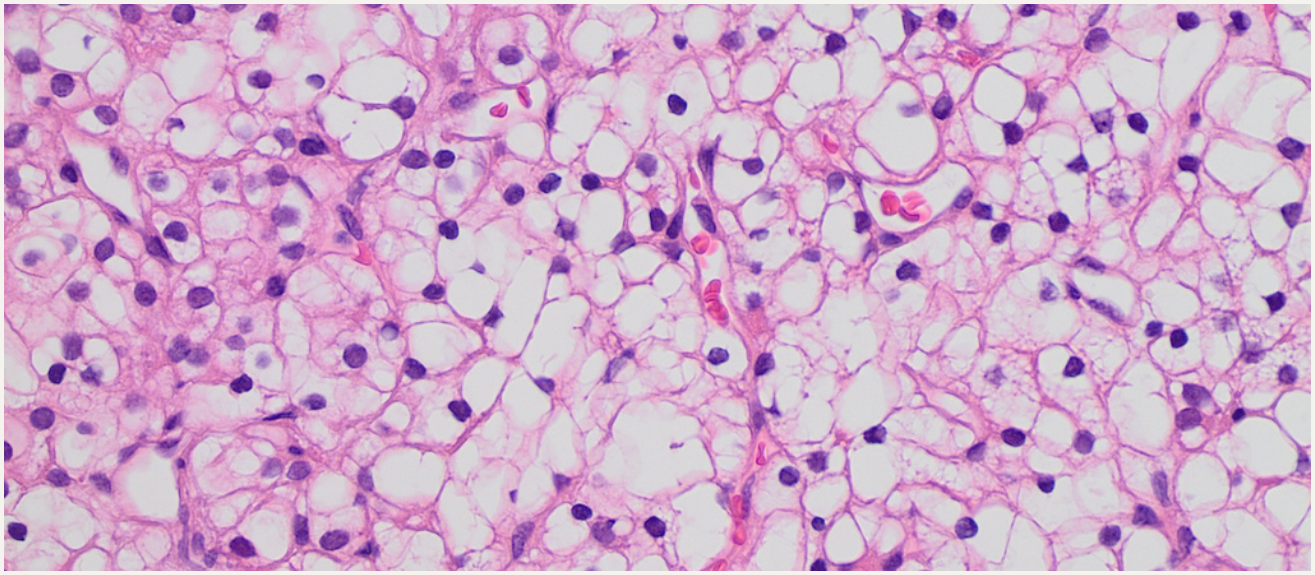
VOLUME 13 | ISSUE 1 | OCTOBER 2023

RHO PxCHI post

St. John's University College of Pharmacy & Health Sciences



THIS ISSUE'S FEATURED ARTICLE:

EFFICACY OF CABOZANTINIB, NIVOLUMAB, AND IPILIMUMAB COMBINATION THERAPY IN ADVANCED CLEAR-CELL RENAL-CELL CARCINOMA

About the Rho Chi Post

The Rho Chi Post was developed by the St. John's University Rho Chi Beta Delta Chapter in October 2011 as an electronic, student-operated newsletter publication with a team of three student editors and one Editor-in-Chief. Today, our newsletter boasts 12 volumes, over 90 published issues, and more than 600 unique articles to date with an editorial team of first to sixth year student pharmacists, as well as returning PharmD graduates.

The newsletter is distributed by St. John's University College of Pharmacy and Health Sciences to more than 1,500 students and faculty members. Our monthly electronic mailing list continues to extend readership far beyond campus.

Mission

The Rho Chi Post is an award-winning, 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 and faculty.

Vision

The Rho Chi Post aims to become the most creative and informative 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 sets the stage for the development of individual writing skills, collaborative team work, and leadership.

Contact Information

The Rho Chi Post
St. John's University College of Pharmacy and Health Sciences
8000 Utopia Parkway, Jamaica, NY 11439

Website: http://rhochistj.org/RhoChiPost
Facebook: https://www.facebook.com/RhoChiPost
Instagram: @sjurhochipost
Email: rhochipost@gmail.com

2023-2024 TEAM MEMBERS

RHO Rx CHI post

Editorial Team & Production

Editor-in-Chief
Isabelle Lim

Senior Content-Focused Copy Editors
John Ortiz
Joanne Fung

Content-Focused Copy Editors
Maliha Akter
Bao Qi Chen
Warda Basher
Kristen Joy Mathew

Senior Graphics-Focused Copy Editors
Mandy Zheng
Ruksabha Zaman

Graphics-Focused Copy Editors
Celestine Van Sertima
Nalisha Xu
Zainab Masood

Senior Staff Editor
Sana Ahmed

Staff Editors
Jennalynn Fung
Paulina Maczko
Shakhzoda Rakhimova
Natalia Turowska
Sharupa Azmal
Nimra Gul

Senior Staff Writers
Nancy Yousry
Ashley Dao
Sairah Sheikh

Staff Writers
Urooj K. Malik
John Ortiz
Anureet Kaur
Enjelique R. Adams
Holly Nguyen
Jacob Row
Giavanna Carr
Sheena Nagpal
Ariella Zadrima
Ashley Medina
Sandra Jojo

Social Media & Outreach

Engagement & Outreach Managers
Anjali Thykattil
Nancy Yousry
Ashley Dao

Advisors

Dr. Ketan Patel
MPharm, PhD
Dr. Joseph Etzel
BS Pharm, PharmD
Dr. Mohammad Rattu
PharmD, BCOP, BCPS, BCGP

The Rho Chi Society

Executive Board

President
Geraldine Ciaccio
Vice President
Javeria Amir
Secretary
Anjali Rana
Treasurer
Giavanna Carr
Historian
Christine Mauceri
Development & Outreach Coordinator
Sammi Wu
Academic Committee Coordinators
Daya Biju
Angel Gao

TABLE OF CONTENTS

FROM THE EDITOR

A Message from the Editor-in-Chief, Isabelle Lim

It is with great honor that I introduce the Rho Chi Post's 13th volume! With the help of our Editorial Team, we have been able to increase the article count in this issue to nine articles. As finals approach, I thank you for taking time out of your day to read over our newsletter. I hope this issue teaches you something new, whether it be clinical, pharmacy news, or advice from our Rho Chi Talks or 6th Year Perspective. I would like to take a moment to thank our Editorial Team, Executive Board, advisors, and readers as this newsletter would not be possible without them. With this, I leave you to the rest of the issue, and I wish the student body the best as they finish off the Fall 2023 semester!

Frequently Asked Questions

Who can write for the Rho Chi Post Newsletter?

Anyone can write for the Rho Chi Post! Our newsletter is not exclusive to St. John's University students. The Rho Chi Post accepts articles on a daily basis!

How do I submit an article?

You can submit an article by creating an account on our website! Go to www.rhochistj.org/RhoChiPost, click the login button from the upper menu bar, and click register. Upon making an account, you will be able to submit articles to our author inbox.

Who determines article topics?

You are free to choose an article topic of your choice. Take a look at our Author Guidelines for ideas.

What happens after I upload my draft article on the Rho Chi Post website?

Our Editor-In-Chief (EIC) will either edit the article directly or assign the article to a staff editor. If any revisions are needed, the editor will upload the article back to the portal, notifying the author via email. The author can then download the edited article, make the suggested revisions, and reupload the draft back to the portal. Additional drafts will be revaluated by our copy editors and then EIC, repeating this process. Once no further revisions are needed, the article is accepted for publication.

Is there a deadline for authors to send revisions?

There is no deadline to submit revisions for an article. However, the quicker revisions are made, the quicker the article can move through our editing process. Once an article is accepted for publication, it will be moved into a queue to be placed into an upcoming issue.

FDA Grants Approval for AREXVY, the First Respiratory Syncytial Virus (RSV) Vaccine

By: Urooj K. Malik, PharmD Candidate c/o 2024

On May 3, 2023, the United States (U.S.) Food and Drug Administration (FDA) approved Arexvy (RSVPreF3), the first vaccine to combat respiratory syncytial virus (RSV) for adults aged 60 and older.[1]

Overview of RSV

RSV is a common respiratory virus that typically causes mild, cold-like symptoms that can progress to serious lung infections, mainly in infants, older adults, and individuals with serious medical issues.[2] Within most regions of the U.S., RSV season starts during fall and peaks in the winter. This virus is highly contagious and can spread from person to person by traveling through the air through coughing, sneezing, or direct contact. In older adults, RSV is a common cause of lower respiratory tract disease (LRTD), that affects the lungs leading to life-threatening pneumonia and bronchiolitis.[1] Each year in the U.S., RSV has led to approximately 58,000-80,000 hospitalizations among children less than 5 years old and 60,000-160,000 hospitalizations among adults 65 years and older.[3] Compared to other respiratory diseases, RSV is the most common cause of pneumonia and bronchiolitis for children below the age of 1 year.[4] Glaxo-SmithKline (GSK), a global pharmaceutical company, developed the RSVPreF3 vaccine as a means to prevent LRTD in the 60 years and older population.

Summary of the AReSVi-006 Trial

The AReSVi-006 trial is an ongoing placebo-controlled, phase 3 clinical study conducted in North America, Europe, Asia, Africa, and Australia. A total of 24,966 individuals partook in this trial with 12,467 participants receiving the RSVPreF3 vaccine and 12,499 receiving saline placebo. Participants were included in the trial if they did not report an RSV-confirmed acute respiratory illness before day 15. Participants with pre-existing chronic conditions that were stable including diabetes, hypertension, and cardiac disease were approved to participate in the trial if deemed medically stable by the investigator at the time of getting vaccinated. However, immunocompromised participants were excluded. Participants were followed up for the development of an RSV-associated LRTD for up to 10 months. Follow-up was conducted starting from day 15 post-vaccination.[5] The participants will remain in this study through three RSV seasons to evaluate the duration of effectiveness and safety of repeat annual vaccination.

The primary endpoint of this study was the efficacy of the RSVPreF3 vaccine in the prevention of RSV-LRTD in adults at least 60 years of age during the first season.[5] In this study, RSV-LRTD was defined as at least 2 LRTD signs and symptoms including at least 1 LRTD sign for at least 24 hours or at least 3 LRTD symptoms for at least 24 hours.[5] Lower

respiratory symptoms included new or increased sputum, new or increased cough, and/or new or increased dyspnea. Lower respiratory signs consisted of new or increased wheezing, crackles/rhonchi, a respiratory rate of at least 20 respirations per minute, low or decreased oxygen saturation, and need for oxygen supplementation.[5] The secondary endpoint was efficacy against RSV-LRTD in participants with at least 1 comorbidity. Comorbidities of interest included chronic obstructive pulmonary disease (COPD), asthma, other chronic respiratory/ pulmonary diseases, chronic heart failure, diabetes mellitus type 1 or type 2, and advanced liver or renal disease.[5]

Results from the first RSV seasons became recently available which led to the FDA's approval of the vaccine. It was seen that 82.6% of participants achieved overall efficacy against RSV-LRTD with the vaccine and reduced the risk of developing severe RSV-associated LRTD by 94.1%. The most commonly reported (incidence of ≥10%) adverse reactions were injection site pain (60.9%), fatigue (33.6%), myalgia (28.9%), headache (27.2%), and arthralgia (18.1%). Serious adverse events of atrial fibrillation were reported in 10 participants who received the RSVPreF3 vaccine and 4 participants that received placebo. There was a 94.6% efficacy against RSV-LRTD in participants with at least 1 comorbidity.[5] There is still ongoing surveillance and research being conducted to comprehensively understand the vaccine's long-term effects and its impact on different age groups, specifically adults 75 years and older and those with an underlying medical condition.[6]

Pharmacists' Role in Administrating RSV Vaccines Within New York State (NYS)

On August 8, 2023, the New York State Department of Health, in partnership with the State Education Department, issued a determination letter to make the RSV vaccine to soon be administered to adults ages 60 and older in pharmacies statewide.[7] The vaccine will also be available to be administered by other trusted health care providers. New York Board of Regents Chancellor, Lester W. Young, Jr., shares in the excitement of this new vaccine and the role pharmacists will play in administering it by stating, "[t]his determination is a major victory for access and equity in health care. Research indicates RSV has a major impact on infants and older adults living in communities that often have limited access to health care resources. Pharmacists play a critical role in expanding access and increasing vaccination rates. I applaud Commissioner McDonald for this decision, which takes us one step further toward providing equitable and obtainable health care for all New Yorkers."[7]

In addition, the RSV vaccine will be covered under Medicare Part D, meaning many adults will have greater accessibility to the vaccine in their pharmacies.[6] As New Yorkers prepare for the upcoming fall season when RSV typically spreads, GSK recently announced that their vaccine is now available at major U.S. retail pharmacies.[8] With this milestone, the nation moves one step closer to eradicating the threat of RSV and procuring a healthier future for generations to come.

References

1. FDA Approves First Respiratory Syncytial Virus (RSV) Vaccine. U.S. Food and Drug Administration. Published May 4, 2023. https://www.fda.gov/news-events/press-announcements/fda-approves-first-

respiratory-syncytial-virus-rsv-vaccine
2. Respiratory Syncytial Virus (RSV). Centers for Disease Control and Prevention. Updated August 4, 2023. Accessed September 20, 2023. https://www.cdc.gov/rsv/
3. RSV Research and Surveillance. Centers for Disease Control and Prevention. Published October 28, 2022. Accessed September 18, 2023. https://www.cdc.gov/rsv/research/
4. Symptoms and Care for RSV. Centers for Disease Control and Prevention. Published September 6, 2023. Accessed September 18, 2023. https://www.cdc.gov/rsv/about/symptoms.html
5. Papi A, Ison MG, Langley JM, et al. Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults. *N Engl J Med*. 2023;388(7):595-608. doi:10.1056/NEJMoa2209604
6. Constantino AK. CDC advisory panel backs use of GSK and Pfizer RSV vaccines in adults 60 and older. CNBC. Published June 21, 2023. https://www.cnbc.com/2023/06/21/rsv-vaccine-cdc-panel-pfizer-gsk-shots-adults-over-60.html
7. New York State Department of Health, in Partnership with State Education Department, Takes Steps Necessary to Ensure RSV Vaccine for Adults Over Age 60 Will Be Administered in Pharmacies Statewide. New York State Department of Health.; 2023. Accessed August 19, 2023. https://www.health.ny.gov/press/releases/2023/2023-08-08_rsv
8. GSK announces AREXVY, its respiratory syncytial virus (RSV) vaccine, is now available at all major US retail pharmacies. GSK US. Published August 17, 2023. Accessed August 19, 2023. https://us.gsk.com/en-us/media/press-releases/gsk-announces-arexvy-its-respiratory-syncytial-virus-rsv-vaccine-is-now-available-at-all-major-us-retail-pharmacies/

Zuranolone: An Oral Development in the Treatment of Postpartum Depression

By: Giavanna Carr, PharmD Candidate c/o 2025

Postpartum depression, also known as PPD, is classified as perinatal depression, which is experienced by those who have recently given birth. PPD is the leading complication following childbirth, affecting 1 in 7 women worldwide.[1] Oftentimes, this is the first time the mother suffers from any type of depression, and it is likely to occur in future pregnancies.[1]

Pathogenesis of PPD

Although the pathogenesis of PPD is not yet known, studies show that a combination of the hypothalamic-pituitary-adrenal (HPA) axis, lactogenic hormones, and immunological system are involved in the disease.[2] The HPA axis is involved in the release of cortisol, a stress hormone. Thus, lack of HPA axis function may lead to a poor stress response. The cortisol release is heavily increased during pregnancy and the weeks following childbirth, which may be responsible in part for the disease process of PPD.[2] In addition, during pregnancy, there are rapid changes in estradiol and progesterone which have the potential to lead to depressive episodes in women. The lactogenic hormones, oxytocin and prolactin, are responsible for the synthesis of breast milk as well as the milk let-down reflex.[2] In addition to its lactogenic properties, oxytocin is also nicknamed the "love hormone" due to its release in response to sensory nerve activation, especially during labor, breastfeeding, and skin-on-skin contact between mother and baby.[3] It was noted that low levels of oxytocin simultaneously indicated failure to lactate and onset of PPD.[2] Oxytocin can be related to failure to lactate because this hormone is responsible for lactogenesis, the secretion of milk, and thus without the proper functioning of this hormone, the mother will be incapable of breastfeeding. Additionally, low levels of oxytocin would inhibit the warm interaction typically felt between mother and child shortly after birth. Such setbacks with low oxytocin could result in PPD because inability to breastfeed may accentuate the mother's feeling of worthlessness and guilt, hindering the development of the maternal-fetal bond.[2]

Diagnosis of PPD

It is important to be able to differentiate PPD from the "baby blues." Typically, "baby blues" subside within the first two weeks of giving birth whereas symptoms lasting over 2 weeks could signify PPD. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), PPD is considered in patients with a major depressive episode peripartum onset, meaning the period during or shortly after childbirth, in addition to the following symptoms: depressed mood, loss of interest, insomnia, psychomotor retardation, worthlessness or guilt, fatigue, suicidal ideation, impaired concentration, and change in weight and appetite for up to four weeks.[2] PPD screening is routine during infant wellness checkups. The most common questionnaire to diagnose PPD in the health-

care setting is the Edinburgh Postnatal Depression Scale (EPDS). The EPDS consists of 10 questions regarding mood and thoughts surrounding the mother and their child.4 In addition to diagnosis through the DSM-5 and EPDS, depression may be caused as a side effect of another disease state, such as hyperthyroidism or hypothyroidism. Such disease states can be diagnosed through blood tests taken inpatient.

