

**INTERNATIONAL SYMPOSIUM ON:
INNOVATION IN MEDICAL SCIENCES
AND PUBLIC HEALTH**
Cagliari (Italy), May 19-20, 2017
Highlights

Introduction



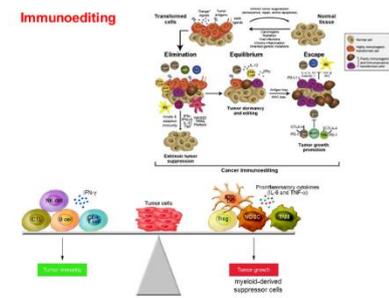
Prof. Mercurio, chairman of the symposium, opened the congress, by highlighting the high scientific level of this meeting, characterized by the involvement of different medical sciences like oncology, cardiology, hematology, regenerative medicine, genomics, metabolomics and coagulation. This congress was a very unique occasion for a very full update in innovation in these medical science, attended by the top researchers of all these field together with young physicians attending the School of Medicine

of the University of Cagliari.

To follow the presentations of this congress, click on the link below:

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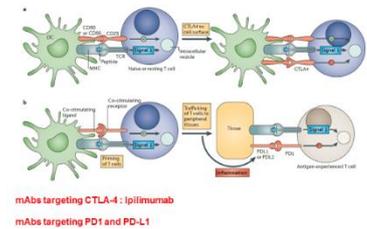
Biological basis of immune response as a therapeutic option



The biological basis of immune response as a therapeutic option, was the topic discussed by Dr. Madeddu in her lecture. The speaker, coming from Cagliari (IT), went deeper in her talk and presented very interesting data on the immunoeediting theory and on the innate and the adaptive immune response. In the main part of her presentation, Dr. Madeddu, talked about the pathways of the immune response against the tumoral cells and presented very interesting data on

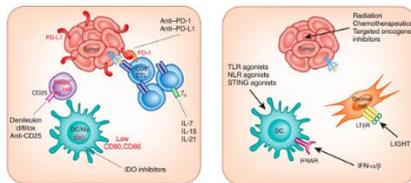
the T-cell activation and on the modulation of the T-cell activity. More in particular Dr. Madeddu presented very interesting data on the relationship between the tumor microenvironment, the T cell response and the therapeutic opportunities. The speaker talked also about a multitargeted approach to the cancer immunotherapy, by highlighting the importance of the modulation of the tumor inflammation for the induction of the T cell anti-tumor activity leading

The blockade of immune checkpoints in cancer immunotherapy



to the inhibition of the immune checkpoints. Finally, Dr. Madeddu spoke about the therapeutic interventions targeting the immune inhibitory pathways and presented very interesting data on the cisplatin-induced antitumor immunomodulation. In conclusion, the speaker pointed out that the promise of immunotherapy depends on the ability to reprogram the suppressive tumor microenvironment for promoting durable anti-tumoral immunity.

Therapeutic interventions targeting immune inhibitory pathways or promoting appropriate immune activation in tumor microenvironment



Nature Immunol 2013; 14: 1014-1022

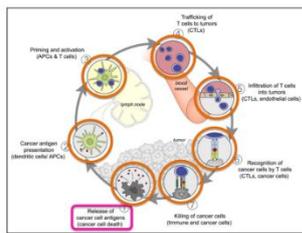
- Are the tumor cells antigenic?
- What are the key points of the T-cell activation and the modulation of the T-cell activity?
- What is the mechanism of action of the blockade of the immune checkpoints in the cancer immunotherapy?
- What is the role of CTL4 and PD1 in the modulation of the immune response?

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Tumour infiltrating lymphocytes (TILs) as a prognostic and predictive factor for immunotherapy

The cancer immunity cycle



Chen and Mellman, Immunity 2013



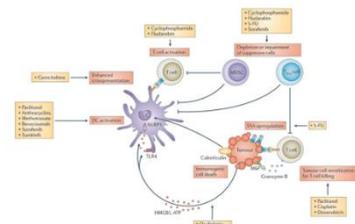
Cinzia Solinas - Cagliari, 19 May 2017



Dr. Solinas from Cagliari (IT), spoke about Tumour infiltrating lymphocytes (TILs) as a prognostic and predictive factor for immunotherapy. The speaker talked about the TILs definition and assessment, their prognostic role, the benefit from treatments and about the biomarkers for immunotherapy. Going deeper in her lecture, Dr. Solinas presented very interesting data on the cancer immunity cycle and its relationships with therapy, more in particular with the immune checkpoint blockade.

In the main part of her lecture, the speaker talked about the role played by TILs in the cancer suppression but also in its progression, depending on the TILs subpopulations involved. Dr. Solinas presented also very interesting data given by clinical studies, on the prognostic role played by TILs in different tumors like the colorectal and the breast cancers. In the second part of her lecture, the speaker talked about the relationship between immunotherapy and TILs, by highlighting that the presence of a lymphocytic infiltrate around the tumor, can raise the efficacy of the anticancer therapy.

Some drugs can induce an immunogenic cell death



Gallucci, Nature Reviews Drug Discovery 2012

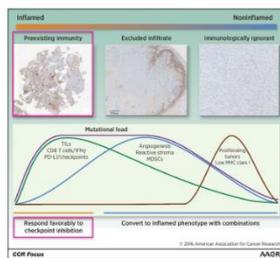


Cinzia Solinas - Cagliari, 19 May 2017



Finally, Dr. Solinas presented very interesting data on the predictive role played by TILs on immunotherapy, by highlighting that a higher concentration of CD8+T cells, predicts a better response to immunotherapy. In conclusion, the speaker pointed out that the immunotherapy approach can be guided on the basis of the immunological involvement of any specific tumor.

The tumor immunity continuum



Hedge et al. Clin Canc Res 2016



Cinzia Solinas - Cagliari, 19 May 2017



- Why are TILs important in cancer immunotherapy from the speaker point of view?
- What are the TILs subpopulations leading to the cancer suppression, based on the data presented by the speaker?
- What's about the prognostic role played by TILs in the melanoma cancer, based on the data presented by the speaker?
- What are the immune effects of the monoclonal antibodies from the speaker point of view?

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Clinical development of immunotherapy in gastrointestinal tumours

Immunotherapy: The Rising Star

Type of response	MSI (N=10)	MSS (N=18)
Complete response	0%	0%
Partial response	40%	0%
Objective Response Rate	40%	0%
Disease control Rate	90%	11%

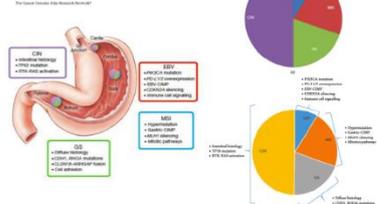
Mod from Lo DT et al. N Engl J Med 2015

The clinical development of immunotherapy in gastrointestinal tumours, was the topic Dr. Pusceddu spoke about in his lecture. The speaker coming from Cagliari (IT), started his talk, by presenting very interesting data on the role played by the immunotherapy in the colon, gastric and pancreatic cancers. Talking about the immunotherapy in the colon cancer, Dr. Pusceddu highlighted the key role played by the microsatellite instability of the colon cancer

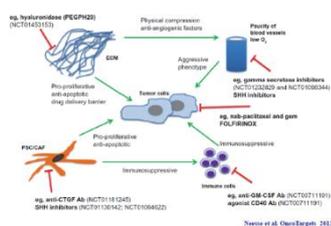
cells leading to a higher mutation tumoral burden and the related immunological reaction. The speaker presented very interesting data given by clinical studies running on colon cancer patients and treated with immunotherapy, where the presence of an important immunological response in the peritumoral area leads to a better response to immunotherapy.

ARTICLE

Comprehensive molecular characterization of gastric adenocarcinoma



Tumor stroma targeting strategies



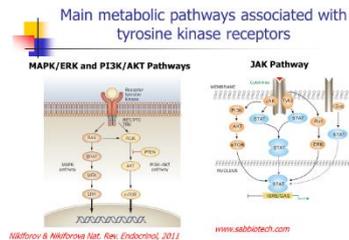
Dr. Pusceddu presented also data on the effects of the immunotherapy in gastric cancer patients, by highlighting that there are almost four different gastric cancer subtypes, characterized by different outcomes. Finally, the speaker talked about immunotherapy and pancreatic cancer, by highlighting the role played by the stroma surrounding the pancreatic tumor and presented very interesting data on the role played by immunotherapy on this tumor.

- What's about immunotherapy in colon rectal cancer patients, based on the data presented by the speaker?
- What is the association between the immunotherapy efficacy and the PD-L1 expression?
- What is the role played by the stroma surrounding the pancreatic cancer, based on the data presented by the speaker?
- What are the main trials in the adjuvant setting with immunotherapy in the pancreatic cancer?

