lipoproteins, lowers LDL-cholesterol on average by 28%. This compound, mipomersen, is injected weekly subcutaneously.

A second agent that inhibits the formation of apoB-containing lipoproteins in liver and gut is an inhibitor of microsomal triglyceride transfer protein (MTP). This compound lowered LDL-cholesterol by 50% in patients with homozygous familial hypercholesterolemia. A side effect of both classes of drugs is the accumulation of fat in the liver.

Proprotein convertase subtilisin/kexin type 9 serine protease (PCSK9) is a protease that induces degradation of LDL-receptors. Statins increase the concentration of PCSK9, thereby attenuating their LDL-cholesterol–lowering effect. Combining statins with inhibitors of PCSK9 has proven to be very effective in LDL-cholesterol lowering: injection of monoclonal antibodies to PCSK9 biweekly on top of maximal statin therapy lowered LDL-cholesterol by an extra 60%. If long-term treatment with these antibodies proves to be safe, this will change the treatment of patients with severe familial hypercholesterolemia. The near future years will also provide the final verdict whether raising HDL-cholesterol by means of inhibition of cholesteryl ester transfer protein (CETP) will be of any benefit.
**Disclosure of Interest:** A. Stalenhoef: consultant for Genzyme.

## ANTI-TNF IN OCULAR DISEASES

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**Summary:** Tumor necrosis factor-alpha (TNF-alpha) plays a role in the process of intraocular inflammation that is the cause that the use of TNF-alpha inhibitor agents is worldwide spread to treat different form of intraocular inflammations. In ophthalmology, anti-TNFs are applied in the treatment of uveitis and immune-vasculitis. The number of TNF-alpha inhibitors is increasing despite the fact that such kind of medication can be used "off-label" in the treatment of inflammations. TNF-alpha inhibitors are effective at first in that form of uveitis that is connected with systemic immunologic diseases: Mo. Behcet, rheumatoid arthritis (especially with juvenile idiopathic arthritis), Mo. Chrohn, Wegener granulomatosis, autoimmune diseases (lupus-like syndrome [LLS]). In cases of vasculitis, it can be used in giant cell arthritis, Takayasu arthritis, primary angiitis of the central nervous system, and Cogan syndrome. Anti–TNF-alpha also are effective in cases of autoimmune, noninfectious diseases of the eye: Mo. Harada, sympathetic ophthalmia. The most frequent anti–TNF-alpha that are used are etanercept, adalimumab, and infliximab. There are 3 other TNF-alpha inhibitors that are less widespread yet: golimumab, certolizumab, and tocilizumab. The advantage of the TNF-alpha inhibitors are that they have fewer side effects as corticosteroids and immunsuppressives but are more effective. Their only disadvantage: they are very expensive.
**Disclosure of Interest:** None declared.

## NEW TARGETS IN THE TREATMENT OF RHEUMATOID ARTHRITIS

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**Summary:** With the increasing needs for better outcome, function, and quality of life in arthritides and autoimmune diseases, we have increasing amounts of information on the major pathogenetic pathways underlying rheumatoid arthritis (RA), spondyloarthritides (SpA), lupus, scleroderma, and other rheumatic diseases. After decades of reliance on largely empiric approaches in the therapy of most of these diseases, the introduction of TNF-alpha–blocking agents in the late 1990s revolutionized the therapy of rheumatoid arthritis (RA), other arthritides, and connective tissue diseases. Numerous pathways have been targeted and almost 10 biologics have been registered to treat RA, SpA, and lupus. In addition to anti-TNF biologics, further therapies such as anti–IL-6R, CTLA4-inhibitor, or anti-CD20 agents along with several new experimental approaches have since emerged out of improved understanding of the immunopathogenesis. In addition to biologics, the first small molecular targeted therapies, mostly tyrosine kinase inhibitors, have been developed. Most therapies primarily intended for RA, however, have failed to show or have shown only marginal benefit in other autoimmune rheumatic diseases such as lupus, scleroderma, polymyositis, or vasculitides, all of which continue to have a high unmet medical need. Challenges to identify novel drug candidates and to conduct successful clinical studies for such diseases include the different and highly complex immunopathology as well as clinical trial–related issues (eg, the lack of validated, sensitive, and reliable end points). Recently, promising new therapeutic approaches have emerged. This presentation highlights these advances in autoimmune rheumatic diseases.
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## WHAT IS THE ADDITIONAL VALUE OF ELECTRONIC MEDICAL RECORDS FOR DRUG SAFETY SIGNAL DETECTION? THE EXPERIENCE OF EU-ADR PROJECT

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**Summary:** In the last decades, both regulators and manufacturers have used computerized data-mining techniques on reports of adverse drug reactions from both health care practitioners and consumers to detect drug safety signals, that is, unknown or incompletely documented drug-event associations. The signal detection using data from spontaneous reporting system (SRS) databases is negatively influenced however by under- and selective reporting as well as missing denominators. To overcome some of these shortcomings, in the last 5 years, a number of ongoing international initiatives (Sentinel, Protect, OMOP, EU-ADR) has started to explore longitudinal observational health care data, including electronic health records (EHRs), as an additional source for signal detection. The ultimate goal of the EU-ADR project was to develop an innovative, computerized system for the automatic detection of drug safety signals. Using a database network of 7 databases from 3 countries covering ~30 million European patients, EU-ADR developed new methodologies for signal detection and compared the performance (both in terms of precision and timing) of signal detection using either EHRs or SRS through validation sets. Main findings of the project are that EU-ADR is not powered enough to monitor infrequently used/captured drugs and associations regarding very rare events, while SRS may be more efficient. On the other hand, EU-ADR has the most power for signal detection concerning events with higher incidences rate and not commonly reported to SRS. In this presentation, the overview of methodology and results from EU-ADR will be presented and the potentially additional value of exploring EHRs in the context of pharmacovigilance will be discussed.