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Subcutaneous Semaglutide Reduces Heart Failure-related Symptoms in Obese Patients Having Heart Failure with Preserved Ejection Fraction

Date: September 21, 2023

Heart failure with preserved ejection fraction (HFpEF) is clinically defined as heart failure with a left ventricular ejection fraction larger than 50%. There are currently no standardized treatment regimens for obese patients with HFpEF. Semaglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist, is indicated as an adjunct for chronic weight management. Evidence showing favourable effects in cardiometabolic risk factors using subcutaneous semaglutide was also documented, which underlies its potential benefits on cardiovascular health.

The randomized, double-blind, placebo-controlled STEP-HfpEF trial recruited 529 HfpEF patients with a body-mass index (BMI) larger or equal to 30 across 13 countries. Participants were randomly assigned in a 1:1 ratio to receive either once-weekly subcutaneous semaglutide 2.4 mg (n=263) or placebo (n=266) for 52 weeks. Semaglutide in the treatment group was first initiated at a dose of 0.25 mg and further titrated to the maintenance dose (2.4 mg) by week 16. Dual primary endpoints are the change in the Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS) and the percentage change in body weight over the treatment period. Confirmatory secondary endpoints including changes in the 6-minute walk distance and the hierarchical composite endpoints were also analyzed.

A significant increase in KCCQ-CSS by 16.6 points was observed in the semaglutide group compared with the placebo group at week 52 (estimated difference = 7.8 points; 95% confidence interval [CI], 4.8 - 10.9; P<0.001). Participants receiving weekly semaglutide injection were also found to have a mean body weight reduction of -13.3% while the mean body weight change was 2.6% in the placebo group (estimated difference = -10.7 percentage points; 95% confidence interval [CI], -11.9 - -9.4; P<0.001). Assessments on the confirmatory secondary endpoints also demonstrated the efficacy of subcutaneous semaglutide on exercise function in obese HFpEF patients. Fewer serious adverse events were reported in the semaglutide group (13.3%) than in the placebo group (26.7%).

To summarize, once weekly subcutaneous semaglutide at a dose of 2.4 mg is effective to alleviate heart failure-related symptoms and promote weight loss in obese HFpEF patients.

Source: www.nejm.org

"1+" Mechanism for Hong Kong New Drug Registration Comes Effective on November 1, 2023

Date: October 26, 2023

According to the Pharmacy and Poisons Ordinance (Cap. 138) and existing guidelines, pharmaceutical products containing new chemical or biological entities (NCE) must satisfy the safety, efficacy, and quality criteria for registration before being sold or supplied in Hong Kong. Additional documentary proof with official registration approvals in at least 2 or more reference countries is also required to expedite the evaluation process by the Drug Office of the Department of Health.

The "1+" mechanism was proposed in "The Chief Executive's 2023 Policy Address" in October 2023. Under the new scheme, pharmaceutical products containing NCEs for life-threatening or severely debilitating diseases supported by local clinical data will be allowed to register conditionally in Hong Kong by the submission of one registration approval from any of the reference drug regulatory authorities. Applications submitted under this new arrangement will be evaluated on a case-by-case basis, provided that the pharmaceutical product intended for registration has a local unmet medical need.

The establishment of the "1+" mechanism starting from November 1st, 2023, is expected to allow Hong Kong to be more proactive in facilitating new drug approval so that patients can gain early access to drugs in long run.

Source: www.drugoffice.gov.hk

Osimertinib-Chemotherapy Regimen Prolongs Progression-Free Survival in Patients with EGFR-Mutated Advanced Non-Small Cell Lung Cancer

Date: November 8, 2023

Patients with advanced non-small cell lung cancer (NSCLC) are often genetically tested for the presence of molecular derangements before choosing their subsequent treatment plans. Osimertinib is a third-generation epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) that has been widely used as the first-line treatment against metastatic NSCLC carrying EGFR exon 19 deletion, T790M or L858R mutations. Other chemotherapeutic options are considered only when disease progression is observed during EGFR-targeted therapy.

