University HOSPITAL
Newark, NJ

Pharmacy News

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Special Points of Interest:

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- University Hospital Formulary Patches informational
- Natural Killer Cell Therapy
- Dapagliflozin: The Recent Indication for Heart Failure With Reduced Ejection Fraction
- Welcome New Pharmacists
- National Pharmacy Week

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P&T Update

Formulary Additions

1. ***Teprotumumab (Tepezza®) Formulary addition request follow up***
   Formulary addition of Teprotumumab for 6 months through the White Bag Process ONLY. Further discussion for permanent formulary addition after accrual of 6 months of medication usage data
   – APPROVED
2. ***Tranexamic Acid 1g/100ml premix Line extensions***
   The formulary line extension of tranexamic acid premixed
   – APPROVED

Formulary Deletions

- NONE

Formulary Restriction Modification

1. **Rasburicase Restriction Revision**
   Rasburicase is indicated for the hyperuricemia of malignancy currently being formulary restricted to the Nephrology and Oncology Services. It is priced at about $800/ 1.5 mg vial. The usual dose is 3 mg, which could be repeated if the desired uric acid reduction is not obtained. Formulary restriction expansion on rasburicase to include the intensivists besides the Oncology/Nephrology services.
   – Approved

Policies & Procedures/Floor stocks

1. **707-400-108 Resuscitation Equipment/Emergency Boxes (update)**
   The policy is presented to update the handling processes for anaphylaxis kit and resuscitation equipment used in pediatrics department.
   – Approved
2. **707-500-110 HRHA & LASA Medications (update)**
   Policy updated to include that the hospital will not have labeling on HRHA because medications are getting stuck when pulled from pyxis. Instead, these medications will have barcoding alerts.
   – Approved
3. **707-600-127 Refrigeration units & Temperature monitoring, validation & documentation (update)**
   – Approved
4. **B-1 Diet Manual Policy Approval**
   – Approved by P&T
5. **707-600-182 Medication Reconciliation Policy**
   The policy is presented to include the comprehensive details of medication reconciliation at various phases of the patient care by different disciplines.
   – Approved

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P&T Update

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6. **707-500-115 Standard Concentration for IV Infusion Medications- Policy Update**
   An update to the existing policy is presented outlining the revised standard infusion concentrations for pediatrics/ neonatal patient population on fentanyl.
   – Approved
7. **707-600-117 Investigational Drug Services (IRB) Policy Update**
   The policy is updated with the revised IRB dispensing fee schedule and a clarified language on how the training for the 24 hours coverage studies would be performed.
   – Approved

Medication/Clinical Guidelines:

1. **Alaris Drug Library Revision Approval**
   – Approved
2. **UH Adult Staphylococcus aureus Bacteremia (SAB) Guideline: September 2020**
   – Approved
3. **UH Diabetic Ketoacidosis (DKA) Guideline for adult patients**
   – Approved

Cefiderocol: Expanding Our Antimicrobial Arsenal

Cefiderocol also known by its trade name FETROJA®, is a new FDA-approved siderophore cephalosporin antibiotic that has just been added to the University Hospital formulary with restriction to antimicrobial stewardship and infectious diseases approval.

How does Cefiderocol work?

This is a beta-lactam antibiotic structurally similar to ceftazidime and cefepime that can inhibit cell wall synthesis through binding to penicillin binding protein 3. A siderophore antibiotic like Cefiderocol, is able to chelate ferric ions and use bacterial transport systems in order to translate into high antibiotic concentrations in the periplasmic space of Gram negative organisms. This unique mechanism of action provides Cefiderocol with the ability to overcome different types of beta-lactam resistance mechanisms ranging from enzymatic hydrolysis to efflux pumps, and even porin channel mutations.

What is the spectrum of activity of Cefiderocol?

Cefiderocol has been FDA-approved for the following treatment indications:

- Complicated urinary tract infections (cUTI), including pyelonephritis
- Hospital-acquired bacterial pneumonia (HAP)
- Ventilator-associated bacterial pneumonia (VAP)

In vitro and in vivo testing have confirmed its activity against multidrug-resistant isolates of *Enterobacterales, Pseudomonas aeruginosa, Acinetobacter baumannii, and Stenotrophomonas maltophilia.* In vitro testing have observed its activity against carbapenem-resistant *Enterobacterales, carbapenem-resistant Pseudomonas aeruginosa*, and carbapenem-resistant *Acinetobacter baumannii.* Additional resistance mechanisms that Cefiderocol has demonstrated activity against include extended-spectrum beta-lactamases (ESBLs), AmpC, serine-carbapenemases (eg, KPC, OXA-48), and even metallo-carbapenemases (eg, NDM, VIM).

