METABOLIC BONE DISEASE SATELLITE MEETING
EUROMEDLAB 2017

JUNE 10 2017
ATHENS WAR MUSEUM ANNEX “SAROGLIO MANSION”

www.athens2017.org/go/satellite

FINAL PROGRAM

IFCC-IOF Working Group for the Standardization of Bone Markers
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Professor Etienne Cavalier
University of Liège, CHU Sart-Tilman, Domaine du Sart-Tilman, B-4000 Liège, Belgium.

Professor Evangelos Terpos
Medical School, University of Athens, Greece

Dr. Konstantinos Makris Ph.D
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Symeon Tournis, MD, PhD
Laboratory for Research of Musculoskeletal System, University of Athens, KAT Hospital, Athens, Greece

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Dear Colleagues and Friends,

On behalf of the Organizing Committee it is a great pleasure to invite you to the Metabolic Bone Disease Satellite Meeting being held in conjunction with EuroMedlab Athens 2017 Congress. This meeting will bring together leading metabolic bone disease clinicians with laboratory medicine specialists providing clinical laboratory services to support their patients. Topics will address new therapies for osteoporosis, clinical practice for metabolic bone disease as a consequence of chronic kidney disease and other diseases of bone. These will be accompanied by presentations on the requirements from the clinical laboratory to optimise patient outcomes for these patients.

Other subjects include the latest developments in our understanding of the clinical usefulness of bone turnover markers for evaluating and following treatment of the osteoporotic patient as well as biomarkers for osteoarthritis and rare bone diseases. From the clinical laboratory, experts will address the role of the latest generation of parathyroid hormone assays, the clinical impact of standardization of 25-hydroxyvitamin D assays and interpretation of their concentrations for the individual patient.

This satellite meeting will provide the opportunity for delegates to network with the international faculty and other specialists both clinical and from the laboratory. Being held in conjunction with EuroMedlab Athens 2017 registrants have the opportunity to attend the Satellite Meeting only or to combine your experience with the most important congress in Laboratory Medicine in Europe. EuroMedlab 2017 provides information on the state of the art and latest innovations of Laboratory Medicine for the 21st century.

Don’t miss this important event in historic Athens. Book the dates and keep an eye on our website. We look forward to seeing you in Athens in June 2017!

Professor Howard Morris
University of South Australia, Adelaide, Australia
Body Jean-Jacques
Professor Jean-Jacques Body received his training at the “Université Libre de Bruxelles” (ULB, Free University of Brussels) and at the Mayo Clinic (Rochester, MN, USA). He is an internist, an endocrinologist and a medical oncologist. He is now Professor Emeritus since March 2017. He was until then Full Professor of Internal Medicine at ULB and Head of the Department of Medicine at University Hospital Brugmann in Brussels. He has been Head of the Internal Medicine Clinic at Institute J. Bordet, the Cancer Center of ULB. He developed the Supportive Care Department at the same Institute. During this period, he created the first National Course on Supportive and Palliative Care. He also created the “Groupe Européen francophone d’étude des Métastases Osseuses (GEMO)”, of which he was the first President. He is also President of the “Belgian Bone Club” and is a member of the “Committee of Scientific Advisors” of “International Osteoporosis Foundation (IOF)”. He is a member of several professional organisations, including ASBMR, ECTS, IBMS, ASCO, ESMO, SIOD, MASCC, ENDO Soc.

His particular research interests are tumor bone disease, osteoporosis, and markers of bone turnover. He was involved in numerous trials in cancer patients with all bisphosphonates available in Europe and with denosumab from phase I to phase IV. More recently, he become interested in risk factors for osteoporotic fractures in postmenopausal women. He has authored or co-authored more than 250 international peer-reviewed papers and more than 60 book chapters or proceedings and he counts more than 200 invited lectures for international meetings.