In this phase 3, international and open-label FLAURA2 trial, 557 patients with locally advanced or metastatic non-squamous NSCLC are randomized in a 1:1 ratio to receive oral osimertinib 80 mg once daily plus pemetrexed and a platinum-based agent intravenously (n=279) or oral osimertinib 80 mg once daily only (n=278). The osimertinib-chemotherapy group was given the chemotherapy on day 1 of the 21-day cycle for 4 cycles, followed by pemetrexed maintenance therapy every 3 weeks despite daily osimertinib intake. Tumor assessments were conducted in week 6, 12 and then every 12 weeks from randomization until disease progression. The primary endpoint was investigator-assessed progression-free survival, whereas the objective response and medication safety were also investigated.

The osimertinib-chemotherapy group was observed to have a significantly longer overall investigator-assessed progression-free survival than the osimertinib monotherapy group (hazard ratio=0.62; 95% confidence interval [CI], 0.49-0.79; P<0.001). Consistent results were also applicable when participants were classified into different subgroups according to their sex, race, type of EGFR mutation and the presence of central nervous system metastases. Reports of grade 3 or higher adverse events from any cause in the osimertinib-chemotherapy group (64%) were more notable than the osimertinib group (27%), yet these can be explained by the established profiles of individual chemotherapy agents used in the study.

The concurrent use of osimertinib and chemotherapy significantly improves progression-free survival in patients with EGFR-mutated advanced NSCLC, especially for patient groups with poor prognosis.

Source: www.nejm.org

Apixaban Reduces Stroke Risk in Subclinical Atrial Fibrillation Patients, but Raises Bleeding Concerns

Date: November 12, 2023

Subclinical atrial fibrillation is asymptomatic or only produces short-lasting, nonspecific symptoms. This type of atrial fibrillation is difficult to diagnose by standard clinical means but is typically detected by using long-term continuous cardiac rhythm monitors. This condition is associated with a 2.5-fold increase in the risk of stroke, but the benefits of initiating oral anticoagulant treatments remain uncertain.

The ARTESIA double-blind, double-dummy, randomized trial was conducted at 247 clinical sites across 16 European and North American countries to evaluate whether apixaban would result in a lower risk of stroke or systemic embolism than aspirin, among patients with subclinical atrial fibrillation as detected by a pacemaker, defibrillator, or implantable cardiac monitor (ICM). Patients were randomly assigned to receive either apixaban 5 mg twice daily (2.5 mg twice daily when indicated) or aspirin 81 mg once daily. The primary efficacy outcome, stroke or systemic embolism incidence, was assessed in the intention-to-treat population and the primary safety outcome, major bleeding, was assessed in the on-treatment population.

A total of 4012 patients (2015 in the apixaban group and 1997 in the aspirin group) with a mean (±SD) age of 76.8±7.6 years and a mean CHA2DS2-VASc score of 3.9±1.1 were included in the analysis. After a mean follow-up of 3.5±1.8 years, stroke or systemic embolism occurred in 55 patients in the apixaban group (0.78% per patient-year) and in 86 patients in the aspirin group (1.24% per patient-year) (hazard ratio, 0.63; 95% confidence interval [CI], 0.45 to 0.88; P=0.007). In the on-treatment population, the rate of major bleeding was 1.71% per patient-year in the apixaban group and 0.94% per patient-year in the aspirin group (hazard ratio, 1.80; 95% CI, 1.26 to 2.57; P=0.001). Fatal bleeding occurred in 5 patients in the apixaban group and 8 patients in the aspirin group.

In conclusion, among patients with subclinical atrial fibrillation, apixaban resulted in a lower risk of stroke or systemic embolism than aspirin but is associated with a higher risk of major bleeding.

