

PEDIANNEWS

The Official Newsletter of RxPups - Student Society of Pediatric Advocates

PediaNews Coordinator: Veli Uzunova | Pharm.D Candidate 2023

Editors

Linda Logan, Pharm.D, BCPS, BCPP, BCACP | Faculty Advisor

Aubrey Slaughter, Pharm.D | PGY-2 Pharmacy Resident

OUR MISSION

The Student Society of Pediatric Advocates is a student organization affiliated with the University of Georgia College of Pharmacy. We are a student group associated with the Pediatric Pharmacy Advocacy Group. The Mission of the SSPA is to bring awareness to the proper use of medication therapy in pediatric populations through various service and education-based initiatives. Service activities center around lending our medication-based knowledge to pediatric patients and their parents in our community. Educational activities are directed toward student members in an effort to safely and effectively extend pharmacy practice to pediatric populations by building relationships with mentors and professionals in the health care community, as well as supplementing didactic coursework with lectures by specialists and our peers. Overall, SSPA advocates for the safety and happiness of young patients while learning and having fun along the way. The purpose of our newsletter is to educate pharmacy students about pediatric pharmacy and advocate for pediatric patients within the University of Georgia College of Pharmacy.

2021-2022 EXECUTIVE BOARD

PRESIDENT: GIGI SANI

PRESIDENT-ELECT: KARA PHILLIPS

VICE PRESIDENT: MADISON O'NEAL

TREASURER: VICTOR NGUYEN

SECRETARY: ELIZABETH SEVIER

PUBLIC RELATIONS CHAIR: KAITLIN GROUT

MIRACLE LIAISON: MARWAH ALZER

MIRACLE LIAISON: ASHTON DICKINSON

FUNDRAISING CHAIR: SARINA DESAI

DISTANT CAMPUS LIAISONS: LAURA RAMIREZ

INSIDE THIS ISSUE

**THE FUTURE OF DOLUTEGRAVIR
IN FIRST- OR SECOND-LINE
TREATMENT FOR HIV-1
INFECTION IN CHILDREN AND
ADOLESCENTS - PAGE 2**

**COMPARISON OF PEDIATRIC
TREATMENTS FOR SCABIES -
PAGE 4**

**PEDIATRIC AND NEONATAL
SEPSIS - PAGE 6**

**RIKAFTA: A REVOLUTIONARY
NEW TREATMENT FOR CYSTIC
FIBROSIS - PAGE 9**



**UNIVERSITY OF
GEORGIA**
College of Pharmacy

The Future of Dolutegravir in First- or Second-Line Treatment for HIV-1 Infection in Children and Adolescents

Written by Emma Peacock, Pharm.D Candidate 2025

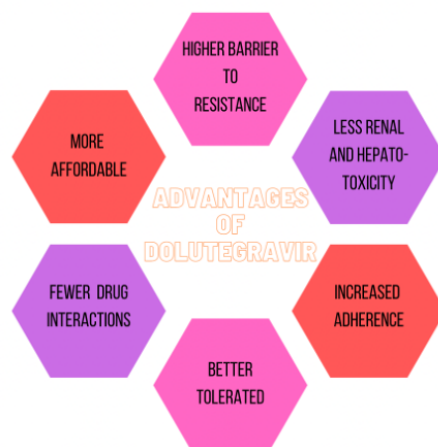
Nearly 1.8 million children and adolescents under the age of 15 are infected with human immunodeficiency virus (HIV), and specifically HIV-1. HIV damages a person's immune system, inhibiting its ability to fight off infections. This damage happens at a significantly faster rate in children than adults. [1] Symptoms of HIV-1 in pediatric patients include persistent fevers, loss of appetite, frequent diarrhea, poor weight gain or rapid weight loss, persistently swollen lymph nodes, extreme fatigue that shows no remittance, white spots in the oral cavity, and recurring or unusual infections. While there is no cure, early diagnosis and effective treatment has a significant impact on keeping patients' healthy quality and length of life. [1] Anti-retroviral therapy (ART) can be complicated by common HIV complications such as tuberculosis and other serious viruses. Common side effects of antiretrovirals include bone loss, heart disease, liver damage, increased incidence of diabetes, kidney damage, and psychosis. Additionally, common medications have multiple drug interactions, a high cost, and demonstrate toxic effects. [2]