Cefiderocol does not possess activity against Gram-positive bacteria or anaerobic bacteria.

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What clinical data exists to support the use of Cefiderocol?

- *APEKS-cUTI trial*
  - Cefiderocol received its initial FDA approval as a result of the APEKS-cUTI trial which compared Imipenem/cilastatin to Cefiderocol for the treatment of complicated urinary tract infections, including pyelonephritis. This was a multicenter, double-blind, randomized trial where patients were randomly assigned to receive either drug for a duration of 7 to 14 days without transition to oral step-down therapy. Patients were excluded if they had a urine culture with more than 2 pathogens, presence of a fungal pathogen, or carbapenem-resistant pathogens. The most prevalent pathogens identified included *E. coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa.* The primary endpoint included composite outcome of clinical response and microbiologic response at the test-of-cure assessment of about 7 days after antibiotic treatment. This was achieved in 72.6% of the Cefiderocol group compared with 54.6% of the Imipenem/cilastatin group. Based on an adjusted treatment difference of 18.6% (95% CI, 8.2% to 28.9%; p=0.0004), Cefiderocol met the non-inferiority margin criteria. As a result of the outcomes of this study, Cefiderocol was determined to be a sufficient option for the treatment of complicated urinary tract infections, including pyelonephritis in adult patients at risk for multidrug-resistant infections.
- APEKS-NP trial
  - This was a randomized, double-blind, phase 3, non-inferiority trial that compared Cefiderocol to high-dose extended-infusion Meropenem for the treatment of nosocomial pneumonia (hospital-acquired pneumonia and ventilator-associated pneumonia). Patients were randomly assigned to receive either drug for a duration of 7 to 14 days in addition to at least 5 days of Gram positive coverage with linezolid. The majority of baseline pathogens included *E. coli, Klebsiella pneumoniae, Pseudomonas aerginosa, and Acinetobacter baumannii.* Of note, 68% of patients were in the intensive care unit at time of randomization. The primary endpoint of all-cause mortality at day 14 was 12.4% with Cefiderocol compared to 11.6% in the Meropenem group. Treatment-emergent adverse events were also similar between groups. These results demonstrated non-inferiority of Cefiderocol to Meropenem for the treatment of nosocomial pneumonia.
- CREDIBLE-CR trial
  - This last trial compared Cefiderocol to Best Available Therapy (BAT) for treatment of serious infections caused by carbapenem-resistant Gram negative bacteria. This was a randomized, open-label, multicenter, phase 3 trial where patients were randomly assigned to receive either Cefiderocol or treatment specified by the investigator for a duration of 7 to 14 days. The Cefiderocol treatment arm was able to be utilized in combination with another agent, excluding polymyxins, cephalosporins, and carbapenems. The primary endpoint was clinical cure at test of cure of about 7 days after the end of antibiotic treatment. Clinical cure for nosocomial pneumonia was achieved by 50% of patients in the Cefiderocol group 53% in the BAT; for patients with bloodstream infection or sepsis, clinical cure was achieved by 43% in the Cefiderocol group and 43% in the BAT therapy group. The results of this study concluded that Cefiderocol had similar clinical and microbiological efficacy compared to BAT for infections caused by carbapenem-resistant Gram negative bacteria resulting in its utility for patients with limited treatment options.

How is Cefiderocol administered?

Cefiderocol comes in a 1-gram powder vial for reconstitution for IV infusion in either 100mL of Normal Saline or 5% Dextrose. The following are the intravenous dosing recommendations:

CrCl (mL/min)	Dose	Frequency	Infusion Time
>120	2 grams	Every 6 hours	Over 3 hours
60-119	2 grams	Every 8 hours	
30-59	1.5 grams	Every 8 hours	
15-29	1 gram	Every 8 hours	
ESRD (CrCl <15) with or without intermittent hemodialysis	0.75 grams	Every 12 hours	

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Cefiderocol: Expanding Our Antimicrobial Arsenal

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	Effluent Flow Rate	Dose Recommended
Continuous renal replacement therapy	2 L/hr or less	1.5 grams every 12 hours
	2.1 to 3 L/hr	2 grams every 12 hours
	3.1 to 4 L/hr	1.5 grams every 8 hours
	4.1 L/hr or greater	2 grams every 8 hours

How does Cefiderocol compare to the other broad-spectrum antibiotics on the UH formulary?

