2020-2021 Residency Project List

Resident	Study Team	Project Title	Project Results
Alexa Plutt PGY1 Pharmacy Practice	Michael Stanton, Anthony Zembillas, Catie Renna, Libby Dahl	Determination of tolerability of a continuous infusion administration of ifosfamide in a pediatric patient population	Ifosfamide is an anti-tumor agent with activity against various malignancies in pediatric patients. As a prodrug, ifosfamide requires metabolic activation, which occurs via a saturable, multi-step equilibrium-based process. Due to these metabolic characteristics, the method of administration can affect its therapeutic and toxic effects. This single center, case series describes the tolerability of continuous infusion and bolus administration ifosfamide in 10 pediatric patients with Ewing sarcoma. The primary objective was to report the hematological toxicities of patients with differing administration methods. Secondary objectives included collecting information on non-hematological toxicities and incidence of treatment delays and dose reductions. Ultimately, 48 cycles of ifosfamide were administered as bolus dose and 24 as continuous infusion. Patients receiving bolus administration had lower hemoglobin and platelet nadirs resulting in more transfusions and treatment delays when compared proportionally to continuous infusion. With the results of this case series, continuous infusion ifosfamide appears to be safe and feasible for outpatient administration and may offer an advantage from a hematological adverse event profile, but would need to be confirmed in a larger cohort.
Emily Wings PGY1 Pharmacy Practice	Jamie Eckardt, Michael Spinner	Evaluation of Clotrimazole Effect on Tacrolimus Trough Concentrations in Kidney Transplant Recipients	174 patients were included in the study, with 81 patients having received clotrimazole prophylaxis post-transplant and 93 patients having received no clotrimazole prophylaxis. **Primary Endpoint:** Following discontinuation of clotrimazole, the median tacrolimus trough concentration decreased significantly from 10.5 ng/mL (IQR 8.4-12.2) to 6.6 ng/mL (IQR 5-8.7, p<0.0001). A median of 12 days (IQR 7-17) were required to attain a goal tacrolimus trough concentration (8-12 ng/mL) after clotrimazole discontinuation. **Secondary Endpoints:** The median time to first goal tacrolimus trough concentration, after tacrolimus initiation post-transplant, was 10 days (IQR 7-14) among patients who received routine clotrimazole prophylaxis and 13 days (IQR 8-20) among patients who did not receive clotrimazole prophylaxis (p=0.0023). No statistically significant differences were seen in the rate of for-cause allograft biopsies (4.9% vs. 9.7%, p=0.264) or incidence of candidiasis (1.2% vs. 5.4%, p=0.217) between groups.
April Chapman PGY1 Pharmacy Practice	Marina Feldman, Myaa Lightfoot, Dave Popa	Assessment and Management of Delirium in Hospitalized Stroke Patients at a Large Academic Medical Center	159 patients admitted to the non-ICU neurology units at Cleveland Clinic Main Campus between May 1, 2016 and July 31, 2019 were screened. Sixty-five patients (34 male; median age 74 years) with a stroke diagnosis were included in this study. **Primary endpoint:** Twenty-four patients (44.4%) received antipsychotics when they were bCAM negative (n=54). **Secondary endpoints:** The median number of antipsychotic days was 2 (interquartile range [IQR], 1-6 days) and the median length of stay was 7 days (IQR,

			5-14 days). Fifty-one (78.5%) patients received at least one antipsychotic during admission. The most frequently used antipsychotic agent was quetiapine (n=36, 55.4%), followed by haloperidol (n=6, 9.2%) and aripiprazole (n=4, 6.2%). Twenty-three patients (35.4%) were discharged on antipsychotic medications. **Conclusion:** The findings of this study identify important opportunities for pharmacists to help steward the use of antipsychotic agents in stroke patients with delirium. These opportunities include identifying patients who may not need antipsychotics on discharge and recommending taper plans to prevent long-term or unnecessary antipsychotic use.
