Drug & Poison Information Center—Faculty of Pharmacy—Tanta University

Drug & Poison Information Bulletin

SUMMER 2017, VOLUME 4, ISSUE 2

Summary of New & Modified 2017 ACC/AHA/ HFSA Recommendations for the Management of Heart Failure

1. For patients at risk of developing heart failure (HF), natriuretic peptide biomarker–based screening followed by team-based care, including a cardiovascular specialist optimizing *guideline-directed management and therapy* (GDMT), can be useful to prevent the development of left ventricular dysfunction (systolic or diastolic) or new-onset HF. *(New)*

2. In patients presenting with dyspnea, measurement of natriuretic peptide biomarkers is useful to support a diagnosis or exclusion of HF. *(Modified)*

3. Measurement of baseline levels of natriuretic peptide biomarkers and/or cardiac troponin on admission to the hospital is useful to establish a prognosis in acutely decompensated HF. *(Modified)*

4. During a HF hospitalization, a predischarge natriuretic peptide level can be useful to establish a postdischarge prognosis. *(New)*

5. In patients with chronic HF, measurement of other clinically available tests, such as biomarkers of myocardial injury or fibrosis, may be considered for additive risk stratification. *(Modified)*

6. The clinical strategy of inhibition of the renin angiotensin system with angiotensin converting enzyme (ACE) inhibitors, or angiotensin -receptor blockers (ARBs), or angiotensin receptor–neprilysin inhibitors (ARNI) in conjunction with evidence based beta blockers, and aldosterone antagonists in selected patients, is recommended for patients with chronic heart failure with reduced ejection fraction (HFrEF) to reduce morbidity and mortality. (New)

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7. Patients with chronic symptomatic HFrEF New York Heart Association (NYHA) class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended. (New)

8. ARNI should not be administered concomitantly with ACE inhibitors or within 36 hours of the last dose of an ACE inhibitor. In addition, ARNI should not be administered to patients with a history of angioedema. *(New)*

9. Ivabradine (new therapeutic agent that selectively inhibits the I_f current in the sinoatrial node, providing heart rate reduction) can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HF*r*EF (left ventricular EF ≤35%) who are receiving *guideline-directed evaluation and management* (GDEM), including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest. *(New)*

10. In appropriately selected patients with heart failure with preserved ejection fraction (HF*p*EF) "with ejection fraction ≥45%, elevated B-type natriuretic peptide.levels, HF admission within 1 year, estimated glomerular filtration rate >30 mL/min, creatinine <2.5 mg/dL or potassium <5.0 mEq/L", aldosterone receptor antagonists might be considered to decrease hospitalizations. *(New)*

11. Routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or quality of life in patients with HF*p*EF is ineffective. *(New)*

12. In patients with NYHA class II and III HF and iron deficiency (ferritin <100 ng/mL or 100 to 300 ng/mL if transferrin saturation is <20%), intravenous iron replacement might be reasonable to improve functional status and quality of life. *(New)*

13. In patients with HF and anemia, erythropoietin stimulating agents should not be used to improve morbidity and mortality. *(New)*

Reference: ***Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2017 Apr 28.***

By: Bassant Maher, B. Sc.

First Vaccine-based Treatment for HIV Virus

Most people with HIV need to take antiretroviral drugs (ART) each day to stop the virus from replicating and causing damage to their immune system.

These have to be taken over a lifetime because the virus can hide away in tissues such as lymphoid and gut cells; if ART is stopped, the virus quickly re-emerges from these cells. Although effective, ART is expensive, time consuming and can cause nasty side effects.

Vaccinations are generally used prophylactically to provoke preexisting immunity designed to prevent infection or disease. However, it seems possible that a vaccine could be used therapeutically, to evoke an immune response in someone already infected with a pathogen so as to improve the outcome of infection or to reduce dependence on rare or expensive treatments.

