

New Frontiers to beat Cardiovascular Disease Rome (IT), September 07-08, 2017 Highlights

Introduction



Prof. Volpe, chairman of the symposium, opened the congress, by highlighting the topics of this meeting, focusing on the future of cardiology, in order to reduce the burden of the cardiovascular disease mortality. The main topics discussed in this symposium were about ischemic heart disease and diagnosis, clinical presentations, acute coronary syndromes, Imaging and finally about heart failure. The congress has been attended by many of the top researchers of this field coming from all the world and by many young physicians attending the university of Rome.

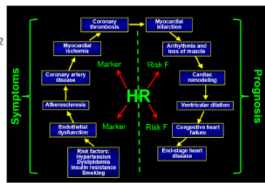
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Novel therapeutic approaches in angina

New perspectives on: **prognostic role of HR reduction related to the CV continuum, marker vs risk factor**

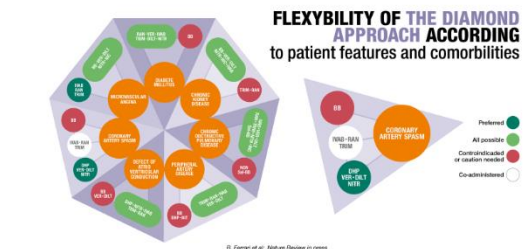
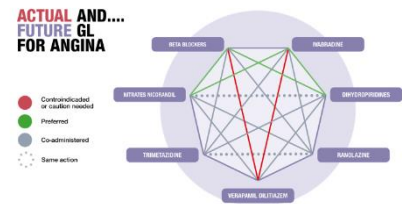
- **Normal LV function:** HR reduction improves transient O₂ consumption **reduction of symptoms (marker)**
- **Impaired LV function:** HR reduction attenuates remodelling **prognosis improvement (risk factor)**



Novel therapeutic approaches in angina, was the topic discussed by Prof. Ferrari in his lecture. The speaker, coming from Ferrara (IT), went deeper in his talk and presented very interesting data on the role of revascularization and pharmacotherapy in patients affected by chronic angina. Speaking about revascularization, prof. Ferrari highlighted that his application is decreasing, shifting forward ACS. In the main part of his presentation, the speaker presented

very interesting data on pharmacotherapy, more in particular he spoke about angina event prevention, starting from the improvement in preventive programs till the emerging role of anticoagulation and antiaggregation. Prof. Ferrari presented very interesting data on the role played by beta-blockers in preventing new events, but only in patients with a previous MI, where the reduction of HR attenuates the remodelling process. In the second part of his lecture, the speaker talked about the new view of the chronic angina pathogenesis, by highlighting the role played by the coronary microcirculation in the onset of the myocardial ischaemia. Finally, Prof. Ferrari talked about

ACTUAL AND... FUTURE GL FOR ANGINA



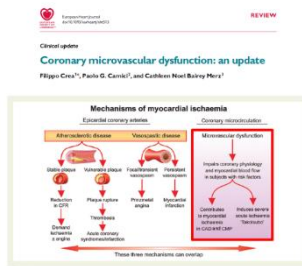
therapy, pointing to the so called “Diamond therapeutic approach” according to the typology of any patient and his comorbidities. The speaker presented very interesting data on the metabolic drugs like ranolazine, ivabradine and trimetazidine. In conclusion, Prof. Ferrari, pointed out that it is the time to reconsider the actual guidelines and that the “diamond approach” could be a suggestion.

- What is the role of the coronary sinus reduction, based on the data presented by the speaker?
- What’s about the role of pharmacotherapy from the speaker point of view?
- What is the prognostic role of beta blockers in chronic angina patients?
- What’s about the new insights of the chronic angina pathogenesis, based on the data presented by the speaker?
- What’s about the emerging role of the microvascular angina, based on the data presented by the speaker?
- What are the key points of the “therapeutic diamond approach” in chronic angina patients, based on the data presented by the speaker?

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The critical role of microcirculatory network

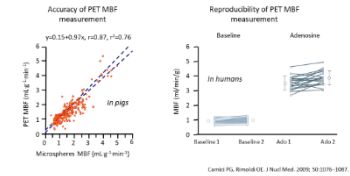


Prof. Camici from Milan (IT), spoke about the critical role of the microcirculatory network. Going deeper in his lecture, the speaker presented very interesting data on the coronary microvascular dysfunction. Prof. Camici talked also about the classical view of the myocardial ischemia due to the epicardial stenosis and about the new view characterized by the presence of the microvascular dysfunction

without coronary occlusion or stenosis. The speaker presented very interesting data on the main pathogenic mechanisms at the basis of the microvascular dysfunction. In the main part of his lecture, Prof. Camici, talked about the symptoms associated with the

PET: the gold standard for the non-invasive measurement of myocardial blood flow

PET with $H_2^{15}O$ or $^{15}NH_3$ allows accurate, reproducible and non-invasive measurement of absolute (ml/min/g) myocardial blood flow in man



coronary microvascular dysfunction and the techniques to be applied for the diagnosis of these patients. The speaker presented also very interesting imaging data on other techniques able to detect the microvascular angina, like the acetylcholine test typically to be used in patients at the first phases of the disease.

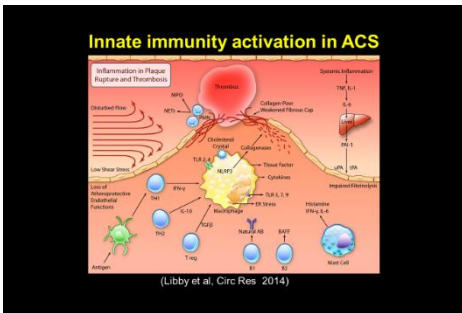


- What are the main mechanisms of the coronary microvascular dysfunction, based on the data presented by the speaker?
- What's about the flow reserve detection for the diagnosis of patients affected by microvascular angina, based on the data presented by the speaker?
- What are the main symptoms associated with the coronary microvascular angina, based on the data presented by the speaker?
- How to detect the microvascular spasm, based on the data presented by the speaker?

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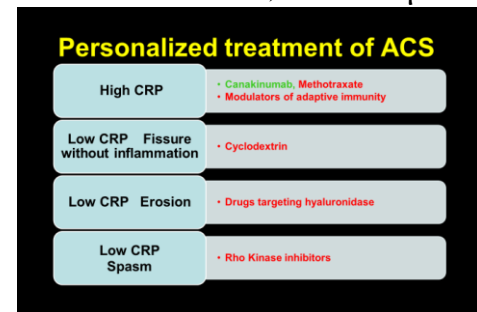
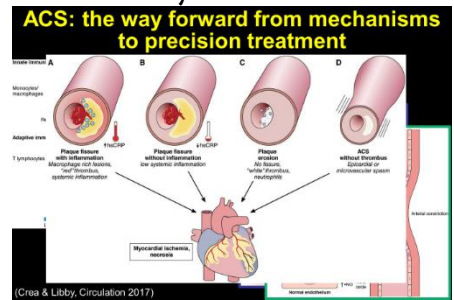
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How to view the myth of unstable plaque today



How to view the myth of unstable plaque today, was the topic Prof. Crea spoke about in his lecture. The speaker coming from Rome (IT), presented very interesting data on the dynamic nature of the coronary artery lesions. Going deeper in his lecture, Prof. Crea talked about the vulnerable plaques, by highlighting that it is difficult to predict events in chronic angina patients, only based on the risk level of the coronary plaques. In the main part of his talk, the speaker presented very interesting data on the dynamic nature of the

coronary artery lesions, pointing to the role played by the inflammation in the onset of the plaque fissure. Prof. Crea presented also very interesting data on the effect of canakinumab in chronic angina patients with high CRP levels, by highlighting that this drug was able to reduce the events compared to placebo. The speaker talked also about other mechanisms leading to the plaque erosion and fissure other than inflammation, more in particular Prof. Crea highlighted



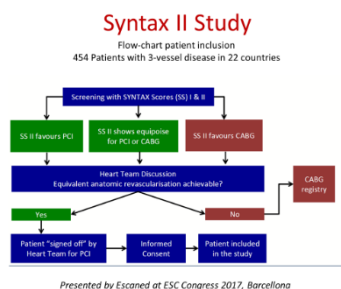
that the pathophysiology of the plaque erosion and fissure are very different. Finally, the speaker talked about the new challenge of targeting ACS patients not associated to an inflammatory outburst in order to implement a personalized treatment. In conclusion, Prof. Crea pointed out that the new frontier of the chronic angina patients' management is characterized by the management of ACS patients associated to low CRP.

- What's about the correlation between AMI and high CRP levels, based on the data presented by the speaker?
- What's about the mechanical triggers of plaque fissure, based on the data presented by the speaker?
- What are the main pathophysiology mechanisms of plaque fissure, based on the data presented by the speaker?
- What's about the correlation between inflammation, atherosclerosis and ischemic events, based on the data presented by the speaker?

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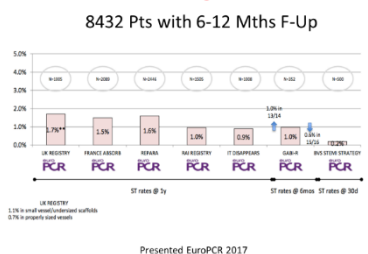
New solutions to manage coronary disease in the cath-lab



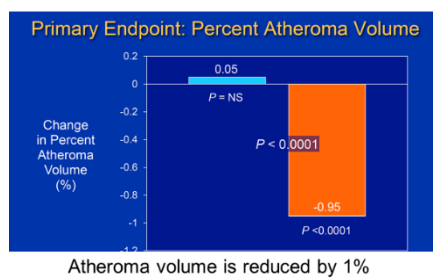
New solutions to manage coronary disease in the cath-lab, was the topic discussed by Prof. Di Mario. The speaker, coming from Florence (IT), talked about interventional cardiology. Going deeper in his lecture, Prof. Di Mario, presented very interesting data on the results of the new generation drug eluting stents and highlighted that despite the stents evolution the burden of CVD death is yet too heavy. In the main part of his lecture, Prof. Di Mario talked about

the Syntax II study, its inclusion-exclusion criteria and its results. The speaker presented also other very interesting data on the effect of the P2Y12 inhibitor administration, together with the consideration that the further reduction of TLR, restenosis and stent thrombosis do not translate into meaningful prognostic improvements due to the disease progression. In the second

7 Dedicated National Registries with ABSORB



GLAGOV: PCSK-9



part of his lecture, Prof. Di Mario, went deeper in presenting a huge amount of data related to the disease progression in patients who underwent to PCI and highlighted that in order to improve the primary and secondary prevention, it is necessary to take advantage of the imaging techniques already available. Finally, the speaker talked about the effect of new drugs like the PCHK9 inhibitors, on the reduction of the atheroma volume and about the customized treatment based on the plaque type.

