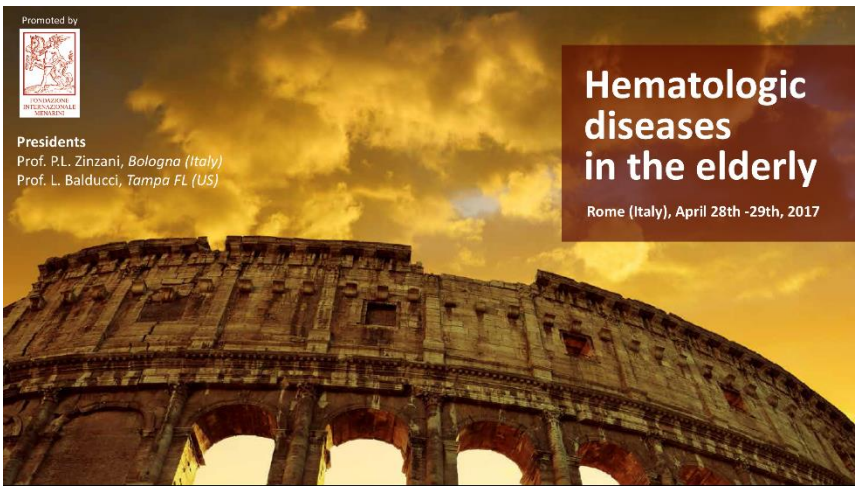
# *Hematologic diseases in the Elderly*

## *Highlights*

### *Rome (Italy), April 28-29, 2017*

## Introduction




Prof. Balducci and Prof. Zinzani, chairmen of the symposium, opened the congress, by highlighting the high scientific level of this meeting focusing on Hematologic diseases in the Elderly and the improvement in this field of Medicine performed in these last 15 years. The Symposium was organized by the Institute of Hematology "L. e A. Seràgnoli", University of Bologna. Many top researchers in hematology, coming from all the world attended this symposium together with young physicians. This congress represented a very unique occasion for a full update on hematology, aging and precision medicine.

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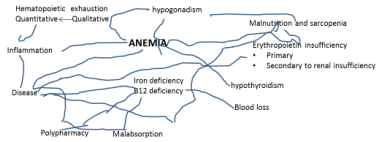
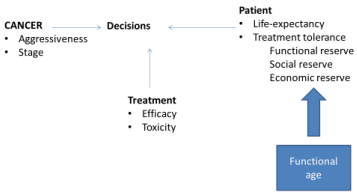
# Hematology of aging coming of age: why do we meet today

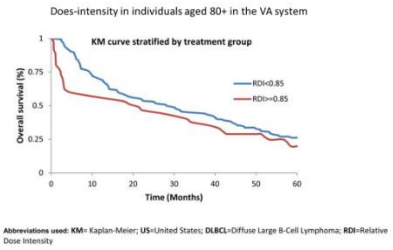
Hematology of aging coming of age: why do we meet today, was the topic discussed by Prof. Balducci in his lecture. The speaker, coming from Tampa (USA), went deeper in his talk starting from one clinical case, by highlighting that to be interested in geriatric hematology, looks like swimming against the current. In the main part of his talk, Prof. Balducci spoke about anemia, its causes, its pathogenesis, the investigations to be performed and finally about the benefits of treating anemia. More in particular, the speaker highlighted that one of the main problems is characterized by the diagnosis of the iron deficiency in the presence of chronic inflammation, as a reversible component of anemia in old people. Prof. Balducci, spoke also about the definition of age, by highlighting the role played by allostasis and genomic in the aging process. In the last part of his lecture, the speaker talked about two other clinical cases of elderly patients affected by lymphoma the first and by prostate cancer the second one. Prof. Balducci spoke about the treatment-related decisions and about the knowledge of the prognosis and the effects of treatment, by highlighting that in older people the use of R-CHOP can lead to very high rates of overall survival. In conclusion, the speaker pointed out that age is a poor prognostic factor for virtually all lympho-proliferative disorders.

The threads of the carpet




Treatment-related decisions




Carson et al, J Ger Oncol, 2015, 6, 211

- How to diagnose different causes of anemia in the same patient?
- How to diagnose iron deficiency in the presence of chronic inflammation?
- Will the reversal of anemia be beneficial to patient function and survival?
- Will reversal of anemia reverse other factors related to aging?
- How to define age, based on the data presented by the speaker?

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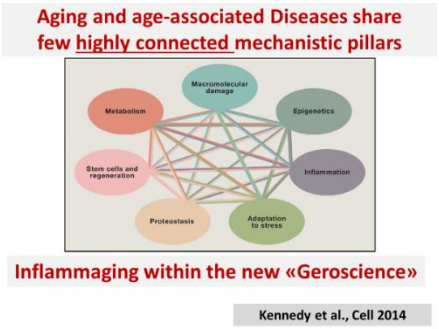
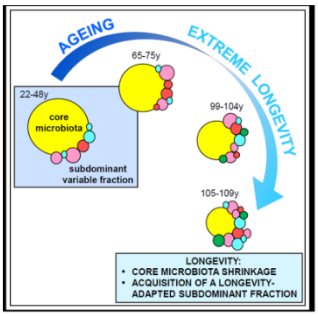
# Biology of aging

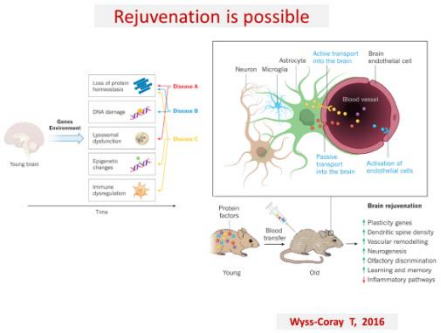



Prof. Franceschi from Bologna (IT), spoke about the biology of aging, by presenting very interesting data on the concept of geroscience as the science bridging aging to chronic diseases. Going deeper in his lecture, Prof. Franceschi presented very interesting data on the so called "seven pillars" of the process that links age with the age-associated diseases. In the main part of his lecture, the speaker talked about these seven pillars starting from Inflammation, by highlighting that this is the first one pillar of this process. More in particular Prof. Franceschi presented very interesting data on centenarians with their high blood levels of anti-inflammatory agents, counteracting the inflammatory compounds. The speaker talked also about the mechanisms underpinning inflammaging, by highlighting that the circulating mitochondrial DNA is one of the main factors responsible for the inflammatory response. Prof. Franceschi presented very interesting data on the correlation between GUT microbiota, the Central Nervous System and the capacity of adaptation of healthy ageing people to the aging-induced accumulation of oxidative and chronic inflammatory conditions. In conclujsion, the speaker highlighted that aging and inflammaging are very deep related and reinforced by age-related chronic diseases, but rejuvenation is possible through the activation of the cellular reprogramming to pluripotency as shown in the animal models.

The adaptive remodeling of gut microbiota with age




Biagi et al., *Curr Biol* 2016




- How rejuvenation is possible from the speaker point of view?
- What are the seven pillars of the process linking age with age-sustained diseases?
- What's about the role of the GUT microbioma in the processes counteracting age-inflammatory processes?
- What's about clonal hemopoiesis and cardiovascular risk, based on the data presented by the speaker?
- What is the role played by the senescent cells in the onset of the inflammatory processes?

