BRAC UNIVERSITY School of Pharmacy

PHARMA HIGHLIGHTS

ISSUE 101 | February 2023

Leadership Lessons: A Pharmaceutical Marketer's Perspective

Leadership skills are essential for any successful business or organization. They enable teams to work more efficiently and effectively, achieve goals, and maintain a positive workplace culture. Strong leadership is extremely important in pharmaceuticals as the sector requires good judgment and clarity of direction because it is an industry where professionals have a direct impact on people's lives.

As part of our **'Toolbox for Success'** series designed by the School of Pharmacy, Brac University, a seminar on "Leadership Lessons: A Pharmaceutical Marketer's Perspective" was organized on February 13, 2023, to provide the students with insight into the leadership skills required to succeed in the field of pharmaceutical marketing.

The distinguished speakers of the seminar were Dr. Jamil and Mr. Sikder who shared their experiences and a few leadership lessons that motivated or inspired the audience on their own journey. Dr. M. Jamil is a commercial leader in the pharmaceutical industry with two decades of strategic and operational experience in matrix organizations across geographies, Dr. Jamil has extensively worked with clinical development teams to commercialize breakthrough therapeutics including the first small molecule targeted therapy and the first aPD-1 immunotherapy. Dr. Jamil is currently working at Merck & Co. and responsible for commercialization of oncology pipeline assets. He is also an adjunct Professor at Columbia Business School in New York. Previously Dr. Jamil worked in marketing and commercial roles of increasing responsibility at Bayer, Eli Lilly and Novartis in US, Europe, Middle East and Emerging Markets to launch multiple products in numerous therapeutic areas. Dr. Jamil got his Ph.D. in Marketing from Kelley School of Business, Indiana University. Hafiz Sikder is the CEO and founder of Axiom Healthcare Strategies, a think-tank style consulting firm with a core focus in Oncology & Rare Disease. Axiom HCS seeks to challenge management's internal axioms to pressure-test and eliminate competitive blind spots. Mr. Sikder has also founded the Axiom REACH Foundation, a 501(c)3 cancer nonprofit organization. REACH speaks to his internal ethos of giving back, putting the community first, and fighting for those without a voice. The Foundation has supported hundreds of patients with rent, groceries, utilities, and more over the past two years as well as supported a cohort of future caregivers at Rutgers University. In addition, Mr. Sikder serves as a board member on the American Cancer Society's CEOs Against Cancer, Metro New York Chapter. Previously, Mr. Sikder held several marketing and competitive intelligence roles, at Bristol-Myers Squibb, Quest Diagnostics, and Sanofi-Aventis. He received his MBA from the Thunderbird School of Management and attended Louisiana State University.

Their discussion explored the fundamentals of entrepreneurship - identifying new opportunities, and strategies for success. They also talked about the obstacles to entrepreneurship including access to capital, ability to take risks, and optimizing resources. Furthermore, they provided insight into ways of developing a business-oriented mentality and illustrated its potential to bring about beneficial changes in our community.

The seminar was moderated by Ms. Farzana Islam, Lecturer, School of Pharmacy, Brac University. Faculty members, Teaching Assistants and students of the School of Pharmacy attended the seminar.

Written by: School of Pharmacy

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On-demand Male Contraceptives

An experimental contraceptive drug developed by Weill Cornell Medicine investigators temporarily stops sperm in their tracks and prevents pregnancies in preclinical models. The study, published in *Nature Communications* on Feb. 14, demonstrates that an on-demand male contraceptive is possible.The discovery could be a "game-changer" for contraception, according to the study's co-senior authors Dr. Jochen Buck and Dr. Lonny Levin, who are professors of pharmacology at Weill Cornell Medicine.

Drs. Buck and Levin noted that condoms, which have existed for about 2000 years, and vasectomies have been men's only options to date. Research on male oral contraceptives has stalled, partly because potential contraceptives for men must clear a much higher bar for safety and side effects. Because men do not bear the risks associated with carrying a pregnancy, the field assumes men will have a low tolerance for potential contraceptive side effects. The team discovered that mice genetically engineered to lack sAC are infertile. Then in 2018, Dr. Melanie Balbach, a postdoctoral associate in their lab, made an exciting discovery while working on sAC inhibitors as a possible treatment for an eye condition. She found that mice that were given a drug that inactivates sAC produce sperm that cannot propel themselves forward. The team was reassured that sAC inhibition might be a safe contraceptive option by another team's report that men who lacked the gene encoding sAC were infertile but otherwise healthy.

Soluble adenylyl cyclase (sAC: ADCY10) is an enzyme involved in intracellular signaling. Inhibition of sAC has potential therapeutic utility in a number of areas. For example, sAC is integral to successful male fertility: sAC activation is required for sperm motility and ability to undergo the acrosome reaction, two processes central to oocyte fertilization. Pharmacologic evaluation of existing sAC inhibitors for utility as on-demand, nonhormonal male contraceptives suggested that both high intrinsic potency, fast on and slow dissociation rates are essential design elements for successful male contraceptive applications.

