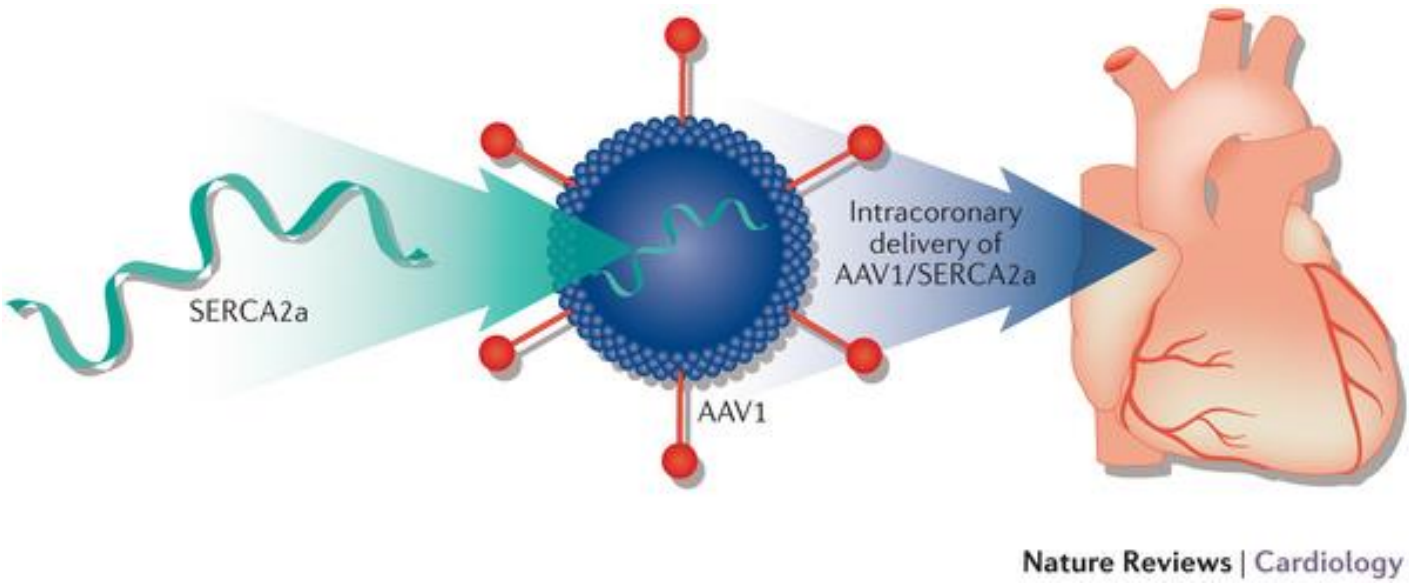
BRAC UNIVERSITY School of Pharmacy

PHARMA HIGHLIGHTS

ISSUE 100 | January 2022

Gene Therapy for Heart Failure



Heart failure is a condition where the heart is incapable of supplying sufficient blood flow to fulfill metabolic requirements for systemic venous return (Kemp & Conte, 2012). From 2010 to 2030, there will be a 25% increase in prevalence and 21% increase in direct medical costs associated with HF (Heidenreich et al., 2011). In order to treat heart failure, it is urgently necessary to investigate novel therapeutic modalities, and gene therapy has become a promising substitute. Cardiac gene therapy holds significant promise in heart failure treatment for patients with currently very limited or no treatment options.

The introduction of adeno-associated virus (AAV) gene vector changed the paradigm of cardiac gene therapy, and now it is the primary vector of choice for chronic heart failure gene therapy in clinical and preclinical studies. One main target for intervention in HF is the modulation of Ca^{2+} handling in cardiomyocytes, since this is pivotal in ensuring normal cardiac function.

Recently, there has been significant progress towards clinical translation in this field spearheaded by AAV-1 mediated sarcoplasmic reticulum Ca^{2+} ATPase gene therapy targeting chronic advanced heart failure patients. The first clinical trial was based on restoration of sarcoplasmic Ca^{2+} ATPase levels which is downregulated in failing hearts and the result was improved heart function. Based on this study, the CUPID trial was the first clinical attempt to use AAV gene therapy to treat HF enrolling 39 patients with symptomatic HF and the result showed reduction in HF hospitalization and significant improvement in both symptoms and functional parameters.

The efficacy of AAV1.SERCA2a in patients is being evaluated (Fish & Ishikawa, 2015). Current research focuses on gene repair, in order to treat hereditary forms of HF, in vivo. Other trials are still ongoing, effective viral vectors are being invented and encouraging novel potential targets are being identified. In future, cardiac gene therapy might be proved as an available and economical treatment option for HF patient (Gabisonia & Recchia, 2018).

