

An award-winning, bimonthly, electronic, student-operated newsletter publication by the St. John's University College of Pharmacy and Health Sciences Rho Chi Beta Delta chapter











THE RHO CHI SOCIETY

The Rho Chi Society encourages and recognizes excellence in intellectual achievement and advocates critical inquiry in all aspects of Pharmacy.

The Society further encourages high standards of conduct and character and fosters fellowship among its members.

The Society seeks universal recognition of its members as lifelong intellectual leaders in Pharmacy, and as a community of scholars, to instill the desire to pursue intellectual excellence and critical inquiry to advance the profession.



St. John's University College of Pharmacy and Health Sciences 8000 Utopia Parkway, Jamaica, NY 11439 Website: http://rhochistj.org/RhoChiPost Facebook: http://fb.com/RhoChiPost Twitter: http://twitter.com/RhoChiPost Technical Support: (347) RHO-CHI-1

CURRENT EXECUTIVE BOARD



Left to Right: Soumik, Nidhia, Alexandra, Daniya, Tolulope, Patrick, Stephanie, Abigail

President: Tolulope Omisakin Vice President: Patrick Kohn Secretary: Daniya Mathew Treasurer: Nidhia John Historian: Soumik Ghosh Development & Outreach Coordinator: Abigail Radoncic Academic Committee Coordinators: Stephanie D'Elia, Alexandra Ilsey Chapter Advisor: Dr. Joseph Etzel Have something interesting to say?

Wish to publish your poster presentation?

Want to review a new drug on the market?

Write to us at RhoChiPost@gmail.com or visit our website:

http://rhochistj.org/ RhoChiPost/

Remember, Rho Chi Honor Society membership is NOT a requirement for submitting articles to the Rho Chi Post!

RHO CHI post

We are always looking for creative and motivated students to join our team! If you are interested in becoming a Rho Chi Post editorial team member, visit:

rhochistj.org/RhoChiPost/ Application



TABLE OF CONTENTS

Issues of Stigma When Addressing Schizophrenia & Mental Illness	
By: William Obilisundar, PharmD Candidate c/o 2023	5
Binghamton University School of Pharmacy and Pharmaceutical Sciences	
Metastatic Breast CancER+ Treatment	7
By: Lyana Sayilar, PharmD Candidate c/o 2020	· · · ·
COVID-19 and the vaccine development process: A closer look	
By: Jason Ifeanyi, PharmD Candidate c/o 2022	9
Novel agents in the treatment of chronic lymphocytic leukemia	10
By: Nishanth Viswanath, PharmD Candidate c/o 2022	13
A Closer Glance at Mycobacterium Avium Complex (MAC) Infection and Treatment	
By: Dana Weinstein, PharmD Candidate c/o 2022	16
Team Members	18
Back Cover	22

QUOTE OF THE MONTH

Wherever the art of medicine is loved, there is also a love of humanity

HIPPOCRATES

Issues of Stigma When Addressing Schizophrenia & Mental Illness

By: William Obilisundar, PharmD Candidate c/o 2023, Binghamton University School of Pharmacy and Pharmaceutical

One of the most interesting events hosted by the Binghamton University School of Pharmacy during the 2019-2020 academic year was a seminar entitled, "Mental Health Awareness: A Focus on Suicide & Stigma," presented by Dr. Carolyn M. Tyler, Ph.D., neuroscientist and Medical Science Liaison from Otsuka Pharmaceuticals' newly promoted PsychU. PsychU is an online platform whose mission is to improve mental health treatment for all individuals in the health care community, including patients, friends of patients, and providers. The main take away points from the seminar were that stigma contributes to the negative attitudes, beliefs, and behaviors of healthcare providers toward people with mental health disorders; mental illness is not the same as other diseases, such as diabetes and heart disease, and that stigma remains a barrier to recovery and social integration.¹ Being introduced to PsychU, I found a pertinent online service that provides a well-rounded presentation of a variety of topics relating to mental health. Nevertheless, as with any such platform, there is always room for improvement in developing accurate statements for sensitive topics like mental health and the stigma that surrounds it.²

The data presented during the seminar resonated with me. Roughly 40 to 50 percent of patients with schizophrenia consider suicide and their life expectancy is reduced by approximately 25 years due to the risk of suicide.^{1,3} The numbers hit me in a very personal way, as I contemplated about a population with which I identify. I have schizophrenia; however, I do not have suicidal ideation. When it came time for Q&A, upon attempting to ask how to deal with emotional abuse targeted at those with mental illness, the data and personal dilemmas became an overwhelming weight on me, and I was hit with raw emotion, bawling with tears as I asked my questions. I had to cover my face with my palm. My thoughts on the university's advocacy for mental health transitioned into my thinking solely about committing faux pas - now I would be labeled mentally ill and at risk for suicide at my school, an untrue label.

Following the event, I thought about voicing my opinions on the topic. Simultaneously, my tears caused the university administration to be notified and consequently email me campus resources for mental health. While the school may not be wrong in forwarding me available resources, there are a few questions to be had – does a display of raw emotion and feelings contribute to stigma? Does an identity dissipate upon being recognized as one with mental illness? Moreover, does data crunching sample statistics further the problem of stigma? What concerns me the most amid all the possible questions is the entirely paradoxical component to addressing mental health and stigma in that a full-blown effort can contradict itself and even exacerbate the issue. Inevitably, I became a sheer number assumed to death by suicide in the eyes of a few of my peers, whereas neither my question nor any other considerations took place.

RHO

CHI

While I would like to be open about having schizophrenia and possibly advocate for the illness, it is not an easy task. Dr. Tyler mentioned during her presentation that one of the largest problems in treating schizophrenia is that many of the first generation antipsychotics (FGAs) are derived from mid-19th century treatments, with a seeming purpose of keeping schizophrenics complacent in society, rather than improving quality of life outcomes.¹ The issue of stigma for those with schizophrenia deviates into a sociocultural dilemma in which a society cannot interpret unaccustomed events; therefore, the conditions and outcomes of a disease state are reaffirmed by numbers which are written off by healthcare professionals.

To the point, rhetoric drives into the perception and interpretation of data. In an improved outreach over the topic this year, Otsuka developed an infographic to reframe ways to deal with stigma. One is not mentally ill, but instead has a mental illness.² Phrasing alters the perceived insult.² Although looking at data crunching, the effect of a number in statements seems unmalleable. PsychU's webinar on the topic not only addresses Dr. Tyler's overview, but also several contributors to institutionalized stigmatization of mental health.³ One of many reasons why negative rhetoric matters in the context of people living with mental illness is because the expectation of a negative prognosis contributes to stigma.³ The aforementioned data in Dr. Tyler's seminar may as well have been translated as, 'those with schizophrenia are a coin flip ticking time bomb.' While the numbers are high, other contemporaneous conversations show different numbers, and some explain in other words that the shortened lifespan and standardized mortality ratio for those living with schizophrenia is two to four-fold the general population.^{4,5} At the same time, another psychiatric expert expresses that those with schizophrenia have life expectancies reduced by 10 to 20 years on account of functional issues, including other physical and metabolic illnesses related to inflammation.⁶ This phrase makes a world of difference in terms of perception and interpretation of the data. While statistics may seem immortal, their explanations are broader than their actual presentation.

The issue of stigma lapses further in rhetorical nuances at the hands of healthcare professionals. A single nuance can mislead an audience over matters at hand. For example, a PsychU webinar presented by Dr. René Kahn, M.D., Ph.D., and Dr. Christoph Correll, M.D., outlines many coherent cognitive facets of



schizophrenia, yet amid the presentation is a diagram listing primary or negative cognitive symptoms in schizophrenia, among them being mental retardation and substance misuse.⁶ While a subset of people living with schizophrenia do experience cognitive impairments, I am not mentally retarded, and my pursuit of a career in pharmacy demonstrates the antithesis. The referenced article, dated 2014, fails to acknowledge diagnostic terminology pursued in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), dated 2013.7 In addition, there are other nuances in metapsychiatry that stigmatize schizophrenia to a greater degree. The referenced article is of the few studies that list substance misuse as a symptom. In the American Psychiatric Association's 2004 edition of the, "Practice Guideline for the Treatment of Patients with Schizophrenia," substance use is described as a plausible comorbidity, common contributor to system relapse, and a common comorbid condition.⁴ In the current 2019 draft of the same guideline, substance use is described as plausibly concomitant, co-occurring, or a common co-occurring condition.⁵ This shift in phrasing dangerously misleads individuals in the health care community and beyond into thinking substance use defines the epidemiology of schizophrenia; all the while, the shift presents a professional environment with slurs at best. There may be a percentage of people living with schizophrenia who present with substance abuse, but I can assure you it is not everyone and not me substance use neither produced my disease state nor is it resultant from my disease. Thus, rhetoric or misappropriation of words in some cases proves a challenge to the cause of raising awareness for such mental illnesses and their stigmata by amplifying the stigmata rather than mitigating them.