Nicole Babiak PGY1 Pharmacotherapy	Jason Yerke, Andrea Pallotta, Matt Siuba, Ryan Miller	Characterization of treatment and outcomes following aspiration events in critically ill patients	• 253 patients were included: 118 patients were categorized as having hospital aspiration and 135 patients with community aspiration. • In patients with community and hospital aspiration 134 (99.3%) and 111 (94.1%) patients received antimicrobials, respectively. • Following aspiration, respiratory cultures were obtained in 99 (39.1%) patients. About 2/3 of these cultures obtained had no growth, candida species, or normal respiratory flora. • In hospital mortality was seen in 24 (17.8%) and 28 (23.7%) patients with community and hospital aspiration, respectively. • Findings in this study highlight that nearly all patients admitted to a MICU as a result of aspiration receive antimicrobials and most receive them for more than 48 hours. Patients that have initial respiratory compromise following aspiration but have improvement during the first 48 to 72 hours could be candidates for antimicrobial de-escalation or discontinuation.
Molly Wheeler - Large PGY2 Pharmacotherapy	Jeff Ketz , R Davis, A Brant	Hypoglycemia Prediction and Proactive Intervention	• 1371 patients included in control group, 1455 in intervention group. Difference in occurrence of any hypoglycemia during the admission was 26.3% vs 22.4% (p = 0.06) among high risk patients (809 control, 839 intervention) • Will conduct sensitivity and specificity analysis to improve tool and implement updates
Molly Wheeler – Small PGY2 Pharmacotherapy	Katie Rivard, PICU Pharmacist	Evaluation of vancomycin dosing in pediatric RRT patients	• 18 patients were included; 19 courses were included for CRRT with 115 levels. Most first levels were subtherapeutic and most strategies were dose by level. A small number of courses with PD and IHD were included. • CRRT dosing protocol will change to scheduled levels initially with a dose prior to 3rd or 4th dose rather than initial dose by level
Jessica Ward – Large PGY2 Critical Care	Mollie Lumpkin, Stephanie Bass; Jason Yerke; Aanchal Kapoor; Christina Lindenmeyer	Evaluation of protocol for rifaximin discontinuation in patients on broad-spectrum antibiotics	159 adult patients admitted to the medical intensive care unit at Cleveland Clinic were screened for inclusion. 32 patients were included in both the pre-protocol group (broad-spectrum antibiotics for ≥3 days of 75% of antibiotic duration) and the post-protocol group (broad-spectrum antibiotics without rifaximin for ≥3 days).

			Baseline characteristics were well balanced with the exception that post-protocol group had higher norepinephrine requirements and more often received deep sedation. **Primary Outcome:** Median days alive and free of delirium and coma to day 14 were similar between the groups [pre-protocol 3 (0,8) vs post-protocol 2 (0,9.5); p=0.93]. **Secondary Outcomes:** Mortality rates were similar between the groups (40.6% vs 46.9%; p=0.61). ICU length of stay was similar (10 (4.5, 20.5) vs 11 (7,17); p=0.73). Days of MICU combination therapy were reduced during the protocol pilot [6 (3,9.5) vs 1 (0,1); p<0.01]. Adherence to the protocol was 91.4% and the most common reason for non-adherence was non-qualifying antibiotic regimens. Time to rifaximin discontinuation was approximately 1 day in the post-protocol group. Protocol implementation was associated with significant reductions in per-patient costs of rifaximin therapy [$494.64 (247.32, 783.18) vs $82.44; p,0.01]. **Conclusions:** A pharmacist-driven protocol for rifaximin discontinuation was not associated with an increase in days alive and free of delirium and coma in critically ill patients with liver disease treated with broad-spectrum antibiotics. No differences were noted in other clinical or safety outcomes. This study demonstrates the feasibility of a pharmacist-driven protocol for rifaximin discontinuation and the significant cost-savings that could result from such an initiative.
Jessica Ward – Small PGY2 Critical Care	Benjamin Hohlfelder, Mike Militello, Heather Torbic, Sudhir Krishnan	Therapeutic versus prophylactic anticoagulation in venovenous extracorporeal membrane oxygenation	Not completed during residency due to COVID-19-related delays. To be completed during 2021.
