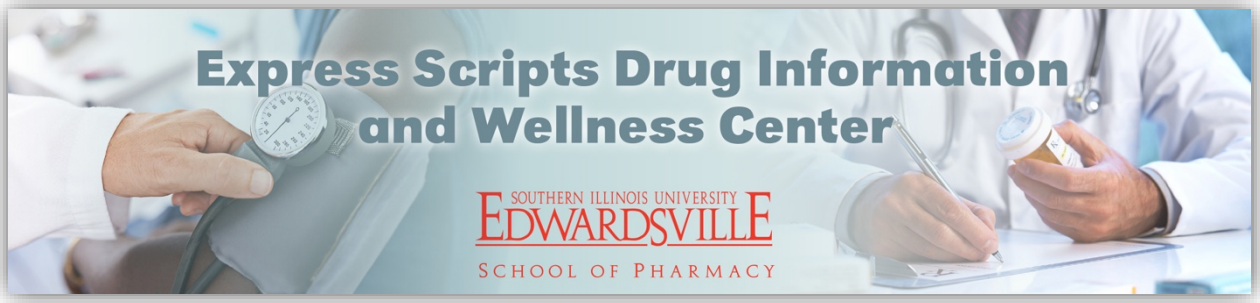

PHARMACY IN THE NEWS

Biotin Decreases Troponin Levels

- On November 5, 2019, the FDA issued an update to their 2017 safety statement that the use of biotin (vitamin B7) may interfere with lab testing; specifically, the test to detect troponin levels in the body.
- Biotin can falsely lower levels of troponin which can interfere with the diagnosis of heart attack. This could lead to serious outcomes for patients.
- The FDA recommends that health care providers discuss any biotin containing supplements with their patients and be aware that it can be found in many over-the-counter items including prenatals, dietary supplements, and multivitamins. These dietary supplements can contain levels up to 650 times the daily biotin recommendation.
- Any other assay that uses biotin technology, such as hormone testing, can be affected as well.
- The FDA also recommends making the lab aware that the patient is taking biotin and if the lab ordered does not result as hypothesized, consider the interference of biotin for error.
- If the patient experiences an adverse effect due to the potential for an incorrect lab value it should be reported to the FDA and the lab test manufacturer.

Source

Revolutionary Cystic Fibrosis Treatment

Trikafta (elexacaftor 100 mg/tezaclaftor 75 mg/ivacaftor 75 mg; 150 mg)

This is the first drug for cystic fibrosis to treat the cause of the disease rather than mitigating the symptoms

What this means for current practice: Trikafta has the potential to vastly improve the lives of many patients with cystic fibrosis and may completely change cystic fibrosis care and outcomes.

- Treatment arms: Trikafta vs current standard of care (ivacaftor/tezacaftor)
- Primary Outcome: the absolute change in percent predicted forced expiratory volume in one second (ppFEV1) from baseline to 4 weeks
- Results: absolute difference between treatment arms in ppFEV1 = 10.0; (95 % CI 7.4 to 12.6; P<0.0001)
- Safety: no patients receiving the study drug had any severe adverse event, all adverse events were reported as mild to moderate and consisted of cough, nasopharyngitis, oropharyngeal pain, upper respiratory infection, headache, hemoptysis, and pulmonary exacerbation

Source

IN THIS ISSUE:

The Drug Information & Wellness Center has moved!

Come visit us at University Park 200, Suite 240!
In between the SOP faculty office and Dean suites

Check out the latest video tutorial on searching PubMed effectively.

NEWLY APPROVED DRUGS

Trikafta (elexacaftor/ivacaftor/tezacaftor); Vertex Pharms INC: 10/21/19

USE: To treat patients > 12 years with the most common gene mutation that causes cystic fibrosis

MOA: Elexacaftor, ivacaftor, and tezacaftor are CFTR modulators. Elexacaftor and tezacaftor bind to separate targets of the defective CFTR protein and potentiate an additive effect to modulate and correct F508del-CFTR. Ivacaftor helps to facilitate the opening of chloride channels resulting in increased CFTR mediated chloride transport.