Healthcare professionals have the tools to address mental health and the stigma associated with it. My only qualms are that some healthcare professionals fail to see potential flaws in their efforts. In the future, I hope to see the language used in discussing mental illness evolve for the better, not only for my sake, but for the sake of others who live with mental illnesses as well.

Sources:

1. Tyler CM. Mental Health Awareness: A Focus on Suicide & Stigma. Seminar presented at: Binghamton University School of Pharmacy and Pharmaceutical Sciences;11/06/2019; Johnson City, NY.

2. Overcoming Stigma in Mental Health. PsychU website. https://www.psychu.org/patient-caregiver/overcoming-stigmain-mental-health/. Published 02/2020. Updated 05/04/2020. Accessed 06/12/2020.

3. Self R, Archuleta B. Mental Health Awareness: A Focus on Suicide & Stigma. PsychU website. https://www.psychu.org/ mental-health-awareness-a-focus-on-suicide-stigma/. Published 05/27/2019. Accessed 06/12/2020. 4. American Psychiatric Association. Practice Guideline for the Treatment of Patients with Schizophrenia. 2nd ed. Washington, DC: American Psychiatric Association; 2004. https:// psychiatryonline.org/pb/assets/raw/sitewide/ practice_guidelines/guidelines/schizophrenia.pdf. Accessed 06/12/2020.

5. American Psychiatric Association. The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia. Washington, DC: American Psychiatric Association; 2019. https://www.psychiatry.org/File%20Library/Psychiatrists/ Practice/Clinical%20Practice%20Guidelines/APA-Draft-Schizophrenia-Treatment-Guideline-Dec2019.pdf. Accessed 06/12/2020.

6. Correll C, Kahn R. Cognitive Function & Neuroprotection In Schizophrenia. PsychU website. https://www.psychu.org/ cognitive-function-neuroprotection-in-schizophrenia/. Published 06/26/2019. Accessed 06/12/2020.

7. Intellectual Disability. American Psychiatric Association Website. https://www.psychiatry.org/File%20Library/ Psychiatrists/Practice/DSM/APA_DSM-5-Intellectual-Disability.pdf. Published 2013. Accessed 06/16/2020.

Figure 1: Tips from PsychU Professionals for Dealing with Mental Health Stigma.^a

TIPS | Ways to Deal With Stigma

- Get Treatment You might be afraid to get help because you don't want to be identified as someone with a mental health condition. But your care team can help you create a treatment plan and reduce your symptoms.
- Be Kind to Yourself You may think your condition is a sign of weakness and that you should be able to control it without help. But getting help is important. People with medical conditions all need treatment. Your condition is not your fault.
- Understand You Are Not Your Illness Don't say, "I am bipolar." Say, "I have bipolar disorder." Avoid using insulting terms for mental illness.
- Educate Yourself and Others Knowing the facts about your condition can help build confidence. It can also help others understand it is a medical condition that you are managing.
- Talk About It It can be hard to talk with family and friends about your condition. Sharing your feelings and what you are going through can help the important people in your life understand your condition. Talking may help you feel less alone. Friends and family can offer encouragement and support.
- Find Support There are groups, like the National Alliance on Mental Illness (NAMI), that offer local support programs and Internet resources to help lessen stigma through education. Connecting and talking with others who have similar conditions can provide mutual support, kindness, and compassion.
- Speak Out Against Stigma If you're able to, consider sharing your experiences and views with others. You may help others who are facing mental health issues.
- $\checkmark\,$ Speak Up Tell your provider if you feel you are not being treated fairly.

©2020 Otsuka Pharmaceutical Development & Commercialization, Inc.

Metastatic Breast CancER+ Treatment

By: Lyana Sayilar, PharmD Candidate c/o 2020

Approved on April 17, 2020, tucatinib (TukysaTM) is indicated to aid in the treatment of human epidermal growth factor receptor 2 (HER2) positive metastatic breast cancer and could be a potential add-on therapy.³ Among the different types of breast cancers, an increase of HER2, a transmembrane glycoprotein consisting of intracellular and extracellular domains, on the surface of breast cancer cells leads to proliferation and may metastasize to other parts of the body. Therefore, HER2-targeted therapy is useful for this type of breast cancer.⁸

The first-line therapy of HER2+ metastatic breast cancer is pertuzumab + docetaxel + trastuzumab. Although there is no experimental causation of docetaxel altering the permeability of the blood brain barrier to increase the entry of tumor cells into the brain, there is an association that brain metastases increase while on taxane treatment.⁴ In many other countries, paclitaxel is used instead of docetaxel because it further increased progression-free survival and reduced the occurrence of neutropenia.¹⁰ The second-line agent for HER2+ metastatic breast cancer, ado-trastuzumab emtansine (Kadcyla®), consists of a humanized monoclonal antibody covalently bound to a cytotoxin. Third-line treatment is a combination of lapatinib, a tyrosine kinase inhibitor, and an antimetabolite, capecitabine.^{5,6,8}

Furthermore, tucatinib is a highly selective tyrosine kinase inhibitor of the intracellular domain of HER2, a tyrosine kinase protein, preventing phosphorylation of HER2 receptors on tumor cells and proliferation of tumor cells. It is indicated for use in neurologically stable patients with brain metastases who are not in need of urgent surgery or radiation and in patients without brain metastases, either of whom have tried treatment with at least one medication against the proliferation of HER2 receptor. Tucatinib is taken along with the anti-HER2 antibody, trastuzumab, and capecitabine.¹

A randomized (2:1), double-blind, placebocontrolled trial, HER2CLIMB, was conducted at 157 sites worldwide with the majority of the patients white females and less than 75 years old.² The primary endpoint of the trial was duration of progression-free survival. The first 480 patients were randomized to receive tucatinib + trastuzumab + capecitabine or placebo + trastuzumab + capecitabine. There was a median 2-month difference in progression-free survival, favoring the tucatinib combination.¹ In one year, the progression-free survival of the tucatinib combination was 33.1 percent as compared to 12.3 percent with placebo combination (95% CI [0.42-0.71]; p-value <0.001).²

RHO CHI

Additionally, secondary endpoints, such as overall survival and progression-free survival in patients with brain metastases, were measured in 612 patients. At 2 years, 44.9 percent in the tucatinib combination survived as compared to 26.6 percent in the placebo combination group (95% CI [0.50-0.88]; p= 0.005). The median survival at 2 years was 21.9 months for the tucatinib combination and 17.4 months for the placebo combination. Progressionfree survival in 1 year in patients with brain metastases was 24.9 percent for the tucatinib combination and 0 percent for the placebo combination (95% CI [0.34-0.69]; p-value <0.001). There was a median 2-month difference in progression-free survival, favoring the tucatinib combination.² The data seems promising for patients with brain metastases. Since tucatinib and lapatinib are in the same drug class, comparing tucatinib + trastuzumab + capecitabine and lapatinib + trastuzumab + capecitabine in brain metastatic patients may be beneficial, although there is no head-to-head trial comparing the two combinations. In a study in China, patients who took lapatinib + trastuzumab + capecitabine as first-line for brain metastases had a statistically significant median progression-free survival of 20.7 months than if taken as second-line therapy (12.3 months) or third-line therapy (7.3 months).⁹ Therefore, the lapatinib combination seems more effective when taken earlier, which may foreshadow the benefit of tucatinib in brain metastatic patients.

Tucatinib resulted in fetal deformities in animal studies and should be avoided in pregnant women. Women of reproductive age should be reminded to use contraception during treatment with tucatinib + trastuzumab + capecitabine and for one week after the last dose. The combination should be avoided during breastfeeding as it may appear in breast milk. Another warning to note is it may cause sterility in men and women.¹

Additionally, drug-drug and drug-food interactions must be considered. Concomitant use of tucatinib with strong CYP3A4 inducers, moderate CYP28C inducers, strong CYP2C8 inhibitors, or with P-gp substrates result in dose adjustments. Renal and hepatic function should be assessed prior to initiating tucatinib + trastuzumab + capecitabine.



The combination is not recommended if the CrCl is less than 30 mL/min. For patients with Child-Pugh C hepatic impairment, the dose should be reduced from 300 mg tucatinib orally twice daily to 200 mg twice daily.¹

Tucatinib can be considered as a treatment option for HER2+ metastatic breast cancer with and without brain metastases. Up to 50 percent of patients with HER2+ metastatic breast cancer suffer from brain metastases and half of those patients unfortunately lose their lives, but there is hope for improvements as research continues.⁷

Sources:

1. TUKYSA[™] (tucatinib) [package insert]. Bothell, WA; Seattle Genetics, Inc.; Revised 04/17/2020.

2. Murthy RK, Loi S, Okines A, et al. Tucatinib, Trastuzumab, and Capecitabine for HER2-Positive Metastatic Breast Cancer. N Engl J Med. 2020;382(7):597-609. doi: 10.1056/ NEJMoa1914609

3. Goodman A. Emerging Alternatives in the Third-Line Setting for Metastatic HER2-Positive Breast Cancer. The ASCO Post. https://www.ascopost.com/issues/december-10-2019/ emerging-alternatives-in-the-third-line-setting-for-metastaticher2-positive-breast-cancer/. Published 12/10/2019.

