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INPHARMATION
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Resident Fall CE Summaries

Liz Ferengul, PharmD

Multisystem Inflammatory Syndrome in Children (MIS-C) is a disease state that arose from the COVID-19 pandemic. At first it was thought to be Kawasaki Disease then it was discovered to be its own disease state. Children would present weeks to months after having COVID-19. It is a hyperinflammatory response that involves at least 2 organ systems. Children present with a fever, rash and elevated inflammatory markers. First line treatment is IVIG, glucocorticoids, and aspirin. Biologic agents are used if first line treatment in contraindicated or in refractory disease. The long-term effects are still being studied.

Roxana Palacios, PharmD

The prevalence is high for patients presenting to the emergency department (ED) for acute pain management. Although opioids may be a great option for some patients, not all patients should receive an opioid to manage their pain. The opioid crisis continues to affect many patients in the United States. As pharmacist, we need to work together with other health care clinicians to provide the best treatment options for acute pain management in the ED. Using a multi-modal approach for the most common complaints of acute pain, we can reduce the number of opioids being dispensed, decrease the adverse events associated with opioids, and provide a more targeted approach for acute pain management.

Emilie Muvundamina, PharmD

Tacrolimus is a calcineurin inhibitor whose mechanism involves the formation of a complex with FKBP-12 to inhibit calcineurin from allowing NFAT entry into the nucleus. This results in decreased formation of the IL-2 cytokine and a diminished immune response. This drug is common in patients post solid organ transplant, therefore pharmacists can play an influential role in tacrolimus management. First, pharmacists can assess general pharmacokinetic principles affecting a patient's ability to respond to tacrolimus including variable elimination post -transplant and variable elimination for each formulation. Second, pharmacists play an instrumental role in recognition of patient specific pharmacokinetic co-variates significantly affecting drug dosing such as the presence of the CYP3A5 genotype, time from transplant, changes in hematocrit, and total body weight. Finally, advising on adverse effects, toxicity, interactions, therapeutic drug monitoring, and formulation variations conclude some of the ways that pharmacists can contribute to tacrolimus management.

Rhea Soltau, PharmD

Status epilepticus affects up to 100,000 patients per year with a mortality rate of up to 30%. Despite the significant morbidity and mortality, appropriate treatment is often underutilized for various reasons. The American Epilepsy Society updated their guidelines in 2016 to reflect literature updates on appropriate selection and dosing of antiepileptics. A major change that was incorporated included a higher loading dose of levetiracetam. The ESETT Trial evaluated the efficacy and safety of levetiracetam, fosphenytoin and valproate use and dosing in refractory status epilepticus. While the results of the trial found similar efficacy between all three interventions, it also found less adverse events with levetiracetam, even when using a higher dose of 4500 mg. The use of high-dose levetiracetam is a safe and effective option for treating status epilepticus and should be employed when treating refractory status epileptics.

New Pharmacist Spotlight

Liliana Pimental, PharmD, BCIDP

I grew up in Tampa Bay and graduated from the University of Florida college of pharmacy (go Gata!). After PGY1, I moved up to Brooklyn for my PGY2 in ID and eventually over to Baton Rouge for my dream job at OLOL! I love ID because change is inherent in this field, and while new challenges continue to arise, pharmacotherapy remains at the core of treatment. Outside of work, I like to discover new places, reconnect with old friends, and post up in a cozy tea shop. Some fun facts about me: I adore all things Japanese, my favorite holiday is Halloween, and I have 6 kitties (bonus points if you can guess their names).

Featured Studies

An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes [1] Analysis by Roxana

Objective: To determine if teplizumab treatment would prevent or delay the onset of clinical type 1 diabetes in high-risk persons

Methods: Phase 2, placebo-controlled, double blind RCT

Intervention: Teplizumab, a single 14-day course , follow up to progression to clinical type 1 diabetes using oral glucose-tolerance test at 6-month intervals

Patient population: ≥ 8 years of age, nondiabetic relatives of patients with type 1 DM, evidence of dysglycemia during an oral glucose-tolerance test , ≥ 2 diabetes related autoantibodies detected

Results:

- Primary outcome: median time to the diagnosis of type 1 diabetes was 48.4 months in the teplizumab group vs 24.4 months in the placebo group; HR 0.41 (95% CI, 0.22 to 0.78); P=0.006
- Type I DM diagnosed in 43% of teplizumab vs. 72% in the placebo group
- Annualized rates of diagnosis of diabetes were 14.9% per year in the teplizumab group and 35.9% per year in the placebo group

Safety: In the teplizumab group lymphocyte count decreased to a nadir on day 5 (total decrease, 72.3%; IQR, 82.1 to 68.4; P<0.001) and spontaneous resolving rash occurred in 36% of the patients on teplizumab

Limitations: small trial, mostly non-Hispanic white participants, drug was given for only one course although repeated doses may provide additional benefits

Clinical applications/role in practice: Teplizumab delayed progression to clinical type 1 diabetes in high-risk participants

Trial of Sodium Phenylbutyrate–Taurursodiol for Amyotrophic Lateral Sclerosis [2] Analysis by Emilie

Objective: To assess if sodium phenylbutyrate-taurursodiol will result is slower functional decline than placebo

Methods: Multicenter, randomized, double-blind phase 2 clinical trial. From June 2017 to September 2019.

