BWPath

BELGIAN WEEK OF PATHOLOGY

9th BELGIAN WEEK OF PATHOLOGY

19.10 > 20.10.18

@ WILD GALLERY - BRUSSELS

FRIDAY

SATURDAY

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Ex-factory price (exclu. VAT)		
OPDIVO®	40 mg	€588,80
OPDIVO®	100 mg	€1.472,00

OPDIVO® (nivolumab)

Extending life of people fighting cancer*

Lung | Renal | Melanoma | Hodgkin | Head & Neck | Urothelial

*Based on Overall Survival data across approved indications. Opdivo SmPC

Bristol-Myers Squibb
Leading the Way in Immuno-Oncology

1506BE18PR03246 - May 2018

OPDIVO® (nivolumab)

Ex-factory price (excl. VAT)
OPDIVO® 40 mg € 588,80
OPDIVO® 100 mg € 1.472,00

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions. **1. NAME OF THE MEDICINAL PRODUCT** OPDIVO 10 mg/mL concentrate for solution for infusion. **2. QUALITATIVE AND QUANTITATIVE COMPOSITION** Each mL of concentrate contains 10 mg of nivolumab. One vial of 4 mL contains 40 mg of nivolumab. One vial of 10 mL contains 100 mg of nivolumab. One vial of 24 mL contains 240 mg of nivolumab. Nivolumab is produced in Chinese hamster ovary cells by recombinant DNA technology. Excipient with known effect Each mL of concentrate contains 0.1 mmol (or 2.5 mg) sodium. For the full list of excipients, see section 6.1. **3. PHARMACEUTICAL FORM** Concentrate for solution for infusion (sterile concentrate). Clear to opalescent, colourless to pale yellow liquid that may contain few light particles. The solution has a pH of approximately 6.0 and an osmolality of approximately 340 mOsm/kg. **4. CLINICAL PARTICULARS 4.1 Therapeutic indications** Melanoma OPDIVO as monotherapy or in combination with ipilimumab is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults. Relative to nivolumab monotherapy, an increase in progression-free survival (PFS) and overall survival (OS) for the combination of nivolumab with ipilimumab is established only in patients with low tumour PD-L1 expression (see sections 4.4 and 5.1). Adjuvant treatment of melanoma OPDIVO as monotherapy is indicated for the adjuvant treatment of adults with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection (see section 5.1). Non-Small Cell Lung Cancer (NSCLC) OPDIVO as monotherapy is indicated for the treatment of locally advanced or metastatic non-small cell lung cancer after prior chemotherapy in adults. Renal Cell Carcinoma (RCC) OPDIVO as monotherapy is indicated for the treatment of advanced renal cell carcinoma after prior therapy in adults. Classical Hodgkin Lymphoma (cHL) OPDIVO as monotherapy is indicated for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma after autologous stem cell transplant (ASCT) and treatment with brentuximab vedotin. Squamous Cell Cancer of the Head and Neck (SCCHN) OPDIVO as monotherapy is indicated for the treatment of recurrent or metastatic squamous cell cancer of the head and neck in adults progressing on or after platinum-based therapy (see section 5.1). Urothelial Carcinoma OPDIVO as monotherapy is indicated for the treatment of locally advanced unresectable or metastatic urothelial carcinoma in adults after failure of prior platinum-containing therapy. **4.2 Posology and method of administration** Treatment must be initiated and supervised by physicians experienced in the treatment of cancer. Posology *OPDIVO as monotherapy* The recommended dose of OPDIVO is either nivolumab 240 mg every 2 weeks **or** 480 mg every 4 weeks (see section 5.1) depending on the indication, as presented in Table 1. Table 1: Recommended dose and infusion time for intravenous administration of nivolumab monotherapy Recommended dose and infusion time per Indication* Melanoma: 240 mg every 2 weeks over 30 minutes or 480 mg every 4 weeks over 60 minutes Renal Cell Carcinoma: 240 mg every 2 weeks over 30 minutes or 480 mg every 4 weeks over 60 minutes Non-Small Cell Lung Cancer: 240 mg every 2 weeks over 30 minutes Classical Hodgkin lymphoma: 240 mg every 2 weeks over 30 minutes Squamous Cell Cancer of the Head and Neck: 240 mg every 2 weeks over 30 minutes Urothelial Carcinoma: 240 mg every 2 weeks over 30 minutes *As per monotherapy indication in section 4.1. If melanoma or RCC patients need to be switched from the 240 mg every 2 weeks schedule to the 480 mg every 4 weeks schedule, the first 480 mg dose should be administered two weeks after the last 240 mg dose. Conversely, if patients need to be switched from the 480 mg every 4 weeks schedule to the 240 mg every 2 weeks schedule, the first 240 mg dose should be administered four weeks after the last 480 mg dose. *Adjuvant treatment of melanoma* The recommended dose of OPDIVO is 3 mg/kg nivolumab administered intravenously over 60 minutes every 2 weeks. For adjuvant therapy, the maximum treatment duration with OPDIVO is 12 months. *OPDIVO in combination with ipilimumab Melanoma* The recommended dose is 1 mg/kg nivolumab in combination with 3 mg/kg ipilimumab administered intravenously every 3 weeks for the first 4 doses. This is then followed by a second phase in which nivolumab monotherapy is administered intravenously at either 240 mg every 2 weeks **or** at 480 mg every 4 weeks, as presented in Table 2. For the monotherapy phase, the first dose of nivolumab should be administered; 3 weeks after the last dose of the combination of nivolumab and ipilimumab if using 240 mg every 2 weeks; or 6 weeks after the last dose of the combination of nivolumab and ipilimumab if using 480 mg every 4 weeks. Table 2: Recommended doses and infusion times for intravenous administration of nivolumab in combination with ipilimumab *Nivolumab:* Combination phase, every 3 weeks for 4 dosing cycles: 1 mg/kg over 30 minutes / Monotherapy phase: 240 mg every 2 weeks over 30 minutes or 480 mg every 4 weeks over 60 minutes *Ipilimumab:* Combination phase, every 3 weeks for 4 dosing cycles: 3 mg/kg over 90 minutes Treatment with OPDIVO, either as a monotherapy or in combination with ipilimumab, should be continued as long as clinical benefit is observed or until treatment is no longer tolerated by the patient. Atypical responses (i.e., an initial transient increase in tumour size or small new lesions within the first few months followed by tumour shrinkage) have been observed. It is recommended to continue treatment with nivolumab for clinically stable patients with initial evidence of disease progression until disease progression is confirmed. Dose escalation or reduction is not recommended. Dosing delay or discontinuation may be required based on individual safety and tolerability. Guidelines for permanent discontinuation or withholding of doses are described in Table 3. Detailed guidelines for the management of immune-related adverse reactions are described in section 4.4. Table 3: Recommended treatment modifications for OPDIVO or OPDIVO in combination with ipilimumab Immune-related adverse reaction *Immune-related pneumonitis: Severity:* Grade 2 pneumonitis *Treatment modification:* Withhold dose(s) until symptoms resolve, radiographic abnormalities improve, and management with corticosteroids is complete *Severity:* Grade 3 or 4 pneumonitis *Treatment modification:* Permanently discontinue treatment *Immune-related colitis: Severity:* Grade 2 diarrhoea or colitis *Treatment modification:* Withhold dose(s) until symptoms resolve and management with corticosteroids, if needed, is complete *Severity:* Grade 3 diarrhoea or colitis - OPDIVO monotherapy *Treatment modification:* Withhold dose(s) until symptoms resolve and management with corticosteroids is complete *Severity:* Grade 3 diarrhoea or colitis - OPDIVO+ipilimumab *Treatment modification:* Permanently discontinue treatment *Severity:* Grade 4 diarrhoea or colitis *Treatment modification:* Permanently discontinue treatment *Immune-related hepatitis: Severity:* Grade 2 elevation in aspartate aminotransferase (AST), alanine aminotransferase (ALT), or total bilirubin *Treatment modification:* Withhold dose(s) until laboratory values return to baseline and management with corticosteroids, if needed, is complete Grade 3 or 4 elevation in AST, ALT, or total bilirubin *Treatment modification:* Permanently discontinue treatment *Immune-related nephritis and renal dysfunction: Severity:* Grade 2 or 3 creatinine elevation *Treatment modification:* Withhold dose(s) until creatinine returns to baseline and management with corticosteroids is complete *Severity:* Grade 4 creatinine elevation *Treatment modification:* Permanently discontinue treatment *Immune-related endocrinopathies: Severity:* Symptomatic Grade 2 or 3 hypothyroidism, hyperthyroidism, hypophysitis, Grade 2 adrenal insufficiency Grade 3 diabetes *Treatment modification:* Withhold dose(s) until symptoms resolve and management with corticosteroids (if needed for symptoms of acute inflammation) is complete. Treatment should be continued in the presence of hormone replacement therapy[a] as long as no symptoms are present *Severity:* Grade 4 hypothyroidism Grade 4 hyperthyroidism Grade 4 hypophysitis Grade 3 or 4 adrenal insufficiency Grade 4 diabetes *Treatment modification:* Permanently discontinue treatment *Immune-related skin adverse reactions:* Grade 3 rash *Treatment modification:* Withhold dose(s) until symptoms resolve and management with corticosteroids is complete *Severity:* Grade 4 rash *Treatment modification:* Permanently discontinue treatment *Severity:* Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) *Treatment modification:* Permanently discontinue treatment (see section 4.4) *Other immune-related adverse reactions: Severity:* Grade 3 (first occurrence) *Treatment modification:* Withhold dose(s) *Severity:* Grade 3 myocarditis *Treatment modification:* Permanently discontinue treatment *Severity:* Grade 4 or recurrent Grade 3 ; persistent Grade 2 or 3 despite treatment modification ; inability to reduce corticosteroid dose to 10 mg prednisone or equivalent per day *Treatment modification:* Permanently discontinue treatment Note: Toxicity grades are in accordance with National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.0 (NCI-CTCAE v4). [a] Recommendation for the use of hormone replacement therapy is provided in section 4.4. OPDIVO or OPDIVO in combination with ipilimumab should be permanently discontinued for: Grade 4 or recurrent Grade 3 adverse reactions; Persistent Grade 2 or 3 adverse reactions despite management. Patients treated with OPDIVO must be given the patient alert card and be informed about the risks of OPDIVO (see also package leaflet). When OPDIVO is administered in combination with ipilimumab, if either agent is withheld, the other agent should also be withheld. If dosing is resumed after a delay, either the combination treatment or OPDIVO monotherapy could be resumed based on the evaluation of the individual patient. *Special populations Paediatric population* The safety and efficacy of OPDIVO in children below 18 years of age have not been established. No data are available. *Elderly* No dose adjustment is required for elderly patients (≥ 65 years) (see sections 5.1 and 5.2). Data from NSCLC, SCCHN, and adjuvant melanoma patients 75 years of age or older are too limited to draw conclusions on this population. *Renal impairment* Based on the population pharmacokinetic (PK) results, no dose adjustment is required in patients with mild or moderate renal impairment (see section 5.2). Data from patients with severe renal impairment are too limited to draw conclusions on this population. *Hepatic impairment* Based on the population PK results, no dose adjustment is required in patients with mild hepatic impairment (see section 5.2). Data from patients with moderate or severe hepatic impairment are too limited to draw conclusions on these populations. OPDIVO must be administered with caution in patients with moderate (total bilirubin > 1.5 × to 3 × the upper limit of normal [ULN] and any AST) or severe (total bilirubin > 3 × ULN and any AST) hepatic impairment. Method of administration OPDIVO is for intravenous use only. It is to be administered as an intravenous infusion over a period of 30 or 60 minutes depending on the dose (see Tables 1 and 2). The infusion must be administered through a sterile, non-pyrogenic, low protein binding in-line filter with a pore size of 0.2-1.2 μm. OPDIVO must not be administered as an intravenous push or bolus injection. The total dose of OPDIVO required can be infused directly as a 10 mg/mL solution or can be diluted with sodium chloride 9 mg/mL (0.9%) solution for injection or glucose 50 mg/mL (5%) solution for injection (see section 6.6). When administered in combination with ipilimumab, OPDIVO should be given first followed by ipilimumab on the same day. Use separate infusion bags and filters for each infusion. For instructions on the preparation and handling of the medicinal product before administration, see section 6.6. **4.3 Contraindications** Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. **4.8 Undesirable effects** Summary of the safety profile *Nivolumab used as monotherapy or in combination with ipilimumab* In the pooled dataset of nivolumab 3 mg/kg as monotherapy across tumour types (n = 2578) with minimum follow-up ranging from 2.3 to 28 months, the most frequent adverse reactions (≥ 10%) were fatigue (30%), rash (17%), pruritus (13%), diarrhoea (13%), and nausea (12%). The majority of adverse reactions were mild to moderate (Grade 1 or 2). With a minimum of 24 months follow-up in NSCLC, no new safety signals were identified. In the pooled dataset of nivolumab 1 mg/kg in combination with ipilimumab 3 mg/kg in melanoma (n = 448) with minimum follow-up ranging from 6 to 28 months, the most frequent adverse reactions (≥ 10%) were rash (52%), fatigue (46%), diarrhoea (43%), pruritus (36%), nausea (26%), pyrexia (19%), decreased appetite (16%), hypothyroidism (16%), colitis (15%), vomiting (14%), arthralgia (13%), abdominal pain (13%), headache (11%), and dyspnoea (10%). The majority of adverse reactions were mild to moderate (Grade 1 or 2). Among the patients treated with nivolumab 1 mg/kg in combination with ipilimumab 3 mg/kg in CA209067, 154/313 (49%) had the first onset of Grade 3 or 4 adverse reactions during the initial combination phase. Among the 147 patients in this group who continued treatment in the single-agent phase, 47 (32%) experienced at least one Grade 3 or 4 adverse reaction during the single-agent phase. *Nivolumab used as monotherapy for adjuvant treatment of melanoma* In the dataset of nivolumab 3 mg/kg as monotherapy for the adjuvant treatment of melanoma (n = 452), the most frequent adverse reactions (≥ 10%) were fatigue (46%), rash (29%), diarrhoea (24%), pruritus (23%), nausea (15%), arthralgia (13%), musculoskeletal pain (11%), and hypothyroidism (11%). The majority of adverse reactions were mild to moderate (Grade 1 or 2). Tabulated summary of adverse reactions Adverse reactions reported in the pooled dataset for patients treated with nivolumab monotherapy (n = 2578) and for patients treated with nivolumab in combination with ipilimumab (n = 448) are presented in Table 4. These reactions are presented by system organ class and by frequency. Frequencies are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from available post-marketing data). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness. Table 4: Adverse reactions *Infections and infestations Nivolumab monotherapy:* Common: upper respiratory tract infection Uncommon: pneumonia[a], bronchitis *Nivolumab in combination with ipilimumab* Common: pneumonia, upper respiratory tract infection Uncommon: bronchitis *Neoplasms benign, malignant and unspecified (including cysts and polyps) Nivolumab monotherapy:* Rare histiocytic necrotising lymphadenitis (Kikuchi lymphadenitis) *Blood and lymphatic system disorders Nivolumab monotherapy:* Very common: neutropaenia[a,b] Uncommon: Eosinophilia *Nivolumab in combination with ipilimumab* Common: Eosinophilia *Immune system disorders Nivolumab monotherapy:* Common: infusion related reaction[c], hypersensitivity[c] Rare anaphylactic reaction[c] Not known solid organ transplant rejection[h] *Nivolumab in combination with ipilimumab* Common: infusion related reaction, hypersensitivity Uncommon: sarcoidosis Not known solid organ transplant rejection[h] *Endocrine disorders Nivolumab monotherapy:* Common: hypothyroidism, hyperthyroidism Uncommon: adrenal insufficiency, hypopituitarism, hypophysitis, thyroiditis, diabetes mellitus Rare diabetic ketoacidosis *Nivolumab in combination with ipilimumab* Very common: hypothyroidism Common: adrenal insufficiency, hypopituitarism, hypophysitis, hyperthyroidism, thyroiditis Uncommon: diabetic ketoacidosis[c], diabetes mellitus[c] *Metabolism and nutrition disorders Nivolumab monotherapy:* Common: decreased appetite Uncommon: dehydration, metabolic acidosis Not known tumour lysis syndrome[i] *Nivolumab in combination with ipilimumab* Very common: decreased appetite Common: dehydration Not known tumour lysis syndrome[i] *Hepatobiliary disorders Nivolumab monotherapy:* Uncommon: hepatitis[c] Rare cholestasis *Nivolumab in combination with ipilimumab* Common: hepatitis[c] *Nervous system disorders Nivolumab monotherapy:* Common: peripheral neuropathy, headache, dizziness Uncommon: polyneuropathy, autoimmune neuropathy (including facial and abducens nerve paresis) Rare Guillain-Barré syndrome, demyelination, myasthenic syndrome, encephalitis[a,c] *Nivolumab in combination with ipilimumab* Very common: headache Common: peripheral neuropathy, dizziness Uncommon: Guillain-Barré syndrome, polyneuropathy, neuritis, peroneal nerve palsy, autoimmune neuropathy (including facial and abducens nerve paresis), encephalitis[c] *Eye disorders Nivolumab monotherapy:* Uncommon: uveitis, blurred vision, dry eye Not known Vogt-Koyanagi-Harada syndrome[h] *Nivolumab in combination with ipilimumab* Common: uveitis, blurred vision Uncommon: Not known Vogt-Koyanagi-Harada syndrome[h] *Cardiac disorders Nivolumab monotherapy:* Uncommon: tachycardia Rare arrhythmia (including ventricular arrhythmia)[d], atrial fibrillation, myocarditis[c,f] *Nivolumab in combination with ipilimumab* Common: tachycardia Uncommon: arrhythmia (including ventricular arrhythmia)[a,c], atrial fibrillation, myocarditis[c,f] *Vascular disorders Nivolumab monotherapy:* Common: hypertension Rare vasculitis *Nivolumab in combination with ipilimumab* Common: hypertension *Respiratory, thoracic and mediastinal disorders Nivolumab monotherapy:* Common: pneumonitis[a,c], dyspnoea[a], cough Uncommon: pleural effusion Rare lung infiltration *Nivolumab in combination with ipilimumab* Very common: dyspnoea Common: pneumonitis[a,c], pulmonary