4. Bernatz S, Ilina El, Devraj K, et al. Impact of Docetaxel on blood-brain barrier function and formation of breast cancer brain metastases. *J Exp Clin Cancer Res.* 2019;38(1):434. doi: 10.1186/s13046-019-1427-1.

5. Shah N, Mohammad AS, Saralkar P, *et al.* Investigational chemotherapy and novel pharmacokinetic mechanisms for the treatment of breast cancer brain metastases. *Pharmacol Res.* 2018;132:47-68. doi: 10.1016/j.phrs.2018.03.021

6. KADCYLA® (ado-trastuzumab emtansine) [package insert]. South San Francisco, CA; Genentech, Inc.; Revised 05/20/2019.

7. Duchnowska R, Loibl S, Jassem J. Tyrosine kinase inhibitors for brain metastases in HER2-positive breast cancer. Cancer Treat rev. 2018;67:71-77. doi: 10.1016/j.ctrv.2018.05.004

8. Schott A. Systemic treatment for HER2-positive metastatic breast cancer. UpToDate. <u>https://www-uptodate-</u> com.jerome.stjohns.edu/contents/systemic-treatment-for-her2positive-metastatic-breast-cancer?search=her2%20positive% 20metastatic%20breast%

<u>20cancer&source=search_result&selectedTitle=1~150&usage_t</u> <u>ype=default&display_rank=1</u>. Published 01/28/2020. Last Updated 05/06/2020.

9. Li Y, Gong C, Lu Q, et al. Real-World Data of Triplet Combination of Trastuzumab, Lapatinib, and Chemotherapy in 10. Bachelot T, Ciruelos E, Schneeweiss A, et al. Preliminary safety and efficacy of first-line pertuzumab combined with trastuzumab and taxane therapy for HER2-positive locally recurrent or metastatic breast cancer (PERUSE). ScienceDirect. <u>https://www-sciencedirect-com.jerome.stjohns.edu/science/article/pii/S0923753419311615?via%3Dihub#!.</u> Published 01/06/2020.

RHO CHI post

COVID-19 and the vaccine development process: A closer look

By: Jason Ifeanyi, PharmD Candidate c/o 2022

Severe acute respiratory syndrome coronavirus 2 (SARS -CoV-2), the viral strain responsible for causing COVID-19, continues to have a profound impact on communities at a local, national and global level. As of August 20, 2020, nearly 5.7 million confirmed cases exist in the United States with a total of over 175,000 deaths. In the State of New York alone, there have been over 450,000 confirmed cases with nearly 33,000 deaths.¹² While there are many clinical trials currently taking place which are investigating the safety and efficacy of certain pharmacological treatments against COVID-19, many people around the world are focused on one thing - the development of a vaccine for COVID-19. In the news, researchers and scientific experts assert that a COVID-19 vaccine could very well be approved and available for administration by the end of 2020. The vaccine's ability to mitigate the damage this pandemic has caused has been a major topic of debate and there have been varied reactions from the public. Some patients are skeptical of these assertions, some fully believe these assertions, and some are confused as to why a vaccine has not already been developed and made available to the public. These patients' questions and concerns are legitimate, and as aspiring pharmacists, we are among the most accessible healthcare professional patients can consult to get answers. The nature of our profession not only requires us to possess sufficient knowledge on the nature of various medications, but also requires us to effectively communicate that knowledge to a concerned public in times of crisis so that they are better able to make informed decisions and live healthier lives. As student pharmacists, we owe it not only to ourselves, but to our communities and our profession, to ensure our knowledge on the COVID-19 vaccine development process remains current.

A vaccine is a form of medicine that contains the same infectious pathogen responsible for causing disease. The key difference with a vaccine is that the infectious pathogen has either been killed or weakened to the point that it does not make a person sick; in other words, it will not cause an infection. As a result, the vaccine stimulates one's immune system to produce antibodies the same way it would if they had been exposed to the disease.² After receiving the vaccine, one develops immunity to the disease, without having contracted it in the first place. This makes vaccines a preventative form of therapy because the goal is not to treat the disease. Rather, the goal is to prevent individuals from getting the disease in the first place.

Vaccines can be developed using one of a few different strategies. The first type of vaccine one can develop is an inactive vaccine. This type of vaccine is composed of an inactivated form of the infectious pathogen. Although it retains the major components of the pathogen required to stimulate an immune response, it will not cause an infection. A second and recent method for developing vaccines involves more recombinant DNA technology. This method involves pulling out components of the virus (parts of its genetic sequence, instead of the full genetic code), and utilizing that as the major component of the vaccine, so that the immune system will recognize it and build up antibodies without getting an infection. The third type of vaccine is live attenuated. This vaccine makes use of a heavily weakened strain of the infectious pathogen so that it does not cause infection after being administered.¹¹

Safety and effectiveness aside, there are five steps in the vaccine development process. The first step involves generating the antigen. As mentioned earlier, the ultimate goal is to stimulate the immune system to produce antibodies in response to an infectious pathogen. For this reason, the vaccine must have some form of the infectious pathogen. This could involve the growth and harvesting of the pathogen itself for later inactivation or isolation of a subunit. It could also involve the generation of a recombinant protein (a protein made from DNA technology) derived from the pathogen. Bioreactors are manufactured devices or systems used to support a biologically active environment. Oftentimes, these are the devices used to grow and culture bacteria. For many viral vaccines, this process begins with small amounts of virus that can be grown in cells. Various cell types can be used such as chicken embryos or cell lines that reproduce repeatedly. 7

The second step of vaccine development involves releasing the antigen, including remnants of proteins from bacteria or viruses, from the cells and isolating it from the materials used in its growth. The third step is purification. For vaccines made from recombinant proteins, this may involve chromatography, a strategic way of separating materials, as well as ultrafiltration. Inactivation of the antigen may also occur during this phase. The fourth step involves strengthening the main vaccine components. This may involve the addition of an adjuvant, which is a material that nonspecifically enhances the immune response. Vaccines may also include stabilizers to prolong shelf-life, as well as preservatives, to allow multi-dose vials to be used safely. The last step in the vaccine development process involves distribution. In this step, all the components that make up the final vaccine are combined and mixed uniformly in a single vessel. The vaccine is then filled into a vial or syringe, sealed with sterile stoppers or plungers and labeled for widespread distribution.⁷

It is important to emphasize that the five steps described above are a general overview of the vaccine development process. More specifically, the first four steps are components of preclinical studies where the antigen's structure is researched, and toxicity and pharmacokinetic profiling are evaluated prior to initiating clinical trials with human participants. All this research on safety and efficacy is included in an Investigational New Drug (IND), which must be submitted prior to commencing to clinical trials.¹⁰

Before a vaccine can be labeled for widespread distribution, which is the fifth and final step in development, it must first be approved for use by the Food and Drug Administration (FDA). In order to obtain approval, the vaccine must adequately demonstrate both safety and effectiveness in three phases of clinical trials in which human participants are enrolled. This is the key step which takes the longest period of time to complete and is the reason why as of August 20, 2020 no COVID-19 vaccine has been FDAapproved for widespread distribution. This key step can be broken down into 4 phases.

Phase 1 marks the first stage of research involving human participants. The enrolled participants in Phase 1 studies are relatively small, usually 20 healthy volunteers.³ The vaccine is given at different doses to each of the volunteers, and this helps researchers determine the right dose for the next step in the testing process that is sufficient to elicit an immune response. Phase 1 clinical trials are also meant to rule out major safety concerns. After completing Phase 1, the vaccine proceeds to Phase 2 clinical trials, which involves a larger group of participants consisting of approximately one hundred to two hundred enrollees. This phase may include up to one thousand patient volunteers if multiple Phase 2 trials are necessary. In this phase, the dose that was determined in Phase 1 is administered alongside other routine vaccines to the healthy volunteers. This phase is meant to ensure that the vaccine provides a consistent immune

response. In addition to monitoring participants for common adverse effects, including local swelling and fever, researchers monitor for less common and potentially more severe adverse effects. Subsequently, the vaccine progresses to Phase 3 clinical trials. This phase involves thousands of healthy volunteers. This phase determines whether the vaccine protects against natural infection and allows researchers to identify rare problems not observed in smaller studies. If the vaccine passes all these stages of clinical trials, there are additional regulatory components that must be satisfied before it proceeds to Phase 4, also known as Post-Marketing Surveillance. ⁶

RHO CHI

The FDA center for Biologics Evaluation and Research (CBER) is responsible for regulating vaccines in the United States. Once clinical trials have been completed, the sponsor of the new vaccine must submit a Biologics License Application (BLA). This application serves as a request for permission to introduce, or deliver for introduction, a biologic product into the market. This process involves presentations of clinical trial findings to FDA's Vaccines and Related Biological Products (VRBPAC). Advisory Committee Additionally, the manufacturing facility will be inspected, and tests will be done to assess usability and labeling of the vaccine. Only once these requirements have been met, and the BLA has been approved, will the vaccine be introduced to market.²

In Phase 4, the vaccine undergoes widespread distribution and is continuously monitored for side effects and long-term adverse events that were not observed in preclinical and clinical trials. The Vaccine Adverse Event Reporting System (VAERS) is a national vaccine surveillance program cosponsored by the FDA and CDC. It is strongly encouraged for all concerned individuals to make a report of any unexpected side effects that occur. This includes patients, parents, pharmacists, physicians and vaccine manufacturers. ² With this information in mind, one can see why an established vaccine against COVID-19 has yet to be approved for widespread use. There are many steps involved not only in developing the actual vaccine, but in the testing of the vaccine to ensure its safety and efficacy. Additionally, the necessary approval process of the FDA and other regulatory boards is a crucial step that furthers slows the entire process down.

