

**NEW STRATEGIES
FOR REDUCING CARDIOVASCULAR RISK:
FROM OLD RISK FACTORS TO
EMERGING DIAGNOSTIC AND
THERAPEUTIC OPPORTUNITIES**
Naples (Italy), February 09-011, 2017
Highlights

Introduction



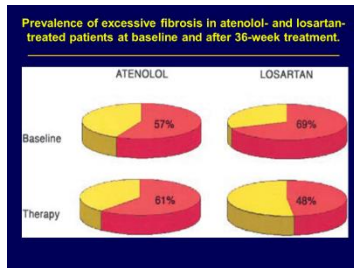
Prof. Filardi, chairman of the symposium, opened the congress, by highlighting the high scientific level of this meeting. This congress focused on the new strategies for reducing the cardiovascular risk, through the presentation of very updated data on pathophysiology, biomarkers, imaging, new but also “old” drugs accounting for quite new effects, Mediterranean diet and life style behaviour. More than 100 cardiologists and young physicians attended the symposium, coming from Italy and other countries from Europe.

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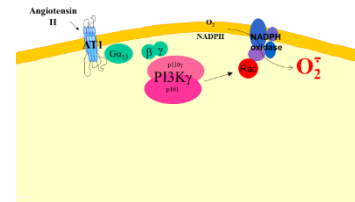
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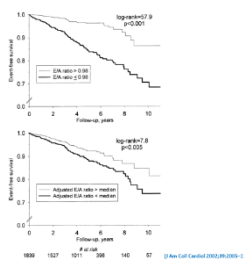
New insights in the pathophysiology of hypertension



Prof. Trimarco from Naples (IT), spoke about the pathophysiology of hypertension and its new insights. The speaker went deeper in his talk, by presenting very interesting and impressive data about the effects of the GPCR-activated phosphoinositide 3-kinase PI3K γ factor. Speaking about this enzyme, Prof. Trimarco pointed out that its effects depend on the AT1 receptor-



angiotensin II activation and it is responsible for the superoxide production and the onset of cardiac hypertrophy. The speaker highlighted that the ACE-inhibitors are unable to inhibit the PI3K γ activity and presented some data given by animal studies, showing



that the PI3K $\gamma^{+/+}$ mice, but not the PI3K $\gamma^{-/-}$ ones are exposed to the onset of cardiac hypertrophy and remodelling due to the constriction of the Transverse Aorta. Finally, in order to find a correlation between animal and human data, Prof. Trimarco spoke about the effect of the diastolic dysfunction due to cardiac hypertrophy and remodelling on the event-free survival in hypertensive patients.

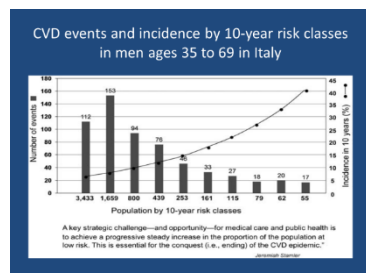
- What's about the survival rates during pressure overload in PI3K $\gamma^{-/-}$ and PI3K $\gamma^{+/+}$ mice?
- What's about the left ventricular growth during chronic pressure overload based on the data presented by the speaker?
- What is the prevalence of excessive fibrosis in atenolol and losartan treated patients?
- What is the mechanism leading to the superoxide production mediated by the phosphoinositide 3-kinase enzyme?
- What's about the effect of the diastolic dysfunction due to cardiac hypertrophy and remodelling on the event-free survival in hypertensive patients, based on the data presented by the speaker?

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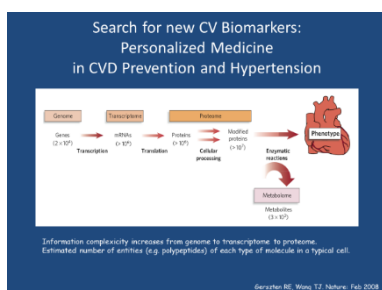
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Refining CV risk in asymptomatic subjects: the role of biomarkers



The role of biomarkers in refining CV risk in asymptomatic subjects was the topic at the core of the lecture discussed by Prof. Volpe. At the beginning of his talk the speaker, coming from Rome (IT), presented very interesting data derived from clinical studies on the CV incidence in general population. Going deeper in his presentation, Prof. Volpe highlighted that from a population-based approach point of view the CV incidence is higher in low-medium risk classes, the opposite of the individual-based approach. From a risk stratification point of view, the presence of more than one risk factor even at low risk-level is related to a higher CV risk level, the speaker pointed out. How to detect this risk factors as intermediate endpoints?



With this question the speaker addressed the audience and, in order to find a comprehensive answer, he presented very interesting data on the biomarkers used in CVD diagnosis. Prof. Volpe spoke about TN, BNP, CRP and MAU. Finally, the speaker pointed out that there is the need for developing new biomarkers starting from genome to proteome in order to find a new personalized CVD and hypertension prevention.

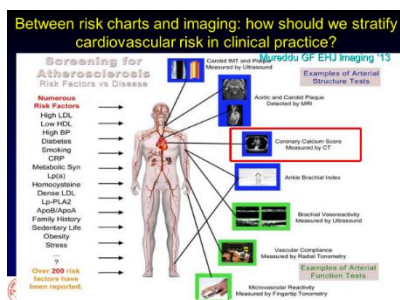
- What's about the search of new biomarkers based on the data presented by the speaker?
- What is the clinical value of the different biomarkers presented by the speaker?
- Which characteristics should a biomarker fulfil to be clinically useful?
- What kind of biomarkers are actually used in CV disease prevention and therapy?
- What's about the residual cardiovascular risk in individuals, based on the BP-lowering treatment from the speaker point of view?
- What's about the global cardiovascular risk assessment based on either Framingham risk score or ESC score in young hypertensive individuals?

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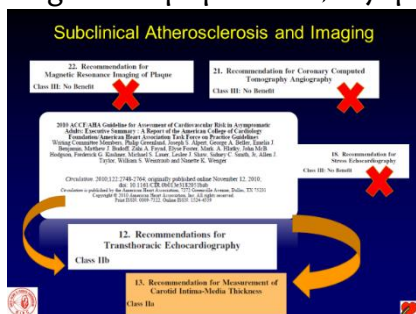
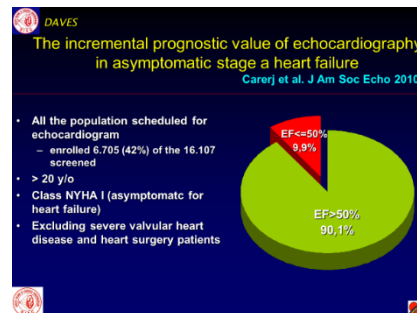
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Subclinical organ damage: the role of imaging



