358. Comparison of Voriconazole (VORI), Isavuconazole (ISAV), and Posaconazole (POSA) in the Initial Treatment of Patients With Invasive Aspergillosis (IA)

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Background. While VORI is recommend as first-line therapy for patients with IA, ISAV, and POSA have been approved for the treatment and prophylaxis of IA, respectively. We evaluated treatment responses among patients with IA receiving triazole antifungals.

Methods. We performed a retrospective cohort study at our center in patients diagnosed with probable or proven IA between March 2015 and January 2018 who were initially treated with VORI, ISAV, or POSA. Patients were followed until April 2018. Baseline characteristics, laboratory parameters, and clinical evolution were documented. We captured changes in antifungal therapy due to lack of drug efficacy (clinical, radiographic, or mycological progression) and changes in response to drug toxicities.

Results. A total of 73 patients were diagnosed with IA (55 probable, 18 proven) during the study period. Median age was 61 years (range, 19–80) and 37 (50.7%) were male. At IA diagnosis, 57 (78.1%) had an active hematological malignancy, 27 (37%) had undergone hematopoietic-cell transplantation, and 10 (13.7%) had undergone solid organ transplantation. Sixty-two patients (84.9%) were neutropenic, 42 (57.5%) were on glucocorticoids > 0.3 mg/kg/day prednisone-equivalents in the 3 weeks preceding diagnosis, and 43 (58.9%) were on other T-cell immunosuppressants. Thirty-six patients were initially treated with VORI for a median of 20 days (range, 1–453), 29 with ISAV for a median of 35 days (range, 1–714), and 8 with POSA for a median of 15 days (range, 2–399). Pulmonary-only IA was treated initially with POSA in 87.5%, VORI in 86.1% and ISAV in 65.5% of patients. ISAV was more commonly used in patients with extrapulmonary involvement (44.5%) compared with VORI (13.9%) or POSA (12.5%). Antifungal changes due to lack of efficacy or drug toxicities were: 2.8% and 22.2% for VORI, 24.1% and 3.4% for ISAV, and 37.5% and 25.0% for POSA. In an analysis based on initial treatment not accounting for later changes, the EORTC/MSG clinical success rate at 6 weeks was 33.3%, 31.0%, and 12.5% for VORI, ISAV, and POSA, respectively.

Conclusion. While the drug efficacy and toxicity rates varied among agents, the 42-day clinical success rate did not. Further research is warranted to determine the optimal antifungal agent for patients with IA.

Disclosures. **F. M. Marty**, Merck: Consultant and Investigator, Consulting fee, Research support and Speaker honorarium. Astellas: Consultant and Investigator, Consulting fee and Research support. Chimerix: Consultant and Investigator, Consulting fee and Research support. Fate Therapeutics: Consultant, Consulting fee. GlaxoSmithKline: Consultant, Consulting fee. LFB: Consultant, Consulting fee. Roche Molecular Diagnostics: Consultant, Consulting fee. Shire: Consultant and Investigator, Consulting fee and Research support. **S. Hammond**, Merck: Investigator, Research support.

359. Baseline Serum *Aspergillus* Galactomannan Index Among *Aspergillus* Species in Hematologic Malignancies Patients With Invasive Pulmonary Aspergillosis

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Background. Most of the information regarding serum *Aspergillus* galactomannan (sAGM) index in patients with invasive pulmonary aspergillosis (IPA) and hematological malignancies (HM) is derived by infections caused by *Aspergillus fumigatus*, the predominant *Aspergillus* species causing IPA. It is unclear if differences exist in sAGM in IPA caused by non-*fumigatus Aspergillus* species.

Methods. We analyzed all consecutive patients with proven or probable culture-documented IPA (EORTC/MSG criteria) at MD Anderson Cancer Center (2006–2017) who had an sAGM obtain within a week of IPA diagnosis (day −6 to day 0 of fungal culture). The sAGM result was categorized as either undetectable (GM = 0), negative (0.0 > GM < 0.5) or ≥ than a 0.5 index value. Baseline demographic characteristics and 42-day crude mortality after the diagnosis of IPA were collected.