To diagnose and confirm HIV-1 in pediatric patients, two positive virologic assay results are needed. The goals of HIV treatment is to reduce HIV-related mortality and morbidity, restore and preserve immune function, maximize viral replication suppression, minimize drug-related toxicity, maintain normal physical growth and neurocognitive development, as well as improve quality of life. [2] Currently, the Food and Drug Administration (FDA) and World Health Organization (WHO) recommend initiating ART with combination therapy of three drugs that are a dual nucleoside/nucleotide reverse

transcriptase inhibitors (NRTI) backbone and either a non-nucleoside reverse transcriptase inhibitor (NNRTI) or boosted protease inhibitor (PI). The combination therapy chosen should not include more than two of these pharmacologic classes. Current ART for pediatrics is limited, significantly less researched than adult treatment, and statistically has worse outcomes than treatment in adults. [3] Dolutegravir is not currently included in ART pediatric standard of care (SOC).

Dolutegravir is second generation HIV integrase strand-transfer inhibitor (INSTI). While not part of current SOC, dolutegravir (Tivicay) tablets and pediatric drop (PD) tablets for suspension was approved by FDA for use in pediatric patients of at least 4 weeks old and 3 kg weight in combination with other ART drugs on June 12, 2020. [2] Promising clinical trials with adults have led to its inclusion in national treatment protocols and emergence as a first- or second-line treatment for HIV-1 infection.

A recently published open-label, randomized trial, known as the Odyssey trial, conducted 96-week on dolutegravir-based ART conducted between 2016 and 2020 revealed promising results. The Odyssey trial included 707 children and adolescents weighing at least 14 kg (median weight of 30.7 kg) and from the ages of 2 to 18 (median age of 12.2) with 49% of the participants being female. Participants were from Uganda, Zimbabwe, South Africa, Thailand, and Europe. The study was conducted comparing a 1:1 ratio of dolutegravir-based therapy with current standard of care treatment.



As recommended by the FDA and European Medicines Agency (EMA), 5 mg dolutegravir tablets taken once daily were used to initiate therapy followed up by 50 mg film-coated tablets in participants over 20 kg and 25 mg PD tablets in those other administered once daily for maintenance. Throughout the course of the study, participant height, weight, HIV disease stage, WBC, CD4+ count, liver function, BMD, ADR, and adherence were continually assessed. [3]

In the study, dolutegravir-based ART demonstrated superior efficacy when compared to current SOC. [4] Results were consistent when compared across age, weight bands, sex, and NRTI backbone therapies. Additionally, participants receiving dolutegravir-based ART had a 40% lower treatment failure rate, better adherence, no antiviral resistance suggesting a higher barrier to INSTI resistance and protection against NRTI resistance. While side effects and adverse reactions were similar, they occurred at lower rates specifically with better lipid and liver function profiles. [3]

Overall, dolutegravir demonstrated significantly better virologic suppression and protection against drug resistance. Overall, benefits of dolutegravir compared to other drugs include higher effectiveness, well tolerated, easier administration leading to increased adherence, fewer interactions, higher barrier to resistance, and significantly more affordable. Results of similar studies have expedited worldwide interest and treatment of dolutegravir to make it a possible alternative for children living with HIV-1 infection. It is probable that dolutegravir will potentially emerge as a first- or second-line HIV-1 infection treatment option with better long-term maintenance results. [5]

References

1. HIV and AIDS: Information for Families, (n.d.). Retrieved March 18, 2021, from <https://healthychildren.org/English/health-issues/conditions/sexually-transmitted/Pages/HIV-and-AIDS.aspx>
2. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection, (n.d.). Retrieved March 15, 2021, from <https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/regimens-recommended-initial-therapy-antiretroviral-naive-children?view=full>
3. FDA Approves Drug to Treat Infants and Children with HIV, (n.d.). Retrieved March 18, 2021, from <https://www.hiv.gov/blog/fda-approves-new-drug-treat-infants-and-children-hiv>.
4. Guidelines for Use of Antiretroviral Agents in Pediatric HIV Infection, (n.d.). Retrieved March 19, 2021, from <https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/whats-new-guidelines>
5. Turkova A, White E, Mujuru AR, et. al. Dolutegravir as First- or Second-Line Treatment for HIV-1 Infection in Children. *New England Journal of Medicine*. 2021; 385(27):2531-2543. <https://doi.org/10.1056/NEJMoa2108793>

