Alaska Pharmacists Association

Continuing Education Home Study Series

Program 0139-0000-20-201-H04-P/T
Quarterly AKPhA Newsletter
Release Date 4/15/2020
Expiration Date 4/15/2023
CPE Hours: 2.0 (0.2 CEU)

This lesson is a knowledge-based CPE activity and is targeted to pharmacists and technicians in all practice settings.

Learning Objectives

At the completion of this activity, the participant will be able to:

1. State two positive changes you can make to your practice following participation in this series.
2. Summarize three practice updates or changes you acquired while participating in this series.

Disclosure

The author(s) and other individuals responsible for planning AKPhA continuing pharmacy education activities have no relevant financial relationships to disclose.

Fees

CE processing is FREE for AKPhA members. Non-members must submit $20 per quiz at: https://alaskapharmacy.org/payments/

To Obtain CPE Credit for this lesson you must complete the evaluation and quiz linked at the end and score a passing grade of 70% or higher. If you score less than 70%, you may repeat the quiz once. CPE credit for successfully completed quizzes will be uploaded to CPE Monitor within 60 days.

The Alaska Pharmacists Association is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Smoking Cessation in Adult Cancer Patients Receiving Chemotherapy

Authors:
Judy Moua, Pacific University School of Pharmacy, PharmD Candidate 2020
Anne Marie Bott, PharmD, BCPS, BCOP, IHS Alaska Area Oncology Pharmacist

Cigarette smoking presents as a significant source of morbidity and mortality. Its use is responsible for more than 480,000 deaths in the U.S. annually.[1] Filled with carcinogens and other harmful chemicals, cigarettes and tobacco usage affects nearly every organ in the body; causing an array of health problems.[2,3] Not only is smoking linked to a multitude of cancers, there are additional risks with continual use during cancer treatment. Specifically, smoking and tobacco use has the potential to reduce the efficacy of chemotherapy and targeted therapy, ultimately leading to poor treatment outcomes and high mortality.[3,4] Furthermore, tobacco smoke increases the chance of recurrent disease and secondary malignancies.[2,5] Apart from the disease site and stage, continual smoking is the strongest adverse predictor of survival in cancer patients.[3]

What makes it so difficult to quit even after a cancer diagnosis? Cigarettes contain a highly addictive substance called nicotine. Nicotine increases the amount of dopamine, a neurotransmitter, which is released in the body. Dopamine causes improved mood and feelings of pleasure, so when a person smokes they get a temporary "feel-good" experience. However, this effect quickly wears off, leading smokers to light again and eventually leads to nicotine addiction.[2]

Despite the negative impacts, data from the National Health and Nutrition Examination Survey (NHANES), suggests that 64% of cancer survivors continued to smoke post-diagnosis.[6] Patients with cancer who are smokers often demonstrate high-level nicotine dependence, because it serves as a coping mechanism during this difficult time.[4,5] In addition to the strong

chemical addiction to nicotine, some patients may be unaware of the harms related to smoking and assume there are no benefits to smoking cessation after a cancer diagnosis is made.[5] This misconception makes it even more challenging to overcome the complexity of smoking cessation.

Altered Drug Metabolism

Smoking impacts the metabolism of chemotherapy and targeted therapy through effects on the cytochrome P450 (CYP) enzymes by either increasing induction or increasing degradation.[7] This mechanism of interaction is contributed by the presence of polycyclic aromatic hydrocarbons (PAHs), a carcinogen produced from tobacco smoke. PAHs are potent inducers of CYP1A2, a common isoform found in the liver and gut that is responsible for the metabolism of several systemic chemotherapy agents.[7] The increase in transcription leads to increased activity of the enzymes, lowering the plasma concentration of cancer drugs.[7] In a pharmacokinetic study of healthy volunteers, current smokers achieved significantly less erlotinib exposure following a single 150 and 300 mg dose than nonsmokers.[8] This shows how continual smoking during chemotherapy can lead to suboptimal outcomes and may warrant the need to adjust doses in order to target plasma concentrations.[6,7]

