

Revolutionizing resistant hypertension: Unlocking the potential of AprocitentanRahemeen Goraya¹, Mahrukh Nadeem²

Madam, Hypertension is a prevalent disease worldwide; however, the therapies for the treatment of hypertension have not been able to meet the desired blood pressure levels in approximately 15% of patients resulting in resistant hypertension. According to the American Heart Association, resistant hypertension is a condition in which the blood pressure remains elevated despite the use of drugs from three different classes of anti-hypertensives. It has been linked with an increasing risk of organ damage and cardiovascular events including ischaemic heart disease and stroke.¹

Many novel anti-hypertensive drugs have been studied in response to this concern. Aprocitentan, an active metabolite of macitentan, is one of them. It acts as a dual ETA and ETB receptor antagonist blocking the binding of ET-1 to the receptors.² ET-1 is an isoform of endothelin found in the human cardiovascular system. It acts through ETA and ETB receptors and plays a key role in the regulation of blood pressure. Overexpression of both ET-1 and its receptors has been implicated in the pathogenesis of hypertension.³ Aprocitentan antagonizes these receptors and mitigates ET-1 mediated vasoconstriction to lower blood pressure.

Previously, some endothelin receptor antagonists were developed but didn't significantly lower blood pressure which limited their utility. However, a phase III clinical trial using Aprocitentan was conducted. It showed

improvements in blood pressure control among patients using the drug.⁴ The most frequent adverse effects found with the use of this drug were oedema and low RBC count. FDA approved this drug in March 2024 as an add on therapy recognizing its potential. Nevertheless, data on its prolonged safety profile are scarce and additional research is vital to comprehensively assess its delayed complications.¹

Aprocitentan, in combination with other anti-hypertensives holds promise for effectively treating resistant hypertension. It is essential for clinicians to remain informed regarding this drug in order to provide optimal care to patients. Health regulatory authorities should ensure that this revolutionary drug is available to those in need of it.

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