One point that should be noted is the difference between clinical trials for vaccines and clinical trials for medications. A much larger patient population is included in Phase 3 trials for vaccines because researchers want to detect any highly rare side effects caused by the vaccine. There is a

RHO CHI post

much lower tolerance level for side effects in vaccine trials compared to other medicine trials, and for good reason. The patient volunteers, and the future target group for the vaccine, are healthy to begin with.⁶ The last thing researchers want to do is cause a healthy patient to become unhealthy and possibly die, due to receiving a poorly tested vaccine. For these reasons, vaccines can usually take up to ten or more years to develop, costing nearly five hundred million dollars, according to Wellcome Trust, a United Kingdom Charity. Discovery research can take anywhere from two to five years - two years for preclinical trials, one to two years for Phase 1 clinical trials, two to three years for Phase 2 clinical trials, two to four years for Phase 3 clinical trials, and one to two years for regulatory review and approval.⁵

This is a major cause of confusion among patients. On one hand, many politicians and scientific experts are making assertions that an effective vaccine will be available by the end of 2020, yet history has shown us that it takes much longer than 12-18 months to develop a safe and effective vaccine. If a COVID-19 vaccine were to be ready by the end of the year, that would make its development time faster than the current record holder, the Mumps Vaccine, which took 4 years to develop. ⁸ While there is uncertainty as to whether this is a practical timeframe or mere wishful thinking, one thing is certain – researchers and pharmaceutical companies are working relentlessly to fast-track the COVID-19 vaccine development process.

On May 15, 2020, the White House announced a new initiative entitled, Operation Warp Speed (OWS). This initiative aims to fast-track multiple COVID-19 vaccine candidates, with the goal of delivering 100 million doses across America in November 2020, and another 200 million by January 2021.⁹ This initiative entails a partnership among a variety of agencies within the Department of Health and Human Services (HHS) including the Centers for Disease and Control and Prevention (CDC), FDA) the National Institutes of Health (NIH), and the Biomedical Advancement Research and Development Authority (BARDA), partnered with Department of Defense (DoD).9 Currently, there are over one hundred and thirty five vaccine candidates in preclinical trials internationally; twenty in Phase 1 clinical trials, eleven in Phase 2 clinical trials, eight in Phase 3 clinical trials, and two that have been approved, albeit with a large degree of uncertainty, as they have not been FDA approved in the US. One of the vaccines that is not FDA-approved, was developed by CanSino Biologics of China and was developed from an adenovirus called Ad5. Although it was announced on August 9th that they plan on initiating a Phase 3 clinical trial in Saudi Arabia, the vaccine was approved for limited use on June 25, 2020 by the Chinese military. ⁴

More recently, Russia's Gamaleya National Research Institute of Epidemiology and Microbiology launched a Phase 1 clinical trial in June of 2020 for a vaccine called, Gam-Covid-Vac-Lyo. It is a combination of two adenoviruses, Ad5 and Ad6, both engineered with a Coronavirus gene. On August 11, 2020, Russian President Vladimir Putin announced that a Russian healthcare regulator had approved the vaccine, renaming it Sputnik V, before Phase 3 trials began.⁴ It is important to note that a number of US experts have denounced these vaccines due to the haste with which they were approved. One such US expert includes. Dr. Fauci, director of the National Institute of Allergy and Infectious Disease (NSAID). In an interview with ABC news reporter Deborah Roberts, this is what Dr. Fauci had to say. "Having a vaccine, Deborah, and proving that a vaccine is safe and effective are two different things... If we wanted to take the chance of hurting a lot of people, or giving them something that doesn't work, we could start doing this, you know, next week if we wanted to. But that's not the way it works." 1

In conclusion, the vaccine development process is multifaceted. It involves preclinical research, where the structure of the infectious pathogen is determined and manipulated in order to develop a specific vaccine type. Different strategies for developing a vaccine involve recombinant DNA technology, inactivating the infectious pathogen, or weakening the infectious pathogen so that the vaccine is able to stimulate an immune response while simultaneously avoiding the development of an infection. Once researchers determine the type of vaccine that is needed, they then culture, isolate and release, and purify the antigen followed by strengthening the vaccine components. At this point, the vaccine candidate undergoes three phases of clinical trials to determine whether it is both safe and effective in the prevention of COVID-19 in human patients. A variety of American and European pharmaceutical companies are currently in Phase 2 and Phase 3 clinical trials for the COVID-19 vaccine. As aspiring pharmacists, it is imperative that we understand the vaccine development process and its impact on our communities. As we are in the midst of a pandemic, many patients are scared, confused and skeptical of the healthrelated information they are bombarded with every day. They have questions about when the COVID-19 vaccine will be available, why it is taking so long to develop and want



answers to these questions which we can make a conscious effort to provide them with. Although we cannot predict the future, we can stay educated about the vaccine development process, and explain it to our patients in a way they helps them understand it while simultaneously eliminating fear of the unknown.

Sources:

1. Andreano C. Fauci says he has serious doubts Russia's COVID-19 vaccine is safe, effective. abcnews.go.com. https://abcnews.go.com/US/fauci-doubts-russias-covid-19-vaccine-safe-effective/story?id=72309297. Published 08/11/2020. Acceded 08/20/20.

2. Basics of Vaccines. <u>https://www.cdc.gov/vaccines/vpd/vpd-vac-basics.html</u>. Published 03/15/12. Accessed 08/05/20.

3. Commissioner, O. Step 3: Clinical Research. <u>https://</u> www.fda.gov/patients/drug-development-process/step-3clinical-research. Accessed 08/20/20

4. Corum, J., Grady, D., Wee, S., & Zimmer, C. Coronavirus Vaccine Tracker <u>https://www.nytimes.com/interactive/2020/</u> <u>science/coronavirus-vaccine-tracker.html.</u> Published 08/20/20. Accessed 08/20/20.

5. Douglas Broom, S. 5 carts that tell the story of vaccines today. <u>https://www.weforum.org/agenda/2020/06/vaccine</u> -development-barriers-coronavirus/. Accessed 08/05/20.

6. Finnegan, G. How are new vaccines developed? <u>https://www.vaccinestoday.eu/stories/how-are-new-vaccines-</u> <u>developed/</u>. Published 04/12/17. Accessed 08/05/20.

7. How are vaccines made: History of Vaccines. <u>https://www.historyofvaccines.org/content/how-vaccines-are-made</u>. Accessed 08/05/20.



Novel agents in the treatment of chronic lymphocytic leukemia

By: Nishanth Viswanath, PharmD Candidate c/o 2022

Introduction

Chronic lymphocytic leukemia (CLL) is a hematological malignancy of mature CD5 positive B-lymphocytes that primarily affects elderly patients.¹ With the average age of diagnosis being 71, the incidence of CLL is relatively rare in younger populations, though cases have occurred in those under the age of 50.1 CLL is much more prevalent in those of Caucasian descent than those of Asian or African descent. This distinction adds evidence to the genetic morphology of CLL, yet the true reasoning for it remains elusive.² CLL is the most common form of leukemia in the United States. In 2020 it is estimated that approximately 21,040 new cases will be diagnosed and about 4,060 patients will succumb to the disease.³ Due to advancements in therapies and diagnostic measures, the 5-year overall survival rate has increased from sixty-nine percent in 1980 to eighty-eight percent in 2007, and has likely become even higher today.¹ While CLL generally remains an incurable illness, contemporary therapies have rendered it a manageable and tolerable condition for most patients, especially through the latter stages of their lives.