Treatment of PPD

The treatment options for PPD differ depending on the severity of the symptoms experienced by each individual patient. Options include antidepressant medicines such as selective serotonin reuptake inhibits (SSRIs) , serotonin and norepinephrine reuptake inhibitors (SNRIs), or tricyclic antidepressants (TCAs).[5] Antidepressants were found to take 3 to 4 weeks to show effects, and symptoms may return if the medication was stopped too soon. When stopping antidepressant treatment for PPD, providers recommend reducing the dose slowly rather than discontinuing the medication all at once. In addition to medications, psychotherapy as well as participating in a support group are recommended in cases of PPD.[5]

In 2019, Sage Therapeutics received Food and Drug Administration (FDA) approval for an intravenous (IV) drug, Zulresso (brexanolone), for the treatment of PPD, making it the first drug to be approved for this indication by the FDA.[6] If PPD is detected early, a provider may recommend giving IV brexanolone in the hospital. Since the medication is only available through a risk evaluation and mitigation strategy (REMS) program and the infusion time takes 60 hours, Sage Therapeutics worked to develop a drug with a novel mechanism of action that eliminated such complications.[6]

On August 4, 2023, the FDA approved Zurzuvae (zuranolone), the first and only oral treatment approved for the treatment of PPD.[7] Zuranolone is a rapid acting neuroactive steroid that targets the GABA-A receptor. The GABA system is responsible for regulating brain function, and Zuranolone is thought to rebalance the dysregulated neurons to restore brain functions including mood, arousal, behavior, and cognition.[7] Zuranolone was developed by Sage Therapeutics and Biogen and will be available as a once-daily tablet, scheduled as a controlled substance by the Drug Enforcement Administration.[8]

Unlike brexanolone and existing antidepressant therapies for PPD, zuranolone has a rapid onset of action and was seen to reduce depressive symptoms as early as three days after beginning treatment.[6] Additionally, this medication is only taken for a 2-week span, so it may be preferred by patients who do not want to be placed on a long-term therapy.

Clinical Trial of Zuranolone

On June 30, 2021, a randomized clinical trial was published that assessed the efficacy and safety of zuranolone in individuals who suffered from PPD. This was a phase 3, double blind, randomized, placebo-controlled trial which consisted of 153 adult women with PPD.[9] The study focused on female patients, aged 18 to 45 years old, revealing at most 6 months postpartum. All patients had exhibited a major depressive episode diagnosed by the DSM-5. Patients must agree to either cease breastfeeding completely or stop lactating prior and for 7 days after the last dose for a total of 21 days.[9] A total of 275

patients were screened, however 122 were screen failures, thus only 153 patients were randomized. Of the 153 patients who were recruited and enrolled in the trial, 77 were randomized to receive the intervention, 30 mg of zuranolone orally every evening for 2 weeks. The remaining 76 were randomized to receive the placebo capsule for 2 weeks.[9]

The effect of the medication was tested using a 17-item Hamilton Rating Scale for Depression (HAMD-17).[8] At baseline, a score of 26 or higher was necessary to partake in the study, and the primary efficacy endpoint was measured by the change from baseline in HAMD-17 score at day 15. Zuranolone demonstrated significant day 15 HAMD-17 score improvements from baseline vs placebo [−17.8 vs −13.6; difference, −4.2; 95% confidence interval (CI), −6.9 to −1.5; P = .003].[8] This difference was deemed statistically significant being that the 95% confidence interval did not cross 0 and the P value was below 0.05. Secondary endpoints looked at the change from baseline in HAMD-17 score at other time points such as day 3, 8, 21, and 45. Sustained differences in HAMD-17 scores favoring zuranolone were observed from day 3 (difference, −2.7; 95% CI, −5.1 to −0.3; P = .03) through day 45 (difference, −4.1; 95% CI, −6.7 to −1.4; P = .003).[8] Similarly, this difference was deemed statistically significant, being that the 95% CI did not cross 0 and the P-value was below 0.05.

Adverse Reactions

At the end of the study, it was concluded that zuranolone was generally well tolerated being that of the 78 participants in the zuranolone group, only 3 reported having a severe adverse event (4% of the group), and only 2 reported having a serious adverse event (1% of the group).[7] It is of importance to mention that there was the same percentage of participants reporting severe and serious adverse events in the control group as well, 4% and 1%, respectively. The most commonly reported treatment-associated adverse events were somnolence which was reported in 15% of the participants, headache reported in 9%, dizziness and upper respiratory tract infection reported in 8%, diarrhea reported in 6%, and the rest of the adverse events were reported in less than 5% of participants.[9]

Conclusion

Zuranolone demonstrated a statistically significant change from baseline in HAMD-17 score as compared to placebo at every time point tested for both the primary and secondary endpoints tested in the study mentioned above. Zuranolone exhibited both rapid and sustained improvements through its ability to show an effect on day 3 and sustain this effect through day 45.[9] Limitations of this study existed in the areas of follow-up. The patients taking part in the study were only observed up until day 45, therefore any additional effects experienced by patients beyond this window were not recorded. For these reasons, an ongoing open-label study investigating the sustainability of effects as well as any need for retreatment of depressive episodes.[9] A safety precaution required in the study was to cease breastfeeding during the study and for 1 week following the study, a total of 21 days. The safety of zuranolone in breastfeeding women is still unknown and is of interest in future studies.[8] Despite these areas of further research, zuranolone has the potential to be a successful new treatment for patients suffering from PPD looking for an oral treatment option.

References

1. Postpartum depression. March of Dimes. Last Reviewed March 2019. Accessed August 14, 2023. https://www.marchofdimes.org/find-support/topics/postpartum/postpartum-depression
2. Schiller CE, Meltzer-Brody S, Rubinow DR. The role of reproductive hormones in postpartum depression. *CNS Spectr*. 2015;20(1):48-59. doi:10.1017/S1092852914000480
3. Uvnäs-Moberg K, Handlin L, Petersson M. Self-soothing behaviors with particular reference to oxytocin release induced by non-noxious sensory stimulation. *Front Psychol*. 2015;5(1529). doi:10.3389/fpsyg.2014.01529
4. Sit DK, Wisner KL. Identification of postpartum depression. *Clin Obstet Gynecol*. 2009;52(3):456-468. doi:10.1097/GRF.0b013e3181b5a57c
5. Postpartum depression. OASH Office on Women's Health. Last Updated October 17, 2023. Accessed October 20, 2023. https://www.womenshealth.gov/mental-health/mental-health-conditions/postpartum-depression
6. Global Healthcare. Zuranolone approved for postpartum depression but misses out on bigger MDD indication. Clinical Trials Arena. Published August 9, 2023. Accessed August 21, 2023. https://www.clinicaltrialsarena.com/comment/zuranolone-postpartum-depression-misses-out-mdd-indication/
7. FDA Approves Oral Treatment for Postpartum Depression. Formulary Watch. Published August 6, 2023. Accessed August 21, 2023. https://www.formularywatch.com/view/fda-approves-oral-treatment-for-postpartum-depression
8. Zurzuvae (zuranolone) [package insert]. Cambridge, MA; Sage Therapeutics, Inc; Issued August 2023.
9. Deligiannidis KM, Meltzer-Brody S, Gunduz-Bruce H, et al. Effect of Zuranolone vs Placebo in Postpartum Depression: A Randomized Clinical Trial. *JAMA Psychiatry*. 2021;78(9):951-959. doi:10.1001/jamapsychiatry.2021.1559

Rho Chi Talks: Pathway to Pharmaceutical Industry

Featuring: Fawad Piracha, PharmD, MBA, IgCP
By: Holly Nguyen, PharmD Candidate c/o 2024

Fawad Piracha is a '16 alumnus of the St. John's University PharmD program and has since had a storied career. Dr. Piracha is the second of four family members who graduated from St. John's University's College of Pharmacy and Health Sciences (read more about it here: "For the Pirachas, Pharmacy Is a Family Affair"). After graduating, Dr. Piracha completed a Post-Doctoral Fellowship in Pharmacovigilance/Risk Management at Regeneron, where he advanced his career, before accepting a role as Vice President, Clinical Affairs at KabaFusion, the largest privately held home infusion company in the United States. In May 2023, Dr. Piracha earned a Master of Business Administration (MBA) degree from Columbia Business School, where he graduated with distinction. Currently, Dr. Piracha is the Chief Clinical Officer at KabaFusion, where he leads a broad array of activities.

You have a unique family connection within the St. John's University, College of Pharmacy and Health Sciences alumni as mentioned above. How did having your sister attend St. John's first impact your decision to also attend St. John's, and what part did you play in your cousins' decision to do the same?

When I was in high school, my personal goal was to get admitted into an accelerated BS/MD program. If that didn't work out, then I was content with completing a six-year PharmD program. When I was admitted into St. John's, I visited the campus with my sister, Tooba, one day. I remember going into the D'Angelo Center, which was fairly new at the time, where I met my sister's friends, some of whom were in their fourth or fifth year of pharmacy school. Their opinions led me to realize that completing the pharmacy program was far better than aspiring to go to medical school. I sat in on a class as well, which was taught by a professor who teaches biochemistry, Dr. Woon-Kai Low, to get a feel for what it was like to be in a class. After that, I made the decision to accept my admission into pharmacy school. My cousins, Andrew and Zach, and I have always had a good level of respect for each other. They went to a private Catholic school in Long Island, so going to St. John's was a natural progression; having a professional doctorate is respectable and has attractive attributes.

What inspired you to pursue a career in the pharmaceutical industry?

Just before I started pharmacy school, I worked at CVS until I became a pharmacy intern. When I became a pharmacy intern, I began to work at Mount Sinai Hospital. The goal was to expose myself to the profession,

which I accomplished. I was torn between pursuing a residency or a fellowship, so I applied to both. What tipped the scale for me was having a rotation at the FDA. I had a very good preceptor, Jade Pham, who took me under her wing. I had a remarkably positive experience at the FDA, and I enjoyed the professionalism, which involved presenting at meetings, and thinking critically.

What experiences did you have in your fellowship, and how did it best train you for a career in the pharmaceutical industry?

Regeneron was extraordinary. I had a very good experience as a fellow and had a remarkable manager, Romana Hosain, who was an MD with an MPH. In addition to being exposed to risk management and pharmacovigilance, I loved the fast-paced environment. I was deeply involved in working with colleagues from regulatory affairs, clinical sciences, clinical development, and pharmacoepidemiology, which was a tremendous learning experience. I helped with the development of many molecules that eventually became FDA approved and commercialized. I remember working with the marketing team once before a commercial launch. I was also exposed to toxicology and pharmacokinetics and had a sense of what it was like to work on a very sophisticated team, each member of whom had a high degree of excellence in a particular area. One of the most meaningful experiences was when I attended meetings the European Medicines Agency (EMA) office, which was in London at the time. We had an office in London as well, and experiencing a company that had operations in both the US and Europe was quite exciting.

Why did you decide to get an MBA, and how did your education at Columbia Business School complement your career in the pharmaceutical industry?

In 2019, after working at Regeneron for around three years, I had the life-changing opportunity to join the management team of what is now the largest privately held home infusion company in the United States, Kaba-Fusion. That experience was monumental because I transitioned from being a manager to being an executive, and it was a different type of business than what I was exposed to at Regeneron. The company has grown exceptionally fast. When I joined, we had 450 employees, and now we have around 2000 employees (all in the span of around four years).

Since I was a pharmacy student, I aspired to pursue an MBA from a top-tier institution. Being a clinician and having very good technical skills are important, but having a foundational understanding of business was incredibly important in the advancement of my career. Exactly five years after I graduated pharmacy school, I started the MBA program at Columbia Business School in May 2021, and graduated in May 2023. Through CBS, I developed an even broader professional and personal network. I've been fortunate to have very good mentors who I'm still in contact with, and beyond that, friendships that will last a lifetime. Attending CBS was the right decision at the right time, and I feel very complete in my education with the MBA, especially since I developed important skills, which have helped me immensely.

What are your day-to-day responsibilities as Chief Clinical Officer at Kabafusion?

I wear many hats. The first is that we have

several types of clinical research activities and clinical trials. I also meet regularly with key opinion leader physicians, some of whom I have the opportunity to meet on a regular basis, and work with directly and indirectly. We also work with pharmaceutical and medical device manufacturers for the launches of products. We also have programs that are oriented to digitizing the patient experience and leveraging novel technologies to deliver clinical excellence. We're trying to understand how we can incorporate different types of innovations into our company, and expand the company's existing strategies, which involve initiating ambulatory infusion centers throughout the US. I am involved with clinical projects, sales- and marketing-focused initiatives (some of which involve hospitals and health systems), and operational initiatives. I also have the opportunity to meet regularly with our investors and other key stakeholders. Lastly, we have a pharmacy residency and internship program at KabaFusion.

How do you give back to the St. John's University community?

After I graduated from St. John's, I was invited by a number of student organizations to speak on campus. These types of activities have waned in recent years, and I believe it's because I'm a little removed from some of the current students, since I graduated in 2016. However, I have been consistently involved as a mentor through the St. John's University Alumni Mentoring Program. I have had 3 or 4 formal mentees, and I plan to continue being involved from a mentorship perspective.

What tips do you have for students looking to enter the pharmaceutical industry?