embolism[a], cough Uncommon: pleural effusion *Gastrointestinal disorders Nivolumab monotherapy:* Very common: diarrhoea, nausea Common: colitis[a], stomatitis, vomiting, abdominal pain, constipation, dry mouth Uncommon: pancreatitis, gastritis Rare duodenal ulcer *Nivolumab in combination with ipilimumab* Very common: colitis[a], diarrhoea, vomiting, nausea, abdominal pain Common: stomatitis, pancreatitis, constipation, dry mouth Uncommon: intestinal perforation[a], gastritis, duodenitis *Skin and subcutaneous tissue disorders Nivolumab monotherapy:* Very common: rash[e], pruritus Common: vitiligo, dry skin, erythema, alopecia Uncommon: erythema multiforme, psoriasis, rosacea, urticaria Rare toxic epidermal necrolysis[a,f] Stevens-Johnson syndrome[a,f] *Nivolumab in combination with ipilimumab* Very common: rash[e], pruritus Common: vitiligo, dry skin, erythema, alopecia, urticaria Uncommon: psoriasis Rare toxic epidermal necrolysis[a,f] Stevens-Johnson syndrome[f] *Musculoskeletal and connective tissue disorders Nivolumab monotherapy:* Common: musculoskeletal pain[g], arthralgia Uncommon: polymyalgia rheumatica, arthritis Rare Sjogren's syndrome, myopathy, myositis (including polymyositis)[a,f], rhabdomyolysis[a,f] *Nivolumab in combination with ipilimumab* Very common: arthralgia Common: musculoskeletal pain[g] Uncommon: spondyloarthropathy, Sjogren's syndrome, arthritis, myopathy, myositis (including polymyositis)[a,f], rhabdomyolysis[a,f] *Renal and urinary disorders Nivolumab monotherapy:* Uncommon: tubulointerstitial nephritis, renal failure (including acute kidney injury)[a,c] *Nivolumab in combination with ipilimumab* Common: renal failure (including acute kidney injury)[a,c] Uncommon: tubulointerstitial nephritis *General disorders and administration site conditions Nivolumab monotherapy:* Very common: fatigue Common: pyrexia, oedema (including peripheral oedema) Uncommon: pain, chest pain *Nivolumab in combination with ipilimumab* Very common: fatigue, pyrexia Common: oedema (including peripheral oedema), pain Uncommon: chest pain *Investigations*[a] *Nivolumab monotherapy:* Very common: increased AST, increased ALT, increased alkaline phosphatase, increased lipase, increased amylase, hypocalcaemia, hyperglycaemia[c], lymphopaenia, leucopaenia, thrombocytopaenia, anaemia, hypercalcaemia, hyperkalaemia, hypokalaemia, hypomagnesaemia, hyponatraemia Common: increased total bilirubin, hypoglycaemia, hypermagnesaemia, hypernatraemia, weight decreased *Nivolumab in combination with ipilimumab* Very common: increased AST, increased ALT, increased total bilirubin, increased alkaline phosphatase, increased lipase, increased amylase, increased creatinine, hyperglycaemia[c], hypoglycaemia, lymphopaenia, leucopoenia, neutropaenia, thrombocytopaenia, anaemia, hypocalcaemia, hyperkalaemia, hypokalaemia, hypomagnesaemia, hyponatraemia Common hypercalcaemia, hypermagnesaemia, hypernatraemia, weight decreased [a] Fatal cases have been reported in completed or ongoing clinical studies [b] Frequencies of laboratory terms reflect the proportion of patients who experienced a worsening from baseline in laboratory measurements. See "Description of selected adverse reactions; laboratory abnormalities" below. [c] Life-threatening cases have been reported in completed or ongoing clinical studies. [d] The frequency of adverse events in the cardiac disorders system organ class regardless of causality was higher in the nivolumab group than in the chemotherapy group in post-CTLA4/BRAF inhibitor metastatic melanoma population. Incidence rates per 100 person-years of exposure were 9.3 vs. 0; serious cardiac events were reported by 4.9% patients in the nivolumab group vs. 0 in the investigator´s choice group. The frequency of cardiac adverse events was lower in the nivolumab group than in the dacarbazine group in the metastatic melanoma without prior treatment population. All were considered not related to nivolumab by investigators except arrhythmia (atrial fibrillation, tachycardia and ventricular arrhythmia). [e] Rash is a composite term which includes maculopapular rash, rash erythematous, rash pruritic, rash follicular, rash macular, rash morbilliform, rash papular, rash pustular, rash papulosquamous, rash vesicular, rash generalised, exfoliative rash, dermatitis, dermatitis acneiform, dermatitis allergic, dermatitis atopic, dermatitis bullous, dermatitis exfoliative, dermatitis psoriasiform, drug eruption and pemphigoid. [f] Reported also in studies outside the pooled dataset. The frequency is based on the program-wide exposure. [g] Musculoskeletal pain is a composite term which includes back pain, bone pain, musculoskeletal chest pain, musculoskeletal discomfort, myalgia, neck pain, pain in extremity, and spinal pain. [h] Post-marketing event (also see section 4.4). [i] Reported in clinical studies and in the post-marketing setting. The overall safety profile of nivolumab 3 mg/kg for the adjuvant treatment of melanoma (n = 452) was consistent with that established across tumour types for nivolumab monotherapy. Description of selected adverse reactions Nivolumab or nivolumab in combination with ipilimumab is associated with immune-related adverse reactions. With appropriate medical therapy, immune-related adverse reactions resolved in most cases. Permanent discontinuation of treatment was required in a greater proportion of patients receiving nivolumab in combination with ipilimumab than in those receiving nivolumab monotherapy for immune-related colitis (16% and 0.8%, respectively), immune-related hepatitis (9% and 1%), and immune-related endocrinopathies (2.7% and 0.1%). Among patients who experienced an event, high-dose corticosteroids (at least 40 mg prednisone equivalents) were required in a greater proportion of patients receiving the combination regimen than in patients receiving nivolumab monotherapy for the management of immune-related colitis (46% and 15%, respectively), immune-related hepatitis (46% and 21%), immune-related endocrinopathies (27% and 7%, respectively), and immune-related skin adverse reaction (7% and 4%, respectively). The management guidelines for these adverse reactions are described in section 4.4. *Immune-related pneumonitis* In patients treated with nivolumab monotherapy, the incidence of pneumonitis, including interstitial lung disease and lung infiltration, was 3.4% (87/2578). The majority of cases were Grade 1 or 2 in severity reported in 0.8% (21/2578) and 1.7% (44/2578) of patients respectively. Grade 3 and 4 cases were reported in 0.7% (19/2578) and <0.1% (1/2578) of patients respectively. Grade 5 cases were reported in < 0.1% (2/2578) of patients in these studies. Median time to onset was 3.6 months (range: 0.2-19.6). Resolution occurred in 63 patients (72.4%) with a median time to resolution of 6.1 weeks (range: 0.1+-96.7+); + denotes a censored observation. In patients treated with nivolumab in combination with ipilimumab, the incidence of pneumonitis including interstitial lung disease, was 7.8% (35/448). Grade 2, Grade 3, and Grade 4 cases were reported in 4.7% (21/448), 1.1% (5/448), and 0.2% (1/448) of patients, respectively. One of the Grade 3 pneumonitis cases worsened over 11 days with a fatal outcome. Median time to onset was 2.6 months (range: 0.7-12.6). Resolution occurred in 33 patients (94.3%) with a median time to resolution of 6.1 weeks (range: 0.3-35.1). *Immune-related colitis* In patients treated with nivolumab monotherapy, the incidence of diarrhoea, colitis, or frequent bowel movements was 13.1% (339/2578). The majority of cases were Grade 1 or 2 in severity reported in 8.5% (220/2578) and 3.0% (78/2578) of patients respectively. Grade 3 cases were reported in 1.6% (41/2578) of patients. No Grade 4 or 5 cases were reported in these studies. Median time to onset was 1.8 months (range: 0.0-26.6). Resolution occurred in 296 patients (88.1%) with a median time to resolution of 2.1 weeks (range: 0.1-124.4+). In patients treated with nivolumab in combination with ipilimumab, the incidence of diarrhoea or colitis was 46.7% (209/448). Grade 2, Grade 3, and Grade 4 cases were reported in 13.6% (61/448), 15.8% (71/448), and 0.4% (2/448) of patients, respectively. No Grade 5 cases were reported. Median time to onset was 1.2 months (range: 0.0-22.6). Resolution occurred in 186 patients (89.4%) with a median time to resolution of 3.0 weeks (range: 0.1-159.4+). *Immune-related hepatitis* In patients treated with nivolumab monotherapy, the incidence of liver function test abnormalities was 6.7% (173/2578). The majority of cases were Grade 1 or 2 in severity reported in 3.5% (91/2578) and 1.2% (32/2578) of patients respectively. Grade 3 and 4 cases were reported in 1.6% (41/2578) and 0.3% (9/2578) of patients, respectively. No Grade 5 cases were reported in these studies. Median time to onset was 2.1 months (range: 0.0-27.6). Resolution occurred in 132 patients (76.7%) with a median time to resolution of 5.9 weeks (range: 0.1-82.6+). In patients treated with nivolumab in combination with ipilimumab, the incidence of liver function test abnormalities was 29.5% (132/448). Grade 2, Grade 3, and Grade 4 cases were reported in 6.7% (30/448), 15.4% (69/448), and 1.8% (8/448) of patients, respectively. No Grade 5 cases were reported. Median time to onset was 1.5 months (range: 0.0-30.1). Resolution occurred in 124 patients (93.9%) with a median time to resolution of 5.1 weeks (range: 0.1-106.9). *Immune-related nephritis and renal dysfunction* In patients treated with nivolumab monotherapy, the incidence of nephritis or renal dysfunction was 2.8% (71/2578). The majority of cases were Grade 1 or 2 in severity reported in 1.6% (41/2578) and 0.7% (18/2578) of patients respectively. Grade 3 and 4 cases were reported in 0.4% (11/2578) and <0.1% (1/2578) of patients, respectively. No Grade 5 nephritis or renal dysfunction was reported in these studies. Median time to onset was 2.3 months (range: 0.0-18.2). Resolution occurred in 42 patients (61.8%) with a median time to resolution of 12.1 weeks (range: 0.3-79.1+). In patients treated with nivolumab in combination with ipilimumab, the incidence of nephritis or renal dysfunction was 5.1% (23/448). Grade 2, Grade 3, and Grade 4 cases were reported in 1.6% (7/448), 0.9% (4/448), and 0.7% (3/448) of patients, respectively. No Grade 5 cases were reported. Median time to onset was 2.6 months (range: 0.5-21.8). Resolution occurred in 21 patients (91.3%) with a median time to resolution of 2.1 weeks (range: 0.1+-125.1+). *Immune-related endocrinopathies* In patients treated with nivolumab monotherapy, the incidence of thyroid disorders, including hypothyroidism or hyperthyroidism, was 9.6% (248/2578). The majority of cases were Grade 1 or 2 in severity reported in 4.2% (107/2578) and 5.4% (139/2578) of patients, respectively. Grade 3 thyroid disorders were reported in < 0.1% (2/2578) of patients. Hypophysitis (1 Grade 1, 2 Grade 2, 5 Grade 3, and 1 Grade 4), hypopituitarism (4 Grade 2 and 1 Grade 3), adrenal insufficiency (including secondary adrenocortical insufficiency) (1 Grade 1, 9 Grade 2, and 5 Grade 3), diabetes mellitus (including Type 1 diabetes mellitus) (3 Grade 2 and 1 Grade 3), and diabetic ketoacidosis (2 Grade 3) were reported. No Grade 5 cases were reported in these studies. Median time to onset of these endocrinopathies was 2.8 months (range: 0.3-29.1). Resolution occurred in 117 patients (42.9%). Time to resolution ranged from 0.4 to 144.1+ weeks. In patients treated with nivolumab in combination with ipilimumab, the incidence of thyroid disorders was 25.2% (113/448). Grade 2 and Grade 3 thyroid disorders were reported in 14.5% (65/448) and 1.3% (6/448) of patients, respectively. Grade 2 and Grade 3 hypophysitis (including lymphocytic hypophysitis) occurred in 5.8% (26/448) and 2.0% (9/448) of patients, respectively. Grade 2 and Grade 3 hypopituitarism occurred in 0.4% (2/448) and 0.7% (3/448) of patients, respectively. Grade 2, Grade 3, and Grade 4 adrenal insufficiency (including secondary adrenocortical insufficiency) occurred in 1.6% (7/448), 1.3% (6/448) and 0.2% (1/448) of patients, respectively. Grade 1, Grade 2, Grade 3, and Grade 4 diabetes mellitus and Grade 4 diabetic ketoacidosis were each reported in 0.2% (1/448) of patients. No Grade 5 endocrinopathy was reported. Median time to onset of these endocrinopathies was 1.9 months (range: 0.0-28.1). Resolution occurred in 64 patients (45.4%). Time to resolution ranged from 0.4 to 155.4+ weeks. *Immune-related skin adverse reactions* In patients treated with nivolumab monotherapy, the incidence of rash was 26.4% (680/2578). The majority of cases were Grade 1 in severity reported in 20.1% (518/2578) of patients. Grade 2 and Grade 3 cases were reported in 5.1% (131/2578) and 1.2% (31/2578) of patients respectively. No Grade 4 or 5 cases were reported in these studies. Median time to onset was 1.4 months (range: 0.0-27.9). Resolution occurred in 428 patients (63.8%) with a median time to resolution of 17.1 weeks (0.1-150.0+). In patients treated with nivolumab in combination with ipilimumab, the incidence of rash was 65.0% (291/448). Grade 2 and Grade 3 cases were reported in 20.3% (91/448) and 7.6% (34/448) of patients, respectively. No Grade 4 or 5 cases were reported. Median time to onset was 0.5 months (range: 0.0-19.4). Resolution occurred in 191 patients (65.9%) with a median time to resolution of 11.4 weeks (range: 0.1-150.1+). Rare cases of SJS and TEN some of them with fatal outcome have been observed (see sections 4.2 and 4.4). *Infusion reactions* In patients treated with nivolumab monotherapy, the incidence of hypersensitivity/infusion reactions was 4.7% (121/2578), including 6 Grade 3 and 2 Grade 4 cases. In patients treated with nivolumab in combination with ipilimumab, the incidence of hypersensitivity/infusion reactions was 3.8% (17/448); all were Grade 1 or 2 in severity. Grade 2 cases were reported in 2.2% (10/448) of patients. No Grade 3-5 cases were reported. *Complications of allogeneic HSCT in classical Hodgkin Lymphoma* Rapid onset of GVHD has been reported with nivolumab use before and after allogeneic HSCT (see section 4.4). In 49 evaluated patients from two cHL studies who underwent allogeneic HSCT after discontinuing nivolumab monotherapy, Grade 3 or 4 acute GVHD was reported in 13/49 patients (26.5%). Hyperacute GVHD, defined as acute GVHD occurring within 14 days after stem cell infusion, was reported in three patients (6%). A steroidrequiring febrile syndrome, without an identified infectious cause, was reported in six patients (12%) within the first 6 weeks post-transplantation, with three patients responding to steroids. Hepatic veno-occlusive disease occurred in one patient, who died of GVHD and multi-organ failure. Nine of 49 patients (18.4%) died from complications of allogeneic HSCT after nivolumab. The 49 patients had a median follow-up from subsequent allogeneic HSCT of 5.6 months (range: 019 months). *Laboratory abnormalities* In patients treated with nivolumab monotherapy, the proportion of patients who experienced a shift from baseline to a Grade 3 or 4 laboratory abnormality was as follows: 5.2% for anaemia (all Grade 3), 1.0% for thrombocytopaenia, 1.0% for leucopoenia, 10.0% for lymphopaenia, 1.1% for neutropaenia, 2.1% for increased alkaline phosphatase, 2.7% for increased AST, 2.2% for increased ALT, 1.2% for increased total bilirubin, 0.9% for increased creatinine, 3.8% for hyperglycaemia, 1.0% for hypoglycaemia, 3.5% for increased amylase, 7.9% for increased lipase, 6.4% for hyponatraemia, 1.8% for hyperkalaemia, 1.5% for hypokalaemia, 1.2% for hypercalcaemia, 0.7% for hypermagnesaemia, 0.5% for hypomagnesaemia, 0.7% for hypocalcaemia, and 0.1% for hypernatraemia. In patients treated with nivolumab in combination with ipilimumab, the proportion of patients who experienced a worsening from baseline to a Grade 3 or 4 laboratory abnormality was as follows: 2.8% for anaemia (all Grade 3), 1.2% for thrombocytopaenia, 0.5% for leucopoenia, 6.7% for lymphopaenia, 0.7% for neutropaenia, 4.3% for increased alkaline phosphatase, 12.4% for increased AST, 15.3% for increased ALT, 1.2% for increased total bilirubin, 2.4% for increased creatinine, 5.3% for hyperglycaemia, 8.7% for increased amylase, 19.5% for increased lipase, 1.2% for hypocalcaemia, 0.2% each for hypernatraemia and hypercalcaemia, 0.5% for hyperkalemia, 0.3% for hypermagnesaemia, 4.8% for hypokalaemia, and 9.5% for hyponatraemia. *Immunogenicity* Of the 2022 patients who were treated with nivolumab monotherapy 3 mg/kg every 2 weeks and evaluable for the presence of anti-product-antibodies, 231 patients (11.4%) tested positive for treatment-emergent anti-product-antibodies with fifteen patients (0.7 %) testing positive for neutralising antibodies. Of 394 patients who were treated with nivolumab in combination with ipilimumab and evaluable for the presence of anti-nivolumab antibodies, 149 patients (37.8%) tested positive for treatment-emergent anti-nivolumab antibodies with 18 patients (4.6%) testing positive for neutralising antibodies. Although the clearance of nivolumab was increased by 24% when anti-nivolumab-antibodies were present, there was no evidence of loss of efficacy or altered toxicity profile in the presence of nivolumab antibodies based on the pharmacokinetic and exposure-response analyses for both monotherapy and combination. Elderly No overall differences in safety were reported between elderly (≥ 65 years) and younger patients (< 65 years). Data from NSCLC, SCCHN, and adjuvant melanoma patients 75 years of age or older are too limited to draw conclusions on this population (see section 5.1). Data from cHL patients 65 years of age or older are too limited to draw conclusions on this population (see section 5.1). Hepatic or renal impairment In the non-squamous NSCLC study (CA209057), the safety profile in patients with baseline renal or hepatic impairment was comparable to that in the overall population. These results should be interpreted with caution due to the small sample size within the subgroups. Reporting of suspected adverse reactions Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V. **MARKETING AUTHORISATION HOLDER** Bristol-Myers Squibb Pharma EEIG Uxbridge Business Park Sanderson Road Uxbridge UB8 1DH United Kingdom **8. MARKETING AUTHORISATION NUMBER(S)** EU/1/15/1014/001 EU/1/15/1014/002 EU/1/15/1014/003 **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION** Date of first authorisation: 19 June 2015 **DATE OF REVISION OF THE TEXT** Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