Scenesse (afamelanotide); Clinuvel INC: 10/8/19

USE: An implant which is inserted under the skin to decrease pain associated with light exposure in adult patients with a history of phototoxic (skin damaging) reactions from erythropoietic protoporphyria

MOA: Scenesse is an alpha-melanocyte stimulating hormone analog selective to melanocortin 1 receptor (MC1R). It is a MC1R agonist.

Xenleta (lefamulin); Nabriva: 8/19/19

USE: To treat adults with community-acquired bacterial pneumonia

MOA: Systemic pleuromutilin antibacterial agent which inhibits protein synthesis of bacteria through interactions with A and P sites of peptidyl transferase center (PTC) in domain V in the 23s rRNA of the 50S subunit. Prevents correct position of tRNA.

Reyvow (lasmiditan); Eli Lilly and Co: 10/11/19

USE: To treat adults with acute migraine with or without aura

MOA: Although precise mechanism is unknown, it is thought to be a serotonin agonist at the 5HT-1F receptor.

Aklief (trifarotene); Galderma Research and Development LLC: 10/4/19

USE: To treat acne vulgaris in patients > 9 years

MOA: Believed to be a retinoic acid receptor agonist but exact mechanism is unknown

Beovu (brolucizumab–dbll); Novartis Pharm Corp: 10/7/19

USE: To treat age-related wet macular degeneration

MOA: Human vascular endothelial growth factor (VEGF) inhibitor that binds to VEGF-A (VEGF(110), VEGF(121), and VEGF(165). This results in suppression of vascular permeability, neovasularization, and cell proliferation through prevention of interaction of VEGF-A with VEGFR-1 and VEGFR-2.

Recently approved generics

Viibryd (vilazodone hydrochloride) 9/30/19

Soolantra (ivermectin cream) 9/13/2019

Kyprolis (carfilzomib) 9/9/19

Emend (fosaprepitant) 9/5/19

Relafen (nabumetone) 8/30/19

Orfadin (nitisinone) 8/26/19

Noxafil (posaconazole) 8/21/19

Dyrenium (triamterene) 8/19/19

UP AND COMING

New Alzheimer's Drug Could Slow Progression of Disease

- A biologics license application will be filed for aducanumab in early 2020
- Drug works by targeting amyloid plaques, which are proteins that form abnormal deposits in the brains of people with dementia
- Current Alzheimer's therapies only treat symptoms, they do not affect progression of the disease
- EMERGE trial: showed significant benefit on measures of cognition and function such as memory, orientation, and language
- ENGAGE trial: significant effects were only seen when a subset of the population that received higher doses was analyzed
- Most common adverse events were amyloid-related imaging abnormalities – edema (ARIA-E) and headache
- Edema episodes were usually asymptomatic and resolved in 4-16 weeks without any long- term consequences

Source

PROFESSIONAL WRITING TIPS

Should I use i.e. or e.g.?

- Use e.g. to denote that only a few examples of a wider range of possibilities are being provided.
  - The patient's nausea and diarrhea could be indicative of several other conditions (e.g. ovarian cysts, pelvic adhesions, irritable bowel diseases).
- Use i.e. to indicate that all possibilities are being listed.
  - The patient reports no missed doses of any of his medications (i.e. atorvastatin, metoprolol, Januvia).

Eliminate fluff words such as: *very, rather, little, the*

- "Substitute "damn" for every time you are inclined to write "very;" your editor will delete it and the writing will be just as it should be." - Mark Twain

Example First Draft: Advanced breast cancer is cancer that has been staged at Stage 3 or Stage 4. In Stage 3 breast cancer, the cancer has spread to nearby lymph nodes and muscles, but has not progressed to other organs. Stage 4 breast cancer means that the cancer has metastasized and has spread to distant sites in the body. Regardless of where the cancer spreads to, it is named for the area where it began. Cancer having a primary site/primary tumor/site of origin in the breast will always be classified as breast cancer. An example of this is breast cancer that has spread to the lung; it will be called metastatic breast cancer, not lung cancer.