On the other hand, when smoking increases drug concentrations by inhibiting the CYP enzymes, patients have an increased exposure to the cytotoxic agent and may experience more severe side effects.[7] Some studies have shown that smokers who received erlotinib or gefitinib experienced more side effects compared to non-smokers.[5,7] Generally, smokers receiving chemotherapy will have more treatment-related complications than non-smokers such as fatigue, weight loss, heart and lung complications, and risk for infection.[7]

General Approach to Smoking Cessation

Attempts made to stop smoking immediately after cancer diagnosis may have higher than normal success rates, but cessation is highly encouraged regardless of timing.[6,9] Although several treatment options are available for patients, their attempt to quit should address both the psychological and behavioral dependence of nicotine.[6,9] The National Comprehensive Cancer Network (NCCN) recommends combining pharmacotherapy and behavioral therapy as the most effective approach for smoking cessation.[6]

Pharmacotherapy Agents

First-line medications for tobacco dependence include combination nicotine replacement therapies (NRT) or varenicline. A minimum of 12 weeks of combination NRT or varenicline is recommended for the initial quit attempt. Therapy can be extended to 6 months or longer to achieve continual cessation.[6] Medications should be encouraged for all patients who are seeking to quit smoking except in those where it is medically contraindicated.[6,9]

Behavioral Therapy

In addition to medications, behavioral therapy increases the chance of successful smoking cessation and long-term abstinence. It's recommended to get four or more sessions during each 12-week course of pharmacotherapy with a tobacco treatment specialist or dedicated staff member.[6,9]

Risks

Patients may have concerns about nicotine withdrawal. Since nicotine causes physical dependence and tolerance, cravings for cigarettes and symptoms of nicotine withdrawal can be expected upon cessation.[2] Withdrawal symptoms including anxiety, irritability depression, insomnia, poor concentration, restlessness, increase appetite and urge to smoke (cravings) are temporary and can be treated with pharmacological or behavioral therapies.[2,6,9]

Provider's Role

Health care providers play a vital role in smoking cessation among cancer patients. The American Society of Clinical Oncology (ASCO) suggests incorporating tobacco use screening and cessation services into routine practice. Smoking status should be assessed as a part of the initial intake and updated at each visit.[9] All current tobacco users should be advised to quit. A personalized approach to educate the patient of the risks of continual use and benefits of cessation should be used.[9] By identifying cancer patients who smoke, health care providers are able to offer resources for smoking cessation, or refer them to a tobacco treatment specialist.[8,9]

Conclusion

Literature has demonstrated the benefits of smoking cessation during cancer treatment with chemotherapy and targeted agents. Elimination of cigarette smoking can improve the effectiveness of these treatments and lower the side effects. This in turn, will improve the overall well-being and quality of life for cancer patients regardless of their prognosis. Health care professionals can support cancer patients by ensuring they understand the specific health risks of tobacco use and provide resources to quit. Counseling and medication therapy can increase a patient's chance of successful quitting and should be used in combination to ensure long-term abstinence.

References

1. U.S. Department of Health and Human Services. *Treating Tobacco Use and Dependence: 2008 Update*.Washington, D.C: Public Health Service; 2008.
2. Mayo Clinic Staff. (2018). Nicotine dependence. *Mayo Clinic.* Retrieved from: https://www.mayoclinic.org/diseases-conditions/nicotine-dependence/symptoms-causes/syc-20351584
3. Jassem J. (2019). Tobacco smoking after diagnosis of cancer: clinical aspects. *Translational lung cancer research*. Vol 8, (Suppl 1), S50–S58. doi:10.21037/tlcr.2019.04.01
4. Gritz ER, Fingeret MC, Vidrine DJ, et al. Successes and failures of the teachable moment: Smoking cessation in cancer patients. Cancer. 2006;106:17–27.
5. (2019). Tobacco Key Facts. World Health Organization. Retrieved from: https://www.who.int/news-room/fact-sheets/detail/tobacco