1506BE18PR04434-Date of preparation July 2018

INVITED LECTURES

Dear Colleagues and Friends,

On behalf of the Belgian Society of Pathology, we would like to welcome you to the 9th Belgian Week of Pathology (BWP), here at the Wild Gallery in Brussels.

The previous editions of the BWP were a huge success. Based on these experiences we decided to bring the BWP back to Brussels, as a central place in our country and in the heart of Europe.

I'm happy to announce an exciting scientific program to update and exchange our knowledge on diagnostic and molecular pathology. The Key Note lecture of this year will be on Melanocytic lesions, presented by Prof. Dr. Wolter Mooi from Amsterdam, The Netherlands. The different Working Groups of the Belgian Society of Pathology worked very hard to deliver State-of-the-Art lectures, focusing on areas of direct practical relevance to general surgical pathologists. A comprehensive and rich program covers advances in pathology diagnosis, new classifications, guidelines and quality assessment. An innovative topic on digital pathology will address how artificial intelligence may change the way pathologists work. On Saturday, the Belgian Society of Pathology organizes an Educational Symposium on Immuno-oncology, supported by a special Educational Grant.

We would like to thank the authors of the many abstracts submitted for the Oral and Poster sessions. Best presentations will be awarded by the Belgian Society of Pathology.

Don't miss this year's Pathology Congress dinner on Friday night: here you can reunite with your colleagues and with the expert speakers from around the world. The relationships you forge here will last throughout your career!

Last but not least, the BWP 2018 gratefully acknowledges our partners from the industry for their renewed and ongoing support! It is always a pleasure to continue our constructive collaboration.

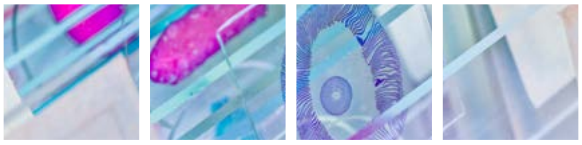
We look forward to seeing you in Brussels at the 9th Belgian Week of Pathology!

Koen VAN DE VIJVER
Belgian Week of Pathology President

INDEX

FRIDAY

SATURDAY



GENERAL INFORMATION

FRIDAY

SATURDAY

Accreditation

Accreditation has been requested for ethics and economy as well a pathology.
Submission is done on the computers available in the exhibition area.
Submission is requested once a day. You will receive a confirmation e-mail after ending the procedure.

Language

The language of the congress is English (British spelling) for abstracts, slides and announcements.

Abstracts

Authors were invited to submit abstracts until September 15, 2018.
The result of evaluation was sent to the first authors on september 20th
- Oral presentations will be presented during the Free paper Session on Saturday from 15:00 to 15:50
- Poster presentations will take place during the morning and afternoon coffee breaks of Friday October 19.