	Ceftazidime-avibactam	Ceftolozane-tazobactam	Cefiderocol
Indication(s)	Treatment of patients with complicated intra-abdominal infections, complicated urinary tract infections (including pyelonephritis), hospital-acquired bacterial pneumonia, and ventilator-associated bacterial pneumonia.	Treatment of patients with complicated intra-abdominal infections and complicated urinary tract infections (including pyelonephritis).	Treatment of patients with limited or no alternative treatment options, for the treatment of complicated urinary tract infections (including pyelonephritis), hospital-acquired pneumonia, and ventilator-associated pneumonia.
Cabrapenemase Activity	KPC, OXA48 (ESBL, AMPC)	None (ESBL, AMPC); Main role is Carbapenem-resistant Pseudomonas sp- activity against pump and porin changes	KPC, OXA48, NDM, VIM (ESBL, AMPC); Carbapenem-resistant Pseudomonas sp- activity against porin changes
Dosing (CrCl >120)	2.5 grams IV every 8 hours	Pneumonia: 3 grams IV every 8 hours Other: 1.5 grams IV every 8 hours	2 grams IV every 6 hours
Drug-Drug and Drug-Food Interactions	• Probenecid: inhibits OAT uptake of avibactam leading to decrease in elimination • Laboratory test: may lead to false-positive reaction for glucose in urine	• No significant drug interactions	• Probenecid: may increase serum concentrations of cephalosporins • Dipstick test: may result in false positive results
Contraindications	Known hypersensitivity to any component of the formulation	Known hypersensitivity to any component of the formulation, piperacillin-tazobactam, or other members of the beta-lactam class	Known hypersensitivity to cefiderocol or other beta-lactam antibacterial drugs
Adverse Reactions	• Hypersensitivity reactions • *Clostridium difficile*-associated diarrhea • Central nervous system reactions	• Hypersensitivity reactions • *Clostridium difficile*-associated diarrhea	• Increase in all-cause mortality in patients with CRGNO infections • Hypersensitivity reactions • *Clostridiodes difficile*-associated diarrhea • Seizures and other central nervous system adverse reactions • Development of drug-resistant bacteria
Cost Per Day	$1,002.72	$637.14 for 3g dose $318.57 for 1.5g dose	$1,364 for 2g IV q6h dose

Any other questions?

Feel free to reach out to your friendly neighborhood antimicrobial stewardship pharmacists, Arun Mattappallil and Katie McCrink, for additional information.

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University Hospital Formulary Patches Informational

At University Hospital, their formulary includes patches as follows: Nicotine, Estradiol, Clonidine, Lidoderm, Nitroglycerin, Fentanyl, and Transderm Scop. Patch or Transdermal delivery system (TDS) are beneficial due to high bioavailability and diversity in controlled release formulations. Mechanisms of release include single drug substance dissolved in a single adhesive, multi-component, multi-adhesive, or multi-laminate matrices. Furthermore, excipients include various adhesive systems, permeation enhancers, rate controlling or non-rate controlling membranes, solubilizers, plasticizers/softeners, or tackifiers, all which can influence the quality and performance attributes of the TDS.[1] Overall, transdermal patches allow adhesive capacity for safe delivery of drug through the human skin.

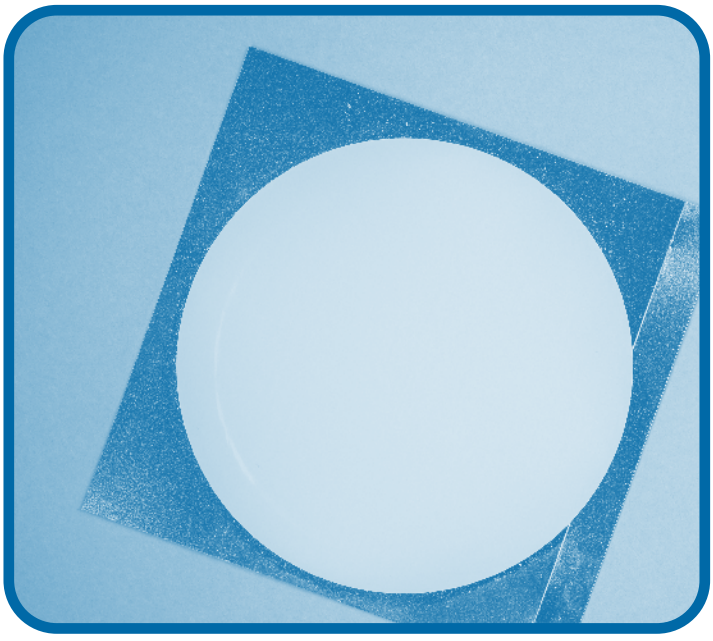
Nicotine (Nicoderm CQ; Nicorette Mini; Nicotrol NS): Nicotine patches are indicated for smoking cessation. Nicotine is delivered from the patches and absorbed through the skin. Nicotine binds to nicotine receptors in the body, lessening nicotine desire and withdrawal symptoms related to smoking.[2]