Source: www.nejm.org

FDA Approves LetsGetChecked's Simple 2 Test: The First At-Home Diagnostic Test for Chlamydia and Gonorrhea

Date: November 15, 2023

On November 15th 2023, the U.S. Food and Drug Administration (FDA) granted marketing authorization to LetsGetChecked for the Simple 2 Test, the first at-home diagnostic test for chlamydia and gonorrhea. Available over-the-counter, the diagnostic test is intended for use in adult patients aged 18 years and older to detect the presence of bacteria Chlamydia trachomatis and Neisseria gonorrhoeae through samples collected at home using vaginal swabs and urine specimens.

The direct-to-consumer test requires the user to activate the collection kit online and fill out a health questionnaire, which would be evaluated by a healthcare provider. After collecting the sample at home, the specimen is sent back to the designated laboratory for testing. Results are delivered online, with follow-up from a healthcare provider in cases of positive or invalid test results.

According to the Centers for Disease Control and Prevention's Sexually Transmitted Infections Surveillance Report, chlamydia and gonorrhea are the most common bacterial STIs in the United States, with rates steadily increasing. In 2021 alone, there were an estimated 1.6 million cases of chlamydia and more than 700,000 cases of gonorrhea. When left untreated, these infections can lead to serious health complications, including infertility. Expanding the availability of STI testing can help patients receive quicker results and access appropriate treatment, potentially curbing the rising rates of STIs.

The Simple 2 Test is the first FDA-authorized diagnostic test with at-home sample collection for any sexually transmitted disease other than HIV. The test and collection kit were validated for use with the cleared Hologic Aptima 2 Combo Assay. The FDA reviewed the Simple 2 Test under its De Novo premarket review pathway and established special controls for labeling and performance testing to ensure safety and effectiveness.

Source: www.fda.gov

Promising Results for mRNA-1345 Vaccine in Preventing Respiratory Syncytial Virus (RSV) in Older Adults

Date: December 14, 2023

Respiratory syncytial virus (RSV) poses a significant threat to older adults, which often leads to severe complications and even death. A phase 1 clinical trial of an mRNA-based RSV vaccine, mRNA-1345, encoding the stabilized RSV prefusion F glycoprotein has shown promising results, but further data are required.

The ongoing ConquerRSV trial is a randomized, double-blind, placebo-controlled study involving 35,541 adults 60 years of age or older in 22 countries. In this phase 2-3 trial, participants were randomly assigned in a 1:1 ratio to receive a single dose of mRNA-1345 (50 μg) or placebo. The study's primary efficacy endpoints were the prevention of RSV-associated lower respiratory tract disease with at least two or three signs or symptoms and the secondary efficacy endpoint was the prevention of RSV-associated acute respiratory disease. Safety evaluations were also conducted.

Out of the total participants, 17,739 participants received the mRNA-1345 vaccine while 17,748 received the placebo. The median follow-up was 112 days. The primary efficacy analyses were conducted once at least 50% of the expected RSV-associated lower respiratory tract disease cases had occurred. The vaccine demonstrated an efficacy rate of 83.7% (95% confidence interval [CI], 66.0 to 92.2) in preventing RSV-associated lower respiratory tract disease with at least two signs or symptoms and 82.4% (95% CI, 34.8 to 95.3) in preventing the disease with at least three signs or symptoms. Furthermore, the vaccine displayed an efficacy rate of 68.4% (95% CI, 50.9 to 79.7) in preventing RSV-associated acute respiratory disease. The vaccine's protection was consistent across age groups and individuals with coexisting conditions. Regarding safety, the mRNA-1345 group experienced a higher incidence of solicited local and systemic adverse reactions compared to the placebo group (58.7% vs 16.2% and 47.7% vs 32.9%) respectively. However, these reactions were mostly transient and mild to moderate in severity. The occurrence of serious adverse events was similar between the vaccine and placebo groups, affecting 2.8% of participants in each group.

In conclusion, the mRNA-1345 vaccine, administered as a single dose, demonstrated a favourable safety profile and significantly reduced the incidence of RSV-associated lower respiratory tract disease and RSV-associated acute respiratory disease in adults aged 60 years and older.

Source: www.nejm.org