References:

Kemp, C. D., & Conte, J. v. (2012). The pathophysiology of heart failure. In Cardiovascular Pathology (Vol. 21, Issue 5, pp. 365–371). https://doi.org/10.1016/j.carpath.2011.11.007

Heidenreich PA, Trogdon JG, Khavjou OA, Butler J, Dracup K, Ezekowitz MD, Finkelstein EA, Hong Y, Johnston SC, Khera A, Lloyd-Jones DM, Nelson SA, Nichol G, Orenstein D, Wilson PW, Woo YJ. Forecasting the future of cardiovascular disease in the United States: a policy
statement from the American Heart Association. Circulation 123(8):933-944, 2011.

Fish, K. M., & Ishikawa, K. (2015). Advances in gene therapy for heart failure. Discovery medicine, 19(105), 285–291.

Gabisonia, K., & Recchia, F. A. (2018). Gene Therapy for Heart Failure: New Perspectives. In Current Heart Failure Reports (Vol. 15, Issue 6, pp. 340–349). Current Science Inc. https://doi.org/10.1007/s11897-018-0410-z

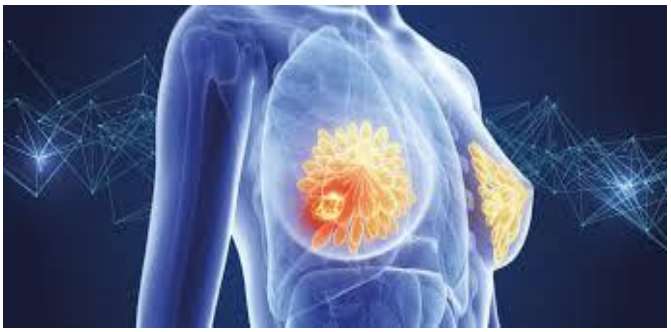
Written by: Puja Biswas (ID: 19146091)

BRAC UNIVERSITY School of Pharmacy

PHARMA HIGHLIGHTS

ISSUE 100 | July 2022

Cancer of the Breast



Cancer of the breast is the most prevalent cancer found among women with a total of 1 in 10 new cancers diagnosed annually. Cancer of the breast is the most popular kind of cancer that result in death among women globally. The progression is always unnoticed. The structure of the breast is that it has a gland that produces milk in front of the chest wall. They are located on the pectoralis major muscle supported by the ligaments which hold the breast against the chest wall. The breast is formed by the circularly arranged fifteen to twenty lobes, and the fat covering the lobes gives the shape and size of the breast.

In addition, each of the lobes is made up of lobules which contain the glands that are obliged to produce milk when stimulated by hormones such as prolactin. Most times women with breast cancer do not notice it until the time of their pregnancy routine screening. Though, some might be discovered accidentally through the observance of the breast lump, the shape and size changes, or due to the discharges from the nipple. However, mastalgia is still common. Physical examination and imaging, such as mammography and tissue biopsy are carried out in order to diagnose breast cancer. The tumor begins to spread lymphatically and hematologically which lead to lengthy metastasis.The Etiology of breast cancer can arise from the following factors:

Age: The age factor is of greater ratio in the population of females.

Gender: Breast cancer is common among women.

Personal history of breast cancer.

Histologic risk factors: The abnormalities of the histologic that are diagnosed by breast biopsy can be another form of breast cancer risk factor. Lobular carcinoma in situ (LCIS) and proliferative changes with atypia are part of these abnormalities.

Family history of breast cancer and genetic risk factors: Five percent to ten percent of all breast cancer cases are a result of genetic factors. However, it can be accounted for 25% of cases in women younger than thirty years. The susceptibility of breast cancer is increased by the effect of BRCA1 and BRCA2 genes.

Reproductive risk factors: Estrogen exposure increases the risk of breast cancer. This includes the beginning of menarche, first live childbirth after 30 years, menopause, and nulliparity.

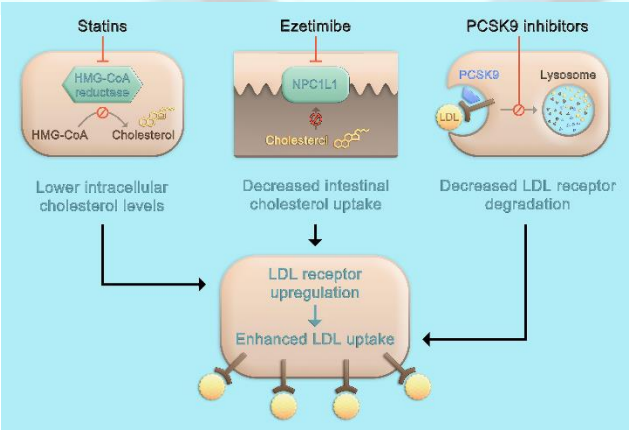
Exogenous hormone use: The intake of supplemental and therapeutic estrogen and progesterone are taken for different reasons. The most common practice is the use of contraceptives in premenopausal women and the use of replacement therapy in postmenopausal women.

