NEW YORK accp American College of Clinical Pharmacy

NYS-ACCP Insider

Touro College of Pharmacy - New York

The official newsletter of SCCP/ACCP TOURO COLLEGE OF PHARMACY 2021

Touro College of Pharmacy's American College of Clinical Pharmacy (TCOP-ACCP) student chapter has been serving students since 2015. In keeping with the mission and core values, our organization provides members with opportunities within clinical pharmacy, advice on professional networking, and ways to strengthen leadership abilities.

On September 10, a team of three students participated in the clinical skills competition in round one, where they applied their knowledge of various therapeutics topics to solve the questions. On September 17, TCOP-ACCP student chapter held its first general body meeting virtually on zoom, and provided information about the chapter's mission and the myriad opportunities, including membership benefits and introducing chapter initiatives.

In Fall of 2020, we participated in a variety of different activities that were aligned with our mission of achieving excellence in education. In September, we participated in the clinical skills competition and had our first virtual general body meeting on zoom. In honor of World Mental Health month in September and World Diabetes month in October, we collaborated with Touro College of Osteopathic Medicine to create educational flyers for Touro Harlem Health Clinic (THHC).

IN THIS ISSUE

In October, we hosted Jeopardy game night quizzing students on diabetes, hyperlipidemia, and hypertension, and provided participants with advice on studying for quizzes and exams. Students shared their study techniques and advice on how to improve academic performance and manage time efficiently.

We also collaborated with the Student Society of Health-System Pharmacy (SSHP) student chapter to provide a CV/interview workshop where students had mock residency interviews with faculty and were given the opportunity to edit their CVs and letters of recommendations for residency applications.

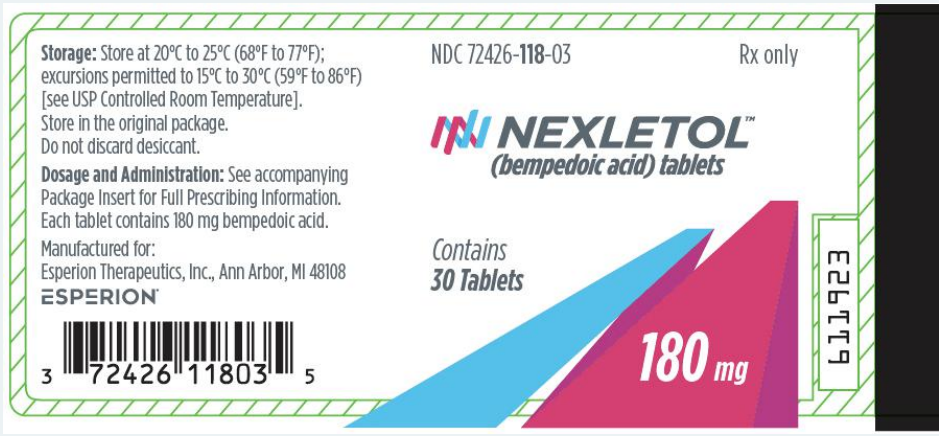
In Spring 2021, we had students compete in the ACCP Clinical Research Challenge Local Competition (CRC) at Touro. Three finalists were chosen to participate in the first round of the Clinical Research Competition on February 15, 2021.

In March, presented a review lecture on HIV and created a fun, interactive game to assess audience knowledge. Students enjoyed the event as they reviewed their topic on HIV before their exams and facilitated their knowledge by answering Kahoot questions.

Our chapter remains devoted to promoting passion for clinical pharmacy and expanding the clinical knowledge of our TCOP students and members.

