Weight loss drug does not increase cardiovascular events

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A weight loss drug does not increase cardiovascular events, according to late breaking results from the CAMELLIA-TIMI 61 trial presented today in a Hot Line Session at ESC Congress and published in the *New England Journal of Medicine*.

Lorcaserin is an appetite suppressant, increasing the sense of fullness after a meal and reducing hunger before meals. It is not approved as a weight loss drug in Europe. The European Medicines Agency has expressed concerns about the potential risk of tumours based on animal data, psychiatric disorders including depression, and problems with heart valves.

The US Food and Drug Administration (FDA) in June 2012 approved the medication for weight loss in overweight adults with a body mass index (BMI) of 30 kg/m2 or greater, or with a BMI of 27 kg/m2 or greater and at least one weight-related health condition such as high blood pressure, type 2 diabetes, or high cholesterol. As with all weight loss agents, the FDA's approval was contingent on postmarketing studies assessing the risk for major adverse cardiovascular events.

The CAMELLIA-TIMI 61 trial was conducted as part of the FDA's postmarketing requirement. The trial examined the safety and efficacy of the drug with regard to major adverse cardiovascular events (MACE) and progression to diabetes in overweight or obese individuals with, or at risk for, cardiovascular disease.

The trial enrolled 12,000 adults from 473 centres in eight countries between January 2014 and November 2015. Participants had a BMI of at least 27 kg/m2 and either 1) established cardiovascular disease3 (with or without diabetes) or 2) diabetes and at least one other cardiovascular risk factor.4 Participants were randomly allocated in a 1:1 ratio to lorcaserin (10 mg twice a day) or matching placebo. All participants were advised to exercise and eat healthily.

The primary safety endpoint was noninferiority of the drug compared to placebo for MACE (cardiovascular death, myocardial infarction, or stroke) after 460 events had occurred. If the safety endpoint was met, the trial would proceed to completion and assess the primary efficacy endpoint of superiority of the drug for MACE plus hospitalisation for unstable angina, heart failure, or any coronary revascularisation. Secondary endpoints included delay or prevention of conversion to type 2 diabetes in those with pre-diabetes at baseline, and the effect on weight, heart rate, blood pressure, lipids, and blood sugar.

The average age of participants was 64 years, 64% were male, and the median BMI was 35 kg/m2. Three-quarters (8,958; 75%) had a history of at least one established cardiovascular disease: 8,153 (68%) had coronary artery disease, 1,129 (9.4%) had cerebrovascular disease, and 657 (5.5%) had peripheral artery disease. More than half (57%) had diabetes, 90% had hypertension, 94% had hyperlipidaemia, and 20% had renal insufficiency.

The interim analysis after 460 events showed that the trial met its primary safety objective. At study completion with a median follow-up of 3.3 years, MACE occurred in 6.1% of those taking lorcaserin and 6.2% of those on placebo, demonstrating noninferiority (p