Expanding CAR-T to Solid Tumors

Authors:
Sarah Noble, Pharm. D. Candidate 2020
Anne Marie Bott, Pharm. D., BCOP, BCPS

Gene therapy may be a hot new topic, but the idea and research that paved the way is anything but new. Gene therapy treats a disease by modifying or correcting the genes of an individual through various methods such as using modified virus vector.[1] Genetic engineering in the 1970s opened doors for being able to clone genes and an ability to transfer them. Retrovirus discovery in the 1980s opened another door to possibilities of gene therapy. The first clinical trials began in 1989 with terminal melanoma patients with the aim to test and treat adenosine deaminase (ADA) deficiency (one form of severe combined immunodeficiency disease (SCID)) in children.[2] Despite hundreds of trials with thousands of patients, little progress was made in the next decade due to ineffective retroviral vectors. An unfortunate death in 1999, due to multiple missteps in the trial process, halted any gene therapy trials while the FDA investigated current trials and revamped the regulatory process. Progress slowly progressed for almost another decade while better, safer vectors were being developed and tested.[2]

The first successful chimeric antigen receptor T-cell (CAR-T) treatment for childhood acute lymphocytic leukemia (ALL) took place in 2012 as a last-ditch effort to help a young girl, Emma Whitehead. After what seemed like a turn for the worst, her immune system began fighting the cancer and she is now a healthy fifteen year old. Although the initial work in the 80s seemed doomed with a lack of progress and then a death, and Emma seemed near death herself, the work started in 1989 led to this success in 2012.[2-4]

CAR-T works by collecting a patient's T-cells; a virus is genetically changed to not cause disease, but to fight cancer; and the T-cells are loaded into the vectors. The end product is transfused back into the patient, the virus/T-cell combination reprograms immune cells to become "serial killer cells" by targeting CD19 (found only on white blood cells) of the cancerous cells that were not being detected.[3-4]

Since 2015, four gene therapies have been approved by the FDA: two products for non-cancer uses and two CAR-T therapies for leukemia and lymphoma.[5] The two CAR-T therapies currently on the market in the oncology setting are: Kymriah® (tisagenlecleucel) and Yescarta® (axicabtagene ciloleucel).[5] In addition to these approved treatments, there are numerous pre-clinical and clinical trials being carried out for SCID-ADA, sickle cell, thalassemia, HIV, and further investigation of various uses for clustered regularly interspaced short palindromic repeats with CRISPR associated protein 9 (CRISPR-Cas9).[2, 6, 7]

Besides the seemingly exorbitant cost, the biggest hurdle is figuring out if and how to apply it to more conditions. As noted above, most conditions being investigated with gene therapy are hematologic or with mutated cells that are easily accessible as far as physiology is concerned. For solid tumors, CAR-T therapy is not able to successfully penetrate to the affected cells and stay active long enough to be effective in fighting the cancer.

Based on new mouse model studies, a "vaccination" of a phospholipid polymer linked to small molecules or peptides will enhance CAR-T cell survival to treat solid tumors.[8] When injected, the polymer complex binds to

albumin, is directed to lymph nodes, and are presented on antigen presenting cells (APCs). The APCs provide stimulatory signals to T-cells that allow them to proliferate, survive, and infiltrate tumor sites at a higher rate. Furthermore, a tandem therapy that used two CARs, one targeting tumor antigen and another targeting fluorescein isothiocyanate (FITC) (used in their initial studies), improved tumor activity against melanoma and breast cancer in mice. This novel complex bypasses major histocompatibility complexes normally needed to build immune responses from vaccination and appears to have an epigenetic effect where native T-cells are able to inherit immune memory for tumor cells without the direct input of CAR-T cells.

More studies on the processes, mechanisms, and effects is warranted, but early results are promising for this polymer-antigen boosted CAR-T treatment of solid tumors. This is one exciting development in the world of current gene therapy studies being investigated. Although there are many questions left to be answered, there are many new paths being developed for relapsed and hard to treat diseases on the horizon.

