New Drug Mechanisms

In this series we draw attention to recently licensed medicines with an entirely new mechanism of action.

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Aliskiren

Indication

Treatment of essential hypertension.

Mechanism

Aliskiren is the first renin inhibitor to be licensed in Europe. It selectively inhibits renin, the first enzyme in the renin–angiotensin system (RAS) cascade, thereby inhibiting the formation of angiotensin I from angiotensinogen (Figure 1). This reduces the production of vasoconstrictor angiotensin II and mineralocorticoid aldosterone, resulting in vasodilation, decreased sympathetic activity and increased excretion of sodium ions by the kidneys with a consequent decrease in blood pressure.

Other antihypertensive drugs, such as angiotensin converting enzyme inhibitors, angiotensin receptor blockers, and aldosterone antagonists exert their actions at later stages in the system. All drugs that block the RAS inhibit the negative feedback of angiotensin II on renin secretion, leading to a compensatory rise in renin concentration. Aliskiren is special because it inhibits the RAS at its origin. Furthermore, in contrast to other RAS-blocking agents, aliskiren decreases plasma renin *activity* despite the compensatory rise in renin *concentration*. Aliskiren does not interfere with the degradation of bradykinin (which is inhibited by angiotensin converting enzyme inhibitors but not by angiotensin receptor blockers).

Adverse effects

Aliskiren causes only mild and transient adverse reactions, of which diarrhoea is the most common. Peripheral oedema, rash, and influenza-like symptoms have been reported.

Literature

1 Siragy HM, Kar S, Kirkpatrick P. Fresh from the pipeline: Aliskiren. *Nat Rev Drug Discov* 2007; 6: 779–80.

Available at <http://www.emea.europa.eu/humandocs/Humans/EPAR/rasilez/rasilez.htm>

Figure 1

Aliskiren inhibits the activity of the enzyme renin at the onset of the conversion cascade within the renin–angiotensin system (RAS), eventually resulting in a decrease in blood pressure. ACE, angiotensin converting enzyme; ACEI, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blockers; AT-R, angiotensin-II receptor