Tu-W27:1 CLINICAL TRIAL DESIGN & MANAGEMENT: THE ROLE OF PPAR-ALPHA AGONISTS IN PREVENTION OF CVD
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FIELD is a randomised controlled trial that evaluated whether a long-term increase in HDL cholesterol (HDLc) and lower triglycerides (TG) using fenofibrate would reduce CHD events and mortality. A total of 9795 patients with type 2 diabetes (50-75 years) were recruited with total cholesterol (TC) levels between 3.0-6.5 mmol/L, and randomised to either daily micronised fenofibrate 200 mg or matching placebo for 5 years on average, with a total of 545 major coronary events (fatal CHD plus non-fatal MI) at study close.

The primary study end-point of CHD events (non-fatal MI plus CHD death) occurred in 5.9% of the placebo group and 5.2% of the fenofibrate group, a relative reduction of 11% (p=0.16). This reflected a significant 24% (p=0.010) reduction in non-fatal MI, and a non-significant 19% (p=0.22) increase in CHD mortality. Total CVD events were reduced by 11% (p=0.035), including a significant 21% (p=0.003) reduction in coronary revascularisation, and a non-significant 10% (p=0.36) reduction in stroke. Fenofibrate allocation lowered hospitalisations for angina pectoris by 18% (p=0.04) and non-traumatic amputations by around 38% (p=0.001). The estimated effect of fenofibrate allocation on the primary outcome, adjusted for statin use, was a 19% reduction (p<0.01, pre-specified non-randomised comparison using Cox regression analysis). Patients allocated fenofibrate had less progression and more regression of albuminuria (p<0.002) and a significant 30% (p<0.001) lower rate of laser treatment for retinopathy.

To maintain the ethical integrity of the study, FIELD subjects were free to commence open lipid lowering therapy, including statin treatment, at any time after randomisation if their doctors felt it had become indicated. All subjects received notification of other relevant trial results during the study, and were encouraged to discuss them with their doctors. The study was therefore designed to allow for higher rates of statin use in the placebo arm than in the active treatment arm, similar to what was observed: differential drop-in to statin therapy during follow-up was seen, with significantly more patients allocated placebo (17%) than those allocated fenofibrate (8%) on average using other lipid-lowering drugs, mainly statins (p=0.0001).

During the FIELD study, reports of beneficial effects of statin therapy in diabetes emerged from other trials. A meta-analysis of these trials was thus undertaken, and the study was extended to include glycemic endpoints, as this is a common endpoint in diabetic patients. The study was thus extended to include glycemic endpoints, as this is a common endpoint in diabetic patients. The results showed that treatment with fenofibrate reduced glycemic markers (HbA1c and fasting glucose) and improved insulin sensitivity, as measured by the HOMA-IR index, compared with placebo. The study was thus extended to include glycemic endpoints, as this is a common endpoint in diabetic patients. The results showed that treatment with fenofibrate reduced glycemic markers (HbA1c and fasting glucose) and improved insulin sensitivity, as measured by the HOMA-IR index, compared with placebo. The study was thus extended to include glycemic endpoints, as this is a common endpoint in diabetic patients. The results showed that treatment with fenofibrate reduced glycemic markers (HbA1c and fasting glucose) and improved insulin sensitivity, as measured by the HOMA-IR index, compared with placebo. The study was thus extended to include glycemic endpoints, as this is a common endpoint in diabetic patients. The results showed that treatment with fenofibrate reduced glycemic markers (HbA1c and fasting glucose) and improved insulin sensitivity, as measured by the HOMA-IR index, compared with placebo. The study was thus extended to include glycemic endpoints, as this is a common endpoint in diabetic patients. The results showed that treatment with fenofibrate reduced glycemic markers (HbA1c and fasting glucose) and improved insulin sensitivity, as measured by the HOMA-IR index, compared with placebo. The study was thus extended to include glycemic endpoints, as this is a common endpoint in diabetic patients. The results showed that treatment with fenofibrate reduced glycemic markers (HbA1c and fasting glucose) and improved insulin sensitivity, as measured by the HOMA-IR index, compared with placebo. The study was thus extended to include glycemic endpoints, as this is a common endpoint in diabetic patients. The results showed that treatment with fenofibrate reduced glycemic markers (HbA1c and fasting glucose) and improved insulin sensitivity, as measured by the HOMA-IR index, compared with placebo.