The role of imaging in the diagnosis of the subclinical organ damage was the topic at the core of the lecture discussed by Prof. Colonna. The speaker, coming from Bari (IT), introduced his talk by presenting data on the European Guidelines on cardiovascular disease prevention in clinical practice, by highlighting the need for a shift from a population based-prevention strategy to an individual based-prevention one. With the intention to find a link between risk charts and imaging, for a better identification of

patients' risk level, the speaker presented very interesting data on the main echocardiographic techniques like B-mode ultrasonography or the Magnetic resonance imaging or the 2D/M-Mode echocardiography. More in particular Prof. Colonna talked about echocardiography as a very useful tool for a prognostic evaluation of the presence of asymptomatic HF in general population, by presenting interesting data on the



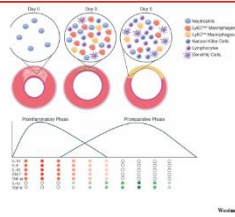
echo parameters available for the detection of diastolic dysfunction. In the second part of his lecture, the speaker talked about the relationship between atherosclerosis and CVD from the echocardiographic point of view, by presenting many data on QIMT and the capacity to measure the treatment effect. In conclusion, Prof. Colonna pointed out that the imaging methods may be considered as risk modifiers especially in those patients at a risk level around the decisional thresholds.

- What are the “Very high risk” category patients based on the 2016 ESC GL?
- How to stratify the cardiovascular risk in clinical practice, based on the data presented by the speaker?
- What is the incremental prognostic value of echocardiography in asymptomatic stage A HF patients' evaluation?
- What is the role of echocardiography and Imaging in HF patients from the speaker point of view?
- What is the clinical utility of DTI in the estimation of the left ventricular filling pressures?
- What is the prevalence of LV diastolic dysfunction in the community, based on the data presented by the speaker?
- What's about the role of Imaging in the detection of subclinical atherosclerosis?

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Epicardial adipose tissue: an emerging opportunity for risk stratification

Inflammation and LV remodeling after MI

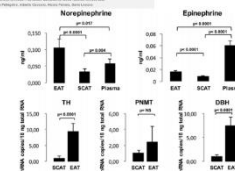


Workshop: ESC/EACV 2014

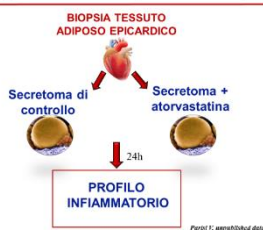
The Epicardial adipose tissue as an emerging opportunity for risk stratification was the topic of Prof. Leosco presentation. The speaker, coming from Naples (IT), talked about the local and the systemic effects of the epicardial fat. More in particular Prof. Leosco presented very interesting and impressive data on the correlation between epicardial adipose tissue and CAD, through the onset of Inflammation and atherosclerosis. Inflammation is also at the core of Heart Failure, the speaker pointed out and in order to better explain this correlation, he went deeper in his talk by presenting other data on the central role played by the sympathoadrenal activity and its link with the body fat composition. Higher is the epicardial adipose tissue concentration lower is the cardiac sympathetic innervation state, the speaker highlighted and this condition worsen the HF symptomatology. In the last part of his presentation, the speaker

Circulation Research

Increased Epicardial Adipose Tissue Volume Correlates With Cardiac Sympathetic Denervation in Patients With Heart Failure



Direct Activity of Statins on Epicardial Adipose Tissue



Parisi F, Angelillo GJ et al.

talked about the correlation between EAT, inflammation and aortic stenosis and finally about the role of treatment and more in particular of statins on the reduction of the epicardial adipose tissue. In conclusion, Prof. Leosco pointed out that EAT is involved in the pathogenesis of CAD, HF and aortic stenosis and that statins are able to reduce the EAT levels.

- What are the main local and systemic effects of the epicardial fat from the speaker point of view?
- What is the correlation between inflammation, atherosclerosis and epicardial fat?
- What's about the relationship between inflammation, HF and epicardial fat?
- What's about body fat and the sympathetic activity?
- What are the main results of the ADMIRE-HF trial, based on the data presented by the speaker?
- What is the relationship between epicardial adipose tissue and aortic stenosis from the speaker point of view?
- What is the effect of statins on the epicardial adipose tissue?

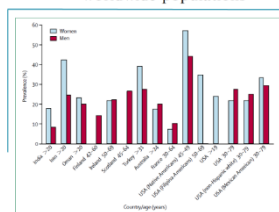
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Metabolic syndrome, insulin resistance and CV risk

The metabolic syndrome: prevalence in worldwide populations

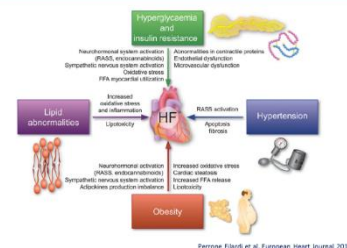


Carron et al. Endocrinol Metab Clin North Am 2004

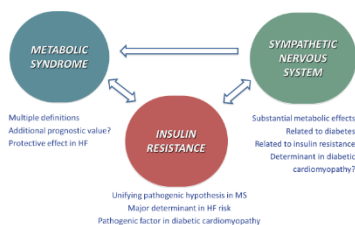
Metabolic syndrome, insulin resistance and CV risk was the topic of Dr. Paolillo presentation. The speaker, coming from Naples (IT), addressed the audience, talking about the main components of the metabolic syndrome, its definition, prevalence in worldwide population, total CVD mortality and finally on cardiovascular risk. Going deeper in her talk Dr. Paolillo spoke

about the role of the metabolic syndrome in the onset of Heart Failure, starting from the so called “obesity paradox” in patients affected by heart failure. More in particular the speaker talked about the correlation between metabolic syndrome, insulin resistance and the sympathetic nervous system, by highlighting that the presence of insulin resistance accounts for more than 90% of patients affected by metabolic syndrome and HF and that the sympathetic nervous system is the main factor linking metabolic syndrome and IR in HF patients. In the main part of her talk, Dr. Paolillo presented very interesting data on these correlations. In conclusion, the speaker pointed out that Insulin Resistance can be considered the central mechanism of Metabolic Syndrome and represents a risk factor for the onset of HF.

The role of metabolic syndrome in heart failure



Ferrero Ffardi et al. European Heart Journal 2015



METABOLIC SYNDROME

Multiple definitions
Additional prognostic value?
Protective effect in HF

SYMPATHETIC NERVOUS SYSTEM

Substantial metabolic effects
Related to diabetes
Related to insulin resistance
Determinant in diabetic cardiomyopathy?

INSULIN RESISTANCE

Unifying pathogenic hypothesis in MS
Major determinant in HF risk
Pathogenic factor in diabetic cardiomyopathy

- What’s about the effect of Metformin on insulin resistance and exercise parameters in HF patients?
- What is the main relationship between Insulin Resistance and HF?
- What’s about the sympathetic nervous activity in IR and non-IR heart failure patients?
- Is the Metabolic Syndrome a sympathetic disease?
- What’s about the pathogenesis of CVD in insulin resistant patients?

