Inclisiran: Adis Evaluation

Clinical Considerations

- First-in-class siRNA directed against PCSK9 mRNA
- Convenient maintenance dosing every 6 months (after initial doses at days 1 and 90)
- Markedly lowers LDL-C levels in patients with, or at high risk of developing, ASCVD who have hypercholesterolaemia, irrespective of whether or not their conventional therapy includes a statin
- Generally well tolerated; only adverse reactions at the injection site occur more often than with placebo

Plain Language Summary

Background and rationale

- Atherosclerotic cardiovascular disease (ASCVD) is a leading cause of death and disability
- 'Statins' are the drugs of choice for reducing elevated levels of low-density lipoprotein cholesterol (LDL-C) in patients with, or at risk of developing, ASCVD
- However, due to multiple factors, including adverse events and/or poor adherence, many patients don't achieve their guideline target LDL-C level on conventional (statin-based) therapy and novel, non-statin lipid-lowering therapies (LLTs) are needed

Clinical findings

- Inclisiran (Leqvio®) is a small interfering RNA (siRNA) drug that works as a LLT by stopping the liver from making an enzyme [proprotein convertase subtilisin/kexin type 9 (PCSK9)] that otherwise reduces its ability to remove LDL-C from the blood
- Subcutaneously injecting inclisiran every 6 months (after initial doses at days 1 and 90) was generally well tolerated and approximately halved LDL-C levels in patients with, or at high risk of developing, ASCVD who had hypercholesterolemia, regardless of whether or not their conventional therapy included a statin

Conclusion

Inclisiran is a potentially valuable additional/alternative antihyperlipidemic agent to a statin because of its infrequent, and therefore more convenient, dosing schedule versus other non-statin LLTs, including anti-PCSK9 monoclonal antibodies