Hermann Markus
Professor Markus Herrmann is a Chemical Pathologist. He studied medicine at the Universities of Regensburg and Würzburg in Germany, where he graduated in 2000. After internships at the Department of Dermatology at the Technical University of Munich (Germany) and the Institute of Sports Medicine at the University of Saarland (Germany) he started his training in Laboratory Medicine at the Institute of Clinical Chemistry and Laboratory Medicine at the University of Saarland (Germany). In 2007 he received a postdoctoral fellowship grant from the Leopoldina Academy and a went for two years to the AN-ZAC Research Institute in Sydney (Australia). Subsequently, he became a fellow of the Royal College of Pathologists Australia and continued working as a chemical pathologist at the Royal Prince Alfred Hospital and Lavaray Pathology in Sydney. In 2008 he became an associate professor at the University of Saarland (Germany). The University of Sydney awarded him the title of a clinical associate professor in 2010. In 2012 Professor Herrmann moved to Italy, where he directs the Department of Clinical Pathology at the Bolzano hospital. Professor Herrmann’s research is focused on bone metabolism and vitamin D. As a collaborator of the FIELD Study he has shown that vitamin D is an independent predictor of vascular disease in diabetic patients. In addition, he has studied the role of homocysteine and B vitamins in age related degenerative diseases, such as osteoporosis, heart failure and thrombosis. He has published about 100 peer-reviewed articles and book chapters. His current interest is the influence of vitamins on telomere biology. Professor Herrmann is a member of the scientific committee of the Italian Society of Laboratory Medicine and since 2015 he serves on the editorial board of Clinical Chemistry and Laboratory Medicine.

Cavalier Etienne
Cavalier Etienne is Professor of Clinical Chemistry at the University of Liège and Head of the Department of Clinical chemistry at the CHU de Liège. He graduated in pharmaceutical sciences, in laboratory medicine and received his PhD in 2010. His main current research concerns bone markers, vitamin D, PTH, vascular calcification markers, markers of acute kidney diseases, glomerular filtration rate (estimation, biomarkers), markers of frailty and sarcopenia and LCMS/MS methods for steroids and peptides quantification. He is member of 14 scientific societies and has published 184 papers and 4 chapter books.

Cristol Jean-Paul
Jean-Paul Cristol is a Biochemist at the Montpellier Medical School. Since 2003, Jean-Paul Cristol is Head of the Federation of Biology and Pathology and co-ordinator of the Department of Biochemistry and Hormonology at the Montpellier University Hospital. Resident then fellow in Nephrology department, he obtained his MD (1989) and his PhD (1990) in Montpellier. The research group, belonging to “Physiologie et Médecine Experimentale INSERM U1046, CNRS UMR9214”, has a long-standing research interest in chronic and acute kidney disease, especially in monitoring of renal function and LCMS/MS methods for steroids and peptides quantification. He is responsible for the working group “Biomarkers of vascular calcifications” on the behalf of “Société de Biologie Clinique” and “Société Française de Néphrologie Diaylyse et Transplantation”.

Delanaye Pierre, MD, PhD
Dr. Delanaye is currently Nephrologist at the University Hospital of Liège (CHU Sart Tilman), Belgium. His daily practice is the care of his dialysis patients. His clinical research interest is the estimation and measurement of glomerular filtration rate, the epidemiology of chronic kidney disease (CKD) and Mineral Bone Disease (MBD) in dialysis patients. In his research, he underlines the strong and necessary links between Nephrology and Clinical Chemistry. He has published extensively on the epidemiology of CKD, on the evaluation of eGFR formulas and CKD-MBD.
Dr. Terpos is chairing the Bone Subgroup of the International Myeloma Tumors, thalassemia, and hemophilia-related osteoporosis. Zoledronic acid, on myeloma bone disease, solid tumors with bone metastases, and the effects of vitamin D and dietary calcium. Professor Terpos is currently the President-Elect of the IFCC; he has served as Chair of the IFCC – International Osteoporosis Foundation Joint Working Group on Standardization of Bone Marker Assays. Vice-President of the IFCC between 2012 and 2014, and Secretary of the Scientific Division of the IFCC.

Papapoulos Socrates

Socrates E. Papapoulos is Professor of Medicine (Diseases of Calcium and Bone Metabolism) and senior medical specialist/advisor at the Leiden Center for Bone Quality, the Netherlands. He received his MD from the University of Athens, Greece and he was trained in Internal Medicine and Endocrinology in Athens, GR and in London, UK. In 1984 he joined the Department of Endocrinology and Metabolic Diseases of the Leiden University Medical Center where he was Director of Bone and Mineral Research between 1989 and 2012. Since 1974 he has been continuously engaged in basic and clinical research, patient care and teaching of disorders of calcium and bone metabolism. Dr. Papapoulos is recipient, among other, of the Bay Frame Memorial Award and the Frederic C Bartter Award of the ASBMR, the John Haddad Jr Award of the IBMS, the JB Johnson Award of the Paget’s Foundation, USA, the Steven Boonen Award of ECTS and The Pierre Delmas Award of the IOF and he is Doctor Honoris Causa of the Universities of Athens and Thessaloniki. He has served on numerous boards and committees including the Board and the Scientific Advisory Board of the IOF, the Board of Directors of the IBMS and of the ECTS, the European Union committee for the prevention of osteoporosis, a WHO task force for the development of a world wide strategy for the prevention and treatment of osteoporosis and he is senior scientific advisor of the European Union project Osteoporosis in Europe.