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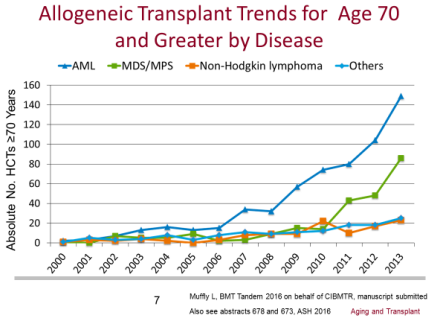
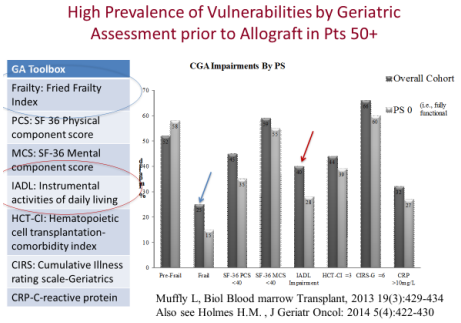
# Physiologic and chronologic age: clinical studies in elderly patients




Physiologic and chronologic age: clinical studies in elderly patients was the topic discussed by Prof. Artz. At the beginning of his talk the speaker, coming from Chicago (USA) presented very interesting data on chronologic age and physiologic age, on allogenic transplant in older adults and finally on his experience in using the physiologic age for informing and optimizing older transplanted patients. Going deeper in his lecture, Prof. Artz spoke about aging and geriatric hematology, by presenting very interesting data given by clinical trials published on AML transplanted patients and highlighted that in these patients age is an unfavourable factor for survival. In the main part of his lecture, Prof. Artz spoke about the geriatric assessment of the patients eligible for transplantation, by highlighting that there is a high prevalence of vulnerabilities from the geriatric assessment (GA) point of view. The speaker presented very impressive data on a biomarker score derived from CRP, albumin and ferritin for AML/MDS patients after HCT from unrelated donors, by highlighting that there is a very high correlation between this score and the transplant related mortality. Prof. Artz spoke also about the neurophysiological testing prior to perform an allogenic transplant in patients over 60 years old and the deep correlation between the rate of impaired patients and the level of the verbal memory. Finally, the speaker presented very interesting data on his personal experience on GA, talking about the transplant optimization program for older adults performed in his hospital. In conclusion, Prof. Artz pointed out that a multi-disciplinary team approach tailored to the physiologic age holds promises to expand treatment options for older patients.




TOP: GA to Inform and Optimizing Transplant

| Domain | Comments | Vulnerability (V) or Asset (A) | Plan |
|---|---|---|---|
| Comorbidity | HCT-CI=2 DM, Depression + OA, Cr clear=50 | V | endocrine on admit Non-NSAID OA Tx |
| Functional | Preserved IADL, Slow 6 minute walk | +/- | Pre-habilitation with PT |
| Cognition | Normal | A | Detailed education in writing |
| Emotional | Coping, anxiety | V | Engage family, psych referral |
| Social support | Initially poor, later strong | A | Family meeting Caregivers in room |
| Nutrition | No weight loss, partial dentures | A | Educate on supplements |
| Polypharmacy | 3 Rx medication One supplement | A | Safety of other medications, stop supplement |

- What's about age as a variable for heme malignancies based on the data presented by the speaker?
- What is the correlation between aging and geriatric hematology?
- What's about the Simple "frailty" score presented by the speaker?
- What's about the prognostic influence of GA in patients over 50 years old after allograft?
- What are the key points of the TO program presented by the speaker?
- What's about the data on survival presented by the speaker on the outcomes of the Allo over 60 years from 2009 to 2016?

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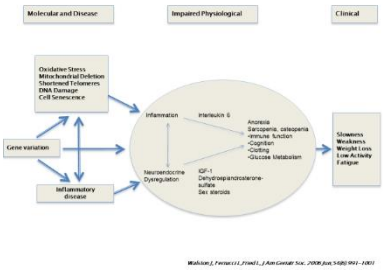
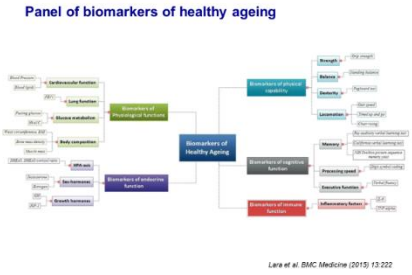
# Biologic Biomarkers of Aging


Biologic Biomarkers of Aging was the topic discussed by Prof. Colloca. The speaker, coming from Rome (IT), introduced his talk by highlighting that aging depends on a lot of variables not only to biological age itself. Going deeper in his lecture, Prof, Colloca spoke about the biomarkers of aging, by highlighting that, based on the American Federation for aging research, these biomarkers have to be in compliance with four major points. In the main part of his lecture, the speaker presented very interesting data on the biomarkers of aging compared to the ones of healthy aging, by highlighting that in our time is easier to speak about biomarkers of healthy aging for healthy is a well-established concept in our society. In conclusion, the speaker pointed out that we need biomarkers, but together with a comprehensive geriatric assessment.




- When should a person be considered old, from the speaker point of view?
- What are the main biomarkers of aging?
- What are the major points characterizing the true biomarkers of age, based on the data presented by the speaker?
- What are the main biomarkers of healthy aging presented by the speaker?

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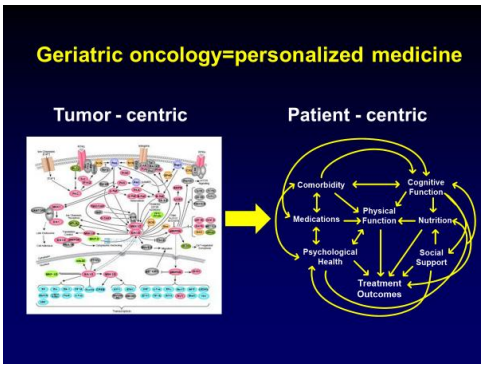
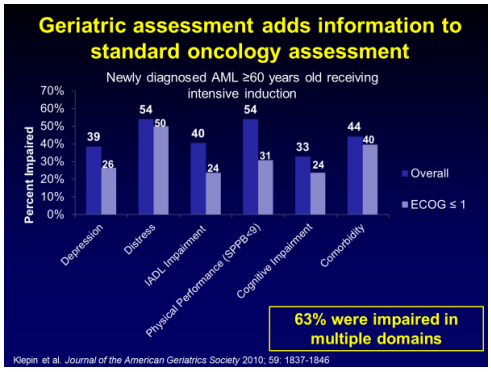
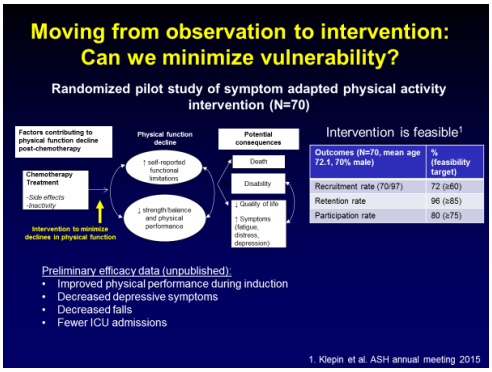
# Functional assessment of the elderly