Estradiol (Climara, Minivelle, Vivelle): Estrogen skin patches contain estradiol. Estrogens are female sex hormones produced by the ovaries. Transdermal Estrogen patches can treat symptoms of menopause such as hot flashes, and vaginal dryness, burning, and irritation. Estrogen patches are also indicated for postmenopausal patients with a uterus to decrease the risk of endometrial cancer. Individuals who have had a hysterectomy generally do not need a progestin.[3]

Clonidine (Catapres TTS): Catapres-TTS is indicated in the treatment of hypertension. It may be employed alone or concomitantly with other antihypertensive agents. Clonidine stimulates alpha-adrenoreceptors in the brain stem. This action results in reduced sympathetic outflow from the central nervous system and in decreases in peripheral resistance, renal vascular resistance, heart rate, and blood pressure.[4]

Lidocaine (LIDODERM): Lidocaine is indicated for pain associated with post-herpetic neuralgia. Its mechanism of action blocks both the initiation and conduction of nerve impulses by decreasing the neuronal membrane's permeability to sodium ions, which results in inhibition of depolarization with resultant blockade of conduction.[5]

Nitroglycerin (NITRO-DUR®): Nitroglycerin indicated for prevention of angina pectoris due to coronary artery disease. It is considered as a vasodilator, and antianginal agent. Nitroglycerin forms free radical with nitric oxide, in smooth muscle nitric oxide activates guanylate cyclase which increases guanosine 3'5' monophosphate (cGMP) leading to dephosphorylation of myosin light chains and smooth muscle relaxation. This in turn produces a vasodilator effect on the peripheral veins and arteries with more prominent effects on the veins.[6]



Fentanyl (DURAGESIC®): indicated for management of persistent, moderate to severe chronic pain which requires continuous around-the-clock opioid administration for an extended period, and cannot be managed by other means such as non-steroidal analgesics, opioid combination products, or immediate-release opioids. Fentanyl is an opioid agonist that binds to receptors at sites within the CNS to increase pain threshold, alters pain reception, and inhibits the ascending pain pathways.[7]

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University Hospital Formulary Patches Informational

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Scopolamine (Transderm Scop): Scopolamine is indicated for motion sickness and post-operative nausea and vomiting. It is an anticholinergic agent that blocks the action of acetylcholine at parasympathetic sites in smooth muscle, secretory glands, and the CNS. Scopolamine also increases cardiac output, dries secretions, and antagonizes histamine and serotonin.[8]

Table

Drug (Patches dosage form)	**Brand Name**	**Wash Area with soap prior to administration**	**Patch can be cut**	**Administration frequency**	**Site of Application**	**Drug free interval needed?**
Nicotine	**Nicoderm CQ; various**	Wash your hands when finished applying the patch	Do not cut patch in half or into smaller pieces	Apply one new patch every 24 hours	Apply on skin that is dry, clean and hairless	none
Estradiol	**Alora; various**	Placed on a clean, dry area	Not recommended by manufacture to cut in half	Apply one new patch every 7 days	Applied of the lower abdomen or the upper quadrant of the buttock	1-week washout period
Clonidine	**Catapres TTS**	Wash hands with soap and water and thoroughly dry them	Do not cut	Applied every 7 days	hairless area of intact skin on the upper outer arm or chest.	none
Lidocaine	**Lidoderm**	Yes, area must be clean and dry	Yes can be cut	Apply for 12 hours within a 24-hour period.	intact skin to cover the most pain area	12 hours free interval
Nitroglycerin	**NITRO-DUR**	clean, dry, hairless skin	Do not cut	Patch on for 12-14 hours	upper arm or body; do not apply to extremities below knee or elbow	10-12 hours patch free
Fentanyl	**DURAGESIC**	Do not use soap, alcohol, over site of application; only use water	Do not cut	Can be worn continuously for 72 hours	chest, back, flank (side of the waist), or upper arm	none
Scopolamine	**Transderm Scop**	hairless area behind one ear	Do not cut	Patch can be worn for 3 days	Behind the one ear	none

University Hospital Formulary Patches Informational

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Natural Killer Cell Therapy

What are Natural Killer Cells?