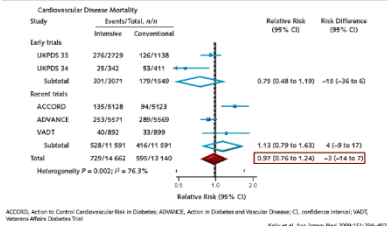
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How low glycated haemoglobin should be in the high-risk patients?

Meta-analysis of ACCORD, ADVANCE, VADT and UKPDS suggests no significant difference in CV mortality

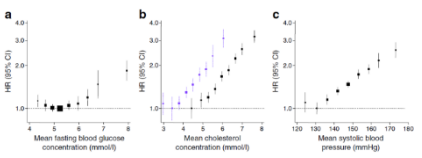


ACCORD, Action to Control Cardiovascular Risk in Diabetes; ADVANCE, Action in Diabetes and vascular Diseases; CI, confidence interval; VADT, Veterans Affairs Diabetes Trial; Kelly et al. Ann Intern Med 2009;151:394-403

Prof. Sesti coming from Catanzaro (IT) spoke about glycated haemoglobin and its recommended levels in high-risk patients, by presenting very interesting data on the effects of the intensive glucose lowering treatment in CVD patients related to the CV outcomes and finally on the recommendations of the international guidelines about the glycemic target. Going deeper in his lecture, Prof. Sesti presented many data given by

meta-analyses and clinical trials on the correlation between the intensive glucose control and the CVD risk. More in particular the speaker talked about UKPDS, ACCORD, ADVANCE and VADT results, in order to find a comprehensive answer for explaining the non-satisfactory effect of the intensive glucose control on CV outcomes and

Comparison of HRs for CHD by long-term average concentrations of fasting blood glucose, total (and non-HDL) cholesterol, and systolic blood pressure



FBG concentrations are non-linearly and moderately associated with risk of CHD, total (or non-HDL-) cholesterol levels and systolic blood pressure are more strongly associated with such risk and show a near log-linear relationship

The Emerging Risk Factors Collaboration. Lancet 375:2215-2222, 2010

on the so called "floor effect". In the second part of his lecture, Prof. Sesti, presented data given by the 2016 European Guidelines and the EASD Guidelines on the glycemic target to be reached in diabetic patients for a very effective cardiovascular prevention, by highlighting that HbA1c level could be less than 7% in order to gain additional microvascular benefits as well as macrovascular protection in new-onset diabetic patients affected by CVD.

Personalized Glycemic Targets

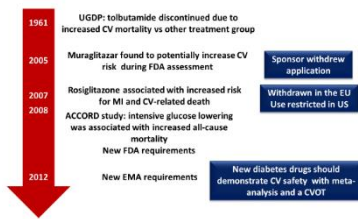
A1c <7.0% (6.5-7.0%)	A1c >7.0% (7.5-8.0%)
<ul style="list-style-type: none"> Short duration of diabetes Long life expectancy No significant cardiovascular disease 	<ul style="list-style-type: none"> Long-standing diabetes Limited life expectancy History of severe hypoglycemia Advanced micro- and macrovascular complications Extensive comorbid conditions Target difficult to attain despite intensive self-management education, and effective doses of multiple glucose-lowering agents, including insulin
<p>May Gain Additional Microvascular Benefit As Well As Macrovascular Protection</p>	

- What are the glycemic recommendations for nonpregnant diabetic adults?
- What's about the 2016 European guidelines recommendations for the managements of diabetic patients with or without CVD?
- What's about the floor effect based on the data presented by the speaker?
- What are the main results of the UKPDS, ACCORD, ADVANCE and VADT meta-analysis about the effect of the intensive glucose control on the CVD risk reduction?

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Anti-diabetic drugs and CV events: what the cardiologist did not expect

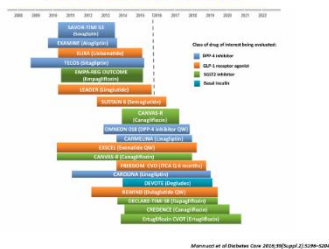
CONTROVERSIAL CV EFFECTS OF GLUCOSE LOWERING DRUGS



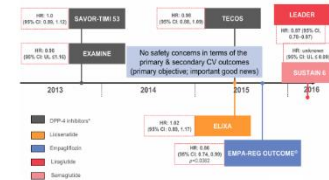
New insights on anti-diabetic drugs and CV events was the topic at the core of Dr. Esposito presentation. The speaker, coming from Naples (IT), presented very interesting data given by clinical studies on the intensive glucose control and the CV outcomes, by highlighting that till now the glucose lowering drugs have presented quite controversial effects on CV prevention and outcomes. Going deeper in his talk, Dr. Esposito talked about the new CV outcomes trials performed with Incretin-based drugs, by presenting many data on the CV effects of DPP-4 inhibitors and GLP-1

receptor agonists, given by the main clinical trials performed with these drugs. In the final part of his presentation, Dr. Esposito spoke about empagliflozin and its effects on CVD outcomes. In conclusion, the speaker pointed out that the new drugs actually under evaluation through the performance of a lot of clinical trials, represent a very interesting opportunity for the cardiovascular disease prevention and treatment in diabetic patients.

FUTURE PERSPECTIVES



CV OUTCOMES TRIALS INCRETIN-BASED THERAPY FOR DIABETES



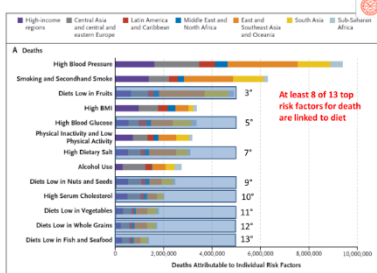
- What are the future perspectives of diabetes from the speaker point of view?
- What is the effect of the intensive glucose control on CV outcomes based on the data presented by the speaker?
- What's about the controversial CV effects of the glucose lowering drugs starting from the studies published in 1961 till the new published studies?
- What are the FDA and EMA Regulatory Requirements for CV outcomes?
- What's about the Incretin-based therapy in Diabetic patients from the CV outcomes point of view?
- What is the role of the DPP-4 inhibitors in heart failure patients?
- What's about the future perspectives based on the data presented by the speaker?