Chemotherapy and Chemoimmunotherapy

Monotherapy with chlorambucil (Leukeran®) has been used the longest of all the available effective CLL regimens due to its low cost, and low toxicity profile.⁴ Other alkylating agents such as fludarabine (Fludara®), cyclophosphamide (Cytoxan®), and bendamustine (Bendeka®) have displayed longer progression-free survival (PFS) and higher response rates, but have made no significant impact on overall survival (OS) and are accompanied by more toxicities than chlorambucil.⁴ Anti-CD20 antibodies such as ofatumumab (Arzerra®) and obinutuzumab (Gazyva®) have been studied alongside chlorambucil for more elderly and frail patients, but have shown only median PFS rates of 22.4 months and 26.7 months respectively.⁵ Side effects such as neutropenia, thrombocytopenia and infusion-related reactions are common with ofatumumab and obinutuzumab as well.^{5,6}

The chemoimmunotherapy regimen of fludarabine, cyclophosphamide and rituximab (Rituxan[®]) (FCR) has been established as the gold standard for younger patients requiring initial pharmacologic treatment, but is not suitable for older patients due to its high rate of treatment related adverse events.⁵ Additionally, though the average PFS in patients treated with first line FCR is fifty-two percent, the same benefit is not seen in patients older than 65 or those who have unfavorable cytogenetic aberrations associated with CLL such as a chromosomal 11q deletion, 17p deletion, or unmutated immunoglobulin heavy chain variable (IGHV) region.¹

Novel Intracellular Oncogenic Pathways

Only recently did studies elucidate the role of B cell receptor (BCR) signaling in the molecular pathogenesis of CLL, and its ability to drive the proliferation of neoplastic B-lymphocytes.⁵ BCR signaling involves both "tonic" and antigen-activated stimulation, which both lead to downstream phosphorylation by kinases to provide for activation of transcription factors such as NF-kB and NFAT.⁷ As BCR signaling is an essential function of normal Blymphocyte survival, its activity in CLL promotes extensive malignancy and over proliferation of B-lymphocytes.⁷ Novel agents that target BCR signaling mechanisms have displaced the use of cytotoxic chemotherapy regimens, and have greatly increased PFS rates in the majority of patients. Bruton's Tyrosine Kinase (BTK) and isoforms of Phosphoinositide 3-Kinase (PI3K) are evidently targetable biomarkers for CLL therapy, while others are currently being evaluated in ongoing research.⁷

BTK Inhibitors

Ibrutinib (Imbruvica®) is a first in class, irreversible, relatively selective inhibitor of BTK.1 BTK is essential in leukemic Bcells for the downstream release of calcium and NF-kB, and for cell survival and proliferation.⁷ Initially approved for patients with relapsed or refractory CLL, ibrutinib has evolved into a reliable option for the first-line treatment of CLL in all age groups and for those exhibiting 17p deletion.^{1,5} When studied against chlorambucil in previously treated patients, seventy percent of patients on ibrutinib therapy experienced PFS as opposed to twelve percent with chlorambucil at 5 years of treatment.⁸ Additionally, when ibrutinib monotherapy was compared to ofatumumab in treatment naive patients for 63 months, the median length of PFS was 44.1 months (95% CI [38.5, 56.9]) and 8.1 months (95% CI [7.8, 8.3]) in the ibrutinib and ofatumumab arms, respectively.⁸ Most notably, when the combination of ibrutinib and rituximab was studied in comparison to FCR, patients on ibrutinib and rituximab displayed a median PFS at 3 years of eighty-nine percent (95% CI [85, 92]), as opposed to seventy percent of patients for FCR (95% CI [61, 78]).8

Acalabrutinib (Calquence[®]), a second generation BTK inhibitor, binds more tightly to the C481 residue of BTK than ibrutinib.9 This pharmacological profile leads to the rationale that second generation BTK inhibitors such as acalabrutinib may diminish the off-target kinase inhibiting properties of ibrutinib, which may lead to arthralgias, atrial fibrillation, rash, hypertension, bleeding and diarrhea.⁹ In clinical studies, the efficacy of acalabrutinib monotherapy has been compared to therapy with chlorambucil acalabrutinib + obinutuzumab and + obinutuzumab, with PFS being the primary endpoint.¹⁰ At a median follow-up time of 28.3 months, the chlorambucil +



obinutuzumab arm displayed a median PFS of 22.6 months [95% CI (20, 28)], while the acalabrutinib + obinutuzumab and acalabrutinib monotherapy arms did not possess average PFS rates as not enough patients displayed progressive disease.¹⁰ Compared to ibrutinib, acalabrutinib offers a lesser risk of cardiovascular comorbidities such as thrombotic risk and atrial fibrillation, but is unsuitable for patients using proton-pump inhibitors (PPI) or medications that are strong CYP-3A4 inducers or inhibitors.¹⁰ Zanubrutinib (Brukinsa[®]), another second generation BTK inhibitor is currently in phase-3 evaluation against ibrutinib for its safety and efficacy in patients with CLL, and may further abridge the risk of BTK inhibitor use in patients with cardiac dysfunctions .¹¹

PI3K Inhibitors

Idelalisib (Zydelig[®]) is a first in class, highly selective inhibitor of PI3K δ that is approved in combination with rituximab for patients with relapsed or refractory CLL.7, 12 PI3K is a multifarious kinase that is expressed as many ubiquitous isoforms such as PI3K α and PI3K β , whereas PI3K δ is found solely in B-lymphocytes.⁷ The activity of PI3K δ allows for the phosphorylation of phosphatidylinositol-bisphosphate (PIP2) creating PIP3, which assists in anchoring BTK to the cell membrane of B-lymphocytes.⁷ The efficacy of idelalisib was displayed in studies assessing it in combination with rituximab versus placebo in combination with rituximab, with PFS being the primary endpoint. Patients enrolled experienced relapsed disease or were refractory to conventional chemoimmunotherapy.¹² At a median follow-up time of 8.3 months, the median PFS for the idelalisib + rituximab arm was 19.4 months (95% CI [12.3, Not Estimable]) versus 6.5 months (95% CI [4.0, 7.3]) in the placebo + rituximab arm.¹²

Duvelisib (Copiktra®) is an inhibitor of PI3K with activity against both PI3K δ and PI3K γ , with additional inhibitory function of T cell migration.¹³ This pharmacological activity sanctions duvelisib as an effective monotherapy for relapsed or refractory patients, as opposed to idelalisib which is only approved in combination with rituximab.^{12,13} Evidently, this efficacy was proven in studies assessing duvelisib monotherapy in comparison to of atumumab monotherapy, where patients were highly treatment experienced (2 prior therapies or more).¹³ With PFS being the primary endpoint, at a median follow-up time of 22.4 months the median PFS in the duvelisib arm was 17.6 months (95% CI [15, 22]) and 9.7 months (95% CI [9, 11]).¹³

Common toxicities in both idelalisib and duvelisib such as neutropenia, anemia, diarrhea, musculoskeletal pain and respiratory infections are synonymous with those of BTK inhibitor therapy.^{12,13} Advantageously however, both idelalisib and duvelisib are plausible options for patients with cardiac comorbidities or hypertension as opposed to ibrutinib and acalabrutinib.^{12,13}

Anti-apoptotic Therapy

B-cell lymphoma 2 (BCL-2) is a regulatory protein exhibited in malignant B-cells that regulates the anti-apoptotic mechanisms of B-lymphocytes.⁵ In CLL this protein, in combination with the TP53 gene, is overexpressed and provides for the prolonged survival and resistance to certain chemotherapeutics against B-lymphocytes.⁵ Venetoclax (Venclexta®) is a selective inhibitor of BCL-2 which assists in regulating the natural apoptosis of leukemic cells and has shown remarkable clinical efficacy in relapsed and refractory CLL as monotherapy, and in combination with obinutuzumab and ibrutinib.5, 14 In combination with other agents venetoclax demonstrates high rates of undetectable minimal residual disease (uMRD) potentiating the possibility of fixed-duration therapies, as opposed to indefinite therapy with other novel agents.⁵ When venetoclax in combination with obinutuzumab was compared against chlorambucil with obinutuzumab with 2-year PFS being the primary endpoint, eighty-eight percent versus sixty-four percent of patients were progression free in each arm respectively (HR = 0.35, 95% CI [0.23, 0.53]).^{5,14} Additionally, the uMRD incidence in the venetoclax + obinutuzumab group was substantial, as fifty-seven percent (95% CI [59, 78]) and seventy-six percent (95% CI [69, 81]) of patients in the venetoclax + obinutuzumab group did not have detectable amounts of leukemic cells in bone marrow and peripheral blood respectively.14

Two-year studies utilizing fixed-duration regimens of ibrutinib as a lead in therapy and venetoclax for the remaining duration have also elucidated considerable uMRD rates.⁵ The synergistic action of BTK inhibitors and venetoclax offers an explorable treatment mechanism with acalabrutinib and zanubrutinib, and moreover a potential cure for CLL.⁵