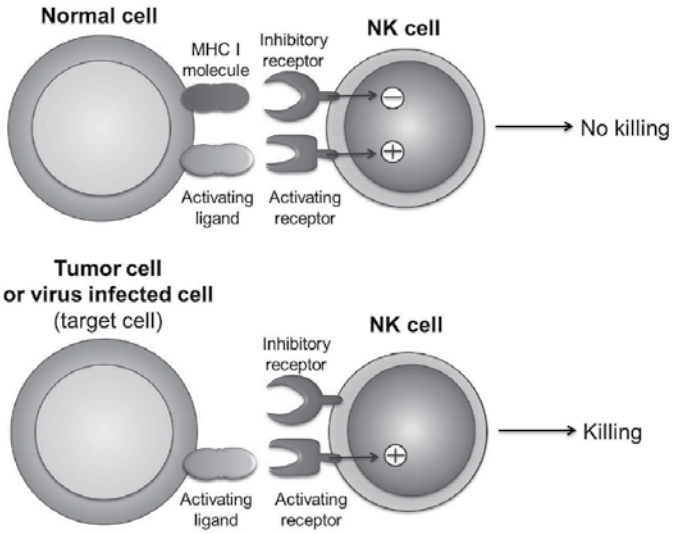
Natural Killer (NK) cells are a part of the innate immune system and both recognize and kill abnormal cells and pathogens.[1] They have a half-life of about 7-10 days and comprise 10-15% of all lymphocytes in peripheral blood.[1] They are distinguished by their larger size and their granules containing perforin and granzyme, mediators of cytotoxicity. They lack specifically rearranged antigens (which are crucial in acquired immunity), but are able to recognize and kill abnormally transformed cells without prior sensitization.

Natural Killer Cells and Cancer

Natural Killer cells are constantly monitoring the body for abnormal cells, such are cancer cells. Tumor cells are easily recognized by the innate immune system because they lack MHC-1, which is expressed on every cell in the body.[4] When these cells are detected, they are destroyed by the NK Cells via the release of perforin and granzymes. Additionally, they recruit other NK Cells, dendritic cells, and T-cells by releasing chemokines.[4] Furthermore, they can further facilitate the development of a proinflammatory environment by releasing cytokines. However, tumor cells have developed means to overcome this constant immune surveillance.[4] Most notably, some cancer cells can mutate to display MHC-1, others can inhibit immune response by displaying PD-1 on their cell surface. Furthermore, the formation of tumors disrupts the normal blood supply, inducing a hypoxic environment. This hypoxic environment impairs the ability of NK cells to function. When NK cells become less cytotoxic or less prolific, tumors have the opportunity to overgrow.

Natural Killer Cell Engineering in Cancer

In order to overcome the effects of the cancer on NK cells, researchers are exploring opportunities to enhance the effects of NK Cells.[4] The average half-life of an NK cell is 7-10 days, which would then require increased dosing frequency. NK cells can be engineered to produce IL-15, which would enhance the persistence of the cells.[1] In some cases, IL-15 enhanced cells have shown to persist 12 months out from the original therapy. Furthermore, NK cells can be engineered with a chimeric antigen receptor (CAR) in order to enhance their specificity, thus limiting side effects.[2]



Koziejowska, Karolina. NK Cells Applications in Immuno-Oncology[4]

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Natural Killer Cell Therapy

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Natural Killer Cell Therapy vs CAR-T

Chimeric antigen receptor T-cell (CAR-T) therapy is a technology that has gained a lot of excitement in recent years. T-cells are removed from a patient's body and reengineered ex vivo to target a specific antigen within the body. Afterwards, the newly formed CAR-T cells are readministered to the body. There are currently two approved autologous CAR-T therapies on the market: Novartis' Kymriah and Gilead's Yescarta. Both of these therapies are only approved for hematologic malignancies and target the CD-19 antigen.[3] There are many limitations to the currently approved CAR-Ts. These include the long vein-to-vein time (17-21 days), the autologous nature, the relatively high rate of cytokine release syndrome (CRS), and high cost.[3] On the other hand, NK cells are naturally off-the-shelf and do not induce graft-vs-host disease and do not appear to cause CRS. As a result, NK cell therapy has a reduced time to administration, which is critical in late-stage cancers, is significantly safer, and will cost much less than CAR-T cell therapy.