Functional assessment of the elderly was the topic of Prof. Klepin presentation. The speaker, coming from Winston Salem (USA), started her lecture, by highlighting that there is a little evidence to guide treatment decisions. Going deeper in her lecture, Prof. Klepin pointed out that any patient deserves an individualized treatment plan, taking in account risks and benefits. More in particular the speaker talked about the correlation between Geriatric oncology and the necessity to apply this science to the specific situation of any patient. In the main part of her presentation, Prof. Klepin talked about the Geriatric assessment (GA), by highlighting that the measurement of the GA factors adds significance to the simple prediction of survival. The speaker presented very impressive data given by clinical and registries studies on the GA in MDL/AML, multiple myeloma and chronic lymphocytic leukemia patients, by highlighting its power in predicting survival and the rate of adverse events. Prof. Klepin spoke also about the so called "G8" screening tool in hematologic malignancies, by highlighting that this is a very affordable tool in term of outcome prediction in patients over 67 years old. In the last part of her talk, the speaker talked about the need for introducing new outcomes other than quality of life, like the decline in physical function, measured through GA. In conclusion, Prof. Klepin pointed out that the measures to be included when scientists design a trial, should be physical and cognitive functions plus comorbidities in order to better measure the real outcomes of patients affected by hematological diseases.




- Can we extrapolate available evidence for any individual patient?
- What are the main research themes of the Geriatric Oncology, based on the data presented by the speaker?
- What are the key points of the GA model presented by the speaker?
- Is it necessary to develop hematologic specific tools for GA in the hematology scale?
- What's about the functional decline from the speaker point of view?

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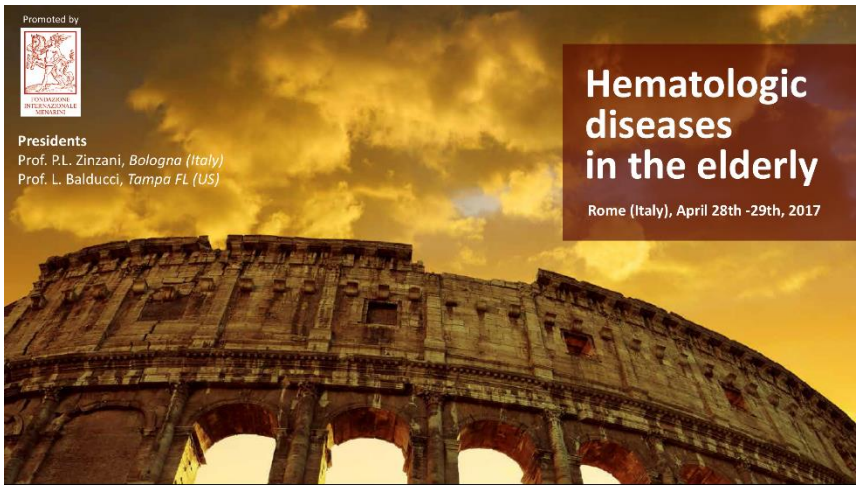
# Frailty as an important concept in geriatric hematololgy




Frailty as an important concept in geriatric hematololgy was the topic of the round table held by Prof. Artz, Balducci, Colloca, Franceschi, and Klepin. The speakers, at the beginning of this talk, addressed the audience by highlighting that frailty is a generic definition. Prof. Klepin pointed out that it is necessary to use this term in a better defined clinical context. Prof. Colloca highlighted that frailty is a condition of high vulnerability in response to external stresses that changes time by time in the same patient. Prof. Franceschi pointed out that frailty looks like a "cargo" concept, characterized by the inclusion of different conditions not well defined, also used in total different clinical settings and it needs to be better defined. Prof. Artz, highlighted that frailty is a very useful term but it is used in unappropriated conditions, it is necessary to restart to use it in a more correct way. All the speakers agreed to use geriatric assessment instead of frailty in the research setting, but not in the clinical setting where frailty is a very useful term. In conclusion, Prof. Balducci pointed out that frailty is not the same of physiologic age and it is very useful in the absence of specific organs damages from the clinical point of view

- What's about the need for using better the term frailty from the speakers point of view?
- Why is frailty considered like a "cargo" term based on the opinion of Prof. Franceschi?
- What's about the U-shaped curve of the salt intake from the speaker point of view?
- What's about the use of these two terms, frailty and geriatric assessment, from the speakers point of view?

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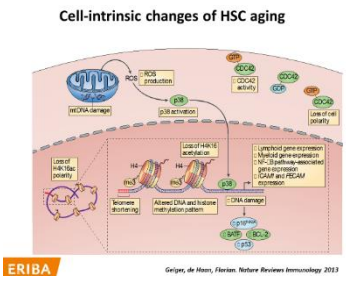
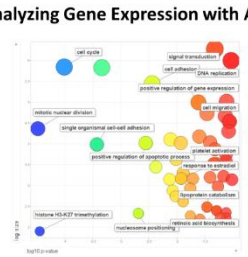
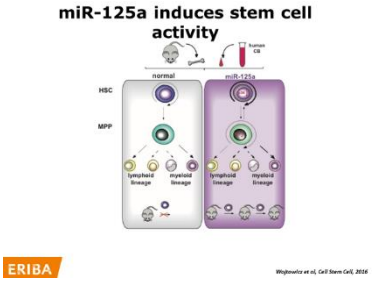
# Hematopoiesis in the elderly




Prof. de Haan, coming from Groningen (the Netherland) spoke about hematopoiesis in the elderly, by presenting very interesting data on the biological cascade leading to the production of the myeloid and lymphoid lineages. Going deeper in his lecture, Prof. de Hann presented very interesting data on the loose of power of the hematopoietic stem cells due to their aging processes. More in particular he spoke about different models like clonal succession, dynamic repetition, clonal stability and stochastic processes. In the main part of his lecture, Prof. de Haan presented very interesting data on the HSC clones, their asymmetric distribution across the skeleton and on the analysis of the gene expression with age, by highlighting that the gene expression changes with age and more in particular talked about the consistently and differently expressed genes and the epigenetic control of aging. In the last part of his lecture, Prof. de Hann presented very interesting data on the microRNA-125a and its effects on hematopoiesis and on the stem cell activity.




- Do pre-hematological diseases result from HSC aging?
- What are the main Cell-intrinsic changes of HSC aging, based on the data presented by the speaker?
- There is an epigenetic control of aging, based on the data presented by the speaker?
- What are the main genes consistently differently expressed with age?
- Can progenitors become stem cells, based on the data presented by the speaker?
- What's about the relationship between the microRNA-125a and the stem cell activity, based on the data presented by the speaker?