Shahnoza Tohirova Pharm.D. candidate class of 2022

NEW DRUG UPDATE: FIRST IN CLASS ORAL MEDICIATION BEMPEDONIC ACID AS AN ADJUNCTIVE TO CURRENT GUIDELINE-RECOMMENDED STATIN THERAPIES FOR PATIENTS WITH HIGH LDL LEVELS DESPITE MAXIMALLY TOLERATED STATIN USE



Introduction

High low-density lipoprotein (LDL) levels have been associated with poor cardiovascular outcomes, therefore it is important to lower it to a target goal. Statins have been established as the first-line drug class in treatment of hyperlipidemia due to their abilities of interfering with arteriosclerotic plague formations and disruption of formed plagues [1]. Additionally, multiple randomized trials have demonstrated the anti-inflammatory effect of statins which contribute to cardiovascular benefits by reducing vascular inflammation [1].

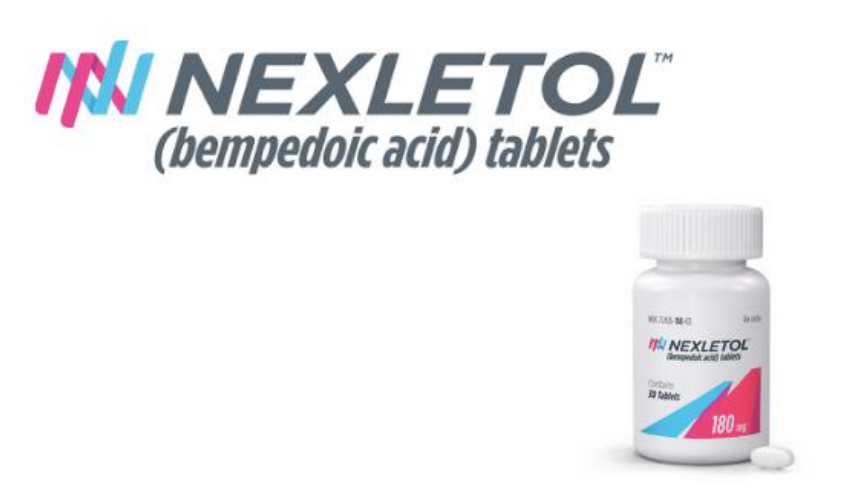
According to 2013 American College of Cardiology/American Heart Association (ACC/AHA) guidelines, statins are recommended for several clinical scenarios: history of a clinical ASCVD event , severe hyperlipidemia defined as LDL ≥190 mg/dL, patients with diabetes and LDL between 70-189 mg/dL, and patients with elevated 10-year ASCVD risk score [2]. In the case of statin intolerance or high LDL levels despite maximum tolerated statins, guidelines recommend additional lipid-lowering agents such as ezetimibe, bile acid sequestrants, and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors. [2] Ezetimibe lowers LDL by 10-15% as monotherapy, and by 25% in combination with statins. PCSK9 inhibitors were reported to lower LDL by 60%, but their use carries a cost barrier for the majority of patients [1].

On February 21, 2020, the Food and Drug Administration approved Nexletol (bempedoic acid) and on February 26, 2020, the FDA approved Nexlizel (bempedoic acid in combination with ezetimibe) [5] [6]. Nexletol is available in the United States as a 180 mg oral tablet recommended for once daily administration, and Nexlizet is bempedoic acid 180 mg/ezetimibe 10 mg oral tablet also for once daily regimen [3] [4]. Both drugs are manufactured by Esperion Therapeutics, Inc., and approved for management of hypercholesterolemia and atherosclerotic cardiovascular disease as adjuncts to diet and maximally tolerated statin therapy for additional lowering of LDL-C [3] [4] [5] [6].

***MOA:** Bempedoic acid is an adenosine triphosphate (ATP) citrate lyase inhibitor, a prodrug which needs to be activated by acyl-CoA synthetase-1 liver enzyme to its active metabolite, bempedoic acid-CoA. It inhibits production of ATP-citrate lyase (ACL) which is used for synthesis of cholesterol. As a result of this process, hepatic production of cholesterol is reduced [5].*

***Clinical trials**: Bempedoic acid use was assessed in phase 2 and 3 clinical trials as monotherapy and in combination with ezetimibe and a statin [1].*

***Clinical outcomes:** significant reduction of LDL-C and cardiovascular risk markers was demonstrated as a result of the trials [1].*



Phase 1 and 2 studies

Evaluation of different dosages of bempedoic acid

Safety and tolerability of bempedoic acid was evaluated in phase 1 and 2 studies, and results showed that the drug is well tolerated at doses of 140 mg, 180 mg and 220 mg daily. The **ETC-1002-004** study included 24 participants who received these dosages daily for the duration of 14 days. LDL reduction up to 36% was observed when 220 mg was taken orally once daily. Side effects were not reported in this study [1].