Rye Jorgensen Niklas

Niklas Rye Jørgensen is professor of Clinical Biochemistry at University of Southern Denmark and head of the Section of Clinical Biochemistry at Copenhagen University Hospital, Glostrup, Denmark. He graduated as Medical Doctor from the University of Copenhagen in 1992. His primary field of research is translational bone biology in which he has worked for more than 20 years. Also, he has a great interest in research in the clinical use of biochemical markers of bone turnover.

Terpos Evangelos

Evangelos Terpos, MD, PhD is an Associate Professor of Hematology in the National and Kapodistrian University of Athens, School of Medicine, Athens, Greece (since 2009). He has also been appointed as Honorary Senior Lecturer in the Department of Hematology, Faculty of Medicine Imperial College London, London, UK (since 2003). His main research interest is the biology of bone disease in hematological disorders, including multiple myeloma and thalassemia. In more than 380 papers in peer-reviewed journals, Dr. Terpos has reported the significant role of receptor activator of nuclear factor-kappa B ligand (RANKL) and osteoprotegerin axis, macrophage inflammatory protein-talpha (CCL3, MIP-1), Wnt signaling (dickkopf-1 protein, Dkk-1, sclerostin) and activin-A antagonists in myeloma bone disease and thalassemia bone loss. He has studied the predictive value of markers of bone remodeling and osteoclast function in both myeloma and thalassemia-associated osteoporosis. He has studied the effect of bisphosphonates, mainly of pamidronate and zoledronic acid, on myeloma bone disease, solid tumors with bone metastases, thalassemia and hemophilia-related osteoporosis.

Dr Terpos is chairing the Bone Subgroup of the International Myeloma Working Group (IMWG) and is co-chairing the Guideline subgroup of the European Myeloma Network (EMN). He has given lectures in the European Hematology Association (EHA), American Society of Hematology (ASH) and American Society for Medical Oncology (ASCO) meetings, Thalassemia International Federation (TIF) meetings, International Myeloma Workshops, International Meetings on Cancer-Induced Bone Disease, and several National meetings. He is reviewer of scientific papers in more than 50 medical journals including the Lancet, Lancet Oncology, Journal of Clinical Oncology, Blood and Leukemia and he has reviewed abstracts for EHA, EBMT and ASH meetings. He is also a member of the Editorial Board of Haematologica.

Evangelos Terpos can be reached via e-mail at eterpos@med.uoa.gr and充沛 clinical experience in treating patients with osteoporosis and research experience and publications on the use of bone turnover markers in the management of osteoporosis. He was Chair of the IOF-IFCC Working Group on Bone Marker Standards in Osteoporosis, which formulated position paper on reference bone turnover markers.

Tournis Symeon

Symeon Tournis, MD, PhD is a clinical Endocrinologist and Senior Research Fellow at the Laboratory for the Research of the Musculoskeletal System of the University of Athens, KAT Hospital. He graduated from the medical school of the University of Thessaloniki and received his PhD degree from the University of Ioannina.

He has published more than 70 papers in peer-reviewed journal, has over 900 citations and an H-index of 15.

Vasikaran Samuel

Dr Samuel Vasikaran is a Chemical Pathologist based in Perth, Western Australia. He was previously Clinical Professor, Pathology and Laboratory Medicine, University of Western Australia until 2016. He has extensive clinical experience in treating patients with osteoporosis and research experience and publications on the use of bone turnover markers in the management of osteoporosis. He was Chair of the IOF-IFCC Working Group on Bone Marker Standards in Osteoporosis, which formulated position paper on reference bone turnover markers.
Welcome
Professor George P. Lyritis  
Chair Organizing Committee and Professor

Professor Howard Morris  
Chair Scientific Committee

Session 1  
Bone Turnover Markers in Osteoporosis  
Chair: Prof. George P. Lyritis

09:00  
The clinical usefulness of bone turnover assays  
Professor Samuel Vasikaran  
Royal Perth Hospital, Perth, Australia

09:30  
Analytical requirements for bone marker assays  
Professor Niklas Rye Jørgensen  
Research Centre for Aging and Osteoporosis,  
Copenhagen University Hospital, Glostrup, Denmark

10:00  
Clinical requirements for new biomarkers of bone metabolism  
Dr. Marie-Hélène Lafage-Proust  
University Hospital Saint-Etienne,  
Université de Lyon, FRANCE

10:30  
Morning Break

11:00  
Plenary Lecture 1  
Chair: Dr. Symeon Tournis

New Therapeutics for Osteoporosis  
Prof. Socrates Papapoulos  
Center for Bone Quality, Leiden University Medical Center, Leiden, Netherlands.