Researches have discovered ***the first vaccine-based treatment to stop the virus from replicating without the use of daily drugs***. They combined two innovative HIV vaccines with romidepsin (a drug usually used to treat cancer) in a study conducted at the IrsiCaixa AIDS Research Institute in Barcelona.

After receiving the treatment, the virus was undetectable in five out of 24 participants and its spread was stopped by their immune systems. One of them has been drug-free for seven months. The other four have been free of detectable virus for six, 14, 19 and 21 weeks, respectively.

The study had been carried out on a small scale but its findings were "interesting and important" raising hopes further research could help prevent AIDS without the need for daily drugs.

References:

- ***http://www.medscape.org/viewarticle/416548***
- ***https://www.newscientist.com/article/mg23331143-900-hiv-infection-stopped-in-its-tracks/***

By: Mai Mousa, Pharm D.

FDA News

FDA approves first cancer treatment for any solid tumor with a specific genetic feature

On May 23, 2017 the U.S. Food and Drug Administration (U.S. FDA) granted accelerated approval to ***pembrolizumab***, a treatment for patients whose cancers have a specific genetic feature (biomarker). This is the first time FDA has approved a cancer treatment based on a common biomarker instead of the location in the body where the tumor originated.

Pembrolizumab is indicated for the treatment of adults and children with unresectable or metastatic solid tumors that have been identified as having a biomarker referred to as microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR). MSI-H and dMMR tumors contain abnormalities that affect the proper repair of DNA inside the cell.

Pembrolizumab works by targeting the cellular pathway known as PD-1/PD-L1 (proteins found on the body's immune cells and some cancer cells). By blocking this pathway, ***pembrolizumab*** may help the body's immune system fight the cancer cells. The FDA previously approved ***pembrolizumab*** for the treatment of certain patients with metastatic melanoma, metastatic non-small cell lung cancer, recurrent or metastatic head and neck cancer, refractory classical Hodgkin lymphoma, and urothelial carcinoma.

Common adverse effects of the drug include fatigue, pruritis, diarrhea, decreased appetite, rash, pyrexia, cough dyspnea, musculoskeletal pain, constipation, and nausea. In addition, ***pembrolizumab*** can cause serious conditions known as immune-mediated adverse events including pneumonitis, colitis, hepatitis, endocrinopathies, and nephritis. Complications or death related to allogeneic hematopoietic stem cell transplantation after using ***pembrolizumab*** have occurred.

References:

- ***https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm560167.htm***
- ***https://www.pharmacist.com/article/fda-approves-first-cancer-treatment-any-solid-tumor-specific-genetic-feature***

By: Bassant Maher, B. Sc.

FDA confirms increased risk of leg and foot amputations with the diabetes medicine canagliflozin

On may 16, 2017 the U.S. FDA issued a drug safety communication regarding the increased risk of leg and foot amputations with diabetes medication ***canagliflozin***.

Canagliflozin is a sodium-glucose cotransporter-2 (SGLT2) inhibitor indicated as an adjunct to diet and exercise to improve blood sugar control in adults with type 2 diabetes. Due to results from two large clinical studies, the FDA is requiring a Boxed Warning be added to drug labeling describing the increased risk of leg and foot amputations.

Recommendations:

* **Patients** taking ***canagliflozin*** should notify there health care professionals (HCPs) right away if you develop new pain or tenderness, sores or ulcers, or infections in your legs or feet. should not stop taking there diabetes medicine without first talking to there HCPs.

* **Health care professionals** should, before starting ***canagliflozin***, consider factors that may predispose patients to the need for amputations. These factors include a history of prior amputation, peripheral vascular disease, neuropathy, and diabetic foot ulcers. Monitor patients receiving ***canagliflozin*** for the signs and symptoms described above and discontinue ***canagliflozin*** if these complications occur.