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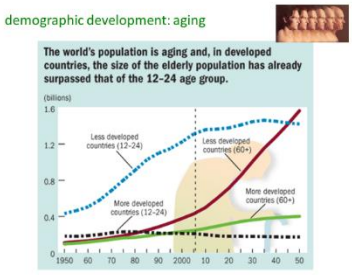
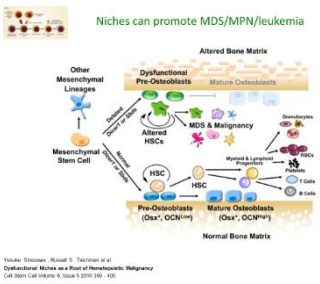
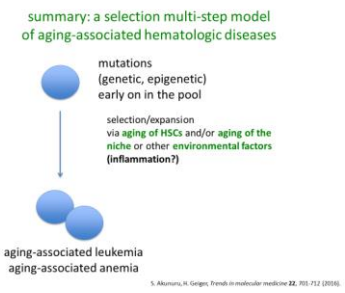
# Microenvironement stroma




Microenvironement stroma was the topic at the core of Prof. Geiger presentation. The speaker, coming from Cincinnati (USA), at the beginning of his presentation, highlighted that aging around the world is dramatically increasing and one of the main consequences is the rise in the prevalence of leukemia. In the main part of his lecture, Prof. Geiger, spoke about the identification of the molecular and cellular mechanisms of aging that cause age-associated tissue dysfunctions and diseases and presented very interesting data given by experimental studies on the main HSCs changes in number and function due to aging. More in particular the speaker talked about the possible mechanisms that can promote leukemia and other diseases like MDS and MPN thanks to the dysfunctional niches and presented very impressive data on an experimental study performed in mice, demonstrating that in the stromal aged stem cells, there is a lack of osteoponin, counteracted by the injection of the OPN fractions. In conclusion, the speaker, based on these data, pointed out that aging is not just time-dependent, but changes upon aging mechanistically contribute to the disease progression.




- How much should we lower blood pressure in the elderly, based on the data presented by the speaker?
- Why are stem cells social entities from the speaker point of view?
- How do aged stem cells respond to young levels of OPN?
- What's about the multi-step model of aging-associated hematologic diseases?

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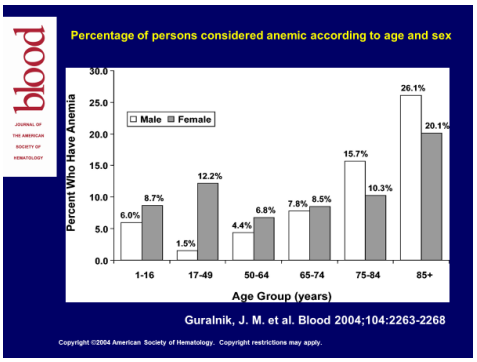
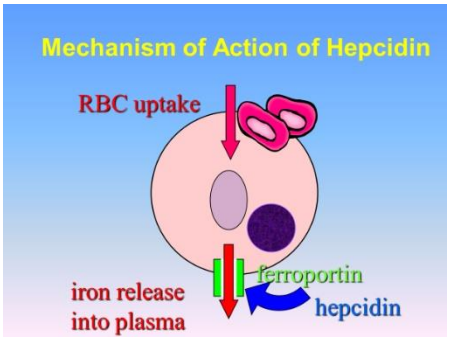
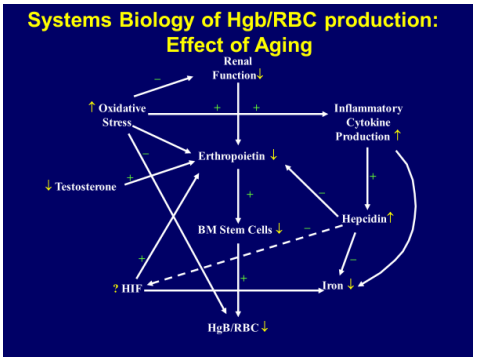
# Anaemias in the elderly




Anaemias in the elderly was the topic discussed by Prof. Cohen. The speaker, coming from Durham (USA), presented very interesting data on the main topics linking anaemia and the elderly. Going deeper in his lecture, Prof. Cohen spoke about the prevalence of anaemia according to age and sex, by highlighting that old age and male sex are the two main factors leading to the rise of the prevalence of anaemia.




In the main part of his lecture, the speaker presented very interesting data on the etiology and on the main characteristics and mechanisms of anaemia in relationship with the chronic diseases, by highlighting the role played by the inflammatory cytokines. Prof. Cohen presented also data on hepcidin, the iron-regulatory hormone and its mechanism of action. In the second part of his lecture, the speaker talked about the unexplained forms of anaemia in the elderly, by highlighting the role played by the stem cell loss, the inhibited erythropoietic stimulus and the state of dyserithropoiesis. Prof. Cohen presented also data demonstrating the dramatic changes in GUT microbiota that influence the hematopoietic processes and spoke about the phenomena which determine the link between stress and hematopoiesis. In conclusion, Prof. Cohen pointed out that the mechanisms leading to anemia in older people are many and quite complexes.




- What's about the etiology of anaemia, based on the data presented by the speaker?
- What are the main characteristics linking anaemia to the chronic diseases?
- What's about hepcidin and its mechanism of action, based on the data presented by the speaker?
- What are the main clinical conditions known to influence the circulating hepcidin levels?
- How does GUT microbiota sustain hematopoiesis?
- What's about the relationship between hematopoiesis and stress?

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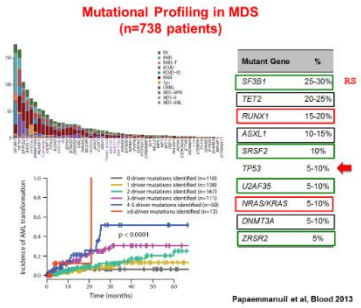
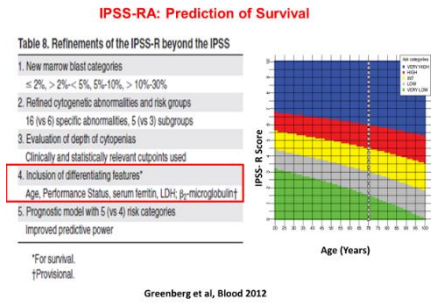
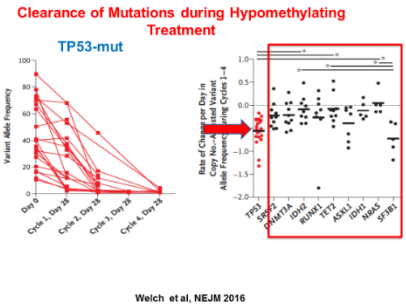
# MDS in the elderly




MDS in the elderly, was the topic discussed by Prof. Voso. The speaker coming from Rome (IT) talked about the Pathogenesis, Prognosis and Treatment of MDS in elderly people. Going deeper in her lecture, Prof. Voso, presented very interesting data given by genetic studies running in 738 patients, on the mutational profiling in MDS, by highlighting that these mutations have a significant impact on prognosis. The speaker pointed out that these mutations are frequently present also in healthy people, but during the life course these healthy people can develop the disease, demonstrating that mutations and aging have a tight relationship with the onset of MDS. In the main part of her lecture, Prof. Voso presented very impressive data on the correlation between aging, the presence of mutation and the onset of MDS but also of other disease like the hereditary myeloid malignancy syndromes and talked about the scores to be applied in MDS elderly patients. In the last part of her presentation, the speaker talked about treatment, by presenting many data on the effect of Lenalidomide, Erythropoietin, Azacitidine and the hypomethylating treatment. In conclusion, Prof. Voso pointed out that somatic mutations play a significant role for the onset and progression of MDS and the elderly are characterized by an higher mutation rates, but the response to Epo, Len and HMT is age-independent.