Ongoing Clinical Trials Exploring Natural Killer Cell Therapy

In a Phase 1/2a clinical trial to treat relapsed/refractory B-cell malignancy, there are no side effects of cytokine release syndrome or neurotoxicity with NK cell therapy which are very common in CAR-T cell therapy.[5] The clinical trial is multicenter and still open for registration on clinicaltrials.gov: NCT04245722. The investigational NK cell therapy given here is FT596 a multi-antigen targeting, chimeric antigen receptor (CAR) natural killer (NK) cell therapy. It was developed with 3 mechanisms of actions.[6] First it targets CD19 receptors. Second it activates the CD16 Fc receptor to enable tumor targeting and enhance antibody-dependent cell cytotoxicity when in combination with monoclonal antibody (mAb). Third it fuses to interleukin-15 receptors, promoting cytokines.

An example of a case was provided by BLOOD on a 76-year-old patient with refractory B-cell lymphoma who failed 8 lines of treatment. She received 30 million cells of FT596 NK cells as monotherapy and within a 28 day follow up the patient did not show any grade 3 or higher side effects. On day 29 the patient's tumor was assessed with Lugano 2014 criteria; the patient's tumor size decreased by 50% and showed a 70% decrease in uptake of 18F-fluorodeoxyglucose. The patient was also being reconsidered to be given a second cycle of NK cell therapy, due to how well she reacted to therapy. Granted that the treatment needs more patients to prove it's safety and efficacy and a longer follow up period to track long term side effects, there was a marked improvement in the patient's disease state. NK cell therapy could have a great impact in the field of treating cancer, as shown with patients who are more compromised and might not be able to bear the side effects from traditional chemo or CAR-T cell therapy.

Mechanism of Actions	Disease	Phase/Ongoing
Ex-Vivo expanded NK Cells	Non B-cell Leukemia/Solid Tumors Myelodysplastic Syndrome/Leukemia	Phase 1, Complete Phase 1/2, Ongoing
IL-2 activated NK Cells	Leukemia Myelodysplastic Syndrome/Leukemia	Phase 2, Complete Phase 1/2, Complete
mbIL21-expanded haploidentical NK	Leukemia	Phase 1/2, Ongoing

Lim, Okjae, et al. "Present and Future of Allogeneic Natural Killer Cell Therapy."

As there is a lot of potential in NK cell therapy, there is further research in its use to treat other related disease states and modifying it to alter different mechanisms of actions.[6] Above is a chart that shows the mechanisms of actions of specific NK therapy platforms in the United States, and the disease state they are addressing. When compared the mode of action in FT596, chimeric antigen receptor natural killer cell have widely differing modes of actions, showing how many promising possibilities the platform could have. It also has the possibility of impacting the market, as when compared to it CAR-T cell therapy, NK-cell therapy is cheaper to produce and could have the possibility to become an off-the-shelf product.

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Dapagliflozin: The Recent Indication for Heart Failure With Reduced Ejection Fraction

Heart failure is becoming more and more prevalent. It is estimated that 6.2 million Americans over the age of 20 had heart failure from 2013 to 2016. While 5.7 million Americans had heart failure from 2009 to 2012. Approximately half of all hospitalized heart failure is characterized by a reduced (systolic) ejection fraction and half by a preserved (diastolic) ejection fraction.[3] Common heart failure symptoms include shortness of breath during day to day activities, trouble breathing while lying down, and weight gain and swelling in the feet, legs, or ankles.

Dapagliflozin, a sodium-glucose transporter 2 inhibitor that blocks glucose reabsorption in the proximal tubule of the kidney and promotes glucosuria, has historically been used for type II diabetes.[4] Through trial studies involving type II diabetes patients, SGLT2 inhibitors have shown favorable cardiovascular effects, including a reduction in the risk of hospitalization for heart failure. Thus, after this trial dapagliflozin has been shown to decrease hospitalizations and death from cardiovascular causes. In May 2020, the Food and Drug Administration approved dapagliflozin for the new indication of heart failure with a reduced ejection fraction to reduce the risk of cardiovascular death and hospitalization for patients with heart failure.

Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

Trial[1]

- Placebo-controlled, phase III trial
- Randomly assigned heart failure patients with New York Heart Association class II, III, or IV and a reduced ejection fraction of 40% or less to receive either dapagliflozin (10mg once daily) or placebo, plus the recommended standard of care

Inclusion Criteria[1]

- Plasma level of N-terminal pro–B-type natriuretic peptide (NT-proBNP) of at least 600 pg per milliliter (or ≥400 pg per milliliter if they had been hospitalized for heart failure within the previous 12 months)
- Patients with atrial fibrillation or atrial flutter on baseline electrocardiogram were required to have an NT-proBNP level of at least 900 pg per milliliter
- Required to receive standard heart failure device therapy (an implantable cardioverter–defibrillator, cardiac resynchronization therapy, or both) and standard drug therapy, including an angiotensin-converting–enzyme inhibitor, an angiotensin-receptor blocker, or sacubitril–valsartan plus a beta-blocker
- Patients with type 2 diabetes continue to take their glucose-lowering therapies, but doses could be adjusted as required

Patients were randomly assigned to receive either dapagliflozin (at a dose of 10 mg once daily) or matching placebo, in accordance with the sequestered, fixed-randomization schedule, with the use of balanced blocks to ensure an approximate 1:1 ratio of the two regimens. Then, the patients were evaluated at 14 days and 60 days post randomization. More evaluations continued at 4 months and at 4-month intervals thereafter.[1]

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Dapagliflozin: The Recent Indication for Heart Failure With Reduced Ejection Fraction

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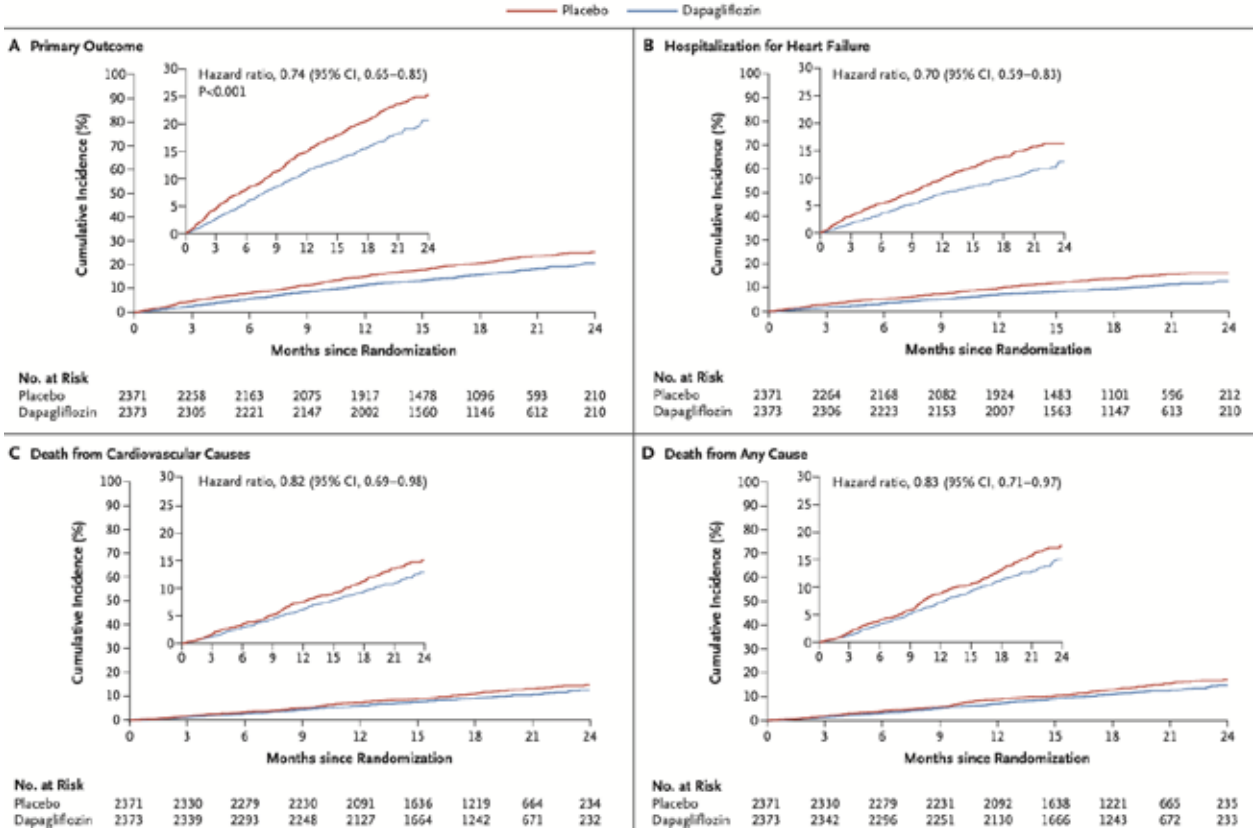
The primary outcome included worsening heart failure or death from cardiovascular causes. Worsening heart failure would include an unplanned hospitalization or urgent care visit leading to the initiation of IV therapy to treat the heart failure symptoms. The secondary outcomes included total number of hospitalizations for heart failure and cardiovascular deaths, change from baseline to 8 months in the total symptom score on the Kansas City Cardiomyopathy Questionnaire, worsening renal failure defined as an eGFR of 50% or greater, end-stage renal disease, and death from any cause.[1]