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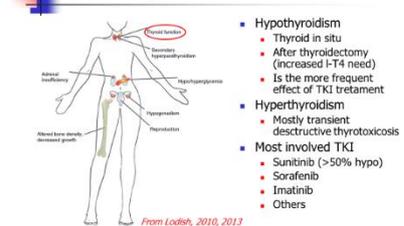
Endocrine effects of anti-cancer drugs



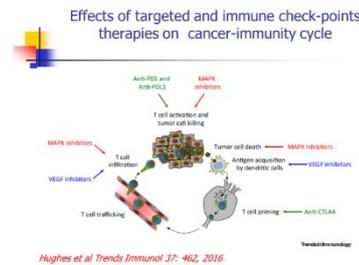
The endocrine effects of anti-cancer drugs, was the topic at the core of the lecture discussed by Prof. Mariotti. At the beginning of his talk the speaker, coming from Cagliari (IT), presented very interesting data on the endocrine effects of the traditional and the new targeted cancer therapies. Going deeper in his lecture Prof. Mariotti talked about the effects of the old anti-cancer agents on the serum thyroid hormone binding proteins and presented

very impressive data on the tyrosine kinase inhibitors already on the market and their main signaling pathways. In the main part of his lecture, the speaker talked about the TKIs endocrine-organs-involved side effects. More in particular He spoke about hypo and hyper-thyroidism, fertility, altered bone metabolism and hypoglycaemia. In the second part of his lecture, Prof. Mariotti presented very interesting data on the Immune check point inhibitors (ICPIs), their efficacy and their immune-related adverse events. Finally, the speaker talked about the TKIs and ICPIs endocrine effects as indicators of

Endocrine organs involved in side effects of tyrosine kinase inhibitors



efficacy and presented very interesting data on the effects of the targeted and immune-check-points therapies on the cancer-immunity cycle. In conclusion, the speaker pointed out that TKIs and ICPIs frequently affect the endocrine glands as true endocrine disruptors, but the potential role of the endocrine dysfunctions as predictive markers of the tumor response to the targeted therapies deserves particular attention for future investigations.



- What are the main endocrine organs involved side effects of TKIs presented by the speakers?
- What's about the TKIs hypoglycaemic effects from the speaker point of view?
- Why are the Immune checkpoint inhibitors the milestone in immunooncology from the speaker point of view?
- What are the main checkpoint pathways of the antigen-specific T cells presented by the speaker
- What's about the main ICPIs immune-related adverse events, based on the data presented by the speaker?

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Effects of tyrosine kinase inhibitors on thyroid function and autoimmunity

TKI and thyroid autoimmunity

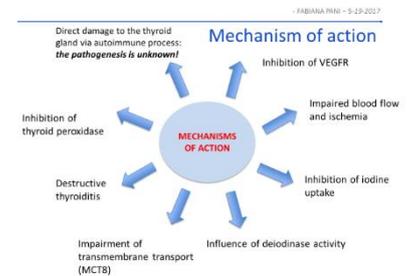
Oncologist and endocrinologist suggest to evaluate thyroid function, but few data are present in literature about thyroid autoantibodies



FNAC demonstrates abundant colloid and follicular epithelial cells organized in sheets and clusters along with lymphocytic infiltration consistent with lymphocytic thyroiditis.

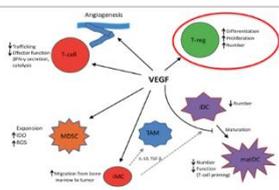
Alexandrescu DT et al 2008 Sunitinib-associated lymphocytic thyroiditis without circulating antithyroid antibodies Thyroid 18: 911.

The Effects of tyrosine kinase inhibitors on thyroid function and autoimmunity was the topic at the core of the lecture discussed by Dr. Pani. The speaker, coming from Cagliari (IT), talked about TKIs, their effects with a particular attention to thyroid dysfunction and autoimmunity, their mechanisms of action and on the future perspectives. Going deeper in her lecture, Dr. Pani presented very interesting data on the correlation between TKIs and hypothyroidism, thyrotoxicosis and thyroid atrophy, by highlighting the decrease in thyroid size diameter and parenchymal vascularization after TKIs treatment. In the main part of her lecture, Dr. Pani talked about TKIs mechanism of action and presented very interesting data given by clinical studies performed by her team of researches on the thyroid



dysfunctions and autoimmunity secondary to TKIs treatment. More in particular the speaker pointed out that patients developing thyroid autoimmunity have a better outcome in survival than patients without any sign of autoimmunity. Finally, Dr. Pani spoke about angiogenesis and immunity and presented the main methods of an animal study designed for understanding the effects of the immune check-points and the endothelial growth factors inhibition as combination therapy for the metastatic melanoma.

Angiogenesis and immunity



Ohl PA et al 2015 Inhibition of immune checkpoints and vascular endothelial growth factor as combination therapy for metastatic melanoma: an overview of rationale, preclinical evidence, and initial clinical data Front Oncol

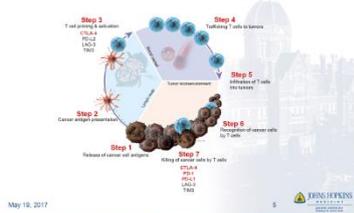
- What is the relationship between hypothyroidism, thyroid autoimmunity and survival based on the data presented by the speaker?
- What's about the thyroid function test evaluation during sunitinib therapy from the speaker point of view?
- What's about the correlation between hypothyroidism and survival based on the data presented by the speaker?
- What are the main mechanisms of action of TKIs based on the data presented by the speaker?

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Ipililumab-induced lymphocytic hypophysitis

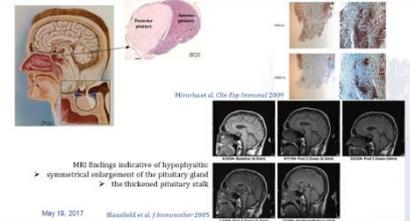
Therapeutic modulation of tumor immunogenicity



Ipililumab -induced lymphocytic hypophysitis was the topic of Dr. Chalan presentation. The speaker, coming from Baltimore (USA), talked about the immunotherapy goals, monotherapy versus combination therapy and about hypophysitis, its presentation, symptoms, incidence and management and the role played by CTLA-4 in its development. Going deeper in her lecture, Dr. Chalan presented data on immunotherapy and

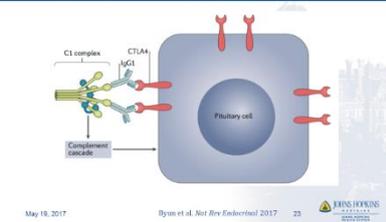
on the therapeutic modulation of the tumor immunogenicity. In the main part of her presentation, the speaker talked about the main clinical studies with ipilimumab in monotherapy and about the main studies with the combination therapy, by highlighting the positive effect of the combination therapy on survival. In the second part of her lecture, Dr. Chalan talked about hypophysitis, its clinical manifestations, its correlation

Hypophysitis (primary & secondary)- clinical manifestation



with the immune checkpoint inhibitors and its correlation with survival, by highlighting that the development of Hypophysitis in patients treated with immune checkpoint inhibitors is associated with a better overall survival. In conclusion, Dr. Chalan pointed out that the use of ipilimumab in combination with other ICPIs is associated with the higher risk of developing hypophysitis, but its development is associated with a better response to the cancer immunotherapy.

The reason ipilimumab- induced autoimmunity targets the pituitary remains unclear

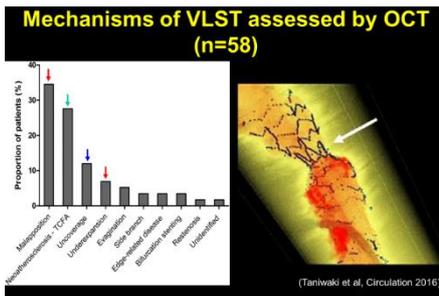


- What's about the management of hypophysitis secondary to immune checkpoint blockade?
- What is the incidence of hypophysitis after monotherapy and combination therapy?
- What's about the immunotherapy-survival curve after monotherapy and combination therapy presented by the speaker?
- What are the main steps of the therapeutic modulation of the tumor immunogenicity presented by the speaker?

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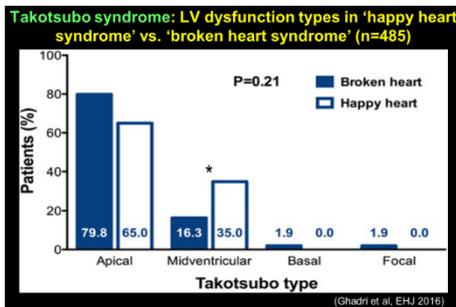
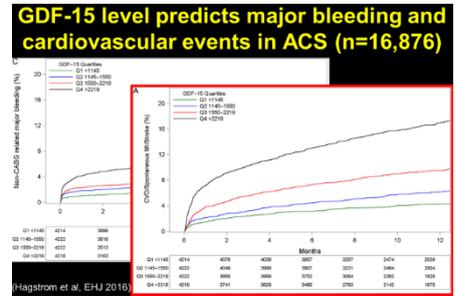
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The year in cardiology 2016: acute coronary syndromes



Prof. Crea coming from Rome (IT) spoke about the year in cardiology 2016: acute coronary syndromes and presented very interesting data on mechanisms, early diagnosis, risk stratification, treatment and outcome. Going deeper in his lecture, Prof. Crea presented very interesting data on atherosclerosis, plaques formation and the related coronary acute syndromes, by highlighting that not all the plaques are involved in inflammatory processes

leading to their rupture. The speaker talked also about diagnosis, by highlighting the lack of advantages of the coronary CT angiography compared with standard procedures in the ACS patients' diagnosis. Prof. Crea presented also very interesting data on the risk stratification and spoke about a risk score calculator based on more than 200.000 in-hospital AMI patients. In the main part of his lecture, Prof. Crea talked about treatment and presented very innovative data on the effects of the anti-thrombotic therapy



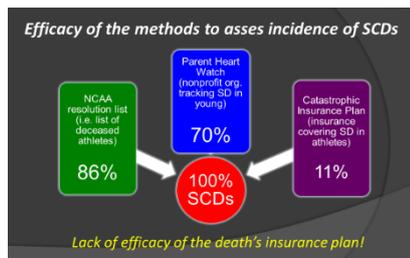
and the effects of morphine in associations with ticagrelor in AMI patients. The speaker presented also data on the effects of the Ω 3-FA on the LV remodeling after AMI and on the interventional approach in older patients. Finally, Prof. Crea talked about outcomes and presented very interesting data on the elderly patients, the variant angina and on the Takotsubo syndrome, by highlighting that recent data show that the emotional stress may have positive effects on the heart.