Posters will be displayed during the congress on the assigned boards in the Exhibition Area.

The Belgian Society of Pathology will award the Best Oral Presentation with a prize of 1.000€

The BWP will award the Best Poster with a prize of 500€.

Venue

Wild Gallery
11 rue du Charroi
B-1190 Brussels – Belgique

Parking available

Underground parking: Avenue du Pont de Luttre/ Luttrebruglaan 86
Outdoor parking: Rue du Charroi 21-23

Hotels

Pullman Brussels Centre Midi: Place Victor Horta 1 – 1060 Brussels – Belgium
Tel: (+32)25289800 – Fax: (+32)25289801

Event Coordinator

DME Events
Pacôme Pescenda – 57, Av. G. Demey – 1160 Brussels – Belgium
Tel: +32 493 68 89 31 / E-mail: pacome.pescenda@dme-events.eu

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Digestive
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Gynecology
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Molecular
Patrick PAUWELS

Surgica
Philippe DELVENNE

Urology
Thomas GEVAERT

SAVE THE DATE

CONGRESS

10TH EDITION

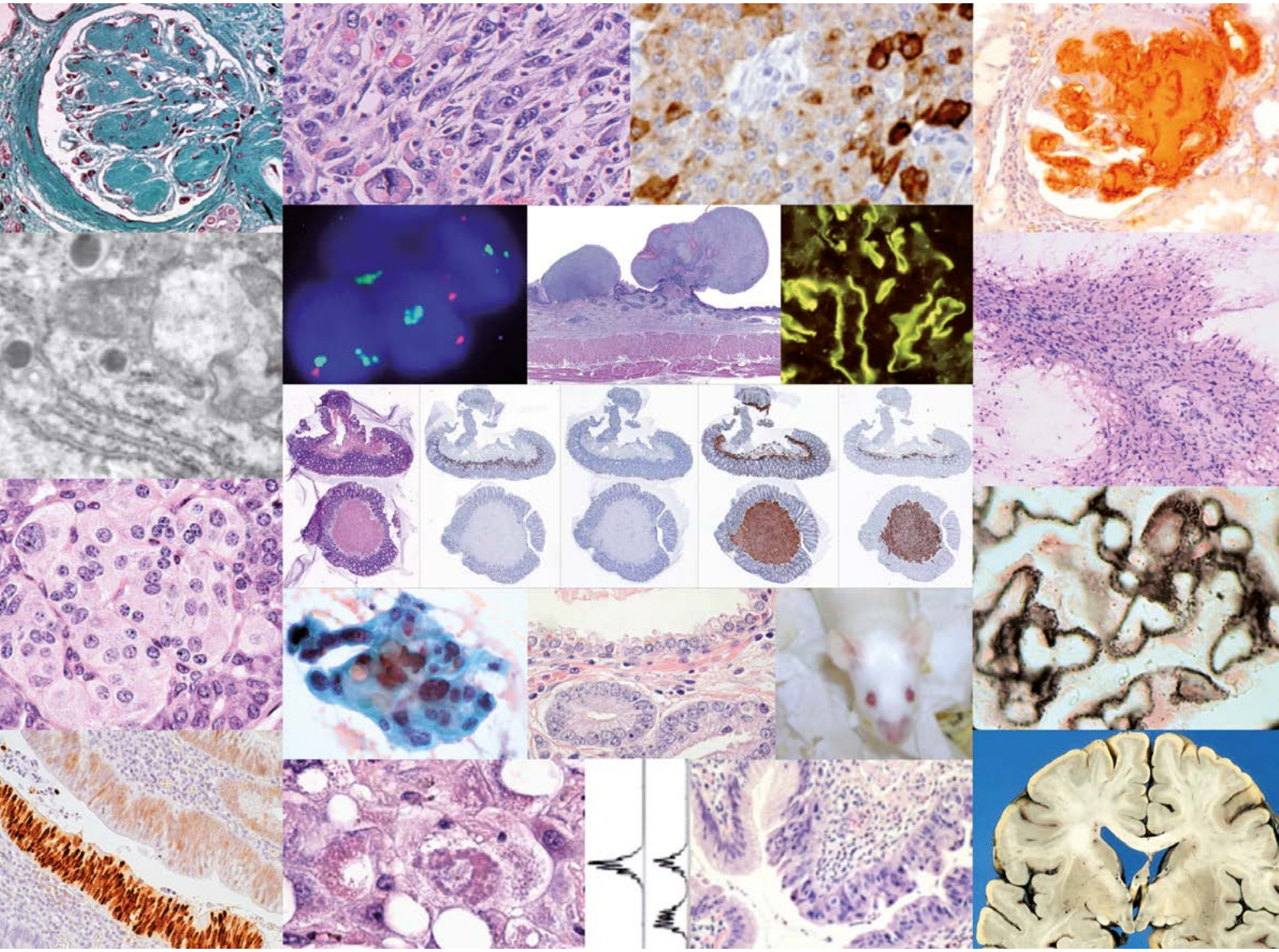
BELGIAN WEEK OF PATHOLOGY

18.10 > 19.10.19

CONFIRMED SPEAKERS:

Prof. Dr. Esther Oliva, Harvard, USA
Prof. Dr. Peter Sadow, Harvard, USA
Prof. Dr. W. Glenn McCluggage, Belfast, UK

BWPath
BELGIAN WEEK OF PATHOLOGY



SECRETARIAT

C/o DME Events SPRL
e-mail: event@bwpcongress.be
Tél: +32 (0)477 27 00 45

ONLINE REGISTRATION

www.bwpcongress.be

Foreign faculty

BEREZOWSKA Sabrina	Bern, Switzerland
COLLECHIA Maurizzio	Milan, Italy
COMPERAT Eva	Paris, France
DE JONG Daphne	Amsterdam, The Netherlands
DE LEVAL Laurence	Lausanne, Switzerland
MARCHIO Catarina	Torino, Italy
MOOI Wolter	Amsterdam, The Netherlands
PARADIS Valérie	Paris, France
PÖLLINGER Alexander	Bern, Switzerland
SEMPOUX Christine	Lausanne, Switzerland
VAN DER LAAK Jeroen	Nijmegen, The Netherlands
VAN KEMENADE Folkert	Utrecht, The Netherlands
VIELH Philippe	Dudelange, Luxembourg
VREULS Celien	Utrecht, The Netherlands

Belgian faculty

COLPAERT Cecile	Antwerp, Belgium
DE SAINT AUBIN Nicolas	Brussels, Belgium
DRIESSEN Ann	Antwerp, Belgium
FERREIRA Ingrid	Brussels, Belgium
FONTANGES Quitterie	Brussels, Belgium
HASPESLAGH Marc	Ghent, Belgium
HOORENS Anne	Ghent, Belgium
KEULEN Lotte	Antwerp, Belgium
KOCKX Mark	Antwerp, Belgium
LAMBRECHT Diether	Leuven, Belgium
ROSKAMS Tania	Leuven, Belgium
ROUMEGUERE Thierry	Brussels, Belgium
SALMON Isabelle	Brussels, Belgium
VAN DEN OORD Joost	Leuven, Belgium
VAN DE VIJVER Koen	Ghent, Belgium
VAN DEN BERGHE Ivo	Bruges, Belgium
VANHAELE Matthias	Leuven, Belgium
VERSET Laurine	Brussels, Belgium
GEVAERT Thomas	Leuven, Belgium
VAN DEN BRANDE Jan	Antwerp,Belgium

FRIDAY

SATURDAY

FRIDAY

2018 PRELIMINARY SCIENTIFIC PROGRAM

FRIDAY October 19

	Auditorium 1	Auditorium 2
08.00-09.00	WELCOME	WELCOME
09.30-11.00	**Surgical Pathology: Digital pathology** (Accreditation for Ethics & Economy requested)	**Breast Pathology: Spindle cell tumors**
11.00-11.30	BREAK + POSTERS SESSION	BREAK + POSTERS SESSION
11.30-12.30	**Surgical Pathology: Digital Pathology (continue)** (Accreditation for Ethics & Economy requested)	**Gynecological Pathology: Practical guidelines**
12.30-14.00	LUNCH + POSTERS SESSION	LUNCH + POSTERS SESSION
	AstraZeneca Satellite Symposium: Exploring diagnostic solutions to meet clinical demands for NSCLC patients	
14.00-15.30	**Gastro-enterological Pathology: Benign and malignant primary liver tumors**	**Hematopathology**
15.30-16.00	BREAK + POSTERS	BREAK + POSTERS
16.00-17.00	**Gastro-enterological Pathology (continue)**	**Lung Pathology**
17.00-18.00	**KEY NOTE Lecture Dermatopathology**	
18.00-19.00	RECEPTION	RECEPTION

20.00-23.00
CONGRESS DINNER
Pullman Zuid Station
Place Victor Horta 1
1060 BRUSSELS – BELGIUM

2018 PRELIMINARY SCIENTIFIC PROGRAM

Saturday October 20

	Auditorium 1	Auditorium 2
08.00-09.00	WELCOME	WELCOME
09.00-10.30	**Urologic Pathology: testicular neoplasms**	**Cytology**
10.30-11.00	BREAK + POSTERS	BREAK + POSTERS
11.00-12.00	**Molecular Pathology**	**Cytology (continue)**
12.00-12.30	**Educational Symposium on Immuno-oncology**	
12.00-13.00	LUNCH + POSTERS	LUNCH + POSTERS
13.00-15.00	**Dermatopathology: Melanocytic tumors**	
15.00-15.50	**Scientific presentations (by trainees)**	
15.50-16.00	**Closing Ceremony + Awards (poster/oral)**	
16.00-16.15	**General Assembly of the BSP**	

SATURDAY

FRIDAY

AUDITORIUM 1

08.00-09.00 **WELCOME**

09.30-11.00 **Surgical Pathology: Digital pathology**

Chairs: Philippe DELVENNE and Ramses FORSYTH

09.30-10.00 • **What can we learn from the Utrecht experience?**
Dr. Celien VREULS

10.00-10.30 • **Digital pathology platform: how to bridge the gap between theory and daily practice?**
Prof. Isabelle SALMON

10.30-11.00 • **How artificial intelligence may change the way pathologists work**
Prof. Jeroen VAN DER LAAK

11.00-11.30 **BREAK + POSTERS**

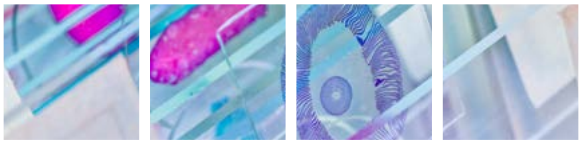
11.30-12.30 **Surgical Pathology: Digital Pathology**

Chairs: Philippe DELVENNE and Ramses FORSYTH

11.30-12.00 • **Digital pathology in routine practice: review of 3 years of experience**
Dr. Ivo VAN DEN BERGHE

12.00-12.30 • **Digital pathology in immuno-oncology – a roadmap for biomarker development**
Dr. Mark KOCKX

12.30-14.00 **LUNCH + POSTERS +**
ASTRAZENECA SATELLITE SYMPOSIUM



AUDITORIUM 1

14.00-15.30 **Gastro-enterological Pathology: Benign and malignant primary liver tumors**

Chairs: Anne HOORENS and Laurine VERSET

14.00-14.30 • **Liver cell adenomas**
Prof. Christine SEMPOUX

14.30-15.00 • **Combined hepatocellular-cholangiocarcinoma**
Prof. Tania ROSKAMS

15.00-15.30 • **Cholangiocarcinoma**
Prof. Valérie PARADIS

15.30-16.00 **BREAK + POSTERS**

16.00-17.00 **Gastro-enterological Pathology:**

Chairs: Anne HOORENS and Laurine VERSET

• **Slide seminar on benign and malignant primary liver tumours**

Dr. Quitterie FONTANGES - Dr. Laurine VERSET
Erasme University Hospital

Dr. Laurine VERSET
Erasme University Hospital

Dr. Matthias VANHAELE - Prof. Tania ROSKAMS
Leuven University Hospital

Prof. Anne HOORENS
Ghent University Hospital

Dr. Lotte KEULEN - Prof. Ann DRIESSEN
University Hospital Antwerp

17.00-18.00 **KEY NOTE Lecture Dermatopathology**

Chairs: Sofie DE SCHEPPER and David CREYTENS

• **Ten mistakes to avoid in the diagnosis of melanomas and naevi**
Prof. Wolter MOOI

18.00-19.00 **WELCOMING RECEPTION IN THE EXHIBITOR AREA**

20.00-23.00 **CONGRESS DINNER AT PULLMAN ZUID STATION**

FRIDAY

AUDITORIUM 2

08.00-09.00 **WELCOME**

09.30-11.00 **Breast Pathology: Spindle cell tumors**

Chairs: Kathleen LAMBEIN and Marcella BALDEWIJNS

09.30-10.15 • **Epithelial and fibro-epithelial lesions of the breast with spindle cell characteristics**