In particular, recent work has increased interest in the use of sAC as a drug target for contraception. Safe, effective new contraceptive strategies for males, particularly nonhormonal methods, represent a profound unmet medical need as globally, approximately half of all pregnancies are unplanned.

The new Nature Communications study demonstrate that a single dose of a sAC inhibitor called TDI-11861 immobilizes mice sperm for up to two and half hours and that the effects persist in the female reproductive tract after mating. After three hours, some sperm begin regaining motility; by 24 hours, nearly all sperm have recovered normal movement.

TDI-11861-treated male mice paired with female mice exhibited normal mating behavior but did not impregnate females despite 52 different mating attempts. Male mice treated with an inactive control substance, by contrast, impregnated almost one-third of their mates. It takes weeks to reverse the effects of other hormonal and nonhormonal male contraceptives in development. sAC inhibitors wear off within hours, and men would take it only when, and as often, as needed, they could allow men to make day-to-day decisions about their fertility.

The team is already working on making sAC inhibitors better suited for use in humans. The next step for the team is repeating their experiments in a different preclinical model. These experiments would lay the groundwork for human clinical trials that would test the effect of sAC inhibition on sperm motility in healthy human males, Dr. Buck said. If the drug development and clinical trials are successful, Dr. Levin said he hopes to walk into a pharmacy one day and hear a man request "the male pill."

Reference:

1. Balbach, M., Rossetti, T., Ferreira, J. et al. On-demand male contraception via acute inhibition of soluble adenylyl cyclase. Nat Commun, 2023 DOI: 10.1038/s41467-023-36119-6
2. Miller, M., Rossetti, T., Ferreira, J., Ghanem, L., Balbach, M., Kaur, N., Levin, L. R., Buck, J., Kehr, M., Coquille, S., van den Heuvel, J., Steegborn, C., Fushimi, M., Finkin-Groner, E., Myers, R. W., Kargman, S., Liverton, N. J., Huggins, D. J., & Meinke, P. T. (2022, November 8). Design, Synthesis, and Pharmacological Evaluation of Second-Generation Soluble Adenylyl Cyclase (sAC, ADCY10) Inhibitors with Slow Dissociation Rates. Journal of Medicinal Chemistry, 65(22), 15208–15226. https://doi.org/10.1021/acs.jmedchem.2c01133

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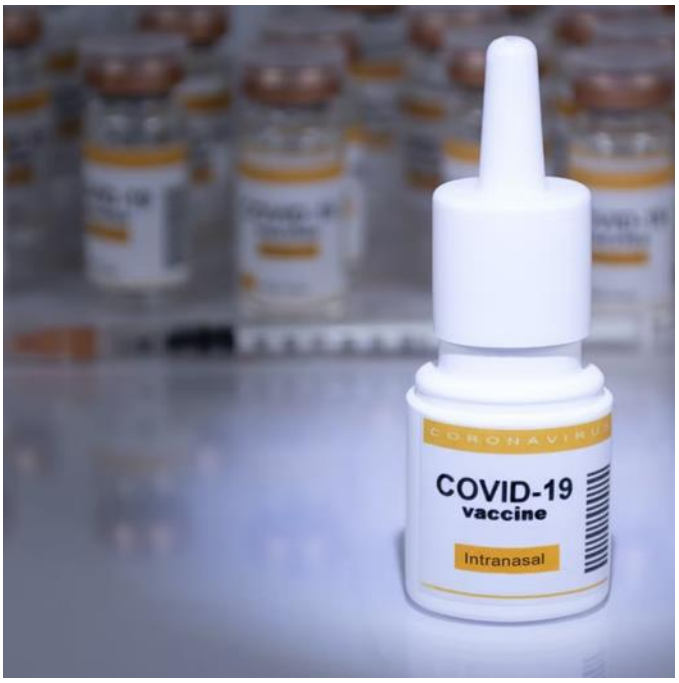
COVID-19 Nasal Vaccine



As the COVID-19 pandemic continues to ravage the world, scientists and researchers are working hard to develop vaccines to protect against the virus. One new approach to vaccine development is the Covid-19 nasal vaccine, which is currently being tested in clinical trials around the world.

Unlike traditional vaccines that are administered via injection, the COVID-19 nasal vaccine is delivered through the nose. The vaccine contains weakened or inactivated virus particles, or fragments of the virus's genetic material, that are delivered directly to the mucous membranes in the nose. This method is thought to be particularly effective since the nasal cavity is one of the primary entry points for the virus into the body.

One of the biggest advantages of the COVID-19 nasal vaccine is that it can be administered without the assistance of a healthcare professional. This makes it easier to distribute the vaccine to large populations, particularly in areas where healthcare resources are limited. Furthermore, the nasal vaccine may also provide a more effective immune response than traditional injectable vaccines since it targets the immune cells lining the nasal cavity, which are the body's first line of defense against respiratory infections.