Session 2  
Clinical impact of assay standardization for Metabolic Bone Disease  
Chair: Prof. Niklas Rye Jørgensen

11:45  
Practical considerations in parathyroid hormone testing  
Prof. Etienne Cavalier  
University of Liège, Belgium

12:15  
Suggestion of vitamin D status – a changing landscape  
Professor Markus Herrmann  
Zentrallabor für Klinische Pathologie / Laboratorio Centrale di Patologia Clinica Bozen (Italien)
12:45  Emerging biochemical markers of osteoarthritis
   Professor Martin Lotz
   Head of Arthritis Research. The Scripps Research Institute, CA

13:15  Lunch break

Session 3
Rare diseases of bone metabolism
Chair: Prof. Samuel Vasikaran

14:30  Hypophosphatasia
   Dr Symeon Tournis
   Laboratory for Research of Musculoskeletal System, University of Athens, KAT Hospital, Athens, Greece

15:00  Bone markers in thalassemia major
   Professor Evangelos Terpos
   University of Athens, Greece

15:30  Inhibitors of bone resorption: from the treatment of cancer hypercalcemia to the prevention of metastases
   Professor Jean-Jacques Body
   University Hospital Brugmann, Dept. of Medicine, Head Université Libre de Bruxelles, Brussels, Belgium

16:00  Afternoon Break

Session 4
Chronic Kidney Disease
Chair: Prof. Jean-Jacques Body

16:30  CKD-MBD – Input from the clinical laboratory
   Professor Jean-Paul Cristol
   University of Montpellier, Montpellier, France

17:00  Bone markers and vascular calcification in CKD-MBD
   Dr. Pierre Delanaye
   University of Liège, Liège, Belgium

Plenary Lecture 2
Chair: Prof. Jean-Jacques Body

17:30  The Clinical Impact of Standardisation of 25-Hydroxyvitamin D Assays
   Professor Howard Morris

Closing remarks
Professor Howard Morris

18:00  Farewell Cocktail
General information

VENUE AND DATES
The Metabolic Bone Disease will take place in Athens, on June 10, 2017 at the Athens War Museum - Annex “Saroglou Mansion” (Address: 1, Rigillis & Vas. Sofias Avenue Athens, Greece 106 75, website: www.laed.gr, Tel.: 0030 210 7212496).

LANGUAGE
The official language of the Meeting will be English.

SHOPPING IN ATHENS
In Athens the usual opening hours for shops are:
- Monday, Wednesday & Saturday from 09.30 - 14.30 hours
- Tuesday, Thursday & Friday from 09.30 - 14.30 hours and from 17.30 - 20.30 hours
These times are not always strictly adhered to. Many shops in tourist resorts are open seven days a week.
Department’s stores and supermarkets are open from 09.00 - 20.00 hours (Monday-Friday) and from 08.00 - 15.00 hrs (Saturday) and are closed on Sunday.
Post offices are open from 07.30 - 14.00 hours (Monday-Friday)

WEATHER
Typically mediterranean climate. Athens enjoys relatively mild winters and lovely, temperate autumns and springs. The climate is pleasant, and sunshine is plentiful. June is warm without being stifling, the swimming is excellent and the temperature ranges from 25°C to 35°C.

TRANSPORTATION
Athens Airport
The Athens International Airport is located in Spata, 27 Kms north-east of Athens and handles all international and domestic flights.
For more information please visit the Eleftherios Venizelos website: http://www.aia.gr
A special feature of this web site is that on the home page you can link to live arrival and departure information by clicking on the link Real Time Flight Information
The Athens International Airport “Eleftherios Venizelos” is linked to the Athens city center by:
From Airport by Bus (www.oasa.gr):
Three express lines serve the Athens International Airport to Athens City Center on a 24 hours basis.
The bus line E95 (Direction Syntagma) serves Athens City center (Syntagma, Constitution Square)
The following timetable is applicable:

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<th>From Airport to Syntagma area</th>
<th>From Syntagma area to Airport</th>
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<td>Every 25’ from 06.30 to 21.20</td>
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<td>Every 25'-35’ from 21.20 to 06.30</td>
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Current ticket price for the airport express line is € 6.
FROM AIRPORT BY TAXI
An average journey by taxi from Eleftherios Venizelos Airport to City Centre should take approximately 30-45 minutes, depending on the traffic. The cost of the ride should be around €38 per way.