Intervention: Sodium phenylbutyrate-taurursodiol, enteral powder x 24 weeks

Patient population: Adults with definite ALS (Amytrophic Lateral Sclerosis) with symptom onset in the 18 preceding months , slow vital capacity > 60% predicted , no riluzole use in the 30 days preceding initial screening for trial

Primary outcome: rate of decline in ALSFRS-R (Amyotrophic Lateral Sclerosis Functional Rating Scale–Revised) from baseline at 24 weeks; modified intention to treat population sodium phylbutyrate-taurursodil vs placebo: -1.24 vs -1.66 points per month (95% CI, 0.03 to 0.81); P=0.03

Safety: There was a higher incidence of severe adverse events in the placebo group, however adverse events were reported in 97% and 96% in intervention and placebo groups respectively.

Limitations: study population is not representative of the whole, primary outcome assessment with combined adjustments for concomitant therapy not provided, power was not met, ALSFRF-R is debatably not an appropriate measurement of ALS severity

Clinical applications/role in practice: Sodium Phenylbutyrate-Taurursodiol has been associated with a decrease in neuronal destruction making it an ideal drug for ALS

1.Herold KC, Bundy BN, Long SA, et al. An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes [published correction appears in N Engl J Med. 2020 Feb 6;382(6):586]. N Engl J Med. 2019;381(7):603-613. doi:10.1056/NEJMoa1902226

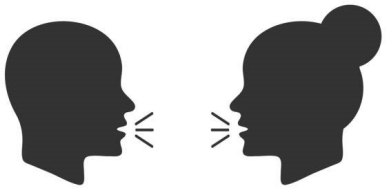
2. Paganoni S, Machlin EA, Hendrix S, et al. Trial of Sodium Phenylbutyrate-Taurursodiol for Amyotrophic Lateral Sclerosis. N Engl J Med 2020; 383:919-930.

Patient Safety Corner

A Diltiazem drip was ordered for a patient with documented AFib with RVR. The patient had a documented allergy of Amlodipine. An I-vent was placed, and the cardiologist was contacted with no response. The primary team was not contacted until the next morning almost 20 hours after the original order was placed to ask about the allergy.

Things to remember when verifying orders

- **Closed loop communication:** if specialist doesn't respond you can also reach out to the primary team
- **Closed loop communication:** hand off any outstanding I-vents or problems to the next shift.
- Always contact provider with an alternative option. Reach out to the clinical team or a friend if you need help
- Do not leave medication in the queue that need to be given urgently
- When in doubt, ask a friend



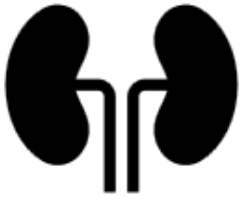
Terlivaz (Terlipressin)

Terlivaz was FDA approved in September of 2022 for adults with hepatorenal syndrome (HRS) with rapid reduction in kidney function. The phase 3 randomized, placebo controlled, clinical trial compared terlipressin plus albumin to placebo. The trial included approximately 300 patients who had HRS-1, cirrhosis, ascites and rapidly progressive kidney failure with a serum creatine of at least 2.25 mg/dL. Patients received 1 mg of terlipressin IV over 2 minutes every 5.5 to 6.5 hours plus albumin 1 g/kg with a maximum of 100 g on day 1 then 20-40 g daily thereafter. The primary end point was verified reversal of HRS which was measured by two consecutive serum creatinine of ≤1.5 mg/dL and survival without renal replacement for at least 10 days. The primary endpoint was statistically significant with a p-value of 0.006. Adverse effects with a higher rate of incidents in the terlipressin group included respiratory failure in 20 patients (10%) verse 3 patients (3%) in the placebo group. Additionally patients experienced more nausea, abdominal pain, and diarrhea in the terlipressin group. The terlipressin group experienced less hepatobiliary disorder overall, 37 patients (18%) verse 29 patients (29%) in placebo. In conclusion, terlipressin shows promise for the rare disease state.

P&T Update

Ceftazidime automatic interchange update

Ceftazidime (Ordered)	Cefepime (Interchange)
1g q8h	2g q12h
2g q12h	
2g q8h	2g q8h



Recent FDA Approvals

Tzield (teplizumab-mzwv)

11/18/22

To delay the onset of stage 3 type 1 diabetes

Elahere (mirvetuximab soravtansine-gynx)

11/14/22

To treat patients with recurrent ovarian cancer that is resistant to platinum therapy

Reyvrio (sodium phenylbutyrate/taurursodiol)

9/29/22

To treat amyotrophic lateral sclerosis (ALS)

References
1. FDA. FDA approved treatment to improve kidney function in adults with HRS.
2. Wong F, Pappas SC, Curry MP, et al. Terlipressin plus Albumin for the Treatment of Type 1 Hepatorenal Syndrome. N Engl J Med. 2021 Mar 4;384(9):818-828.

Word Search—Drugs and Bugs

T H R M V Q M X W X C Y T W C O M R T R
I H N R X D J D B P U L X Q L E J A C Y
M T V B S T R X T C L N M J I L A N G X
M Y T P J K N D M D T D U I N O N T A I
B Z L A E E P P F E U B L E D Z T I D I
D T J T N U W R T Z R C S J A A I B I C
E D A H N L U O M A E Y U N M N V I D E
Z Z Y O P X Z T J L S V F X Y O I O N V
X R M G F D M E R F G P J T C C R T A O
D I D E O V Y U A U C K E Y I U A I C R
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V J U V A T E W O H H E P K L I L Y C V
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P B E X T L I U T P L R N C Y P N I T S
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G E N A V R M W A F M K F D O O A E A C
Q O B L Y V D I P O H U I C Q G E D N J

Proteus Candida Aspergillus

Fluconazole Jirovecii Toxoplasma

Antiviral Pathogen Clindamycin

Antibiotic Culture Fungus

Foscarnet

Wordle