Having a very thoughtful approach to pharmacy school is important. You should aim to get the most out of pharmacy school because a lot of time, energy, and money is being invested into this experience. Striving academically is important. Being involved on campus, in terms of holding meaningful leadership positions, is going to help you hone your leadership skills. Working at a pharmacy as a student is also essential, as it teaches time management and prioritization skills, and gives you an appreciation for what it is like to work hard. If you have the opportunity to speak with people who have completed fellowship or residency programs, then you will better understand what path is best for you. As a student, I was active in speaking with graduates from fellowship and residency programs, and based on those discussions, I decided to pursue postgraduate training. Postgraduate training is not absolutely required but will benefit you in the long-term. And obviously, you've heard this before, networking is important. I don't like the word "networking", but it's good to have genuine long-term relationships with people, and befriend people who can advise, or benefit you directly or indirectly in terms of your career path. You could be the best student who's really involved on campus and know what you want but if you don't have the social and professional connections, you're doing a disservice to yourself. Get out of your comfort zone, try to understand the landscape, then try to make an impact. The future is bright and the opportunities are endless.

On behalf of the Rho Chi Post, we would like to thank Dr. Piracha for sharing his journey through pharmacy with our newsletter!

FDA Falls Behind on Sunscreen Approvals

By: Ashley Dao, PharmD Candidate c/o 2024

Melanoma is the fifth most common cause of cancer in the United States (US). Unprotected exposure to ultraviolet (UV) radiation from the sun is the primary risk factor for developing melanoma.[1] In order to reduce damage from UV exposure, the American Cancer Society (ACS) recommends practices such as avoiding the sun during peak hours, wearing appropriate clothing, and using broad-spectrum sunscreen with a sun protection factor (SPF) of 30 or higher.[2] Sunscreen use has been shown to effectively protect against skin cancer in the general population.[3] Despite the crucial role sunscreens play in melanoma prevention, the US Food and Drug Administration (FDA) has been stagnant in approving new UV filters, with the most recent update in 1999. The FDA sunscreen monograph currently contains 16 approved UV filters (Table 1).[4]

In the US, sunscreens are regulated strictly by the FDA as over-the-counter (OTC) drugs. On the other hand, the European Union (EU) considers sunscreen to be cosmetic, therefore approving products more liberally, but not without a similar rigor of testing.[5] In order to understand why the FDA is lagging behind its international counterparts in terms of sunscreen quality and quantity, the OTC drug approval process must be evaluated.

FDA Sunscreen Approval Process

There are two ways that OTC drugs can be approved by the FDA. One way is through either a New Drug Application (NDA) or an Abbreviated New Drug Application (ANDA). The other option is to go through the OTC Drug Review process, also referred to as the OTC monograph. Drugs that meet the OTC monograph's requirements do not need an NDA/ANDA, nor do they require FDA pre-market approval. Despite the benefits of this process, the FDA previously faced challenges when updating older monographs because any changes required lengthy notice-and-comment rulemaking. This resulted in OTC monographs, including the sunscreen monograph, to be outdated.[6] In 2020, the Coronavirus Aid, Relief, and Economic Security Act (CARES Act) was enacted. This act has since transformed the way in which the FDA regulates OTC monographs. It replaced rule-making with a much quicker administrative order process and allowed the FDA to collect valuable fees from manufacturers. The CARES Act has provided the FDA with the resources needed in order to efficiently revise OTC monographs based on new data and/or safety concerns.[6]

The OTC Monograph M020: Sunscreen Drug Products for OTC Human Use (M020) is a "rulebook" that establishes guidelines, including those regarding active ingredients, labeling, and test procedures, that all OTC sunscreen products must follow. If a product meets the conditions stated in M020, it is deemed "generally recognized as safe and effective" (GRASE) and can be marketed without an NDA/ANDA or FDA premarket approval.[6] The passing of the CARES Act

Table 1. List of UV filter approved in the United States[4,5]

UV Filter	GRASE Status	OTC examples	Mechanism	UV Coverage
Para-aminobenzoic acid (PABA)	Not GRASE*	• N/A	Organic	UVA2
Avobenzone	Not GRASE**	• Supergoop! Unseen Sunscreen SPF 40 • La Roche-Posay Anthelios Cooling Water Sunscreen Lotion SPF 30 • Banana Boat Ultra Sport Sunscreen Lotion SPF 100 • Coppertone Sport Sunscreen Continuous Spray SPF 30	Organic	UVA1/2
Cinoxate	Not GRASE**	• N/A	Organic	UVB
Dioxybenzone	Not GRASE**	• N/A	Organic	UVA2, UVB
Ensulizole	Not GRASE**	• N/A	Organic	UVB
Homosalate	Not GRASE**	• Supergoop! Unseen Sunscreen SPF 40 • La Roche-Posay Anthelios Sunscreen • Sun Bum SPF 50 Spray Sunscreen • Neutrogena Ultra Dry-Touch Sunscreen SPF 70	Organic	UVB
Meradimate	Not GRASE**	• N/A	Organic	UVA2
Octinoxate	Not GRASE**	• EltaMD UV Clear Broad-Spectrum SPF 46	Organic	UVB
Octisalate	Not GRASE**	• Supergoop! Unseen Sunscreen SPF 40 • Neutrogena Ultra Dry-Touch Sunscreen SPF 70 • Sun Bum SPF 50 Spray Sunscreen • La Roche-Posay Anthelios Cooling Water • Coppertone Sport Sunscreen Continuous Spray	Organic	UVB
Octocrylene	Not GRASE**	• Supergoop! Unseen Sunscreen SPF 40 • La Roche-Posay Anthelios Sunscreen • Banana Boat Ultra Sport Sunscreen Lotion SPF 100 • Coppertone Sport Sunscreen Continuous Spray	Organic	UVB
Oxybenzone	Not GRASE**	• La Roche-Posay Anthelios Sunscreen • Banana Boat Ultra Sport Sunscreen Lotion SPF 100 • Coppertone Sport Sunscreen Continuous Spray	Organic	UVA2, UVB
Padimate O	Not GRASE**	• N/A	Organic	UVB
Sulisobenzone	Not GRASE**	• N/A	Organic	UVA2, UVB
Titanium Dioxide	GRASE	• La Roche-Posay Anthelios Sunscreen • EltaMD UV Physical Broad-Spectrum SPF 41 Sunscreen	Inorganic	UVA1/2, UVB
Trolamine Salicylate	Not GRASE*	• N/A	Organic	UVA1/2, UVB
Zinc Oxide	GRASE	• La Roche-Posay Anthelios Sunscreen • EltaMD UV Clear Broad-Spectrum SPF 46 • EltaMD UV Physical Broad-Spectrum SPF 41 Sunscreen	Inorganic	UVA1/2, UVB

* Not GRASE for use in sunscreens because of safety concerns
** Not GRASE for use in sunscreens because additional data needed

required the FDA to post M020 as a Deemed Final Order (DFO); a proposal of significant changes to the DFO was made in September 2021 for the first time since 1999 after the passage of the CARES Act.[7] On September 24, 2021, the FDA proposed an order that would cut down the list of approved safe and effective UV filters from the 16 to 2; under this proposal, para-aminobenzoic acid (PABA) and trolamine salicylate would lose their status as GRASE ingredients due to safety concerns.[8] The other 12 active ingredients would also be categorized as not GRASE due to insufficient data.[8] The implementation of the CARES Act has clearly been promising for those hoping for advancements in the safety and effectiveness of American sunscreen. Hopefully, with this act in place, the time required for the FDA to implement a new OTC monograph will be shortened, and the quicker approval of novel GRASE UV filters will be soon to come as well.

Choosing the Right Sunscreen

Sunscreen has been demonstrated to reduce the risk for skin cancer, prevent photoaging, and reduce sunburns. However, less than 40% of Americans report practicing sun protection including regular sunscreen wear.[3] The lack of sunscreen use is a multifactorial problem. Sunscreen formulations, UV coverage, allergic reactions, and cost are all factors that patients consider when looking for a product. As a consequence of the lack of new sunscreen filters approved by the FDA, some patients have resorted to traveling abroad or using third-party retailers to purchase non-FDA approved products in order to fulfill their desires for what they want in a sunscreen.[5,9]

A study conducted by Xu et al. analyzed the top 1 percentile of sunscreen products being sold on Amazon.com, Inc. as of December 2015. The study found that the most cited positive features of sunscreens were aspects of cosmetic elegance (61% of 325 comments), described with words such as “rub in well,” “positive tactile skin feel,” and “not greasy.” The most notable negative features were concerns with cosmetic elegance (22%), as well as product performance (11%), product ingredients (10%), and expense (9%). Consumers preferred sunscreens with physical UV filters such as zinc oxide and titanium oxide – the two ingredients deemed as GRASE in the FDA’s proposed order.[10] However, despite the popularity of these 2 ingredients, many US consumers are left looking for more in a sunscreen than what these filters can offer. Many titanium dioxide sunscreen formulations can leave a white cast, especially in patients with darker skin tones.[9] Additionally, results from this study showed that physical sunscreens (i.e., those containing zinc and titanium dioxide) are more expensive than chemical ones.[10]

Social media has introduced consumers to well-rated, but non-FDA approved, sunscreens from other countries. Notably, Korean beauty brands have gained popularity lately through reviews posted on YouTube and TikTok. Once sunscreen in particular, Isntree’s Hyaluronic Acid Watery Sun Gel SPF 50, has repeatedly been claimed to be one of the best sunscreens on the market. The sunscreen contains 7 active UV filters: octisalate, homosalate, polysilicone-15, etc. Only 2 of these UV filters are approved by the FDA, while 5 of them are approved by the EU.[11] Another popular Korean sunscreen is Beauty of Joseon Rice Probiotics Sunscreen SPF 50, which contains 2 UV filters: diethylamino hydroxybenzoyl hexyl benzoate and bis-ethylhexyloxyphenol methoxyphenyl triazine.[12] Both UV filters are approved in the

EU, but not in the US.[4,5] The FDA should take note of the popularity of these sunscreens' ingredients among consumers and professionals to expand approved UV filters.

Limitations of US Sunscreen

Furthermore, one key difference between US and EU sunscreen filters is UVA coverage. The EU requires that UVA protection be at least one-third the SPF of the product. On the other hand, the FDA currently does not require sunscreens to provide adequate protection against UVA (the proposed order should revise the DFO to include adequate protection against UVA).[5] Only 7 of the 16 FDA-approved filters provide UVA and UVB protection, including titanium dioxide and zinc oxide.[5] To achieve both UVA and UVB coverage as seen in many EU sunscreens, US manu-facturers must combine UV filters. For example, Supergoop! Unseen Sunscreen SPF 40 is a mix of 1 UVA and 3 UVB coverage filters.[4,5,13]

Research by Matta et al. demonstrated that sunscreens containing popular ingredients such as oxybenzone, homosalate, and octisalate surpassed the FDA safety threshold of 0.5 ng/mL in plasma after single application, hence their categorization as not GRASE in the FDA's proposed order until further safety studies are conducted.[5,8,14] Oxybenzone is a common ingredient found in US and EU sunscreens; it is also, unfortunately, the most frequent allergen in these products. Research demonstrates that oxybenzone has the potential to induce contact allergy, photo contact allergy, and contact urticaria.[5] Despite the concerns surrounding this ingredient, it may be difficult to replace due to the limited number of other GRASE and FDA approved UV filters available in the US.

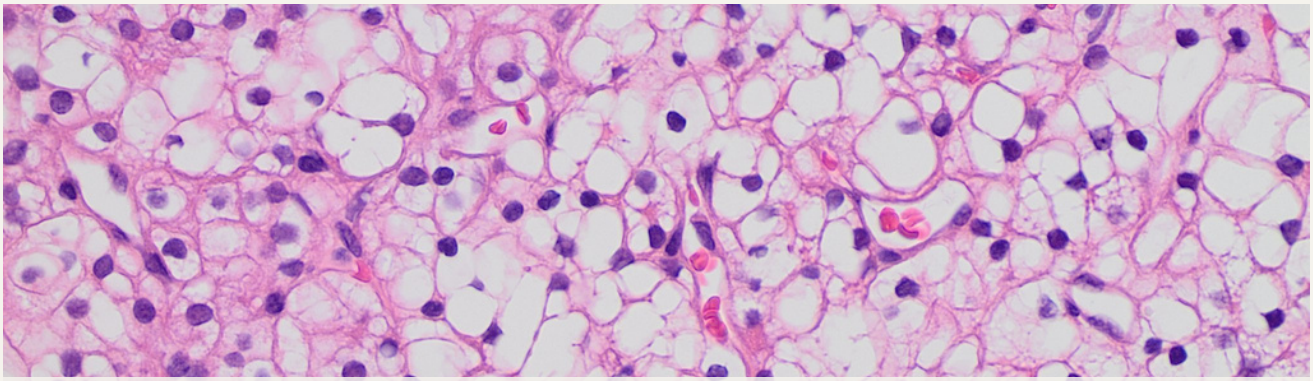
Conclusion

Although it may be a while before the FDA approves any radical changes to the DFO, pharmacists can still play an important role in providing sunscreen recommendations for everyday use. When pharmacists help patients select a sunscreen, they should factor in cosmetic elegance, effectiveness, patient allergies, and cost. Patients should be asked about their preference between physical or chemical UV filters, if they have had previous sensitivity to sunscreens, and how much they are willing to spend. Sunscreens sold in Europe and Asia offer benefits that are not observed in many US formulations. Broad-spectrum coverage from both UVB and UVA radiation and the cosmetic elegance of novel UV filters are some advantages these products have over many US sunscreens. However, pharmacists should caution patients to be mindful when purchasing sunscreens online or abroad, as they may not be approved by the FDA. The power of the CARES Act, along with concerns about current US UV filters and the popularity of EU-approved ingredients among consumers, should hopefully spur the modernization of US sunscreens in the upcoming years.