Comparison of Pediatric Treatments for Scabies

Written by Sam Van Horn, Pharm.D Candidate 2025

Scabies (*Sarcoptes scabiei*), an infection found commonly in children, presents as excessive itching, pervasive rash, and lack of feeding. At the beginning of the latent period, the microscopic mite delves into the epidermis, where the parasite inhabits and breeds. The primary mode of transmission is through skin-to-skin contact, which results in infection rates as high as 300 million people worldwide because of how easily it spreads from close body contact. [1] The prevalence of scabies in children is estimated to be 5-10%, with the highest prevalence being found in children younger than two years of age. [2] Current treatments are permethrin and ivermectin (Soolantra®). Both medications interact with electrolyte channels inside the parasite to cause paralysis and death of the parasite. Although effective for scabies, these anti-parasitic medications have an increasing resistance rate. The United States Food and Drug Administration (FDA) has approved spinosad (Natroba™), as an effective treatment for scabies, providing a new treatment option for pediatric patients with scabies.

Currently, oral ivermectin and topical permethrin are the preferred treatment options. The FDA has approved topical permethrin, topical sulfur, benzyl benzoate, and crotamiton for infantile scabies. However, topical permethrin is not approved for scabies in patients younger than two months old. The recommended treatment for patients younger than two months is either topical crotamiton or sulfur. However, the efficacy of sulfur and crotamiton are significantly lower than ivermectin, permethrin, and spinosad. Permethrin has minimal toxicity and irritation, which makes it very suitable for children and pregnant patients. [3]

Permethrin would be an efficacious option for children under two months, but it has been known to cause eczematous reactions in patients under two months. [2] Although the topical permethrin can treat children younger than ivermectin and spinosad, there is an increasing concern about resistance to the treatment. In a recent study, only 34 patients out of 155 responded to permethrin, which is considered the first-line therapy for scabies. [4] In the same study, 96 patients failed permethrin treatment after a median of two cycles. [4] This raises concern for the effective treatment of infants diagnosed with scabies.

Ivermectin, the only oral medication that treats scabies, has a similar effectiveness with two doses compared to 5% permethrin. [3] The initial concern with ivermectin was the concern for neurotoxicity, but recent studies show that ivermectin is safe. [2] Although effective, the FDA has not approved ivermectin for children less than five years old and less than 15 kilograms. [5] This creates a problem, since children younger than five in lower economic environments are at a higher risk. Without effective treatment, substantial economic burden and mortality can occur in countries experiencing the scabies endemic. In a study using ivermectin, doctors treated fifteen patients under one year of age and below 15 kilograms with ivermectin after the permethrin proved ineffective. [2] Ivermectin cured 13 out of 14 patients after three months. [2] In another study with 30 patients under 15 kilograms, patients were treated with ivermectin. At follow-up, all infants were considered cured, which provides strong evidence for infantile scabies treatment. [2]

As a potential new treatment, spinosad has been studied to determine its efficacy against scabies. The FDA previously approved a 0.9% formulation to treat lice, where it acts as an

insecticide with a low side effect profile compared to ivermectin and permethrin. In a recent study, researchers tested a 0.9% topical suspension against a placebo, and 85% of patients that placed the topical formulation on the skin for at least six hours showed a microscopic cure of scabies on the 28th day. [1] The vehicle showed a 51% microscopic cure on day 28, but this may have resulted from male mites living on the skin surface where they could be rubbed or scratched off. [1] In this study, the age range was 8-40 years old, and adverse events occurred in two subjects. The FDA approved this treatment for patients 4 years or older experiencing a scabies infection. Even with minimal side effects, it is efficacious based on the previous studies, and there is little concern about arising resistance. However, this treatment option still lacks approval in pediatric patients under four years old.