The results were obtained from February 2017 to August 2018 with a total of 4744 patients assigned to either arm. When screening, 42% of patients in each arm had type II diabetes and an additional 3% received a new diagnosis of diabetes. The primary outcome of worsening heart failure or death from cardiovascular causes occurred in 386 patients or 16.3% in the dapagliflozin group and 502 patients or 21.2% in the placebo group. 231 or 9.7% of patients were hospitalized for heart failure in the dapagliflozin arm and 318 or 13.4% of patients in the placebo arm. There were 567 total first and recurrent events (340 hospitalizations for heart failure and 227 deaths from cardiovascular causes in 382 patients) in the dapagliflozin group and 742 total events (469 hospitalizations for heart failure and 273 deaths from cardiovascular causes in 495 patients) in the placebo group. There was an increase in the total symptom score on the Kansas City Cardiomyopathy Questionnaire (indicating fewer symptoms) was greater in the dapagliflozin group than in the placebo group between baseline and month 8.



The Future

Next in the pipeline is the FDA approval of empagliflozin for heart failure with a reduced ejection fraction less than 40%. The result of the EMPEROR-Reduced trial showed empagliflozin is superior to placebo in improving heart failure with patients on already guideline-directed medical therapy, regardless of a diabetes diagnosis. This trial was only published in The New England Journal of Medicine in October 2020 so the future is bright for empagliflozin and patients with HFrEF.[2]

References
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3. Virani, S. S. (2020). Heart Disease and Stroke Statistics—2020 Update: A Report From the American Heart Association. Circulation, 141(9), 139-596.
4. Wiviott, S. (2019). Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. The New England Journal of Medicine, 380(4), 347-357. doi:10.1056/NEJMoa1812389

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Welcome New Pharmacists

Luis Romero, Pharm.D.

Dr. Luis Romero completed his Bachelor of Science in Biology at Fairleigh Dickinson University followed by his Doctor of Pharmacy at Northeastern University in Boston, Massachusetts. Prior to starting at University Hospital, he worked in CVS/Health for four years both as an intern and pharmacist. Luis enjoys learning, working in a team to provide the best care and expanding his knowledge in infectious disease. He is excited to be back home in New Jersey and be a part of the UH family.

National Pharmacy Week

National Pharmacy Week, celebrated the third full week in October, acknowledges the contribution of pharmacists and technicians make to patient care. The pharmacy department has worked tirelessly throughout the year, as many other departments have, to deliver the best possible care during a global pandemic. The staff pharmacists are essential for verifying the large amount of medication orders, staying up to date with rapidly changing protocols, and compounding critical medications. The technicians are vital for ensuring seamless drug delivery and medication availability. The clinical pharmacy team and management team have been instrumental in staying current with COVID-19 treatments, developing optimal medication processes, managing drug shortages, and even treating critically ill patients at bedside. To celebrate, a week of pharmacy games and activities took place to celebrate the staff's invaluable contributions to the hospital (socially distanced, of course!). Staff was encouraged to play pharmacy BINGO, participate in an assortment of games and team building exercises, attend a continuing education lecture hosted by our Emergency Medicine Pharmacist, take pictures, and of course EAT. Thank you to the pharmacy team!