Combination of bempedoic acid with ezetimibe

The following **ETC-1002-008** 12 week trial included 349 patients with or without statin intolerance across 70 clinical sites in the U.S. [7]. “The purpose of this clinical trial is to inform dosing for our Phase 3 program, directly compare the LDL-C lowering efficacy of ETC-1002 versus ezetimibe, and assess safety and tolerability, including muscle-related adverse events, in patients with or without statin intolerance” [7]. Researchers compared the combination of 120 mg or 180 mg of bempedoic acid taken with 10 mg ezetimibe, with monotherapy regimen of each of these drugs. Results demonstrated that bempedoic acid was more effective than ezetimibe as monotherapy, and even more potent in combination, reaching LDL reduction level of 43-48%. Bempedoic acid monotherapy LDL reduction was reported to be 27-30% versus ezetimibe alone of 21%. C-reactive protein (CRP) inflammatory marker was reduced by 30-40% for bempedoic acid alone and 10% for ezetimibe monotherapy [1].

Combination of bempedoic acid with statin

Additional **ETC-1002-035** phase 2 randomized, double-blind, parallel group study included 60 patients on stable atorvastatin 80 mg per day at 20 clinical centers in the U.S. [8]. Patients were randomized to receive either the combination of 180 mg of bempedoic acid and high intensity statin (atorvastatin 80 mg) taken for four weeks or placebo. As the result of the study, LDL was additionally reduced by 13%, and CRP by 34.6% when compared to atorvastatin with placebo [1].

Combination of bempedoic acid with statin and ezetimibe

The double-blind randomized controlled trial (RCT) **triplet therapy trial** was a placebo-controlled, parallel group study which included 63 participants [9]. The goal of this study was to assess the efficacy of bempedoic acid 180 mg, atorvastatin 20 mg and ezetimibe 10 mg once daily for 6 weeks versus placebo [9]. Results of this study demonstrated 63.6% reduction of LDL compared to 3.1% for the placebo group, and 47.7% reduction in CRP versus 2.7% in the placebo arm [1].

Combination of bempedoic acid with evolocumab

In the **ETC-1002-039** study, efficacy of bempedoic acid 180 mg was studied in combination with a PCSK9 inhibitor, evolocumab 420 mg once monthly for 2-month duration. LDL reduction was marked as 27.5% in the experimental group versus 2.8% increase in the control group. CRP was reduced by 34.4% in the combination group and decreased by 1.6% in the placebo group [1].

Bempedoic acid in patients with type 2 diabetes

The **ETC-1002-005** trial included 60 patients with diabetes. One treatment arm was placebo and the other was assigned to take bempedoic acid 80 mg daily for 2 weeks, then 120 mg for 2 weeks or a placebo for 4 weeks. LDL was lowered by 43% in the treatment arm versus 4% in the placebo arm, CRP mean reduction was 41% versus 11% in the placebo group. Therefore, LDL reduction was highly significant in patients with type 2 diabetes and among the highest observed in bempedoic acid monotherapy trials [1].

The **1002FDC-058** study assessed the combination of 180 mg bempedoic acid taken with 10 mg ezetimibe in patients with type 2 diabetes. LDL-C and CRP were reduced by 40% and 25% respectively [1].

Phase 3 studies

The intent of phase 3 studies is to assess long-term safety and efficacy of the new medication.