References:

1. Genetics Home Reference. What is gene therapy?. National Institutes of Health. 2019 Sept 10. https://ghr.nlm.nih.gov/primer/therapy/genetherapy
2. Marks L. Gene therapy. *What is Biotechnology?*. Accessed 2019 Sept 26 and Oct 22. https://www.whatisbiotechnology.org/index.php/science/summary/gene-therapy
3. Kauffman R. Fire with Fire. Red Light Films LLC. 2013. https://vimeo.com/54668275
4. Relapsed leukemia: Emily's story. Children's Hospital of Philadelphia. 2012 Dec. Updated 2017 July. https://www.chop.edu/stories/relapsed-leukemia-emilys-story.
5. FDA. Approved Cellular and Gene Therapy Products. 2019 March 29. https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products.
6. High KA, Roncarolo MG. Gene therapy. *N Engl J Med.* 2019;381:455-64. doi: 10.1056/NEJMra1706910
7. Genetics Home Reference. What are genome editing and CRISPR-Cas9?. National Institutes of Health. 2019 Oct 29. https://ghr.nlm.nih.gov/primer/genomicresearch/genomeediting
8. Singh N, June CH. Boosting engineered T cells. *Science*. 2019 Jul 12;365(6449):119-120. doi: 10.1126/science.aax6331.

Treatment and Prevention of Anthracycline-Induced Cardiotoxicity

Authors:
Zach Swedberg, PharmD Candidate 2020
Anne Marie Bott, PharmD, BCOP, BCPS,
Alaska Native Medical Center

Anthracyclines play a crucial role in the therapy of many types of cancer. These include diseases affecting the white blood cells, such as acute lymphocytic leukemia (ALL) and acute myeloid leukemia (AML); the lymphatic system, such as Hodgkin's lymphoma; connective tissues; and epithelial cells, such as breast and lung.[1] Examples of anthracyclines include doxorubicin, daunorubicin, and epirubicin. These medications work by preventing cell replication and promoting apoptosis through the inhibition of the enzyme topoisomerase II.[2] Topoisomerase II is involved in the "re-fusing" process of DNA during replication following its uncoiling.[2]

Although anthracyclines are important in the treatment of several cancers, caution must be taken. Anthracycline use must be limited due to its incidence of cardiotoxicity. Cardiotoxicity is likely caused by a combination of the production of free radicals and the inactivation of topoisomerase II.[3,5] Minute changes in cardiac function can occur at any point while taking an anthracycline.[4] Therefore, in order to reduce the incidence and severity of cardiotoxicity, cumulative lifetime doses were developed. Other risk factors for cardiotoxicity include age (>65 years old or <18 years old), female gender, African American descent, renal failure, baseline left ventricular dysfunction, hypertension, valvular disease, radiation exposure, or therapy containing other potentially cardiotoxic agents, such as trastuzumab.[1,11]

While preventing patients from receiving cumulative doses above the recommended maximum is important, monitoring patients is just as important. Unfortunately, there has not been a consensus made on the ideal monitoring parameters for cardiotoxicity; however, a couple markers have been found to be reliable. These markers are troponin and B-type natriuretic peptide.[1] Another means of assessing and monitoring for

cardiotoxicity is assessing left ventricular ejection fraction through echocardiograms.[3]

Anthracycline-induced cardiotoxicity preventative and therapeutic measures have been studied recently. One study attempted to prevent the development of cardiotoxicity by increasing infusion duration to reduce the peak concentration within the patient. However, this study found that longer infusions of anthracyclines reduced incidence of cardiotoxicity at the expense of more extravasations. Another attempt was to study liposomal formulations of anthracyclines compared to conventional formualtions. Again, the liposomal formulation had lower incidences of cardiotoxicity yet higher rates of skin toxicity.[4,12]