FROM AIRPORT BY METRO
The metro (Lines 2 and 3) run from about 05:00 am until 2:00 am, every 10 minutes, the trip takes approximately 30 minutes. For further information contact Attiko Metro or through the Internet www.ametro.gr Current ticket price for the metro is €10.

WEB SITE
Up-to-date information regarding the Meeting will be available at the Euromedlab web site: www.Athens2017.org Participants will be able to register and book hotel accommodation on line.

<table>
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<th>FULL REGISTRATION</th>
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<td>EUROMEDLAB REGISTRANT YOUNG REGISTRATION</td>
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The registration fee includes:
• Access to the conference hall
• Coffee and lunch break
• Certification of Attendance

MEETING SECRETARIAT & OFFICIAL TRAVEL AGENCY
For any information regarding Registration, Accommodation, Travel or Sponsoring please contact the Meeting Secretariat & official Travel agency:

ERA LTD 17, Asklipiou Str., 10680 Athens-Greece
Tel.: +30 210 3634944, Fax: +30 210 3631690 E-mail: info@era.gr, website: www.era.gr

The Registration Secretariat and Hospitality desk will operate at the Saroglio Mansion during meeting hours.
Bone Turnover Markers in Osteoporosis

The clinical usefulness of bone turnover markers

Samuel D Vaskaran

Department of Clinical Biochemistry, PathWest Laboratory Medicine WA, Perth, Australia

Osteoporosis is diagnosed by bone mineral density (BMD) measurement, which by itself is insufficient for identifying and her Quantifying bone formation is important, as dis- ease specifically at the bone level, this combination allows early treatment with parathyroid hormone (PTH) and bisphosphonates to be identified. The clinical utility of using bone turnover markers to monitor response to therapy is also demonstrated.

Biocomplexity of bone turnover markers

Bone turnover markers are biochemical molecules released by active bone remodeling, which provides a measure of bone formation and resorption. They are important for monitoring and assessing the effectiveness of treatment for osteoporosis. However, the selection of appropriate markers can be challenging.

Markers of bone turnover

Bone turnover markers can be classified into three groups: those related to osteoclast activity, osteoblast activity, and bone mass.

Osteoclast activity markers

Markers related to osteoclast activity include tartrate-resistant acid phosphatase (TRAP) and cathepsin K. TRAP is used as a marker of osteoclast activity in vivo, whereas cathepsin K is a marker of osteoclast apoptosis.

Osteoblast activity markers

Markers related to osteoblast activity include osteocalcin and bone-specific alkaline phosphatase (BSAP). Osteocalcin is a non-collagenous protein produced by osteoblasts and osteocytes.

Bone mass markers

Markers related to bone mass include bone mineral density (BMD) and bone turnover markers. BMD is measured by dual-energy X-ray absorptiometry (DXA) and is used to classify the severity of osteoporosis.

Conclusion

Bone turnover markers provide valuable information about bone turnover, allowing for the early detection of bone disease and the monitoring of treatment efficacy. However, the selection of appropriate markers requires careful consideration, and the interpretation of results must be approached with caution.
different between “intact” kits. 3rd generation PTH assays, are specific for the 1-84 PTH and do not cross-react with the 7-84 fragments, resulting in less variability. There is a huge problem regarding the standardization of PTH assays. Indeed, results obtained in the same patients, notably CKD patients, can vary as much as 100%. Thus, reference ranges differ between laboratories and a large variability is observed between the results of the same reference laboratories. There is a strong need to have unique standards for each assay to ensure more accurate diagnostic results.