- What's about the mutational profiling in MDS patients?
- What are the main HMM syndromes due to the presence of mutations, based on the data presented by the speaker?
- Is the IPP-R score system sufficient from the prognostic point of view in MDS elderly patients?
- What's about the effect of Azacitidine in a real-world setting, based on the data presented by the speaker?
- What are the main prognostic factors for response, from the speaker point of view?

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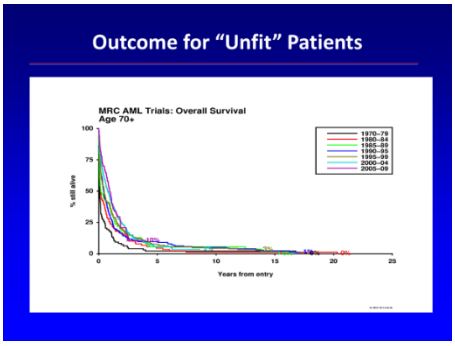
# Acute leukemia in the elderly




Prof. Burnett from Cardiff (UK), presented very interesting data on acute leukemia in the elderly. Going deeper in his lecture, the speaker talked about AML and its dramatically increasing with aging. In the main part of his lecture, Prof. Burnett presented very impressive data on the poor overall survival in patients over 60 years old, not more than 5% at 20 years from the onset of the disease, by highlighting that the problem is not the age per se, but the higher risk of cytogenetic mutations linked with age. More in particular, the speaker talked about the options for the improvement of the intensive treatment starting from the escalation of dose till the alternative formulation of "3+7" and presented very poor effective data given by the main clinical studies running in over>60 years patients treated with these options. Prof. Burnett spoke about the AML17, AMLSG, AML16, CPX-351 and the AML 14 trials, and presented a lot of data on survival, consolidation and maintenance. In the last part of his presentation, the speaker talked about the tolls for the identification of older adults suitable for intensive AML chemotherapy and finally spoke about standard of care, by highlighting that low-dose cytarabine is superior to best supportive care and hydroxyurea. In conclusion, Prof. Burnett pointed out that the present treatments have in general poor results and some new treatments hold promises.

**Determinants of Therapy "Fitness"**

Many individual factors recognized that impact likelihood of treatment-related mortality:

- Age
- Performance status
- Bilirubin
- Albumin
- Hemoglobin
- Neutrophil count
- Albumin
- Creatinine
- Secondary disease
- LDH
- Fibrinogen
- Cytogenetic risk
- Presence of infections
- Etc.

➢ Surrogates for biological age of patient

**New Options**

- Clofarabine
- Sapacitibine
- Vosaroxin or Vosaroxin +/- LDAC
- Demethylation agents (azacytidine/ decitibine)
- LDAC + arsenic trioxide
- LDAC + gemtuzumab ozogamicin
- DMT + HiDAC inhibitors (azacitidine + pacrinostat)
- LDAC + mTOR inhibition
- HSP90 inhibition (Ganetespib)
- NEDD inhibition/ SMO inhibitors
- Polo-like kinase (Plk) inhibitors (volarsertib)
- SINE (Selinexor)
- DMT Combos
- CPX-351

- What's about the real role of age for outcome, based on the data presented by the speaker?
- What are the main options for the improvement of the intensive treatment?
- What are the main questions raised by the speaker about the UK AML16 trial?
- What's about consolidation in the AML16 trial?
- What is the standard of care, based on the data presented by the speaker?
- What's about the new options for treatment of AML older patients, presented by the speaker?

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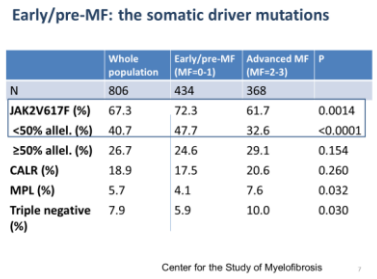
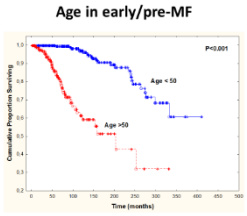
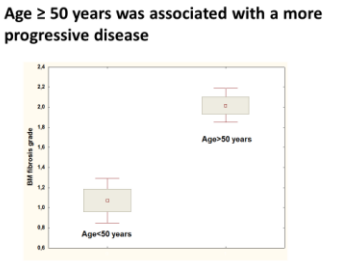
# Myeloproliferative neoplasms in the elderly




Prof. Barosi from Pavia (IT), presented very interesting data on the myeloproliferative neoplasms in the elderly. Going deeper in his lecture, the speaker talked about the contemporary definition of myeloproliferative neoplasms, the main phenotypes, the prognosis and finally about the disease mechanisms, all of these topics correlated with age. In the main part of his lecture, Prof. Barosi spoke about the diagnostic criteria for myelofibrosis by highlighting that bone marrow fibrosis is not a necessary criterion and that this disease is characterized by the presence of mutation at the genetic level. More in particular, the speaker presented very impressive data on the mutations and the subclonal mutations and karyotype leading to the onset of MF, by highlighting that age is a major determinant of the MF phenotype and it is also a key factor for prognosis. In the last part of his lecture, the speaker talked about the correlation between age, inflammation and the onset of the disease. In conclusion, Prof. Barosi pointed out that the hypothesis of his team of Research is that the older age influences the disease progression through the onset of genomic instability.




- What are the main diagnostic criteria for myelofibrosis presented by the speaker?
- What's about the role of age in the early/pre-MF somatic driver mutations presented by the speaker?
- What is the role played by age in the relationship between MF and inflammation?
- What are the main clinical scores for the risk stratification in MF patients presented by the speaker?

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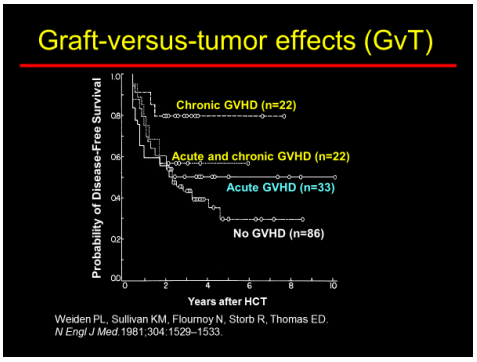
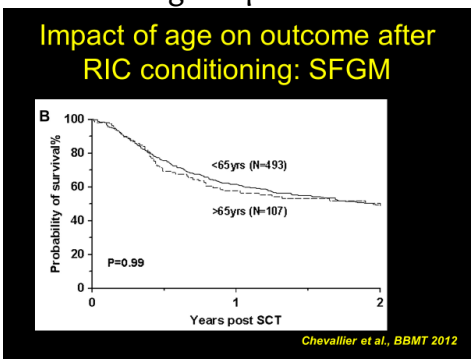
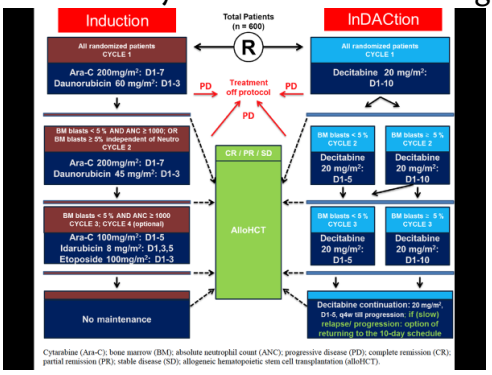
# Stem cell transplantation in older patients