Reaghan Erickson – Large PGY2 Emergency Med	Matt Campbell, Gretchen Sacha, Seth Bauer, Jessica Wesolek	Association of an updated emergency department sepsis order set and delay to administration of second dose piperacillin/tazobactam	3,219 adult patients who received at least two doses of piperacillin/ tazobactam ordered through the ED sepsis order set within in the Cleveland Clinic Enterprise between 5/7/18 to 5/6/20 were included in the study (1,222 pre- order set update group; 1,997 post- group). On average, patients were 65 years old and 55% male with a mean ED lactate of 3. Patients in the pre- group had higher SOFA scores, more sepsis, and more ICU admissions, but similar baseline comorbidity scores than in the post- group. **Primary Outcome:** the proportion of patients who experienced major second piperacillin/tazobactam dose delay was significantly lower in the post- order set update group (32.7% vs 25.6%, p < 0.001). In our logistic regression model, order set update was significantly associated with major delay (OR = 0.64, 95% confidence interval 0.52 to 0.78, p < 0.001), when controlling for confounding factors. **Secondary Outcomes:** patients in the post- order set update group had shorter duration of mechanical ventilation (5.6 vs 4.2 days, p = 0.02), but similar hospital

			length of stay (7.3 vs 7.0 days, p = 0.18) and in-hospital mortality (7% vs 6%, p = 0.29) relative to patients in the pre- group. When controlling for other variables, order set update was not associated with in-hospital mortality (OR 1.02, 95% confidence interval 0.71 to 1.46, p = 0.92). **Conclusions:** Introduction of an ED sepsis order set with scheduled antibiotic frequencies significantly decreased the proportion of patients with major second dose piperacillin/tazobactam dose delay within a large health-system. Future research should be focused on additional strategies to mitigate second dose antibiotic delay.
Alex Taylor – Large PGY2 Infectious Disease	Janet Wu, Katie Rivard	Comparison of antimicrobial prescribing in outpatient settings	This is a retrospective, cohort analysis from June 1, 2019 to May 31, 2020 with the primary objective of comparing antibiotic prescribing habits for cystitis, otitis media, pharyngitis, sinusitis, and URTIs among five ambulatory care departments within the health system: Emergency Department (ED), Express Care (EC), Express Care Online (ECO), Pediatrics (PED), and Primary Care (PC). A total of 261,947 encounters were included at ambulatory care sites (ED:56,766, EC:92,749, ECO:8,783, PED:29,151, PC:74,498) for the treatment of cystitis (30,932), otitis media (22,094), pharyngitis (59,964), sinusitis (53,693), or URTIs (95,264). The population was 63% female with a median age of 34.2 years (IQR: 12.8-56.3). A total of 17% of patients had documented penicillin allergies and 18% of patients had Group A Streptococcus (GAS) testing. Antibiotics were prescribed in 44% of encounters (ED:21,746 [38%], EC:45,652 [49%], ECO:4,622 [53%], PED:10,909 [37%], PC:33,547 [45%]; P <0.001). Guideline concordant antibiotics were prescribed in 65% of encounters (ED:14,338 [66%], EC:31,532 [69%], ECO:3,869 [84%], PED:8,212 [75%], PC:17,263 [51%]; P <0.001). Observed rates of antibiotic and guideline concordant antibiotic prescribing were similar to national published rates of antibiotic prescribing in the ambulatory setting. The variability in antibiotic prescribing demonstrated opportunities for targeted outpatient stewardship efforts.
Nicole Guist – Large PGY2 Informatics	Tyler Tomasek	Evaluation and Implementation of Critical Low Pyxis Setting	**Primary endpoint** – significant reduction of stock-outs 48.6 vs. 55.1 per day; -6.5 [95% CI, -11.5 to -1.6] **Secondary endpoints** – non-significant reduction of stock-out duration 83.3 vs. 93.0 hours per day; -9.7 [95% CI, -23.2 to 3.9] - non-significant increase of unscheduled refills (pharmacy workload) 59.3 vs. 55.1 per day; 4.1 [95% CI, -1.1 to 9.4] **Conclusion** – Critical low functionality is a promising functionality that significantly decreased incidence of stock-outs without significantly increasing pharmacy workload.