Dexrazoxane is another agent that can be used to prevent cardiotoxicity. Dexrazoxane works by reducing the production of free radicals.[6] Through this mechanism, dexrazoxane can preserve left ventricular ejection fraction and limit the release of troponin and B-type natriuretic peptides.[1] Concerns have developed about the use of dexrazoxane limiting the effect of anthracyclines and its potential to lead to hematologic malignancy; however, recent studies have refuted these claims.[1,4] Currently, dexrazoxane is only indicated for anthracycline extravasations and women with metastatic breast cancer, who have received a cumulative dose of doxorubicin in excess of 300mg/m^2, and are continuing to receive doxorubicin for tumor control.[4,5,8,9,10,11]

Trials of ACE inhibitors, ARBs, and beta-blockers for the prevention and reversal of cardiotoxicity are ongoing; however, preliminary results have showed promise. Several small randomized controlled trials have studied the effects of ACE inhibitors, ARBs, and beta-blockers on the change in left ventricular ejection fraction compared to a control group. In many of these studies, ejection fraction was found to remain at baseline or even slightly improve with treatment of an ACE inhibitor, an ARB, a beta-blocker, or a combination of ACE inhibitor with beta-blocker.[4] In a study of 2625 patients that had anthracycline-induced cardiotoxicity (defined as a 10% decrease in ejection fraction from baseline and having an ejection fraction less than 50%) and received enalapril with either bisoprolol or carvedilol, 11% of patient had a complete response with their ejection fraction returning to baseline and 71% had partial recovery, defined as an increase in ejection fraction of at least 5% and increasing to at least an ejection fraction of 50%.[3,7] Other therapies currently being investigated for potential to prevent and/or reverse cardiotoxic effects of anthracyclines including statins, metformin, febuxostat, and ranolazine.[4]

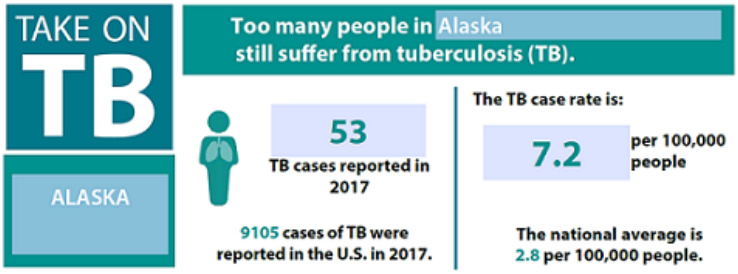
Many oncology patients may benefit from receiving anthracycline therapy due to the variety of malignancies it can treat. However, cardiotoxicity is a major concern with these medications. While a cumulative lifetime dose has been implemented to help prevent cardiotoxicity, many are still effected, even without reaching the lifetime dose. Although vast amounts of research have been performed to find ways to prevent this effect and to help reverse it in individuals that have already been effected, more research is on the way to support these preliminary claims.

References:

1. Henriksen PA. Anthracycline Cardiotoxicity: An Update. JACC [serial online]. 2017. Available from: https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2017/12/21/14/55/anthracycline-cardiotoxicity-an-update. Accessed February 21, 2020.
2. Elsevier Staff. Anthracyclines. ScienceDirect. Available at: https://www.sciencedirect.com/topics/neuroscience/anthracyclines. Accessed February 21, 2020.
3. Farmakis D, Mantzourani M, Filippatos G. Anthracycline-induced cardiomyopathy: secrets and lies. European Journal of Heart Failure. 2018;20(5):907-909.
4. Nohria A. Prevention of Cardiomyopathy in Patients With Cancer. JACC [serial online]. 2016. Available from: https://www.acc.org/latest-in-cardiology/articles/2016/09/29/13/25/prevention-of-cardiomyopathy-in-patients-with-cancer. Accessed February 21, 2020.
5. Geisberg C, Sawyer DB. Mechanisms of Anthracycline Cardiotoxicity and Strategies to Decrease Cardiac Damage. Curr Hypertens Rep. 2010;12(6):404-410.
6. Gianni L, Herman EH, Lipshultz SE, Minotti G, Sarvazyan N, Sawyer DB. Anthracycline Cardiotoxicity: From Bench to Bedside. J Clin Oncol. 2008;26(22):3777-3784.
7. Cardinale D, Colombo A, Bacchiani G, Tedeschi I, Meroni CA, Veglia F, et al. Early Detection of Anthracycline Cardiotoxicity and Improvement With Heart Failure Therapy. Circulation. 2015;131(22):1981-1988.
8. Zinecard [package insert]. Albuquerque, NM: SP Pharmaceuticals LLC; 1998.
9. Totect [package insert]. Nashville, TN: Cumberland Pharmaceuticals Inc.; 2007.
10. Dexrazoxane [package insert]. Eatontown, NJ: West-Ward Pharmaceuticals; 2016.
11. NCCN Staff. Cardiac Toxicity. NCCN. Available at: https://www.nccn.org/patients/resources/life_with_cancer/managing_symptoms/cardiac_toxicity.aspx. Accessed March 5, 2020.
12. NCCN Staff. NCCN Clinical Practice Guidelines in Oncology – Breast Cancer. NCCN. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed March 6, 2020.

Management of Latent Tuberculosis Infection

Authors:
Jenny Rhee, PharmD Candidate 2020
Virginia Commonwealth University
School of Pharmacy
Mary Mackey, PharmD, BCPS
Alaska Native Medical Center



In 2018, the state of Alaska had the highest state-specific incidence of tuberculosis in the country. The average number of tuberculosis cases in the United States in 2018 was 2.8 cases per 100,000 people while Alaska's average was 8.5 cases per 100,000 people—nearly three times the national average.[1] Whereas the number of cases of TB in the United States decreased from 2017 to 2018 from 9,105 to 9,029 cases, the number of cases in Alaska increased from 53 to 63 cases.[1] The management of LTBI is important in American Indian/Alaska Native populations because they have the 2nd highest TB incidence for US-born persons only succeeded by Native Hawaiians/Pacific Islanders and followed by blacks, Asians, and Hispanics. The lowest incidence occurred in whites. Additionally, during 2018, 4.1% of TB cases were reported among persons who experienced homelessness within the year preceding diagnosis.[1] Because treatment of latent TB infection decreases the risk of progression to active TB disease, it is critical that LTBI is managed and treated appropriately.

Latent tuberculosis infection (LTBI) in an infection with *Mycobacterium tuberculosis* without evidence of clinically manifested active TB.[3] It is estimated that up to 13 million people in the US have latent TB.[4] Without treatment, 5-10% of infected persons will progress to TB disease in their lifetime hence the management and treatment of latent tuberculosis infection (LTBI) is critical to the control and elimination of tuberculosis disease (TB) in the United States.[4]

There are two main types of diagnostic testing for latent TB infection. The first one is the tuberculin skin test (TST) which is one of the oldest and most widely used diagnostic tests in medicine. However, there are significant limitations with this method. Operational issues include requiring proper technique for administration and interpretation of the results. In addition, the results must be read within 48-72 hours that poses a barrier in having patients return for the interpretation. Some biological issues include confounding results with patients who received a prior vaccination with Bacille Calmette-Guérin (BCG) vaccination.[6] BCG is a vaccine for tuberculosis (TB) disease that foreign-born people receive in many countries with a high prevalence of TB to prevent childhood tuberculous meningitis and military disease.[7] The TST contains antigens in purified protein derivative (PPD) that are also produced by mycobacterial strains used in the BCG vaccine. Due to this, the specificity of TST in people previously vaccinated with BCG are low and can cause false positives.[6]