The **CLEAR Harmony** 52-week trial evaluated bempedoic acid 180 mg daily in 2,230 patients with ASCVD, hyperlipidemia and elevated LDL despite maximum tolerated statin regimen. 10.9% of patients on bempedoic acid reported adverse events versus 7.1% in the placebo group. Adverse events included myalgia, nasopharyngitis, and upper respiratory tract infections [1].

The **CLEAR Wisdom** trial evaluated LDL reduction at 12 weeks. Patients on bempedoic acid achieved an LDL reduction of 15.1% compared with 2.4% reduction for the placebo group. Adverse reactions were also reported to be higher in bempedoic acid group (17.4%) versus placebo use (12.5%) such as myalgia, increased aspartate aminotransferase level, arthralgia, muscle spasms, cardiac arrest, and fatigue [1].

The **CLEAR Serenity** trial evaluated efficacy of bempedoic acid 180 mg and placebo for a duration of 24 weeks in a statin-intolerant patient population of 345 patients. Results were obtained after 12 weeks and demonstrated reduction of LDL levels by 23.6% in bempedoic acid versus the placebo group. LDL was reduced by 22.1% in patients without lipid lowering therapy, 23.3% in non-statin adjunctive therapy, and 17.4% in low-dose statin background therapy [1].

The **CLEAR Tranquility** trial enrolled 269 statin-intolerant patients with background ezetimibe therapy and either bempedoic acid 180 mg or placebo administered for 12 weeks. As a result, bempedoic acid provided 23.5% LDL reduction versus 5% LDL increase in the placebo group. Similarly to the results of the CLEAR Serenity trial, LDL reduction with bempedoic acid versus placebo was higher in patients who did not receive statin therapy previously (34.7% reduction) compared to patients on statin therapy (20.5%) [1].

The **CLEAR Outcomes** study is an ongoing study that will enroll 12,000 patients and assess cardiovascular risk reduction in statin intolerant patients on 180 mg bempedoic acid in comparison with placebo group [1].

Lastly, the **NCT03337308** clinical trial evaluated safety and efficacy of bempedoic acid 180 mg and ezetimibe 10 mg compared to ezetimibe 10 mg alone, bempedoic acid 180 mg alone, or placebo in high ASCVD risk patients with high LDL and statin intolerance. After 12 weeks, LDL was reduced by 36.2% in the combination group, 17.2% in bempedoic acid alone, 23.2% in the ezetimibe arm alone, and 1.8% in the placebo arm. CRP reduction was 35.1% in the combination group, 8.2% in the ezetimibe group, and 31.9% in the bempedoic acid monotherapy arm.

Adverse Effects

Some studies reported tendon rupture occurring in 0.5% of patients after weeks or months of bempedoic acid use. Ruptures involved rotator cuff, bicep tendons, and Achilles tendon. Risk factors for rupture tendon included 60 years of age or greater, renal failure, prior history of tendon disorders, and usage of corticosteroids or fluoroquinolones. Discontinuation of bempedoic acid is recommended if patients report swelling, inflammation, or pain [1].
Additionally, increase in uric acid levels and occurrence of gout was reported in studies due to competition between uric acid and glucuronide metabolite of bempedoic acid for renal transporters. Increase in uric acid was reported after 4 weeks of treatment, and can be managed with urate lowering drugs [1].

Clinical significance

Since some patients cannot adequately achieve target LDL levels with statin therapy alone or are unable to tolerate statins, other treatment options are needed.Bempedoic acid is an effective option, even despite a lower LDL lowering effect when used in combination with statin versus bempedoic acid monotherapy. This effect is due to a similar mechanism of action affecting the same cholesterol synthesis pathway [1]. Ezetimibe reduces LDL levels significantly, but lacks cardiovascular benefits [1].Bempedoic acid reduces CRP more significantly than ezetimibe, and inflammation plays a major role in progression to ASCVD [1]. PCSK9 inhibitors are highly effective in LDL lowering and reduction of cardiovascular events, but very costly for patients, and not often implemented in clinical practice [1]. Bempedoic acid is more expensive than statins and ezetimibe, cheaper than PCSK9 inhibitors, but effective in lowering LDL, CRP and reducing the risk of cardiovascular events [1]. This agent is recommended as an adjunctive therapy for patients on statins [1].

