ECRONICON OPEN ACCESS

EC ENDOCRINOLOGY AND METABOLIC RESEARCH

Opinion

A Current Assessment of the Cost-Effectiveness, Efficacy, and Safety of the PCSK9 Inhibitors in Patients with Dyslipidemia and/or Cardiovascular Disease

Parth Shah*

Clinical Research Medical Director, Obvio Health (a SPRIM Company), USA

***Corresponding Author**: Parth Shah, Clinical Research Medical Director, Obvio Health (a SPRIM Company), USA.

Received: August 28, 2017; **Published:** September 15, 2017

The cardiovascular disease (CVD) endemic in the United States is the leading cause of mortality with 1 in 4 deaths every year [1]. Approximately 735,000 Americans have a myocardial infarction, and 795,000 have a stroke each year [2]. Hypercholesterolemia, primarily defined by an elevated low-density lipoprotein (LDLC), is a major cardiovascular risk factor, and about one-third of U.S. population has hypercholesterolemia [2]. Historically, the statin therapy has played a crucial role in producing favorable efficacy along with promising cardiovascular outcomes. Despite therapies such as statins, bile-acid binding resins, ezetimibe, and niacin, many patients fail to achieve optimal LDLC lowering due to statin intolerance, expense, lack of insurance coverage, or variations in statin availability [3-7]. Given the previous considerations, it is projected that about 23 million Americans may have suboptimal LDLC lowering despite the best tolerated standard of care (SoC) therapy [8].

The PCSK9 inhibitors, alirocumab and evolocumab, are indicated for patients with familial hypercholesterolemia (FH) and/or CVD who fail to achieve optimal LDLC lowering despite being on the best tolerated SoC therapy. From 2016 to present, there have been new studies which have shed light on PCSK9 inhibitor's pharmaco-economics, its efficacy and safety, and cardiovascular outcomes. The efficacy of PCSK9 inhibitors remains consistent across majority of studies, up to four years, with a LDLC reduction from baseline of 59 - 69%. The safety assessment, including cognitive function, in a large group of patients has shown a favorable safety profile [9-14]. A pooled-analysis of prediabetics, and normoglycemics in 10 phase III ODYSSEY clinical trials up to 104 weeks showed no effects on glycemia [15]. Overall, the safety and efficacy of PCSK9 inhibitors has remained minimally concerning and promising, respectively.

The CVD regression and outcomes studies have brought about the question of true benefits to the patients on PCSK9 inhibitors. In the evolocumab regression study using the intravascular ultrasound, it was shown that there was a significant percent and total atheroma volume reduction with a reduction in LDLC to 36.6 mg/dl in evolocumab plus statin (EVO) versus 93.0 mg/dl placebo plus statin group [16]. The atheroma volume reduction occurred in 64.3% of patients in EVO group and in 80% of patients in the same group whose LDLC was < 70 mg/dl. In the cardiovascular outcomes study done in previous CVD patients on evolocumab with a median follow-up of 2.2 years, a reduction of 15 - 27% was found in the CVD endpoints [17]. Given the substantial LDLC decreases, the percent decrease in CVD endpoints may be disappointing, but a longer follow-up period of > 2 years is needed to get a better assessment of the CVD outcomes. Furthermore, the alirocumab CVD outcomes and regression study results are still pending.

The cost of PCSK9 inhibitors is ~$14,000 - 14,600 per patient per year, and this price tag has raised questions on its cost versus the benefits value. Few studies, using various health-economics models, have suggested that the PCSK9 inhibitor's prices should be reduced to $4,250-4,536 at $100,000 per quality-adjusted life years (QALY) so that the payors may possibly get return on their investment (ROI) [18,19]. Fonarow GC., *et al*. suggested that in the evolocumab patients with CVD and LDLC of 70 mg/dl, with an annual event rate of 6.4/100 patient years, to achieve a threshold of $150,000 per QALY, the annual net price of PCSK9 inhibitors should be adjusted to $9669 [20]. In a case-by-case study of PCSK9 inhibitors costs (~$14,000 - 14,600/year) to CVD benefits in 61 CVD patients, it was found that net costs/patient/year would have been ~$7,000 in the past 10 years on PCSK9 therapy with an assumption of 50% CVD reduction [21].

Furthermore, in the future and at current health-care costs, if the CVD patient were to be on 10-years of PCSK9 therapy and there was a 50% CVD risk reduction, net costs/patient/year would be $12,459 [21]. Overall, as presented above on case-by-case basis, PCSK9 inhibitor's net cost/patient/year will be below $50,000 per QALY [21]. After assessing recent pharmaco-economic studies on PCSK9 inhibitors, at its current price, it still remains debatable whether it is a cost-effective therapy.