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Mediterranean diet, olive oil and CV risk

N Engl J Med 2013; 369:954-964



The Mediterranean diet, olive oil and CV risk was the topic discussed by Dr. Maiorino. The speaker, coming from Naples (IT), presented very interesting data about the main non-communicable diseases and the causes of death based on the WHO publications, by highlighting that the majority of the top risk factors for death are linked to diet. Going

Mediterranean diet



High consumption of minimally processed plant-based foods
Olive oil as the principal source of fat
Low-to-moderate consumption of dairy products, fish, and poultry
Low consumption of red meat
Low-to-moderate consumption of wine with meals

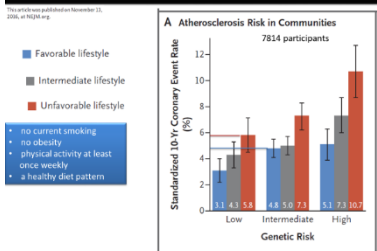
- Mediterranean dietary patterns were associated with lower risk of type 2 diabetes in prospective cohort studies and RCTs
- Mediterranean diets compared with a conventional diet for diabetes management improved glycemic control and insulin sensitivity*

*Esposito K et al. Diabetes Res Clin Pract 2010; 89: 97-102. Estruzzi R, et al. N Engl J Med 2013; 368: 1279-90. Shah L, et al. N Engl J Med 2008; 359: 229-41. Esposito K, et al. Ann Intern Med 2009; 151: 308-14.

deeper in her lecture, Dr. Maiorino presented many data given by clinical studies on the effects of the Mediterranean diet on CV risk through the reduction of metabolic syndrome prevalence, the prevention of type 2 diabetes, the glycemic control in diabetic patients, the reduction of the cardiovascular risk factors, the reduction of the

cardiovascular events and finally through its favourable effect on longevity. The speaker presented a huge amount of data, demonstrating that the adherence to the Mediterranean diet reduces the risk of all mortality and presents beneficial effects on longevity, probably through the reduction of the endothelial dysfunction and other markers of inflammation. In conclusion, Dr. Maiorino, pointed out that also the genetic risk of CAD can be reduced with a correct life style, where the Mediterranean diet plays a major role.

Nature vs nurture; Genetics vs lifestyle



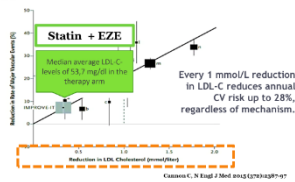
- What is the standard Mediterranean plate proposed by the speaker?
- What's about Genetics and life style, based on the data presented by the speaker?
- What are the main effects of the Mediterranean diet on the endothelial dysfunction?
- What are the main effects of the Mediterranean diet on the metabolic syndrome and its components, according to the data presented by the speaker?
- What's about the prevention of diabetes with Mediterranean diet?

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Targeting LDL in high risk patients: how low we should get? How?

IMPROVE-IT: The Concept of More Aggressive Absolute LDL-Reduction

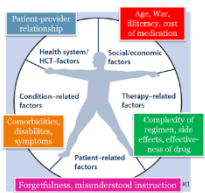


Prof. Calabrò from Naples (IT), spoke about LDL and its recommended level in high-risk patients. At the beginning of his lecture, the speaker presented very interesting data on the key questions on the LDL goals of therapy. More in particular Prof. Calabrò talked about the need for using “goals” in LDL reduction, but how to measure the effect, with the absolute reduction or with the percent

reduction? was the question raised by the speaker and in order to find a very comprehensive answer, presented very interesting data given by the IMPROVE-IT study. Other questions raised by Prof. Calabrò were about the right time for starting the LDL lowering

therapy and the right LDL level to be achieved. In the last part of his presentation, the speaker talked about guidelines, their utilities and the need for cover the gap between guidelines and clinical practice in order to obtain benefits for patients. In conclusion, Prof. Calabrò pointed out that it is essential to find new strategies in order to address the gaps in adherence to lipid lowering therapy.

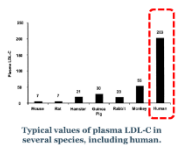
FIVE DIMENSIONS OF ADHERENCE



Adherence is a multidimensional phenomenon. The common belief that patients are solely responsible for taking their treatment is misleading and most often reflects a misunderstanding of how other factors affect people's behaviour and capacity to adhere to their treatment.

Human exception: LDL-supremacy...

In the animal kingdom, modern humans are “outliers” on the LDL scale. Our levels of LDL cholesterol exceed by far that of other species.



J Am Coll Cardiol 2004;93:1002-8

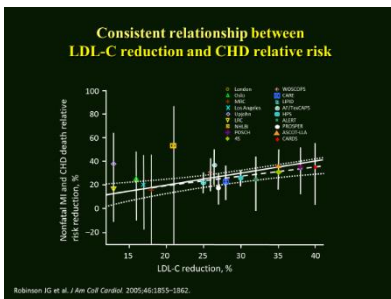
- Should we use LDL-goals in lipid lowering therapy?
- Should we target an absolute or a percent reduction in LDL-C level?
- Is the duration of therapy important?
- There is a lower limit in LDL-C level reduction?
- How soon is too soon for starting a lipid lowering therapy?
- What's about the results of the IMPROVE-IT trial according to the data presented by the speaker?

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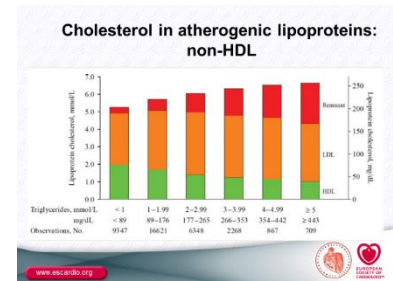
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Beyond LDL: are there additional lipid parameters we should focus on?

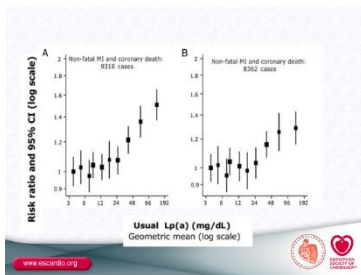


Additional lipid parameters other than LDL, was the topic discussed by Prof. Catapano. More in particular the speaker, coming from Milan (IT) presented very interesting data on the role played by lipoproteins and triglycerides in the onset of the atherosclerotic process. Going deeper in his presentation, Prof. Catapano highlighted the relationship between LDL-C and

CRP in patients affected by atherosclerosis, by presenting very interesting data given by clinical trials like Jupiter and others. In the main part of his lecture, the speaker talked about Triglycerides, “Remnant cholesterol” and their atherogenic effects, by presenting very innovative and impressive data given by many clinical trials on the



correlation between these lipoproteins and the prevalence of Cardiovascular disease. In the last part of his lecture Prof. Catapano spoke about the role played by Lp(a) in the onset of Atherosclerosis, through the presentation of data given by mendelian randomization trials. Finally, the speaker talked about the future challenges in atherosclerosis research by highlighting the importance to go deeper in the role of non-HDL cholesterol, Apolipoproteins and Lp(a).



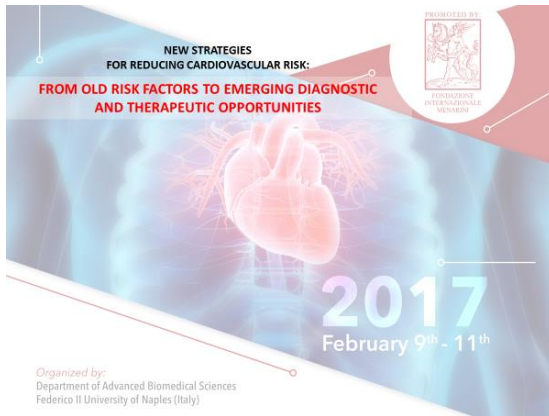
- What is the role of remnants in the development of atherosclerosis?
- What is the relationship between the loss of function in APOC3 and the onset of Coronary Disease?
- What’s about the relationship between Lp(a) and CVD?
- What are the main results of the Copenhagen General Population study?
- What’s about the correlation between triglycerides and CVD?