References

1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. *CA Cancer J Clin*. 2023;73(1):17-48. doi:10.3322/caac.21763
2. The American Cancer Society medical and editorial content team. How do I protect myself from ultraviolet (UV) rays? American Cancer Society. Last Revised July 23, 2019. Accessed September 3, 2023. https://www.cancer.org/cancer/risk-prevention/sun-and-uv/uv-protection.html
3. Saginala K, Barsouk A, Aluru JS, Rawla P, Barsouk A. Epidemiology of Melanoma. *Med*

Sci (Basel). 2021;9(4):63. doi:10.3390/medsci9040063
4. Over-the-Counter Monograph M020: Sunscreen Drug Products for Over-the-Counter Human Use. U.S. Food and Drug Administration. September 24, 2021. Accessed March 30, 2023. https://dps-admin.fda.gov/omuf/omuf/sites/omuf/files/primary-documents/2022-09/Final%20Administrative%20Order%20OTC000006_M020-Sunscreen%20Drug%20Products%20for%20OTC%20Human%20Use.pdf
5. Pantelic MN, Wong N, Kwa M, Lim HW. Ultraviolet filters in the United States and European Union: A review of safety and implications for the future of US sunscreens. *J Am Acad Dermatol*. 2023;88(3):632-646. doi:10.1016/j.jaad.2022.11.039
6. Michele TM. An Exciting New Chapter in OTC Drug History: OTC Monograph Reform in the CARES Act. U.S. Food and Drug Administration. 2020. Accessed April 1, 2023. https://www.fda.gov/news-events/fda-voices/exciting-new-chapter-otc-drug-history-otc-monograph-reform-cares-act
7. Questions and answers: FDA posts deemed final order and proposed order for over-the-counter sunscreen. U.S. Food and Drug Administration. Last Revised December 16, 2022. Accessed September 3, 2023. https://www.fda.gov/drugs/understanding-over-counter-medicines/questions-and-answers-fda-posts-deemed-final-order-and-proposed-order-over-counter-sunscreen
8. FDA proposed order: sunscreen drug products for over-the-counter-human use; proposal to amend and revise the deemed final order established by the Cares Act. U.S. Food and Drug Administration. 2022. Accessed April 2, 2023. https://www.fda.gov/media/153964/download
9. Printz C. Sunscreen slow down: The US FDA's sluggish approval of new sunscreens frustrates physicians, manufacturers, and consumers. *Cancer*. 2015;121(17):2861-2862. doi:10.1002/cncr.29001
10. Xu S, Kwa M, Agarwal A, Rademaker A, Kundu RV. Sunscreen Product Performance and Other Determinants of Consumer Preferences. *JAMA Dermatol*. 2016;152(8):920-927. doi:10.1001/jamadermatol.2016.2344
11. Isntree Hyaluronic Acid Watery Sun Gel. Insntree. Accessed October 1, 2023. https://en.isntree.com/Mobile/Product/Detail/view/pid/216.
12. Rice Probiotics Sunscreen spf50+ pa++++. INCI Decoder. Accessed August 28, 2023. https://incidecoder.com/products/beauty-of-joseon-rice-probiotics-sunscreen
13. Unseen sunscreen SPF 40. Supergoop! Accessed September 9, 2023. https://supergoop.com/products/unseen-sunscreen
14. Matta MK, Florian J, Zusterzeel R, et al. Effect of Sunscreen Application on Plasma Concentration of Sunscreen Active Ingredients: A Randomized Clinical Trial. *JAMA*. 2020;323(3):256–267. doi:10.1001/jama.2019.20747



Efficacy of Cabozantinib, Nivolumab, and Ipilimumab Combination Therapy in Advanced Clear-Cell Renal-Cell Carcinoma

By: Shakhzoda Rakhimova, PharmD Candidate c/o 2024

Renal-cell carcinoma (RCC) is a type of kidney cancer in which malignant epithelial cells are found in the lining of the renal tubules or renal cortex.[1] Clear-cell renal-cell carcinoma (ccRCC) is the most common type, accounting for about 80% of all RCC cases. ccRCC is named aptly for its appearance: transparent tumor cells under the microscope.[2] Common risk factors for RCC include obesity, analgesic abuse, hypertension, family history of RCC, and certain genetic conditions.[3] The two most common genetic abnormalities associated with ccRCC are mutations of the Von Hippel–Lindau (VHL) and protein polybromo-1 (PBRM-1) genes. More specifically, decreased expression of both of these genes results in increased activity of the ccRCC tumor, and decreased expression of the VHL gene alone was associated with a decline in overall survival.[4]

RCC Staging

To understand the extent of the disease and determine an appropriate treatment plan, cancer is classified into stages. The staging classifications are unique to the specific type of cancer. For RCC, there are four stages, each dependent on the size of the tumor and its location. For example, stage I is when the tumor is local to the kidney and is less than or equal to 7 centimeters. Conversely, stage IV is when the tumor can be any size but has spread beyond the kidney into other organs such as the brain, liver, bones, lungs, or distant lymph nodes.[5] The five-year survival rate for localized and distant RCC is 93% and 15%, respectively.[6]

ccRCC Clinical Presentation, Diagnosis & Treatment

The clinical presentation of renal cell carcinoma in adults includes a lump in the abdomen, blood in the urine, unexplained weight loss, loss of appetite, and anemia.[3] Diagnosis consists of a physical evaluation, laboratory testing, and imaging. A physical evaluation includes examining a patient for signs of lumps in the abdominal region. Laboratory testing would include a urinalysis to examine for hematuria, and other factors such as menstruation, infection, or recent strenuous exercise should be ruled out.[7]

Treatment can include surgery, radiation, chemotherapy, or immunotherapy. Surgery can be an option for localized RCC and is usually followed by chemotherapy or radiation to eradicate any remaining malignant cells. Radiation utilizes high-energy rays to eliminate cancerous tumor cells. Chemotherapy can be used, though it has not had a tumor response of over 10% in clinical trials.[5]

Immunotherapy has been utilized at all stages, including as adjuvant therapy in post-nephrectomy or post-radiation patients, and in combination therapy for stage IV or recurrent RCC.[5] Adjuvant immunotherapy can include Keytruda (pembrolizumab) or Sutent (sunitinib). Pembrolizumab is an immune checkpoint inhibitor and targets the programmed cell death protein 1 (PD-1) protein on the surface of T-cells. Sunitinib is a tyrosine kinase inhibitor (TKI) that targets the vascular endothelial growth factor (VEGF) to inhibit tumor growth.[5] First-line treatment for metastatic ccRCC includes a combination of immunotherapies, including Cabometyx (cabozantinib) plus Opdivo (nivolumab), Yervoy (ipilimumab) plus nivolumab, or Lenvima (lenvatinib) plus pembrolizumab.[8]

Cabozantinib, Nivolumab, and Ipilimumab Overview

Protein kinase B (PKB or Akt) and the mammalian target of rapamycin (mTOR) are responsible for tumor cell proliferation and survival.[9] Another mechanism of malignant tumor cell survival is through upregulating hypoxia-inducible factors (HIFs), which are transcription factors responsible for regulating oxygen delivery and can adjust in hypoxic conditions.[10] They are also responsible for mediating factors involved in cell growth, such as transforming growth factor alpha (TGFα), platelet-derived growth factor (PDGF), and VEGF.10 mTOR can be activated by VEGF and PDGF signaling through Akt.10 Approved therapies for ccRCC include targeting VEGF receptors (VEGFRs), PDGF receptors (PDGFRs), or the mTOR/HIF pathway.[10]

Cabozantinib is an oral TKI that targets multiple receptors involved in tumor angiogenesis, including VEGFR.[11] It is indicated for patients with advanced RCC, hepatocellular carcinoma (HCC), and metastatic thyroid cancer.[12] It is also approved to be used in combination with nivolumab for RCC. The recommended dose in RCC is 60 mg as a single agent, or 40 mg when used in combination with nivolumab, once daily without food until disease progression or unacceptable toxicity is administered.[12]

Nivolumab is a monoclonal antibody that blocks the programmed death-receptor 1 (PD-1) receptor, allowing T-cells to attack the metastatic tumor.[13] It is currently indicated for a plethora of cancers, including but not limited to RCC, non-small cell lung cancer (NSCLC), malignant pleural mesothelioma, classical Hodgkin lymphoma, and squamous cell carcinoma of the head and neck.[14] The recommended dose for advanced RCC is 240 mg every two weeks or 480 mg every four weeks when used as a single agent.[14]

Ipilimumab is a monoclonal antibody that inhibits the cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), which allows for increased T-cell activity to be carried out. It is currently indicated for RCC, melanoma, NSCLC, colorectal cancer, HCC, malignant pleural mesothelioma, and esophageal cancer.[15] The recommended dose in advanced

RCC is 1 mg per kilogram intravenously over 30 minutes immediately following nivolumab 3 mg per kilogram intravenously over 30 minutes on the same day, every three weeks for four doses.[15]

Previous Clinical Trials

The clinical trials leading up to the trial analyzing the efficacy of cabozantinib plus nivolumab and ipilimumab for patients with advanced ccRCC include the CABOSUN, the CheckMate 214, and the CheckMate 9ER clinical trials.

The CABOSUN clinical trial was a randomized, open-label, phase II, multicentered trial comparing cabozantinib with standard-of-care sunitinib in patients with advanced RCC which resulted in cabozantinib demonstrating a significant clinical benefit in progression-free survival and overall response over sunitinib.[16] This trial led to the Food and Drug Administration's (FDA's) approval of cabozantinib as the first-line treatment in advanced RCC in 2017.[17]

The CheckMate 214 clinical trial was a randomized, open-label, phase III trial comparing nivolumab plus ipilimumab to sunitinib monotherapy, which resulted in the combination of nivolumab and ipilimumab showing an increase in overall survival.[18] This study led to the 2018 FDA approval of the combination therapy of nivolumab and ipilumumab as first-line treatment for RCC.[19]

The CheckMate 9ER was a randomized, open-label, phase III trial comparing nivolumab plus cabozantinib combination to sunitinib monotherapy and resulted in the combination therapy showing an increase in progression-free survival and overall survival.[20] This trial led to the 2021 FDA approval of the combination of cabozantinib and nivolumab as first-line therapy for advanced RCC.[21]

COSMIC-313 Trial: Efficacy of Cabozantinib Plus Nivolumab and Ipilimumab

The COSMIC-313 trial was a randomized, double-blind, placebo-controlled, phase III clinical trial analyzing the efficacy of cabozantinib plus nivolumab and ipilimumab for patients with advanced ccRCC, conducted by Choueiri et al. Between June 2019 and March 2021, 855 participants from the United States, Canada, Europe, Australia, New Zealand, Latin America, and Asia underwent randomization, which was the intention-to-treat (ITT) population.[22] The experimental group contained 428 patients while the control group contained 427. Those in the experimental group received cabozantinib 40 mg while those in the control group received a placebo. In addition, both groups received nivolumab 3 mg per kilogram of body weight and ipilimumab 1 mg per kilogram intravenously every three weeks for four cycles, followed by nivolumab maintenance therapy 480 mg every four weeks for up to 2 years.[22] The first 550 patients who had undergone randomization were included in the progression-free survival (PFS) population.[22]

Patients 18 years or older with confirmed advanced or metastatic renal-cell carcinoma with a clear-cell component, an International Metastatic Database Consortium (IMDC) risk score of intermediate or poor, a Karnofsky performance-status score of 70 or greater, and a PD-L1-positive tumor cell were deemed eligible for the trial.[22] Patients were excluded if they had received previous systemic anticancer therapy for advanced renal-cell carcinoma (one previous systemic adjuvant

therapy was allowed, except for combination regimens with PD-L1 and CTLA4 inhibitors). Exclusion criteria also included brain metastases or cranial epidural disease (unless the disease was adequately treated and stable), autoimmune diseases, or use of immunosuppressive medications (>10 mg of prednisone or equivalent per day) within 14 days before randomization.[22] Baseline characteristics of participants were well balanced between the experimental and control groups, with the average participant being a white male around 60 years old with an intermediate IMDC risk.[22]

The primary endpoint of this study was progression-free survival in the PFS population, and the secondary endpoint was overall survival in the ITT population. Additional endpoints included objective tumor response, duration of response, and safety.[22] The Kaplan-Meier method was used to estimate the primary endpoint and duration of response confidence intervals. The Clopper-Pearson method was used to calculate the two-sided confidence intervals for each group's point estimate of response. The Cox proportional hazard model was used to estimate the hazard ratios with 95% confidence intervals. The objective tumor response was done by assessing computer tomography (CT) or magnetic resonance imaging (MRI) scans performed at baseline, week ten, then every eight weeks through week fifty, and then every twelve weeks.[22]

It was determined that the 249th event of disease progression or death would provide a hazard ratio of 0.66 with 90% power in the experimental group compared to the control group, as assessed with a two-sided log-rank test at a significance level of 0.05.22 The PFS benefit was shown in the experimental group except for those with an IMDC risk score of poor.[22] It was estimated that 433 deaths in the ITT population would provide a hazard ratio of 0.73 with 90% power in the experimental group compared to the control group.[22] Investigators of the study deemed that data from the trial is not mature enough to assess the secondary endpoint.

In the PFS population, objective tumor response was observed in 43% [95% confidence interval (CI), 37 to 49] of patients in the experimental group and 36% (95% CI, 30 to 42) of patients in the control group. 3% of patients in both groups had a complete response to the assigned regimen.[22] A grade 3 or 4 adverse event occurred in 79% (337 out of 426) of the patients in the experimental group and 56% (236 out of 424) in the control group.[22]

Adverse events that occurred more in the experimental group than in the control group included increased alanine aminotransferase (27% vs. 6%), increased aspartate amino-transferase level (20% vs. 5%), and hyper-tension (10% vs. 3%), respectively. Death that was related to the trial regimen and occurred within 100 days before the last dose of the trial regimen was observed in 5 participants in the experimental group and 4 participants in the control group.[22]

Conclusion

The clinical trial concluded that a triplet regimen of cabozantinib plus nivolumab and ipilimumab in treatment-naive patients with advanced renal carcinoma with intermediate prognostic risk provides longer PFS.[22] Overall survival outcomes could not be concluded as results are still ongoing. Though this triplet therapy did show statistically significant outcomes, it also resulted in a higher inci-

dence of adverse events. At this time, further evaluation with a larger group and longer trial duration is needed to determine whether it should be included in the guidelines for advanced ccRCC.

References

1. Muglia VF, Prando A. Renal cell carcinoma: histological classification and correlation with imaging findings. Radiol Bras. 2015;48(3):166-174. doi:10.1590/0100-3984.2013.1927
2. Clear Cell Renal Cell Carcinoma. National Cancer Institute. Published March 17, 2020. https://www.cancer.gov/pediatric-adult-rare-tumor/rare-tumors/rare-kidney-tumors/clear-cell-renal-cell-carcinoma
3. PDQ® Adult Treatment Editorial Board. Renal Cell Cancer Treatment (PDQ®)-Patient Version. National Cancer Institute. Updated July 21, 2023. Accessed September 11, 2023. https://www.cancer.gov/types/kidney/patient/kidney-treatment-pdq.
4. Högner A, Krause H, Jandrig B, et al. PBRM1 and VHL expression correlate in human clear cell renal cell carcinoma with differential association with patient's overall survival. Urol Oncol. 2018;36(3):94.e1-94.e14. doi:10.1016/j.urolonc.2017.10.027
5. PDQ® Adult Treatment Editorial Board. Renal Cell Cancer Treatment (PDQ®)-Health Professional Version. National Cancer Institute. Updated February 16, 2023. Accessed August 27, 2023. https://www.cancer.gov/types/kidney/hp/kidney-treatment-pdq
6. Survival Rates for Kidney Cancer. National Cancer Institute. https://www.cancer.org/cancer/types/kidney-cancer/detection-diagnosis-staging/survival-rates.html
7. Gray RE, Harris GT. Renal Cell Carcinoma: Diagnosis and Management. Am Fam Physician. 2019;99(3):179-184. https://www.aafp.org/pubs/afp/issues/2019/0201/p179.html
8. Motzer RJ, Jonasch E, Agarwal N, et al. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Kidney Cancer, Version 1.2024. National Comprehensive Cancer Network. Published June 21, 2023. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf
9. Banumathy G, Cairns P. Signaling pathways in renal cell carcinoma. Cancer Biol Ther. 2010;10(7):658-664. doi:10.4161/cbt.10.7.13247
10. Linehan WM, Srinivasan R, Schmidt LS. The genetic basis of kidney cancer: a metabolic disease. Nat Rev Urol. 2010;7(5):277-285. doi:10.1038/nrurol.2010.47
11. Cochin V, Gross-Goupil M, Ravaud A, Godbert Y, Le Moulec S. Cabozantinib : modalités d'action, efficacité et indications [Cabozantinib: Mechanism of action, efficacy and indications]. Bull Cancer. 2017;104(5):393-401. doi:10.1016/j.bulcan.2017.03.013
12. Cabometyx (cabozantinib) [package insert]. Alameda, CA; Exelixis, Inc.; Revised September 2023.
13. Guo L, Zhang H, Chen B. Nivolumab as Programmed Death-1 (PD-1) Inhibitor for Targeted Immunotherapy in Tumor. J Cancer. 2017;8(3):410-416. doi:10.7150/jca.17144
14. Opdivo (nivolumab) [package insert]. Princeton, NJ; Bristol-Myers Squibb Company; Revised October 2023.
15. Yervoy (ipilimumab) [package insert]. Princeton, NJ; Bristol-Myers Squibb Company; Revised February 2023.
16. Choueiri TK, Halabi S, Sanford BL, et al. Cabozantinib Versus Sunitinib As Initial Targeted Therapy for Patients With Metastatic Renal Cell Carcinoma of Poor or Intermediate Risk: The Alliance A031203 CABOSUN Trial. J Clin Oncol. 2017;35(6):591-