Stephen To – Large PGY2 Informatics	Ashley Coccarelli, Jill Wesolowski	Turning on outpatient order contexts so age-based dosing and frequency buttons will appear for prescriptions	**Primary endpoint-** Non-significant increase and decrease in proportion of modified orders and proportion of orders with free-text in the dose field in commonly prescribed pediatric outpatient orders **Secondary endpoint-** - Non-significant increase and decrease in proportion of modified orders and proportion of orders with free-text in the dose field in pediatric outpatient antimicrobial orders, pediatric discharge prescriptions and pediatric prescriptions ordered from the outpatient setting - No significant difference in pharmacist satisfaction with providers' prescribing of pediatric outpatient orders **Conclusion-** Results suggest that there was no statistically significant difference pre- vs post-implementation
Sonya Anderson – Large PGY2 Medication Use Safety and Policy	Meghan Lehmann	Comparison of bupivacaine liposomal to immediate release bupivacaine for post-operative pain control in pediatric patients	**Primary Objective:** Compare total opioid consumption in the first 24 hours after surgery in pediatric patients who received liposomal bupivacaine with those who received IR bupivacaine • There were no significant differences in 24 hour postoperative opioid consumption between LB and IRB (36 MME vs. 41.64 MME, p = 0.445). Additionally, IRB was found to be non-inferior to LB with a less than 63.53% increase in 24 hour postoperative total opioid consumption. **Secondary Objectives** 1. Compare total opioid consumption in the first 72 hours after surgery in pediatric patients who received liposomal bupivacaine with those who received IR bupivacaine • There were also no differences in 72 hour postoperative doses of opioids (70.31 MME vs. 67.26 MME, p = 0.696; 0.95 MME/kg vs. 1.22 MME/kg, p = 0.302). 2. Compare total non-opioid analgesic consumption in the first 24 and 72 hours after surgery in pediatric patients who received liposomal bupivacaine with those who received IR bupivacaine • There were no differences in 24 hour postoperative doses of APAP (1800 mg vs. 2600 mg, p = 0.257), ibuprofen (0 mg vs. 0 mg, p = 0.534), ketorolac use (45 mg vs. 0 mg, p = 0.119), or gabapentin use (0 mg vs. 0 mg, p = 0.179). There were also no differences in 72 hour postoperative doses of ibuprofen (0 mg vs. 0 mg, p = 0.292), ketorolac use (53 mg vs. 0, p = 0.338), and gabapentin use (0 mg vs. 0 mg, p = 0.174). There was however a significant difference in 72 hour postoperative APAP use (3600 mg vs. 5200 mg, p = 0.049). 3. Compare the time to first rescue analgesic use in pediatric patients who received liposomal bupivacaine with those who received IR bupivacaine • There were no significant differences in time to first PRN use of an opioid between LB and IRB (1.25 hours vs. 1.05 hours, p = 0.883) and first PRN use of a non-opioid (33.25 hours vs. 38.38 hours, p = 0.946). 4. Evaluate the differences in total length of stay between pediatric patients who received liposomal bupivacaine and those who received IR bupivacaine

			• There were also no significant differences between LB and IRB in LOS (3.1 days vs. 3.9 days, p = 0.240).