Prof. Catarina MARCHIO

10.15-11.00 • **Spindle cell tumors of the breast (real mesenchymal lesions)**

Prof. Nicolas DE SAINT AUBAIN

11.00-11.30 **BREAK + POSTERS**

11.30-12.30 **Gynecological Pathology: Practical guidelines**

Chairs: Jean-Christophe NOËL and Claire BOURGAIN

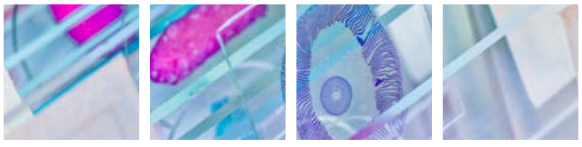
11.30-12.00 • **International Society of Gynecological Pathologists (ISGyP) Endometrial Cancer Project: Guidelines**

Prof. Koen VAN DE VIJVER

12.00-12.30 • **Sentinel node in gynecological cancers (vulva-vagina-cervix-endometrium-ovary)**

Prof. Cecile COLPAERT

12.30-14.00 **LUNCH + POSTERS**



AUDITORIUM 2

14.00-15.30 **Hematopathology**

Chairs: Joan SOMJA and Thomas TOUSSEYN

14.00-14.45 • **The 2016 updated WHO classification of B-cell lymphomas**

Prof. Daphne DE JONG

14.45-15.30 • **The 2016 updated WHO classification of T-cell lymphomas**

Prof. Laurence DE LEVAL

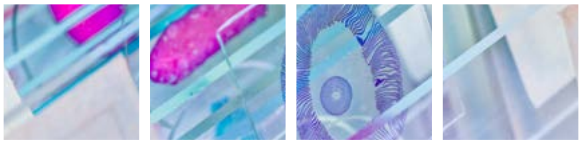
15.30-16.00 **BREAK + POSTERS**

16.00-17.00 **Lung Pathology**

Chairs: Karl D'HAENE and Myriam REMMELINK

16.00-17.00 • **Interstitial lung disease**

Prof. Sabina BEREZOWSKA and Prof. Alexander PÖLLINGER



12.00-12.40

Educational Symposium

Auditorium 1

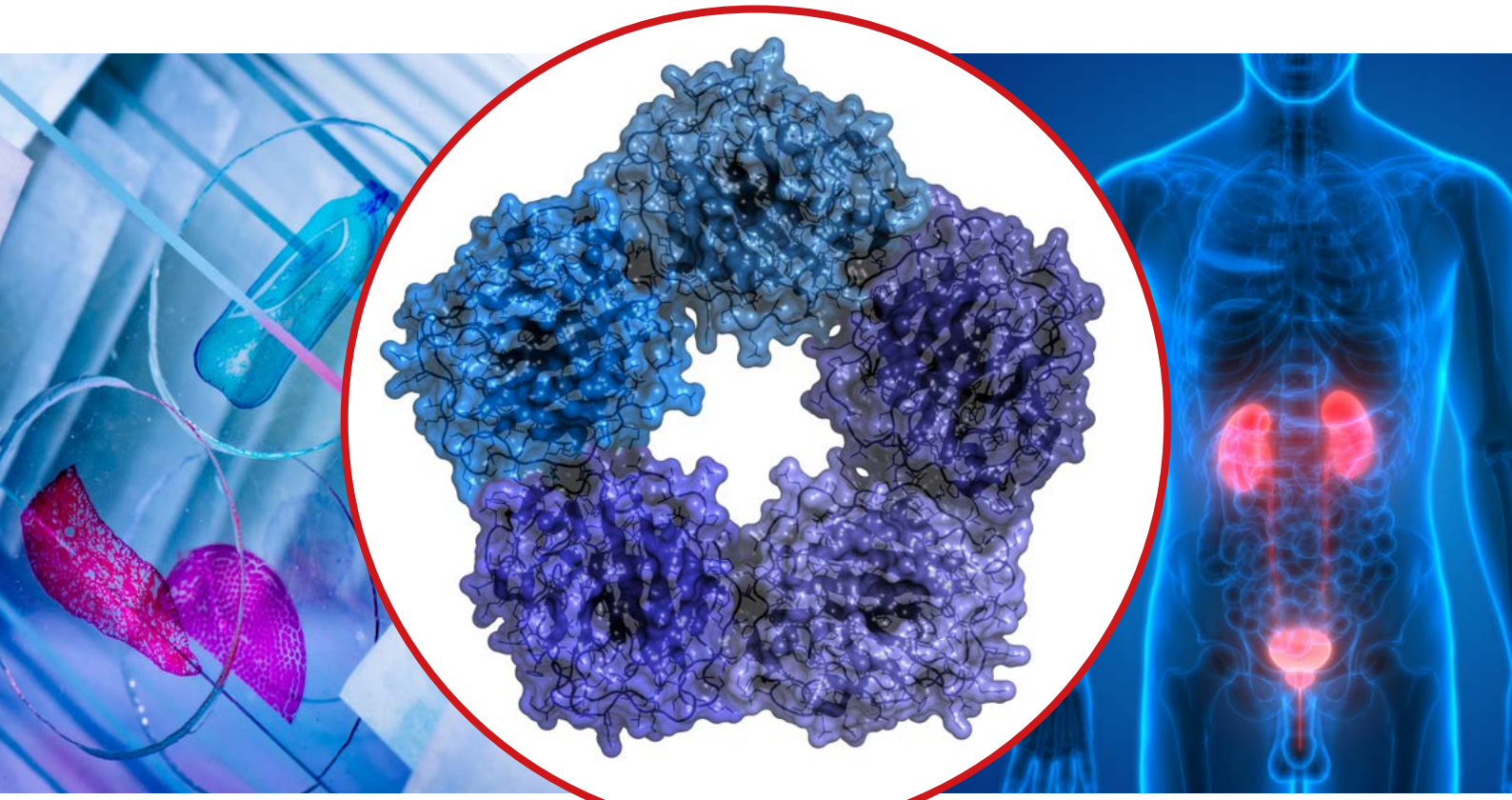
Immuno-oncology in the field of Urological Cancer

Biomarkers in GU cancers (PD-L1)

Dr. Thomas GEVAERT

Immuno-therapy for GU cancers

Dr. Jan VAN DEN BRANDE



Organised thanks to the Educational Grant

with the kind support

AstraZeneca

Bristol-Myers Squibb

Roche

AUDITORIUM 1

08.00-09.00 **WELCOME**

09.00-10.30 **Urologic Pathology: testicular neoplasms**

Chairs: Louis LIBBRECHT & Sandrine RORIVE

09.30-10.00 • **Clinical management of testicular tumors: from diagnosis to treatment**

Prof. Thierry ROUMEGUERE

10.00-10.30 • **Handling and Reporting of Orchidectomy Specimens with Testicular Cancer and Updates in the Eighth Edition of the TNM AJCC Cancer Staging Classification**

Prof. Eva COMPERAT

10.30-11.00 • **Seminoma and spermatocytic tumor**

Prof. Maurizzio COLLECHIA

10.30-11.00 **BREAK + POSTERS**

11.00-12.00 **Molecular Pathology**

Chairs: Nicky D'HAENE and Isabelle VANDEN BEMPT

11.00-12.00 • **DNA repair in cancer: a new target**

Prof. Diether LAMBRECHT

12.00-13.00 **LUNCH + POSTERS**

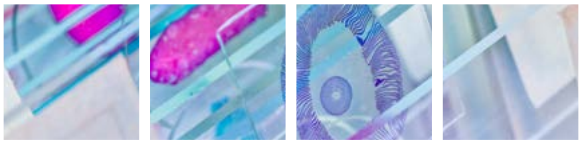
12.00-12.40 **EDUCATIONAL SYMPOSIUM: IMMUNO-ONCOLOGY IN THE FIELD OF UROLOGICAL CANCER**

12.00 – 12.20 • **Biomarkers in GU cancers (PD-L1)**

Dr. Thomas GEVAERT

12.20 – 12.40 • **Immuno-therapy for GU cancers**

Dr. Jan VAN DEN BRANDE



AUDITORIUM 1

13.00-15.00 **Dermatopathology: Melanocytic tumors**

Chairs: Sofie DE SCHEPPER and David CREYTENS

13.00-13.45
- **Biphenotypic naevi: tumour progression that does not indicate malignancy**
  Prof. Wolter MOOI

13.45-14.30
- **Signatures in melanoma**
  Prof. Joost VAN DEN OORD

14.30 -14.45
- **Melanocytic tumours: on the MAPKinase road again!**
  Dr. Ingrid FERREIRA

14.45-15.00
- **Bridging genetics, dermoscopy and pathology (new WHO classification)**
  Prof. Marc HASPESLAGH

15.00-15.50 **Scientific presentations (by trainees)**

Chairs: Martin LAMMENS and Koen VAN DE VIJVER

- **Management of breast lesions of uncertain malignant potential: a Belgian retrospective study.**
  Isabel DE BRABANDER
- **Laboratory variation of molecular testing in metastatic lung cancer in the Netherlands.**
  Chantal KUIJPERS
- **Copy number alterations derived from liquid biopsies support lung cancer subtyping.**
  Lennart RAMAN
- **Combination of postmortem redistribution aspects with pathological findings in drugs-related deaths.**
  Eric LEMAIRE

15.50-16.00 **Awards (poster/oral)**
+ Closing Ceremony of the Congress

AUDITORIUM 2

08.00-09.00 **WELCOME**

09.00-10.30 **Cytology**

Chairs: Birgit WEYNAND and Christine GALANT

09.00 – 09.30 • **HPV-based screening implementation in the Netherlands: knowns and unforeseens**

Prof. Folkert VAN KEMENADE

09.30 – 10.30 • **Cervical cytology: case presentations**

10.30-11.00 **BREAK + POSTERS**

11.00-12.00 **Cytology**

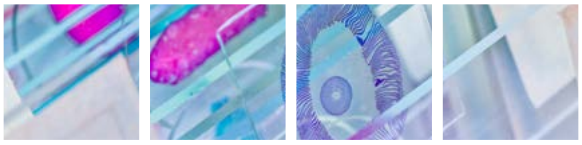
Chairs: Birgit WEYNAND and Christine GALANT

11.00 – 12.00 • **Milan classification of salivary gland tumors**

Prof. Philippe VIELH

12.00-13.00 **LUNCH + POSTERS**

12.45-13.00 **General Assembly of the BSP**



Welcome Drink

FRIDAY 19 AFTERNOON

18:00 - 19:00

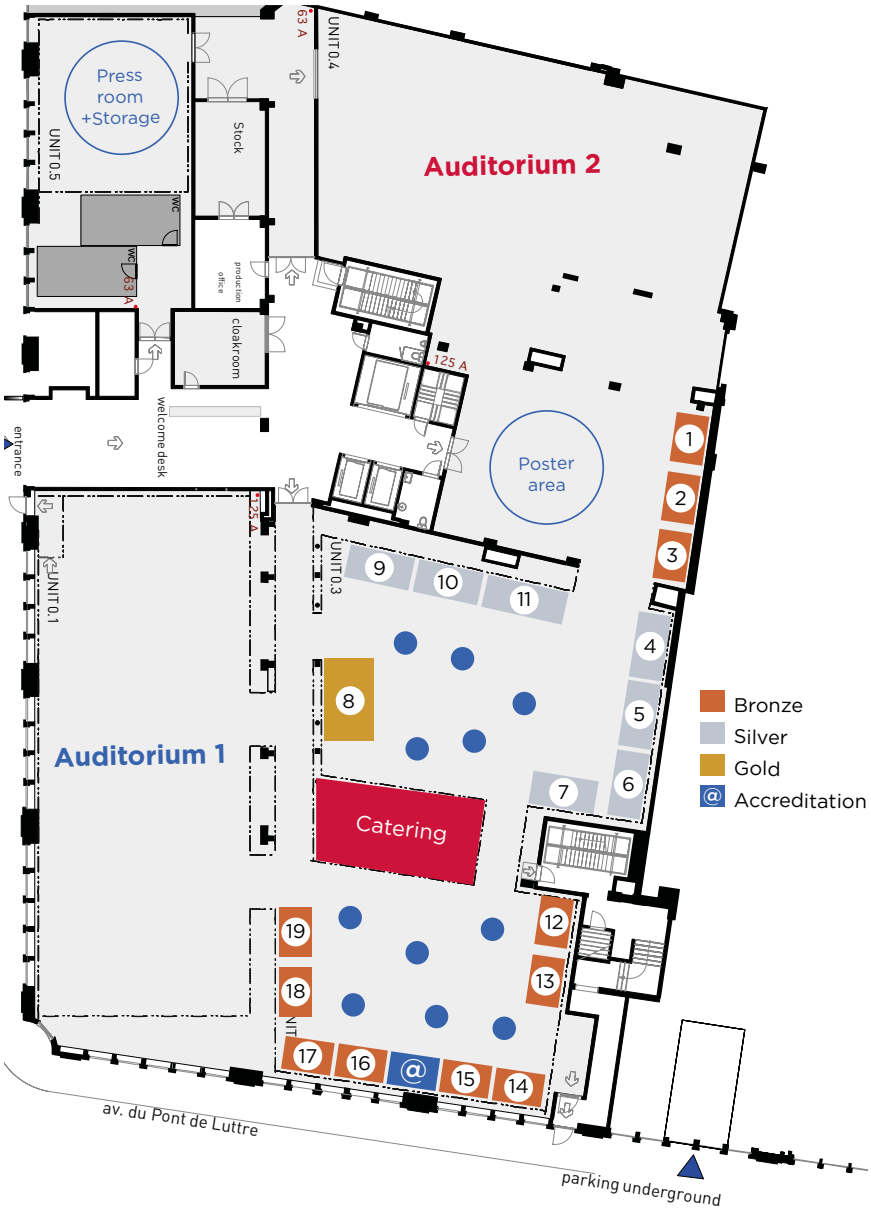
IN THE EXHIBITION AREA

EXHIBITION FLOOR

FRIDAY

SATURDAY

1	What's up doc?
2	Medisquare
3	Elsevier
4	MSD
5	Roche Diagnostic
6	Roche Pharma
7	Sectra
8	BMS
9	Agilent
10	Astra-zeneca
11	Hologic
12	Hamamatsu
13	Menarini
14	Mips
15	Sakura
16	Thermofisher
17	Biocartis
18	Leica
19	Philips



