“Drug Development for Cardiometabolic Disorders – Focusing on the Patient”

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The cardiometabolic syndrome has become a major public health problem worldwide because of its increasing prevalence. Effective treatment of the cardiometabolic syndrome depends on understanding of the underlying molecular mechanisms of key components of this disorder, such as insulin resistance. Large prospective cardiovascular outcome trials (CVOTs) have redefined the benefit of the newer classes of glucose-lowering drugs such as glucagon-like peptide-1 receptor agonists (GLP-1RAs) and sodium/glucose co-transporter-2 (SGLT-2) inhibitors even in non-diabetic patients with cardiovascular diseases. The combination of a GLP-1 agonist and an SGLT2-inhibitor has additive effects on lowering HbA1c and systolic blood pressure, body weight and cardiac risk. In recent years, technical advances have enabled efforts to further understand the complexity of systemic metabolic crosstalk and its underlying mechanisms. Systemic inflammation, oxidative stress, excessive rates of fatty acid release into the bloodstream and alterations in gut microbiome, bioactive lipids, liver function, adipose tissue fatty acid and adipokine metabolism, collectively contribute to multi-organ insulin resistance and pathogenesis of cardiometabolic syndrome. In addition to GLP-1 agonists, SGLT2-inhibitors, dipeptidyl peptidase-4 (DPP-4) inhibitors and metformin, several therapies to treat cardiometabolic disorders are under development. Immunotherapies target cells of the innate and adaptive immunity, cytokines, chemokines and their receptors. Other treatments target altered gut microbiome products and bioactive lipids as inducers of inflammation. Such therapies may complement diet and exercise and existing treatments for cardiometabolic syndrome (such as lipid lowering drugs). With emerging insight into disease mechanisms and new drug options for prevention and treatment of risk factors of cardiometabolic disease, there is need to focus on the patient to treat cardiometabolic syndrome within collaborative interdisciplinary teams of primary care physicians, endocrinologists and cardiologists. After completing this activity, the learners will be able to discuss most recent drugs in development for treatment of cardiometabolic disorders.