Results. We identified 72 (proven in 4, probable in 68) patients with culture-documented IPA. Most common HM was AML in 34 (47.2%) patients and CLL in 15 (20.8%) patients. Most (47/72, 65, 2%) patients developed IPA despite mold-active antifungals. Forty-three (60%) patients had *A. fumigatus*, 19 (26%) *A. terreus*, and 10 (14%) *A. flavus*. Mortality at 42 day was 22.2% (16/72) patients. Serum AGM at the baseline was undetectable in only one (2%) *Aspergillus fumigatus* IPA. Serum AGM positivity was seen in 28 (65%), 10 (53%), and five (50%), among the *Aspergillus fumigatus, terreus*, and *flavus* species, respectively ($P = 0.52$), with a median sAGM level of 1.32 (0.50–9.36), 0.87 (0.50–9.70), and 1.11 (0.57–8.58), respectively, $P = 0.99$. There were not significant differences in baseline neutropenia, extent of lung involvement by chest CT, prior mold-active antifungal use, prior SCT as well as 42-day mortality among patients with IPA caused by each of the three *Aspergillus* species.

Conclusion. In the setting of common prior mold-active antifungal use, we found no apparent differences in sAGM among *Aspergillus* species causing IPA in HM patients. Mortality was comparable and worse in patients with high baseline sAGM levels.

Disclosures. **D. P. Kontoyiannis**, Merck: Consultant, Research support and Speaker honorarium. Pfizer: Consultant, Research support. Astellas: Consultant, Research support and Speaker honorarium. Gilead: Speaker's Bureau, Speaker honorarium. F2G Inc.: Speaker's Bureau, Speaker honorarium. Cidara Inc.: Speaker's Bureau, Speaker honorarium. Jazz Pharmaceuticals: Speaker's Bureau, Speaker honorarium.

360. Breakthrough Invasive Pulmonary *Aspergillosis* During Isavuconazole Prophylaxis in Patients with Hematologic Malignancies: A Single-Center Experience

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Background. Isavuconazole (ISA) is an attractive candidate for prophylaxis against invasive mould infections (IMIs) due to its broad-spectrum activity, ease of dosing, favorable side-effect profile, and limited drug–drug interactions. Clinical experience using ISA prophylaxis in high-risk patients is lacking. We describe our experience using ISA as first-line primary prophylaxis in select patients with hematologic malignancies and hematopoietic cell transplant (HCT) recipients over a 13-month period.

Methods. We conducted a retrospective review of adults with hematologic malignancies and HCT recipients who received ≥7 days of uninterrupted ISA primary prophylaxis between September 1, 2016 and September 31, 2017. Breakthrough IMIs were documented through chart review and classified as probable or proven according to standard criteria. The study was approved by the OHSU IRB.

Results. A total of 135 patients received 184 courses of ISA prophylaxis for AML ($N = 100$), GVHD ($N = 36$), "high-risk HCT" (≥14 days neutropenia immediately prior to HCT; $N = 25$), and other indications ($N = 23$). Ten cases of proven/probable breakthrough IMIs were identified (invasive pulmonary *Aspergillosis* (IPA) = 6, Mucorales = 2, Fusarium = 2). Four cases of breakthrough IPA occurred during prophylaxis for AML, and two occurred during prophylaxis after high-risk HCT. All breakthrough IPA occurred during prolonged neutropenia (median 46 days, range 16–181). The median duration of ISA prophylaxis prior to breakthrough IPA was 15 days (range 10–37). The median serum ISA trough level at breakthrough IPA was 3.7 μg/mL (range 3.1–6.3). During this same time period, there was no breakthrough IPA during 101 courses of voriconazole or posaconazole (POS) prophylaxis in similar patients. Only one case of breakthrough IPA occurred during 244 courses of POS prophylaxis in the 18 months prior to the introduction of ISA prophylaxis. Due to the higher than expected rate of breakthrough IPA, POS replaced ISA as first-line primary prophylaxis in October 2017. Since then there have been no cases of breakthrough IPA on POS prophylaxis.