GOLD

Bristol-Myers Squibb

SILVER

Roche

AstraZeneca

HOLOGIC

MSD

Roche Diagnostics

Agilent Technologies

BRONZE

BIOCARTIS - ELSEVIER - HAMAMATSU - LEICA - MENARINI - MIPS - PHILIPS - SAKURA - SECTRA - THERMOFISHER

FRIDAY

Breast Pathology : Spindle cell tumors

Chairs : Kathleen LAMBEIN and Marcella BALDEWIJNS

Epithelial and fibro-epithelial lesions of the breast with spindle cell characteristics

PROF. CATERINA MARCHIÒ

PhD (2008), Specialist in Pathology (2014), Breast Cancer
Università di Torino

EDUCATION & RELATED TRAINING EXPERIENCES

- MD (2004)
- PhD (2008) : Clinical Research fellow at the Institute of Cancer Research, London (2006-2008)
- Specialist in Pathology (2014) : Visiting Research Scholar at the Dept. of Pathology, Children's Hospital, Boston, USA (2013-2014) ; Research Fellow at the Dept. of Pathology, Memorial Sloane Kettering Cancer Center, New York, USA (2014)

SUMMARY OF THE PRESENTATION

The main research interest resides in breast cancer (BC) pathology, spanning from histopathogenesis of BCs to molecular pathology of special histologic types of BC and genetics of HER2-positive carcinomas. The research work is complemented by a clinical activity as consultant histopathologist at the Pathology Unit of FPO-IRCCS, Candiolo Cancer Institute, where she focused on breast pathology and molecular diagnostics on solid tumors, she is responsible for breast pathology diagnostics, as well as for the Research activities of the Pathology lab.

Following the direct evidence she provided on the co-amplification of the HER2 gene and of the centromere of chromosome 17 in BC, a major interest has been dedicated to the characterization of non classical HER2 patterns in BC leading to a focus on BC showing an equivocal HER2 status. A spore project on double equivocal carcinomas has recently originated and funded in part by PRIN 2015.

http://www.dsm.unito.it/do/docenti.pl/Show?_id=cmarchio#ricerca

Breast Pathology : Spindle cell tumors

Chairs : Kathleen LAMBEIN and Marcella BALDEWIJNS

Spindle cell tumors of the breast (real mesenchymal lesions

PROF. NICOLAS DE SAINT AUBAIN

Soft tissue pathologist at Institut Jules Bordet, Brussels.

FRIDAY

Surgical Pathology : Digital pathology

Chairs : Philippe DELVENNE and Ramses FORSYTH

What can we learn from the Utrecht experience ?

DR. CELIEN VREULS

EDUCATION & RELATED TRAINING EXPERIENCES

2009-2014	resident clinical pathology (Maastricht/Antwerpen)
2009-2014	PHD researcher Maastricht
2014-2017	pathologist, Amphia, Breda
2017-	pathologist UMCU, Utrecht
2013-	assistant editor Functionele histologie, Junqueira

SUMMARY OF THE PRESENTATION

- Advantages digital pathology
- How to implement digital pathology in practice
- Tips for writing a business case

Surgical Pathology : Digital pathology

Chairs : Philippe DELVENNE and Ramses FORSYTH

Digital pathology platform: how to bridge the gap between theory and daily practice ?

PROF. ISABELLE SALMON

Head of anatomo-pathology department in Erasme Hospital
Lab manager of DIAPATH (CMMI) in Gosselies
Strategic manager of CurePath Laboratory in Jumet (Chirec-Tivoli-Erasme)
Professor at the Faculty of Medicine, ULB

EDUCATION & RELATED TRAINING EXPERIENCES

November 1993 :	PhD Thesis : "Contribution of the quantitative description of the chromatin facies for the diagnosis and prognosis of thyroid and nervous system tumors".
April 1991 :	Specialized physician in Anatomo-Pathology.
July 1985 :	Doctor of Medicine – Faculty of Medicine - Université Libre de Bruxelles (ULB).

FRIDAY

Surgical Pathology : Digital pathology

Chairs : Philippe DELVENNE and Ramses FORSYTH

How artificial intelligence may change the way pathologists work

PROF. JEROEN VAN DER LAAK

Jeroen van der Laak is Principle Investigator and associate professor of computational Pathology at the department of Pathology of the Radboud University Medical Center in Nijmegen, The Netherlands and guest professor at the Center for Medical Image Science and Visualization (CMIV) in Linkoping, Sweden. His research focuses on the use of machine learning for the analysis of whole slide images. Application areas include : improvement of routine pathology diagnostics, objective quantification of immunohistochemical markers, and study of novel imaging biomarkers for prognostics. Dr van der Laak holds an MSc in computer science and acquired his PhD from the Radboud University in Nijmegen. He co-authored 100 peer-reviewed publications and is member of the editorial boards of Laboratory Investigation and the Journal of Pathology Informatics. He is member of the board of directors of the Digital Pathology Association and organizer of sessions at the European Congress of Pathology and the Pathology Visions conference. He coordinated the highly successful CAMELYON grand challenges in 2016 and 2017. Dr van der Laak acquired research grants from the European Union and the Dutch Cancer Society, among others. He is frequently invited as a speaker at international conferences.

SUMMARY OF THE PRESENTATION

Advances in machine learning have propelled computational pathology research. Today, computer systems approach the level of humans for certain well-defined tasks in pathology. At the same time, pathologists are faced with an increased workload both quantitatively (numbers of cases) and qualitatively (the amount of work per case ; with increasing treatment options, the data delivered by pathologists is also expected to become more fine-grained). In this presentation I will address the potential of machine learning techniques, and discuss how these may alleviate the challenges of pathologists. Potential solutions range from computer aided support for relatively straightforward tasks to discovery of innovative prognostic and predictive biomarkers.

Gynecological Pathology: Practical guidelines

Chairs: Jean-Christophe NOËL and Claire BOURGAIN

International Society of Gynecological Pathologists (ISGyP) Endometrial Cancer Project: Guidelines

PROF. KOEN VAN DE VIJVER

Koen Van de Vijver is a surgical pathologist with a keen interest in the diagnosis and treatment of cancers of the female genital tract and the breast. Most of his activities involve diagnostic work, teaching, and clinico-pathologic research. His research is mainly focused on the molecular analysis of endocervical and ovarian neoplastic diseases.

He received his MD in 2000 at Antwerp University (Belgium), and did his PhD research both at Antwerp University and Leiden University Medical Center (LUMC, the Netherlands), leading to a PhD on Functional immunogenic glycoconjugates in 2007. In 2008 he became University Docent (Assistant Professor) at Maastricht University (the Netherlands). In 2011-2012 he completed a fellowship with prof. dr. Esther Oliva in Gynaecological Pathology at Massachusetts General Hospital, Harvard Medical School, Boston (USA). After working as a consultant pathologist in the Netherlands Cancer Institute in Amsterdam, he became professor of Gynaecological Pathology at Ghent University Hospital (Belgium) in 2018.

SUMMARY OF THE PRESENTATION

The 2013 Nature publication of the Cancer Genome Atlas Research Network (TCGA) on Integrated Genomic Characterization of Endometrial Carcinoma (EC) initiated an evolution of traditional surgical-pathologic staging and grading towards an integrated molecular-pathologic classification. Histopathological assessment of biopsy/curettage and resection specimens remains the gold standard, but can be extremely difficult in high-grade tumors with morphologic ambiguity. Molecular classification of EC has been shown to be reproducible and is associated with clinical outcomes. The International Society of Gynecological Pathologists (ISGyP) started an Endometrial Cancer Project to propose guidelines and recommendations regarding 1) diagnosis 2) processing / sampling / staging / prognosis and 3) special techniques / ancillary studies after reviewing and discussing the literature. In their paper, published in the International Journal of Gynaecological Pathology, the authors address the value of immunohistochemistry (e.g. p53, ER, PR, MLH1, PMS2, MSH2 and MSH6), ploidy and molecular analysis (e.g. POLE, TP53, MSI, MLH1 hypermethylation) for assessing prognosis, predicting response to hormone therapy and assessing mismatch deficiency in EC. Several different recommendations are made, which will be discussed during this presentation at the BWP2018.

FRIDAY

Gynecological Pathology: Practical guidelines

Chairs: Jean-Christophe NOËL and Claire BOURGAIN

Sentinel node in gynecological cancers (vulva-vagina-cervix-endometrium-ovary)

PROF. CECILE COLPAERT

Cecile Colpaert MD, PhD is a staff member of the department of Pathology of the GZA/ZNA hospitals in Antwerp and consultant pathologist at the University Hospitals of Antwerp and Leuven. She has a special interest in breast, gynaecological and perinatal pathology.

SUMMARY OF THE PRESENTATION

Following the example of sentinel lymph node (SLN) mapping to identify regional lymph node metastases in patients with breast cancer and cutaneous melanoma, in the past decades, lymphatic mapping and SLN biopsy have also been explored in gynaecologic malignancies, including those of vulva, vagina, cervix, uterus and ovary. Clinical trials proved the diagnostic accuracy of SLN mapping: these techniques will increase the rates of detection of lymph node metastasis while decreasing the morbidity associated with lymphadenectomy. Large validation studies are currently being performed in both the United States and Europe.

Based on the results of these trials, the BSP Working Group for Gynaecological Pathology proposes a methodology for the handling, pathological examination and reporting of these SLN biopsies. Caveats for the intra-operative examination of SLN will be also be discussed.

Handling of sentinel lymph nodes in gynaecological cancers (vulva-cervix-endometrium-ovary)

Surgical Pathology : Digital Pathology

Chairs : Philippe DELVENNE and Ramses FORSYTH

Digital pathology in routine practice: review of 3 years of experience

DR. IVO VAN DEN BERGHE

Head of Pathology department in AZ Sint-Jan Bruges since 2002
Chairman of Medical Board in AZ Sint-Jan Bruges since 2014

1995 Doctor of Medicine, Faculty of Medicine, KU Leuven
PhD specialized in Anatomo-Pathology

SUMMARY OF THE PRESENTATION

Overview of validation
Implementation and advantages of digital pathology in daily practice for biopsy diagnosis.

FRIDAY

Surgical Pathology : Digital Pathology

Chairs : Philippe DELVENNE and Ramses FORSYTH

Digital pathology in immuno-oncology – a roadmap for biomarker development

DR. MARK KOCKX

Dr. Mark Kockx founded Histogenex Laboratories in 2001. At the University of Antwerp, Belgium, Dr. Kockx pioneered methodologies to elucidate apoptotic and cytostatic response of cancer patients after treatments with targeted therapies. His subsequent collaborations with global pharmaceutical companies led to the founding of Histogenex Laboratories.

Dr. Kockx is an internationally recognized pathologist-scientist who has operated on the forefront of personalized medicine developments. He continues to lead initiatives to standardize biomarker analysis practices in addition to adapting novel technologies. Dr. Kockx has been extensively involved with the clinical trials that led to the approval of well-known targeted therapies such as EGFR, BRAF and MEK inhibitors. His current passions are two fold. He is introducing practices and workflows for next generation IHC, combining innovations of multiplex staining, quantification and image capture. He has also developed an Immunomics program, a state of the art biomarker program that supports the evolving and numerous needs of immunotherapy development.

SUMMARY OF THE PRESENTATION

Digital pathology offers enticing features, not the least of it as an enhanced microscope platform for viewing, collaboration and distribution. In addition, there are a broad milieu of downstream applications for analyzing the resultant high resolution whole slide image. The combination is especially relevant given the renewed emphasis of assessing the tumor microenvironment (TME) when developing immune-oncology therapeutics. The presentation discusses the varied pressures - such as cost, workflow, initial set up logistics, and regulatory factors - that constrain the use of a technology that seems so obviously suited for the anatomic pathology laboratory. The second part of the presentation reviews the available validation guidelines from the FDA and CAP which primarily addresses manufacturers and clinical laboratories respectively but do not provide guidance for clinical developers. Both guidelines take on different approaches, the FDA unpacks the digital pathology system into components while CAP focuses on what emerges from the "black box." A hybridized model – merging elements of both validation approaches – is presented to the clinical development reader. Finally, the manuscript reviews a series of analysis applications, in particular, the ones that extract valuable data from the TME, and introduces the concept of a laboratory developed digital application (LDDA) that leverages the familiarity of a LDT.