Several companies and research institutions around the world are currently developing COVID-19 nasal vaccines, and early clinical trials have shown encouraging results. In one recent study conducted in India, the Covid-19 nasal vaccine developed by Bharat Biotech was deemed safe and effective in generating an immune response against the virus. Similarly, the University of Alabama at Birmingham's nasal vaccine is also showing promising results in preclinical studies.

However, some concerns have been raised regarding the effectiveness of the Covid-19 nasal vaccine. One issue is that the vaccine may not provide long-lasting immunity against the virus since the mucous membranes in the nose are continually exposed to new pathogens. Additionally, there are concerns about potential side effects, particularly in people with underlying health conditions.

Despite these worries, the COVID-19 nasal vaccine represents a promising development in the fight against the pandemic. The vaccine's ease of administration and ability to target the body's first line of defense against respiratory infections make it a viable option for preventing the spread of the virus, particularly in environments like schools and workplaces where respiratory infections are common.

In conclusion, the COVID-19 nasal vaccine is an innovative approach to vaccine development that has shown positive early results. While concerns remain about its effectiveness and safety, it represents a critical step in the ongoing fight against the pandemic. As scientists and researchers continue to search for effective vaccines and treatments, the COVID-19 nasal vaccine is one of the many promising solutions that offer hope in the fight against this deadly virus.

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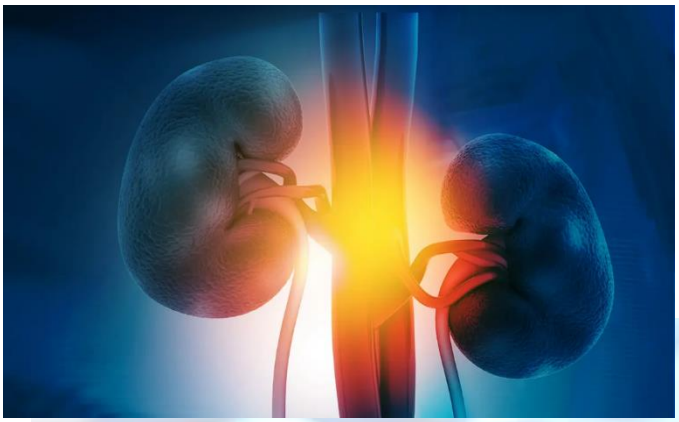
Nivolumab in Combination with Cabozantinib shows Potential for Renal Cell Carcinoma Treatment



The combination of nivolumab (Opdivo) plus cabozantinib (Cabometyx) demonstrated sustained response rate and survival benefits compared with sunitinib in the first-line treatment of advanced renal cell carcinoma (RCC), according to 3-year follow-up data from the phase 2 CheckMate -9ER trial.

Additionally, a biomarker analysis showed improvements in median progression-free survival (PFS) and overall survival (OS) were sustained with the combination, regardless of the individual's programmed death-ligand 1 status. Investigators found that treatment with the combination continued to show a 30% reduction in the risk of death, as well as an improvement of median OS at 49.5 months for the combination and 35.5 for sunitinib. Further, the median OS improved by 11.8 months since the previous data cut at the 32.9 months median follow-up. PFS benefits were also sustained, continuing to double at 16.6 months compared with 8.4 months, respectively. Duration of response (DoR) and objective response rate (ORR) benefits were also maintained. Investigators reported that nearly twice as many individuals responded to the combination with sunitinib at 55.7% compared with 28.4%, respectively, for ORR. The median DoR was 23.1 months compared with 15.2 months, respectively. Complete response (CR) rates were also sustained, with 12.4% of individuals treated with the combination having CR compared with just 5.2% on sunitinib.

Furthermore, approximately 97% of individuals treated with the combination experienced a treatment-related adverse event (TRAE) of any grade compared with approximately 93% of individuals with sunitinib. Approximately 67% and 55% had a grade 3 or greater TRAEs, respectively. The updated results were featured in 1 oral and 1 poster presentation at the American Society of Clinical Oncology 2023 Genitourinary Cancers Symposium (ASCO GU) between February 16 and 18, 2023.

With 44 months median follow-up, the compelling survival benefit further reinforces the value of the cabozantinib and nivolumab combination regimen as a first-line option for patients with advanced kidney cancer.

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1. Opdivo (nivolumab) in combination with Cabometyx (cabozantinib) shows durable survival with over three years of follow-up in the CheckMate -9ER trial in first-line advanced renal cell carcinoma. Bristol Myer Squibb. News release. February 14, 2023. Accessed February 22, 2023. https://news.bms.com/news/details/2023/Opdivo-nivolumab-in-Combination-with-CABOMETYX-cabozantinib-Shows-Durable-Survival-with-Over-Three-Years-of-Follow-Up-in-the-CheckMate--9ER-Trial-in-First-Line-Advanced-Renal-Cell-Carcinoma/default.aspx