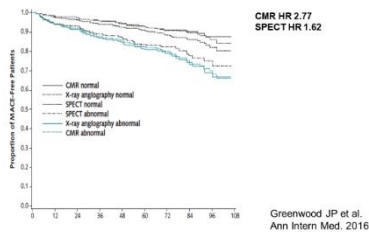
- What's about the vulnerable plaque customized treatment, based on the data presented by the speaker?
- Has interventional cardiology reached maturity, from the speaker point of view?
- What are the main long-term results of the second-generation DES, based on the data presented by the speaker?
- What are the results of the 7 dedicated national registries with ABSORB, presented by the speaker?

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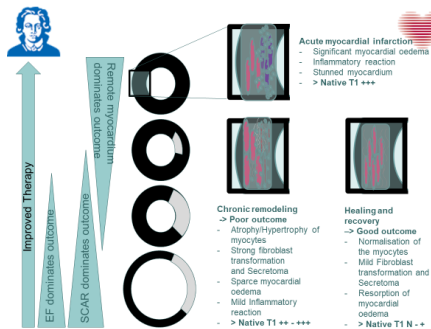
Recent advances in the imaging of cardiomyopathies

 Perfusion CMR is a strong prognosticator



Recent advances in the imaging of cardiomyopathies, was the topic discussed by Prof. Nagel in his keynote lecture. The speaker, coming from Frankfurt (Germany), talked about two main questions, like what are the best tests between the functional versus the anatomical ones and about the replacement of invasive testing with the non-invasive strategies. Going deeper in his lecture, Prof. Nagel, presented very interesting data on the functional flow reserve versus angiography for guiding PCI and highlighted that the perfusion CMR is a strong predictor. In the

main part of his lecture, the speaker talked about the ESC guidelines and highlighted that the degree and location of stenosis do not correlate with the presence and the severity of the ischemia. Prof. Nagel presented very interesting data on the diagnostic performance of the non-invasive myocardial perfusion imaging techniques like CCT, SPECT and PET and highlighted that CMR is probably more useful in the detection of the coronary microvascular disease. Talking about the replacement of invasive



testing with non-invasive strategies, Prof. Nagel presented very interesting data given by many clinical trials and highlighted that the results obtained with non-invasive tests are comparable with the results obtained with the invasive ones. Finally, the speaker in order to give an answer to the last question on the amount of ischemia safely tolerable, presented some data on the effects of the optimal medical therapy with and without PCI and on the main outcomes related to the pathophysiology processes of the myocardium.

- What's about Functional versus anatomical testing, based on the data presented by the speaker?
- What are the best tests from the speaker point of view?
- What are the main results of the replacement of invasive testing with non-invasive strategies presented by the speaker?
- What is the amount of ischemia safely tolerable, from the speaker point of view?

ONLINE FIRST

Diagnostic Accuracy of Fractional Flow Reserve From Anatomic CT Angiography

James Min. JAMA 2012

Table 4. Per-Patient Diagnostic Performance of FFR_{CT} ≤0.80 and CT ≥50% vs FFR ≤0.80 in the Intention-to-Diagnose Sample

	FFR _{CT} ≤0.80		CT ≥50%	
	Estimate, % (95% CI)	No. of Patients in Group	Estimate, % (95% CI)	No. of Patients in Group
Accuracy	73 (67-78)	252	64 (56-70)	252
Sensitivity	90 (84-95)	129	84 (77-90)	129
Specificity	54 (46-63)	123	42 (34-51)	123
PPV	67 (60-74)	172	61 (53-67)	160
NPV	84 (74-90)	80	72 (61-81)	72

Abbreviations: CT, computed tomographic angiography; FFR_{CT}, fractional flow reserve calculated from CT; NPV, negative predictive value; PPV, positive predictive value.

Prevalence 55%

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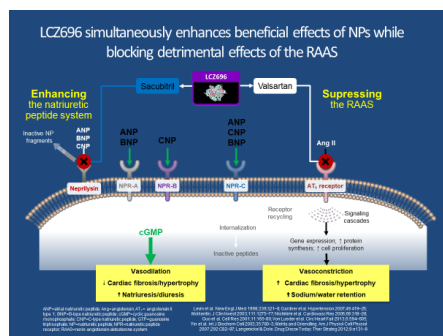
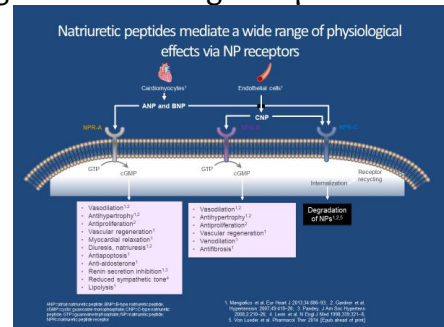
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The balance between the good and the evil: Rebalancing neurohormones in HF

- Emerging relevant pathophysiological aspects of HF
- Geometric remodeling
 - Tissue remodeling
 - Mitral valve regurgitation
 - **RAAS and SNS Dysregulation**
 - Inflammation and oxidative stress
 - Renal reserve → CRS
 - **NPs inappropriately low response and GC-receptors down regulation**

The balance between the good and the evil: Rebalancing neurohormones in HF, was the topic of Prof. Volpe presentation. The speaker, chairman of the symposium, talked about the main emergent and relevant pathophysiological aspects of HF like the RAAS and SNS dysregulation and the NPs inappropriately low response and the GC-receptor down regulation. Going deeper in his lecture, Prof. Volpe presented very interesting

data on the central role of the neurohormonal imbalance in HF and on the role played by the neurohormones in the ventricular remodelling. In the main part of his lecture, the speaker talked about the correlation between the prolonged RAAS activation and its detrimental effect in the HF patients and presented very interesting data on the interactions between NPs and RAAS at the systemic and intracellular



In the second part of his lecture, Prof. Volpe talked about the relationship between the RAAS/SNS hyperactivation and the lack of balance by NPs adaptive response as the main mechanism at the basis of the CHF progression and presented very interesting data on the effects of the neprilysin inhibition and on the NPs activation and simultaneous RAAS blockade. In conclusion, Prof. Volpe pointed out that the current therapeutic approaches for CHF is based on the modulation of the RAAS, the SNS

and the NPs.

- What are the main points of the neurohormonal imbalance in HF patients, based on the data presented by the speaker?
- What are the main physiological effects mediated by the natriuretic peptides, based on the data presented by the speaker?
- Can the heart release natriuretic peptides in response of mechanical stress, based on the data presented by the speaker?
- What are the main NPs and RAAS systemic interactions presented by the speaker?

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HF management: moving towards the integrated neurohormonal approach

LCZ696: sacubitril valsartan sodium
A first in class angiotensin receptor-neprilysin inhibitor

LCZ696 200 mg oral Dose

LCZ696 is a salt complex that comprises the two active moieties:^{2,3}
-sacubitril (AHU377) – a pro-drug, further metabolized to the neprilysin inhibitor LBQ657, and
-valsartan – an AT₁ receptor blocker in a 1:1 molar ratio

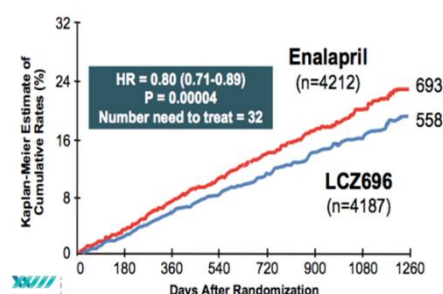
Plasma	AHU377	VAL	Valsartan
AUC equivalent	97 mg	103 mg	160 mg

Go et al. J. Clin. Pharmacol. 2015;55:401-411
Feng et al. Frontiers in Med. 2015;2:279-286

Prof. Senni coming from Bergamo (IT) spoke about “HF management: moving towards the integrated neurohormonal approach” and presented very interesting data on the main unmet medical needs of patients affected by HF. Going deeper in his lecture, Prof. Senni talked about the angiotensin-neprilysin inhibition and presented very interesting data on LCZ696 that is the first in class angiotensin receptor-neprilysin inhibitor. In the main part of his lecture, the speaker talked about

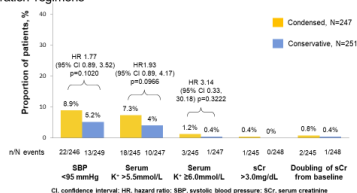
LCZ696 mechanism of action, pointing to the neurohormonal imbalance typical of HF patients and presented very interesting data given by the Paradigm-HF study, comparing the effects of LCZ696 versus Enalapril. In the second part of his lecture, the speaker talked about compliance and highlighted that this new drug is the first one after a lot of years showing to reduce mortality in substitution of the drugs developed in the eighty and the

PARADIGM-HF: Cardiovascular Death



TITRATION primary endpoints: Incidence of pre-specified SBP & lab assessments

No significant differences were observed in the rates of pre-specified thresholds of SBP and laboratory assessments between the two up-titration regimens



ninety years of the last century. Finally, Prof. Senna talked about LCZ696 adverse events, more in particular he presented very interesting data on the incidence of angioedema and amyloid beta accumulation in the brain. The speaker highlighted that there are no evidences of a higher AEs incidence in patients treated with LCZ696 compared to Enalapril. Finally, the speaker presented the main data given by the Titration study aimed to find the best up-titration modality for HF patients treated with LCZ696

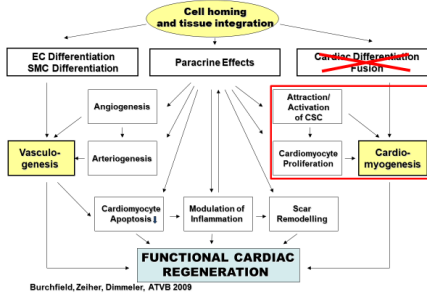
- What’s about the effects of LCZ696 compared to enalapril, based on the data presented by the speaker?
- What are the specific HF patient subgroups representing a challenge for the implementation of LCZ696, based on the data presented by the speaker?
- What’s about the angiotensin receptor-neprilysin inhibitors and the time to insulin initiation in diabetic patients?
- What’s about the angiotensin receptor-neprilysin inhibitors and the glycemic control in diabetic patients, based on the data presented by the speaker?

