Discussion: ODYSSEY (Cost)

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Background: Cost-effectiveness Analysis

Cost-effectiveness Analysis

Do new treatments gain health at a reasonable cost to society and to healthcare payers?

**Incremental cost-effectiveness ratio (ICER):** Metric to assess cost-effectiveness – cost to gain one year of quality-adjusted life (QALY)

\[
\text{ICER} = \frac{\text{Cost}_2 - \text{Cost}_1}{\text{QALY}_2 - \text{QALY}_1}
\]

**Time horizon:** Cost effectiveness of chronic treatments should be assessed within the trial observation period AND over patients’ lifetimes*

**Willingness to pay (WTP):** How much is the payer willing to invest in the new treatment to gain health? Commonly accepted thresholds in the US range from $50,000-$150,000 per QALY gained.

*Ramsey S, et al., Value in Health, 2005
ODYSSEY (Cost): Strengths

- Data on efficacy, health-related quality of life, healthcare utilization all based on values measured directly in the ODYSSEY-Outcomes trial.

- Standard approach to post-acute coronary syndrome survival projections to model expected lifetime QALYs in active and placebo arms.

- Focus on “value based cost” in overall and subgroup analyses (Figure): setting a price point cost-effective for highest benefit patients could incentivize appropriate prescribing & disincentivize low-value prescribing.

ODYSSEY (Cost): Weaknesses
(Based on cost-effectiveness analysis best practices recommendations)*

- **Not all costs considered**: Exclusion of non-cardiovascular disease background costs is not conservative
- All-cause mortality was a secondary outcome in ODYSSEY-Outcomes [CVD mortality effect relatively weaker (12% reduction, NS); driver of statistically significant 15% all-cause mortality benefit unclear & confidence interval wide]
- All-cause mortality by LDL-C subgroup was not a pre-specified analysis

**Full ODYSSEY (Cost) report will require:**
  - Complete cost-effectiveness outcomes ($\Delta$ total costs, $\Delta$ total QALYs)
  - Reporting on uncertainty – especially treatment effects and survival

- Potential “disutility” (inconvenience) of lifelong biweekly injections

*Sanders GD et al., JAMA, 2016; Ramsey S et al., Value in Health, 2005*
ODYSSEY (Cost): Take Home 1

• **Remaining questions:**
  - Will the ODYSSEY (Cost) economic outcomes be robust when uncertainty is considered [e.g., 95% CI of main effect, hazard ratio for all-cause mortality (0.73-0.98)]?
  - What summary cost-effectiveness estimate (ICER) will be reported for the U.S., and based on what U.S. drug price?

• **Patient preferences, perspectives, and costs need consideration**
  - Convenience of biweekly dosing versus patient acceptance of a life-long injectable agent must be explored
  - Past patient-centered experience with insulin, other injectable anti-diabetes and biologics can be considered
Currently, few patients have had access to PCSK9i—due to out-of-pocket costs and other barriers (inset on right).

Rarely has cost-effectiveness analysis had an impact on CVD drug pricing as with PCSK9i: Manufacturers recently slashed U.S. prices.

Past economic analyses of PCSK9i trials set value-based prices (at WTP $100,000/QALY) ranging from $4,000 to $9,000 annually.

Institute for Clinical and Economic Review recommended alirocumab price, based on ODYSSEY-Outcomes (WTP $100,000/QALY):**

- $5,300 if baseline LDL-C >100 mg/dl
- $2,300 all eligible (baseline LDL-C >70 mg/dl)

*Llatky and Kazi, JACC, 2017

**https://icer-review.org/announcements/alirocumab-prelim-evidence-update/
THANK YOU!