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<http://www.fondazione-menarini.it/Archivio-Eventi/2017/New-strategies-for-reducing-cardiovascular-risk-from-old-risk-factors-to-emerging-diagnostic-and-therapeutic-opportunities/Materiale-Multimediale> ...

and, after having logged in, enter in the multimedia area.

New pharmacologic anti-lipidic strategies on the horizon



Prof. Averna from Palermo (IT), spoke about the new therapeutic strategies in dyslipidaemic patients. At the beginning of his talk, the speaker highlighted that there are a lot of unmet medical needs in lipid lowering therapy like High-risk patients with HeFH which do not reach the recommended LDL-C levels or patients with at list one CV event which fail to reach the recommended LDL-C level despite the good adherence to statin therapy. In order to give a available solution to these needs, Prof. Averna presented data on PCSK9 inhibitors clinical studies, by highlighting the impressive effects of the

monoclonal antibodies on the LDL-C reduction in different populations. The speaker presented also data on the effects of these drugs in statin intolerant patients, on the atherosclerosis regression, on cardiovascular outcomes and on their safety profile. Finally, Prof. Averna presented data on the right time for adding these drugs to statins in high risk patients. In conclusion, the speaker pointed out that these drugs will allow the physicians to achieve the LDL-goals in high risk patients and that they have the potential to change the natural history of Atherosclerosis and Cardiovascular Disease.

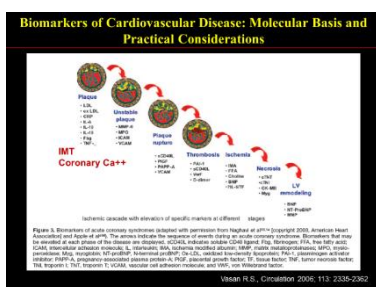
- When add a non-statin therapy in high risk patients based on the data presented by the speaker?
- What are the main adverse reactions imputable to PCSK9 inhibitors from the speaker point of view?
- What are the main results of the PCSK9 inhibitor cardiovascular outcomes trials based on the data presented by the speaker?
- What's about the potential for the atherosclerosis regression based on the data presented by the speaker?
- What is the duration of the LDL-C lowering effects of PCSK9 inhibitors?

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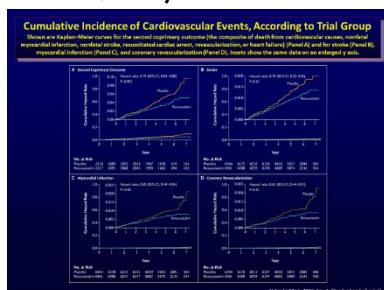
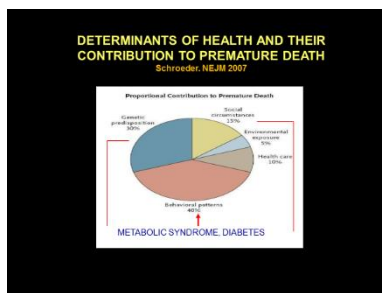
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CV risk prevention in patients at intermediate risk: the message from the HOPE 3 trial



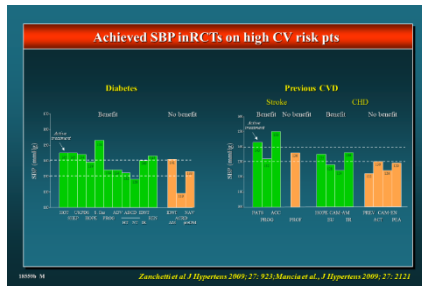
CV risk prevention in patients at intermediate risk was the topic discussed by Prof. Filardi in his lecture. The speaker, chairman of the congress, presented very interesting data on the effects of the prevention strategies to be applied in high risk patients and in the general population by highlighting the deep differences in these two strategies. Going deeper in his lecture Prof. Filardi spoke about some parameters used for the identification of people at risk to develop CVD, by presenting data on intima/media thickness, cardiac computed tomography and circulating and urinary biomarkers. The speaker pointed out that from the guidelines point of view all these parameters are not affordable for the CV prevention in general population. In the second part of his lecture, Prof. Filardi talked about behavioural and other factors, very effective in reducing the CV risk level in general population and presented very impressive data given by the HOPE 3 trial running in CVD patients at intermediate risk. In conclusion, Prof. Filardi pointed out that the risk factors to be monitored for an effective CV prevention on patients at intermediate risk, are the behavioural ones like smoking cessation, diet control, physical activity improvement and body weight reduction together with the intensive LDL-C reduction and the diabetes control.



- What is the cumulative incidence of major cardiovascular events in the HOPE3 hypertensive Arm?
- What is the cumulative incidence of cardiovascular events in all the HOPE3 trial groups?
- What's about the determinants of health and their contribution to premature death based on the data presented by the speaker?
- What's about the recommendations for imaging methods presented by the speaker?
- What is the net reclassification index?

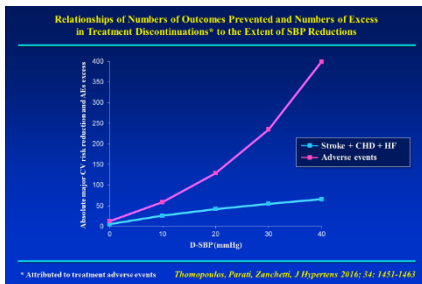
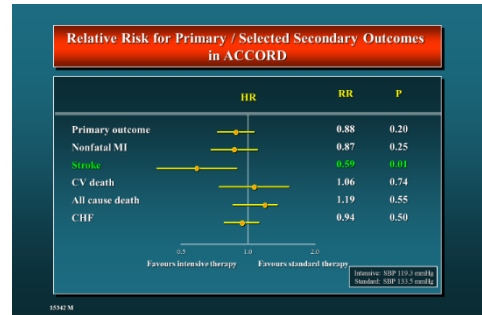
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Reconciling SPRINT and HOPE 3 trials: is intensively reducing blood pressure useful?



Prof. Mancia from Milan (IT), presented very interesting data on the real utility of the intensively reduction of BP levels. More in particular the speaker talked about the BP target to be achieved with the antihypertensive treatment, starting from the 2013 ESH/ESC recommendations in different populations like the high risk patients and the elderly. Going deeper in his lecture Prof. Mancia presented data given by SPRINT, ACCORD and ONTARGET trials about the BP level reduction, but also on the antihypertensive medications and on mortality. In the main part of his lecture, the speaker addressed the audience with a very key question: “do SPRINT results just reflect the benefit of treatment when conventionally measured SBP is reduced above to below 140 mmHg?”

and in order to find a very comprehensive answer he went deeper, by presenting very interesting data on clinical studies and meta-analyses about the BP lowering effects, the adverse ones included. Prof. Mancia presented also data given by HOPE 3 trial, showing that in high-intensively treated patients there were more CV events in the treated group than in the placebo group. In conclusion, the speaker pointed out that in order to reduce the residual risk in treated hypertensive patients it is necessary to improve the control of the associated risk factors and to expand the BP targets for treatment, based on the characteristics of any singol patient.