The main topic at the core of Prof. Baron presentation, was the stem cells transplantation in older patients. The speaker, coming from Liège (Belgium), presented very interesting data on the ALLO-HCT candidacy, on the impact of age on the ALLO-HCT outcomes and on the immune recovery and finally on the best way to prepare AML patients to ALLO-HCT. Going deeper in his lecture Prof. Baron talked about the Graft-versus-tumor effects, by highlighting that the major part of the efficacy of the allogenic HCT is due to these effects. In the main part of his talk, the speaker presented a lot of data on the impact of age on the allo-HCT outcomes by highlighting that age does not have a very significant impact on the overall survival. Speaking about the impact of age on immune recovery, Prof. Baron highlighted that older patients present a thymic recover less strong than younger patients. Finally, the speaker talked about the best way to prepare AML patients to allo-HCT and presented very interesting data comparing 10 days decitabine versus conventional chemotherapy followed by allografting in AML patients over 60 years old. In conclusion, Prof. Baron pointed out that the disease characteristics, the pre-transplant comorbidities, the donor type and the patients' general fitness should be taken into account in addition to age in order to find those patients definable as good transplant candidates.




- What's about the correlation between Graft-versus-tumor effects and the allogenic HCT, from the speaker point of view?
- What's about the role of the conditioning regimens?
- What's about the immune recovery after allo-HCT in younger patients compared to older patients, based on the data presented by the speaker?
- What's about the impact of age on the thymic recovery, based on the data presented by the speaker?

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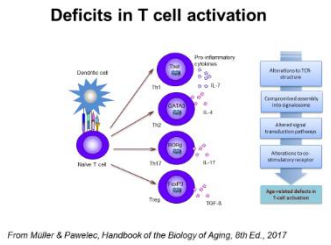
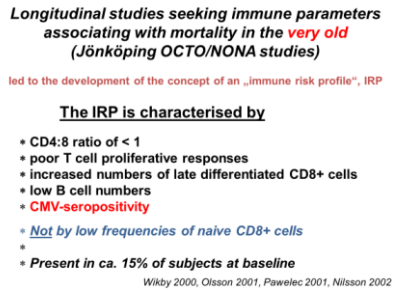
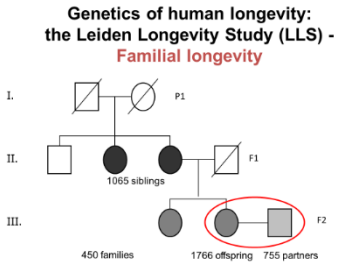
# The immune system in the elderly?



From Müller & Pawelec, Handbook of the Biology of Aging, 8th Ed., 2017

The main topic at the core of Prof. Pawelec presentation, was "what's about the immune system in the elderly". The speaker, coming from Tübingen (Germany), presented very interesting data, starting from the concept that immunity decreases with the age. Going deeper in his lecture, Prof. Pawelec talked about the relationship between age and Immunity, by highlighting that there is a decrease in B and T cells starting from their progenitors due to aging. More in particular, the speaker presented very interesting and innovative data on the main defects leading to the immunosenescence process, characterized by the loss of the naïve T-cells. In the main part of his lecture, Prof. Pawelec talked about the relationship between the loss of naïve T-cells and the age-associated immune changes and presented very interesting data given by clinical studies on the immune risk profile and on the context-dependent models. More in particular the speaker talked about the results of the OCTO/NONA studies and about the L85+, BELFRAIL and Leiden Longevity Family studies. In conclusion Prof. Pawelec pointed out that the risks factors for disease and mortality may be different in younger and older people, they are influenced by genetics and by the differences present in different populations.




- What are the main pre-requisite for a well-functioning immunity system?
- What are the two major problems leading to immunoscenescence based on the data presented by the speaker?
- How long does immune memory last?
- What are the main examples of context-dependency presented by the speaker?
- What's about the differences in survival between women and men in the BELFRAIL study?

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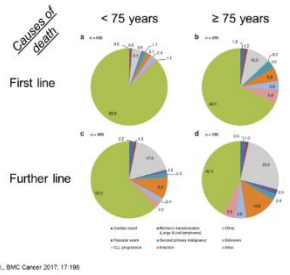
# CLL and related disorders




The main topic at the core of Prof. Goede presentation, was "CLL and related disorders". The speaker, coming from Köln (Germany), presented very interesting data on older people affected by CLL and talked about the main characteristics of the disease and its diagnostic and therapeutic management. Going deeper in his lecture, Prof. Goede presented very interesting data on the main disease deletions and mutations and on the main causes of death depending by age and highlighted that age is a very important factor influencing CLL presentation and evolution. Talking about the patients features, the speaker pointed out that today there is no epidemiological data available in CLL for the main important characteristics of the patients like the polypharmacy intake, the symptomatology, the clinical and physical status. In the main part of his talk, Prof. Goede presented very interesting data on the CLL diagnostic management, speaking about the CLL International Prognostic Index and the related score risk group. In the last part of his lecture, the speaker talked about the CLL therapeutic management, by presenting a lot of data given by RCTs running in CLL older patients from the efficacy and the safety point of view. In conclusion, Prof. Goede pointed out that there is a growing evidence on the prognostic impact of comorbidities and on the ongoing treatment improvement in CLL patients.

CLL International Prognostic Index (CLL-IPI)

| Variable | Adverse factor | Grading |
|---|---|---|
| *TP53* (17p) | Deleted and/or mutated | 4 |
| IGHV | Unmutated | 2 |
| B2M, mg/L | > 3.5 | 2 |
| Age | > 65 years | 1 |
| Stage | Binet B/C or Rai I-IV | 1 |
| Total Score | | 0 – 10 |

| Score | Risk Group |
|---|---|
| 0 – 1 | Low risk |
| 2 – 3 | Intermediate risk |
| 4 – 6 | High risk |
| 7 – 10 | Very high risk |

The International CLL-IPI Working Group
Lancet Oncol 2016

Current treatment paradigm in elderly CLL at a glance

| | |
|---|---|
| 1L - Fit | R-FC or R-B |
| 1L - Unfit | G-CLB, O-CLB, R-CLB or IBRUT |
| 1L - Del17p | IBRUT (or R-IDELA) |
| >1L - early | IBRUT or R-IDELA (or VEN) |
| >1L - late | Re-use of CIT possible |

Eichhorst et al., Ann Oncol 2015; 55:v78-84
Zelenetz et al., 2015; www.nccn.org
Stauder et al., Ann Oncol 2017; 28:218-227

- What is the prognostic value of the geriatric assessment in CLL patients?
- What is the prognostic value of the comorbidities in CLL patients?
- What's about the novel molecular risk factors in CLL elderly patients, based on the data presented by the speaker?
- What is the current treatment paradigm in elderly CLL patients from the speaker point of view?
- What are the main safety aspects of the new oral drugs available for the CLL treatment, from the speaker of view?