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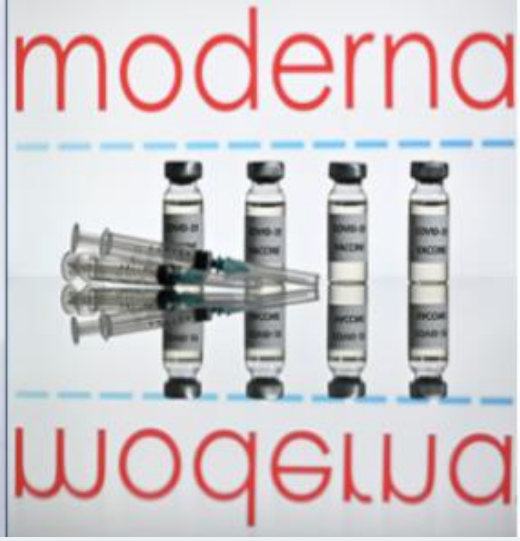

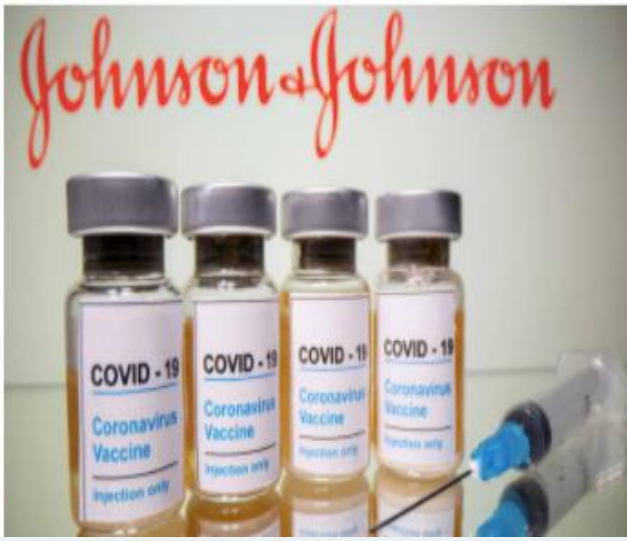

A Comparative Review and Short Analysis of the Current COVID-19 Vaccines Available in the United States (Pfizer-BioNTech vs. Moderna vs. Johnson & Johnson)

The two available mRNA vaccines by Pfizer-BioNTech and Moderna are similar in respect to the entirely new approach utilized in order to prevent SARS-CoV-2 infection [4]. The key similarity between both manufacturers lies in the technology behind messenger RNA. The vaccines contain mRNA (genetic material/information matching that of SARS-CoV-2) in a lipid shell [6][7].Once they are administered to a patient, a target protein is instructed to elicit an immune response against the spike protein contained on the surface of the coronavirus [4]. Ultimately, the immune system will be enhanced and prepared to terminate future infection from the virus through the formation of antibodies that will have the capability to block the virus from invading healthy cells [4] [6][7]. Both vaccines are currently under the use of emergency use authorization and have not been approved by the FDA and are also administered in two-time doses [1][2][3]. In comparison, side effects and reactions are considered to be similar between the two manufacturers. These reactions include pain and soreness at the injection site, fatigue, headache, myalgia, arthralgia, fever, and erythema at the injection site [1][3][6].

Key differences between the Pfizer-BioNTech and Moderna vaccines lie in their ingredient lists in regard to excipients, indicated age for use, proper storage, volume per dose, time frame of waiting period between both doses for each vaccine, dispensing strategy, and efficacy. These differing characteristics can be reviewed in the chart below detailing each manufacturer's product attributes.