Forward Studies

The action of BCR signalling antagonists and venetoclax have offered a multitude of novel treatment options that have revolutionized the therapeutic landscape of CLL. Conventional chemotherapy regimens have been widely superseded by immunotherapies, offering patients more effective and less toxic treatment options. More research is required, however, to determine the most effective combination regimens of venetoclax, BRC signalling antagonists and CD20 antagonists. The introduction of an anti-apoptotic agent with venetoclax has resulted in the most substantial rates of uMRD in patients, especially in combination with obinutuzumab and rituximab which are approved for 1 year and 2 year fixed-duration regimens, respectivley.¹⁴ Further studies must be conducted to identify the most suitable BTK or PI3K agent to be used in combination with venetoclax for a non-invasive, simplified regimen. Additionally, as ibrutinib has gained mass acceptance as the most reliable and definitive BTK inhibitor, toxicities such as neutropenia, diarrhea, arrhythmias and hypertension are common and frequently lead to discontinuation of therapy.⁵ Acalabrutinib diminishes such adverse effects to some extent, but is unsuitable for those receiving PPIs or strong inducers or inhibitors of CYP-3A4. The PI3K inhibitors available to date



present with less toxicities but have not demonstrated the clinical efficacy of ibrutinib and acalabrutinib. Investigational BCR signalling antagonists such as zanubrutinib, vecabrutinib, ARQ-531 and umbralisib may offer even stronger clinical efficacy than currently available agents and reinforce the use of venetoclax as a fixed-duration regimen.¹⁵

Conclusion

The treatment landscape of CLL has evolved over the last decade, shifting from chemotherapy to chemoimmunotherapy and immunotherapy. Due to existing combination regimens of BTK inhibitors, PI3K inhibitors, CD20 antagonists, and venetoclax, patients have experienced remarkable lengths of PFS and OS and now commonly present with uMRD. Traditionally, the onset of CLL results in a permanent and enduring malignancy with therapy focused on prolonging PFS. Today, studies of new BCR signalling antagonists may elucidate a curative regimen for CLL.

Sources:

1. Woyach JA, Byrd JC. Chronic Lymphocytic Leukemia. In: Jameson J, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J. eds. Harrison's Principles of Internal Medicine, 20e. McGraw-Hill; Accessed 07/05/2020.

2. Fabbri G, Dalla-Favera R. The molecular pathogenesis of chronic lymphocytic leukaemia. Nat Rev Cancer. 2016;16 (3):145-62. doi: 10.1038/nrc.2016.8.

3. American Cancer Society. Key Statistics for Chronic Lymphocytic Leukemia. https://www.cancer.org/cancer/chroniclymphocytic-leukemia/about/key-statistics.html. Accessed 07/5/2020.

4. Burger JA, Tedeschi A, Barr PM, et al. Ibrutinib as Initial Therapy for Patients with Chronic Lymphocytic Leukemia. N Engl J Med. 2015;373(25):2425-37. doi: 10.1056/ NEJMoa1509388

5. Sengar M, Jain H, Rajendra A, Rengaraj K, Thorat J. Frontline Therapy of Chronic Lymphocytic Leukemia: Changing Treatment Paradigm. Curr Hematol Malig Rep. 2020;15 (3):168-176. doi: 10.1007/s11899-020-00580-7.

RHO CHI A Closer Glance at Mycobacterium Avium Complex (MAC) Infection and Treatment

By: Dana Weinstein, PharmD Candidate c/o 2022

Mycobacterium avium complex (MAC) infection in humans species, Mycobacterium is caused by two main avium and Mycobacterium intracellulare. These species are difficult to differentiate and therefore are collectively referred to as Mycobacterium avium-intracellulare (MAI).¹ These acid-fast, atypical nontuberculosis mycobacterium (NTM) are the most common cause of lung disease in the U.S.² MAC is an easilydisseminated primarily pulmonary pathogen that is chiefly known to affect immunocompromised patients and is seen less often in immunocompetent hosts. Likely examples of MAC-susceptible patients would be those with AIDS (<10 CD₄⁺ T cells/ μ L), underlying lung disease, hairy cell leukemia, genetic TNF-alpha and IFNgamma deficiency or immunosuppressive chemotherapy.¹

MAC has been isolated from certain sources including but not limited to, plumbing systems, household and hospital water supplies, bathrooms, hot tubs, aerosolized water, house dust, soil, birds, farm animals, and cigarette components.¹ Unlike in the setting of tuberculosis (TB), where secondary cases are often identified, when clusters of patients infected with similar isolates of MAC are found, the link is usually a common water source.³ Once the pathogen is inhaled into the respiratory tract and ingested into the gastrointestinal tract, it then translocates across mucosal epithelium, infects the resting macrophages in the lamina propria and spreads in the submucosal tissue. This directly translates to the fact that virtually all patients will present with a chronic or recurring cough leading to fatigue and a lower quality of life.4,5 MAC is then carried to the local lymph nodes by the lymphatic system.¹ It can be disseminated into the spleen and bone marrow and potentially invade and colonize in intestinal cells if the species is gastric acid resistant, which appears to be a likely result in HIV-infected populations.³

Suspected MAC-infected pulmonary patients must have evident nodular or cavitary opacities on a chest radiograph and a least two positive sputum cultures or, in the absence of sputum specimens, at least one positive bronchoscopic specimen to meet the microbiologic criteria.³ Once the diagnosis is established, treatment regimen selection depends on susceptibility to macrolides; most MAC isolates, particularly in patients who have not been treated before, are macrolide-susceptible. Initial treatment of patients with MAC pulmonary disease is comprised of a threedrua regimen containing a macrolide, a rifamycin. and ethambutol (Myambutol®). For patients who have cavitary or advanced (severe) nodular bronchiectasis disease, a parenteral aminoglycoside is also often used in the initial phase of treatment.^{4,5} The therapy recommendations for nontuberculous mycobacteria from the American Thoracic Society and Infectious Diseases Society of America are shown below:

	Initial Therapy for Nodular/Bronchiectatic Disease*	Evidence Quality [†]	Initial Therapy for Cavitary Disease	Evideno Quality	Advanced (Severe) or te Previously Treated Disease	Evidence Quality [†]
Macrolide	Clarithromycin 1,000 mg TIW or azithromycin 500–600 mg TIW	B, II C	Clarithromycin 500 ⁴ –1,000 mg/d or azithromycin 250–300 mg/c	A, II	Clarithromycin 500 ¹ –1,000 mg/d or azithromycin 250–300 mg/d	B, II
Ethambutol	25 mg/kg TIW	1	5 mg/kg/d		15 mg/kg/d	
Rifamycin	Rifampin 600 mg TIW	R	lifampin 450 [‡] –600 mg/d		Rifabutin 150 ⁴ -300 mg/d or rifampin 450 ⁴ -600 mg/d	
IV aminoglycosid	de None	S	treptomycin or amikacin ⁵ or non	e	Streptomycin or amikacin ⁵	

Not recommended for severe or previously treated disease

¹ Rating for entire multidrug regimen, not necessarily for individual agents. For evidence quality, see Table 1.

[‡] Lower dose for weight < 50 kg ⁵ See text for dosing recommendation

As shown in the table, regimen selection is initially based on severity and radiologic criteria. However, antibiotic susceptibility, macrolide resistance, drug interactions, and drug intolerance also play a key role in deciding optimal treatment administration. The macrolide of choice is typically azithromycin (Zithromax[®]) but can be substituted with clarithromycin (Biaxin®) for the renally impaired, although this drug tends to have worse tolerance. Rifampin (Rifadin®), the hallmark example drug for drug-drug interactions, can be replaced with rifabutin (Mycobutin®). In both cases of drug-intolerant patients or macrolide-resistant infections, patients are recommended to receive clofazimine (Lamprene®) or moxifloxacin (Avelox®) depending on antimicrobial susceptibility testing. Additionally, use of a parenteral aminoglycoside, such as amikacin, has been associated with augmenting treatment outcomes in patients with macrolide-resistant diseases.6

Once treatment is initiated, monitoring parameters include a complete blood count and a comprehensive metabolic panel for all patients. Patients receiving a macrolide, fluoroquinolone, or clofazimine should get an electrocardiogram to assess QT interval. An audiogram should be performed for patients receiving a macrolide or aminoglycoside and a visual acuity and color discrimination should be performed for patients receiving ethambutol.⁶ A successful patient response to therapy should be documented by sputum cultures negative for MAC. Therefore, acid-fact bacillus smears and cultures of sputum should be obtained monthly during therapy for pulmonary MAC disease to assess response. Patients should show clinical improvement within 3 to 6 months and should convert their sputum to negative within 12 months on macrolide-containing regimens.⁴

Ultimately, from a clinical and pharmaceutical standpoint, a MAC patient taking such a rigorous course of antibiotics likely brings into question the implementation of a probiotic. Probiotics help the body maintain a healthy community of microorganisms or help the body's community of microorganisms return to a healthy condition after being disturbed. Although probiotics



have an extensive history of apparently safe use in healthy people, few studies have looked at the safety of probiotics in detail. The risk of harmful effects from probiotics is greater in people with severe illnesses or compromised immune systems. Possible harmful effects of probiotics include infections, production of harmful substances by the probiotic microorganisms, and transfer of antibiotic resistance genes from probiotic microorganisms to other microorganisms in the digestive tract.⁷ As a team, the prescriber, the patient, and the pharmacist should work together to consider the decision and impact of implementing a probiotic in order to provide optimal treatment for each individual MAC patient.