597. doi:10.1200/JCO.2016.70.7398
17. Center for Drug Evaluation and Research. FDA grants regular approval to Cabometyx for first-line treatment of advanced renal cell carcinoma. U.S. Food and Drug Administration. Published December 19, 2017. Accessed August 26, 2023. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-regular-approval-cabometyx-first-line-treatment-advanced-renal-cell-carcinoma
18. Motzer RJ, Tannir NM, McDermott DF, et al. Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma. N Engl J Med. 2018;378(14):1277-1290. doi:10.1056/NEJMoa1712126
19. FDA approves nivolumab plus ipilimumab combination for intermediate. U.S. Food and Drug Administration. Published April 16, 2018. Accessed August 26, 2023. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nivolumab-plus-ipilimumab-combination-intermediate-or-poor-risk-advanced-renal-cell
20. Choueiri TK, Powles T, Burotto M, et al. Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma. N Engl J Med. 2021;384(9):829-841. doi:10.1056/NEJMoa2026982
21. FDA approves nivolumab plus cabozantinib for advanced renal cell carcinoma. U.S. Food and Drug Administration. Published January 11, 2021. Accessed August 26, 2023. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nivolumab-plus-cabozantinib-advanced-renal-cell-carcinoma
22. Choueiri TK, Powles T, Albiges L, et al. Cabozantinib plus Nivolumab and Ipilimumab in Renal-Cell Carcinoma. N Engl J Med. 2023;388(19):1767-1778. doi:10.1056/NEJMoa2212851

It's in Our Blood: An Exploration of Gene Therapies for Hemophilia A and B

By: Holly Nguyen, PharmD Candidate c/o 2024

Hemophilia is a severe hereditary hemorrhagic disorder derived from gene mutations that make clotting factors VIII and IX for hemophilia types A and B, respectively.[1] The sex-linked hemophilia recessive allele on the X chromosome gives sons a 50% chance of inheriting the hemophilia allele from a heterozygous or homozygous recessive mother, and the son who inherits the hemophilia allele from his mother will have hemophilia.[2,3] Daughters have a 50% chance of inheriting the hemophilia allele as carriers from a heterozygous mother, homozygous recessive mother, or homozygous recessive father and may experience the symptoms of mild hemophilia.[3,4] In the search to find cures for rare diseases, pharmaceutical and biotechnology companies are capitalizing on the novel gene therapy market. Gene transfer therapy involves mutated gene replacement or recovery of gene function with a different gene. All genetic changes are compressed and then transferred to the patient in an intravenous vector injection or through a sample of vector-exposed cells performed in the laboratory.[5] Genome editing snips parts of the deoxyribonucleic acid (DNA) sequence for insertion, replacement, or deletion; the most advanced genome editing tool, clustered regularly interspaced short palindromic repeats (CRISPR), was released in 2009.[6] In the past 12 months, gene therapies for hemophilia A and B have either received Food and Drug Administration (FDA) approval or are undergoing the final phases of clinical development, and the prospect of these new therapies is exciting for the future of hemophilia treatments.

Hemophilia gene therapies are specialized in-vivo recombinant adenoassociated viruses (AAV) produced by transiently transfected human HEK293 cells or baculovirus infected Sf9 insect cells in the liver, and are thus prone to hepatotoxicity and capsid-immune responses; the latter results in the decline of factor activity and necessitates treatment with immunomodulating agents.[7] Valoctocogene roxaparvovec-rvox (Roctavian) by BioMarin Pharmaceutical Inc. received FDA approval for hemophilia A in June 2023, and is the sole contender of the post-marketing surveillance space.[8] The decision was supported by a safety and efficacy study of 112 adult male patients between 18 to 70 years old previously treated with factor VIII replacement therapy; a yearly mean bleeding rate decrease from 5.4 to 2.6 bleeds per year reduced the use of factor replacement by 96.8% compared to baseline.[9,10] BioMarin will price Roctavian at $2.9 million with an outcomes-based warranty program, set to "fully reimburse government and commercial payers if expectations are not met, and partially reimburse patients who lose response to the therapy in the first four years after dosing".[10] Starting plans to launch in Germany, BioMarin is currently guiding physicians through the concerns of opioid use post-AAV therapy and identifying eligible

patients to receive the first treatments of Roctavian worldwide.[11]

Expanding on in-vivo recombinant AAV viruses, gene therapies for hemophilia B benefit from the discovery of the Padua variant for the factor IX gene, resulting in 5-10 times higher factor IX activity and higher levels of factor IX.[12] Etranacogene dezparvovec (Hemgenix) by CSL Behring received FDA approval in November 2022 and is also the only gene therapy in the post-marketing surveillance space for hemophilia B.[13] The safety and efficacy trial evaluated 57 adult male patients between 18-75 years, diagnosed with severe or moderately severe hemophilia B, and 54 participants displayed a 54% reduction in annual bleeding rates compared to baseline, in addition to a rise of factor IX activity levels and a decreased need for factor IX replacement therapy.[13] Hemgenix is a single-dose IV infusion priced at $3.5 million per dose, currently holding the spot as the most expensive drug in the world.[13,14] Exceeding the Institute for Clinical and Economic Review's (ICER) recommended price of $2.9 million, it is unknown whether CSL Behring will cede to a price reduction, since it argues that healthcare systems already spend over $20 million on prophylactic and therapeutic treatments of moderate to severe hemophilia B.[14] While CSL Behring continues to navigate the post-marketing stages for Hemgenix, Pfizer announced the FDA acceptance of its Biologics License Application for its hemophilia B gene therapy, fidanacogene elaparvovec, in June 2023.[15] In its Phase 3 BENGENE-2 study, 45 participants were enrolled with a prior six-month prophylactic therapy of factor IX therapy, followed by an IV dose of fidanacogene elaparvovec at 5e11 vg/kg; the primary endpoint of decreased annual bleeding rates of 1.3 for 12 months was superior to an annual bleeding rate of 4.43 during prophylactic therapy.[16] With grants for breakthrough Regenerative Medicines Advanced Therapy (RMAT) and orphan drug designations, Pfizer is working to meet the Prescription Drug User Fee Act (PDUFA) goal set by the FDA for the second quarter of 2024.[15]

Roctavian, Hemgenix, fidanacogene elaparvovec, and the overall impact of hemophilia gene therapy reaches beyond the hemophilia and hematology communities. Spearheaded by the latest AAV technologies and meticulous implementation of the final Phase III trials, hemophilia gene therapies are the first of many opportunities to lock in cells and genes as sustainable solutions for the future of rare inherited and degenerative diseases.

References

1. Berntorp E, Fischer K, Hart DP, et al. Haemophilia. *Nat Rev Dis Primers*. 2021;7(1):45. doi:10.1038/s41572-021-00278-x.
2. Hemophilia Inheritance Patterns. Centers for Disease Control and Prevention. Accessed August 19, 2023. https://www.cdc.gov/ncbddd/hemophilia/course/Hemophilia_Patterns_v3.pdf.
3. How Hemophilia is Inherited. Centers for Disease Control and Prevention. Updated July 12, 2023. Accessed August 19, 2023. https://www.cdc.gov/ncbddd/hemophilia/inheritance-pattern.html.
4. The Scenarios of Females Inheriting Hemophilia. Indiana Hemophilia and Thrombosis Center. Accessed August 19, 2023. https://www.ihtc.org/women-with-hemophilia.
5. How does gene therapy work? MedlinePlus. Accessed August 20, 2023. https://medlineplus.gov/genetics/understanding/therapy/procedures/. 6. What is genome

editing? Genome. Accessed August 20, 2023. https://www.genome.gov/about-genomics/policy-issues/what-is-Genome-Editing
7. Samelson-Jones BJ, George LA. Adeno-associated Virus Gene Therapy for Hemophilia. Annu Rev Med. 2022(74):231-247. doi:10.1146/annurev-med-043021-033013.
8. June 29, 2023 Summary Basis for Regulatory Action ROCTAVIAN. U.S. Food and Drug Administration. Accessed August 20, 2023. https://www.fda.gov/media/170455/download.
9. FDA Approves First Gene Therapy for Adults with Severe Hemophilia A. U.S. Food and Drug Administration.. Published June 29, 2023. Accessed August 20, 2023. https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapy-adults-severe-hemophilia.
10. Liu A. BioMarin's hemophilia gene therapy Roctavian lands FDA nod with 'glimmers' of enthusiasm among doctors. Fierce Pharma. Published June 29, 2023. Accessed August 20, 2023. https://www.fiercepharma.com/pharma/biomarins-hemophilia-gene-therapy-roctavian-lands-fda-nod-glimmers-enthusiasm-among-doctors.
11. Liu A. BioMarin's hemophilia gene therapy may have a chance at winning over Europe: analysis. Fierce Pharma. Published June 14, 2023. Accessed August 20, 2023. https://www.fiercepharma.com/marketing/biomarins-hemophilia-gene-therapy-may-have-chance-winning-over-europe-analysts.
12. Miesbach W, Klamroth R, Oldenburg J, Tiede A. Gene Therapy for Hemophilia – Opportunities and Risks. Dtsch Ärztebl Int. 2022(119):51-52. doi:10.3238/arztebl.m2022.0353.
13. FDA Approves First Gene Therapy to Treat Adults with Hemophilia B. U.S. Food and Drug Administration.. Published November 22, 2022. Accessed August 20, 2023. https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapy-treat-adults-hemophilia-b.
14. Becker Z. Sporting a $3.5M price tag, CSL and uniQure's hemophilia B gene therapy crosses FDA finish line. Fierce Pharma. Published November 13, 2022. Accessed August 20, 2023. https://www.fiercepharma.com/pharma/csl-and-uniqures-hemophilia-b-gene-therapy-scores-approval-35-million-price-tag.
15. FDA Accepts Pfizer's Application for Hemophilia B Gene Therapy Fidanacogene Elaparvonec. Pfizer. Published June 27, 2023. Accessed August 20, 2023. https://www.pfizer.com/news/press-release/press-release-detail/fda-accepts-pfizers-application-hemophilia-b-gene-therapy.
16. Pfizer Announces Positive Top-Line Results from Phase 3 Study of Hemophilia B Gene Therapy Candidate. Published December 29, 2022. Accessed August 20, 2023. https://www.pfizer.com/news/press-release/press-release-detail/pfizer-announces-positive-top-line-results-phase-3-study.

6th Year Perspective: A Guide to Application-Based APPEs

By: Sarah Adly, PharmD Candidate c/o 2024

Applying to advanced professional pharmacy experience (APPE) rotations can be a daunting experience. After all, this is the last opportunity most pharmacy students have to deeply explore their interests. But not to worry! As someone who was in your shoes a year ago, I will let you in on some helpful tips for choosing APPEs that will diversify your experience. When I was ranking sites last winter, I sought guidance from my mentor, who gave me advice that indisputably changed my life: there are application-based APPE rotations separate from the ones listed on Core Elms. These particular APPEs have been like gold mines to me, which have helped me deeply experience various realms of pharmacy, including ones that I had not been exposed to previously.

What makes application-based APPEs unique?

Application-based APPEs give students the opportunity to explore non-traditional sectors of pharmacy which can help to guide their career pathways. These sites can expose students to multiple fields of interest, including the pharmaceutical industry, medical writing, policy reforms and research, and so much more. It is important to fully immerse yourself into these niche areas of pharmacy when you are given the chance; being on APPE rotations is the best time to gather real-world experience and apply what you have learned over the previous six years. Personally, these unique experiences have provided me with the time and place to network and broaden my skill set. One application-based APPE I had was one with the National Association of Chain Drug Stores (NACDS) located in Arlington, Virginia. During my time with NACDS, I was able to hone my presentation and advocacy skills during my topic discussion on Empowering Health and Wellness: The Vital Role of Pharmacists. This experience also provided me with other transferable skills such as time/project management and effective communication. I am currently completing another APPE at Bristol Myers Squibb, where I have grown much more familiar with ways to identify gaps in practice for healthcare providers. During this rotation, I have also been working on a project regarding ulcerative colitis that has really pushed me to develop my research and data-collection skills. This period has also given me the opportunity to have one-on-one meetings with fellows, managers, and directors within the company in order to discuss career paths and their current projects. . Overall, these two application-based APPEs have offered me the chance to not only grow as a student pharmacist, but to develop a clearer understanding of what I want to pursue in the future as well.

Where do I find these application-based APPEs, and what are the requirements?

In Core Elms, under the document library, there is a file titled "APPEs Requiring Applications Outside of the Lottery." This is a document that contains important information about application-based APPEs, including descriptions and links/instructions to apply. For most of these application-based APPEs, you will need to submit a curriculum vitae (CV) and letter of intent. Some sites may also require 2 to 3 letters of recommendation and/or a cover letter. For your CV, you should put your most recent work, leadership, research/publications, and volunteer experiences from the last 2 to 4 years. Some of these application-based APPEs require an interview in which you may be asked to expand upon experiences on your CV, so make sure that you can speak in depth about everything you include. Your letter of intent should include your thoughts on what you will gain by completing the rotation as well as its impact on your future career. For letters of recommendation, it is a good idea to ask various supervisors like professors, employers, pharmacy mentors, etc. Make sure to look at deadlines and ask for recommendations well ahead of time, as you would like to be respectful of everyone's time. I suggest reaching out at least 8 weeks prior to the due date. Also, consider sending them your CV as well as your interests so that they can be specific in your letter of recommendation. Some programs may require applicants to submit cover letters, which is a concise letter that showcases your passion and qualifications. You should mention the positions you are applying to and how you discovered these positions, highlight our relevant experiences and transferable skills, and explain why you are interested in the specific company. Make sure to show that you researched the company by discussing their mission and how it may align with your goals. In any letter that you submit, make sure that it is free of any grammar and spelling errors, and always sign off appropriately.

What should I expect regarding interviews for APPE sites?

As mentioned before, some of these applications require an interviewing process. If that is the case, dress professionally, practice with a mock interview, and get comfortable using the STAR method. The STAR method is a technique used to answer behavior-based interview questions by illustrating a specific situation, task, action, and result. A common question I was asked by interviewers was, "Can you give an example of a conflict you faced with a team member and explain how you resolved it?" In your answers, the setting of your example can vary; for instance, the conflict can be one from work or from school. Just be sure to be concise while making sure you hit all the points emphasized in the STAR method. I have also received "out-of-the-box" questions such as, "If you could be any animal, what would you be and why?" For these types of questions, it is important to know that they do not care so much about the particular animal, but rather your rationale. All in all, just remember to present yourself authentically and explain your answers fully!

When should I expect a response about my application?

Certain sites will state when they will make their decisions by on their website, however some will not give you a specific date at all. With that, I would say the best action plan

during this waiting period is to check your emails frequently. Be sure you check your spam as well! I had one of my determinations go to my spam – luckily for me, they emailed again, but that will not always be the case.

What if I get rejected?