Bibliography

1. CDC, *Underlying Cause of Death 1999-2013 on CDC WONDER Online Database. Data are from the Multiple Cause of Death Files, 1999-2013, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. (2015)*.

2. Mozaffarian D., *et al*. "Heart disease and stroke statistics--2015 update: a report from the American Heart Association". *Circulation* 131.4 (2015): e29-e322.

3. Glueck CJ., *et al*. "Vitamin D deficiency, myositis-myalgia, and reversible statin intolerance". *Current Medical Research and Opinion* 27.9 (2011): 1683-1690.

4. Hsia SH., *et al*. "Differences in cholesterol management among states in relation to health insurance and race/ethnicity across the United States". *Journal of Clinical Lipidology* 7.6 (2013): 675-682.

5. Khayznikov M., *et al*. "Statin Intolerance Because of Myalgia, Myositis, Myopathy, or Myonecrosis Can in Most Cases be Safely Resolved by Vitamin D Supplementation". *North American Journal of Medical Sciences* 7.3 (2015): 86-93.

6. Mann D., *et al*. "Trends in statin use and low-density lipoprotein cholesterol levels among US adults: impact of the 2001 National Cholesterol Education Program guidelines". *Annals of Pharmacotherapy* 42.9 (2008): 1208-1215.

7. Waters DD., *et al*. "Lipid treatment assessment project 2: a multinational survey to evaluate the proportion of patients achieving low-density lipoprotein cholesterol goals". *Circulation* 120.1 (2009): 28-34.

8. Glueck CJ., *et al*. "Eligibility for PCSK9 treatment in 734 Hypercholesterolemic patients referred to a regional cholesterol treatment center with LDL cholesterol >/= 70 mg/dl despite maximal tolerated cholesterol lowering therapy". *Lipids in Health and Disease* 15 (2016): 55.

9. El Shahawy M., *et al*. "Efficacy and Safety of Alirocumab Versus Ezetimibe Over 2 Years (from ODYSSEY COMBO II)". *American Journal of Cardiology* 120.6 (2017): 931-939.

10. Giugliano RP., *et al*. "Cognitive Function in a Randomized Trial of Evolocumab". *New England Journal of Medicine* 377.7 (2017): 633-643.

11. Hirayama A., *et al*. "One-Year Efficacy and Safety of Evolocumab in Japanese Patients- A Pooled Analysis from the Open-Label Extension OSLER Studies". *Circulation Journal* 81.7 (2017): 1029-1035.

12. Koren MJ., *et al*. "Long-term Low-Density Lipoprotein Cholesterol-Lowering Efficacy, Persistence, and Safety of Evolocumab in Treatment of Hypercholesterolemia: Results Up to 4 Years from the Open-Label OSLER-1 Extension Study". *JAMA Cardiology* 2.6 (2017): 598-607.

13. Shah P., *et al*. "Efficacy, safety, Low density lipoprotein cholesterol lowering, and calculated 10-year cardiovascular risk reduction of alirocumab and evolocumab in addition to maximal tolerated cholesterol lowering therapy: a post-commercialization study". *Lipids in Health and Disease* 16.1 (2017): 19.

14. Toth PP., *et al*. "Pooled Safety Analysis of Evolocumab in Over 6000 Patients From Double-Blind and Open-Label Extension Studies". *Circulation* 135.19 (2017): 1819-1831.

15. Leiter LA., *et al*. "Lipid-lowering efficacy and safety of alirocumab in patients with or without diabetes: A sub-analysis of ODYSSEY COMBO II". *Diabetes, Obesity and Metabolism* 19.7 (2017): 989-996.

16. Nicholls SJ., *et a*l. "Effect of Evolocumab on Progression of Coronary Disease in Statin-Treated Patients: The GLAGOV Randomized Clinical Trial." *JAMA* 316.22 (2016): 2373-2384.

17. Sabatine MS., *et al*. "Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease." *The New England Journal of Medicine*, 376.18 (2017): 1713-1722.

18. Arrieta A., *et al*. "Economic Evaluation of PCSK9 Inhibitors in Reducing Cardiovascular Risk from Health System and Private Payer Perspectives." *PLoS One* 12.1 (2017): e0169761.

19. Kazi DS., *et al.* "Cost-effectiveness of PCSK9 Inhibitor Therapy-Reply." *JAMA* 316.20 (2016): 2152.

20. Fonarow GC., et al. "Cost-effectiveness of Evolocumab Therapy for Reducing Cardiovascular Events in Patients With Atherosclerotic Cardiovascular Disease." *JAMA Cardiol* (2017).

21. Shah P., *et al*. "Pharmacoeconomics of PCSK9 inhibitors in 103 hypercholesterolemic patients referred for diagnosis and treatment to a cholesterol treatment center." *Lipids in Health and Disease* 15.1 (2016): 132.

Volume 1 Issue 2 September 2017