Reference

Alkabban, Fadi M., Troy Ferguson. “Breast Cancer - Statpearls - NCBI Bookshelf.” National Library of Medicine, https://www.ncbi.nlm.nih.gov/books/NBK482286/.

Written by: Owowo Wisdom Chikaodir (ID: 22146104)

PCSK9 inhibitors: New Cholesterol-lowering Medicine



According to WHO, the biggest cause of death worldwide CVDs claim 17.9 million lives annually. Globally, CVD was estimated to be responsible for 19.1 million deaths in 2020 according to American heart association. The percentage of LDL reduction is not enough only with statins so, new class of drug named proprotein convertase subtilisin/kexin type 9 added a new dimension to combat this problem. It is an enzyme that is produced in humans by the PCSK9 gene on chromosome 1. It is the ninth member of the family of proteins called proprotein convertases that trigger additional proteins. Studies have shown that naturally high PCSK9, are linked to high levels of cholesterol. Alirocumab, evolocumab, and

inclisiran are three FDA approved monoclonal antibodies that suppress PCSK9 activity. Alirocumab, evolocumab treatment was linked with a larger decline in LDL-C, according to a network meta-analysis of clinical trials.
Combination of Ezetimibe and statin decreases LDL-C up to 15-20%, while PCSK9I with statin decrease LDL-C up to 54-74%. Evolocumab alone decreases 14-20% more LDL-C compared with Alirocumab. MACE reduced LDL-C less than 70mg/dl.
According to the results of the clinical studies FOURIER and ODYSSEY OUTCOMES, Evolocumab or alirocumab coupled to statin therapy in patients with CVD confers additional CV benefit above that achieved by statin alone. In the FOURIER trial, participants were monitored for 2.2 years while receiving either evolocumab or a matching placebo. 27, 564 patients with steady atherosclerotic disease on statin therapy were included in the study. The primary difference between the FOURIER and ODYSSEY Outcomes studies was that the latter revealed a statistically significant decrease in all-cause mortality, which the researchers cautiously interpreted as a nominally meaningful outcome. In both studies, the relative risk decrease was 15%. Contrary to predictions, PCSK9i are not as widely utilized as may be expected mostly because of their high price and obstacles posed by regulatory health authorities.

Written by: Anikah Lubaba (ID: 19146073)

What is known and what should be done in Covid BF.7 subvariant

One of the worrisome sub-variants of Omicron that is responsible for the present deadly Covid-19 pandemic outbreak in China is the BF.7. Compared to the original Omicron, the BF.7 sub-variant is two to three times more contagious. This variation has been classified as a "Variant of Concern" by the World Health Organization. This indicates that BF.7 has to be carefully watched, and new regulating mechanisms should be implemented if necessary. The BF.7 variation was first discovered in Europe in August, when infection was on the decline in those nations, before being discovered in China. There is no widespread immunity against Covid among the sizable population of the nation. But lately, when China's zero-Covid regulation was eased, the BF.7 sub-variant caused the infection to spread quickly over the mainland. On the other hand, Omicron infection is common in most of the world's countries, including Bangladesh, which has led to broad protection against this form. Therefore, it is anticipated that there will be minimal probability of a catastrophic catastrophe even if the BF.7 sub-variant penetrates Bangladesh. Observations show that BF.7 is less virulent but more infectious than other sub-variants of Omicron. A substantially decreased incidence of hospitalization and severe COVID is associated with BF.7 infection. However, those over the age of sixty who also have diabetes, renal illness, high blood pressure, or other concomitant conditions may also experience severe BF.7 infection. Current Covid vaccines have been created targeting the original Wuhan variety and are indicated for use in individuals who have received two doses of the Covid vaccination or have previously been afflicted with the illness. Variants of Omicron have undergone several alterations. The inability of vaccine-induced immunity to stop Omicron infection stems from this. However, the human immune system is able to combat any coronavirus types because of the adaptive immunity that is built up in the body through vaccination or natural infection. As a consequence, when vaccinated individuals become ill, they have very minor symptoms and recover within 5-7 days. Therefore, receiving at least two vaccination injections is highly recommended for everyone. We now understand that it is very hard to halt the international spread of Covid variations. However, by implementing appropriate control mechanisms, its spread can be slowed down. No significant action is required to prevent the arrival of the BF.7 because it is not a fatal variation. Lastly, we have to maintain proper hygiene and wear masks to stay safe.

Reference:
https://www.thedailystar.net/health/disease/coronavirus/news/covid-bf7-subvariant-what-we-know-and-what-do-3210846