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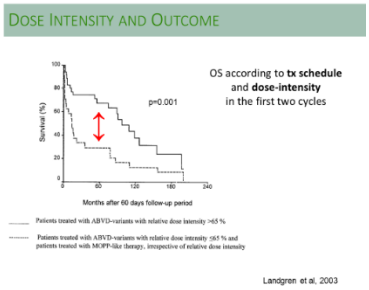
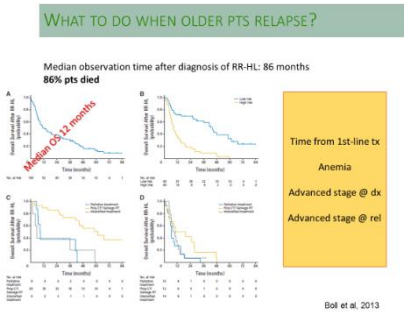
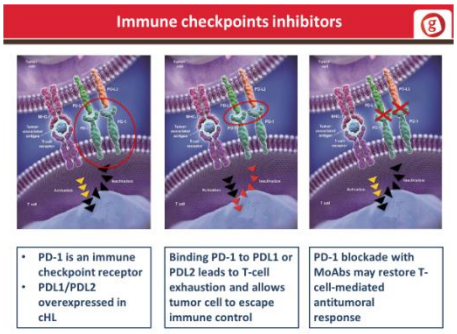
# Hodgkin lymphoma




Hodgkin lymphoma, was the topic at the core of Prof. Spina presentation. The speaker coming from Pordenone (IT), talked about incidence, outcome, risk factors and treatment of the HL patients, by highlighting that HL is an aggressive disease requiring an aggressive therapy, but many HL patients are compromised and frails and they need a less intensive approach. Going deeper in his lecture, Prof. Spina presented very interesting and impressive data given by many clinical trials running in HL patients on incidence and outcome, by highlighting that aging significantly worsens the failure-free survival and the overall survival of the HL patients. In the main part of his lecture, Prof. Spina talked about therapy and presented a huge amount of data given by the main clinical trials published in the last 20 years on the different therapeutic approaches of HL patients. More in particular he talked about the relationship between dose intensity and outcome, the ABVD tolerability in the older and in the compromised patients and the best adapted treatment to be applied for, the procedures for older relapsed patients and finally about the new drugs like Brentuximab Vedotin and the Anti PD1 compounds. In conclusion, Prof. Spina pointed out that for the elderly HL patients, despite all the clinical trials designed for the detection of the best therapy regimens, we are still searching for a well affordable standard of care.




- What are the main biological risk factors presented by the speaker?
- How important is the Epstein Barr Virus infection from the outcome point of view in the HL patients?
- What to do when older patients relapse?
- What's about the compromised patients, is a less intensive therapy viable?
- What's about the Anti PD1 compounds from the speaker point of view?
- Why is the Comprehensive Geriatric Assessment important in HL patients based on the data presented by the speaker?

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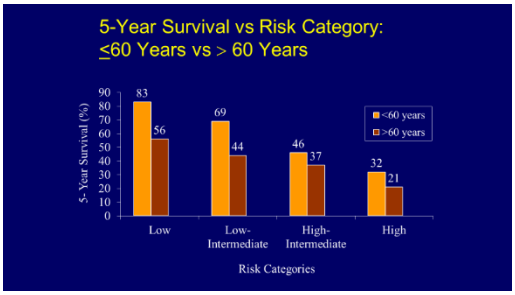
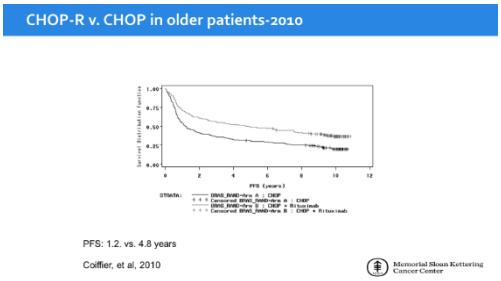
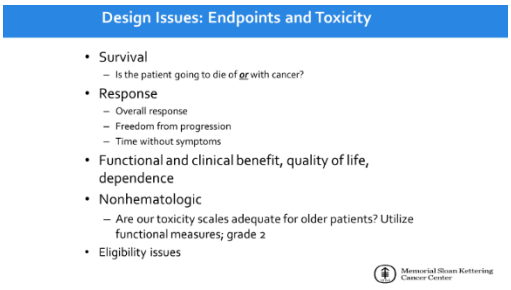
# Non-Hodgkin lymphoma




Non-Hodgkin lymphoma, was the topic Prof. Lichtman talked about. The speaker coming from Commak (USA), presented very interesting data on the non-Hodgkin lymphoma. More in particular, he spoke about incidence, determinants of outcome, predictive factors, treatment and finally about the eligibility issues of the clinical trials running in the elderly patients. Going deeper in his lecture, Prof. Lichtman pointed out that NHL is a typical disease of the elderly with its incidence raising in patients over 60 years old. Talking about the determinants of outcome, the speaker presented very interesting data on the effect of the age related to the arbitrary treatment dose reductions. In the main part of his speech, Prof. Lichtman talked about the prognostic factors for survival and about the Primary Treatment and presented a huge amount of data on the main treatment regimens studied for the NHL patients. In the second part of his lecture, the speaker presented very impressive data on the comparison between the Comprehensive Geriatric Assessment and the Clinical Judgment, by highlighting that CGA is better than the clinical judgment for identifying the best treatment regimen for the NHL patients. Finally, Prof. Lichtman spoke about the under representation of older patients in the clinical trials, a very important problem for a disease mainly present in elderly people, the speaker highlighted. In conclusion, Prof. Lichtman pointed out that CHOP-R is the standard of care in patients who meet the standard eligibility criteria up to age of 75 years old, but the patients over 80 years will continue to be a therapeutic challenge from the treatment regimens choice point of view.




- What's about the relationship between NHL subtype incidence and age?
- What are the main determinants of outcome presented by the speaker?
- What's about the CHOP vs CHOP-R treatment in older patients, based on the data presented by the speaker?
- What's about the alternative regimens from the speaker point of view?
- What are the main effects of comorbidities presented by the speaker?
- What are the main issues of the Clinical Trials in the Elderly presented by the speaker?