Example Final Draft: Advanced breast cancer is at Stage 3 or Stage 4. Stage 3: cancer spread to nearby lymph nodes and muscles, but not progressed to other organs. Stage 4: cancer metastasized and spread to distant sites in the body. Regardless of the stage, cancer is named for where it originated: primary site/primary tumor/site of origin in the breast will always be classified breast cancer. Ex: breast cancer spread to the lung is metastatic breast cancer, not lung cancer.

APPS

Epocrates via AthenaHealth
Free version: insurance formulary drug coverage, guidelines (updated weekly), pill identification, and drug interaction checker
Full access ($174.99/year)

ADA Standards of Care

Free version: Tools include A1c target individualization, glycemic management, drug/patient specific treatment options
NOTE: The app is *not a living document* and does not receive updates each time the Standards of Care online version does.
- Most recent update to the guidelines issued July 31, 2019, section 13.63: "If glycemic targets are no longer met with metformin ± basal insulin, liraglutide therapy should be considered in children 10 years or older, if no history or family history of medullary thyroid carcinoma or MEN2."
- App still states, "If the A1c target is no longer met with metformin monotherapy, or if contraindications of intolerable side effects of metformin develop, basal insulin therapy should be initiated."

PODCASTS

CorConsult Rx: Great coverage of guideline updates, disease state reviews, and walk-throughs of complicated patient cases.

HelixTalk: Podcast from the faculty at Rosalind Franklin University School of Pharmacy; geared towards supplementing study materials for students. Episodes focus on the indications, counseling points, and adverse effects of the top 200 drugs.

Pharmacy Podcast Show: Focuses primarily on issues affecting the profession and changing technology.

Pharmacy Residency Podcast: Interviews and advice on building a professional brand and networking

Drug Information Question of the Month

Question: What literature exists for the long-term use of angiotensin converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), and the development of lung cancer?

Response: The theory that ACEIs could be related to the development of cancer arises from the accumulation of bradykinin that they cause in the lung. High levels of bradykinin have been reported to encourage the growth of lung neoplasms.[1] ACEIs also lead to an accumulation of substance P, which has been associated with tumor growth and vascularization.[1,2] ARBs have not been associated with an accumulation of either of these neuropeptides in the lung.[3]

ARBs, and to a lesser extent ACEIs, have also been theorized to exert a protective effect against the development of cancer. Angiotensin I-Converting Enzyme (ACE) is largely responsible for the activities of the renin angiotensin system (RAS). ACE is expressed in many different anatomical locations and contributes to tumor development by enabling the proliferation, migration, and angiogenesis of malignant cells.[4] This information suggests that drugs directly inhibiting the enzyme, or the action of its downstream products via Angiotensin II, may be beneficial in the prevention or perhaps the progression of certain cancers.

There is no mention of ACEIs or ARBs in the current small cell and non-small cell lung cancer treatment guidelines from the National Comprehensive Cancer Network (NCCN).[5,6]

A search was conducted in PubMed to evaluate the relationship between the use of ACEs and ARBs and subsequent new diagnoses of lung cancer. There is a large body of evidence concerning this topic, though most of the observational studies and meta-analyses focus specifically on ARBs. The literature evaluating the use of ACEs and the development of lung cancer is lacking. Current evidence is conflicting in nature; some studies found an increased risk, some found a protective effect, and some found no apparent association between the two drug classes and the incidence of lung cancer.[3,7-11]

A retrospective cohort study published in 2018 evaluated the incidence of lung cancer associated with use of ACEs and ARBs. The cohort included 992,061 patients treated with either ACEs, ARBs, or other hypertension medication. Participants were followed for a mean (SD) of 6.4 (4.7) years. The most common ACEs were ramipril, lisinopril, and perindopril. Statistical models were adjusted for several covariates, including smoking status, history of lung diseases, and alcohol-related disorders. Although smoking status was accounted for, two other factors that have been associated with lung cancer incidence were not addressed: smoking intensity and duration. Regarding baseline characteristics, ACEI users were more likely to be cigarette smokers. This study found an increased risk of lung cancer among patients taking an ACEI in comparison to patients taking an ARB (HR 1.14, CI 1.01 to 1.29). Hazard ratios increased with longer durations of use and peaked after the ten-year mark (HR 1.31, CI 1.08 to 1.59). There was no significant association between ACEI use and lung cancer in patients who used the drug for less than 5 years (HR 1.10, CI 0.96 to 1.25). Smoking status was determined by investigators to have no significant effect on the association.[3]