Gastro-enterological Pathology: Benign and malignant primary liver tumors

Chairs: Anne HOORENS and Laurine VERSET

Liver cell adenomas

PROF. CHRISTINE SEMPOUX

Dr. Sempoux is Full Professor of Pathology at the University of Lausanne (Switzerland) and Head of the Surgical Pathology Unit in the Institute of Pathology at the Lausanne University Hospital (CHUV). She earned her medical degree at the Louvain Medical School in Belgium and completed her residency training in Pathology at the Cliniques universitaires Saint-Luc, Bruxelles, Belgium. The first research field of investigation in which she was involved, in Belgium at that time, aimed at study the histopathological aspects of congenital hyperinsulinism, a disease affecting the endocrine pancreas. This work was the subject of her PhD thesis and was awarded by the scientific prize Alvarenga de Piauhy from the "Académie Royale de Médecine de Belgique". Today, hepatobiliary, pancreatic and gastrointestinal pathology represents her daily clinical diagnostic and teaching activities, while her current research interest focuses on liver pathology, and more specifically on liver tumors. In this field, and especially in hepatocellular adenoma, she has a recognized expertise and international collaborations. Dr. Sempoux has authored around 250 scientific publications including reviews and texbook chapters. She is member of several national and international scientific societies, including the Swiss Society of Pathology, the Laennec Liver Pathology Society, and the European Society of Pathology where she serves currently as secretary of the Digestive Diseases Working Group.

SUMMARY OF THE PRESENTATION

Her presentation will focus on hepatocellular adenomas. Since their first recognition in 1973, great progresses have been made in understanding these benign liver tumors occurring in childbearing women. The first important step date back from 2007 when a phenotype-genotype correlation deciphered this entity and demonstrated the existence of several subtypes, with different clinical behavior. More recently, the identification of a new subtype, a better understanding of the risk of malignant transformation and of its pathogenesis, the discovery of some translational markers to make the correct diagnosis preoperatively in correlation with imaging techniques, and the identification of new clinical contexts favoring their development has largely extend the knowledge in this field. The talk will focus on all these new developments in a comprehensive way for the routine practice of the pathologists.

FRIDAY

Gastro-enterological Pathology: Benign and malignant primary liver tumors

Chairs: Anne HOORENS and Laurine VERSET

Combined hepatocellular-cholangiocarcinoma

PROF. TANIA ROSKAMS

TANIA ROSKAMS obtained her MD degree in 1989 and her PhD in 1995 at K.U.Leuven. She spent 2 years (1994-1995) in Oklahoma transplant institute under supervision of Prof Van Thiel and Prof Demetris. She is a clinical liver pathologist since 1996 and involved in liver research since 1989. She is the head of the liver research group of the department of Morphology and Molecular Pathology since 1996. Since 2008, she is also coordinating the whole department of Morphology and Molecular Pathology, including gastroenterology, nephrology, uropathology, hematology and breast cancer research programs. She is a specialist in liver progenitor cells, their niche and their role in carcinogenesis. Being a clinical liver pathologist and half time researcher, she has extensive experience in rodent and large animal models and their representativity for human liver diseases. She is member of the scientific committee of the European gastroenterology Federation and coordinates an international consensus panel on a new classification of primary liver carcinomas. She already coordinated an international consensus panel on new nomenclature of human progenitor cells and was first author on the nomenclature paper (see relevant publications.). T Roskams is holder of the "F.C. Donders" Chair at the University of Utrecht, The Netherlands (a guest professorship with the purpose of fairing the research on "Tissue Repair" in different faculties of the University of Utrecht).

Gastro-enterological Pathology: Benign and malignant primary liver tumors

Chairs: Anne HOORENS and Laurine VERSET

Cholangiocarcinoma

PROF. VALÉRIE PARADIS

Valérie Paradis, MD PhD and Professor in Pathology, is the chairman of Pathology department (Beaujon hopsital) and leader of the INSERM team "From inflammation to neoplasia in digestive diseases" (INSERM UMR 1149 Paris). Fields of interest and research include pathological and molecular aspects of liver tumorigenesis with a specific interest of hepatocellular carcinomas developed in patients with metabolic syndrome. Her team has developed original in situ proteomic approach (MALDI imaging) for identification of tissue biomarkers, and ex vivo culture model of human tumor slices for evaluation of therapeutic molecules.

V. Paradis is involved in educational activities, chairing the specialty "Epithelium: interface structure" (Master 2 "Cellular biology-Physiology-Pathology"). She is co-coordinator of the DHU UNITY "Unmet Needs for Innovation in HepaTology and GastroenterlogY" (Coordinator Pr DC Valla) and task leader (WP2: cross sectional clinical study)) of the RHU QUID-NASH (coordinator Pr DC Valla) aiming to identify novative noninvasive diagnostic markers of NASH in diabetic patients.

SUMMARY OF THE PRESENTATION

Cholangiocarcinomas (CC) define a heterogeneous entity based upon their anatomic localization along the biliary tree from the liver to the pancreas. In the liver, it accounts for the second most frequent primary malignancy, following hepatocellular carcinoma (HCC). Significant heterogeneity is also observed within CC since a majority of them develop in a normal background liver without any evident risk factor, while others occur in the context of chronic liver diseases and cirrhosis. Morphologically, CC is characterized by a prominent fibrous stroma, composed of cancer-associated fibroblasts and extracellular matrix components, which may play a role in the poor prognosis of this tumor. More recently, using an integrative genomic analysis, 2 main biological classes of CC (inflammatory and proliferative) have been identified, with a worse prognosis for the proliferative one. The identification of new CC biomarkers is a key-issue for improving the management of patients with CC and developing targeted therapies.

Hematopathology

Chairs: Joan SOMJA and Thomas TOUSSEYN

The 2016 updated WHO classification of B-cell lymphomas

PROF. DAPHNE DE JONG

EDUCATION & RELATED TRAINING EXPERIENCES

2014-present	Full professor Hematopathology, VU University, Amsterdam, the Netherlands
2012-present	Hematopathologist, VU University Medical Center, Amsterdam, the Netherlands
1993-2012	Staff pathologist, Netherlands Cancer Institute, Amsterdam, the Netherlands
1989-1993	Residency Surgical Pathology, Leiden University Medical Center, the Netherlands
1989	PhD, Leiden University Medical Center, Leiden the Netherlands, The origin and clonal evolution of follicle center cell lymphomas (cum laude)
1986	Full license as physician in the Netherlands (MD)

SUMMARY OF THE PRESENTATION

The revised WHO classification for myeloid and lymphoid malignancies has been published in early 2017. Using research findings on the oncogenesis, biology and clinical features of malignant lymphoma for the past 8 years and largely based on discussions in the hematopathology community as during the yearly diagnostic workshops of the European Association for Haematopathology and Society for Hematopathology on how to implement this knowledge in daily practice, definitions of known disease entities have been set and new entities described.

The basis of the new classification has been unchanged after the first globally accepted WHO classification in 2001 : recognized entities are well defined on the basis of clinical, morphological and (patho-)biological criteria. In the previous WHO classification, which was published in 2008, a start was made with the implementation of molecular definitions in addition to the classical criteria. The current revised WHO classification takes this thinking further and where ever possible, works towards complete integration of molecular data.

As compared to previous versions, the present lymphoma classification stands out by its focus on stratification within existing entities, rather than the definition of completely novel entities. This reflects in the definition of pathobiological variants and subclasses based on morphological, immunophenotypic or molecular characteristics or, conversely, prognostic subdivision within a further pathologically homogeneous entity. A few groups of lymphoproliferative disorders have been changed in an essential way and are now being distributed in a truly different way. While the impact of genetic information may have become more dominant, the diagnosis of lymphoid malignancies remains a preeminently multidisciplinary process and integration of the four defining modalities morphology, immunophenotype, genetic information and clinical context remains key to our diagnostic approach and our role in patient management.

Using examples of diagnostic dilemma's that are regularly encountered in daily practice, aspects of the new WHO classification and how to implement these will be discussed.

Hematopathology

Chairs: Joan SOMJA and Thomas TOUSSEYN

The 2016 updated WHO classification of T-cell lymphomas

PROF. LAURENCE DE LEVAL

EDUCATION & RELATED TRAINING EXPERIENCES

Dr. Laurence de Leval is full Professor of Pathology and Director of the Institute of Pathology at the University Hospital of Lausanne, Switzerland. Laurence de Leval graduated M.D. at the University of Liège, Belgium, in 1994, where she trained in pathology and obtained a PhD degree in experimental pathology in 1998. She completed a 2-year postdoctoral fellowship in hematopathology at the Massachusetts General Hospital, Harvard Medical School, Boston.

From 2000 to 2009 she was staff pathologist at the University Hospital, Liège and senior researcher of the Belgian National Fund for Scientific research. She is holding swiss licences for pathology and molecular pathology and her diagnostic activities are mainly in hematopathology and molecular pathology. Dr. de Leval is an internationally recognized expert in hematopathology. Her research on non-Hodgkin lymphomas was awarded Prize for Clinical Research of the Inbev-Baillet Latour Fund (Belgium) in 2009 and she received the Benjamin Castleman award presented by the United States and Canadian Academy of Pathology in 2008 for her discovery of the follicular helper T-cell (TFH) derivation of angioimmunoblastic T-cell lymphoma. Her current research is focused on exploring the molecular pathogenesis of NK/T-cell malignancies. Other interests include implementing and optimizing tools for the molecular diagnosis of hematological malignancies and other cancers. Dr. de Leval has authored more than 220 scientific publications and several chapters for reference textbooks in pathology and hematology. She is a member of several national and international scientific societies, member of the executive board and of the pathology group of the LYSA (the Lymphoma Study Association, France). She was elected member of the International Lymphoma Study Group in 2011, and corresponding member of the Belgian Royal Academy of Medicine.

SUMMARY OF THE PRESENTATION

In her talk she will present the main changes introduced in the recently revised WHO classification of lymphomas for neoplasms derived from T and NK cells. These represent a heterogeneous group of uncommon malignancies, accounting for less than 15% of all non-Hodgkin lymphomas worldwide, which are characterized by a usually aggressive clinical course, and important epidemiological variations in different parts of the world. She will review the recent high-throughput molecular and genomic profiling studies which have generated important changes and refinements of diagnostic criteria incorporated into the revised classification. Her presentation will focus on the most commonly encountered entitites, i.e. angioimmunoblasdtic T-cell lymphomas and other lymphomas of follicular helper T-cell derivation, anaplastic large cell lymphomas, peripheral T-cell lymphoma not otherwise specified, and selected extranodal non-cutaneous lymphomas. The practical implications of the revised diagnostic criteria will be emphasized. She will also discuss newly recognized entities consisting of indolent clonal T-cell lymphoproliferative disorders.

FRIDAY

Gastro-enterological Pathology

Chairs: Anne HOORENS and Laurine VERSET

Slide seminar on benign and malignant primary liver tumours

DR. QUITTERIE FONTANGES
Erasme University Hospital

DR. LAURINE VERSET
Erasme University Hospital

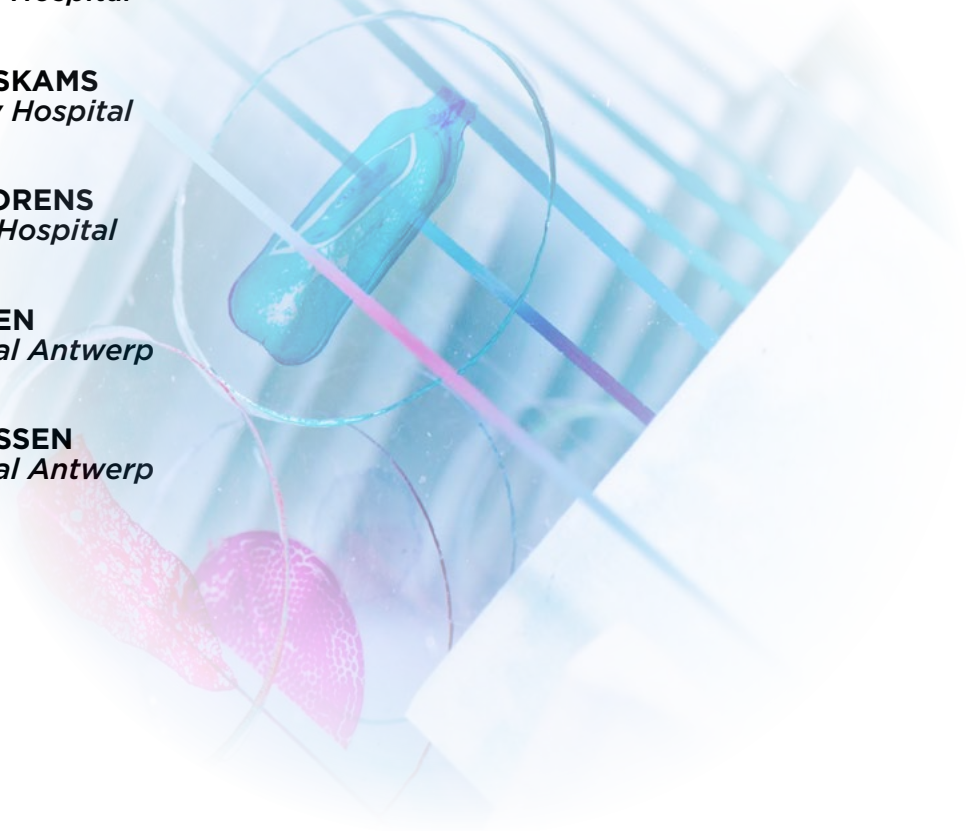
DR. MATTHIAS VANHAELE
Leuven University Hospital

PROF. TANIA ROSKAMS
Leuven University Hospital

PROF. ANNE HOORENS
Ghent University Hospital

DR. LOTTE KEULEN
University Hospital Antwerp

PROF. ANN DRIESSEN
University Hospital Antwerp



Lung Pathology

Chairs: Karl D'HAENE and Myriam REMMELINK

Interstitial lung disease

DR. SABINA BEREZOWSKA

EDUCATION & RELATED TRAINING EXPERIENCES

Dr. Berezowska serves as a consultant at the Institute of Pathology of the University of Bern since 2014, where she is head of the diagnostic and research group on non-neoplastic and neoplastic lung diseases. She was a visiting scholar in Ann Arbor, MI, in 2015, and is a member of national and international pathology groups focusing on thoracic pathology.