All three treatments, oral ivermectin, topical permethrin, and topical spinosad, provide effective relief for scabies infections. However, there are various limitations to these medications and unpleasant adverse effects make some of these treatments undesirable. In patients under two months of age, topical permethrin was reported to cause eczematous reactions [2] and oral ivermectin adverse effects include mildly elevated creatinine kinase levels, eczema flare-ups, diarrhea, vomiting, transient nervousness and irritability, transient pruritus, and pustular skin reactions. [2] For topical spinosad, patients tolerated the treatment well with no safety concerns. Ivermectin is only approved for those above five years old and above 15 kilograms due to concerns of neurotoxicity and encephalopathy. [6]

Permethrin has not been approved for scabies patients younger than two months old due to neurotoxicities. [6] Although permethrin is most commonly used, there is increasing concern regarding the resistance of scabies to permethrin. Because of these issues, sulfur is commonly used in patients under two months old. However, the cure rate for ivermectin is higher than sulfur after one to two weeks of treatment, as well as after six weeks of treatment. [7] With spinosad, there is increased effectiveness in the cure of scabies, no signs of arising resistance, and a low side effect profile, but the FDA has only approved it for patients older than 4 years old. With additional studies for patients under four years old, spinosad could become the new preferred treatment and cure for the under-recognized topical disease, scabies, which affects over 300 million people globally.

References

1. Seiler JC, et al. Spinosad at 0.9% in the treatment of scabies: Efficacy results from 2 multicenter, randomized, double-blind, vehicle-controlled studies. *Journal of the American Academy of Dermatology*. 2022;86(1): 97-103. doi:10.1016/j.jaad.2021.07.074
2. Lobo Y, Wheller L. A narrative review of the roles of topical permethrin and oral ivermectin in the management of infantile scabies. *The Australasian Journal of Dermatology*. 2021;62(3): 267-277. doi:10.1111/ajd.13654
3. Motswaledi HM, et al. Clinical diagnosis and treatment of scabies, a neglected tropical disease. *South African Family Practice*. 2021;63(1): e1-e6. doi:10.4102/safp.v63i1.5224
4. Balestri R, et al. Scabies is becoming less sensitive to permethrin therapy. *Journal of the European Academy of Dermatology and Venereology*. 2021;35(12): e889-e891. doi:10.1111/jdv.17538
5. Chiu S, Argaez C. Ivermectin for Parasitic Skin Infections of Scabies: A Review of Comparative Clinical Effectiveness, Cost-Effectiveness, and Guidelines. *Canadian Agency for Drugs and Technologies in Health*. 2019.
6. Thomas C, et al. Treatment practices in the management of scabies in infants younger than two months. *Pediatric Dermatology*. 2021;38(2): 431-435. doi:10.1111/pde.14523
7. Mila-Kierzenkowska C, et al. Comparative Efficacy of Topical Permethrin, Crothamiton and Sulfur Ointment in Treatment of Scabies. *Journal of Arthropod-borne Diseases*. 2017;11(1): 1-9.

Pediatric and Neonatal Sepsis

Written by Maddie Marsh, Pharm.D Candidate 2023

According to the World Health Organization (WHO), sepsis has a huge impact on global mortality. [1] Children have a high incidence of sepsis, especially neonates, with an estimated 3 million babies affected worldwide and mortality ranging from 11 to 19%. [2] Approximately 85% of all sepsis cases and sepsis-related deaths worldwide occurred in low- and middle-income countries. [1] If not recognized early, sepsis can lead to septic shock, multiple organ failure, and death. Behind pre-term birth, infections including sepsis are the leading cause of neonatal death worldwide. [1]

What is sepsis?

People assume that sepsis and bacteremia are the same disease state, but they actually are different. Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. [1] In order to adequately treat a patient with sepsis, the disease must be recognized quickly. With neonates and children, there are specific signs and symptoms that indicate sepsis. Symptoms and signs of sepsis in adults include altered mental status, rapid breathing, fever, increased heart rate, weak pulse, low blood pressure, and low urine output. [1] Children and neonates cannot communicate these symptoms to their parent or guardian. Instead, the parent might notice a fever, fast breathing, pale cold skin, and lethargy in their child. [3] For neonates, the signs are less clearly indicative of sepsis – difficulty feeding, repeated vomiting, and lack of urination. [3]

Sepsis diagnosis includes the use of a scoring system called the Sequential (Sepsis-Related) Organ Failure Assessment (SOFA). By looking at respiration, coagulation, liver, cardiovascular, central nervous system, and renal lab markers, the SOFA score shows the extent of sepsis-induced organ dysfunction. If the SOFA score changes by 2 or more units from baseline, the patient most likely has sepsis. [4]