- What is the role played by the microbiota in the intravascular plaque rupture from the speaker point of view?
- What is the role played by neutrophils in the post-myocardial infarction healing, based on the data presented by the speaker?
- What's about the role of the coronary CT angiography for the ACSs diagnosis based on the data presented by the speaker?
- What's about the effect of ticagrelor in association with morphine in AMI patients, based on the data presented by the speaker?

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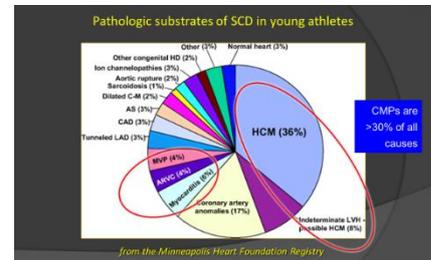
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Preventing sudden cardiac death in athletes

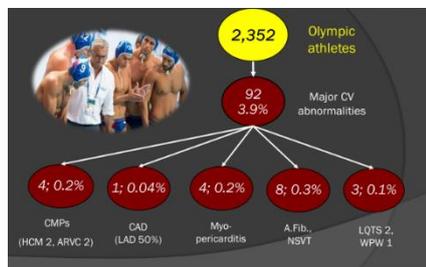


Preventing sudden cardiac death in athletes, was the topic at the core of Prof. Pelliccia presentation. The speaker, coming from Rome (IT), presented very interesting data on the SCD in athletes starting from the incidence of disease to the mechanisms, causes and finally on the primary and secondary prevention. Going deeper in his lecture, Prof. Pelliccia talked about SCD incidence, by

highlighting that there are huge discrepancies in its detection. The speaker talked also about the main causes leading to SCD and presented very interesting data in young and adult athletes, by highlighting that the youngest die for ventricular arrhythmias, but the adults for ischemic heart disease. In the main part of his lecture Prof. Pelliccia spoke about primary prevention and presented very interesting data on the national screening programs, by highlighting that the 2% of people which underwent to screening procedures present CV abnormalities. Finally, Prof. Pelliccia talked about the screening of the Olympic athletes, by



highlighting that the 3.9% of these athletes are affected by major CV abnormalities. The speaker also presented data on secondary prevention, by highlighting the efficacy of the defibrillator procedures applied to athletes. In conclusion, Prof. Pelliccia pointed out that the preparticipation screening is very effective in identifying athletes at risk and is able to reduce the incidence of SD in young athletes.



- Why the SCD incidence is so variable based on the data presented by the speaker?
- What are the main methods used for assessing the SCD incidence?
- What are the main substrates of SCD in young athletes presented by the speaker?
- What are the key points of the national screening program presented by the speaker?
- What is the global perception of the CV screening from the speaker point of view?

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New trends in cardiovascular pharmacology

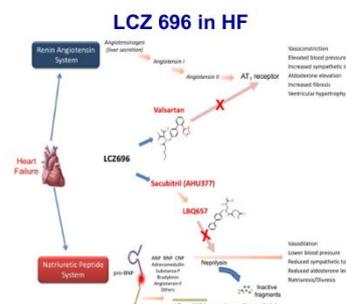
NEP inhibitors (NEPI)

NEP inhibitors (candoxatril and thiorphan) induce an increase of natriuretic peptides, P-substance and bradikinin levels

Nevertheless, clinical trials showed that the administration of candoxatril is associated with an increase of ANP levels, but it doesn't correlate with an improvement of symptoms or haemodynamic function in patients with HF.

↓ Angiotensin II + ↓ Endothelin

Prof. Capuano from Naples (IT), spoke about new trends in pharmacology, by presenting very interesting data on LCZ696 and PCHK9 inhibitors. Going deeper in her lecture, Prof. Capuano spoke about the physiopathological roles of RAAS and about the pharmacological approaches to RAAS starting from the ACEi synthesis in the 60ies till the LCZ969 development. In the main part

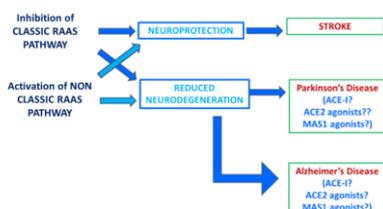


of her lecture, Prof. Capuano presented very interesting data on the LCZ969 pharmacology and the effects on the natriuretic peptides and other vasoactive peptides as bradykinin, endothelin-1 and angiotensin I and II. The speaker talked also about the NEP inhibitors, their effects on ANPs and the rationale for their association with an angiotensin inhibitor. Finally, Prof. Capuano presented very interesting data on the ACE 2

drugs which through the conversion of ANG II to A1-7 or Ang I to A1-9 counterbalance the RAAS classic effects. The speaker talked also about the non-cardiovascular effects of Ang 1-7-MAS 1 axis, more in particular on the reduction of the fibrosis, inflammation and angiogenesis processes and on the increase of the cerebrovascular protection, metabolism and reproduction. In conclusion, Prof. Capuano pointed out that the brain RAAS plays a role in both the cardiovascular and neurological diseases.

RAAS effects on CNS

The same balance is important also when neurological diseases are considered!

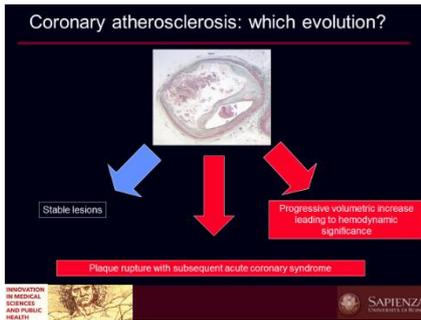


- What is the effect of LCZ969 in HF patients, from the speaker point of view?
- What are the main effects of the MAS1 activation in the ACE-2-angiotensin 1-7-MAS1 pathway based on the data presented by the speaker?
- What are the main RAAS effects on CNS, based on the data presented by the speaker?
- What are the main non-cardiovascular effects of the Ang 1-7-MAS 1 axis presented by the speaker?
- What are the new RAAS inhibitors under investigation presented by the speaker?

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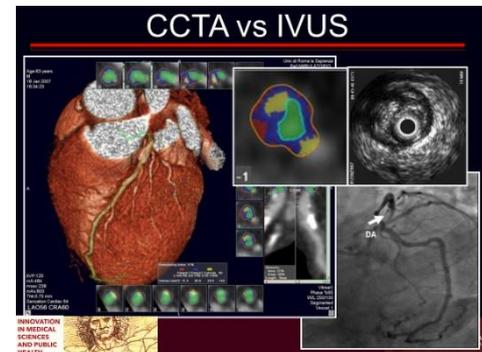
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Advanced imaging of coronary vulnerable plaque

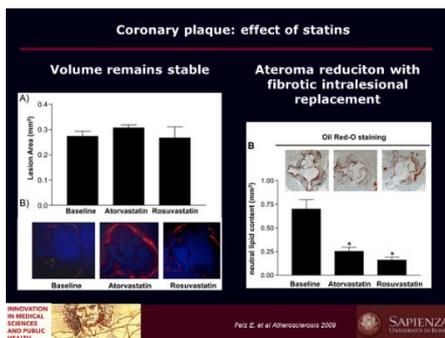


The advanced imaging of coronary vulnerable plaque, was the topic discussed by Prof. Francone from Rome (IT), more in particular the speaker presented very interesting data, starting from the concept of vulnerability of the atherosclerotic plaque. Going deeper in his lecture, Prof. Francone talked about the three main scenarios of the coronary atherosclerosis evolution, like stable lesion, plaque rupture

and progressive volumetric increase leading to an hemodynamic significance. In the main part of his lecture, the speaker presented very interesting data on the main imaging techniques used for detection, risk stratification, therapeutic management and finally for the pathophysiology in-vivo evaluation of the coronary vulnerable plaques. More in particular Prof. Francone spoke about the comparison between CT and MRI, by highlighting pros and cons of these two techniques. The speaker spoke also about the comparison between CCTA and IVUS and their very similar results despite the more complexity, costs and invasiveness of IVUS. In the



second part of his lecture, Prof. Francone spoke about the new applications of CCT and presented very interesting data on the Dual Energy CT. Finally, the speaker talked about the plaque imaging and its prognostic implications and about the plaque regression-progression evaluation. In conclusion, Prof. Francone pointed out that the plaque imaging is useful for the detection of culprit lesions in a pre-clinical phase, but the therapeutic follow-up of the plaque regression is still controversial.