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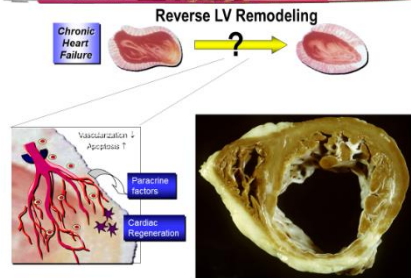
The results of HF trials with progenitor cells

Putative mechanisms for cardiac regeneration



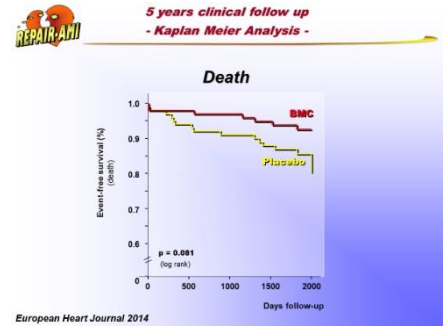
regeneration and highlighted the possibility to induce the cardiomyocyte proliferation and the cardio-myogenesis. More in particular, Prof. Zeiher presented very interesting

Challenges of Cell Therapy in Chronic Post-Infarction Heart Failure



therapy in congestive HF patients and by the REPEAT sub-study on the continuous monitoring of the cardiac function. Finally, the speaker talked about the future and more in particular about the need for developing other stem cells, or direct reprogramming procedures or also microRNA therapeutics.

Prof. Zeiher from Frankfurt (Germany), spoke about the results of HF trials with progenitor cells and presented very interesting data starting from the global proposition paper on CV regenerative medicine. Going deeper in his lecture, Prof. Zeiher presented very interesting data on the clinical trials pointing to the regenerating capacity of the heart thanks to the injection of bone marrow-derived cells. In the main part of his lecture the speaker talked about the putative



data on the cell therapy application in AMI patients, by highlighting that this therapy is able to reverse the adverse LV

remodelling typical in these patients. In the second part of his lecture, the speaker talked about the cell therapy application in chronic post-infarction HF patients and presented very interesting data given by the CHART-1 study, designed for testing the effect of the regenerative

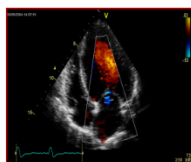
- What are the main bone marrow-derived cells used in such clinical trials presented by the speaker?
- What are the main applications of the cell therapy in CVDs, based on the data presented by the speaker?
- What's about the metaanalysis data on the use of the cell therapy in AMI patients, presented by the speaker?
- What's about the strategies for future heart regeneration, presented by the speaker?
- What are the main preliminary data of the REPEAT sub-study, presented by the speaker?
- What are the main results of the CHART-1 trial presented by the speaker?

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Valve repair to improve HF outcomes. The surgical approach

Secondary (Functional) Mitral Regurgitation (ischemic or non-ischemic)



Normal valve morphology

- Changes in LV geometry
- Papillary muscles dislocation
- Leaflet tethering
- Annular dilatation
- Decreased closing forces
- Dyssynchrony in contraction
- Failure of leaflet expansion

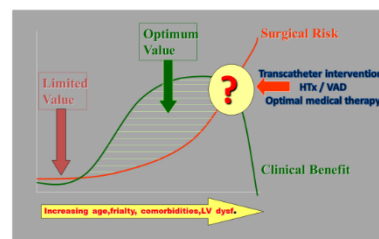


Levine, R. A. et al. Circulation 2005;112:745-758

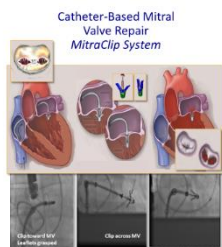
Prof. Alfieri from Milan (IT), spoke about “valve repair to improve HF outcomes. The surgical approach”. More in particular, the speaker talked about the secondary mitral regurgitation and the methods for its repair. Going deeper in his lecture, Prof. Alfieri presented very interesting data on the secondary mitral regurgitation characterized by normal valve morphology and highlighted that the SMR has a bad impact in the HF patients. SMR produce a vicious circle through the increase of the overload that

increases the annular-ventricular dilation, the speaker pointed out. In the main part of his lecture, Prof. Alfieri talked about the recommendations for the mitral valve intervention in chronic SMR patients and highlighted that for many patients, surgery is not an option. Prof. Alfieri presented also very interesting data on the methodology for the evaluation of surgical risk at the valve and the ventricular levels. In the second part of his lecture, Prof. Alfieri talked about the options

Surgical Risk vs Benefit in MR



for operable patients affected by SMR and presented very interesting data on undersized anuloplasty, anuloplasty and procedures on the subvalvular apparatus and on valvular replacement. In the last part of his lecture, the speaker talked about the expected results of surgery and highlighted that no data on survival improvement are produced till now. Finally, Prof. Alfieri presented very interesting data on the Mitra-Clip System and highlighted that its application can promote the reverse remodelling.

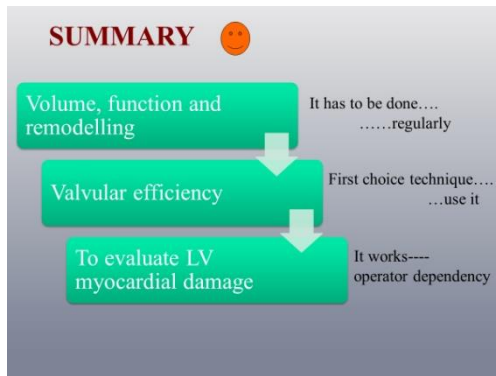


- What is the impact of SMR on the HF prognosis, based on the data presented by the speaker?
- What are the main indications for mitral valve intervention in chronic SMR patients presented by the speaker?
- What’s about the surgical risk vs benefits, from the speaker point of view?
- How to characterize patients with SMR, based on the data presented by the speaker?
- What are the main options for operable patients with severe SMR?
- What can we expect from surgery, from the speaker point of view?

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Imaging the new CV imaging



Imaging the new CV imaging, was the topic discussed by Prof. Lombardi from Milan (IT), more in particular the speaker talked about echocardiography in CHD, the multimodality ultrasound applications, the CCT applications and the CMR ones. Going deeper in his lecture, Prof. Lombardi presented very interesting data on the left ventricle reconstruction based on the echo data and on the role played by echocardiography in the diagnostic assessment of HF patients. In the

main part of his lecture, the speaker talked about the imaging application in ruling out CAD and presented very interesting data on the multidetector CT. Prof. Lombardi presented also other very interesting data on the imaging application for the evaluation of the left ventricle damage, but highlighted that this technique is not enough standardized for its use in a clinical practice setting. In the second part of his lecture, the speaker talked about the MR application in the prognostic evaluation of patients with myocardial

3. TO EVALUATE LEFT VENTRICLE DAMAGE

Late enhancement using multisection row computer tomography: A feasibility study with low dose 80 kV protocol

Arja J. Reimann*, Axel Klattner*, Bernhard Klump*, Martin Hoeschmid*, Felix Schumacher*, Matthias Teitel*, Toren Beck*, Christof Baerentzen*, Stefan Schneider*, Claus D. Claussen*, Andreas F. Egg*[†]

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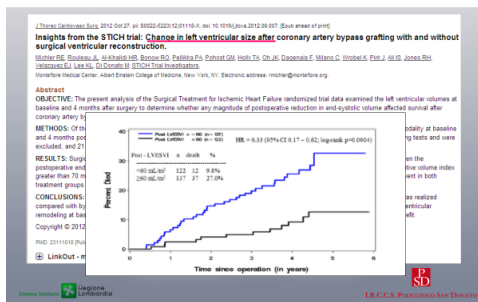
- Delayed Time: 5 – 10 min
- Tube Voltage: 80 kV
- Tube Current: 420 mA
- Collimation: 64x0.625 mm
- Crantry Rotation Time: 350 msec
- ECG-gating: prospective ECG

Se	Sp	NPV	PPV
78%	100%	100%	97%

Effective Radiation Dose: 1.13 – 1.51 mSv

fibrosis. Finally, Prof. Lombardi talked about the myocardial scar evaluation through the MR application and the importance of the scar intramyocardial location from a prognostic point of view and presented new data on the 4D flow analysis in post-ischemic HF patients, that is a very innovative technique developed by the speaker in collaboration with the Politecnico of Milan. In conclusion, the prof. Lombardi pointed out that in HF patients, multimodality is a real neediness either for clinical and for research purposes.

LEFT VENTRICLE RECONSTRUCTION



- What is the role of Echocardiography in the diagnosis of HF older adult patients, based on the data presented by the speaker?
- What's about the multidetector computed tomography for ruling out CAD, based on the data presented by the speaker?
- What's about the evaluation of the left ventricle damage with the new CV imaging, from the speaker point of view?
- What's about the CMR main applications for the scar tissue evaluation in ischaemic HF patients, presented by the speaker?

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Atrial fibrillation: Emergent solutions for an emergent epidemic

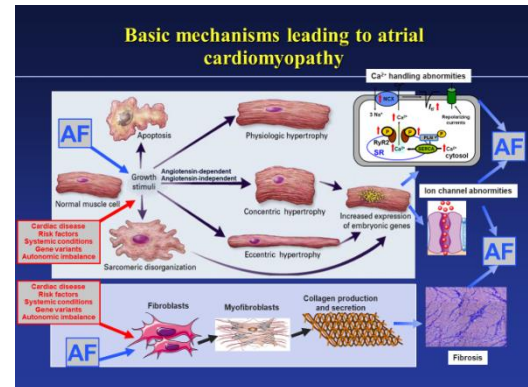
Key questions for managing the risk of STROKE in subclinical AF



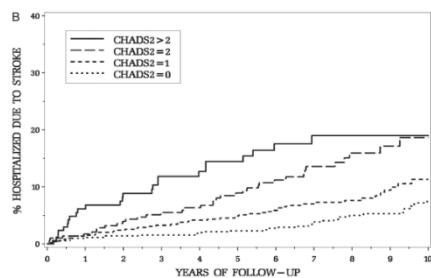
- What amount of AF is significant for stroke risk?
- What amount of AF (ie, what threshold of AF burden) can justify to initiate oral anticoagulation according to CHA₂DS₂ VASc in specific settings?

cardiomyopathy, starting from its classification divided into four classes. More in particular Prof. Capucci, talked about the basic mechanisms leading to the atrial cardiomyopathy and highlighted that AF is an epi-phenomenon of the atrial cardiomyopathy affecting the atrium, not the leading cause of stroke. In the second part of his lecture, the speaker presented very interesting data on the main methods for the atrial cardiomyopathy detection and prognosis, like ECG, MRI and CHADS₂ vasc score. Prof. Capucci talked also about the novelties about antiarrhythmic drug therapy in atrial fibrillation patients

“Atrial fibrillation: Emergent solutions for an emergent epidemic” was the topic of Prof. Capucci presentation. The speaker, coming from Ancona (IT), presented very interesting data starting from the prevalence of AF by CVD classification and gender. Going deeper in his lecture, Prof. Capucci talked about AF detected by CIEDs and the risk of stroke. In the main part of his presentation, the speaker presented very interesting data on AF in patients affected by atrial



ROLE OF THE CHADS₂ SCORE IN ACUTE CORONARY SYNDROMES: RISK OF SUBSEQUENT STROKE IN PATIENTS WITHOUT ATRIAL FIBRILLATION



Poçi D. et al. CHEST 2012; 141(6):1431-1440



and presented very interesting data on the state of the art, like the use of ranolazine in association with amiodarone or dronedarone in patients affected by paroxysmal atrial fibrillation. Finally, the speaker talked about the upstream therapies like the mineralocorticoid receptor antagonists, statins, ACE-i and cardiac rehabilitation procedures. In conclusion, Prof. Capucci pointed out that the clinical management of the AF patients needs for and “holistic” and “personalized” clinical approach.

