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ISPOR Europe 2023
12-15 November | Copenhagen, Denmark

EE164

Cost-Effectiveness of Inclisiran as Add-on Therapy to Standard-of-Care for the Secondary Prevention of Cardiovascular Events in Patients with Elevated LDL Cholesterol

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INTRODUCTION & OBJECTIVE

- Inclisiran is a small interfering RNA that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9) with published effectiveness in lowering elevated low-density lipoprotein cholesterol (LDL-C) but without cardiovascular (CV) outcomes in patients on standard-of-care therapy yet. Meanwhile, monoclonal antibodies PCSK9 inhibitors evolocumab and alirocumab have published effectiveness on CV outcomes.
- The Agency for Care Effectiveness (ACE) is the national health technology assessment (HTA) agency in Singapore to guide health policy, drive appropriate use of treatments and inform technology funding decisions. Given inclisiran has a different mechanism of action compared with evolocumab and alirocumab, an initial assessment of its value as add-on therapy compared to placebo from Singapore healthcare system's perspective using LDL-C as a surrogate outcome was conducted.

METHODS

- A Markov model with health states for CV events such as stroke was adapted from a Norwegian study. The model differentiated between first year of CV event and subsequent years.
- The effectiveness of inclisiran in lowering LDL-C was informed by ORION-11 while effectiveness of reduction in LDL-C on lowering probabilities of cardiovascular events were taken from the Cholesterol Treatment Trialists' Collaboration (CTTC) meta-analysis.
- Health state utilities were sourced from literature while cost were sourced from public healthcare institutions in Singapore.

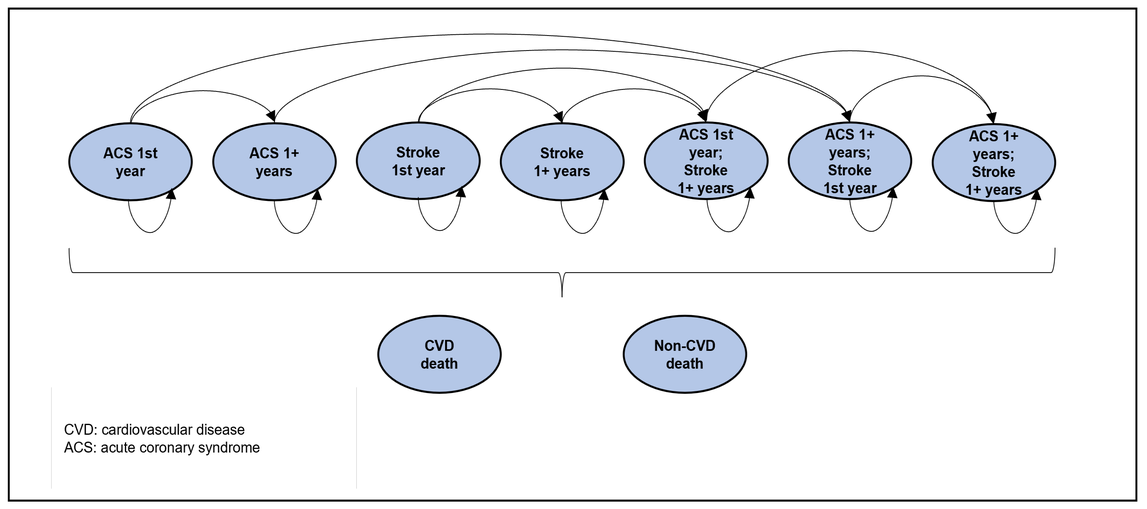

Figure 1. State transition diagram

RESULTS

- Treatment with inclisiran added on to standard-of-care, compared with placebo, was associated with higher costs (S$30,100 [USD 22,600]) and higher effectiveness (0.51 QALY gained) which resulted in an incremental cost-effectiveness ratio (ICER) of S$58,500 (USD 44,000) per quality-adjusted life-year (QALY) gained.
- Sensitivity analyses show the ICER ranged from S$55,500 to S$65,700 per QALY (USD 44,000 to 47,000) when using the upper and lower bound of the 95% confidence interval on the estimated LDL-C effect on reducing probability of cardiovascular events respectively.

	Accrued total cost (SGD)	Incremental accrued total cost (SGD)	Accrued total QALYs	Incremental QALYs	ICER
Placebo	$15,300	$30,100	7.56	0.51	$58,500
Inclisiran	$45,400		8.08		

Table 1. Accrued cost and QALYs

CONCLUSION

- This study provides an initial assessment of the value of inclisiran using LDL-C as a surrogate outcome but remains highly uncertain given the lack of CV outcomes data. The findings from our cost-effectiveness analysis, alongside other considerations, will be useful to inform policy makers on funding decisions.
- As CV outcomes from trials will take longer to publish, there will be a continued need to model the cost-effectiveness of hypercholesterolemia treatments using only LDL-C as a surrogate outcome. As such, it will be useful to update the findings when CV outcomes are reported from the trials of inclisiran and compare the predicted effects with trial outcomes. This may inform on future cost-effectiveness models on drugs with a similar mechanism of action.