- What is the rationale of the vulnerable plaque imaging?
- What is the evolution of the coronary atherosclerosis based on the data presented by the speaker?
- What's about the risk biomarkers from the speaker point of view?
- What are the main pro and cons of the coronary vulnerable plaque detection with MRI?
- What's about CCTA vs IVUS from the speaker point of view?
- What are the prognostic implications of the plaque imaging, from the speaker point of view?
- What the main limitations of CT from the speaker point of view?

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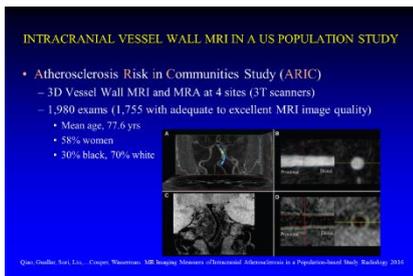
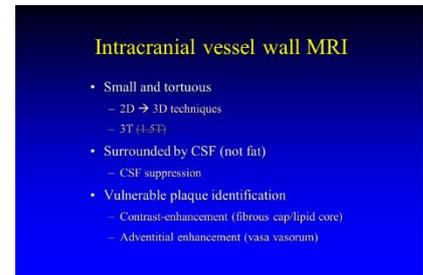
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Advanced imaging of intracranial atherosclerosis



on the MRI features of the carotid plaque leading to stroke. In the main part of his presentation, the speaker talked about the intracranial vessel wall MRI and the main characteristics of this technique able to identify the typical lesions. Prof. Wasserman

Prof. Wasserman from Baltimore (USA), spoke about the advanced imaging of intracranial atherosclerosis. More in particular, the speaker talked about the plaque identification and characterization, the related techniques, their applications and impact. Going deeper in lecture, Prof. Wasserman presented very interesting data



presented also other data on the 3D high isotropic resolution BBMRI at 3T and its application in a US population study. In conclusion, the speaker pointed out that the vessel wall MRI of the intracranial atherosclerosis is useful for the detection of the angiographically occulted lesions, the culprit lesions and of the features of the plaque vulnerability.

- What's about the main characteristics of the ARIC study presented by the speaker?
- What are the main characteristics of the contrast-enhanced black blood MRI presented by the speaker?
- What are the MRI features of the carotid plaques leading to stroke, presented by the speaker?
- What are the main topics of the intracranial vessel wall MRI presented by the speaker?
- What's about the 3D high isotropic resolution BBMRI at 3T from the speaker point of view?

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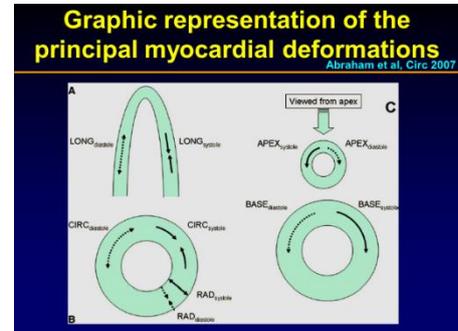
Multimodality Imaging in Cardiology

Multimodality Imaging in Cardiology

- Early diagnosis (ischemic heart disease, heart failure)
 - Coronary stenosis
 - Early myocardial dysfunction
- Refined diagnosis
 - Perfusion abnormalities
 - 3D volumes/motion analysis
 - 3D valvular analysis
- Exclusive diagnosis
 - Resynchronization
 - Atrio appendage function

CT multislice
Ultrasounds
Cardiac M resonance
SPECT / PET

The multimodality imaging in Cardiology, was the topic discussed by Prof. Colonna from Bari (IT), more in particular the speaker talked about ultrasound, MRI, multislice CT and nuclear methods. Going deeper in his lecture, Prof, Colonna presented very interesting data on the early diagnosis related to the coronary arteries studied with the echocardiography techniques for the stenosis evaluation and for the early myocardial dysfunction. Talking about the refined diagnosis Prof. Colonna presented very interesting data on the perfusion abnormalities thanks to the myocardial flow quantification with real time perfusion and intravenous sonovue infusion and spoke about the detection of the mechanisms of the contrast enhancement through the Gd-DTPA application. The speaker presented also very interesting data on the 3D valvular analysis and its application for the evaluation of the valvular defects, like the mitral stenosis. Finally, Prof. Colonna presented the data on two registries the first one in Europe and the second one in Italy, by highlighting the deep differences between them and the need for a better involvement of different professionalities like cardiologists and radiologists.



RESEARCH Open Access
European cardiovascular magnetic resonance (EuroCMR) registry – multi national results from
Contents lists available at ScienceDirect
European Journal of Radiology
ELSEVIER
Journal homepage: www.elsevier.com/locate/ejrad
Italian registry of cardiac magnetic resonance

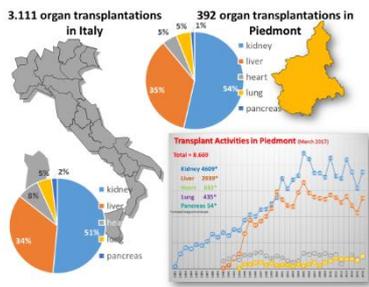
	Reader: cardiologist	Reader: Radiologist	Reader: Team	Gadolinium	% stress
European registry (cardiology)	71 %	3 %	26 %	92 %	37 %
Italian registry (radiology)	3 %	80% (13% double)	17 %	75 %	3 %

- What are the main applications of the multimodality imaging in cardiology presented by the speaker?
- What are the main coronary arteries studied with the echocardiography techniques?
- What's about the detection through imaging of the early myocardial dysfunction from the speaker point of view?
- How to detect the perfusion abnormalities with the echocardiography based on the data presented by the speaker?
- What are the main characteristics of the 3D valvular analysis?

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From genetics to transplant genomics

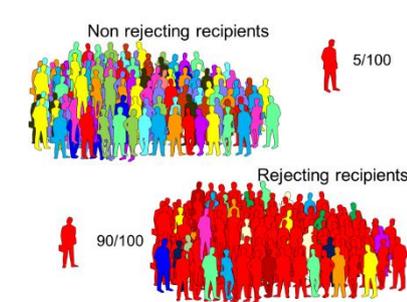


Prof. Amoroso from Turin (IT), presented very interesting and impressive data on genetics to transplant genomics. More in particular the speaker talked about the human genome, by highlighting that it contains more than 3 billion of nucleotides. Going deeper in his lecture, Prof. Amoroso presented very interesting data on a global view of the organ transplantation around the world, in Italy and more in particular in Piemonte. The speaker highlighted that

every ten minutes a person is added to a national transplant waiting list and an average of almost twenty people die each day while waiting for a transplant. In the main part of his lecture, Prof. Amoroso talked about the donor and recipient genomes contributions to the nucleic acids that are relevant for transplantation from the genetic point of view. Prof. Amoroso presented also very impressive data given by association studies on the effects of the HLA mismatches and the non-HLA factors on the graft survival. More in particular he spoke about an ongoing genome-wide association study designed for the detection of the donor-recipient genomic incompatibilities that influence the acute renal



- Although great progress has been made in the field of transplantation, whether in surgical techniques, diagnostic methods or efficient immunosuppressive therapy, the gap between supply and demand continues to be wide.
- Every ten minutes, a person is added to a national transplant waiting list; on average, twenty-two people die each day while waiting for a transplant.
- Three most important issues in solid organ transplantation today are as follows:
 - need for more organs,
 - longer graft survival rates,
 - reduction of rates of rejection.



rejection. At the basis of this project there is the suggestion that the donor-recipient SNP represent an unrecognized risk for the allograft acute rejection in the solid organ transplant recipients, the speaker pointed out and presented very interesting preliminary data given by this study. In conclusion, Prof. Amoroso pointed out that the development of the genomic research in the organ transplantation field can help in improving the long-term graft function.

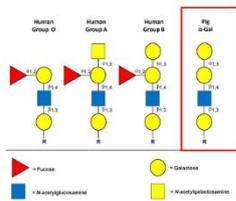
- What is the first one transplanted organ around the world and in Italy, based on the data presented by the speaker?
- How many people is waiting for a transplant in USA, based on the data presented by the speaker?
- What are the three most important issues in solid organ transplantation presented by the speaker?
- How to recognize non-HLA genes relevant in transplantation?
- What is the rate between rejecting and non-rejecting recipients based on the data presented by the speaker?
- What are the main preliminary results of the immunological studies presented by the speaker?
- What's about the possible effects of the CARC1 variants from the speaker point of view?