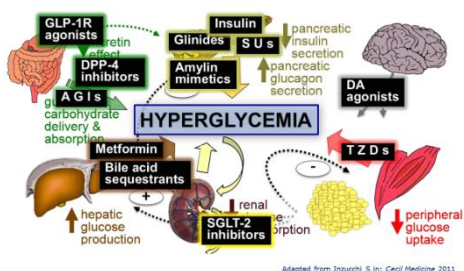
- What amount of AF is significant for stroke risk, from the speaker point of view?
- What amount of AF can justify the initiation of the oral anticoagulation, based on the data presented by the speaker?
- What are the basic mechanisms leading to the atrial cardiomyopathy, from the speaker point of view?
- What’s new in antiarrhythmic drug therapy for atrial fibrillation, based on the data presented by the speaker?
- What’s about the effect of ranolazine in AF patients, based on the data presented by the speaker?
- What’s new in upstream therapies for atrial fibrillation, based on the data presented by the speaker?

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The new age of diabetes and CV disease

Multiple pathophysiologically-based therapies for T2DM

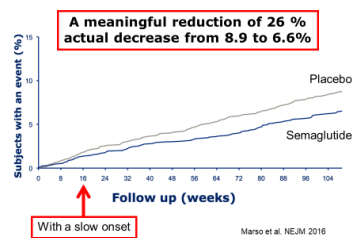


The main topic of Prof. Cosentino presentation was “The new age of diabetes and CV disease”. The speaker, coming from Stockholm (Sweden), presented very interesting data on the relationship between CVD and diabetes starting from the historical perspective till the contemporary trials and the main contributions from the most recent ones. Going deeper in his lecture, Prof. Cosentino presented very interesting data on the multiple complex pathophysiological abnormalities in T2DM patients, the related therapies and their effects on the heart. In the main part of his lecture, the speaker talked about the correlation between the T2DM therapies and the CV system through the presentation of the main results of the outcome trials running in these patients. More in particular, Prof. Cosentino presented very interesting data on the contemporary trials with glucose lowering agents with a particular attention to their objective and structure and highlighted that more than 120000 people have been enrolled in these trials. In the last part of his lecture, the speaker highlighted that the new drugs do not present differences in results from an efficacy and safety point of view, with the only exceptions of the SGLT2 inhibitors and the GLP-1 RA

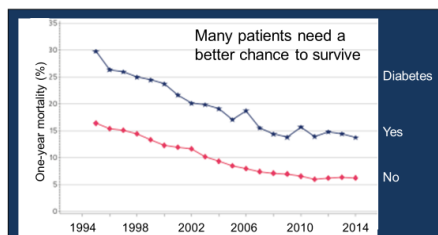
which demonstrate a very effective reduction in CV-death or MI or stroke compared to placebo in T2DM patients. Finally, Prof. Cosentino presented very interesting data on the most recent trials like the SUSTAIN 6 trial and the CANVAS program. In conclusion, the speaker pointed out that the outcome of EMPA-REG, CANVAS, LEADER and SUSTAIN 6 represents a paradigm shift in the treatment of T2DM patients.

SUSTAIN 6 Primary endpoint

First of CV-death, nonfatal myocardial infarction or stroke



Diabetes and myocardial infarction Time trends in 1-year mortality – Swedish RIKS-HIA 1995-2014

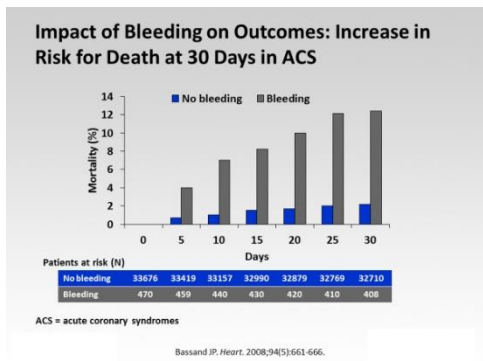


- What are the main recent trials running in diabetic patients, presented by the speaker?
- What should be the impact of these studies on guidelines?
- What should be the impact of these studies in research and clinical practice?
- What's about the multiple complex pathophysiological abnormalities in T2DM from the speaker point of view?

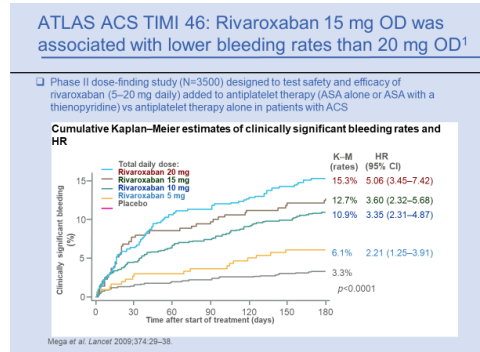
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New anticoagulants and SCA



Prof. Di Minno from Naples (IT), spoke about new anticoagulants and SCA and presented very interesting data on aspirin and aspirin plus clopidogrel in ACS. Going deeper in his lecture, the speaker talked about the impact of bleeding on outcomes and the related risk of death. In the main part of his lecture Prof. Di Minno presented very interesting data given by the MATCH study and the results on bleeding leading to the possibility to withdraw aspirin in these patients. More in particular the speaker talked about the relationship between bleeding and the Triple therapy in AF patients. In the second part of his lecture, Prof. Di Minno presented very interesting data on the pathophysiological mechanisms leading to bleeding in these patients and talked about the introduction of DOACs in therapy. The speaker presented also very interesting data given by clinical studies running in ACS patients treated with DOACs plus DAPT. More in particular he talked about the ATLAS ACS TIM 46 and 51 studies, the Gemini ACS 1 study, the PIONEER AF-PCI, the RE-DUAL PCI study and the AUGUST study. In conclusion, Prof. Di Minno, pointed out that the 2016 ACC/AHA guidelines have been updated more in particular on the duration of DAPT in ACS patients.



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2016 ACC/AHA Guideline update on duration of DAPT in patients With ACS

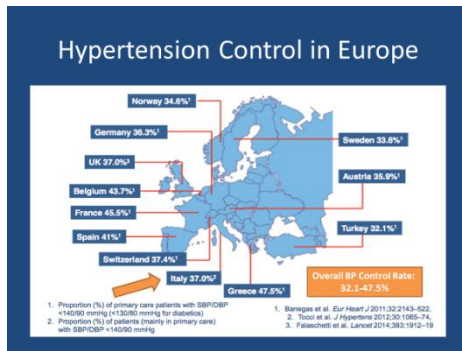
Strategies	ACC/AHA Recommendations	Strength of the Recommendation	Level of Evidence
Use of potent antiplatelet agents	Ticagrelor is a reasonable choice over clopidogrel in patients with ACS treated with DAPT after PCI Prasugrel is a reasonable choice over clopidogrel in patients with ACS treated with DAPT after PCI who are not at high risk for bleeding complications and who do not have a history of stroke or TIA Prasugrel should not be administered to patients with a prior history of stroke or TIA	Moderate Benefit >>Risk	Moderate-quality evidence from 1 or more RCTs; meta-analyses of moderate-quality RCTs
Addition of direct oral anticoagulants to DAPT	No address in 2016 update		
Optimizing the duration of DAPT	Patients with ACS treated with DAPT after PCI should be given P2Y12 inhibitor for at least 12 months Patients with ACS treated with DAPT after PCI without bleeding complications and are not at high risk of bleeding may continue DAPT for longer than 12 months Patients with ACS treated with DAPT who develop high risk of bleeding, are at high risk of severe bleeding complications, or develop overt bleeding may discontinue P2Y12 inhibitor after 6 months	Strong Benefit >>>Risk Weak Benefit >Risk Weak Benefit >Risk	Moderate-quality evidence from 1 or more RCTs; meta-analyses of moderate-quality RCTs High-quality evidence from more than 1 RCT; meta-analyses of high-quality RCTs, or more RCTs corroborated by high-quality registry studies Randomized or nonrandomized observational or registry studies with limitations of design or execution; meta-analyses of such studies; physiological or mechanistic studies in human participants

- Is ASA Necessary in Triple Therapy, for the speaker point of view?
- Can we find EGFR T790M in the blood, based on the data presented by the speaker?
- What are the main pharmacological characteristics of DOACs, based on the data presented by the speaker?
- What are the PIONEER AF-PCI results, presented by the speaker?
- What are the new strategies for managing the DOACs-related bleeding, based on the data presented by the speaker?

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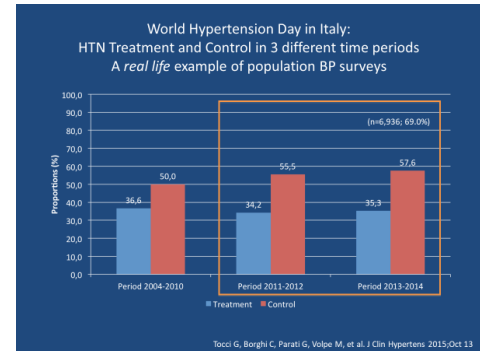
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Hypertension therapy: how to approach the 100% goal



Hypertension therapy: how to approach the 100% goal, was the topic discussed by Prof. Tocci from Rome (IT). More in particular the speaker presented very interesting data on the hypertension control in Europe and in Italy. Going deeper in his lecture, Prof. Tocci talked about the hypertension control rate in Europe and highlighted that it is less than 50%. In the main part of his lecture, Prof. Tocci presented very interesting data on the blood pressure targets

related to SBP and DBP and the results achieved in Italy. More in particular the speaker talked about the key points of the SIIA strategy for improving the BP control in Italy, pointing to the SIIA objective of obtain the 70% BP control in hypertensive patients. In the second part of his lecture, Prof. Tocci talked about the hypertension drug therapy and more in



Conclusive Remarks

- BP control is still suboptimal, although significant improvements have been achieved in Europe, and also in Italy.
- Current US and EU guidelines still identify a priority role for monotherapy. Yet, combination therapy has been widely used in clinical trials and is reported to reach BP control up to 90% in a setting of clinical practice.
- Practical tools, such as a therapeutic platform for the use of combination therapy, may support physicians' management of hypertension and ensure higher adherence and better BP control.
- Future guidelines for hypertension should be consistent with the observation that the vast majority of hypertensives require combination therapy and support the use of single-pill combination approach, also in order to face the low adherence problem.

particular on the effects of the combination therapy in the achievement of the BP control. Finally, the speaker presented very interesting data on the analysis of new large databases, like the "street BP, the GP database and the European networks. In conclusion, Prof. Tocci pointed out that the BP control is still suboptimal also in Italy, but the new generation of physicians has a concrete chance to control about the 100% of the hypertensive patients.