- When is it necessary to start with the improvement of lifestyle habits and antihypertensive drug treatment in low risk patients based on the 2013 ESH/ESC hypertension guidelines?
- What is the relationship between outcomes prevented and adverse events due to treatment based on the data presented by the treatment?
- What’s about the mortality in SPRINT trial?
- What’s about Risk of primary/secondary outcomes in SPRINT based on the data presented by the speaker?

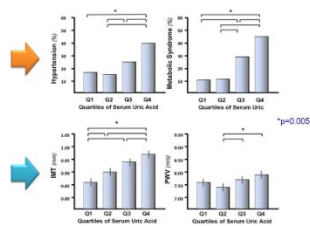
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Hyperuricemia, blood pressure and metabolic syndrome: linking uric acid to CV events

Quartiles of SUA and prevalence of CV risk factors and TOD in the cohort of the Brisighella Heart Study

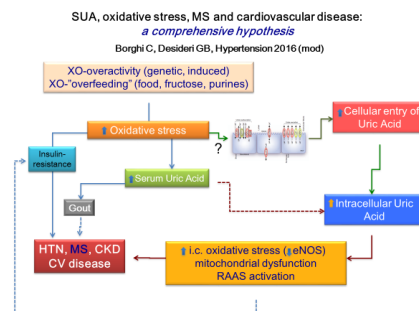


Borghgi C et al, J Hypertens 2013

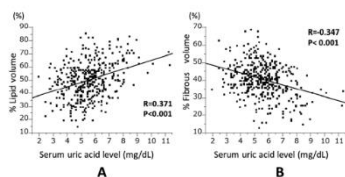


The main topic at the core of Prof. Borghgi presentation, was the role of hyperuricemia, as a link between high blood pressure and metabolic syndrome in the CV events manifestation. The speaker, coming from Bologna (IT), presented very interesting data given by the main studies running in hyperuricemic patients, on the correlation between SUA, hypertension and metabolic syndrome. Going deeper in his lecture,

Prof. Borghgi spoke about the effects of fructose ingestion with and without allopurinol administration in rat, showing that SUA modulates the intracellular fat accumulation induced by fructose. In the main part of his presentation the speaker talked about the possible mechanisms leading to the onset of the Metabolic Syndrome in patients with elevated SUA levels from an epidemiology, biochemistry and genetic point of view. In the last part of his lecture, Prof. Borghgi spoke about the evolutionary legacy adaptive mechanism, leading to the Uricase mutation and the pathophysiologic hyperactivation of the XO pathway leading to the onset of atherosclerosis through the higher intracellular UA levels responsible for the RAAS activation, the increase of the insulin resistance and the oxidative stress. In conclusion, Prof. Borghgi pointed out that Hyperuricemia is widely represented in the population and can contribute to the new-onset of hypertension, Metabolic Syndrome and CVDs.



Simple linear regression analysis showing the relationship between serum uric acid levels and coronary plaque components: (A) % lipid volume and (B) % fibrous volume



Ando K, et al, J Atheroscler Thromb, 2016 Mar 5

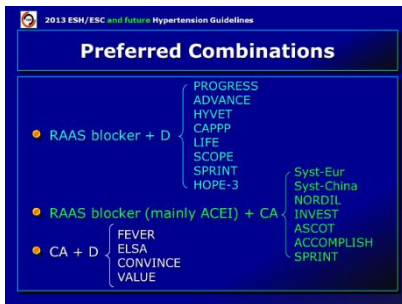
- What is the relationship between Uric Acid, AT1 receptors and Atherosclerosis?
- What's about the relationship between SUA, oxidative stress, MS and cardiovascular disease based on the data presented by the speaker?
- What's about the Uricase mutations?
- What's about the association of genetic urate score with CVD risk factors and CHD?
- What are the mean urate levels and the prevalence of gout across the genetic urate score presented by the speaker?
- What is the Metabolic syndrome prevalence in different countries based on the data presented by the speaker?

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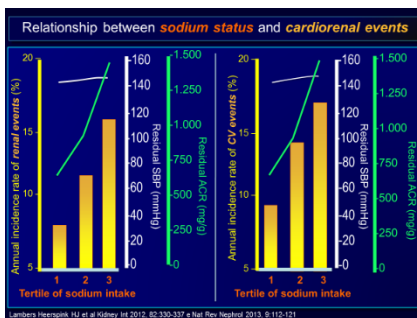
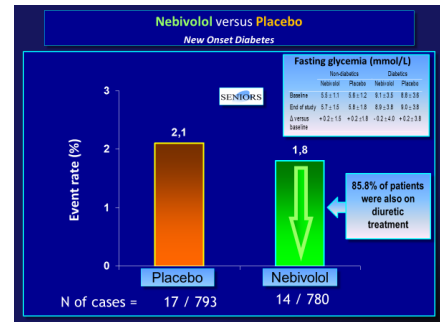
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Traveling through the anti-hypertensive drug combinations: how the choice should be guided



The main topic at the core of Prof. Grassi presentation, was the antihypertensive drug-combination therapy. The speaker, coming from L'Aquila (IT), presented very interesting data, starting from the 2013 ESH/ESC hypertensive guidelines recommendations on monotherapy vs combination therapy for achieving the BP targets. Going deeper in his talk, the speaker presented many data given by clinical studies and meta-analyses on the drugs to be used in the combination treatment protocols. More in particular Prof. Grassi spoke about which drugs are to be preferred for first line and combination therapy, by presenting data on Guidelines, patients' adherence, the non-pharmacological management and finally on the practical approach to the daily life. In conclusion, the speaker pointed out that the antihypertensive therapy can start either with the mono or the combo approach, depending on the patient' profile, but combination therapy is often necessary and the fixed combinations increase the patients adherence.



- What's about the practical approach to the daily life, based on the data presented by the speaker?
- What are the main characteristics of the non-pharmacological BP management from the speaker point of view?
- What about patients adherence based on the data presented by the speaker?
- What is the position of the ESH Guidelines on the drug combination antihypertensive therapy?
- What's about the effect of ACE-In and ARBs on CV outcomes in patients free from LV dysfunction based on the meta-analysis presented by the speaker?
- What are the main preferred combination-therapies based on the data presented by the speaker?

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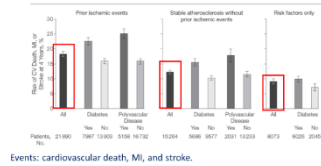
Prolonging DAPT in the chronic patients: in whom? For how long?

