Key points regarding:

**ODYSSEY ALTERNATIVE**
Efficacy and safety of alirocumab vs. ezetimibe, in patients with statin intolerance defined by placebo run-in and statin rechallenge arm

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Disclosures

- Research Grants - National Institutes of Health
  - NHLBI
  - NIDDK
  - BD2K consortium

- Diabetes Clinical Trials Adjudication Committee
  - Merck and Company
What we learned from this trial

• 1. The PCSK9 monoclonal antibody alirocumab lowers LDL cholesterol (LDL-C) impressively

• 2. In statin intolerant patients, alirocumab reduced LDL-C significantly more than ezetimibe
  - A commonly used agent in statin intolerant patients

• 3. In these statin intolerant patients, Q 2 week SQ dosing of alirocumab was fairly well tolerated and better tolerated than atorvastatin in terms of skeletal muscle adverse effects
  - p= .042 for any skeletal muscle TEAE
4. Many patients that are labelled as statin intolerant can, in fact, tolerate a statin.
   - Skeletal muscle TEAE leading to discontinuation showed no statistically significant differences between the 3 groups
   - While 25% of the atorvastatin assigned group withdrew due to TEAEs, that means 75% successfully completed the study
What we still don’t know…

1. How does LDL-C lowering with alirocumab compare to LDL-C lowering with atorvastatin
   - We were shown the LDL-C lowering results in comparison to ezetimibe but not atorvastatin

2. Will alirocumab ultimately prove more tolerable than other LDL-C lowering agents
   - Remember, skeletal muscle TEAE leading to *discontinuation* were similar between the groups
What we still don’t know...

3. Will alirocumab prove safe in longer studies
   - Human PCSK9 loss-of-function mutations give some comfort that this therapy will be safe
   - In this study, neurocognitive disorders were numerically higher, although statistically insignificant, in the alirocumab group (2.4%)
   - Longer term safety data needed

4. Finally, and of utmost importance, will alirocumab improve cardiovascular outcomes.
   - Need for large scale, longer duration trial with hard cardiovascular outcomes
Take home points

- This study suggests that many statin intolerant patients might be able to be successfully treated with a statin
  - The comparator used in this study was atorvastatin 20 mg

- There is a subgroup of patients who are truly statin intolerant for whom the PCSK9 monoclonal antibody alirocumab may have a role

- As with all new therapies, long term safety and efficacy of alirocumab must first be demonstrated.