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Advances in xenotransplantation

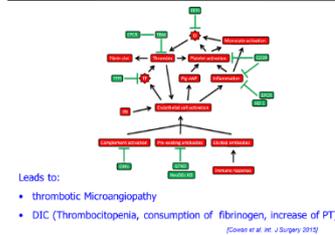
Xenograft immunogenicity: the importance of the sugars



The main topic at the core of Prof. Cozzi presentation, was the advances in xenotransplantation. The speaker, coming from Padua (IT), presented very interesting data on xenotransplantation, starting from the definition. Going deeper in his lecture, Prof. Cozzi talked about the relationship between xenotransplantation and the advanced preclinical research in immunology and oncology. In the main part of his talk, the speaker presented very interesting

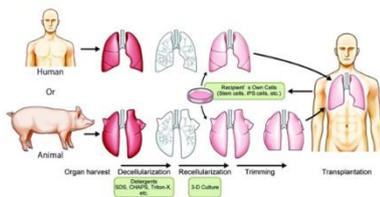
data on immunology, physiology, biosafety, ethics and regulations of the clinical xenotransplantation. Speaking about immunology, Prof. Cozzi, presented experimental data on the effects of the sugars as the most important immunogenic agents and other data on the cell-mediated rejection, by highlighting the role played by the xenogeneic porcine cells. Talking about physiology and biosafety, Prof. Cozzi presented very interesting data on the risk of zoonosis in xenotransplantation, more in particular he spoke about the search for potential unknown pathogens and about the use of the molecular engineering for

Coagulation dysfunction



addressing the safety aspects. Finally, Prof. Cozzi presented experimental data on the best results in pig-to primate xenotransplantation, more in particular the speaker talked about the kidney and the heart xenotransplantation and about the application of the xenotransplantation in the regenerative medicine applied to the heart, kidney and lung regeneration. In conclusion, Prof. Cozzi pointed out that in particular conditions, the xenotransplantation can represent an attractive solution to the shortage of the human organ.

Xenotransplantation and new frontiers of regenerative medicine



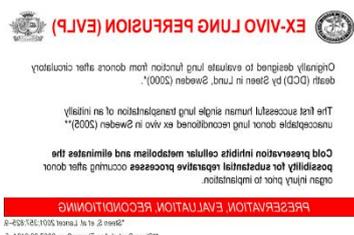
[Tsuchiya et al. Organogenesis 2014]

- What is the definition of xenotransplantation from the speaker point of view?
- What are the xenotransplantation possible areas of application based on the data presented by the speaker?
- What are the major advantages of the clinical xenotransplantation from the speaker point of view?
- What's about the main immunological barriers of the clinical xenotransplantation?
- What is the role played by the sugars as immunogenic agents, based on the data presented by the speaker?
- What are the key aspects of the genetic engineering?
- How to build a Heart based on the data presented by the speaker?

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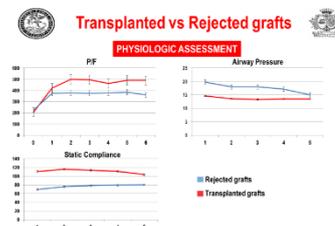
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The transplant of regenerated lungs

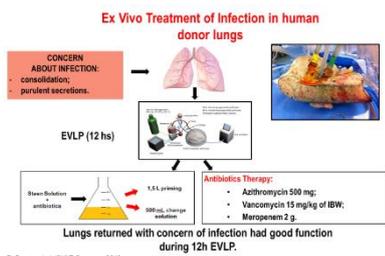


problems like the ischemia reperfusion injury and the primary graft dysfunction. The speaker presented the main surgical procedures applied in the lung transplantation in accordance with the ex-vivo lung perfusion Toronto protocol and discussed

The transplant of regenerated lungs was the topic of Prof. Rinaldi presentation. The speaker, coming from Turin (IT), presented very interesting data, starting from the number of lung transplants by year and the applied procedures. Going deeper in his lecture, Prof. Rinaldi talked about the ex-vivo lung perfusion transplantation and its major



the ELVP successful rate in term of outcomes and rejection reduction. In the main part of his lecture, the speaker talked about the advantages of the ELVP procedure and presented very interesting data on the increase of the lung transplant activity, the better donor/recipient size matching, the better evaluation of the graft and finally on the specific therapies that use the perfusion as a reliable platform.



- What is the number of lung transplants reported by year and procedure type, presented by the speaker?
- What are the key points of the ischemia reperfusion injury and the primary graft dysfunction?
- What are the main advantages of the ex-vivo lung perfusion based on the Toronto protocol?
- What's about the ex-vivo treatment of infection in human donor lungs, based on the data presented by the speaker?

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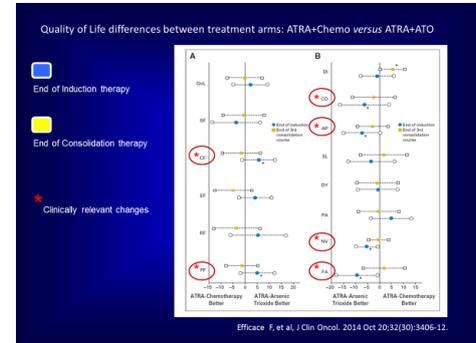
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Health related quality of life in hemato-oncology

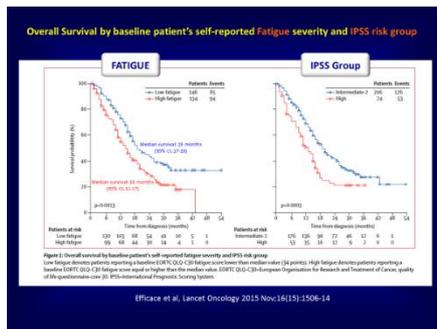


Prof. Efficace from Rome (IT) spoke about Health-related quality of life in hemato-oncology. Going deeper in his lecture the speaker addressed the audience pointing to the differences between quality of life and toxicity. More in particular Prof. Efficace presented data on the common terminology criteria for adverse events, by highlighting that the toxicity criteria cannot capture the patient's quality of life. In

the main part of his lecture, the speaker talked about quality of life, starting from the FDA definition. The quality of life refers to the patient's perspective and gives additional information on the treatment effectiveness, Prof. Efficace pointed out. The speaker discussed some problems linked with the patient's perspective as the sustainability of specific therapeutic protocols like chemotherapy, radiation and biological therapy, bone marrow transplantation and targeted therapy. More in particular Prof. Efficace presented very interesting data on the relationship between the new therapeutic protocols in onco-hematology and the patients' QoL, like the



use of Arsenic in APL patients and the QoL in patients affected by myelodysplastic syndromes treated with lenalidomide. Finally, Prof. Efficace spoke about QoL as a prognostic/predictive factor and presented very interesting data on the patient-reported fatigue index and the survival probability in patients affected by myelodysplastic syndromes. In conclusion, Prof. Efficace, pointed out that the information collected with the QoL questionnaires have a particular value for a better understanding of the real effects of the therapies in humans.



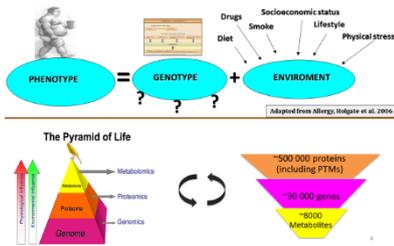
- What are the main differences between quality of life and toxicity, from the speaker point of view?
- What's about the new targeted therapy in onco-hematology and its relationship with the patient's QoL from the speaker point of view?
- What's about the relationship between Arsenic and QoL in APL patients, based on the data presented by the speaker?
- Does the patient-reported fatigue add prognostic information in survival, based on the data presented by the speaker?

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The theoretical and methodological bases of metabolomics

Metabolomics=study of phenotype



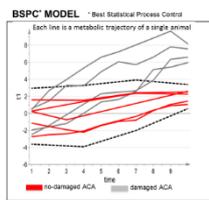
The theoretical and methodological bases of metabolomics was the topic at the core of Dr. Noto presentation. The speaker coming from Cagliari (IT), talked about the meaning of metabolomics and the relationship between metabolomics and cardiac arrest. Going deeper in his lecture, Dr. Noto presented very interesting data on metabolomics as the way capable to reflect the state of the cell, organ or organism which may change in response to a physiological status. In other words, metabolomics refers to the study of phenotype, the speaker pointed out. Speaking

about the relationship between metabolomics and the cardiac arrest, Dr. Noto presented very interesting experimental data given by animal studies performed in pigs with cardiac arrest induced through asphyxia and ventricular fibrillation procedures. In conclusion, the speaker pointed out that this metabolomics study demonstrates for the first time that the asphyxial procedures are different from the ventricular ones and that, thanks to this study was possible to identify biomarkers as early predictors of outcome.

DESIGN of EXPERIMENT (DoE)

- 20 pigs were instrumented
 - Asphyxia was induced by clamping the endotracheal tube while Ventricular Fibrillation was induced using a pacing wire.
 - Cardiac Arrest (CA) remained untreated for 5 min.
 - Resuscitation was performed according to the guidelines.
-
- Return of Spontaneous Circulation (ROSC) was defined as the presence of an organized cardiac rhythm with a mean arterial pressure of at least 50 mmHg.
 - From baseline to ROSC, blood was drawn every minute, and every hour for the first 4 hours and 24 hours after ROSC.
 - Blood samples were centrifuged and serum samples were immediately frozen at -80° C before analysis.