Conclusion. Our institutional experience indicates that additional studies are needed to determine the role of ISA for prophylaxis in certain high-risk hematologic malignancy patients.

Disclosures. **J. S. Lewis II**, Merck: Consultant, Consulting fee

361. Changing Epidemiology of *Blastomyces dermatitidis* Infection in Quebec, Canada: A Retrospective Multicenter Study

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Background. In the wake of the increased incidence of blastomycosis in Quebec province, Canada, clinicians have observed a possible increase of severity in patients, with occasional death. This study aimed to assess temporal changes in blastomycosis severity and mortality in Quebec, and to identify risk factors for mortality of blastomycosis.

Methods. A retrospective multicenter cohort study of patients with confirmed blastomycosis identified in a database at the provincial laboratory (Laboratoire de santé public du Québec) between 1988 and 2016. Severe cases were defined as patients with septic shock and/or acute respiratory distress syndrome and/or requiring mechanical ventilation. Immunosuppression included corticosteroid use, HIV, immunosuppressive therapy for inflammatory disease, chemotherapy, and transplantation. The primary outcome was 90-day all-cause mortality. Risk factors for mortality were identified by multivariate logistic regression.

Results. Over the study period, 220 blastomycosis cases were identified. Medical charts for 176 patients from 17 institutions were available and complete for data collection. The median age of patients was 55.3 years (interquartile range 45–67). Infection

led to hospitalization of 119 patients (68%). Pulmonary involvement was recorded for 81% of cases (142/176) and two organs or more were involved in 35% (61/176). An increase in severity was observed mainly in recent years [1988–1997: 1/32 (3%); 1998–2007: 9/54 (17%); 2008–2016: 19/89 (21%); $P = 0.05$]. The overall mortality was 17.6% (31/176); 6% (2/33) in 1988–1997, 20% ($n = 11/54$) in 1998–2007 and 20% in 2008- 2016 ($n = 18/89$) ($P = 0.15$). There was also a significant increase in age at diagnosis ($P = 0.005$), the proportion of diabetic patients ($P = 0.03$) and the proportion of immunocompromised patients ($P = 0.009$) over time. The independent risk factors of mortality were age (aOR 1.03 for each additional year, 95% CI 1.0–1.06, $P = 0.05$) and immunosuppression (aOR 3.62, 95% CI 1.54–8.49, $P = 0.003$).

Conclusion. The severity of blastomycosis observed in Quebec over the past 30 years has increased. These changes could be explained in part by an increase in the number of immunosuppressed patients. However, mortality has remained stable in recent years.

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

362. Species Distribution and Trends of Invasive Candidiasis in the United States, 2009–2015, Using a Large Electronic Medical Record Database

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Background. While 50% of invasive candidiasis (IC) has historically been caused by *C. albicans,* the changing epidemiology and rise in drug-resistant *Candida* necessitates understanding the contribution of specific *Candida* species to IC. To date, species and site-specific trends in IC have not been reported on a large scale using US clinical data.

Methods. Using the Cerner *Health Facts* electronic health record (EHR) dataset, inpatient hospitalizations with any *Candida* spp. isolated from blood or a sterile site (SS) (abdominal or other) were identified from 2009 to 2015. Patient characteristics were described by species. Significant relationships ($P \leq 0.05$) were assessed using chi-squared or exact binomial tests. Annual percent change in IC incidence by site and species were assessed via Poisson regression.

Results. Overall, 19,310 *Candida* isolates from 10,313 patients were identified. Of these, 46% of isolates were *C. albicans*, 22% *C. glabrata*, 14% *C. parapsilosis*, 7% *C. tropicalis*, and 11% other/unspeciated; no *C. auris* infections were identified. The overall incidence of IC was 99 cases/100,000 patients. Compared with *C. albicans*, isolation of other species was 35% more frequent from blood, and 43% and 30% less frequent from non-blood abdominal and non-abdominal SSs, respectively (Table 1). Total IC increased by 1% (95% CI = 0.2–2%) annually; while abdominal and SS IC significantly increased by 6% (4–8%) and 11% (9–13%) per year, respectively, candidemia decreased significantly by 4.5% (3–6%) annually. Among *C. albicans*infections candidemia decreased by 6.5% (5–8%) annually, while abdominal (5%, 3–8%) and other SS infections (10%, 7–13%) increased (Figure 1). Candidemia incidence remained unchanged for the other species. SS infections increased for every species, and abdominal infections increased for all but *C. parapsilosis* (Figure 2).