45,227 pts with CAD, cerebrovascular disease, or PAD or with multiple risk factors for atherothrombosis

REACH study

Follow up: 4 year

Patients with prior ischemic events remain at high risk for events

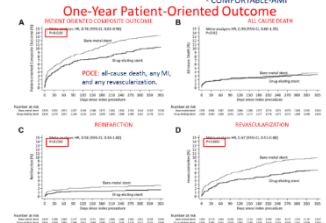


Events: cardiovascular death, MI, and stroke.

Bhatt DL et al. JAMA 2010

Dr. Silverio from Salerno (IT) spoke about prolonging DAPT in the chronic patients, by focusing on the type of patient and on the therapy duration. Going deeper in his talk the speaker presented very interesting data given by clinical trials in STEMI and non-STEMI patients, starting from the epidemiology of MI recurrence and the importance of DAPT in patients in the first year

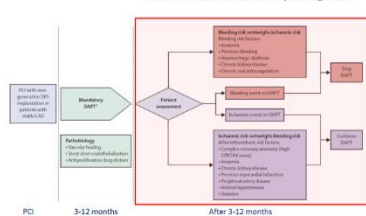
2,655 STEMI pts from 2 trial comparing BMS vs newer DES - EXAMINATION



...remains to be determined whether the differences in favor of newer-generation DES are sustained during long-term follow-up". Sabaté M et al. JACC 2014

after stent implantation for avoiding reinfarction. In the main part of his talk Dr. Silverio presented also data comparing old stents vs the new ones by highlighting that the new stents present significant benefits compared to the old ones. Speaking about DAPT duration after DES, the speaker pointed out that the data do not present a definitive answer, because in many studies long-term DAPT is better in preventing STENT thrombosis but is worse in major bleeding complications. In the second part of his talk Dr. Silverio spoke about the patient selection for DAPT prolongation, by presenting very interesting data on DAPT SCORE, PRECISE – DAPT score and PARIS risk score. Finally, the speaker spoke about the ongoing studies like GLOBAL LEADERS and the EYESHOT Post – MI. In conclusion, Dr. Silverio pointed out that the benefit offered by long-term DAPT duration reflects the ischemic vs bleeding risk status of patients

Patients selection for DAPT prolongation



Modified from Piccolo R et al. The Lancet 2015

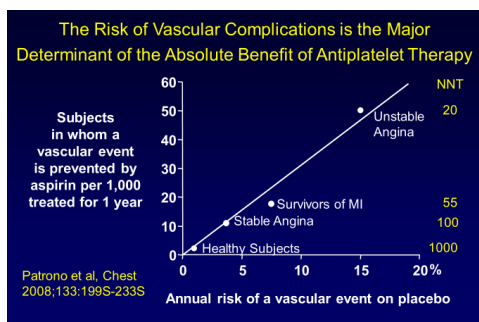
- What are the main characteristics of PARIS risk score?
- What's about PRECISE-DAPT score from the speaker point of view?
- What are the main results of the DAPT study in bleeding adverse effects compared to thrombosis prevention?
- How to select patients for long-term DAPT based on the data presented by the speaker?
- What's about the PEGASUS study results based on the data presented by the speaker?

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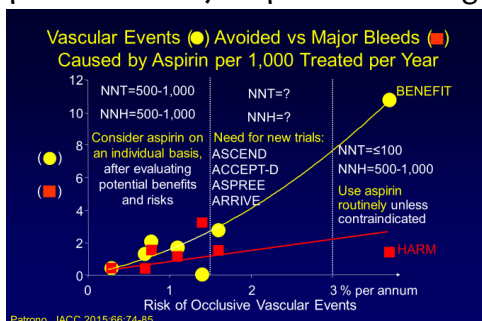
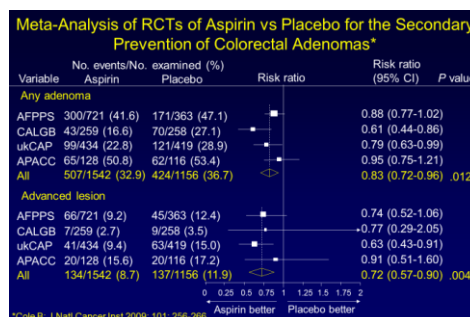
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Aspirin in primary prevention: what more we need to know



Aspirin in primary prevention was the topic at the core of Prof. Patrono presentation. The speaker coming from Rome (IT), at the beginning of his lecture talked about the risk of vascular complication avoided by Aspirin compared to the risk of GI ulcers, in patients affected by stable or unstable angina and in the MI survivors, by highlighting that the balance between benefits and harms depends on the clinical status and

on the age of patients. Going deeper in his lecture, Prof. Patrono presented data given by meta-analyses and guidelines recommendations, by highlighting that there is no consensus about the aspirin administration in primary prevention. The speaker talked also about the effect of aspirin on the gastrointestinal cancer and presented very impressive data given by observational



studies, randomized trials and a post-hoc meta-analysis of 51 randomized controlled trials on the mechanism of action of aspirin leading to the reduction of cancer incidence also in primary prevention. The speaker highlighted that the data are very indicative for the anticancer effect of aspirin. In conclusion Prof. Patrono pointed out that the use of aspirin in primary prevention depends on the exposure of any single patient to the CVD risk and that it is useful even for the GI cancer

prevention.

- What's about the US recommendations on Aspirin use for the primary prevention of CVD and colorectal cancer?
- What's about the cancer incidence reduction due to the use of aspirin in primary prevention based on the meta-analysis presented by the speaker?
- What are the fingerprints of the chemopreventive effects of aspirin against colorectal cancer in cardiovascular trials?
- What's about the incidence of adenoma and advanced lesions in patients treated with aspirin or placebo for the secondary prevention of colorectal adenoma?
- What's about the use of aspirin in primary prevention?

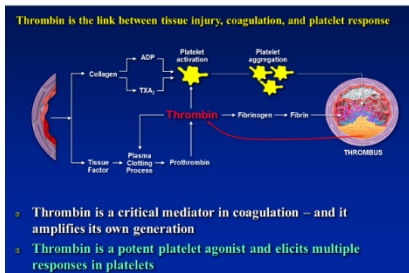
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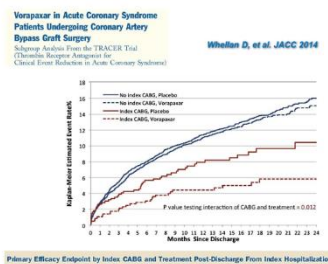
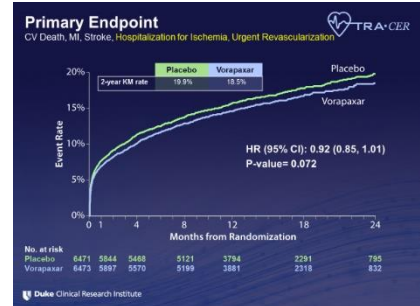
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The role of the thrombin receptor antagonists

Thrombin: Center of Coagulation Process



The role of the thrombin receptor antagonists was the topic at the core of Prof. Ambrosio presentation. The speaker coming from Perugia (IT), at the beginning of his lecture talked about the Tissue Factor and Thrombin pathway leading to Coagulation, by highlighting that, in particular conditions, Thrombin plays a pathophysiological role besides coagulation. Going deeper in his talk, Prof. Ambrosio presented very impressive data given by phase III clinical studies on the effects of the thrombin receptor antagonist SCH530348 in NSTEMI and post-MI patients for the treatment of atherothrombosis together with other data on the effects of SCH530348 in type 2 diabetic patients with MI, in ACS patients undergoing CABG surgery and in patients affected by peripheral artery diseases. In conclusion, Prof. Ambrosio pointed out that the unchecked stimulation of coagulation and all the other linked pathways may actually become a mechanism of disease occurrence and/or progression.