ASPHYXIAL PRE-ARREST PERIOD ACA group



Metabolite	Variation in time	P	R ²
Adiponitrone	↑	<0.001	0.2
Ala	↑	<0.001	0.2
Succinate	↑	<0.001	0.7
Urea	↑	0.1	0.1
Oxirane	↑	0.046	0.3
Glycine	↑	0.03	0.3
Glutamate	↓	<0.001	0.7
Aspartate	↑	0.201	0.3
Tyrosine	↑	0.027	0.3
Phenylamine	↑	0.003	0.3
Leucine/iso	↑	0.038	0.3

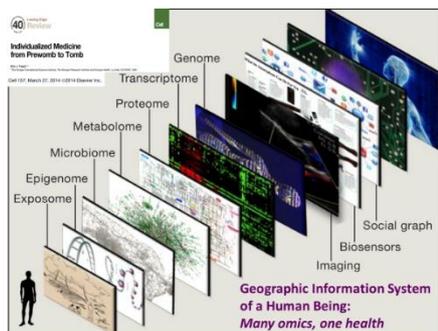
↑/↓ mean +/− relative variation (standard deviation) in the independent variable (P < 0.05) in the regression model

- What are the main correlations between metabolomics, genetics and phenotype, from the speaker point of view?
- What are the typical metabolomics work flows presented by the speaker?
- What's about MRI, Gas chromatography and Mass spectrometry in relationship with metabolomics?
- What are the main analysis models applied to metabolomics, presented by the speaker?

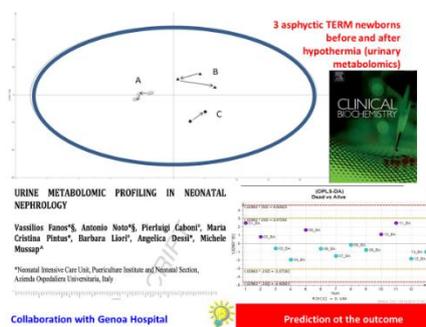
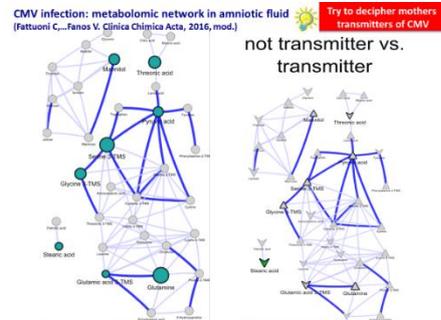
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The paradigm of metabolomics in perinatology



The paradigm of metabolomics in perinatology was the topic at the core of Prof. Fanos presentation. The speaker coming from Cagliari (IT), talked about metabolomics applied in obstetrics, maternal milk, neonatology and in perinatal programming. Going deeper in his lecture, Prof. Fanos presented very interesting data on the main omics cycles in relation to Health and on the main samples used in perinatal and pediatric metabolomics. Talking about the metabolomics in obstetrics, the speaker presented the top metabolites involved in the great obstetrical syndromes. Prof. Fanos talked also about metabolomics and the maternal milk and presented very interesting data on the clinical impact of the metabolomics of the human breast milk and on the role of the human breast milk stem cells.



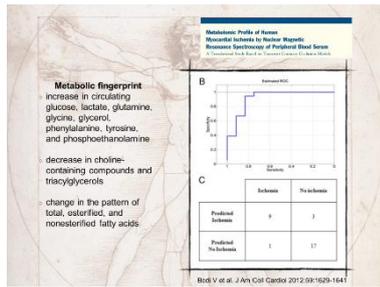
The speaker talked about metabolomics in newborns and presented very interesting data on the diagnostic and the prognostic value of metabolomics applied to neonatology. Finally, Prof. Fano presented very interesting data on the relationship between metabolomics and the perinatal programming able to identify the future of the newborns. In conclusion, the speaker pointed out that the metabolomics are able to make possible the future for people affected by specific defects in metabolism leading to chronic diseases.

- What are the new languages of Medicine based on the data presented by the speaker?
- How many are the publications on Metabolomics in PubMed, based on the data presented by the speaker?
- What's about the relationship between metabolomics and the fetal-neonatal nutrition?

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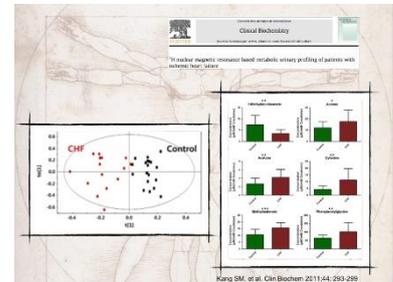
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Metabolomics approach to cardiovascular diseases

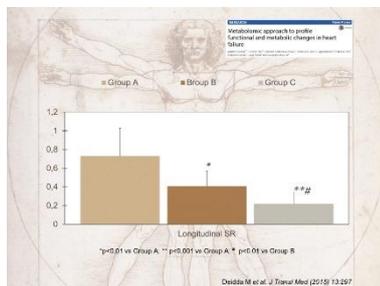


The Metabolomics approach to cardiovascular diseases was the topic of Prof. Deidda presentation. The speaker coming from Cagliari (IT), talked about the main publications on metabolomics applied to the cardiovascular disease. Going deeper in his lecture, Prof. Deidda, presented very interesting data on a metabolomics study running in patients affected by myocardial ischemia, aimed to

identify a specific predictive metabolic pattern for the outcome. Speaking about heart failure, Prof. Deidda presented other very interesting data on six metabolites involved in the Krebs cycles and significantly associated with the outcomes. Finally, the



speaker presented data given by metabolomics studies performed in his team of researchers, more in particular on ischemic and heart failure patients. In conclusion, Prof. Deidda pointed out that metabolomics is emerging as a useful tool for the investigations in cardiology and its use can improve the physician's diagnostic and prognostic capacities and identify the metabolic pathways as new markers of outcomes.

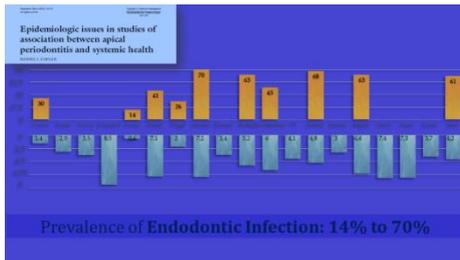


- What are the main metabolites identified in the coronary heart disease metabolomics study presented by the speaker?
- What's about the metabolic disturbances identified in the plasma of patients affected by heart failure, presented by the speaker?
- What are the main results of the metabolomics study on patients affected by heart failure presented by the speaker?
- What are the main metabolomic fingerprints in scleroderma patients, based on the data presented by the speaker?

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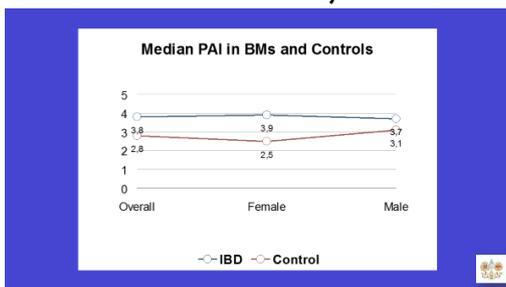
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Odontogenic infection and systemic disease: correlation and clinical and forensic aspects



Odontogenic infection and systemic disease: correlation and clinical and forensic aspects was the topic Prof. Cotti talked about. The speaker coming from Cagliari (IT), spoke about the relationship between the odontogenic infections and the systemic health and the role of the immune modulators on the odontogenic infections. Going deeper in her lecture, Prof. Cotti, presented very interesting data on

the effects of a chronic dental infection on the heart leading to the development of CVDs. Speaking about systemic inflammation, Prof. Cotti highlighted the role played by the apical periodontitis to its increase. In the main part of her lecture, the speaker presented very interesting data on the relationship between periodontitis and diabetes, by highlighting the correlation between periodontitis, glycemic control and the risk for developing diabetes. Prof. Cotti spoke also about the effects of the systemic diseases on the odontogenic infections and presented very interesting data on the effects of diabetes on periodontitis and on the periapical lesions. In the last part of her presentation, Prof. Cotti spoke about the correlation between inflammatory bowel diseases treated with biological medications and/or immunomodulatory agents and the apical periodontitis, by highlighting the tight relationship between the dental diseases and the chronic inflammatory diseases treated with biologics.



In conclusion, Prof. Cotti pointed out that patients with autoimmune chronic inflammatory diseases treated with biologic agents need a dental and endodontic screening in association with premedication if in

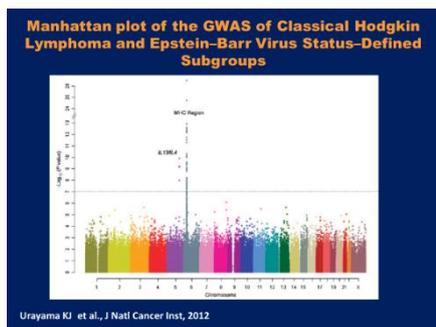
treatment for AP.

- What is the prevalence of the periodontitis based on the data presented by the speaker?
- How can an oral infection cause distant site consequences, from the speaker point of view?
- What are the main correlations between periodontitis and diabetes from the speaker point of view?
- What are the main effects of the systemic diseases on the odontogenic infections, based on the data presented by the speaker?