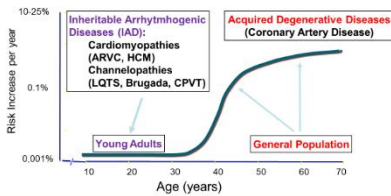
- What's about the hypertension control in Europe, based on the data presented by the speaker?
- How to improve BP control in daily clinical practice of hypertension, from the speaker point of view?
- What are the Key Points of the SIIA Strategy for improving BP control in Italy presented by the speaker?
- What is the New Mission of the Italian Society of Hypertension (SIIA), presented by the speaker?

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Prediction and prevention of sudden death

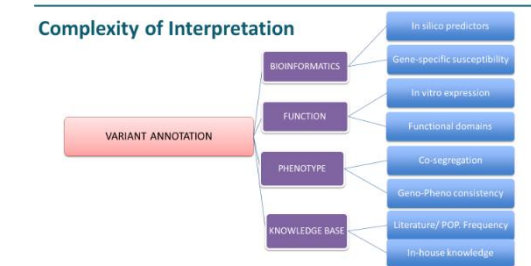
Age-Specific Risk and Causes for Sudden Death



Prof. Priori from Milan (IT), spoke about the prediction and prevention of sudden death. More in particular, the speaker talked about the age-specific risks and causes for Sudden Death. Going deeper in her lecture, Prof. Priori presented very interesting data on the problem of predicting SCD and on the importance of CAD as a its cause in the general population. In the main part of her lecture, the speaker talked about the risk factors for SCD in CAD patients, pointing to the role played by the left ventricular ejection fraction as the most important marker of SCD. More in particular Prof. Priori talked about prevention in the general population starting from the guidelines recommendations in patients affected by CAD. The speaker presented also very interesting data on the main therapies for patients with LV dysfunction, administered with the intention to prevent SCD. In the second part of her presentation, Prof. Priori talked about the data of the COMPANION trial, demonstrating that the association of a defibrillator to the cardiac-resynchronization therapy, significantly reduces the risk of death. Finally, the speaker talked about the role played by the family history and the genetic risk score in the general population for the prediction of SCD. Prof. Priori presented also very interesting data

Prediction of SCD in the General Population The Role of Family History

- Two large population studies:
 - Jouven et al. (1999) showed that parental history of SCD increases risk of SCD by **1.8**. History of SCD on maternal and paternal families increases risk to **9.4**.
 - Friedlander et al. (2002) demonstrated that risk for SCD increases by **1.57** in the presence of a family history MI or CA.



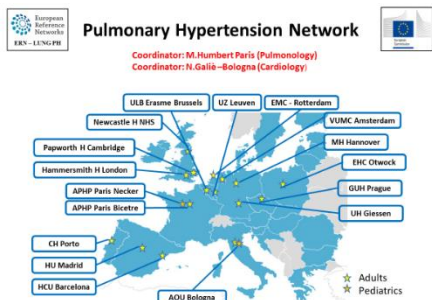
on the inherited arrhythmogenic diseases like any type of cardiomyopathy and on the population screening and the genetic testing as procedures to be implemented for the early recognition of these diseases. In conclusion, Prof. Priori pointed out that the screening programs should be implemented for the prevention of SCD, only when specifically trained personnel is available.

- What's about the Age-Specific Risk and Causes for Sudden Death, based on the data presented by the speaker?
- What Are the Risk Factors for SCD in Coronary Artery Disease?
- How to Implement Early Recognition of Inherited Arrhythmogenic Diseases?
- What's about the application of the genetic testing for the early recognition of the inherited arrhythmogenic diseases, based on the data presented by the speaker?

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Novel strategies to fight pulmonary hypertension

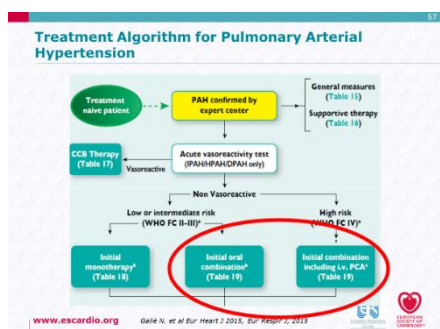


Novel strategies to fight pulmonary hypertension, was the topic discussed by Prof. Galiè from Bologna (IT), more in particular the speaker talked about the main characteristics of the pulmonary circulation anatomy and the PH definitions and classifications. Going deeper in his lecture, Prof. Galiè presented very interesting data on the haemodynamic and clinical PH classification and about the main pathologies of the distal pulmonary arteries in different types of PH. More in particular the speaker divided

these patients in in four groups, defined as PAH, LHD, LD and CTEPH. In the main part of his presentation, Prof. Galiè presented very interesting data on survival divided for all these four types of PH and on the prevalence of PAH and CTEPH in the Bologna Province area. The speaker talked also about the main clinical features of these four groups of patients and about mortality, pointing out that the use of the drugs approved for the treatment of CHF patients is armful in PH patients for the increase of the mortality rate. Finally, Prof. Galiè



presented very interesting data on the Bologna Balloon Pulmonary Angioplasty program and its main results from a clinical and haemodynamic point of view and on the approved drugs for these patients divided into these four groups, basically divided between monotherapy and sequential combination therapy. In conclusion, the speaker pointed out that the correct therapy strategy has to be selected based on the classification of the PH patients also for the presence of comorbidities.

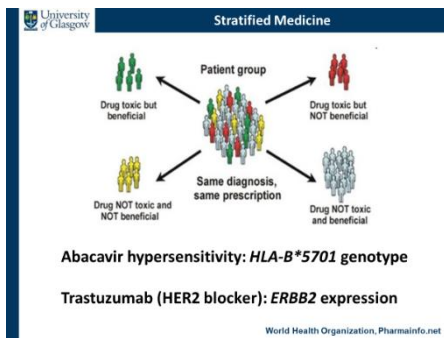


- What's about the haemodynamic classification of the PH, based on the data presented by the speaker?
- What is the prevalence of PAH and CTEPH in the Bologna Province area, based on the data presented by the speaker?
- What's about the mortality in RCTs treated with PAH approved drugs in CHF, based on the data presented by the speaker?
- What are the key points of the Bologna BPA Program presented by the speaker?
- What's about the contribution of neovascularization to the plaque growth, based on the data presented by the speaker
- What is the Treatment Algorithm for Pulmonary Arterial Hypertension, presented by the speaker?

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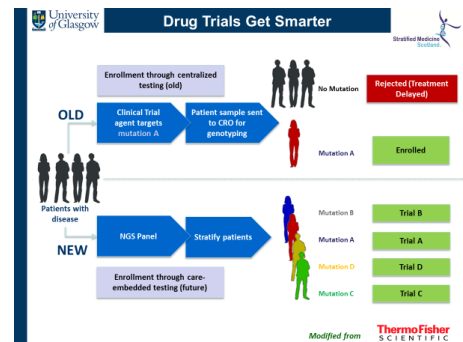
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Precision Medicine in hypertension

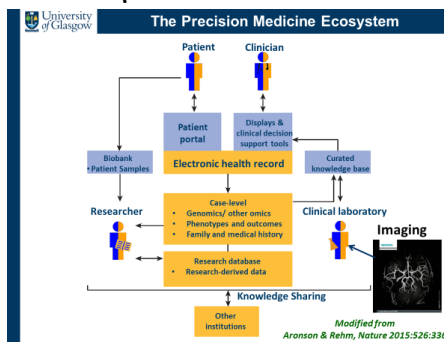


Prof. Delles from Glasgow (UK), presented very interesting data on Precision Medicine in hypertension, starting from the concept of the stratifying medicine. Going deeper in his lecture, Prof. Delles talked about the precision medicine topics across the lifeline and presented very interesting data on its real meaning. In the main part of his lecture, Prof. Delles talked about hypertension, pointing to his multifactorial etiology and the related complexity of the disease. The speaker

presented very interesting data on the high worldwide prevalence of hypertension and the related health economic burden. Prof. Delles talked also about Omics and the techniques developed for an integrated analysis, more in particular the speaker presented very interesting data on the Biology System and its relationship with Omics. In the second part of his lecture, Prof. Delles presented very



interesting data on the application of the precision medicine rules for the diagnosis and treatment of hypertension and other cardiovascular diseases. More in particular the speaker highlighted that, thanks to precision medicine, could be possible to better stratify patients based on their gene mutations. Finally, Prof. Delles talked about the precision medicine ecosystem, where patients and clinicians are linked through electronic systems.



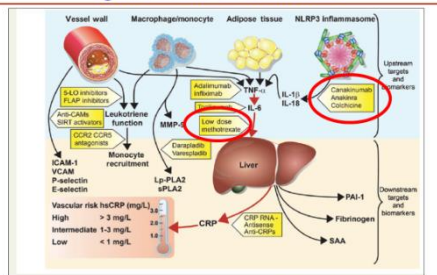
- What are the domains of the Stratified Medicine, based on the data presented by the speaker?
- What are the key points of the Omics Techniques for Integrated Analysis, presented by the speaker?
- What's about CKD 273, based on the data presented by the speaker?
- What is the Path to Precision Medicine, presented by the speaker?

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Inflammatory markers for a better risk stratification and prediction

Inflammation and Coronary disease – genetics and clinical trials



Ridker et al. Eur Heart J 2014

Prof. Landmesser from Berlin (Germany), spoke about “Inflammatory markers for a better risk stratification and prediction” and presented very interesting data starting from the presentation of a clinical case of a patient affected by ACS. Going deeper in his lecture, Prof. Landmesser talked about the clinical classification of the plaque morphology in the coronary disease. In the main part of his lecture, the speaker presented very interesting data on the main therapeutic strategies for the control and treatment of the

atherosclerotic CVD, starting from the role of inflammation in the development of the atherosclerotic plaque. Prof. Landmesser presented very interesting data on the correlation between inflammation and cardiovascular risk, given by the main clinical trials running in patients affected by CVD and treated with the new monoclonal agents like canakinumab. The speaker presented also other very interesting data on the relationships between Immunity, Inflammation and Cancer, by highlighting the role played by inflammation on the increase of the cancer risk

Immunity, Inflammation, and Cancer



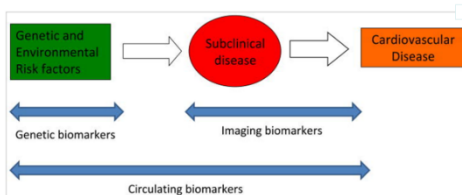
Sub-clinical chronic inflammation increases cancer risk (hsCRP is also a risk factor for certain cancers, in particular lung cancer)

Inflammation in the tumor micro-environment impacts upon tumor initiation, progression, invasiveness, and metastatic progression

Grivnaniuk, Greten, Karin. Cell 2016;146:883-99.

and on the tumor initiation and progression. Finally, Prof. Landmesser presented very interesting data on the cardiovascular risk stratification and risk prediction, by highlighting the importance to identify genetic, imaging and circulating biomarkers for the CVD risk stratification.