Vitamin D status – a changing landscape

Prof. Dr. med. habil. Markus Herrmann
Department of Clinical Pathology, Bolzano Hospital Lorenz-Bonfils-Str. 3, 39100 Bolzano (Italy)

Vitamin D deficiency is associated with an increased incidence as well as the progression of a broad range of diseases including osteoporosis, rickets, cardiovascular disease, cancer, and type 2 diabetes. Until recently, low serum 25-OHD levels are considered a marker of vitamin D status in the general population. However, recent studies suggest that the term “25-OHD level” might be misleading (e.g., vitamin D status might be suboptimal even in the presence of high 25-OHD levels). The concept of vitamin D status has changed significantly over the past years, and the current definition of vitamin D sufficiency is based on the Vitamin D Council’s Vitamin D Sufficiency Index (25-OHD ≥ 75 nmol/L). The current definition of vitamin D deficiency is based on the Vitamin D Council’s Vitamin D Insufficiency Index (25-OHD < 75 nmol/L). The current definition of vitamin D insufficiency is based on the Vitamin D Council’s Vitamin D Insufficiency Index (25-OHD < 75 nmol/L).

Vitamin D insufficiency is associated with an increased incidence as well as the progression of a broad range of diseases including osteoporosis, rickets, cardiovascular disease, cancer, and type 2 diabetes. Until recently, low serum 25-OHD levels are considered a marker of vitamin D status in the general population. However, recent studies suggest that the term “25-OHD level” might be misleading (e.g., vitamin D status might be suboptimal even in the presence of high 25-OHD levels). The concept of vitamin D status has changed significantly over the past years, and the current definition of vitamin D sufficiency is based on the Vitamin D Council’s Vitamin D Sufficiency Index (25-OHD ≥ 75 nmol/L). The current definition of vitamin D deficiency is based on the Vitamin D Council’s Vitamin D Insufficiency Index (25-OHD < 75 nmol/L). The current definition of vitamin D insufficiency is based on the Vitamin D Council’s Vitamin D Insufficiency Index (25-OHD < 75 nmol/L).

Vitamin D deficiency is associated with an increased incidence as well as the progression of a broad range of diseases including osteoporosis, rickets, cardiovascular disease, cancer, and type 2 diabetes. Until recently, low serum 25-OHD levels are considered a marker of vitamin D status in the general population. However, recent studies suggest that the term “25-OHD level” might be misleading (e.g., vitamin D status might be suboptimal even in the presence of high 25-OHD levels). The concept of vitamin D status has changed significantly over the past years, and the current definition of vitamin D sufficiency is based on the Vitamin D Council’s Vitamin D Sufficiency Index (25-OHD ≥ 75 nmol/L). The current definition of vitamin D deficiency is based on the Vitamin D Council’s Vitamin D Insufficiency Index (25-OHD < 75 nmol/L). The current definition of vitamin D insufficiency is based on the Vitamin D Council’s Vitamin D Insufficiency Index (25-OHD < 75 nmol/L).
Tumor bone disease is most commonly seen in breast, prostate, lung and kidney cancer, as well as multiple myeloma. Bone metastases often lead to skeletal complications typically referred to as skeletal-related events (SREs). Bone destruction is significant enough to cause pain, the normal bone resorbing cells, whose activity and proliferation are increased in the presence of tumor cells. Inhibitors of bone resorption, first the bisphosphonates and, later, denosumab, have been shown to be effective to prevent SREs. Before the introduction of inhibitors of bone resorption, a significant proportion of patients with cancer developed bone metastasis. In breast cancer and bone metastases. It was in the early eighties that the bisphosphonate pamidronate was shown to correct cancer hypercalcaemia in most cases. A significant increase in bone resorption could be effectively reduced in 90% of the cases. In the last two decades, the bisphosphonates and denosumab have become established as a valuable additional approach to the range of current treatments in patients with tumor bone disease. Multiple, randomized, controlled trials have clearly demonstrated that they are effective in reducing skeletal morbidity from metastatic cancer. Zoledronic acid has been shown to be more effective than pamidronate in breast cancer metastasis to bone and, compared to zoledronic acid, denosumab has been shown to further reduce the skeletal morbidity rate in patients with solid tumors and bone metastases. Inhibitors of bone resorption have also been shown to counteract cancer treatment-induced bone loss. Anderson et al showed that bone resorption also increase disease-free and overall survival in postmenopausal women with breast cancer when used in the adjuvant setting. Bone targeted agents may disrupt tumor cell / bone cell interactions, and thereby affect survival, and migration of tumor cells to other distant sites. The results of large adjuvant trials in breast cancer have demonstrated the ability of bisphosphonates to prevent metastases and improve disease outcomes in women with low levels of female hormones. The improvement in disease outcomes in both the zoledronic acid and oral clodronate trials were predominantly mediated by a reduction in bone metastases as the first distant metastatic site. A formal individual patient data meta-analysis of data from more than 18,000 women randomized to placebo and bisphosphonates showed that bisphosphonates reduced the risk of distant metastases. Bisphosphonates are likely to become part of routine clinical practice in the adjuvant management of CTIBL in ‘at risk’ patients and prevention of metastases in patients with low level of female hormones. Ongoing trials of denosumab will add important knowledge to the new role of adjuvant anti-resorptives in CTIBL and metastases prevention.