The second test, the interferon gamma release assay (IGRA), addresses many of the limitations found with the TST. The biggest advantage is significantly improved specificity over TST. IGRA only utilizes two or three TB specific antigens to stimulate the immune response as opposed to the hundreds found in PPD. In addition, the antigens in IGRA are not produced by the mycobacterial strains that compose BCG that decreases the confounding results for patients who have received the BCG vaccination. This method also only requires a simple blood draw, so no return visit is required. IGRA is preferred by the CDC, American Thoracic Society, and IDSA when testing people who previously received the BCG vaccination; however, it is limited by its higher cost.[6]

Signs and Characteristics of LTBI[5]:

- Positive tuberculin skin test (TST) or interferon gamma release assay (IGRA)
- Normal chest x-ray and negative sputum test
- Presence of Mycobacterium tuberculosis in body but inactive
- No clinical signs or symptoms of disease
- Noncontagious
- Can progress to TB disease if immune system is compromised
- Need treatment to prevent progression to TB disease

Table 2: Treatment of LTBI

Drugs	Duration	Indicated Age	Frequency	Total doses	Indicated special pop.
Isoniazid (INH) and Rifapentine (RPT)	3 months	Adults and children ≥2 years	Once weekly	12	LTBI with HIV infection with acceptable DDIs
Isoniazid (INH) and Rifampin	3 months	Adults and children	Daily	90	---
Rifampin (RIF)	4 months	Adults and children	Daily	120	Preferred in children <2 years
Isoniazid (INH)	9 months	Adults and children	Daily or twice weekly	76 or 270	Preferred tx for pregnant women with Vit B6 supp

There are four algorithms available for the treatment of LTBI. Although the different treatment regimens have comparable efficacy, therapies with shorter treatment durations are preferred because they have higher rates adherence and treatment completion.[2]
In 2018, the CDC expanded the Isoniazid (INH) and rifapentine (RPT) treatment to[2]:

1. Persons with LTBI aged 2-17 years
2. Persons with LTBI who have a HIV infection, including AIDS, and are taking antiretroviral medications with acceptable DDI's with rifapentine (i.e. efavirenz or raltegravir)
3. By directly observed therapy (DOT) or self-administered therapy (SAT) in persons aged ≥2 years

Although only the twice-weekly isoniazid treatment is required to be administered through DOT[8] it is highly recommended that DOT be used over self-administered therapy (SAT) as DOT enhances adherence and improves treatment outcomes compared to SAT.[9]

Unfortunately, drugs used in the treatment of LTBI are followed by significant adverse effects, and it requires careful consideration looking at patients' medical history, current medications, and risk factors to determine the best therapy. One of the most significant limitation with rifamycins are the drug-drug interactions (DDI). Because rifamycins are potent Cytochrome P450 enzyme inducers, it increases clearance of multiple drugs which lead to lower concentrations and possibly subtherapeutic levels of drug in the body. Some notable interactions include warfarin, birth control, antiretroviral agents, and methadone. Other adverse effects include GI effects like nausea and vomiting and orange discoloration of bodily fluids. Hepatotoxicity with rifapentine has been seen and hematologic effects like thrombocytopenia, neutropenia, and acute hemolytic anemia has been recorded for rifampin.[10]

The most notable side effect of Isoniazid is hepatotoxicity. It has a Black Box Warning for hepatitis so monitoring of liver function through liver function tests to test for transaminases, bilirubin, and INR is critical while on isoniazid therapy. Avoiding alcohol consumption when on therapy with isoniazid is an important counseling point. In addition, Peripheral neuropathy can occur among patients on LTBI regimens containing isoniazid due to interference with metabolism of pyridoxine. This can be prevented with pyridoxine supplementation (25 to 50 mg daily). The administration of pyridoxine is especially important for patients with conditions that can predispose to neuropathy (including diabetes, uremia, alcoholism, malnutrition, and HIV infection) as well as in the setting of pregnancy and seizure disorders.[11] Adverse effects associated with the use of combination Rifamycins and isoniazid include hypotension and syncope and flu-like syndrome.[10,11]

Management of LTBI can certainly be very overwhelming and difficult for patients to manage and pharmacists can play a very prominent role to improve the quality of life of our patients. Whether it is in an in-patient or out-patient setting, there are many opportunities for pharmacist intervention like DOT and/or encouraging medication adherence, monitoring for adverse effects and DDI's, patient education, and providing important counseling points.