The empiric recommendations for antibiotic treatment of sepsis change based on the age of the patient. Antibiotics need to be given within the first hour of the recognition of sepsis. If sepsis occurs within the first 7 days of life in a full-term newborn or 72 hours of life for a baby admitted to the neonatal intensive care unit (NICU), the term early-onset sepsis (EOS) is used. Late-onset sepsis (LOS) begins after 72 hours of a baby in the NICU or 7 days of life for a full-term newborn. Empirical EOS treatment is ampicillin plus gentamicin to target the possible source of *Listeria monocytogenes*. For LOS, the infection is typically hospital-acquired, making them at risk for multidrug-resistant bacterial infections. Children outside of the EOS or LOS categories can be treated with a third-generation cephalosporin, such as ceftriaxone. Physicians should consider adding vancomycin if MRSA risks are prevalent. [5]

Outside of antibiotics, sepsis treatment requires multiple supportive therapies. Fluid therapy and hemodynamic support are crucial for patient survival. Aggressive fluid resuscitation is the most important step after empiric antibiotics. Crystalloids are the fluid of choice at a quantity of 30 mL/kg within 3 hours. Assessing therapeutic endpoints in adults is typically mean arterial pressure. In young children, capillary refill time, urine output, and peripheral pulses are more reliable markers. [6]

How do we prevent sepsis from occurring in kids and neonates?

The answer to this question can be split into three different perspectives: before birth, during labor, and after delivery. Before birth, the mother's health is of the utmost importance. The mother delivers nutrients and immunity to the baby while the baby is still in the womb. Thus, healthcare providers can promote appropriate vitamin and calorie intake. They can also promote the importance of immunizations such as tetanus and influenza so that the immunity can cross the placenta and protect the baby.

During labor, it is important to maintain clean delivery practices and handwashing to prevent infections. Studies have shown that giving intrapartum antibiotic prophylaxis to mothers in developed countries has been highly effective in reducing early-onset neonatal bacterial and maternal sepsis. After delivery, mothers who are able to breastfeed can give their babies additional immunity through breast milk. Breast milk contains secretory IgA, lactoferrin, and lysozymes, but not all mothers are able to produce adequate amounts of breast milk to support a growing baby. Research shows that supplementing vitamin A in a baby's diet also leads to reductions in neonatal mortality and respiratory disease. [7]

Sepsis is one of the leading causes of death in the first few years of life. By preventing the development of sepsis or quickly identifying and aggressively treating sepsis, neonatal deaths will hopefully decrease.

References

1. Sepsis. World Health Organization. <https://www.who.int/news-room/fact-sheets/detail/sepsis>.
2. Molloy EJ, Bearer, CF. Pediatric and neonatal sepsis and inflammation. *Pediatr Res.* 2022;91:267-9. <https://doi.org/10.1038/s41390-021-01918-4>
3. Surviving sepsis campaign international guidelines: Pediatric critical care medicine. LWW. https://journals.lww.com/pccmjournal/fulltext/2020/02000/surviving_sepsis_campaign_international_guidelines.20.aspx.
4. Jones AE, Trzeciak S, Kline JA: The Sequential Organ Failure Assessment score for predicting outcome in patients with severe sepsis and evidence of hypoperfusion at the time of emergency department presentation. *Crit Care Med* 2009; 37:1649-1654. doi: 10.1097/CCM.0b013e31819def97
5. Mariani M, Parodi A, Minghetti D, et al. Early and Late Onset Neonatal Sepsis: Epidemiology and Effectiveness of Empirical Antibacterial Therapy in a III Level Neonatal Intensive Care Unit. *Antibiotics.* 2022;11(2):284. <https://doi.org/10.3390/antibiotics11020284>
6. Pont-Thibodeau GD, Joyal JS, Lacroix J. Management of Neonatal Sepsis in Term Newborns. *F1000Prime Rep.* 2014; 6:67. doi: 10.12703/P6-67
7. Edmond K, Zaidi A. New approaches to preventing, diagnosing, and treating neonatal sepsis. *PLoS Med.* 2010;7:e1000213.