Sonya Anderson – Small PGY2 Medication Use Safety and Policy	Mandy Leonard	Rifaximin Use in Non-ICU Adult Patients	**Primary Objective:** To describe prescribing practices of rifaximin in non-ICU adult patients at Cleveland Clinic Main Campus. • While inpatient, the majority of patients were prescribed rifaximin for HE prophylaxis (42.6%), HE treatment (40.7%), and SIBO (14.7%). A small portion of patients also utilized rifaximin for IBS-D (1.0%) and other indications such as pouchitis (1.0%). For HE prophylaxis, the majority of patients were on rifaximin for continuation of therapy (93.1%). For HE treatment, while the majority of patients were on rifaximin for continuation of therapy (55.4%), there were a significant number of new starts while inpatient (44.6%). For SIBO, the majority of patients were new starts (66.7%). For IBS-D, rifaximin for continuation of therapy (50.0%) and new starts (50.0%) were evenly split. Lastly, for pouchitis, all patients were on rifaximin for continuation of therapy (100%). **Secondary Objectives** 1. To assess adherence to formulary restriction criteria for rifaximin in non-ICU adult patients at Cleveland Clinic Main Campus • The majority of rifaximin use was appropriate (76.5%) (Table 6). Reasons for inappropriate use consisted of use in SIBO (63.8%), lactulose not being previously failed (14.9%), home lactulose not being restarted while inpatient (10.6%), patient refusing lactulose (4.3%), use in IBS-D (4.3%), and use in pouchitis (2.1%). 2. To evaluate the consistency of rifaximin's dosing scheme with the selected indication • For dosing strategy, the majority of patients were prescribed rifaximin 550 mg twice daily (BID) (90.2%), with a small proportion of patients being prescribed 550 mg three times daily (TID) (7.8%), 400 mg TID (0.5%), and other dosing strategies (1.5%). 3. To identify the inpatient services or consultants responsible for prescribing rifaximin • Primary services mostly consisted of Gastroenterology/Hepatology (57.0%), with additional services consisting of Internal Medicine (22.5%), Transplant (6.5%), General Surgery (2.0%), and other services (12.0%). Consulting services were not typically the ones to initiate rifaximin (12.0%), with Gastroenterology/Hepatology initiating rifaximin in 11.5% of patients and Infectious Disease initiating rifaximin in 0.5% of patients.
Clare Dyczkowski – PGY2 Oncology	Joslyn Rudoni, Heena Patel, Austin Kurkowski, Simon Lam, Dr. Brian T. Hill, Dr. Allison Winter	Characterization of Frequency and Timing of Tumor Lysis in Patients with Lymphoid Malignancies Treated with Venetoclax	The majority of laboratory TLS events (84.6%) in studied patients with CLL, SLL, WM, and MCL occurred during the first two dose weeks. The incidence of laboratory TLS decreased from 11.8% on week 1 to 4.8% on week 2 and further lowered to 1.1% between week 3 and 5. One patient (1.5%) experienced a second episode of laboratory TLS. Clinical TLS was reported in 5.9% of patients during week 1 only; no episodes of clinical TLS were identified thereafter. Baseline risk was correlated with an incidence of laboratory TLS (p=0.002) but not incidence of clinical TLS (p=1.000). Isolated laboratory abnormalities that did not meet criteria for TLS were seen in a frequency of 0-30.9% and were managed with standard of care without sequelae.

			This study provides data that incidence of TLS decreases with each subsequent venetoclax ramp-up with the highest risk during initiation. Institutional venetoclax ramp-up policy was modified based on results. Future studies may be conducted to assess safety and benefits of this approach.