Sources:

- Koirala, J., 2020. Mycobacterium Avium Complex (MAC) (Mycobacterium Avium-Intracellulare [MAI]): Background, Pathophysiology, Etiology. [online] Emedicine.medscape.com. Available at: https://emedicine.medscape.com/article/222664- overview#showall> [Accessed 14 June 2020].
- 2. MAC lung disease | American lung association. Lung.org. https://www.lung.org/lung-health-diseases/ lung-disease-lookup/mac-lung-disease. Accessed July 11, 2020.
- Daley CL. Mycobacterium avium Complex Disease. Microbiol Spectr. 2017;5(2): 10.1128/ microbiolspec.TNMI7-0045-2017.
- Griffith DE, Aksamit T, Brown-Elliott BA, et al. An official ATS/IDSA statement: Diagnosis, treatment, and prevention of nontuberculous Mycobacterial diseases. Am J Respir Crit Care Med. 2007;175(4):367-416.
- Charles L. Daley, Jonathan M. Iaccarino Jr., Christoph Lange, et al. Nontuberculous Mycobacterial (NTM) Diseases. IDSA Home. https://www.idsociety.org/practiceguideline/nontuberculous-mycobacterial-ntm-diseases/. Accessed July 31, 2020.
- UpToDate. Uptodate.com. https://www.uptodate.com/ contents/treatment-of-mycobacterium-avium-complexpulmonary-infection-in-adults?search=treatment%20of% 20mycobacterium%20avium%20complex% 20pulmonary%

20infec-

tion&source=search_result&selectedTitle=1~150&usage _type=default&display_rank=1. Accessed June 17, 2020.

 Probiotics: What you need to know. Nih.gov. https:// www.nccih.nih.gov/health/probiotics-what-you-need-toknow. Accessed July 2, 2020.

BACK TO COVER



RHO CHI POST: TEAM MEMBERS



Catharine Russo Augusta Aug 6th Year, STJ; Editor-in-Chief

The Rho Chi Post as been a forum for students, faculty, and staff to advance their knowledge in the field of pharmacy since 2011. The platform allows for students to practice their written communication skills while offering an innovative and creative workspace to bring together various aspects of the pharmacy profession. I am proud to continue this tradition by fostering a publication suited to keep our readers up-to-date, especially in these unprecedented times during the COVID-19 pandemic.

@ Shireen Farzadeh, PharmD

Graduate Copy Editor [Content-Focused] I am excited to join Rho Chi Post and contribute to the award-winning newsletter for students to share ideas, opinions, and pertinent topics! Writing for the Rho Chi Post is an opportunity to express our appreciation for pharmacy and educate ourselves and our peers. I hope to inspire students to discover their passion for writing and to stay up to date on our evolving profession!



@ Kathleen Horan, PharmD

Graduate Copy Editor [Content-Focused] I have always loved writing, and I hope to couple my passion for writing with my interest in clinical pharmacy by becoming a writer and staff editor for the Rho Chi Post. As a writer and staff editor for the Rho Chi Post, I hope to write and edit informative and interesting articles that relate to the world of healthcare and pharmacy. I am so excited to join this team of student pharmacists and writers.



@ Nicollette Pacheco, PharmD Graduate Editor [Graphics-Focused]

As a member of the Rho Chi Post team, I have a vast appreciation of what it means to be a pharmacist in the rapidly evolving world of healthcare. As a graduate editor, I will continue to bring my passion for science and creativity to the Rho Chi Post.



Throughout my time in the PharmD program, my understanding of pharmacy as a profession has evolved and deepened as much as

my desire to create awareness, particularly to non-science students, about the diverse role pharmacy plays in various healthcare and non -healthcare settings. I have always had an affinity for writing and look forward to combining my interests in literary composition, editing and pharmacy to produce relevant issues which both pharmacy students and nonpharmacy students alike will find relatable and take an interest in.

@ Sarah Hewady, PharmD

@ Anna Diyamandoglu, PharmD

Graduate Copy Editor [Content-Focused]

The importance of staying updated on relevant healthcare matters cannot be overstated. I appreciate the mission of Rho Chi Post in that it successfully compiles clinically relevant and up-to-date information for its audience. Wanting to contribute to this cause is what sparked my interest to become a staff editor. I hope to broaden the scope of knowledge of the public as well as aid healthcare practitioners in the clinical decision-making process.

Ø Jonathan Mercado, PharmD

Graduate Copy Editor [Content-Focused]

The Rho Chi Post breaks barriers for students that want a glimpse of their future and acts as an inspiration to work harder to achieve their goals. It is an embodiment of the motivation and intelligence that drives pharmacy students to be the most informed and capable professionals they can be. I am glad to a part of that mission and to channel my passion and interests through this newsletter.

@ Joseph Eskandrous, PharmD Graduate Staff Writer

In the world of pharmacy, knowledge becomes outdated within hours of when you learned it. The miracle drug that used to be considered the standard of therapy is replaced by the latest and greatest. My role as a Staff Writer for the Rho Chi Post is to bring these changes to the forefront in order to empower future pharmacists and to improve the quality of patient care.







RHO CHI POST: TEAM MEMBERS



② Daniela Farzadfar, PharmD Graduate Staff Writer

Pharmacy is a constantly evolving profession. Writing for the Rho Chi Post gives me the opportunity to enlighten my peers and myself on changes occurring in the field that we are often not taught in the classroom. The Rho Chi Post serves as a creative outlet where students can express their opinions and share new information by combining their passion for writing and the pharmacy profession. I hope that my contribution to this newsletter inspires others to improve patient outcomes by staying up to date on recent changes.



@ Maryam Sekhery, PharmD Graduate Staff Writer

I have always looked forward to reading Rho Chi Post's newsletters and can now proudly say that I am a member of the Rho Chi Post team! The field of pharmacy is always changing, and Rho Chi Post is one-way students can stay up to date regarding current events in the profession and express their views on the dynamic aspects of pharmacy. I look forward to contributing to Rho Chi Post as a staff writer and am grateful for the opportunity to create original content for the newsletter.

@ Judy Koag

6th Year, STJ; Copy Editor [Graphics-Focused]

I am so excited to join the Rho Chi Post, a newsletter which strives to create high quality and creative content. I look forward to working with the team to promote the profession of pharmacy and communicate ideas that inspire and attract readers through the use of graphic design. Graphic design has always been my passion and I hope my contributions continue the Rho Chi Post's mission.







@ Michael Lim, PharmD Graduate Staff Writer

In the spirit of advancing the pharmacy profession, the Rho Chi Post never ceases to produce valuable content showcasing the innovation and diversity of the career. As a Staff Writer for the Post, I am honored to have the opportunity to use writing to both educate and push readers to strive for excellence in their professional pursuits. I hope that my contributions to the newsletter are able to foster growth in an informative and accessible manner.

@ Evanthia Siozios, PharmD Graduate Staff Writer

Rho Chi Post is a newsletter that gives students the opportunity to learn and write about novel topics and broaden their knowledge while demonstrating their writing skills. For me, being involved with this newsletter is not just about learning something new but also sharing relevant topics which have an impact on patients' lives. I have learned so much from writing for the Rho Chi Post and hope to inspire others with my words. As a future pharmacist I want to learn to teach and get to give.

@ Alisha Kuriakose

5th Year, STJ; Finance & Outreach Manager

I wanted to be part of Rho Chi Post as it provides a platform for students to express their ideas and educate others on global healthcare issues. As a future pharmacist, this is my way of contributing to the change I want to see in our growing profession and make my voice heard. I am very excited for the privilege to work alongside the editorial board to produce a newsletter and serve as the 2020-2021 Finance and Outreach Manager!



BACK TO COVER



RHO CHI POST: TEAM MEMBERS



@ Jason Ifeanyi

5th Year, STJ; Social Media Manager

The Rho Chi Post has a clear mission: to advance the profession of pharmacy by instilling the desire in others to pursue intellectual excellence and critical inquiry. I could not be more excited to join the Rho Chi Post. This an interactive platform that affords me a unique opportunity to contribute to the process of educating readers on advances made in drug discovery and development, modifications in treatment guidelines, and the implications these changes have on the practice of Pharmacy. I am eager to work on this team of equally motivated students, and I look forward to utilizing my skills, past work and volunteer experiences to assist the Rho Chi Post in achieving their goals.