This is bound to happen if you apply to multiple APPEs, as these sites only accept a few students per period and have a large pool of applicants. Do not let these decisions bring you down or lower your confidence. Whether or not you get accepted, this whole process will serve as valuable practice for the future as you apply for jobs, residencies, or fellowships. Use this as a way to learn and do some self-reflection on what you think you could improve on in the future. Also, although this is a rather cliché saying, it definitely holds true: remember that everything happens for a reason.

Okay, I got accepted! What should I do next?

Congratulations! This next step is VERY crucial: make sure to accept and thank the site's APPE committee via email within the timeframe they give you to do so. During this time, the site may also ask you when you would like to schedule this rotation. If this is the case, check the Core Elms document library for your year's APPE schedule. If this is a site you really want to complete prior to fellowship or residency season so you can add it to your CV, try fitting it before Period 4 or 5 for fellowship and Period 7 or 8 for residency. Additionally, please email your experiential coordinator and let them know the following information: confirmation of your acceptance, the period in which you and your site agreed upon, the domain of the site, and the name/contact information of your preceptor. For the domain of the site, this would entail if the site fell under elective, advanced community care, ambulatory care, general inpatient, or focused inpatient. You should also check and see what the requirements are for your year. For my year, we had to have two faculty and two patient-focused electives out of the four electives.

Final thoughts on trying out something new

If this sounds like a lot, it may be, but I promise you it will help immensely with your project management skills, and you will not regret stepping out of your comfort zone. To be frank, I never pushed my limits much during school, but applying for the NACDS has been one of the best choices I have made for myself! I truly do not regret this decision one bit. I am incredibly grateful for these opportunities as well as for my mentor, who gave me the advice to explore more outside of my bubble in the first place. I encourage you all to do the same, as you never know where your journey will take you. Try to explore the non-traditional paths! Good luck with everything, and have a great year!

The Rho Chi Post would like to thank to Sarah for taking the time to explain application-based APPEs and share her experiences with us! If you have any questions about APPEs or pharmacy school in general, please feel free to email Sarah at: sarah.adly18@stjohns.edu

The Current Landscape of Treatment Options for Alzheimer's Disease

By: Anureet Kaur, PharmD Candidate c/o 2024

Alzheimer's disease (AD) is an epidemic. Currently, the neurodegenerative disorder holds the title of the seventh leading cause of death in the United States (U.S.), disproportionately affecting older adults.[1] In fact, the National Institute on Aging reports that the number of people with AD doubles about every five years beyond the age of 65 years.[2] While AD is not a normal part of aging, age-related changes in the brain may increase the risk of disease. Ongoing research also suggests that vascular conditions, lack of social engagement, diet, and genetics may play a role in disease progression.[2]

The probable pathophysiology of AD is twofold; proposed mechanisms involve an accumulation of abnormal plaques as well as the formation of neurofibrillary tangles in the brain. In the healthy brain, naturally occurring beta-amyloid proteins are broken down by enzymes. In the brain of a person with AD, abnormal levels of beta-amyloid protein clump together to form insoluble plaques that collect between neurons and disrupt cell function.[3] Furthermore, in the healthy brain, tau proteins bind to and stabilize microtubules to support neurons. Abnormal chemical changes in those with AD cause tau to misfold. This creates tangles inside neurons, disrupting normal synaptic communication. These two mechanisms cause a variety of neurotransmitter deficits, with loss of acetylcholine being one of the most notable.[4] Acetylcholine carries messages from the brain to nerve cells; thus, its deficiency may lead to memory loss, confusion, and delusions.[5] Four clinical phases of AD are currently recognized. The pre-clinical stage is distinguished by mild memory loss with no decline in performance of daily living activities. The mild stage is when several symptoms start to develop including poor memory, disorientation of place and time, depression, and decreased concentration. The moderate stage is when the disease spreads to other areas of the brain, leading to a subsequent loss of control, increased memory loss, and issues with reading, writing, and speaking. Agitation, paranoia, and delusion become more prominent during this period as well. Lastly, the severe stage comprises of significant cognitive, neuropsychiatric, and functional deterioration. By this phase, the disease has spread to the entire cortex of the brain. The patient loses the ability to perform basic tasks such as speaking, walking, and swallowing. Complications from the severe stage can contribute to the patient's death.[5]

Despite the significant public health issue it poses, treatments for AD are limited. The mainstay of therapy for this disease includes three cholinesterase inhibitors (ChEIs) and one N-methyl-D-aspartate receptor antagonist (NMDA). These drugs do not alter the course of the disease, but rather work to control symptoms of AD.[5]

Current guidelines recommend initiating AD treatment with any of the ChEIs as opposed to an NMDA antagonist. Choice of ChEI therapy

is individualized based on patient preference, drug interactions, affordability, and ease of use. The major mechanism behind cholinesterase inhibitors involves restoration of the cholinergic pathway by inhibiting acetylcholinesterase, the enzyme responsible for acetylcholine hydrolysis. There are 3 drugs in this class: Aricept (donepezil), Exelon (rivastigmine), and Razadyne (galantamine). These medications are typically well tolerated by patients, but some common side effects of nausea, vomiting, and diarrhea have been observed. Syncope, bradycardia, atrial arrhythmias, and myocardial infarction are other less common, yet significant side effects. Due to its cardiovascular effects, a contraindication to ChEI use is a heart rate below 50 beats per minute.[4]

Donepezil is the leading choice of therapy for those with AD. This medication is available in a variety of formulations: a(n) standard oral tablet, oral dissolving tablet, oral solution, and transdermal patch. All of donepezil's dosage forms are approved for use in any stage of AD, unlike rivastigmine and galantamine.[4] Another advantage of donepezil is that it only requires once-a-day dosing due to its extensive half-life of 70 hours. Patients are generally initiated on 5 mg daily, for both oral and transdermal formulations. The dose may be titrated to 10 mg after 4 to 6 weeks based on clinical response.[6] Patients should be advised to take oral formulations of donepezil in the evening due to their tendency to cause significant dizziness and irregular heartbeat.[6] However, this drug, like other ChEIs, has also been reported to cause sleep disturbances – in patients experiencing such side effects, it may be recommended to take the dose in the morning instead.[4]

Rivastigmine is available as a(n) oral capsule, oral solution, and transdermal patch. Both oral formulations of rivastigmine are approved for mild and moderate AD, while the transdermal patch is only approved for severe cases.[4] Oral formulations are dosed twice daily due to the drug's short half-life of 1.5 hours. They should be taken with meals to mitigate gastrointestinal (GI) side effects. The oral solution may be mixed in water, cold fruit juice, or soda, and stored at room temperature for up to 4 hours before administration.[7] Initial oral dosing is 1.5 mg twice daily and may be increased by 3 mg daily every 2 weeks based on tolerability for a maximum recommended daily dose of 12 mg. Initial transdermal dosing is one 4.6 mg/24-hour patch applied daily. After a minimum of 4 weeks, the clinician may increase the dose to 9.5 mg/24 hour as tolerated and continue to titrate to a maximum dose of 13.3 mg/24-hour patch. In contrast to other ChEIs, rivastigmine carries a distinct low body weight warning – for patients weighing less than 50 kilograms, close monitoring for toxicity, which can manifest as excessive nausea and vomiting, is advised.[7]

In contrast to the other ChEIs, galantamine is only available in oral formulations including a standard tablet, solution, and extended-release capsule. Given its short half-life of 7 hours, regular release oral formulations are dosed twice daily. The drug should be taken with meals to avoid GI side effects like other ChEIs.[8] Galantamine oral solution can also be mixed with water, cold fruit juice, or soda; however, unlike rivastigmine, this medication must be administrated right away after mixing.[9] The regular-release tablet or solution is initiated at 4 mg twice daily for 4 weeks and, if tolerated, doubled every 4 weeks to a maximum of 24 mg daily in 2 divided doses. The extended-release capsule is initiated at 8

mg once daily for 4 weeks. The dose may be doubled every 4 weeks to a maximum of 24 mg daily as a single dose.[8] Renal and hepatic dosing is necessary for both rivastigmine and galantamine. Lastly, interruptions in ChEI therapy for 3 or more days require retitration.[4]

Memantine's mechanism of action differs from the aforementioned AD drugs. It is a partial antagonist of NMDA receptors which cause neuronal loss when overactivated.[10] The drug is indicated for use in moderate and severe AD. It can be used as monotherapy and in conjunction with a ChEI, to enhance therapeutic response and mitigate GI side effects. Common adverse events of memantine include headache, constipation, confusion, and dizziness.[4] Similar to donepezil, memantine has an extensive half-life of 60 to 80 hours, allowing for once-a-day initial dosing. The medication is available as a tablet, oral solution, and extended-release capsule. Immediate-release preparations are initiated at 5 mg once daily and increased by 5 mg every week as tolerated to a target maximum dose of 20 mg/day. Extended-release capsules are initiated at 7 mg once daily and increased by 7 mg every week as tolerated to a target maximum dose of 28 mg once daily. Renal and hepatic dosing is necessary.[4] Unlike the other oral solutions, memantine oral solution cannot be mixed with other liquids; however, capsules may be opened, and contents may be sprinkled into applesauce to aid in administration.[4]

AD is a complex condition to manage – an interprofessional approach is recommended to improve quality of life and achieve therapeutic outcomes. Pharmacists can contribute to this process by considering factors such as comorbidities and patient preferences as they personalize medication regimens with ChEIs and NMDA antagonists. Although current options are limited and may only provide symptomatic relief, there appears to be a promising future for AD therapy. The Food and Drug Administration recently approved two new medications that may potentially delay decline from dementia. AD is currently a challenging condition to deal with, but with the proper care and pharmacological therapy, there is potential to better manage the disease.

References

1. 2023 Alzheimer's disease facts and figures. Alzheimers Dement. 2023;19(4):1598-1695. doi:10.1002/alz.13016
2. What Causes Alzheimer's Disease? National Institute on Aging. Reviewed December 24, 2019. https://www.nia.nih.gov/health/what-causes-alzheimers-disease.
3. Sheppard O, Coleman M. Alzheimer's Disease: Etiology, Neuropathology and Pathogenesis. In: Huang X, ed. Alzheimer's Disease: Drug Discovery. Brisbane (AU): Exon Publications; December 18, 2020.
4. Zimmerman KM, Peron EP, Crouse EL, Sargent LJ, Hobgood SE. Alzheimer Disease. In: DiPiro JT, Yee GC, Haines ST, Nolin TD, Ellingrod VL, Posey L. eds. DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition. McGraw Hill; 2023. Accessed November 12, 2023. https://accesspharmacy.mhmedical.com/content.aspx?bookid=3097&sectionid=267240515
5. Breijyeh Z, Karaman R. Comprehensive Review on Alzheimer's Disease: Causes and Treatment. Molecules. 2020;25(24):5789. doi:10.3390/molecules25245789
6. Aricept (donepezil hydrochloride) [package insert]. Woodcliff Lake, NJ: Eisai Co., Ltd.; Revised 2018.

7. Exelon (rivastigmine tartrate) [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; Revised 2018.
8. Razadyne® (galantamine hydrobromide) [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; Revised 2021.
9. Galantamine Hydrobromide (galantamine hydrobromide solution) [package insert]. Berkeley Heights, NJ: Hikma Pharmaceuticals USA Inc.; Revised 2022.
10. Folch J, Busquets O, Ettcheto M, et al. Memantine for the Treatment of Dementia: A Review on its Current and Future Applications. J Alzheimers Dis. 2018;62(3):1223-1240. doi:10.3233/JAD-170672

Interested in writing for the Rho Chi Post?

Go to http://rhochistj.org/RhoChiPost and click on the login option from the menu bar to make an account! With an account, you'll have access to the article submission portal where you can submit your writing for publication in an upcoming issue!

Remember, you do NOT have to be a member of Rho Chi, a member of the editorial team, or a student of St. John's to write for our newsletter!

If you have any questions, feel free to email us at rhochipost@gmail.com!

Health-Related Mechanisms Behind Exercise

By: Sairah Sheikh, PharmD Candidate c/o 2024

Increased physical activity is often touted as a lifestyle choice that improves bodily health dramatically. Over recent years, there has been an increase in research showing that exercise can help to prevent chronic diseases. Physical activity exerts its benefit through a wide variety of mechanisms.

Exercise can improve the health of cancer patients undergoing chemotherapy, immunotherapy, or radiation. Research conducted by Memorial Sloan Kettering's Exercise Oncology Service revealed that patients who had been treated with chemotherapy for three months experienced a 15% decline in their fitness levels, which is equal to physically aging 10 years in three months. When observing the effect of regularly exercising during treatment periods, these researchers found that it significantly decreased physical aging.[1] Additionally, a study published in the Nation-al Library of Medicine showed the benefits of exercise in mice with cancer. In this study, mice were injected with 4T1 mammary carcinoma, equivalent to triple-negative breast cancer. They were then split into two groups: an active and a sedentary group. The active group ran on the treadmill for 30 minutes per day for five days a week, while the other mice were kept in their home cages. Both groups were treated with radiotherapy and programmed cell death-1 (PD-1)-blocking immunotherapy. The study determined that tumor growth was substantially lower in the mice that exercised, with an average tumor size of 203 $\pm$ 52 mm^3 versus 325 $\pm$ 83 mm^3 in the sedentary control group.[2] This occurred as a result of a reduc-tion in myeloid-derived suppressor cells (MDSCs) along with an increase in natural killer (NK) and CD8 T-cell activation. MDSCs are immunosuppressive and ultimately pro-mote the growth of tumors, as well as bodily resistance against immunotherapy.[3] The pow-er of exercise is not limited to the treatment of oncology patients.

Another mechanism behind the health benefits of exercise involves the hypothalamic-pituitary-adrenal axis (HPA) and its interaction with the sympathetic nervous system (SNS). These systems mediate the body's stress response, with the HPA axis releasing glucocorticoids such as cortisol, and the SNS releasing epinephrine and norepinephrine.[4] Heightened glucocorticoid levels normally stimulate the mobilization of immune cells. However, with prolonged glucocorticoid activation, immunosuppressive effects take place to prevent high inflammation due to the overactivity of these cells. Glucocorticoid resistance can also develop as a result of sustained high cortisol levels, which can eventually culminate in chronic inflammation and a higher risk of developing inflammatory disorders.[4]

Exercise buffers against these effects by optimizing HPA and SNS responses.[4] It has been observed that physically active individuals have a different physiological response to stress-inducing situations when compared

to non-physically active individuals. In situations with high physical and non-physical stress, physically fit people have been observed to experience significantly lower HPA responses. They had decreased cortisol and heart rate, along with significantly improved mood.[4] SNS reactivity has been seen to be improved as well because those who are more physically active exhibit a more rapid recovery from stressors compared to less physically active individuals.[4] Less physically fit individuals demonstrated higher HPA responses, higher cortisol and heart rate responses, less calmness, and higher anxiety overall. This shows how effective exercise is in improving a person's overall physical and mental health in the presence of stressors, which is especially critical in society today. The effect physical activity has on lowering inflammation in the body should also not be overlooked.