References:

1. Talwar, A., Tsang, C. A., & Price, S. F. (2019, March 22). Tuberculosis - United States, 2018 | MMWR. Retrieved July 18, 2019, from https://www.cdc.gov/mmwr/volumes/68/wr/mm6811a2.htm
2. Borisov AS, Bamrah Morris S, Njie GJ, et al. Update of Recommendations for Use of Once- MMWR Morb Mortal Wkly Rep 2018;67:723–726. DOI: http://dx.doi.org/10.15585/mmwr.mm6725a5
3. Latent tuberculosis infection (LTBI). (2018, June 08). Retrieved July 22, 2019, from https://www.who.int/tb/areas-of-work/preventive-care/ltbi_faqs/en
4. LTBI | Data & Statistics | TB | CDC. (2018, September 28). Retrieved July 22, 2019, from https://www.cdc.gov/tb/statistics/ltbi.htm
5. Fact Sheets | General | Latent TB Infection vs. TB Disease | TB | CDC. (2014, October 20). Retrieved July 22, 2019, from https://www.cdc.gov/tb/publications/factsheets/general/ltbiandactivetb.htm
6. Schluger, N. W. (2017). Improving the Diagnosis of Latent TB Infection. *Chest,151*(6), 1207-1208. doi:10.1016/j.chest.2017.04.161
7. Fact Sheets | Infection Control & Prevention | Fact Sheet - BCG Vaccine | TB | CDC. (2016, May 4). Retrieved July 22, 2019, from https://www.cdc.gov/tb/publications/factsheets/prevention/bcg.htm
8. Latent tuberculosis infection in children. (2018, November 29). Retrieved July 22, 2019, from https://www-uptodate-com.proxy.library.vcu.edu/contents/latent-tuberculosis-infection-in-children?search=latent tuberculosis&topicRef=115049&source=see_link#H242217269
9. Alipanah N, Jarlsberg L, Miller C, et al. Adherence interventions and outcomes of tuberculosis treatment: A systematic review and meta-analysis of trials and observational studies. *PLoS Med.*2018; 15(7):e1002595.
10. Rifamycins (rifampin, rifabutin, rifapentine). (2018, April 8). Retrieved July 23, 2019, from https://www-uptodate-com.proxy.library.vcu.edu/contents/rifamycins-rifampin-rifabutin-rifapentine?search=Rifamycins (rifampin, rifabutin, rifapentine)&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H9
11. Isoniazid: An overview. (2019, October 30). Retrieved July 23, 2019, from https://www-uptodate-com.proxy.library.vcu.edu/contents/isoniazid-an-overview?search=isoniazid§ionRank=1&usage_type=default&anchor=H13&source=machineLearning&selectedTitle=2~149&display_rank=1#H16

Continuing Education Quiz and Evaluation

Complete the quiz and evaluation online at:

https://alaskapharmacy.org/ce-events/home-study-ce/ce-quiz-quarterly-akpha-newsletter-second-quarter-2020/

Program 0139-0000-20-201-H04-P/T

Quarterly AKPhA Newsletter

Release Date 4/15/2020

Expiration Date 4/15/2023

CPE Hours: 2.0 (0.2 CEU)

The authors and the Alaska Pharmacists Association disclaim any liability to you or your patients resulting from reliance solely upon the information contained herein.

Fees CE processing is free for AKPhA members. Non-members must submit $20 per quiz at: https://alaskapharmacy.org/payments/

To Obtain CPE Credit for this lesson you must complete the evaluation and quiz linked above and score a passing grade of 70% or higher. If you score less than 70%, you may repeat the quiz once. CPE credit for successfully completed quizzes will be uploaded to CPE Monitor within 60 days.

The Alaska Pharmacists Association is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.