Cardiac Myosin Inhibitors as an effective pharmacological treatment for patients of severe drug-refractory hypertrophic cardiomyopathy

Syed Huzaifa Alam Raza, Jawad Sarwar, Jawad Ishtiaq

Madam, Hypertrophic cardiomyopathy (HCM) is the most common genetic cardiovascular disease with an estimated prevalence of its gene carriers at 1 in 200 people[1]. It can be defined as a thickening of the heart muscle; usually the septum, which may result in a phenomenon called left ventricular outflow tract obstruction (LVOT). HCM may present with various cardiac symptoms with related presentations, including dyspnoea, dizziness, and syncope. However, the most severe complication is sudden cardiac death (SCD) due to ventricular arrhythmia, which is often the first disease presentation in young people with mild to no symptoms[2]. Previous pharmacological treatments of HCM included β-blockers, non-dihydropyridine calcium channel blockers and disopyramide which mainly provided sub-optimal symptomatic relief without addressing the disease-specific molecular abnormalities[3]

A new class of myosin inhibitors, mavacamten, was granted Food and Drug Administration (FDA) approval on 28th April 2022[4]. It is a disease specific drug which reduces myocardial hypercontractility by inhibiting cardiac myosin ATPase and its subsequent binding to actin. In a recent double-blind trial, the VALOR-HCM explored the effects of mavacamten on severely symptomatic drug-refractory obstructive HCM (oHCM) patients eligible for septal reduction therapy (SRT), i.e., surgical myectomy or alcohol ablation recommended to oHCM patients with intractable symptoms despite maximal medical therapy[5]. The trial's results showed that the addition of mavacamten to maximally tolerated background medical therapy of HCM patients resulted in significant reduction in guideline eligibility for SRT and a reduction in LVOT gradients with improvement in patient reported outcomes ($p<0.001$)[5].

Such an alternative to SRT is of interest particularly in Pakistan because SRT is an invasive, expensive and risky procedure. Furthermore, SRT demands intensive post-operational care expert surgeons and is performed in only a few institutions in Pakistan, all the more stressing the need for an alternative pharmacological treatment to HCM like mavacamten. More detailed analysis of the phase-3 clinical trial, VALOR-HCM is needed to substantiate the efficacy and safety of mavacamten. Moreover, further development and long-term study of the same class of drugs are required to meet the need of HCM patients in Pakistan for relatively inexpensive and safe treatment.

Submission completion date: 22-09-2022
Acceptance date: 29-12-2022

Disclaimer: None to declare.

Conflict of Interest: None to declare.

Funding Sources: None to declare.

References

1. Semsarian C, Ingles J, Maron MS, Maron BJ. New perspectives on the prevalence of hypertrophic cardiomyopathy. J Am Coll Cardiol 2015; 65: 1249-54.
2. Jordà P, García-Álvarez A. Hypertrophic cardiomyopathy: Sudden cardiac death risk stratification in adults. Glob Cardiol Sci Pract 2018; 2018: 25.
3. Zampieri M, Argirò A, Marchi A, Berteotti M, Targetti M, Fornaro A, et al. Mavacamten, a Novel Therapeutic Strategy for Obstructive Hypertrophic Cardiomyopathy. Curr Cardiol Rep 2021; 23: 79.
4. Novel drug approvals for 2022: [Online] [Cited 2022 Sept 1]. Available from: URL: https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drug-approvals-2022.
5. Desai MY, Owens A, Geske JB, Wolski K, Naidu SS, Smedira NG, et al. Myosin Inhibition in Patients with Obstructive Hypertrophic Cardiomyopathy Referred for Septal Reduction Therapy. J Am Coll Cardiol 2022; 80: 95-108.

1st Year MBBS Student, Dow University of Health Sciences, Karachi, Pakistan.
Correspondence: Syed Huzaifa Alam Raza. Email: shuzaifa.raza@gmail.com
ORCID ID. 0009-0009-5796-1164

DOI: 10.47391/JPMA.7971