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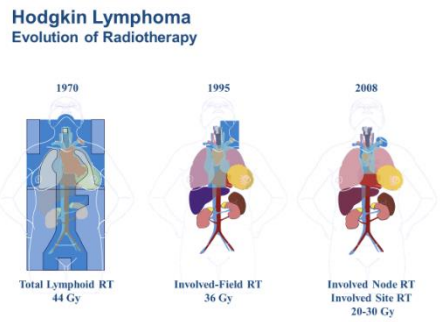
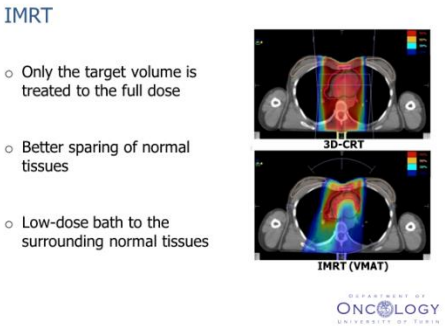
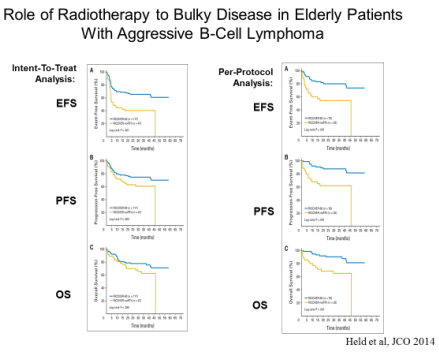
# Role of radiotherapy in the treatment of lymphomas




Role of radiotherapy in the treatment of lymphomas, was the topic at the core of Prof. Ricardi presentation. The speaker coming from Turin (IT), presented very interesting data on the application of this therapeutic procedure in the Hodgkin and in the Diffuse Large B-cell Lymphomas. Speaking about HL, the speaker presented data about the early stage HL treatment and the evolution of radiotherapy, pointing to the concepts of Involved node and Involved site radiotherapy. In the main part of his lecture, Prof. Ricardi talked about the radiotherapy dosages with a special attention to the elderly and presented very interesting data given by the main clinical trials running in these patients. The speaker presented also data on the Intensity-modulated radiotherapy, by highlighting that this procedure is increasing its application in these last years. In the last part of his lecture, Prof. Ricardi talked about the relationship between chemo and radiotherapy and the need for a better balance of these two fundamental therapeutic procedures in Lymphomas patients, more in particular in the elderly. Finally, the speaker presented very interesting data on the role of RT in the DLBCL patients, by highlighting that RT + chemotherapy in the elderly patients affected by aggressive B-cell lymphomas is very effective in improving progression-free, event-free and overall survival compared to chemotherapy alone also in the R-CHOP era. In conclusion, Prof. Ricardi pointed out that a more familiarity with the role of RT is essential for the optimal care of elderly lymphoma patients.




- What's about the "Low dose" RT in indolent lymphomas from the speaker point of view?
- What's about IMRT in lymphoma patients from the speaker point of view?
- What's about chemotherapy alone compared to chemotherapy plus RT in Lymphoma patients from the speaker point of view?
- What are the main characteristics of the BLBC lymphomas in the elderly, based on the data presented by the speaker?
- Which patients do benefit most from RT based on the data presented by the speaker?
- Is there benefits from RT in R-CHOP era, from the speaker point of view?

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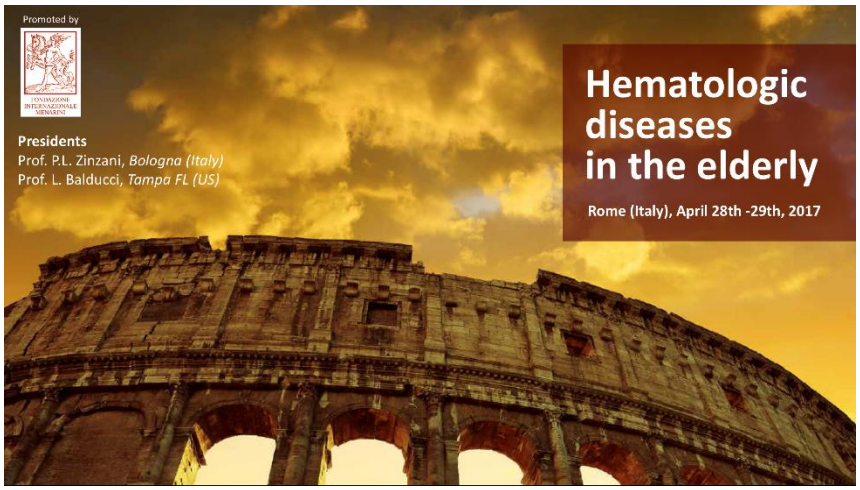
# ROUND TABLE ON LYMPHOMAS




Prof. Balducci, Ferreri, Lichtman, Ricardi, Spina, and Zinzani took part in the second-round table on lymphomas and more in particular on these three topics: "Indolent lymphoma: when to treat the elderly patient?", "How to treat primary CNS lymphoma?" "Burkitt lymphoma. What to do?". Speaking about indolent lymphomas, Prof. Ferreri pointed out that the principal parameters to be taken in account for therapy are the CGA criteria, Prof, Spina highlighted that rituximab alone or in combination with CVP is the better treatment protocol for these patients. Prof. Balducci highlighted that CVPR is a quite appropriate approach, better than BR. Speaking about the treatment of primary CNS lymphomas, Prof. Ferrari highlighted that relapsing has a dramatic effect in these patients. Speaking about the new biological agents, Prof. Ferrari pointed out that these drugs are able to maintain patients in stable conditions for years also after relapse. Prof. Balducci, highlighted that methotrexate is the therapy of reference in CNS lymphomas patients. Speaking about patients affected by Burkitt lymphomas, Prof. Spina highlighted that the better approach depends on the patient conditions.

- What's about radiotherapy in indolent lymphomas patients from the speakers point of view?
- What's about the differences between clinical and research settings for the RT responses in CNS lymphomas patients, from the speakers point of view?
- What is the therapy of reference in CNS lymphomas patients from the speakers point of view?

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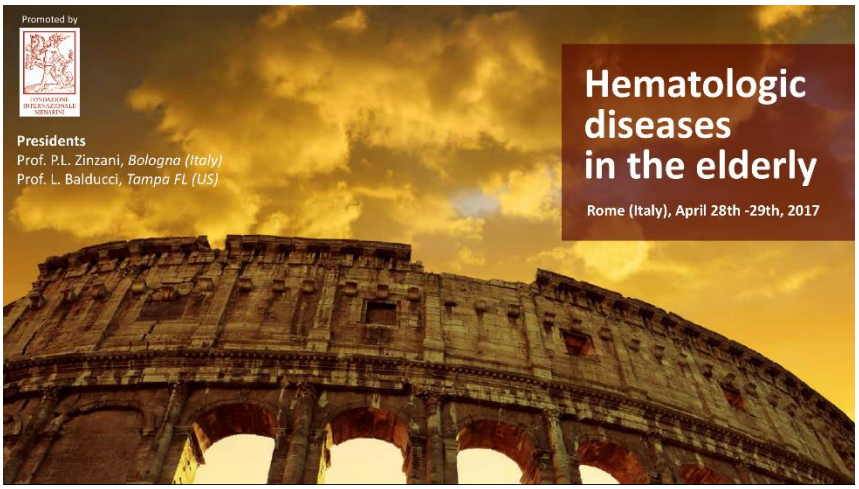


In conclusion, Prof. Balducci pointed out that aging is to be studied in a dynamic prospective and can be defined as a progressive reduction in person functional reserve, but in the main time new protocols of cancer treatment can became available, depending on their tolerability. In this view, there are two new dynamics: different aging and different protocols of cancer treatment the speaker pointed out. Finally, Prof. Balducci proposed the creation of a framework for better define a program for the cancer hematological malignancies of aging and other hematological diseases, starting from the bases put in this congress and also for better define a program available for the collection of real data with well-defined and shared rules, especially for prevention, through alternative ways other than the traditional clinical trials not more reasonable due to the dynamic nature of aging.

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

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

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