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

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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
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