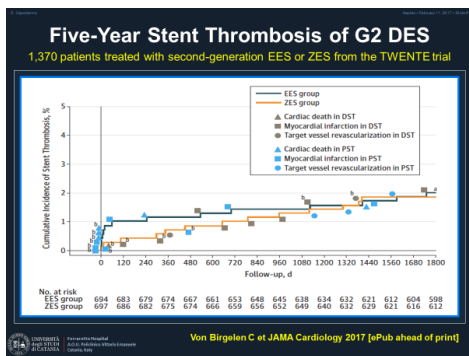


- What's about the effects of SCH530348 on ischemic events stratified by diabetic status based on the data presented by the speaker?
- What are the main characteristics of the TRA2P trial presented by the speaker?
- What are the effects of SCH530348 on myocardial infarction in the TRA-CER trial?
- What is the primary combined endpoint of the TRA-CER trial?
- What are the main effects of PARs in the Tissue Factor and Thrombin pathway based on the data presented by the speaker?

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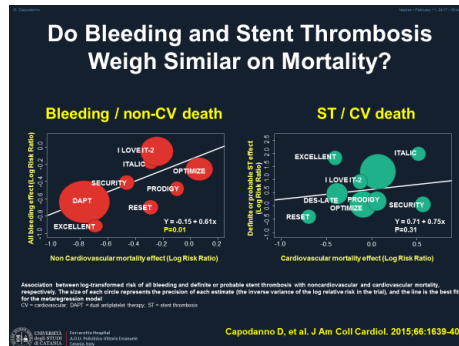
[http://www.fondazione-menarini.it/Archivio-Eventi/2017/New-strategies-for-reducing-cardiovascular-risk-from-old-risk-factors-to-emerging-diagnostic-and-therapeutic-opportunities/Materiale-Multimediale](http://www.fondazione-menarini.it/Archivio-Eventi/2017/New-strategies-for-reducing-cardiovascular-risk-from-old-risk-factors-to-emerging-diagnostic-and-therapeutic-opportunities/Materiale-Multimediale...) ... and, after having logged in, enter in the multimedia area.

The need for DAPT after last generation DES



The need for DAPT after last generation DES was the topic Dr. Capodanno talked about. The speaker coming from Catania (IT), at the beginning of his lecture presented very interesting data on the evolution of the DES technology and on the impact of the strut thickness on thrombogenicity. Going deeper in his talk, Dr. Capodanno presented a huge amount of data on thrombosis due to

Stents, by highlighting that the second-generation DES are characterized by a significant reduction in thrombosis events compared to the first-generation ones. In the main part of his lecture, the speaker discussed very interesting data given by the main clinical trials running in patients undergoing DAPT after DES implantation, with the aim



Trials of DAPT Duration After PCI
15 studies, ~40,000 patients randomized

Study	Journal	Patients	Hypothesis	Result
RESET	JACC 2012	N=2,117	3 months noninferior to 12 months	✓
OPTIMIZE	JAMA 2013	N=2,199	3 months noninferior to 12 months	✓
SECURITY	JACC 2016	N=1,399	6 months noninferior to 12 months (stopped)	✓
ISAR SAFE	EJH 2015	N=4,000	6 months noninferior to 12 months (stopped)	✓
I-LOVE-IT 2	CIRC CV 2016	N=1,829	6 months noninferior to 12 months	✓
OPTIMA-C	TCTAP 2015	N=1,368	6 months noninferior to 12 months	✓
EXCELLENT	Circulation 2015	N=1,443	6 months noninferior to 12 months	✓
IVUS XPL	JACC: CI 2016	N=1,400	6 months comparable to 12 months	✓
NIPPON	ESC 2016	N=2,772	6 months noninferior to 18 months (stopped)	✓
ITALIC	JACC 2015	N=1,822	6 months noninferior to 24 months (stopped)	✓
PRODIGY	Circulation 2012	N=1,970	24 months more effective than 6 months	✗
ARCTIC	Lancet 2014	N=1,259	≥18 months more effective than 12 months	✗
DAPT	NEJM 2014	N=8,961	30 months more effective than 12 months	✓
DES LATE	Circulation 2014	N=5,045	36 months superior to 12 months	✗
OPTIDUAL	EJH 2015	N=1,385	48 months superior to 12 months (stopped)	✗

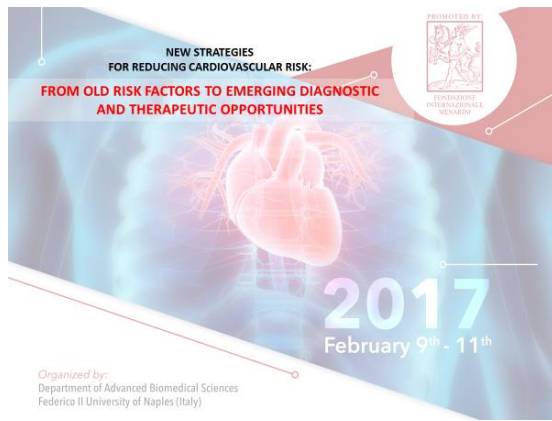
Source: Capodanno D. Personal communication

to compare the short DAPT trials with the long DAPT ones. After this very interesting analysis Dr. Capodanno spoke about the main characteristics of the risk scores for DAPT duration through the comparison of DAPT, PARIS and PRECISE-DAPT and about the different guidelines recommendations on the DAPT duration. In conclusion, the speaker pointed out that the optimal DAPT duration has to be largely determined by the prevention of new atherothrombotic events than the nuisance of stent-related thrombotic complications.

- What are the main ongoing studies examining the abbreviated DAPT duration?
- What's about the DAPT duration after BVS implantations from the speaker point of view?
- What are the main characteristics of the risk scores for DAPT duration presented by the speaker?
- Do bleeding and Stent thrombosis weigh similar on mortality?
- What are the main trials on DAPT duration after PCI presented by the speaker?
- What's about the ABSORB II trial data on the very late scaffold thrombosis presented by the speaker?

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These are only some of the topics addressed in the congress's sections

For a deeper knowledge on these topics, please visit the International Menarini Foundation web site where You can find all the speeches in their full version.

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