Progression from risk factors to overt cardiovascular disease: Role of imaging



Adapted from Wang; Circulation 2011; 123: 551-565

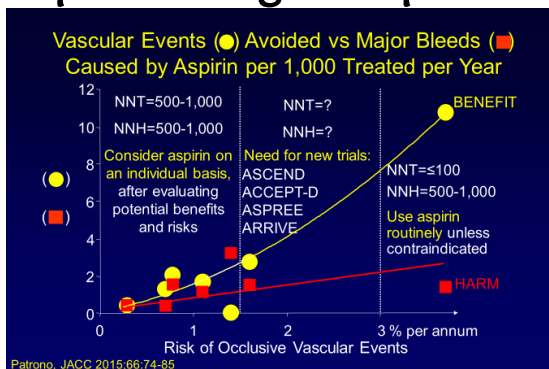
In conclusion, the speaker pointed out that thanks to this new approach, patients will receive more benefits also from a therapeutic point of view, more in particular in a secondary prevention setting.

- What’s about the role of Inflammation in CV Disease, based on the data presented by the speaker?
- What’s about the Inflammation and Coronary disease, based on the data presented by the speaker?
- What’s about the therapeutic inhibition of the inflammatory pathways in CV Disease, based on the data presented by the speaker?
- What are the key points of the cardiovascular risk stratification, from the speaker point of view?

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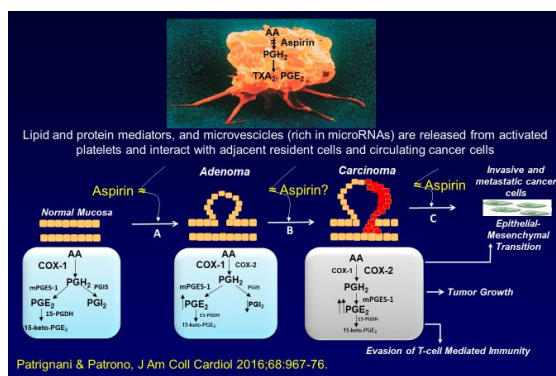
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Aspirin and global prevention

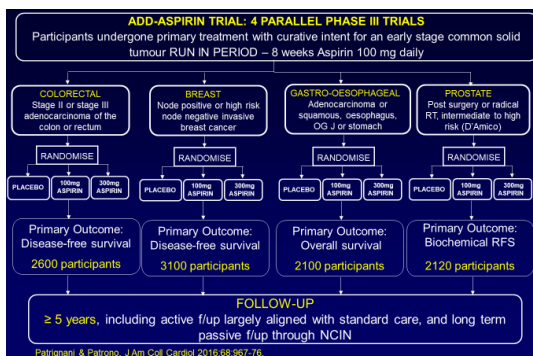


Aspirin and global prevention, was the topic discussed by Prof. Patrono from Rome (IT), more in particular the speaker talked about the role played by Aspirin in cardiovascular and cancer prevention. Going deeper in his lecture, Prof. Patrono presented very interesting data on Aspirin, its discover by Dr. Felix Hoffmann in 1897, its mechanism of action, developed in 70th years of the last century, its application in the cardiovascular setting and its major problems due to the high risk of bleeding. In

the main part of his lecture, Prof. Patrono, presented new data on the effect of aspirin on the prevention of the gastrointestinal cancers and highlighted that the number need to treat for obtain benefits in cancer prevention is significative lesser than the number need to harm for the development of AEs like bleedings. The speaker talked also about many trials supporting the evidence of a chemopreventive effects of aspirin against the gastrointestinal cancers and presented very interesting data on some features of the chemopreventive effect of Aspirin. Finally, Prof. Patrono talked about the potential cellular targets of low-dose aspirin, like platelets,



megakaryocyte and intestinal epithelial/stromal cells cox1 and presented very interesting data given by a clinical trial running in patients undergoing CRC screening, treated with aspirin at the dose of 100 mg daily for 7 days. In conclusion, the speaker pointed out that in order to investigate the effect of aspirin in secondary cancer prevention, a study is actually ongoing in UK running on patients affected by colorectal, breast, gastro-oesophageal and prostate cancers.

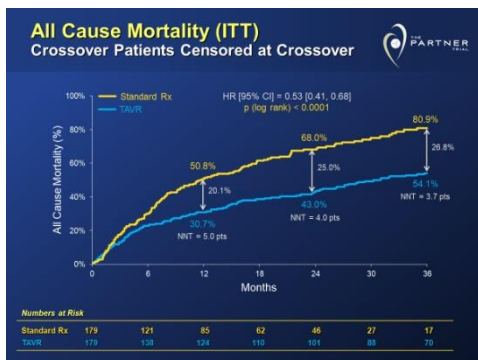


- What's about the Guidelines on the Use of Aspirin in Primary Prevention, based on the data presented by the speaker?
- What are the sources of evidence supporting a chemopreventive effect of Aspirin against Gastrointestinal Cancers, presented by the speaker?
- What are the potential cellular targets of low-dose Aspirin, presented by the speaker?
- What's about the cancer incidence during six randomised trials of daily low-dose Aspirin in primary prevention of vascular events, based on the data presented by the speaker?
- What are the key points of the ADD-Aspirin Trial, presented by the speaker?

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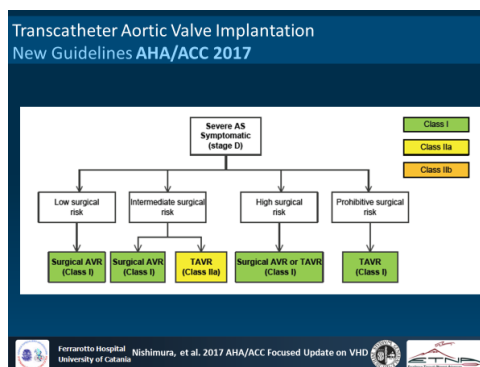
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Valvular disease, the interventional approach

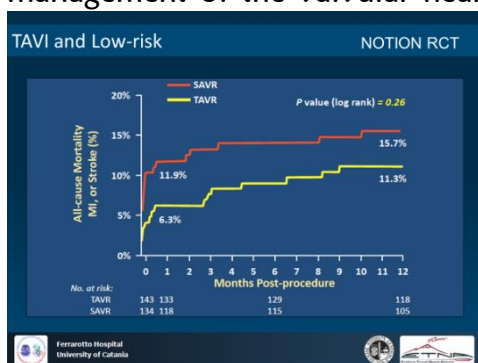


Prof. Tamburino from Catania (IT), spoke about the interventional approach of the valvular disease and presented very interesting data starting from the estimated global TAV implantation growth. Going deeper in his lecture, Prof. Tamburino talked about the main clinical trials running on patients which underwent to TAVI like the Partner and the CoreValve trials. In the main part of his lecture, the speaker presented very interesting data on these TAVI patients compared to the ones treated with surgical procedures and highlighted

that in such high-risk patients, TAVI reduces the all-cause of mortality and stroke. Prof. Tamburino talked also about the main TAVI AEs, mainly characterized by aortic regurgitation and presented other very interesting data on the effect of TAVI through the transfemoral approach, in patients affected by aortic stenosis, compared to the surgical approach. Based on these data, the speaker pointed out that send patients with aortic stenosis to the surgeon, has the consequence to lose more patients. In the second part of his lecture, Prof.



Tamburino talked also about the changes of the guidelines recommendations for the management of the valvular heart disease and presented also very interesting data on the TAVI durability, higher than the one of the surgical procedures and on the TAVI optimization, characterized by an early discharge. In the last part of his lecture, Prof. Tamburino talked about the Mitraclip procedures and presented a lot of data on the main devices produced by the industry, the most for HF patients. In conclusion, Prof. Tamburino pointed out that TF-TAVI is the definite treatment for intermediate-risk patients. Low risk patients and early treatment are the next step.



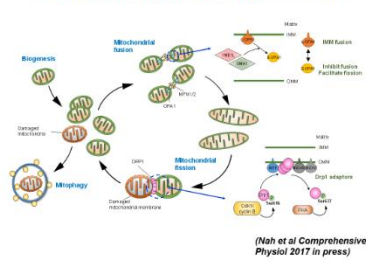
- What is the Partner study design, based on the data presented by the speaker?
- What's about the all-cause of mortality and stroke in the CoreValve study, presented by the speaker?
- What's about total Aortic Regurgitation, based on the data presented by the speaker?
- What are the New Guidelines AHA/ACC 2017 on the Transcatheter Aortic Valve Implantation, based on the data presented by the speaker?
- What's about the TAVR risk assessment, based on the data presented by the speaker?

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The role of autophagy: from injury to self-protection

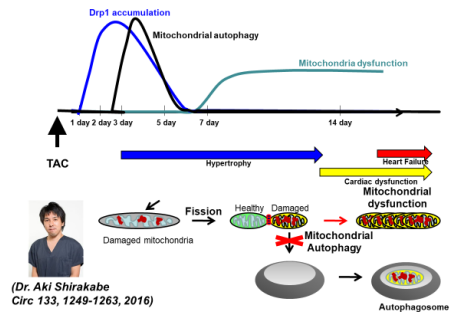
Mitochondria quality control mechanisms



“The role of autophagy: from injury to self-protection” was the topic discussed by Prof. Sadoshima. The speaker coming from Newark-NJ (USA), presented very interesting data on the mitochondria quality control mechanisms. Going deeper in his lecture, Prof. Sadoshima talked about the mitochondria degrade mechanisms like autophagy and mitophagy. In the main part of his lecture, the speaker presented very interesting and innovative data on some experiments conducted in his lab. Unit on the main

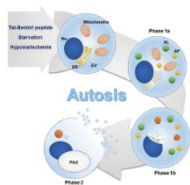
mechanisms of the mitochondrial autophagy, pointing out that mitophagy is activated after the induction of a pressure over-load. More in particular, the speaker talked about an experiment aimed to induce mitophagy in the heart through the daily injection in mice of a peptide called TAT-Beclin 1. The speaker pointed out that this injection has improved the cardiovascular functions in these animals affected by HF. In the second part of his lecture, Prof. Sadoshima presented other very interesting

Mitophagy is suppressed chronically during heart failure



data on the molecular mechanisms of mitophagy and on the alternative pathways involved in the degradation of mitochondria in the cardiomyocytes. More in particular the speaker highlighted that ischemia but also reperfusion activates autophagy mainly through the ulK-1 pathway. Finally, Prof. Sadoshima presented very interesting data on other effects of autophagy on the heart, like the damaging ones, more in particular in those cases of an excessive mitophagy activation.