More recently, a new vaccine has been developed by Janssen Pharmaceuticals from Johnson & Johnson and authorized for emergency use by the FDA. Foregoing the differences between Pfizer and Moderna as stated above, the most significant differences with the Johnson & Johnson vaccine are the dosing frequency, which is only single-shot dose, and overall efficacy percentage. (66.3%) concluded from the manufacturer’s clinical trials[8][9]. Lastly, as opposed to the aforementioned mRNA vaccines (Pfizer-BioNTech, Moderna)- the Johnson & Johnson approach is of a different type of vaccine technology referred to as a viral vector; in which it contains an altered and harmless virus (different from that of the virus that causes COVID-19) and serves as a vector [10]. Upon entry into human cells, the vector instructs cells to create a harmless piece of the virus that causes COVID-19 (the spike protein found on the surface of SARS-CoV-2) [10]. This specific process ultimately leads to the activation of an immune response with newly produced antibodies that can help prevent future infection [10].

Manufacturer	**Pfizer-BioNTech** (BNT162b2 mRNA Covid-19 Vaccine) Issued by FDA on 12/11/2020	**Moderna** (mRNA-1273 SARS-CoV-2 Vaccine) Issued by FDA on 12/18/2020	**Johnson & Johnson** (Ad26.COV2.S Covid-19 Vaccine) Issued by FDA on 02/27/2021
Ingredient List	mRNA, lipids ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 2 [(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 1,2-Distearoyl-sn-glycero-3-phosphocholine, and cholesterol), potassium chloride, monobasic potassium phosphate, sodium chloride, dibasic sodium phosphate dihydrate, and sucrose [1].	mRNA, lipids (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), tromethamine, tromethamine hydrochloride, acetic acid, sodium acetate, and sucrose [2].	recombinant, replication-incompetent adenovirus type 26 expressing the SARS-CoV-2 spike protein, citric acid monohydrate, trisodium citrate dihydrate, ethanol, 2-hydroxypropyl-β-cyclodextrin (HBCD), polysorbate-80, sodium chloride [8].
Dosing Frequency/Dose Route	Two dose series; administered 3 weeks apart (21 days), both intramuscularly [1][3].	Two dose series; administered one month apart (28 days); both intramuscularly [2].	Administered as single dose; intramuscularly [8].
Volume	The volume to be administered for the Pfizer-BioNTech vaccine is 0.3ml after reconstitution with 1.8ml of 0.9% NS [1][6].	The volume for the Moderna vaccine is 0.5ml in a direct draw without reconstitution [2][7].	The volume for the Johnson & Johnson vaccine is 0.5ml and is not to be mixed with a diluent. [8][9].
Proper Storage and Handling/Temperature	The Pfizer-BioNTech vaccine is to be stored in a refrigerator between 2°C and 8°C (36°F and 46°F) for up to 120 hours (5 days). Once the vials are mixed- they may be stored and left at room temperature 2°C to 25°C for up to 6 hours [3].	The Moderna multiple-dose vials are stored frozen between -25° to -15°C (-13° to 5°F) and should be in their original carton to protect from light. Unpunctured vials may be stored between 8° to 25°C (46° to 77°F) for up to 12 hours [2].	The Johnson and Johnson vaccine is to be stored between 2°C and 8°C (36°F and 46°F) for up to 6 hours or at room temperature (up to 25°C or 77°F) for 2 hours. Store vials in a refrigerator. Do not freeze [8].
Indicated Age of Use	The indicated age use for Pfizer-BioNTech is 16 years of age and older [1][6].	18 years of age older for Moderna [2][7].	Individuals 18 years of age and older [8][9].
Efficacy	The Pfizer-BioNTech vaccine trials concluded the vaccine to be 95% effective in their study population [1][3][4][5][6].	Moderna vaccine trials concluded their product to be 94.1% effective in preventing SARS-CoV-2 infection [4][7].	The Johnson & Johnson vaccine trials concluded their product to be 66.3% effective in preventing COVID-19 illness in patients with no prior history of previous illness due to COVID-19 infection [8][9].

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