Trikafta: A Revolutionary New Treatment for Cystic Fibrosis

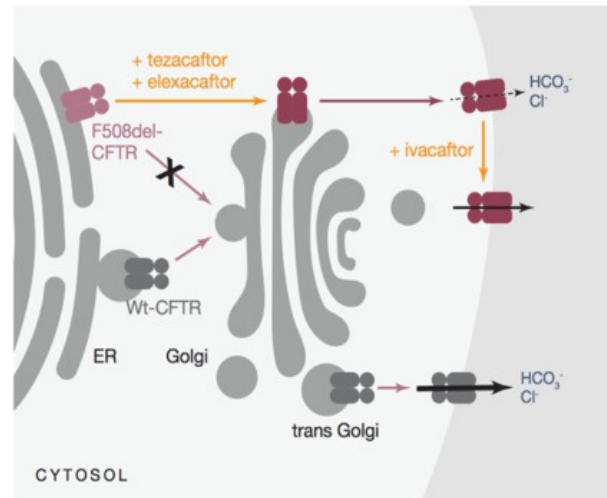
Written by Emma Covington and Alex Ruehman, Pharm.D Candidates 2025

Cystic fibrosis (CF) is a genetic disorder affecting the cells that produce mucus, sweat, and digestive fluid. In patients with CF, the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene is homozygous dominant and leads to the buildup of mucus that blocks lung airways. CF affects more than 30,000 people and approximately 1,000 new cases are diagnosed each year [1] Previous treatments include CFTR modulator therapies like Tezacaftor/Ivacaftor (Symdeko) and Lumacaftor/Ivacaftor (Orkambi), have demonstrated only modest efficacy in F508del-homozygous patients. The FDA has recently approved a triple combination therapy of Elexacaftor/Tezacaftor/Ivacaftor (Trikafta) for CF patients that are 12 years and older, which showed improved outcomes.

The deletion of phenylalanine at position 508 (F508del) is the most prevalent CF-causing mutation affecting approximately 82% of the CF population. [1] This mutation leads to CFTR protein misfolding that is not processed by the endoplasmic reticulum and prematurely destroyed by proteasomes. Target drug therapies aim to enhance the proper expression and stability of defective CFTR proteins.

There are two main mechanisms of CF drugs: potentiators and correctors. A potentiator works on the mutated CFTR channels at the plasma membrane by enhancing the opening and subsequent efflux of chloride ions. Ivacaftor (IVA) is the only FDA approved potentiator currently on the market. [2] Correctors work by restoring the natural function of the misfolded CFTR protein. Elexacaftor (ELX) is termed a next generation corrector because it binds to a different site on the CFTR protein to previous others of its kind, such as Tezacaftor (TEZ). [2] Although little is known regarding the targets of ELX

versus TEZ, clinical outcomes are measurably different, which provides the rationale for a combination approach. [2]



In evaluating the efficacy of Trikafta, clinical trials were conducted in populations 12 years and older. The first trial was a 24 week, randomized, double-blind, placebo-controlled study. This study had 403 participants who were unresponsive to previous therapy options due to their specific allelic mutations. [3] The second study was a 4 week, randomized, double-blind, active-controlled trial in 107 patients, which compared the previous dual combination product, Symdeko, to the new triple combination therapy Trikafta. [3]

Both trials of Trikafta primarily looked at the increases in percent predicted Forced Expiratory Volume in one second (ppFEV1). In the first trial, the mean ppFEV1 increased 13.8% from baseline compared to placebo and resulted in improvements in sweat chloride, number of pulmonary exacerbations, and body mass index (BMI). [3] The second trial showed an increase of 10% ppFEV1 from baseline compared to Tezacaftor/Ivacaftor (Symdeko). [3]

The FDA recently granted Trikafta orphan drug designation and a rare pediatric disease priority review voucher for the current trials in progress to expand approval to children as young as 2 years old. If approved by the FDA, this decision will revolutionize potential treatment options for children with CF.

References

1. About cystic fibrosis. Cystic Fibrosis Foundation. (n.d.). Retrieved March 19, 2022, from <https://www.cff.org/intro-cf/about-cystic-fibrosis>
2. Zaher, A., ElSaygh, J., ElSori, D., ElSaygh, H., & Sanni, A. (2021). A Review of Trikafta: Triple Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulator Therapy. *Cureus*. 2021;13(7):e16144. doi:10.7759/cureus.16144
3. FDA. (2019, October 21). FDA approves new breakthrough therapy for cystic fibrosis. U.S. Food and Drug Administration. Retrieved March 19, 2022, from <https://www.fda.gov/news-events/press-announcements/fda-approves-new-breakthrough-therapy-cystic-fibrosis>