Autophagy: protective or damaging?



Molecular mechanism of Autosis

- A compound library screen revealed that Na⁺K⁺-ATPase participates in regulating autosis.
- Cardiac glycosides (chemical inhibitors of the Na⁺K⁺-ATPase) inhibit autosis and dramatically reduce brain damage in neonatal rats subjected to brain ischemia.
- Cardiac glycosides available target alpha1 subunit of the Na⁺K⁺-ATPase in humans but not in rodents.

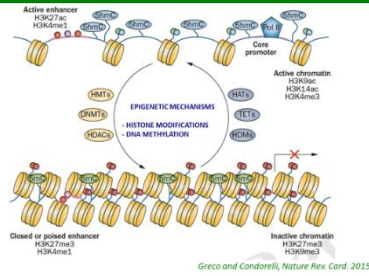
- What is the role of Mitophagy on the heart, based on the data presented by the speaker?
- What are the molecular mechanisms of mitophagy, presented by the speaker?
- What are the two forms of mitophagy in the heart, presented by the speaker?
- Is Autophagy protective or damaging?

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Epigenetics in cardiovascular diseases: A practical view

Epigenetics: a variety of mechanisms modulating the expression of genes without modifying the DNA sequence

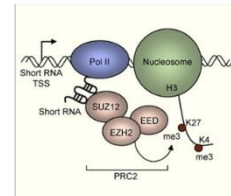


Prof. Condorelli from Milan (IT), spoke about “Epigenetics in cardiovascular diseases: a practical view”. More in particular, the speaker talked about the DNA sequencing technologies applied to the heart. Going deeper in his lecture, Prof. Condorelli presented very interesting data starting from the challenges of the modern Medicine, mainly due to Precision Medicine and Omics. In the main part of his lecture, the speaker talked about epigenetics, starting from his meaning characterized by a variety of mechanisms modulating the expression of the genes without modifying the DNA sequence.

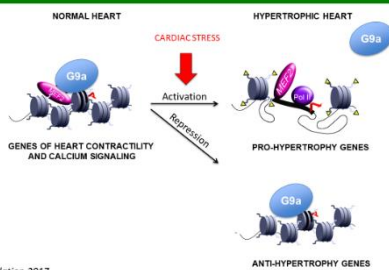
Prof. Condorelli, presented also very interesting data given by animal experiments running in his lab, on the transcription regulation through the histone methylation and highlighted the role played by G9a as a true transcriptional repressor.

Question 2

As G9a is implicated in histone methylation, what is its role in myocardial homeostasis in physiology and disease?



Hypothetical mechanism of action



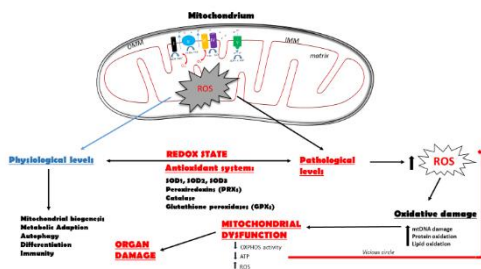
In the second part of his lecture, the speaker presented very interesting data on the effects of the G9a inhibition in the heart and on the role played by G9a in the development of the cardiac hypertrophy. Finally, Prof. Condorelli talked about other experiments aimed to verify the relevance of epigenetics in the myocardial human diseases and presented very interesting data on a study performed on tissue specimens given by patients affected by cardiomyopathy.

- What’s about Epigenetics and the evolution of the species, based on the data presented by the speaker?
- How does histone methylation regulate transcription?
- What is the role of G9a in myocardial homeostasis, in physiology and disease?
- Is G9a required for cardiac hypertrophy?
- What is the relevance of epigenetics in myocardial human disease?

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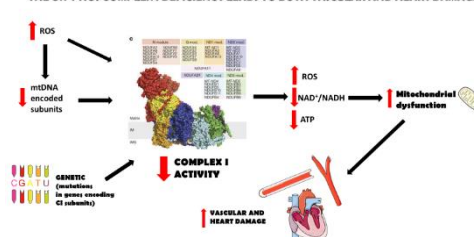
Mitochondrial-related redox genes



Mitochondrial-related redox genes, was the topic discussed by Prof. Rubattu from Rome (IT), more in particular the speaker talked about mitochondria as the key producers of energy for the hearth. Going deeper in her lecture, Prof. Rubattu presented very interesting data on the link between mitochondrial dysfunction and the cardiovascular diseases. In the main part of her presentation, the speaker talked about the role of the

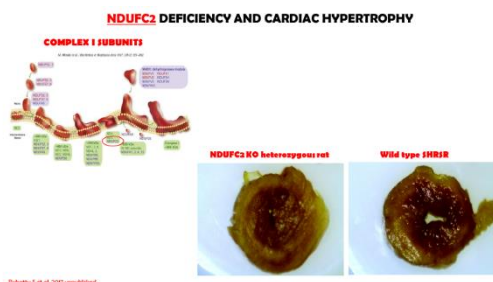
mitochondrial dysfunction for the development of CVD and presented very interesting data on the effects of the mitochondrial antioxidant system on the hearth and on the consequences of his damage. Prof. Rubattu presented a lot of experimental data on the ox-phos complex I deficiency and the Ndufc2 Gene inhibition, able to determine mitochondrial dysfunction and cardiac hypertrophy. In the second part of his lecture, the speaker talked about the role of the mitochondrial dysfunction in the transition from compensated to decompensated cardiac

THE OX-PHOS COMPLEX I DEFICIENCY LEADS TO BOTH VASCULAR AND HEART DAMAGE



disease, as a

model of HF and presented very interesting experimental data on the correlation between mitochondrial damage and HF. Finally, Prof. Rubattu presented very interesting data on mitochondria as therapeutic target in CVD. In conclusion, Prof. Rubattu pointed out that the mitochondrial dysfunction is strong correlated with CVD and the development of cardiac dysfunction.

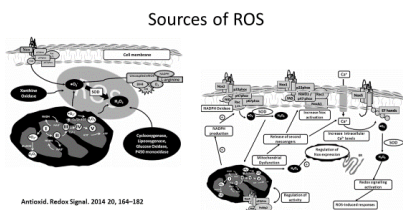


- What's about the correlation between mitochondrial dysfunction and CVD, based on the data presented by the speaker?
- What is the role of the mitochondrial antioxidant system on the heart, based on the data presented by the speaker?
- What's about the Ndufc2 deficiency and the cardiac hypertrophy, based on the data presented by the speaker?
- What's about mitochondria as a target in cardiovascular diseases?

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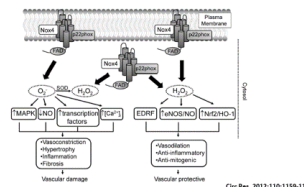
Oxidative stress and vascular damage



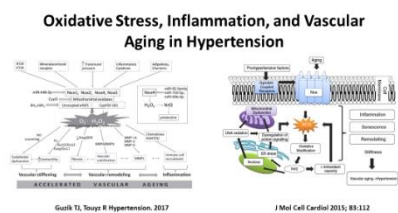
Prof. Savoia from Rome (IT), presented very interesting data on the oxidative stress and the vascular damage, starting from the concept that the production of increased reactive oxygen species correlates with the vascular damage. Going deeper in his lecture, Prof. Savoia presented very interesting data on the ROS production in the hypertensive cardiovascular disease. In

the main part of his lecture, the speaker talked about the sources of ROS and on the Nox isoforms, like the NOX4, deeply involved in many pathways leading to vascular damage, but also protection. Prof. Savoia presented also very interesting data on the main ROS activated pathways and on the role played by aldosterone and Ang. II as the

Role of Nox4 in vascular pathophysiology



major activators of the Nox isoforms. The speaker discussed also about the main molecular mechanisms involving some proteins like the s-Src in the onset of the oxidative stress at the vascular level and presented very interesting data on the correlation between oxidative stress, inflammation and Vascular aging in Hypertensive patients.



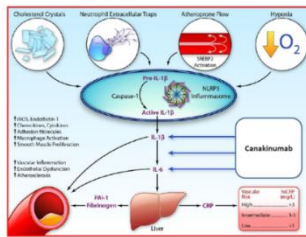
- What is the role of Aldosterone and Ang. II on the Nox activation, based on the data presented by the speaker?
- What's about the role played by the oxidative stress in the acceleration of the vascular aging, based on the data presented by the speaker?
- What is the role played by aldosterone in the onset of the vascular aging, based on the data presented by the speaker?
- What is the correlation between the mineralocorticoid receptor blockade and the vascular aging, based on the data presented by the speaker?

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New alternative strategies for lipid-related cardiovascular damage

Canakinumab

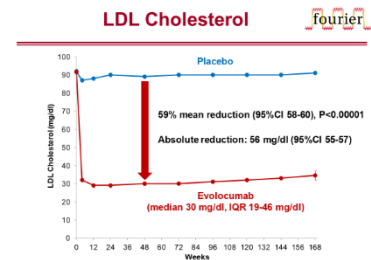


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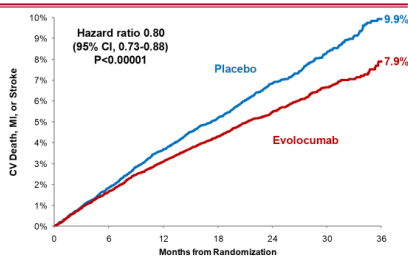
Prof. Pedersen from Oslo (Norway), spoke about “New alternative strategies for lipid-related cardiovascular damage” and presented very interesting data on PCSK9 inhibitors and on Canakinumab. Going deeper in his lecture, Prof. Pedersen talked about the PCSK9 inhibitors and presented very interesting data given from the main clinical trials running in hypercholesterolemic patients treated with these drugs. In the main part of his lecture, the speaker

talked about Canakinumab and highlighted the too high cost of this drug, unaffordable also for a rich country like Norway. Speaking about Evolucomab, Prof. Pedersen presented very interesting data given from the Fourier study, running in more than 27.000 hypercholesterolemic patients. More in particular

the speaker talked about the effect of this new drug on LDL cholesterol, CV death, MI, stroke and the hospitalization for UA. The effects on LDL cholesterol was about the 59% reduction, the speaker pointed out. In conclusion, Prof. Pedersen pointed out that the PCSK9 inhibitors and the monoclonal antibodies against interleukin offer new opportunities to reduce the cardiovascular events, but their high cost is currently preventing a widespread use.