Conclusion. In this first large-scale study on trends in IC using US hospital EHR data, the species distribution of IC isolates varied between blood and non-blood SSs. The incidence of candidemia is decreasing, but not for potentially drug-resistant species such as *C. glabrata,* which continue to pose treatment challenges.

This work was supported in part by the Division of Intramural Research, NIAID, NIH

Table 1. Patient demographics by species

	C. albicans N (col %) = 5447	*C. glabrata* N (col %) = 2492	*C. parapsilosis* N (col %) = 1369	*C. tropicalis* N (col %) = 778	Other N (col %) = 608
Gender					
Female [N (%) = 5008 (48)]	2639 (48)	1322 (53)*	598 (44)*	358 (46)	279 (46)
Male [5336 (52)]	2807 (52)	1170 (47)*	770 (56)*	420 (54)	329 (54)
Age					
<1 year [N (%) = 173 (2)]	86 (2)	11 (0)	57 (4)	10 (1)	13 (2)
1 – 17 years [274 (3)]	134 (2)	16 (1)	62 (5)	35 (4)	48 (8)
18 – 39 years [1155 (11)]	657 (12)	210 (8)	155 (11)	102 (13)	121 (20)
40 – 64 years [4368 (42)]	2340 (43)	1029 (41)	604 (44)	335 (43)	245 (40)
65+ years [4343 (42)]	2230 (41)	1226 (49)	491 (36)	296 (38)	181 (30)
Neonate (≤4 weeks) [N (%) = 106 (1)]	59 (1.1)	≤5 (NR)	34 (2.5)*	≤5 (NR)	≤5 (NR)
Race					
African American [N (%) = 2127 (21)]	947 (17)*	555 (22)	379 (28)*	189 (24)*	121 (20)
Caucasian [7173 (70)]	3965 (73)*	1710 (69)	837 (61)*	512 (66)*	424 (70)
Other [820 (8)]	426 (8)	191 (8)	119 (9)	65 (8)	47 (8)
Unknown [193 (2)]	109 (2)	36 (1)	34 (2)	12 (2)	16 (3)
Census region					
Midwest [N (%) = 1818 (18)]	1106 (20)*	461 (18)	173 (13)*	112 (14)*	104 (17)
Northeast [3239 (31)]	1713 (31)	778 (31)	469 (34)*	205 (26)*	167 (27)*
South [4123 (40)]	1937 (36)*	980 (39)	611 (45)*	406 (52)*	274 (45)*
West [1133 (10)]	691 (13)*	273 (11)	116 (8)*	55 (7)*	63 (10)
Patient encounters (with ≥1 culture positive)	N (%) = 5668	N (%) = 2598	N (%) = 1431	N (%) = 808	N (%) = 629
Infection type (encounters)					
†Candidemia [N (%) = [6011 (55)]	2650 (47)*	1776 (68)*	885 (62)*	503 (62)*	401 (64)*
‡Abdominal [2437 (22)]	1567 (28)*	499 (19)*	103 (7)*	156 (19)*	132 (21)
¤Other sterile [2531 (23)]	1451 (26)*	323 (12)*	444 (31)*	149 (18)*	96 (15)*