Several systematic reviews have been published on this topic; only one meta-analysis was found that included trials with an ACEI treatment group. The review included 31 studies published between 1998 and 2014: the results of 17 observational studies and 14 randomized controlled trials were assessed. Seven of the studies assessed dual therapy with ACEs and ARBS, 24 studies investigated ARBS only, and only 8 trials evaluated ACEI monotherapy. ACEs (RR 0.84, CI 0.72 to 0.99) and ARBs (RR 0.91, CI 0.84 to 0.99) demonstrated a protective effect on the incidence of cancer in the observational studies, but no benefit was seen among ARBs or dual therapy in the randomized controlled trials. The observational studies also suggested a significant reduction in incidence of lung cancer among both ACEI and ARB users (RR 0.85, CI 0.75 to 0.97); the randomized controlled trials did not. The protection noted was not statistically significant when adjusted for follow-up time. The observational studies had a larger study population and longer duration of follow-up, which could have impacted the detection of cancer.[7]

The compiled results of reviews that investigate the use of ARBs indicate that an increased risk of cancer is not strongly supported. A 2010 analysis performed by Sipahi et al. included studies that assessed use of telmisartan, losartan, and valsartan. The analysis revealed that patients randomly assigned to an ARB had an increased risk of any cancer diagnosis in comparison to patients receiving a different hypertension medication (RR 1.08, CI 1.01 to 1.15). It is important to note that although the confidence interval was statistically significant, there was only an absolute 1.2% difference in the number of new cancer diagnoses between groups (7.2% of patients in the ARB group and 6.0% of patients in the non-ARB group). Only 3 of the included trials had cancer as a prespecified endpoint; there was a significant increase in cancer risk in those assigned to ARBs versus control (RR 1.11, CI 1.04 to 1.18). The other major finding of the review was a significant increase in the occurrence of lung cancer in cohorts receiving ARBs (p = 0.01). The major limitation of this review is the number of included studies: although the largest and longest trials were part of their analysis, the review included only half of the studies that were available at the time.[8]

Two meta-analyses published subsequently did not corroborate these findings. A meta-analysis of 15 clinical trials published in 2011 revealed no significant increase in the incidence of overall (OR 1.00, CI 0.95 to 1.04) or site-specific cancer (lung: OR 1.01, CI 0.90 to 1.14) among participants randomized to ARBs versus non-ARB controls.[9] Similarly, a Danish nationwide cohort found no increased risk of lung cancer (RR 0.92, CI 0.82 to 1.02) or increased risk of any cancer with increasing duration of exposure (RR 0.99, CI 0.99 to 1.00), in comparison to ACEI use. This analysis also revealed a similar risk profile for each ARB in the class and no preference for one over another regarding safety.[10] A more recent cohort that compared cancer incidence between telmisartan users and other ARB users supported this finding.[11]

The body of evidence for ARB use and the subsequent development of lung cancer is extensive. The literature indicates that an increased risk of cancer is unlikely. The risk surrounding ACEI use is less clear and future studies need to be completed before any well-supported conclusions can be drawn. Ethical implications will prevent the design of any randomized controlled trials and our data will be limited to that which is produced by observational studies. The exposure period, follow-up time, and numerous covariates are the greatest limitations to the existing data. Even exposure to a potent carcinogen, e.g. tobacco smoke, is unlikely to cause cancer after a few years.9 Although the relationship between long-term ACEI and ARB use and the development of lung cancer has yet to be defined, the cardiovascular benefit of these two drug classes is well-established. Patients that have been prescribed an ACE or an ARB should continue taking their medication due to the lack of consistent evidence stating otherwise. The cohort study published in 2018 may provide a reason to switch to or start your patient on an ARB; however, these decisions should be individualized to the patient.

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Thank you to Lisa Gosa, Allison Hotop, and Anna White for their contributions to this newsletter.