References:

- ***https://www.fda.gov/Drugs/DrugSafety/ucm557507.htm source=govdelivery&utm_medium=email&utm_source=govdelivery***
- ***https://www.pti-nps.com/nps/index.php/drug-update-may-2017/***

By: Bassant Maher, B. Sc.

Antidotes for New Oral Anticoagulants

Idarucizumab injection for intravenous use

Mechanism of action:

Idarucizumab is a specific reversal agent for ***dabigatran***. It is a humanized monoclonal antibody fragment (Fab) that binds to ***dabigatran*** with very high affinity, approximately 300-fold more potent than the binding affinity of ***dabigatran*** for thrombin. The ***idarucizumab-dabigatran*** complex is characterised by a rapid on-rate and extremely slow off-rate resulting in a very stable complex. ***Idarucizumab*** potently and specifically binds to ***dabigatran*** and its metabolites and neutralises their anticoagulant effect.

Dosage form, dosage and administration:

* Injection: 2.5 g/50 mL solution in a single-use vial.
* Restricted to hospital use only.
* The recommended dose is 5 g (2x2.5 g/50 mL).

Adverse reactions:

* **1-10%:**
  Hypokalemia (7%), delirium (7%), constipation (7%), pyrexia (6%), and pneumonia (6%).
* **Frequency Not Defined:** Thromboembolic events & Hypersensitivity.

Warning and Precautions:

* **Thromboembolic risk:** Reversing ***dabigatran*** therapy exposes patients to the thrombotic risk of their underlying disease. Resume anticoagulant therapy as soon as medically appropriate.
* **Re-elevation of coagulation parameters:** In patients with elevated coagulation parameters and reappearance of clinically relevant bleeding or requiring a second emergency surgery/urgent procedure, an additional 5 g dose of ***idarucizumab*** may be considered.

Warning and Precautions (cont.):

* **Hypersensitivity reactions:** Discontinue administration and evaluate.

* **Risks of serious adverse reactions in patients with hereditary fructose intolerance due to sorbitol excipient.**

Contraindications: None.

Date of first authorization: 20 November 2015.

References:

- ***https://www.medicines.org.uk/emc/medicine/31243***
- ***https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/761025lbl.pdf***
- ***http://reference.medscape.com/drug/praxbind-idarucizumab-1000042#5***

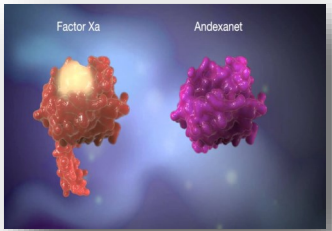
Anticoagulant Antidotes Under Investigation

1-Andexanet alfa (Factor Xa Inhibitor Antidotes)

It is a Novel agent currently in **Phase III** trials, pending FDA approval for patients receiving a Factor Xa inhibitor who suffer a major bleeding episode or who may require emergency surgery.

Mechanism of Action:

Acts as a Factor Xa decoy that targets and sequesters with high specificity both direct (eg, apixaban, rivaroxaban) and indirect Factor Xa inhibitors in the blood.



References:

- ***http://www.nejm.org/doi/full/10.1056/NEJMoa1607887#t=article***
- ***http://reference.medscape.com/drug/formulary/andexxa-andexanet-alfa-999945***

2-Ciraparantag (PER977)

Ciraparantag is now being investigated in **Phase II** human trials to be used as a broad-spectrum reversal agent for anticoagulants.

Mechanism of Action:

It is a synthetic small, water-soluble molecule has been shown to form a complex with large molecules such as unfractionated heparin and LMWH, as well as with smaller molecules such as ***fondaparinux***, ***apixaban***, ***edoxaban***, ***rivaroxaban***, and ***dabigatran***. Once these complexes are formed, subsequent interactions with antithrombin and activated clotting factors are inhibited .

References:

- ***http://www.ajhp.org/content/73/10_Supplement_2/S27?sso-checked=true***
- ***https://www.ncbi.nlm.nih.gov/pubmed/27470323***

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