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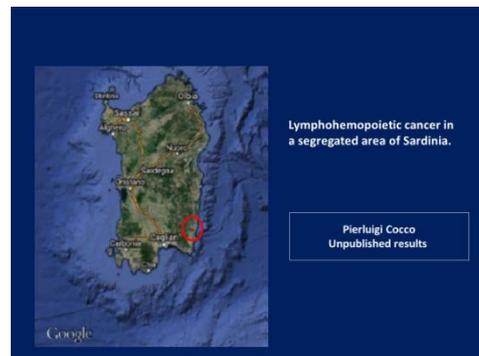
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Gene environment interactions



Gene environment interactions was the topic Prof. Cocco talked about. The speaker coming from Cagliari (IT), spoke about carcinogenesis and its main steps like initiation, promotion, pre-malignant progression and finally malignant conversion. Going deeper in his lecture, Prof. Cocco, presented very interesting data on the G side of the gene-environment interactions. More in particular he spoke about the lymphohemopoietic cancer developed in a segregated area of Sardinia and

presented very interesting data on the risk for non-Hodgkin lymphoma, Hodgkin lymphoma, multiple myeloma and leukemia. Speaking about the E side of the gene-environment interactions, Prof. Cocco presented data on the study requirement for the gene-environment interactions, more in particular in NAT1 and NAT2 rapid acetylator phenotypes and on the relationship between the occupational risk factors and the common gene polymorphisms in the CLL, MDD and LQTs etiologies. Finally, the speaker



talked about the future and more in particular on genome vs exposome, by highlighting there is the need for developing methods with the same precision for an individual's environment as we have for the individual's genome. In conclusion, Prof. Cocco, pointed out that the environmental data are representative of current exposures, whilst a long latency separate exposure and the clinical appearance of the chronic diseases.

Interaction between dietary and lifestyle risk factors, and the NAT2 slow acetylator phenotype

Lifestyle factors	NAT2		P for interaction
	slow	rapid	
Never smokers + ex smokers	1.0	4.6	0.586
Current smokers	1.6	0.8	
Coffee less than daily	1.0	3.3	0.223
1 coffee daily	0.4	1.7	
Heterocyclic amines intake			0.961
< median	1.0	4.0	
> median	0.7	1.2	
Folate			0.198
< median	1.0	2.4	
> median	0.3	4.2	
Hair dyes, never	1.0	5.3	0.009
Hair dyes, ever	29.7	0.3	

Cocco P et al., J Environ Analytical Toxicol, 2015

- What is the spatial distribution of the NHL risk in Sardinia, based on the data presented by the speaker?
- What's about the NHL prevalence in Muravera and San Vito, based on the data presented by the speaker?
- What's about the interactions between dietary and lifestyle risk factors and the NAT1 rapid acetylator phenotype, presented by the speaker?
- What is the exposome definition presented by the speaker?

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AhR activation and risk of lymphoma subtypes



Aim of the study

- AhR (Aryl Hydrocarbon Receptor) activation is the first step by which several chemicals induce the expression of genes implicated in the phase I metabolism of xenobiotics.
- Tetrachlorodibenzo-p-dioxin (TCDD) is one of such chemicals. Due to high cost of direct TCDD serum measurement, studying AhR activation by the serum of study subjects is a quick and unexpensive way to detect TCDD negative samples, allowing to cut the cost of direct TCDD laboratory assays.
- At the same time, as xenobiotics other than TCDD may also activate the AhR, the assay might indicate the role of its activation, by external chemicals of lifestyle, environmental or occupational origin, in lymphomagenesis.

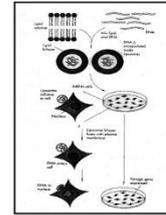
Prof. Cocco talked about AhR activation and risk of lymphoma subtypes. The speaker coming from Cagliari (IT), presented the main data of this study, starting from its aim: the investigation of the aryl hydrocarbon receptor activation by xenobiotics other than TCDD in order to have an indication on the role of its activations by external chemicals

derived from lifestyle, environmental or occupational habits in lymphomas. Going deeper in his lecture, Prof. Cocco presented very interesting data on the mechanism of action of TCDD, the reaction scheme, the dual luciferase assay system and finally on the results of this study.



The dual luciferase assay system

The detector system



Transfection of Hep G2 cells (Fagene HD, Promega) with liposomes encapsulating plasmids containing the luciferase reporting gene.

- What is the aim of the study presented by the speaker?
- What is the clinical significance of the AhR activation, based on the data presented by the speaker?
- What are the mechanism of action of TCDD, presented by the speaker?
- What are the results of this study presented by the speaker?

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AhR activation and DNA damage

Viability vs Time Differences

Correlations			
Days	Pearson Correlation Sig. (2-tailed)	Days	VIABILITY
		1	-.397*
		39	.012
VIABILITY		-.397*	1
		39	
		N	39

*. Correlation is significant at the 0.05 level (2-tailed).

AhR activation and DNA damage was the topic at the core of Dr. Amini Nia presentation. The speaker coming from Cagliari (IT), spoke about the aim of this study, that is to find prone gene polymorphisms related to DNA damage in Sardinia population. Dr. Amini presented the methodology used in her study and finally the results, by highlighting the

correlations between SNPs the related genes and their functions. In conclusion, the speaker pointed out that AHR activation is not related to the DNA damage.

Final table

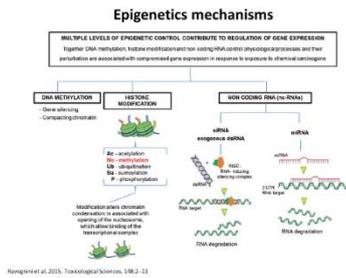
SNP	Gene	function	AHR
*124125	TNF	Cytokine secreted by macrophages	RF 0.02
		Role in L-selectin ligand biosynthesis, lymphocyte homing and lymphocyte trafficking.	RF 0.023
*36686	B3GNT3		LD 0.0004 PRO
*179959	NAT2	DRUG RESPONSE	LD 0.053 PRO
*45497	IL11A	cytokine	LD 0.042 PRO
*178382	nc RNA		LD 0.022 RF

- What's about the correlations between SNPs, gene and function based on the data presented by the speaker?
- What is the methodology applied in this study?
- What's about viability vs time differences based on the data presented by the speaker?

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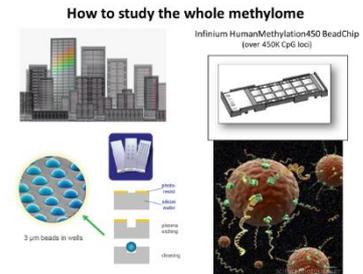
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Methylation, xenobiotics, and risk of chronic lymphocytic leukemia

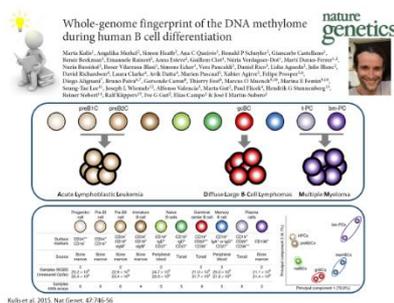


Dr. Zavattari talked about methylation, xenobiotics, and risk of chronic lymphocytic leukemia. The speaker coming from Cagliari (IT), presented very interesting data on epigenetics, their control on the organism development and the relationships between environment and the body. Going deeper in her lecture, Prof. Zavattari spoke about the epigenetic inheritance, the

exposure to chemical compounds and the related DNA methylation processes starting in the CpG gene islands. In the main part of her lecture, the speaker presented very interesting data on the methods used for the whole methylome study.



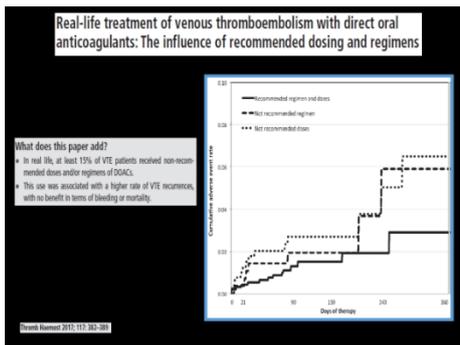
More in particular Prof. Zavattari spoke about the Beta value, that is the ratio between methylated probe intensity and the total probe intensity and about the differential methylation analysis of CLL or CRC and the related controls. Finally, the speaker presented the preliminary results of the CLL altered molecular functions. In conclusion, Prof. Zavattari pointed out that epigenetics can be remodelled, so their detection may change the evolution of specific pathologies.



- What's about the epigenetic mechanisms that regulate the organism development, based on the data presented by the speaker?
- What are the epigenetic mechanisms that regulate the relationships between environment and body?
- What are the main epigenetics mechanisms presented by the speaker?
- What's about the DNA methylation the methylated and unmethylated loci?

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Direct oral anticoagulants (DOACs) and warfarin in the real life



The Direct oral anticoagulants (DOACs) and warfarin in the real life was the topic Prof. Marongiu talked about. The speaker coming from Cagliari (IT), introduced his talk by presenting the data comparing DOACs and Warfarin in RCTs. Going deeper in his talk. Prof. Marongiu spoke about the outcomes in a warfarin-treated population with AF and highlighted that warfarin

presents an incidence of major bleeding less than 2%. In the main part of his lecture, Prof. Marongiu talked about the FCSA-START study, an ongoing registry that investigates the bleeding and the thrombotic events in an Italian prospective cohort of patients treated with DOAC and presented the main characteristics of the study, together with its results on the bleeding and thrombotic

START-Register
 SURVEY ON ANTICOAGULATED PATIENTS - REGISTER
 Registro computerizzato per la raccolta dei dati di pazienti trattati con anticoagulanti
FCSA-START Study: bleeding and thrombotic events in an Italian prospective cohort of patients treated with DOAC

Antonucci E, Migliaccio L, Marongiu F, Pengo V, Poli D, Testa S, Tripodi A, Guazzaloca G, Moia M, Palareti G on behalf of the FCSA-START-Register participating centers



XXIV Congresso Nazionale
 Abano 9-12- Novembre 2016



events and the comparison with the clinical trials and the real-life data. Finally, the speaker presented the data produced in his clinical center on 1344 patient, their basal characteristics and highlighted that in general DOACS are not superior to warfarin if well managed. In conclusion. Prof. Marongiu pointed out that the results of the START Register indicate that both DOACs and VKA can reduce the rate of the haemorrhagic risk around the 2%.