C. albicans and *C. parapsilosis* had 1 patient each with unknown gender
*p≤0.05 compared to total sample population
Other species include: *C. catenulate, C. ciferrii, C. dubliniensis, C. famata, C. guilliermondii, C. haemulonii (pan-susceptible), C. kefyr, C. lambica, C. lipolytica, C. lusitaniae, C. magnoliae, C. norvegensis, C. pelliculosa, C. pulcherrima, C. rugosa, C. sphaerica, C. stellatoidea, C. utilis, C. zeyalnoides*
≤5 (NR) – Number of cases ≤5, exact count and percentage not reported to preserve data anonymity
†Candidemia with or without disseminated infection; ‡Abdominal sterile source without candidemia; ¤Non-abdominal sterile source without candidemia

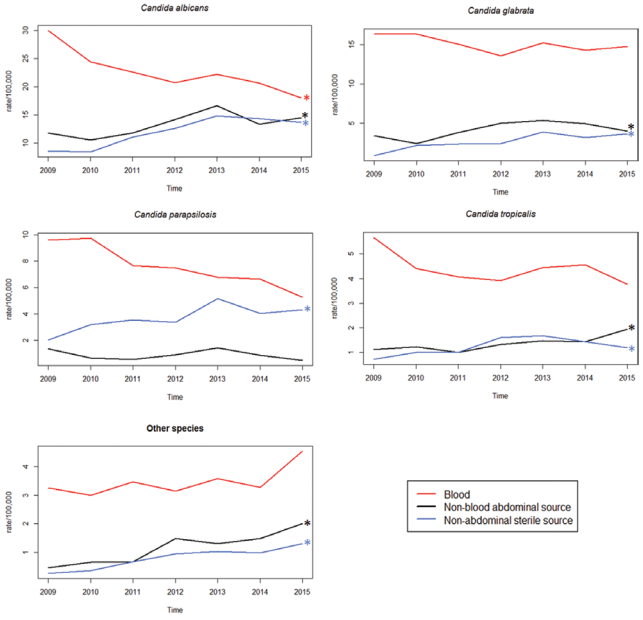

Figure 1. Source-specific incidence trends by species. Significance determined by Poisson regression denoted by *.

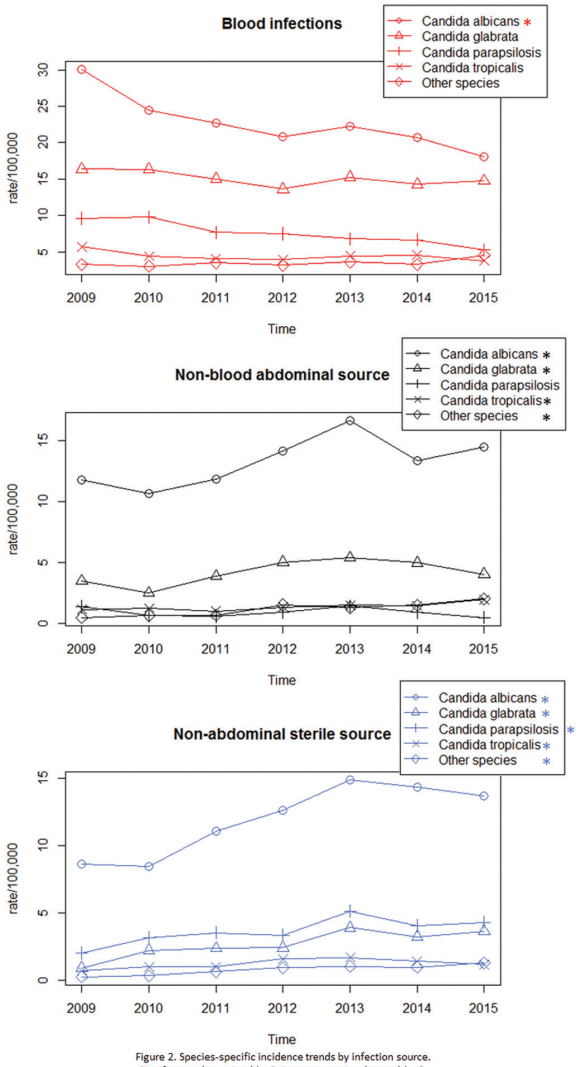

Figure 2. Species-specific incidence trends by infection source. Significance determined by Poisson regression denoted by *.

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