[EL 1; NE]). The ODYSSEY OUTCOMES trial is ongoing to determine the efficacy of the alirocumab for the reduction of the same composite cardiovascular events outcome (640 [EL 4; NE]. Additional PCSK9 inhibitor formulations, including an annual vaccine and oral version, are currently in development (641 [EL 4; NE]).

Imaging Studies

The Global Assessment of Plaque Regression With a PCSK9 Antibody as Measured by Intravascular Ultrasound (GLAGOV) study compared treatment with the PCSK9 inhibitor evolocumab (420 mg monthly subcutaneous injection) and placebo over 76 weeks in order to evaluate the effect of PCSK9 inhibition on coronary atherosclerosis in statin-treated individuals (334 [EL 1; RCT]). Percent atheroma volume (PAV) change was measured via intravascular ultrasound at baseline and again at 78 weeks in 968 study participants. The results showed that individuals taking evolocumab had PAV decreased by 0.95% (P<.001) compared with a PAV increase of 0.05% in the placebo group (between-group difference, –1.0% [95% CI, –1.8% to –0.64%]; P<.001). Similarly, total atheroma volume was not significantly changed from baseline in the placebo group (–0.9 mm^3, P = .45), but decreased by 5.8 mm^3 in the evolocumab group (P<.001). In addition, more evolocumab-treated individuals exhibited PAV regression compared with placebo (64.3% vs. 47.3%, P<.001).

Other options

Two new treatment options for individuals with HoFH are lomitapide (MTP inhibitor) and mipomerson (antisense apolipoprotein B oligonucleotide). These new agents, which may be associated with hepatotoxicity, are available with restricted distribution (520 [EL 4; NE]; 562 [EL 4; NE]) and may be useful for individuals with HoFH not responsive to PCSK9 therapy.

Special Considerations: Drug Therapy in Women

In light of the diagnostic challenges that present when trying to identify ASVCD in women, prevention and treatment of dyslipidemia are essential considerations in this population. However, efforts to manage dyslipidemia in women have often been inadequate. While lipid-lowering treatments are used routinely for men, they are frequently underprescribed for women (267 [EL 1; MRCT]). Furthermore, although lowering LDL-C significantly reduces ASVCD risk in women, the unique roles of hormonal change over the lifetime of a woman, HDL-C, and TG must also be addressed.

For women at high risk, the following treatment approach is recommended (37 [EL 4; NE]):

- lipid-lowering pharmacotherapy (preferably with a statin) regardless of LDL-C level;
- niacin or fibrate therapy in the presence of low HDL-C or elevated non-HDL-C; and
- a diet low in saturated fat (<7%), cholesterol (<200 mg/day), and *trans* fat.

For women at intermediate risk, the following treatment approach is recommended (37 [EL 4; NE]):

- lipid-lowering pharmacotherapy (preferably with a statin) in the presence of an LDL-C level greater than 130 mg/dL; and
- niacin or fibrate therapy in the presence of low HDL-C, or elevated non-HDL-C after LDL-C goal is reached.

Supporting Data: Statins

Most early studies of the relationship between dyslipidemia and ASCVD included only middle-aged men (267 [EL 1; MRCT]). Although few clinical trials have evaluated lipid-lowering in women specifically (162 [EL 4; NE]), men and women have been equally represented in most major statin trials (267 [EL 1; MRCT]). In a meta-analysis of 5 randomized, placebo-controlled primary and secondary prevention trials (N = 30,817) to assess the impact of statins on ASCVD development and mortality, statins significantly lowered LDL-C and similarly reduced the risk of major coronary events, coronary mortality, and all-cause mortality in men and women (267 [EL 1; MRCT]). The HPS, a randomized, placebo-controlled trial of simvastatin to reduce LDL-C, reported similar findings in a population of 20,536 men and women with ASCVD, other occlusive arterial disease, or diabetes (25 [EL 1; RCT]). Although sex subgroup analyses were not performed, HPS investigators found no evidence for an LDL-C threshold below which further lowering did not reduce risk (25 [EL 1; RCT]).

The JUPITER study was a primary prevention trial that enrolled a large number of women (N = 6,800) with LDL-C levels less than 130 mg/dL and hsCRP levels 2 mg/L or greater. JUPITER found that women taking rosuvastatin 20 mg daily versus placebo showed a 46% reduction in cardiovascular events, very similar to the reduction in men of 42% (320 [EL 1; RCT]). A reduction in all-cause mortality in women has not yet been demonstrated in a randomized controlled trial.

Supporting Data: Niacin and Fibrates

In numerous studies, both niacin and fibrates have been shown to favorably affect all components that characterize atherogenic dyslipidemia (low HDL-C, elevated TG, and increased numbers of small dense LDL-C particles) (10 [EL 4; NE]). Treatment with these drugs also produces a moderate decrease in ASCVD risk (10 [EL 4; NE]).

Several trials of the lipid-lowering effects of extended release niacin have specifically evaluated cholesterol-lowering efficacy in women. In a meta-analysis of 5 trials (N = 432), extended-release niacin improved HDL-C, LDL-C,