Session 4: Chronic Kidney Disease

CKD-MBD – Input from the clinical laboratory

Professor Jean-Paul Cristol

AS Bargnoux, AM Dupuy, M Moreau, Montpellier University Hospital, Montpellier, France

Since 2005, the term “Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD)” should be used to describe the broader clinical syndrome encompassing mineral abnormalities of calcium, phosphorus PTH and vitamin D metabolisms, or abnormalities in bone turnover, mineralization, volume, linear growth, or strength that impact the soft issue calcification. The CKD-MBD guidelines were originally published in 2009 and a draft of a 2016 update has been released in August 2016.

The recommendations for biological parameters assessment are still based on regular monitoring of calcium, phosphorus, PTH, phosphate alkalase (PAL) and vitamin D levels. Source of variations included physiologic parameters such as age, death and bone remodeling biomarkers and eventually bone biopsy could help to define the indications or to the monitoring of activity of future treatments.

Inhibitors of bone resorption: from the treatment of cancer hypercalcaemia to the prevention of metastases

Professor Jean-Jacques Body

Univ. Libre de Bruxelles (ULB), Brussels, Belgium

Plenary Lecture 2

The Clinical Impact of Standardisation of 25-Hydroxyvitamin D Assays

Howard Morris

Chemical Pathology Directorate, SA Pathology and School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, South Australia

A high prevalence of vitamin D deficiency continues to be reported internationally stimulating significant public health and individual patient concerns. Several factors contribute to variations in vitamin D levels and these have implications for the interpretation of kinase status. Standardisation of vitamin D levels is essential in order to facilitate the progression of these trials.

The VDSP has verified protocols to retrospectively standardize assays from prior research including the US NHANES and German KIGGS surveys. Reanalysis of such standardized data with clinical significance has varied. Perhaps the most critical clinical significance from a retrospective standardization has been the loss of the so-called J-curve of the relationship between vitamin D and all-cause mortality. Unlike some original results, current data indicate increased all-cause mortality with levels less than 50 nmol/L (20 ng/mL) and no increase at levels greater than 100 nmol/L (40 ng/mL). The standardisation of vitamin D by the VDSP provides the first agreement of clinically significant cut points at 20 nmol/L for plasma mineral homeostasis and 50 nmol/L for other clinical outcomes including bone mineral homeostasis and all-cause mortality.

Bone markers and vascular calcification in CKD-MBD

Pierre Delanaye, MD, PhD

Nephrology-Dialysis-Transplantation, University of Liège, Belgium

Patients with chronic kidney disease (CKD), and still more, patients treated by dialysis, have an increased risk of cardiovascular mortality. This over-mortality is explained, at least in part, by the presence of early, severe and very progressive vascular calcifications (VC). There is a strong link between calcium, phosphate and parathormone concentrations and cardiovascular mortality. Interestingly, both the abnormalities of bone turnover (high and low bone turnover) and bone volume (osteopenia or osteoporosis) are associated with the presence and progression of VC in dialysis patients. In this context, we will briefly review bone biomarkers which have in the diagnosis and management of these bone abnormalities. Basic researches have also focused on the active phenomena involved in the pathogenesis of VC. If parathormone level has a central role, several biomarkers as osteocalcin, D-dimer and matrix Gla protein (MGP) are available. Inhibitors of bone resorption also increase disease-free and overall survival in postmenopausal women with breast cancer when used in the adjuvant setting. Bone targeted agents may disrupt tumor cell / bone cell interactions, and thereby affect survival, and migration of tumor cells to other distant sites. The results of large adjuvant trials in breast cancer have demonstrated the ability of bisphosphonates to prevent metastases and improve disease outcomes in women with low levels of female hormones. The improvement in disease outcomes in both the zoledronic acid and oral clodronate trials were predominantly mediated by a reduction in bone metastases as the first distant metastatic site. A formal individual patient data meta-analysis of data from more than 18,000 women randomized to placebo and bisphosphonates showed that bisphosphonates reduced the risk of distant metastases. Bisphosphonates are likely to become part of routine clinical practice in the adjuvant management of CTIBL in ‘at risk’ patients and prevention of metastases in patients with low level of female hormones. Ongoing trials of denosumab will add important knowledge to the new role of adjuvant anti-resorptives in CTIBL and metastases prevention.