Exercise has a positive impact on cardiovascular function as well. Since cardiovascular disease is the leading cause of death in the world,[5] it is important to note the mechanisms behind exercise as a method to improve cardiac activity. One mechanism is the mitochondrial adaptations that occur in the body. Exercise can improve VO2 max, which is the maximum amount of oxygen our body takes in when performing any physical activity and is used to measure long-term cardiorespiratory fitness. It does this by "increasing the mitochondrial content and desaturation of myoglobin in skeletal muscle tissue."[5] Exercise also enhances mitochondrial biogenesis in cardiomyocytes, which may be due to increased activation of AMP-activated protein kinase (AMPK) which leads to increased mitochondrial PGC-1α expression.[5] PGC-1α is a protein that helps regulate cellular energy metabolism by stimulating mitochondrial biogenesis to make the muscle tissue more oxidative and less glycolytic.[6] Additionally, exercise helps the heart as it causes mitochondria to increase oxidation of fatty acids leading to an increase in the capacity for adenosine triphosphate (ATP) synthesis.[5] Exercise has also been found to increased expression of endothelial nitric oxide synthase (eNOS), which is associated with inhibition of platelet aggregation and reduction in the onset of atherosclerosis, thrombosis, ischemia, or other cardiac events.[5,6]

Additionally, physical activity has been proven to have an immensely beneficial impact on neurological health. Higher amounts of gray and white matter in the brain allow for information processing and bodily processes to be carried out more effectively.[7] Imaging studies have suggested that adequate exercise is linked with increased volume and integrity of gray and white matter integrity, especially in the prefrontal cortex and hippocampus.[4] Additionally, regions of the brain that are associated with stress and aging seem to benefit from a physically active lifestyle which shows that exercise promotes cognitive activity.[4] If hippocampus volume increases due to exercise, it is also associated with higher BDNF levels. BDNF, or brain-derived neurotrophic factor, is a molecule that improves cognitive function and regulates heart function and energy metabolism.4 About 30% of the body's interleukin 6 (IL-6) levels are found in adipose tissue, so if a person is physically fit, they will likely have less adipose tissue and thus have less inflammation in their body. Furthermore, in a Treatment with Exercise Augmentation for Depression (TREAD) study, inflammatory biomarkers such as C-reactive protein (CRP)

were shown to be lower in physically fit persons compared to those who are not fit.[8] Patients in the study who had major depressive disorder and whose symptoms did not improve after being given a selective serotonin reuptake inhibitor (SSRI) were given an exercise plan. Patients who followed their exercise plan were found to have significantly lessened depressive symptoms.[8]

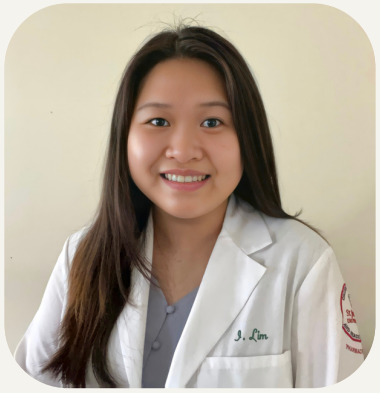
The aforementioned mechanisms make it clear that exercise is beneficial in both preventing disease and reducing its severity. In a country where 60% of the adult population is battling a chronic disease,[9] it is especially beneficial to become educated about healthy lifestyle choices such as exercise so that we can lessen symptom burden and improve quality of life.

References

1. How exercise can help treat and prevent cancer. Memorial Sloan Kettering Cancer Center. https://www.mskcc.org/videos/how-exercise-can-help-treat-and-prevent. Accessed February 2, 2023.
2. Wennerberg E, Lhuillier C, Rybstein MD, et al. Exercise reduces immune suppression and breast cancer progression in a preclinical model. *Oncotarget*. 2020;11(4):452-461. Published 2020 Jan 28. doi:10.18632/oncotarget.27464
3. Law AMK, Valdes-Mora F, Gallego-Ortega D. Myeloid-derived suppressor cells as a therapeutic target for cancer. Cells. 2020;9(3):561. Published 2020 Feb 27. doi:10.3390/cells9030561
4. Silverman MN, Deuster PA. Biological mechanisms underlying the role of physical fitness in health and resilience. Interface Focus. 2014;4(5):20140040. doi:10.1098/rsfs.2014.0040
5. Pinckard K, Baskin KK, Stanford KI. Effects of exercise to improve cardiovascular health. Front Cardiovasc Med. 2019;6:69. Published 2019 Jun 4. doi:10.3389/fcvm.2019.00069
6. Liang H, Ward WF. PGC-1alpha: A key regulator of energy metabolism. Adv Physiol Educ. 2006;30(4):145-151. doi:10.1152/advan.00052.2006
7. Filley CM, Fields RD. White matter and cognition: making the connection. J Neurophysiol. 2016;116(5):2093-2104. doi:10.1152/jn.00221.2016
8. Toups MSP, Greer TL, Kurian BT, et al. Effects of serum brain derived neurotrophic factor on exercise augmentation treatment of depression. J Psychiatr Res. 2011;45(10):1301-1306. doi:10.1016/j.jpsychires.2011.05.002
9. National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP). Chronic diseases in America. Centers for Disease Control and Prevention. Last Updated December 13, 2022. Accessed August 13, 2023. https://www.cdc.gov/chronicdisease/resources/infographic/chronic-diseases.htm

Meet the 2023-2024 Team Members

Editorial Team & Production

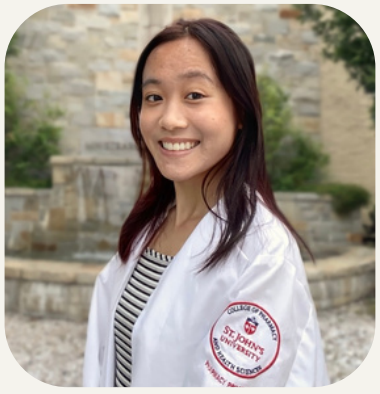


Isabelle Lim
Editor-in-Chief

The Rho Chi Post serves as a platform for students and faculty to collaborate in sharing their knowledge and ideas with the pharmacy community while offering a unique experience to develop writing skills outside of the classroom. As future pharmacists, it is important that we continuously keep ourselves updated as well as voice our opinions on healthcare matters. I am honored to be a part of the Editorial Team and look forward to serving as this year's Editor-in-Chief!

John Ortiz
Senior Content-Focused Copy Editor

Rho Chi Post is an opportunity for students to foster their writing and investigative skills concerning the pharmacy practice. Through Rho Chi Post, students are also exposed to novel information and perspectives that are present in the pharmacy community and in our own student body. By honing our understanding of new innovations and developments in pharmacy, we will be better adept at providing accurate information to readers and maintaining the continuous education expected of pharmacists.



Joanne Fung
Senior Content-Focused Copy Editor

To me, Rho Chi is a great opportunity for all pharmacy students to advance themselves. This society offers something to everyone, whether you are a member of the society, a part of the newsletter staff, or a student taking advantage of the resources offered by Rho Chi. The effort put forth by every person affiliated with Rho Chi is amazing, and I will always appreciate this society's mission and values.

MEET THE TEAM

Maliha Akter
Content-Focused Copy Editor

In my pursuit of becoming a knowledgeable and skilled pharmacist, I remain committed to staying informed about disease treatment and public-health policy. Being a part of Rho Chi Post provides an excellent platform for continuous education and knowledge-sharing with peers. Engaging with individuals from diverse backgrounds fosters critical viewpoints and discussions, all focused on enhancing patient-centered care. Additionally, the newsletter enables me to nurture my lifelong passion for writing while staying updated on the latest healthcare developments. As I embrace this transformative journey, I am dedicated to adapting, learning, and making a positive impact on patient well-being as a compassionate and competent pharmacist.

Bao Qi Chen
Content-Focused Copy Editor

The Rho Chi Post is a bridge between students and the world we will soon enter once we graduate. My ambition is to promote intellect, values, and opportunities that not only allow students to be heard but also impact the pharmacy profession as a whole. I am honored to be a part of the Rho Chi Post's editorial team and work with colleagues who share this ambition. I am excited and grateful for this opportunity, and I look forward to working with everyone!

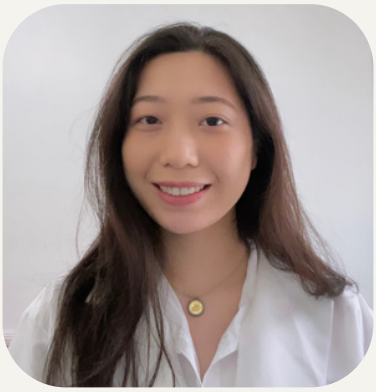
Warda Basher
Content-Focused Copy Editor

Joining this esteemed team excites me with the opportunity to gain invaluable experience and insights into the latest trends in pharmacy. I am eager to expand my professional network and make significant contributions to the field. As a member of the editorial team, I'll be at the forefront of disseminating the most current news and knowledge, effectively impacting pharmacy professionals worldwide with timely and relevant information.

Kristen Joy Mathew
Content-Focused Copy Editor

Being a part of the Rho Chi Post is a rewarding experience where I can work with other students and colleagues to bring forth educational and pertinent information in a renowned newsletter publication. This is a rewarding experience to express my passion for pharmacy and spread awareness of current issues. Collaborating with other students, faculty, alumni, and professionals, it is an incredible experience to continually learn from numerous perspectives and incorporate such experiences into a publication. Working as a Content-Focused Copy Editor, I am happy to be alongside this wonderful team in producing well-researched articles in a respected and widely read newsletter.

MEET THE TEAM



Mandy Zheng
Senior Graphics-Focused Copy Editor

The Rho Chi Post allows pharmacy students the opportunity to be well informed about the amazing contributions in the field of pharmacy. It is a great platform for students to report current advancements in healthcare. My passionate for writing began at a young age as I began to understand just how powerful words can be to communicate. I look forward to being a part of the editorial team and to share new information to my peers. I am so excited to be a part of the Rho Chi Post team.

Ruksabha Zaman
Senior Graphics-Focused Copy Editor

It is an honor to be able to contribute to the Rho Chi Post, a publication that promotes intellect, values, and inclusivity in order to allow student voices to make an impact not only in our school but in the pharmacy profession as a whole. The role of pharmacists is constantly evolving and it is more important than ever for us to not only be aware of the changes and new discoveries that are occurring in our field of practice but to be able to collaborate with other professionals on our team as well. The Rho Chi Post serves as a bridge between students, faculty, pharmacists, and other healthcare professionals outside of the classroom. I look forward to gaining new knowledge on current events from my peers and providing my own insight to further the excellence of this newsletter.

Celestine Van Sertima
Graphics-Focused Copy Editor

When applying to the Rho Chi Post, I was initially fascinated by their goals of providing the highest quality of information to the St. John's community through a student operated newsletter that cultivates both student spirit and expansion of knowledge. Through my passion for writing and health care, combined with my experience in graphic designing, I look forward to what I can contribute to the Rho Chi Post.

Nalisha Xu
Graphics-Focused Copy Editor

By becoming a part of the Rho Chi editorial team, I wish to learn more about the pharmacy field and community by gaining insight through our publications. This position will not only allow me to broaden my views on the profession of pharmacy, but also explore topics related to the medical field as a whole. Through Rho Chi's team, I will utilize this experience to grow professionally, develop leadership skills, and be more involved in our community to improve my confidence and professionalism on my journey to becoming a pharmacist.

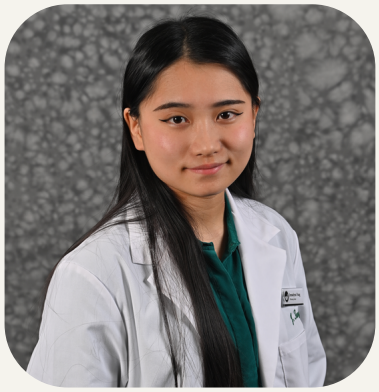
MEET THE TEAM

Zainab Masood
Graphics-Focused Copy Editor

Being part of Rho Chi Post, which provides information on discoveries and research to others, is an honor. Taking insight from professionals and peers to educate others is a rather significant effort in the expanding and evolving role of pharmacists. I look forward to collaborating with the team in pushing this effort further while also learning from them.

Sana Ahmed
Senior Staff Editor

I believe Rho Chi Post is a means to serve the university and impact its professional and health-oriented student community through its various stories. With exposure to a myriad of areas of the healthcare field throughout my work experience, I have secured much knowledge from assisting a diverse array of patients. I will prioritize staying up to date and aiding student writers in presenting the latest pharmaceutical and medical advancements. Through Rho Chi Post, I intend to promote the pharmacy profession through creativity and effective communication. I am honored to serve as a Staff Editor for this organization and hope it will facilitate meaningful connections with my peers.



Jennalynn Fung
Staff Editor

I am thrilled to have the opportunity to express my creativity, critical thinking, and research skills through contributing to the Rho Chi Post. The mission to promote intellectual discourse and showcase diverse perspectives aligns with my values; I look forward to putting my writing and editing experience to use in each issue, and hope that my involvement can ensure that future cohorts will also have this valuable platform available to them.

Paulina Maczko
Staff Editor

As pharmacy students, I believe we have an obligation of staying informed on current healthcare topics, topics that the Rho Chi Post sheds light on. To be part of such a team is an honor, as students are granted the opportunity of a creative outlet, whether that is by writing the articles or organizing the newsletter. As a copy editor, I look forward to seeing first-hand how students voice their opinions, thoughts, and academic learnings. I'm grateful to be part of a team that allows students to understand what they are capable of, and simultaneously advance their writing, comprehension, and communication skills.

MEET THE TEAM

Shakhzoda Rakhimova
Staff Editor

As a staff editor for the Rho Chi Post, I am thrilled to have the opportunity to be part of a team that is dedicated to providing high-quality and thought-provoking content that is relevant to pharmacists, healthcare professionals, and the broader public. I am excited to bring my skills and knowledge to the table as we work together to create meaningful and impactful content for our readers.

Natalia Turowska
Staff Editor

Joining the Rho Chi Post is an opportunity I am immensely grateful for! I am very excited to be a part of an award-winning publication that promotes the pharmacy profession through creativity and effective communication like the Rho Chi Post. In being a Staff Editor, I look forward to reading about ideas, opinions, and innovations, as well as seeing these topics blossom into articles for others to enjoy. I know that throughout holding this position, I will grow in terms of professionalism, teamwork, and creativity, which are all key attributes in the pharmacy world!

Sharupa Azmal
Staff Editor

The Rho Chi Post serves as a notable forum for pharmacy students who wish to expose themselves to medical journalism. Being a staff editor of the Rho Chi Post means amplifying the voices of our writers and educating our readers regarding current events in healthcare. This role provides me with the opportunity to present insightful stories that are relevant to the pharmacy community and contribute to the advancement of the profession through writing.

Nimra Gul
Staff Editor

My name is Nimra Gul and I am currently entering my 6th year of the pharmacy program at St. Johns. Being involved in a cause that serves to educate those pursuing a career in the healthcare field allows me to contribute to the knowledge that these very people will utilize in practice. I hope that my time with the Rho Chi Post Editorial Team will be memorable with much to contribute!

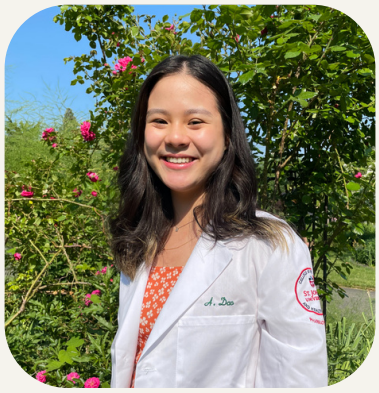
MEET THE TEAM

Nancy Yousry
Senior Staff Writer

It was such an amazing opportunity to become part of Rho Chi Post's Editorial Board last year, and I am really excited to continue being a part of Rho Chi Post this year! I believe one of our responsibilities as Student Pharmacists is to be aware of the current events impacting our profession as well as the critical and unique role Pharmacists play in a variety of healthcare settings. As a Staff Writer and Engagement & Outreach Manager, I look forward to bringing these current events to light and to serve as an educational resource for passionate readers and writers alike.