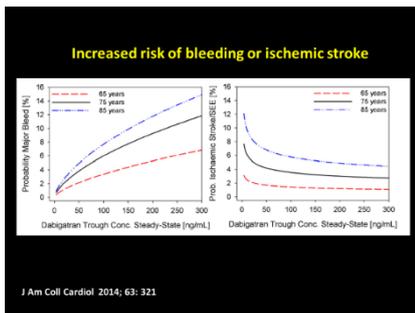
Patients	DOAC YES	DOAC NO
254	121 (47,6 %)	133 (52,4 %)
With AF	96	105
With VTE	15	38

- What's about the results of DOACs compared to Warfarin in the RCTs presented by the speaker?
- What' about the ischemic risk of DOACs in AF patients, based on the data presented by the speaker?
- What are the main outcomes of patients treated with DOACs and Warfarin, based on the data presented by the speaker?
- What are the main results of the START Registry presented by the speaker?

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DOACs, laboratory and follow-up



DOACs, laboratory and follow-up was the topic presented by Prof. Barcellona. The speaker coming from Cagliari (IT), talked about DOACs and the related laboratory tests to be performed in the patients available for the treatment with DOACs. In the main part of her presentation, Prof. Barcellona presented very interesting data on the laboratory tests to be performed in these patients during treatment and on the high variability response to dabigatran and the increased risk of bleeding or ischemic stroke. More in particular the speaker presented data on the on-range concentration, INR, PTT, TT and ECT. Finally, Prof.

DOAC plasma concentration

Drug	Dose, mg	Trough concentration ng/ml		Peak concentration ng/ml	
		Median	5 th to 95 th	Median	5 th to 95 th
dabigatran	150 bid	90	31-225	184	64-443
rivaroxaban	20 daily	26	6-87	270	189-419
apixaban	5 bid	103	41-230	171	91-321
edoxaban	60 daily	22	10-40	170	120-250

Below on-therapy range On-therapy range Above on-therapy range

0 5th percentile trough Drug level 95th percentile peak

Hematology Am Soc Hematol Educ Program, 2015; 2015: 117-24

**Apixaban
Rivaroxaban
Edoxaban**

Blood sampling:

- at through
- 2 hour after

**Best choice:
Specific anti-Xa activity**

Test	Xa inhibitors	
	Normal	Abnormal/prolonged*
APTT	Does not exclude on-therapy levels	On-therapy or above on-therapy levels likely present
PT	Does not exclude on-therapy levels	On-therapy or above on-therapy levels likely present
Anti-Xa assay (DOAC calibrated)	Likely excludes clinically significant levels	May be used to quantify drug levels

**PT ratio in emergency,
when the other test are not available**

Barcellona, spoke about the ant-Xa activity, by highlighting that this test has a good linear correlation with the DOAC plasma concentration and about POCT to be performed in patients undergoing surgical procedures and thrombolysis. In conclusion, Prof. Barcellona pointed out that DOACs should not be monitored as warfarin should be, but there are some critical situations that need for a better knowledge of their plasma concentration levels.

- What are the main laboratory tests to be performed in patients available for DOACs, based on the data presented by the speaker?
- Why is it necessary to perform the laboratory tests in DOACs patients, based on the data presented by the speaker?
- What's about the high variability response to DOACs, based on the data presented by the speaker?
- Why could be useful detect the DOACs plasma concentrations, from the speaker point of view?
- What is the on-therapy range presented by the speaker?
- Which are the main lab tests useful in the real life for DOACs patients?

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Practical problems in prescribing DOACs

	DABIGATRAN	RIVAROXABAN	EDOXABAN	APIXABAN
P-glycoprotein inhibitors Amiodarone, Mequinol, Lubricants and lubricant emulsions, Macrolides, Antiepileptics, Cyclosporin, Rifampicin	Yes	Yes	Yes	Yes
P-glycoprotein inducers Carbamazepine	Yes	Yes	Yes	Yes
CYP3A4 inhibitors Macrolides, Carbamazepine, Danazol, Antiepileptics, Cyclosporin, Antiepileptics, Cyclosporin, Rifampicin	No	Yes	Yes	Yes
CYP3A4 inducers Carbamazepine, Phenytoin, Macrolides, Phenytoin, Rifampicin, Antiepileptics, Cyclosporin, Danazol, Carbamazepine	No	Yes	Yes	Yes
NSAIDs Nonsteroidal anti-inflammatory drugs	Yes	Yes	Yes	Yes
Antiplasmat agents	Yes	Yes	Yes	Yes

Dr. Cornacchini talked about practical problems in prescribing DOACs. The speaker coming from Cagliari (IT), presented very interesting data on the antithrombotic therapy and their actual problems, like the bad compliance, the possibility to develop AEs during follow-up, the costs and the availability of only one antidote. In the

main part of her presentation, Prof. Cornacchini spoke about the main characteristics of the patients eligible for the DOACs and about the rules stated by AIFA for the DOACs dispensation and prescription. Finally, the speaker, talked about the main contraindications to DOACs and the main procedures to be applied for raising the adherence to these drugs, by highlighted that it is

Valutare se il paziente, specie se anziano, é autosufficiente nella gestione della terapia



Dove vive?
Con chi vive?

Coinvolgete un parente stretto

mandatory to perform follow-up visits with the aim to avoid the risks linked with the poor adherence to therapy. In conclusion, Prof. Cornacchini pointed out that DOACs represent a very therapeutic revolution, but not all the patients are eligible for this therapy, therefore it is mandatory to perform a very effective selection of the right patients.

Situazione attuale:
300 Centri FCSA



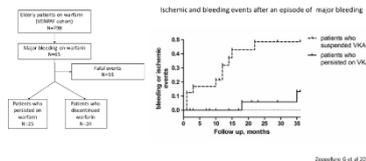
- What are the main problems of the antithrombotic therapy, based on the data presented by the speaker?
- What are the procedures to be performed before starting the DOAC therapy?
- What are the eligible patients for the DOAC therapy?
- What are the main procedures to be applied for raising the adherence to DOACs from the speaker point of view?
- How many antithrombotic center are available in Italy, based on the data presented by the speaker?

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DOACs and difficult clinical cases

Anticoagulation in elderly patients with non valvular atrial fibrillation after a major bleeding



Diaperstein G et al 2017

elderly patients with non valvular atrial fibrillation treated with warfarin and presented the data on the bleeding and ischemic events in those patients who suspended the VKA. In the main part of his talk, the speaker presented many data on other very important clinical issues, like the cardioversion in the emergency room, or the therapeutical decisions in low risk patients with CHADVASC 0,1 in men or 2 in women. Finally, Prof. Pengo spoke about a questionnaire presented to a selected cohort of Italian expert cardiologists and highlighted that among this cohort of 178

Dose reduction in Phase III apixaban study

Apixaban 2,5 mg bid in patient with at least 2 of the following 3 criteria:
 -> AGE > 80 anni
 -> WEIGHT < 60 kg
 -> Creatinin > 1,5 mg/dL (133 µmol/L)

DOACs and difficult clinical cases was the topic Prof. Pengo talked about. The speaker coming from Padua (IT), presented very interesting data on the difficult decisions in patients with AF and in the postoperative AF ones. Going deeper in his presentation, Prof. Pengo talked about a study, performed in his clinical center, running in

DELPHI consensus—Young men with paroxysmal AF and CHA2DS2-VASc=1AND the patient suffer from less than 1 episode a year

	DISAGREE	A	G	R	E	AGREE	Yes
I do not treat the patients with anticoagulants	25	48	46	25	31	178	37%
I will treat the patients with warfarin	109	62	4	3	0	178	60%
I will use a DOAC	50	64	37	15	12	178	64%
I will use anticoagulants only in the presence of renal insufficiency	42	66	48	14	8	178	61%

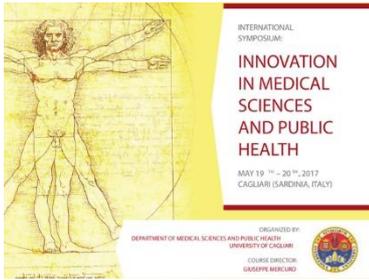
expert physicians there is a lack of uniformity in answers also in the case of very simple questions. In conclusion, Prof, Pengo pointed out that it is important to follow the guidelines, to know the main clinical pictures of the patients and finally to consider the patient's opinion if possible, before taking any important therapeutic decision on DOACs in

difficult clinical cases.

- What are the main difficult decisions in AF patients presented by the speaker?
- What are the main problems with AF postoperative patients, from the speaker point of view?
- What's about the cardioversion in the emergency room?
- What's about the main answers of the questionnaire presented by the speaker?

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