Since 2005, the term “Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD)” should be used to describe the broader clinical syndrome encompassing mineral abnormalities of calcium, phosphorus PTH and vitamin D metabolisms, or abnormalities in bone turnover, mineralization, volume, linear growth, or strength that impact the soft issue calcification. The CKD-MBD guidelines were originally published in 2009 and a draft of a 2016 update has been released in August 2016.

The recommendations for biological parameters assessment are still based on regular monitoring of calcium, phosphorus, PTH, phosphate alkalase (PAL) and vitamin D levels. Source of variations included physiologic parameters such as age, death and bone remodeling biomarkers and eventually bone biopsy could help to define the indications or to the monitoring of activity of future treatments.

Plenary Lecture 2

The Clinical Impact of Standardisation of 25-Hydroxyvitamin D Assays

Howard Morris

Chemical Pathology Directorate, SA Pathology and School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, South Australia

A high prevalence of vitamin D deficiency continues to be reported internationally stimulating significant public health and individual patient concerns. Several factors contribute to variations in vitamin D levels and these have implications for the interpretation of kinase status. Standardisation of vitamin D levels is essential in order to facilitate the progression of these trials.

The VDSP has verified protocols to retrospectively standardize assays from prior research including the US NHANES and German KIGGS surveys. Reanalysis of such standardized data with clinical significance has varied. Perhaps the most critical clinical significance from a retrospective standardization has been the loss of the so-called J-curve of the relationship between vitamin D and all-cause mortality. Unlike some original results, current data indicate increased all-cause mortality with levels less than 50 nmol/L (20 ng/mL) and no increase at levels greater than 100 nmol/L (40 ng/mL). The standardisation of vitamin D by the VDSP provides the first agreement of clinically significant cut points at 20 nmol/L for plasma mineral homeostasis and 50 nmol/L for other clinical outcomes including bone mineral homeostasis and all-cause mortality.
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**Roche Elecsys® Bone Turnover Marker**

*Complete solution for osteoporosis*

The most complete fully automated bone metabolism panel

<table>
<thead>
<tr>
<th>What does Roche offer?</th>
<th>What does it detect?</th>
<th>What is its intended use/clinical value?</th>
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<tbody>
<tr>
<td>Elecsys β-CrossLaps/serum (CTx)</td>
<td>Degradation products of type I collagen during bone resorption</td>
<td>Aid in the assessment of bone resorption rate, monitoring anti-resorptive therapies such as bisphosphonates</td>
</tr>
<tr>
<td>Elecsys total P1NP* (Procollagen I N-terminal peptide)</td>
<td>Degradation products of type I collagen during bone formation</td>
<td>Aid in monitoring therapy of osteoporosis in post-menopausal women and in patients diagnosed with Paget’s disease of the bone</td>
</tr>
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<td>Elecsys N-MID Osteocalcin</td>
<td>Non-collagenous protein in bone matrix, synthesized by osteoblasts during bone formation</td>
<td>Aid in the control of antiresorptives therapeutic efficiency, e.g. for patients with osteoporosis or hypercalcemia</td>
</tr>
<tr>
<td>Elecsys Vitamin D total II</td>
<td>Vitamin D3 (25-OH) and vitamin D2 (25-OH)</td>
<td>Aid in the assessment of vitamin D sufficiency</td>
</tr>
<tr>
<td>Elecsys PTH (Parathyroid hormone)</td>
<td>Parathyroid hormone secreted by parathyroid glands</td>
<td>Differential diagnosis of hypercalcemia and hypocalcemia and monitoring of parathyroid surgery</td>
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* Not available in the US

**Bone remodelling cycle**

Osteoclast
- Recruitment
- Differentiation
- Activation

Osteoblast
- Recruitment
- Differentiation
- Activation

<table>
<thead>
<tr>
<th>Lining cells</th>
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<th>Osteoclast</th>
<th>Apoptosis</th>
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<td>P1NP</td>
<td>CTX-1</td>
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<tr>
<td>Formation</td>
<td>Matrix synthesis</td>
<td>Osteoblast</td>
<td>Recruitment</td>
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