Ashley Dao
Senior Staff Writer

Rho Chi Post is an opportunity for students to be involved in publication regardless of their year or interest. I have always had an interest in writing and research, and I was afraid I would lose these skills in pharmacy school. Being part of Rho Chi Post has allowed me to continue writing and learning beyond the classroom!



Sairah Sheikh
Senior Staff Writer

Ever since I was little, writing has always been a passion of mine. As a senior staff writer for Rho Chi Post, I am excited to merge the knowledge I have gained in pharmacy school with my love for writing to create thought-provoking pieces for our community to read. Since pharmacy is an ever-evolving profession, it is important for our community to stay informed on the latest events in our field and I am looking forward to playing a part in that as a member of the incredible Rho Chi editorial team,

Urooj K. Malik
Staff Writer

The Rho Chi Post is a valuable platform that connects students and faculty with the most up-to-date information within the pharmacy profession. The field of pharmacy is constantly expanding with vital developments, so it is important for us to stay informed in the world of healthcare. The Rho Chi Post serves as a creative outlet for student pharmacists to voice their various perspectives and ideas for others to utilize as an educational resource. As a staff writer, I hope to channel my passions and interests through this newsletter in an effort to impact those around me.

MEET THE TEAM

John Ortiz
Staff Writer

Rho Chi Post is an opportunity for students to foster their writing and investigative skills concerning the pharmacy practice. Through Rho Chi Post, students are also exposed to novel information and perspectives that are present in the pharmacy community and in our own student body. By honing our understanding of new innovations and developments in pharmacy, we will be better adept at providing accurate information to readers and maintaining the continuous education expected of pharmacists.

Anureet Kaur
Staff Writer

Professional writing is a powerful tool. As pharmacists, amongst many other things, we can use our writing to advocate for our profession, to summarize new guidelines, and to spread the word about novel drugs. Thus, being a part of the Rho Chi Post 2023-2024 Editorial Team will help me strengthen the skills I need to be a capable pharmacist in the future. I am very excited to contribute to RCP!

Enjelique R. Adams
Staff Writer

Being a member of the Rho Chi Post will qualify and enable me to branch out to network and connect with others who are older than me and are a part of the Rho Chi Honor Society and others who are a U1, U2, or P1 who have an interest in writing. This opportunity that was blessed and given to me can expand my passion and love for writing to another level. Writing for this post can grant me the chance to learn more about my level of pharmacy through a different scope by reading about current events on insurance, Big Pharma, the FDA, and new medications coming out but also use the knowledge I have from my classes and working at an independent community pharmacy and apply it to my work. Rho Chi Post is an additional additive to the list of organizations and extracurriculars that I partake in; however, this is a new step to a new beginning for my P2 year that I cannot wait to take on.

Holly Nguyen
Staff Writer

Being a member of the Rho Chi Post will qualify and enable me to branch out to network and connect with others who are older than me and are a part of the Rho Chi Honor Society and others who are a U1, U2, or P1 who have an interest in writing. This opportunity that was blessed and given to me can expand my passion and love for writing to another level. Writing for this post can grant me the chance to learn more about my level of pharmacy through a different scope by reading about current events on insurance, Big Pharma, the FDA, and new medications coming out but also use the knowledge I have from my classes and working at an independent community pharmacy and apply it to my work. Rho Chi Post is an additional additive to the list of organizations and extracurriculars that I partake in; however, this is a new step to a new beginning for my P2 year that I cannot wait to take on.

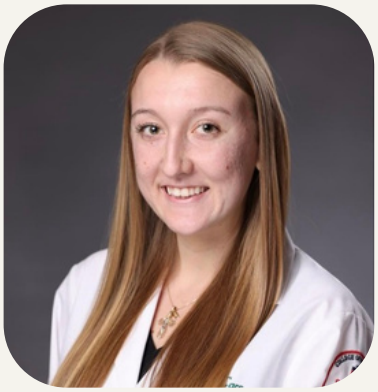
MEET THE TEAM

Bhojranie Brahmanand
Staff Writer

The Rho Chi Post uses its platform to spread knowledge of groundbreaking discoveries that are changing the standard of care for society. It delivers a creative and innovative scope of the pharmacy world. As a school of pharmacy, it is pivotal to become aware of healthcare matters. In turn, we can strengthen our understanding of the field and become more competent pharmacy practitioners. I am excited to be joining the team this year as a staff writer. I look forward to working alongside like-minded individuals in cultivating writing pieces that will share the importance of this profession.

Giavanna Carr
Staff Writer

Rho Chi is a society with members who all have the same goal, which is to excel in their academic careers. As a member of this society, we use our skills and knowledge in order to better our education as well as assist our peers in the process. Being part of this society has been so rewarding thus far, and I look forward to further developing Rho Chi in my time with the organization!



Sheena Nagpal
Staff Writer

As the world is constantly changing in the world of medicine, it can be difficult as a pharmacy student to keep up. The Rho Chi Post is a way for students, educators and practitioners to stay up to date with new developments, discoveries and research. Thus, I am excited to be joining the Post as a new Staff Writer and to be a voice in the community to integrate new ideas and innovations so that we may advance as future pharmacists!

Ariella Zadrima
Staff Writer

As a pharmacy student and future pharmacist, I believe it is a quintessential duty to educate ourselves on current media regarding the medical field and continuously adapt to the new ideas we may face as we enter the pharmacy profession. With topics from emerging diseases to scientific advances made, it is important to be accustomed to new ideas that pertain to our potential responsibilities as a pharmacist. As a Rho Chi Staff Writer, I hope to discuss matters that will inform not only pharmacy students but the St. John's community as a whole on topics that have to do with general health and scientific developments. With my interest in writing and the pharmacy field, I hope to touch upon subjects passionate to me that can benefit our community and inspire our readers to integrate themselves into the ever-growing profession of pharmacy.

MEET THE TEAM

Ashley Medina
Staff Writer

It is an honor to be welcomed as a new member of a prestigious team of students contributing to the pharmacy profession through its publications that reach an audience beyond our campus. The Rho Chi Post has provided students with an opportunity to express themselves creatively and fosters professionalism through impactful communication. Joining the team will allow me to give back through writing that will embody the ideas and ambition that house my passion for the pharmaceutical profession. I am looking forward to providing relevant and up-to-date information to my audience and am eager to operate with fellow students to provide high-quality content that is devoted to the advancement and encouragement of our student body.

Sandra Jojo
Staff Writer

Hi everyone, I am excited to join Rho Chi Post's team as a staff writer. As a P4 student who has read many of the articles published throughout my college career, I am motivated to write articles that inspire conversation among students. The Rho Chi Post gives students the freedom to research and learn about topics beyond the classroom setting. I am looking forward to conveying knowledge about new developments to other rising healthcare professionals in efforts to advance patient care.

MEET THE TEAM

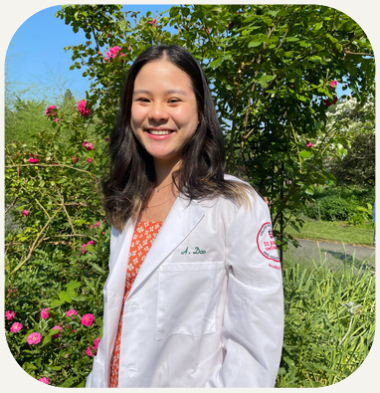
Social Media & Outreach

Anjali Thykattil
Engagement & Outreach Manager

I am beyond grateful for this opportunity, and I am excited to have the honor of serving on the Executive Board as the Engagement and Outreach Manager. The Rho Chi Post is not only a creative outlet for students, but also one that is invariably relevant to the ever-changing world of healthcare. In this position, I aim to further expand the growth of the Rho Chi Post among pharmacy students here at St. John's. Let's not forget, it is us students who will become the healthcare leaders of tomorrow.

Nancy Yousry
Engagement & Outreach Manager

It was such an amazing opportunity to become part of Rho Chi Post's Editorial Board last year, and I am really excited to continue being a part of Rho Chi Post this year! I believe one of our responsibilities as Student Pharmacists is to be aware of the current events impacting our profession as well as the critical and unique role Pharmacists play in a variety of healthcare settings. As a Staff Writer and Engagement & Outreach Manager, I look forward to bringing these current events to light and to serve as an educational resource for passionate readers and writers alike.



Ashley Dao
Engagement & Outreach Manager

Rho Chi Post is an opportunity for students to be involved in publication regardless of their year or interest. I have always had an interest in writing and research, and I was afraid I would lose these skills in pharmacy school. Being part of Rho Chi Post has allowed me to continue writing and learning beyond the classroom!

Advisors

Dr. Ketan Patel
MPharm, PhD

It is an honor to serve as a faculty advisor of Beta Delta Chapter of a 100-year-old prestigious society of pharmaceutical professionals – The Rho Chi Society. With great enthusiasm, I am committed to assist the Rho Chi member's endeavors in: (1) disseminating the latest information/technology in healthcare system; (2) promoting pharmaceutical field & career propulsive networking of current students, alumni, and faculties; and (3) facilitating the scholastic activities and recognizing the scholars.

Dr. Joseph Etzel
BS Pharm, PharmD

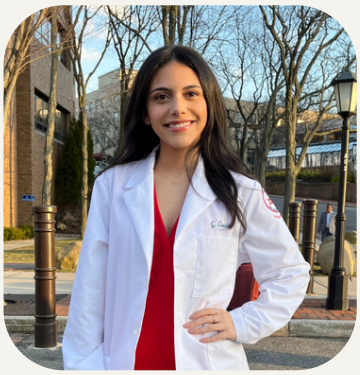
Dr. Etzel served as the Rho Chi Post's interim faculty advisor for the 2022-2023 academic school year and continues to aid the Rho Chi Honor Society as we welcome in our new advisor. Dr. Etzel is not new to our organization, as he has previously served as the faculty advisor for the Rho Chi Honor Society. He has been a huge influence to the success of Rho Chi in the past, and we look forward to continue working with him!

Dr. Mohammad Rattu
PharmD, BCOP, BCPS, BCGP

I am thankful to have been the 2012 editor-in-chief of the Rho ChiPost newsletter, as well as on the 2019 alumni honor roll of the national Rho Chi organization. This is one of the most successful longitudinal projects at my alma mater, as evidenced by its decade-long persistence and teams of highly-motivated students. I remain available for professional support and assistance with the new year's initiatives.

The Rho Chi Society

Executive Board



Geraldine Ciaccio
President

The Rho Chi Society prides itself on fostering intellectual achievement and cultivating professional development. It provides opportunities for students, faculty, alumni, and colleagues to expand their knowledge of pharmacy practice. Through events, seminars, and fundraisers, Rho Chi allows pharmacy students to develop leadership skills that are vital to the profession. I have learned valuable lessons about pharmacy and myself from Rho Chi thus far, and I am honored to be able to give back to the organization. I am humbled to hold such a position and work with a dedicated executive board.

Javeria Amir
Vice President

The Rho Chi Society is an organization that contributes to the development of intellectual leaders in pharmacy. Through this, Rho Chi Society fosters collaboration and initiatives to advance learning in the field of pharmacy. Being part of this organization has allowed me to reach out for help when needed, and continuously improve my skills as a future pharmacist. To be a part of the executive board that will continue to uphold these initiatives is an honor and responsibility I take on with pride. Wishing all a wonderful and successful academic year ahead of us!

Anjali Rana
Secretary

Being a part of Rho Chi has provided me with invaluable opportunities for professional development, connection, and mentorship. The society's commitment to academic excellence and ethical pharmacy practice has inspired me to strive for continuous improvement in my studies and future career. Serving on this year's executive board, provides a sense of belonging among a supportive and inclusive community.

Giavanna Carr
Treasurer

The Rho Chi Honor Society encourages and recognizes intellectual achievements, stimulates critical inquiry in order to advance the future of pharmacy, provides its members with the ability to develop into intellectual leaders, promotes high ethical standards for its members, and fosters collaboration. Through being a member of Rho Chi, we are able not only to grow ourselves, but to help uplift our colleagues and allow them the chance to excel academically through the events we provide. Rho Chi has been a great influence on my studies during my time in this program and being given the opportunity to serve on the executive board allows me to become the influence for the younger students in our program. I'm inspired by every member of this years executive board and can't wait to see all we're able to accomplish together this year!

The Rho Chi Society

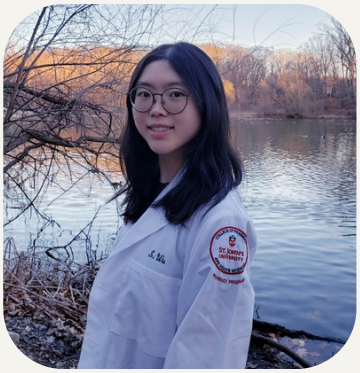
Executive Board

Christine Mauceri
Historian

Rho Chi is an amazing organization that encourages leadership and support among its members. Not only does it offer a space where all pharmacy students can help each other academically, but the opportunities for networking and professional growth are endless. I am proud to be a part of an organization that has helped me immensely throughout my studies, and I am excited to give back to my pharmacy community!

Sammi Wu
Development and Outreach Coordinator

The Rho Chi Society is committed to the development of future pharmacists that excel in both areas of professional expertise and acts of service. It forms a community for pharmacy students to motivate each other's academic growth and provide support within a challenging degree program. It also keeps students informed on news related to breakthroughs in drug therapy and patient care. I am honored to accept my position on the executive board for this upcoming academic year and I hope to fulfill my duties so Rho Chi can continue to have its positive impact on the pharmacy profession!



Daya Biju
Academic Committee Chair

The Rho Chi Honor Society is a distinguished academic organization that recognizes excellence in pharmaceutical studies. It promotes ethical conduct, leadership, and research in pharmacy education. With chapters across the United States, Rho Chi fosters a sense of community and offers valuable networking and mentorship opportunities. Members actively engage in service projects to improve public health awareness. I am truly honored to serve this esteemed organization and embrace the opportunities it offers for personal and professional growth.

Angel Gao
Academic Committee Chair

Rho Chi fosters a community where students can collaborate with each other, upholding the core principles of service and professional development. Being a part of this supportive community is an honor, and I take pride in contributing to the culture of excellence that Rho Chi cultivates.

RHO PX CHI post

St. John's University College of Pharmacy & Health Sciences

OCTOBER

SUN	MON	TUE	WED	THU	FRI	SAT
1	2	3	4	5	6	7
8	**9**	**10**	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

NOVEMBER

SUN	MON	TUE	WED	THU	FRI	SAT
			1	2	3	4
5	6	7	**8**	9	**10**	**11**
12	13	14	15	16	17	18
19	20	21	**22**	**23**	**24**	**25**
26	27	28	29	30		

Oct 9: Fall Mini Break - University closed/No classes
Oct 10: Monday classes meet
Nov 8: Friday classes meet
Nov 10: Veterans Day observed - University closed/No classes
Nov 11: Veterans Day - University closed/No classes
Nov 22: Thanksgiving Recess - No classes
Nov 23-25: Thanksgiving Recess - University closed/No classes

The Rho Chi Post wants to wish everyone luck on tests and midterms!

Interested in writing for the Rho Chi Post?

Go to http://rhochistj.org/RhoChiPost and click on the login option from the menu bar to make an account! With an account, you'll have access to the article submission portal where you can submit your writing for publication in an upcoming issue!

Remember, you do NOT have to be a member of Rho Chi, a member of the editorial team, or a student of St. John's to write for our newsletter!

If you have any questions, feel free to email us at rhochipost@gmail.com!