@ Carolina Guerreiro 6th Year, STJ; Staff Editor

As a student of the arts and sciences all my life, I have always been interested in the intersection between the two. The most exciting part about being a Staff Editor for the Rho Chi Post is not only the ability to share the most exciting and clinically relevant healthcare news with our audience, but also having the opportunity to tap into my creative side while relying on my clinical knowledge and previous scientific writing experience. When I'm not busy editing, I am working to capture stories that raise awareness about the diverse roles pharmacists can play in healthcare settings worldwide. I strive to share my vision of untamed areas of pharmacy practice and hope to inspire you as readers to explore them for yourselves.

@Rubab Hassan 5th Year, STJ; Staff Writer

The Rho Chi Post gives pharmacy students the opportunity to explore their interests, whether it be editing, writing, or graphics, while also enhancing their skills and knowledge as student pharmacists. I am excited to be a part of the Rho Chi Post because it is a great way to expand on what I have learned during my time in pharmacy school and also keep developing my writing skills. Being a writer gives me an outlet to raise awareness on the advancements that are constantly happening in the field of pharmacy and allows me to be part of an amazing team in hopes of providing other students with our best work.

@ Tobin Kuriakose 6th Year, STJ; Staff Writer

The world of pharmacy is constantly making advancements day after day in order to better care for patients and allow them to return to their healthy lives. Rho Chi Post serves as an outlet for students to update themselves without the hassle of having to debate whether the information is accurate or not. I look forward to working with the Rho Chi Post staff to educate students about the growth within the field of pharmacy and to be source of enrichment during a busy school schedule.



@Edwin Gruda

5th Year; STJ; Staff Writer

My name is Edwin and I am a Doctor of Pharmacy student at St. John's University. My favorite aspect of pharmacy school is learning about the clinical and therapeutic components of drugs and diseases. As a kid, I was interested in both the math and sciences. The reason I chose pharmacy over other health care professions is because a lot of people rely on their medications to make them feel better. Pharmacists are the most accessible healthcare providers and are able to help patients optimize their drug therapy in order to improve their health. Throughout the beginning of pharmacy school, I volunteered at Columbia University Medical Center on the oncology department for one year. After that, I have been working as a pharmacy intern at Sandcastle Pharmacy, which is primarily an HIV specialty pharmacy. As a staff writer, I want to highlight the critical role of clinical pharmacists within an interdisciplinary team, in improving and enhancing a patient's quality of life.



5th Year STJ; Staff Writer

The profession of pharmacy and what a pharmacist entails is an ever evolving journey. Rho Chi Post becomes an excellent resource in tracking these advances. It provides student pharmacists to not only read and become educated on what other paths might be in store for them, but to become part of the team and create their path. I am so thankful and excited for the opportunity to become a staff writer for the RCP; allowing myself to use my creative ability to not only create my path, but write content to shed a light on all the amazing opportunities that of being a pharmacist entails.

@ Jeremy Mesias

5th Year, STJ; Staff Writer

The field of pharmacy is constantly growing and improving with every coming day. Today's headlines become tomorrow's history. As healthcare leaders in a dynamic field, it is important to stay up to date. The Rho Chi Post serves as an excellent tool to help students become more informed about our profession, as well as providing them with the opportunity to contribute their own two cents to the conversation. I am excited to join the team and look forward to contributing to keeping students on top of current pharmacy advancements.

@ Aiša Mrkulić

5th year; STJ; Staff Writer

It is admirable of the Rho Chi Post to provide us student pharmacists with a platform to use our voice. Home to the free-exchange of thoughts, opinions & ideas, all are welcome to contribute—so don't count yourself out! Eager to use my voice more than ever before, I counted myself in. As a Staff Writer, patient advocacy, furthering of public health initiatives & diversifying public perception of pharmacists all suddenly become possible. After all, who if not us is to showcase the value of America's most-trusted healthcare professional? I encourage both our loyal & first -time readers to please, read on with us. To learn to read is to learn to write and to learn to write is to become better communicators—disseminators of information. When this occurs, the quality of patient care improves...& that is always the goal.

St. JOHN'S UNIVERSITY College of Pharmacy and Health Sciences







BACK TO COVER



RHO CHI POST: TEAM MEMBERS



@ Nicole Ng

5th Year, STJ; Website Liaison

Being able to join the Rho Chi Post not only gives me the opportunity to expand my knowledge of the profession of pharmacy, but also allows me to be a part of educating students about the constant changes within the field. Through my involvement, I hope to increase the accessibility of our content and motivate students to broaden their knowledge and stay up-to-date. I am excited to work with the team to produce a newsletter that effectively and efficiently communicates all news that affects our healthcare profession.



@ Tolulope Omisakin 5th Year, STJ; Staff Editor

As an avid reader, I have always taken an interest in how things were written. Whether it be novels, journal articles, or magazine columns, there is always a peculiar way in which a writer tells a story. The real story is only 50% of what is written and the rest is in how the writer decides to disseminate that information. The Rho Chi Post serves as an amazing outlet for student pharmacists, allowing us to delve into the intricacies of different perspectives and ideas in the world of pharmacy. It also gives us the opportunity to decide how we want to detail these new found perspectives and ideas to our audience. As an incoming editor for The Rho Chi Post, I hope to enhance and curate the way each writer tells their stories and help them reach their audience at new levels.



@ Shivani Shah

6th Year, STJ; Staff Writer

As students in an dynamic healthcare profession, it is important to keep up to date with literature and publications regarding the pharmacy profession. Rho Chi Post serves as a great outlet for students to catch up on pharmaceutical innovations and progress going on in the career. Being a staff writer motivates me to constantly research and share new, exciting advancements with fellow students. I look forward to reading articles in the Post and hope to spark others curiosity and interest!



@ Preethi Samuel

6th Year; STJ; Staff Writer

As future drug experts, we student pharmacists have a responsibility to take initiative and educate ourselves on advancements in healthcare, so as to improve the quality of patient care. The Rho Chi Post serves as a great platform for students to get information that is both accessible and accurate. To be a voice for my future, fellow pharmacists is to be heard and my patients cared for---as pharmacists are their best, sometimes their only, advocates. I hope that my contributions to the RCP spark readers' curiosity, and inspire conversations of how we may become better pharmacists.



@ Mah Noor 6th Year, STJ; Staff Writer

Rho Chi Post is an amazing student-operated newsletter publication that is doing an astonishing job delivering updated news as well as giving students the opportunity to give back to the pharmacy community. As a staff writer, I hope to play a key role in educating students on the different aspects of pharmacy and how much growth takes place in this field. Reading the Post since freshman year has helped me gain a better understanding of what it means to be a pharmacist and I hope to achieve that same understanding in students who read my articles.

O Nishanth Viswanath 5th Year, STJ; Staff Writer

profession The o f pharmacy is continuously expanding to meet new demands and offer novel platforms for innovation in healthcare. With an abundance of new information and guidance being published everyday, it can become difficult for students and professionals to stay updated with relevant information and find new outlets to learn. The Rho Chi Post not only allows us to be informed about the current state of our profession, but also allows students to voice their opinions and connect with each other through literature. I am excited to be part of its team, and hope to provide meaningful and resourceful contributions.

Dana Weinstein 5th Year; STJ; Staff Writer

I am so excited to be a part of the Rho Chi Post team. This opportunity allows both myself and my peers to be well informed about the ever-changing profession of pharmacy and the vital developments in science and healthcare. Beyond the classroom setting, this newsletter fills in the gaps for the most up-to-date and current advancements for students and faculty. As a staff writer, I look forward to acting as an educator, a motivator, and an executor to further the mission and goals of the Rho Chi Post.



Page 22 VOLUME 9, ISSUE 6

BACK TO COVER

MISSION

The Rho Chi Post is an award-winning, monthly, electronic, student-operated, faculty-approved publication that aims to promote the pharmacy profession through creativity and effective communication. Our publication is a profound platform for integrating ideas, opinions, and innovations from students, faculty, and administrators.

VISION

The Rho Chi Post aims to become the most exciting and creative student-operated newsletter within St. John's University College of Pharmacy and Health Sciences

Our newsletter continues to be known for its relatable and useful content

Our editorial team continues to be known for its excellence and professionalism

The Rho Chi Post essentially sets the stage for the future of student-operated publications in pharmacy VALUES

Opportunity

Teamwork

Respect

Excellence

GOALS

To provide the highest quality student-operated newsletter with accurate information

To maintain a healthy, respectful, challenging, and rewarding environment for student editors

To cultivate sound relationships with other organizations and individuals who are like-minded and involved in like pursuits

To have a strong, positive impact on fellow students, faculty, and administrators

To contribute ideas and innovations to the Pharmacy profession

St. JOHN'S UNIVERSITY College of Pharmacy and Health Sciences

RHO CHI post