Key Secondary Endpoint Fourier

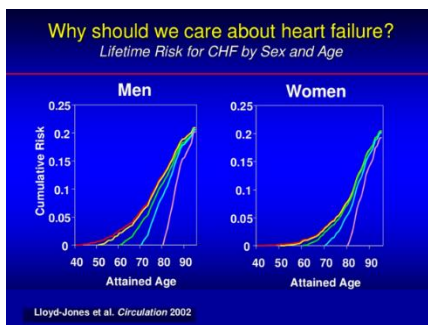


- What’s about Canakinumab, based on the data presented by the speaker?
- What are the main results of the Cantos study, presented by the speaker?
- What’s about Evolocumab from the speaker point of view?
- What are the main results of the Fourier study presented by the speaker?

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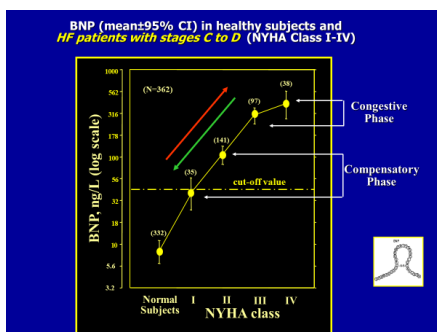
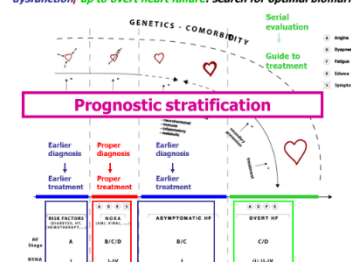
The changing face of natriuretic peptides



The changing face of natriuretic peptides, was the topic discussed by Prof. Emdin from Pisa (IT), more in particular the speaker talked about the correlation between natriuretic peptide and heart failure. Going deeper in his lecture, Prof. Emdin, presented the main correlations between natriuretic peptides and the brain, the heart and the kidney. In the main part of his lecture, Prof. Emdin talked about biomarkers and their clinical value starting from the risk conditions up to overt heart failure. More in particular, the speaker presented

very interesting data on the natriuretic peptides triggers for production, their actions from the heart to the kidney, vessels and brain and their main pathophysiologic aspects. Prof. Emdin talked also about the neurohormonal unbalance in HF patients and the deep involvement of NPS. The speaker presented very interesting data on the seven major classes of biomarkers contributing to the biomarker profile in HF, where NPs play a major role. In the second part of his lecture, Prof. Emdin talked about BNP, starting from its synthesis derived

From risky conditions, through acute damage and ventricular silent dysfunction, up to overt heart failure: search for optimal biomarker



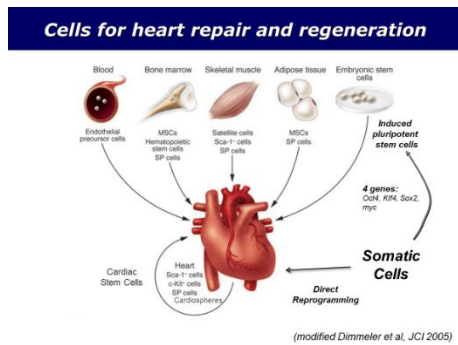
from the pro-BNP molecule and went deeper in presenting very interesting data on its activity and the data derived from its screening tool. In the last part of his lecture, the speaker talked about NPs as prognostic indicators and as markers of the therapeutic response. Finally, Prof. Emdin presented very interesting data on the use of Troponin and sSCT2 in HF patients as biomarkers for a prognostic evaluation, more in particular in those ones with a reduced ejection fraction.

- Why should we care about heart failure, from the speaker point of view?
- What's about the clinical value of biomarkers, based on the data presented by the speaker?
- What are the 7 major classes of biomarkers contributing to the biomarker profile in HF patients, presented by the speaker?
- What are the main biomarkers useful to inform on mechanisms and to determine the prognosis, based on the data presented by the speaker?
- What are the main limitations of NPs in HF patients, from the speaker point of view?

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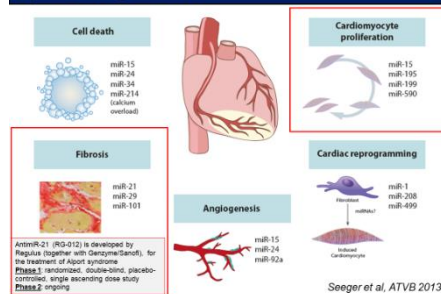
Cardiovascular regeneration: current status and perspectives



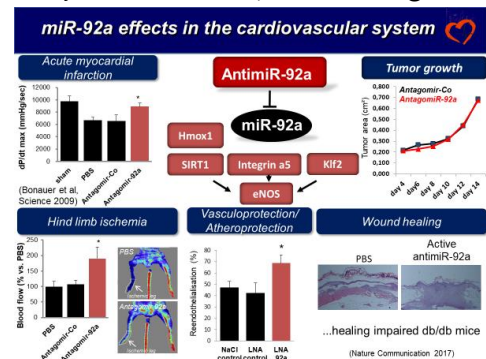
Prof. Dimmeler from Frankfurt (Germany), spoke about “Cardiovascular regeneration: current status and perspectives” and presented very interesting data starting from the main strategies for the heart regeneration. Going deeper in her lecture, Prof. Dimmeler talked about the main challenges in cell-based therapies. In the main part of her lecture, the speaker talked about the regenerative potential of the heart and presented very interesting data on the main strategies for inducing or

activating the endogenous regeneration. More in particular Prof. Dimmeler talked about the role played by the non-coding RNAs in repair and regeneration. The speaker presented very interesting data on the non-coding DNA and the non-coding RNAs also called microRNAs, their main functions, their role in post infarction repair and regeneration and talked about the

MicroRNAs and postinfarction repair & regeneration



activity of the miR-92 on the regulation of angiogenesis and vessel formation. Prof. Dimmeler presented a huge amount of data given by experimental tests running in her lab. Center on the effect of the inhibition of miR-92a in the heart after AMI. Finally, the speaker talked about the miR-92a inhibition mechanism of action and presented very interesting data on the effects of the MicroRNAs on the cardiomyocyte proliferation.

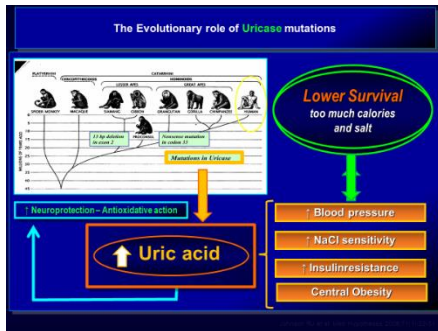


- What are the main cells for the heart repair and regeneration, based on the data presented by the speaker?
- What are the key strategies for heart regeneration, presented by the speaker?
- What’s about the strategies to induce or activate endogenous regeneration, from the speaker point of view?
- What are the miR-92a effects in the cardiovascular system, based on the data presented by the speaker?

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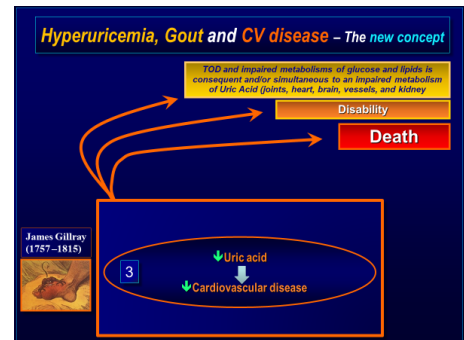
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Metabolic disorder and cardiovascular disease: the uprising role of uric acid

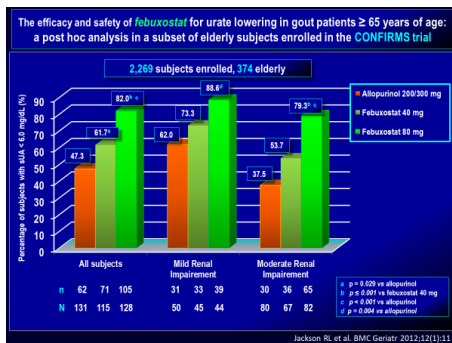


“Metabolic disorder and cardiovascular disease: the uprising role of uric acid” was the topic discussed by Prof. Ferri. The speaker, coming from L’Aquila, (IT), presented very interesting data starting from the evidence that the modern lifestyle leads to the onset of the metabolic syndrome. Going deeper in his lecture, Prof. Ferri talked about the correlation between Uric Acid and the metabolic syndrome. In the main part of his lecture, the

speaker presented a lot of very interesting data given from the main clinical trials running in patients affected by CVD with and without high Uric Acid serum levels. More in particular Prof. Ferri, presented very interesting data on the neuroprotection activity of UA, and its counteracting effect at higher level, leading to the stimulation of the synthesis of amyloid in the neuronal cells. The speaker



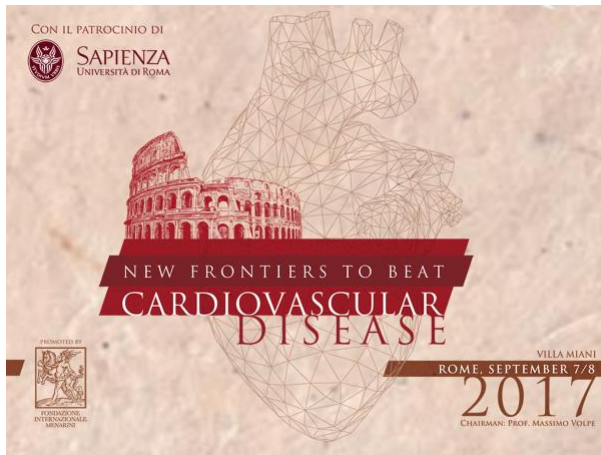
presented also very interesting data on the correlation between hyperuricemia and the increment in the CV and peripheral vascular disease mortality. In the second part of his lecture, Prof. Ferri talked about the possible correlation between the reduction of the CVD incidence and the UA reduction and presented very interesting data on the effects of the Xanthine inhibitors. Finally, Prof. Ferri presented very interesting data on the correlation between UA levels and the assumption of nutraceuticals.



- What is the Evolutionary role of the Uricase mutations, based on the data presented by the speaker?
- There is a correlation between Uric Acid and the risk of peripheral vascular disease, from the speaker point of view?
- What’s about Uric Acid and Nutraceuticals, based on the data presented by the speaker?
- What’s about a possible correlation between Uric Acid and the brain infarcts, based on the data presented by the speaker?

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