Sotorasib: Adis Evaluation

Clinical Considerations

- First approved drug that inhibits $KRAS^{G12C}$; irreversibly binds to the unique cysteine residue at codon 12
- Once daily oral treatment
- Clinically relevant objective response rate observed in patients with *KRAS G12C* mutation-positive NSCLC
- Manageable tolerability profile

Plain Language Summary

Background and rationale

- KRAS is a protein that is involved in cell signalling pathways, including those that are associated with cell growth and differentiation.
- *KRAS* mutations are detected in 23% of patients with non-small cell lung cancer (NSCLC), with the *G12C* mutation being the most common.
- G12C-mutant KRAS ($KRAS^{G12C}$) is kept in an activated state, which is associated with cancer.

Clinical findings

- Sotorasib (LUMAKRAS™ in the USA and LUMYKRAS™ in the EU), which is taken orally once daily, is the first approved drug that inhibits $KRAS^{G12C}$; it permanently binds to $KRAS^{G12C}$ and locks it in an inactivated state.
- Sotorasib is approved for adults who have advanced, previously treated, *KRAS G12C* mutation-positive NSCLC.
- In a clinical trial in patients with *KRAS G12C* mutation-positive NSCLC, a clinically relevant proportion of patients responded to sotorasib treatment. Furthermore, the duration of effectiveness with sotorasib was considered to be clinically relevant.
- Adverse reactions with sotorasib treatment were manageable; the dose may be decreased and/or sotorasib treatment may be temporarily stopped to manage adverse reactions.

Conclusion

Overall, sotorasib is a promising treatment option for patients with *KRAS G12C* mutation-positive NSCLC who have received at least one prior systemic therapy.