Richa Shah – Large PGY2 Oncology	Madeline Waldron, Caitlin Siebenaller, Kelly Gaffney	Oral chemotherapy dosing during maintenance therapy for young patients with Acute Lymphoblastic Leukemia	A total of 13 patients were included in this analysis. Median weekly starting doses of MTX and 6MP were 19.6 and 511.6 mg/m^2, respectively. Twelve of the 13 patients experienced toxicity that required dose adjustments. Hepatotoxicity was the most common (n=8), followed by neutropenia (n=5), GI toxicity (n=5), thrombocytopenia (n=3), pancreatitis (n=2), and infection (n=1). A total of 130 dose adjustments were issued. Seventy six of the 130 adjustments were dose interruptions, 5 were dose reductions, and 49 were dose escalations. Of the dose interruptions, the most common reasons were hepatotoxicity (n=28 interruptions), neutropenia (n=23), and pancreatitis (n=11).Of the dose escalations, all but nine were re-escalations after doses were previously interrupted and restarted at a lower dose due to hepatotoxicity (n=13) or hematologic toxicity (n=21). Dose reductions were rare and occurred due to hepatotoxicity (n=1), GI toxicity (n=1), weight decrease (n=1), or multiple reasons (n=2). For hepatotoxicity, the most common adjustment type was interruption. Median durations of interruption were 8, 16, and 20 days for grades 1, 2, and ≥3, respectively. When doses were re-initiated, most cases had AST/ALT elevations ≤ grade 1. Doses were restarted at a lower doses in approximately half of the cases with a median dose reduction of 30-40%. Doses were re-escalated approximately monthly at a median of 12.5% per re-escalation. All cases of neutropenia were managed by dose interruptions. Most occurred when ANC was below 1000. Median durations of interruption were 9 and 18 days for ANC 500-1000 and <500, respectively. When doses were re-initiated, 18 cases occurred with ANC WNL and three with ANC between 500-1000. Doses were restarted at a reduced dose in 15 of the 23 interruptions, with a reduction of 25-30% and 35-40% for ANC 500-1000 and <500, respectively. Dose re-escalations occurred approximately monthly at a median of 12.5% per re-escalation. Pancreatitis led to 11 dose interruptions due to grade 3 (n=2) and grade 4 (n=9) toxicity. In all cases, 6MP and/or MTX were held until resolution of symptoms and normalization of serum lipase with a median duration of interruption of 36 days. Doses were re-initiated at a lower doses in four of the nine cases of grade 4 pancreatitis at a median of 50% dose reduction. Dose re-escalations after grade 4 pancreatitis occurred in six cases approximately monthly at a median of 15.2% per re-escalation.

			Seven of the 13 patients completed maintenance therapy with a median duration of 2.2 years from day 1 of interim maintenance. Three had ongoing treatment at time of data cutoff. Four relapses occurred, three of which occurred during maintenance therapy. The average dose intensities did not differ between patients who did and did not relapse. Based on the dose adjustment information found, dose adjustment guides based on toxicity were proposed.
Yanni Koukounas – Small PGY2 Oncology	Anthony Zembillas, Jessica Hoover, Elizabeth Dahl	Assessing short-term adverse events associated with anti-thymocyte globulin administration in pediatric bone marrow and solid organ transplantation	**Primary Objective:** Characterize the frequency and timing of febrile events during the BMT conditioning and SOT induction phases when ATG is included as part of the preparative regimen • BMT (median fevers per ATG window): ATG_1 = 2; ATG_2 = 2; ATG_3 = 3; ATG_4 = 0; ATG_5 = 1 • SOT (median fevers per ATG window): ATG_1 = 5; ATG_2 = 4; ATG_3 = 2; ATG_4 = 1; ATG_5 = 0 • Fevers were observed most during the first three ATG windows, which was expected since all patients in the study received at least three doses of ATG **Secondary Objectives:** 1. Identify daily dose requirements of each premedication 24 hours following the completion of the final ATG infusion • BMT: ~1 mg/kg methylprednisolone & diphenhydramine & famotidine; ~20-30 mg/kg acetaminophen • SOT: tapered methylprednisolone (~15 mg/kg, ~2 mg/kg, ~1 mg/kg); ~1 mg/kg diphenhydramine; 0 mg/kg famotidine; ~30-50 mg/kg acetaminophen 2. Describe infusion-related events during the BMT conditioning and SOT induction phases • BMT: A median of 3 events of hypotension per ATG window; minimal events of tachycardia and decreased oxygen saturation (median 0 for both per ATG window) • SOT: More frequent hypotensive events (6-9 per ATG window); minimal events of tachycardia and decreased oxygen saturation (median 0-1 for both per ATG window) 3. Describe antimicrobial usage during the BMT conditioning and SOT induction phases • BMT: almost all received systemic antimicrobial prophylaxis against bacteria, viruses, fungi, and PJP • SOT: most received antibacterial prophylaxis in the form of surgical prophylaxis with cefazolin, but few patients received other prophylactic antimicrobials during the ATG administration period.

			• Thirty-six additional cultures/tests were obtained outside of standard ones that are used for monitoring purposes. While patients did experience fevers throughout the ATG administration period, there was only one positive blood culture that speciated as Klebsiella, which ultimately required an escalation in antibiotics.