. All TCD recipients received myeloablative conditioning (MA) and all cord recipients received reduced intensity conditioning (RIC). For conventional transplant, 65.9 and 26.8% of the patients received RIC and MA, respectively. One hundred and sixty-eight (97%) patients had normal liver function tests (LFT) at VCZ initiation. One hundred and twenty-nine (74.6%) patients started VCZ by D7 and 95% by D15. Median duration of VCZ AFP was 68D (IQR 22–91). Abnormal LFTs was the most frequently encountered TEAE (42/58, 72%), followed by neurologic/visual TEAE (11/58, 19%) leading to VCZ D/C. Median time to VCZ D/C due to neurologic/visual TEAE (4D, IQR 4–9) was significantly shorter than abnormal LFTs (25D, IQR 16–42) (P < 0.05). Eight (5%) breakthrough proven/probable IFIs were observed by D180, without significant difference based on transplant types and AFIP duration. Duration and reasons for VCZ D/C were shown in Table 1 by HCT type.

**Conclusion.** 75% of the patients started VCZ per SOC and 95% by D15. Most TEAE leading to VCZ D/C were abnormal LFTs in all HCT types, and most commonly in cord HCT. 3) Neurologic/visual TEAE were similar across types. Rates of IFI were 3–4% in CONV and TCD and 12% in UCB.

**Table 1. Duration and Reasons for Discontinuation of Voriconazole by Transplant Type**

|                | CONV | UCB | TCD |
|----------------|------|-----|-----|
| Total n | 82   | 26  | 65  |
| VCZ Start Day, D from HCT, Median (IQR) | 8 (7,12) | 7 (7,9) | 7 (7,7) |
| Duration of VCZ AFP, D, Median (IQR) | 63 (22–90) | 82 (19–94) | 77 (21–90) |
| Completed VCZ per SOC, N, % | 63 (77) | 14 (54) | 48 (74) |
| Discontinuation due to abnormal LFTs | 13 (16) | 10 (38) | 19 (30) |
| Discontinuation due to CNS/Vis TEAE | 3 (4) | 2 (7) | 6 (9) |
| Discontinuation due to DDI | 16 (20) | 0 | 1 (2) |
| IFI by D180 from HCT | 3 (4) | 3 | 2 (3) |
| IFI, D from HCT, Mean | 111 | 80 | 142 |

**Figure 2. Reasons of Voriconazole Discontinuation Before Cessation of Immunosuppression or Day 100 Post-allo-HCT**

**Figure 3. Treatment Emergent Adverse Events Lead to Voriconazole Discontinuation**

**Disclosures.** Y. T. Huang, Merck & Co: Grant Investigator, Research grant. M. A. Perales, Merck: Consultant, Grant Investigator and Investigator, Consulting fee and Research grant. Astella: Consultant, Grant Investigator and Investigator, Consulting fee and Research grant. G. Papnicolaou, Astellas Pharma: Consultant and Grant Investigator, Consulting fee, Research grant and Research support. Merck &Co: DSC member and Investigator, Consulting fee, Research grant and Research support

157. **Natural History of Non-CNS Disseminated Coccidioidomycosis**

**Background.** The number of patients with coccidioidomycosis continues to increase yearly. Patients with CNS disease require lifelong antifungal therapy due to the high morbidity and mortality of this disease. However, the morbidity and mortality in non-CNS disseminated disease has not been well characterized.

**Methods.** We conducted a retrospective study of 373 VA-armed forces coccidioidomycosis patients diagnosed between 1955 and 1958 and followed to 1966. Groups were identified as non-disseminated disease, non-CNS disseminated disease with and without multisite dissemination, and disseminated disease to the CNS with and without multisite dissemination. Clinical variables including demographic information, duration and severity of symptoms, coccidioidal serologies, type of infection and complications, time to disseminated disease, and mortality were abstracted from patient charts.

**Results.** Mortality attributed to coccidioidomycosis in the non-disseminated group was 0.3% (1/297) compared with the non-CNS disseminated group of 8.5% (4/47, median survival 12 months, range 12–24 months, P = 0.0002). Mortality in the CNS disseminated group was 86% (19/22, median survival of 12 months, range 12–156 months, P < 0.0001 compared with non-CNS disseminated). The single site non-CNS disseminated group had a mortality of 4.1% (1/24, survival of 12 months) compared with the multiple site non-CNS disseminated group of 13% (3/23, median survival of 18 months, range of 12–24 months, P = 0.57).

**Conclusion.** This retrospective cohort study demonstrates significant mortality differences between different forms of disseminated coccidioidomycosis. CNS dissemination exhibited the highest mortality rate; however, non-CNS dissemination also exhibited an unexpectedly high mortality rate. There was no significant difference in mortality between single site non-CNS disseminated disease and multiple site non-CNS disseminated disease.

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

158. **Presentation and Outcome of Cryptococcal Infection Varies by Predisposing Illness**

Krunal Raval, MD; William Powderly, MD and Andrej Spec, MD; 1Infectious Diseases, Barnes Jewish Hospital – Washington University of St. Louis, St. Louis, Missouri; 2Division of Infectious Diseases, Washington University, St. Louis, Missouri; 3Infectious Disease, Washington University, St. Louis, Missouri

**Session:** 44. Clinical Mycology

**Thursday, October 5, 2017: 12:30 PM**