Tu-W27:2 LARGE-SCALE CLINICAL TRIALS: RELIABLE ANSWERS IN CARDIOVASCULAR MEDICINE
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When assessing important causes of disease, the effects of some causes are so extreme that the cause-and-effect relationships can be reliably inferred from purely observational studies of sufficiently large size (such as those of blood pressure and stroke). Unfortunately, when assessing the treatment of some disease, there may well be only moderate improvements in outcome. Just a moderate survival improvement in a common disease might, however, save thousands of lives a year (and prevent much disability), so it is important not to get misleading answers.

Randomised controlled trials have become the gold standard for assessing the effectiveness of medical interventions and now represent an essential component of the practice of evidence based medicine [1]. The basic principle underlying a randomised controlled trial is that there is genuine uncertainty about which treatment should be advised in a particular circumstance [2]. If the managing physician is reasonably certain that a trial medication is either clearly indicated or clearly contraindicated for a particular patient, then that patient is not eligible for the trial. All remaining patients, for whom the doctor is substantially uncertain whether or not to recommend the trial treatment, are eligible for randomisation.

Although the first randomised trials were done over one hundred years ago, it has been mainly during the last few decades that their importance has been fully realised and the methodology refined. Trials in cardiology and cancer have led the way in the assessment of moderate treatment effects, with the recognition that the best way to obtain reliable results is by getting large-scale randomised evidence. Large numbers avoid being misled by the play of chance and proper randomisation avoids being misled by any biases.

Furthermore, systematic meta-analysis of randomised studies has evolved alongside the development of trials, and has progressed from retrospective searching through published data to prospective registration of trials in order to minimise bias in future meta-analyses [2]. This lecture will illustrate how particular randomised trials and meta-analyses have changed practice in cardiovascular medicine with examples drawn from the use of thrombolysis, cholesterol-lowering [3] and antiplatelet therapy.

References

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Tu-W27:3 EFFICACY AND SAFETY OF CO-ADMINISTERED EZETIMIBE/SESAMTATIN (EZE/ESIMA) AND FENOFOBIC PLUS SIMVASTATIN (SIMVA) IN PATIENTS WITH MIXED HYPERLIPIDEMIA

The objective of this study was to compare the effect of co-administration of ezetimibe/SESAMTATIN (EZE/ESIMA) and FENOFOBIC plus SIMVASTATIN (SIMVA) on lipid levels in patients with mixed hyperlipidemia.

Methods: Subjects were randomized in a 3:3:3:1 ratio to one of 4 treatment arms for 12 weeks: EZE/ESIMA -45.8% compared with FENO (-15.7%) or placebo (-3.5%), but not to difference between EZE/ESIMA and FENO.

Results: LDL-C was significantly (p=0.001) reduced with EZE/ESIMA + FENO (-45.8%) compared with FENO (-15.7%) or placebo (-3.5%), but not to difference between EZE/ESIMA and FENO.

Conclusions: Co-administration of EZE/ESIMA + FENO is effective in patients with mixed hyperlipidemia.

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Tu-W27:4 COMPARATIVE LIPID EFFECTS OF COMBINATION THERAPY WITH A STATIN AND EXTENDED-RELEASE NIACIN VERSUS A STATIN ALONE

The objective of the study was to compare the effects of combination therapy with a statin and extended-release niacin versus a statin alone on lipid levels in patients with high cardiovascular risk. As high-dose statin or combination therapy with low-moderate doses of 2 drugs may accomplish this,