Interstitial lung disease

DR. ALEXANDER PÖLLINGER

EDUCATION & RELATED TRAINING EXPERIENCES

Dr. Pöllinger serves as a consultant and is head of Thoracic Imaging, Department of Diagnostic, Interventional and Pediatric Radiology, Inselspital, Bern University Hospital, Switzerland. His research interest comprises imaging of various lung diseases with emphasis on fibrosis, emphysema and lung cancer both by computed tomography and by magnetic resonance imaging.

SUMMARY OF THE PRESENTATION

Multidisciplinary discussion (MDD) is firmly established as the gold standard in the diagnosis of interstitial lung diseases (ILD). In this presentation, we want to focus on the importance of pathological-radiological correlations in the diagnostic process. Exemplified by cases from the diagnostic routine, we will demonstrate the diagnostic criteria of selected entities. Most importantly, we aim to show when the radiological picture truly matters for rendering a valid pathological diagnosis.

Dear Colleagues,

During the 2018 BWP, Professors Dr Berezowska and Dr Pöllinger will give a lecture on Interstitial Lung Disease on Friday 19/10/2018 at 16.00. Digital images of the 6 cases 01,03,07,09,15 and 17 are now on-line available for personal study and preparation. Please visit the site via link : https://www.iap-bonn.de/series/diagnostik-interstitieller-lungenerkrankungen-im-multidisziplinaeren-team/?cat=481 or QR-code.

FRIDAY

KEY NOTE Lecture Dermatopathology

Chairs: Sofie DE SCHEPPER and David CREYTENS

Ten mistakes to avoid in the diagnosis of melanomas and naevi

PROF. WOLTER MOOI

EDUCATION & RELATED TRAINING EXPERIENCES

W.J. (Wolter) Mooi was born in Groningen, 1956. After studying medicine at the University of Leiden, and pathology at the Universities of Amsterdam and London, Wolter obtained his registration as consultant pathologist and his PhD degree (University of Amsterdam) in 1986. He joined the Netherlands Cancer Institute as research fellow, consultant pathologist and head of the Department of Pathology. Professorships at the VU University Amsterdam (1991) and the Erasmus University of Rotterdam (1996) followed. After a period of four years as head of department at Erasmus University Rotterdam, Wolter went back to Amsterdam, where is was appointed professor of pathology at the University of Amsterdam and, for the second time, at the VU University of Amsterdam, where he is now stationed and divides his time between surgical pathology, undergraduate teaching and research.

Wolter is (co-) author of 184 peer-reviewed articles, 3 monographs and numerous chapters on various topics of melanocytic and pulmonary pathology. He is laureate of various pathological societies, and in 2011 he was chosen, among 2000 competitors, as teacher of the year of VU University Amsterdam.

KEY NOTE Lecture Dermatopathology

Chairs: Sofie DE SCHEPPER and David CREYTENS

SUMMARY OF THE PRESENTATION

It goes without saying that misdiagnosis of melanomas and naevi carries significant and potentially grave negative consequences for the patient. Failure to recognize melanoma is amongst the mistakes most dreaded by pathologists.
How should one minimize the chance of falling into the trap of missing the diagnosis of melanoma? Some practical general advice, based on a significant number of cases I have seen in consultation during the past three decades, will be provided in the lecture.
To summarize these:

- Do not issue an unequivocal diagnosis of naevus on the basis of a small, traumatized specimen, especially when detailed clinical information is lacking;
- Encourage your clinical colleagues to provide detailed information (patient characteristics; lesion characteristics including site; size; shape; delineation; colour - or colours; changes in time or other relevant aspects of the history of the lesion; dermatoscopic features; if possible: photographic information) ;
- Embed the pigmented lesion entirely; do not limit yourself to one central block ;
- Always allow yourself the 20-30 extra seconds to investigate each naevus at low, intermediate and high power ;
- Pay extra attention to areas of biopsy trauma, which appear least inviting to dwell on in detail ;
- Do levels in each instance the histology is not that of a completely banal naevus ;
- Investigate difficult cases at your leisure; do not yield to pressure to issue a diagnosis when you are not ready to do so ;
- Use detailed knowledge on naevus and melanoma subtypes, since diagnostic criteria cannot be consistently applied across the entire spectrum of naevus and melanoma subtypes ;
- Consult colleague pathologists inside or outside your department whenever you feel unsure or whenever you intend to issue a verdict of 'uncertain malignant potential' ;
- Don't accept a 'panel diagnosis' if you are unhappy with it.

Most initially underdiagnosed melanomas that I have reviewed, came with a very brief microscopic description, which strongly suggests that the pathologist did not realize the difficulty of the case. However, at review, most of these underdiagnosed melanomas could be recognized for what they were. The most common mistake appears to be made in a matter of seconds, rather than after mature consideration.

12.00-12.40

Educational Symposium

Auditorium 1

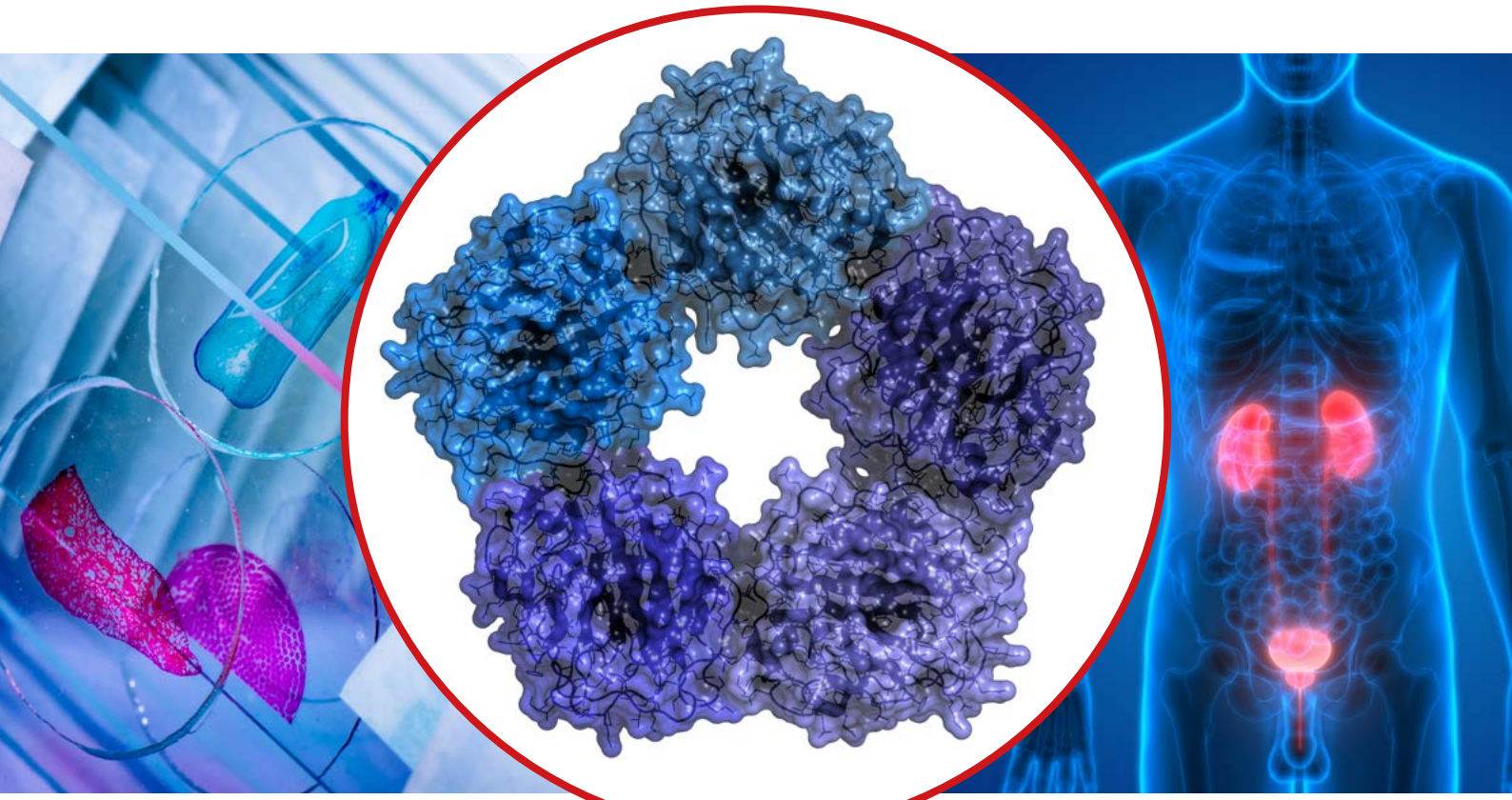
Immuno-oncology in the field of Urological Cancer

Biomarkers in GU cancers (PD-L1)

Dr. Thomas GEVAERT

Immuno-therapy for GU cancers

Dr. Jan VAN DEN BRANDE



Organised thanks to the Educational Grant

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Cytology

Chairs: Birgit WEYNAND and Christine GALANT

HPV-based screening implementation in the Netherlands: knowns and unforeseens
Cervical cytology: case presentations

PROF. FOLKERT VAN KEMENADE

Professor Folkert van KEMENADE has been head of the anato-mo-pathology department in Erasmus MC since March 2013. Before that, he worked as a pathologist in VUmc during 14 years. (Specialized in endocrinology, cytopathology and orthopedics)

He was more than 12 years regional coordinating pathologist for the region Middenwest regarding 0cervical cancer screening and involved in the trials of the research group HPV (pathology VUmc) with trials such as Pobascam, Vusascreen and Prohtect trials.

He has written about 80 publications and acquired with Prof. GA Meijer and Lucy Overbeek a large BBMRI project for the Dutch National Tissue Portal (RB 8 in 2012).

Cytology

Chairs: Birgit WEYNAND and Christine GALANT

Milan classification of salivary gland tumors

PROF. PHILIPPE VIELH

Dr. Philippe Vielh directed the Cytopathology Unit at Institut Curie (Paris, France) for 13 years before moving to Gustave Roussy Comprehensive Cancer Center (Villejuif, France) where he headed the Cytopathology Unit from 2003 until 2015, the Histo-Cytopathology unit of the Translational Research Laboratory (2007-2014), and the Institutional Biobank (2011-2014). He presently works at the Laboratoire National de Santé (Dudelange, Luxembourg) where he is in charge of Cytopathology and Molecular pathology. He is Professor of Pathology affiliated at the faculty of Medicine of the University of Porto (Portugal) since December 2017.

Dr Vielh is interested in the study of omics of breast and thyroid tumors and has authored more than 300 articles in peer-reviewed journals, 6 books and 22 book chapters.

Philippe Vielh is the series' Editor of the Karger collection of books entilted "Monograph in Clinical Cytology". He is on the editorial board and reviews for Diagnostic Cytopathology, Cancer Cytopathology, Acta Cytologica, Journal of the American Society of Cytology, Journal of Pathology and Translational Medicine, Cytopathology, and Cytojournal. He holds a number of national and international society memberships including the fellowship of the International Academy of Cytology (FIAC). He served as the President of the French Society of Cytology (SFCC) for 9 years (1996-2006), had chaired the 31st European Congress of Cytology in 2005 (Paris, France) and served as Secretary General of the European Federation of Cytology Societies (EFCS) from 2005-2012. He recently chaired the 18th International Congress of Cytology (May 2013 in Paris), served as President of the International Academy of Cytology (IAC) from May 2013 until June 2016 and is now IAC Past-President.

Philippe is the recipient of the 2007 L.C. Tao "Educator of the Year" award given by the Papanicolaou Society of Cytopathology and the Maurice Goldblatt 2016 Award given by International Academy of Cytology (IAC).

Belgian Week of Pathology. October 20, 2018.

The Milan System for Reporting Salivary Gland Cytopathology.
Philippe Vielh MD, PhD, FIAC

Department of Anatomic and Molecular Pathology National Laboratory of Health, Dudelange, Luxembourg.

In the absence of a uniform classification for reporting salivary-gland fine-needle aspiration and tiered diagnostic framework limiting the overall effectiveness of the test, we organized a task force of cytopathologists, surgical pathologists and head and neck surgeons under the umbrella of the American Society of Cytopathology and the International Academy of Cytology.

The Milan System for Reporting salivary Gland Cytopathology initiative was planned to consist of a limited number of categories, with clear definitions that most cytopathologists can apply in daily practice, associated with an implied risk of malignancy based up evidence from the existing literature paired with a clinical management algorithm.The six diagnostic categories with recommendations as well as their corresponding risk of malignancy and suggested management will be presented.

By addressing the critical need for a uniform and internationally accepted system for reporting salivary-gland fine-needle aspiration, it is hoped that this will lead to a better communication between cytopathologists and treating clinicians, between institutions, and result in overall improved patient care.

Urologic Pathology : testicular neoplasms

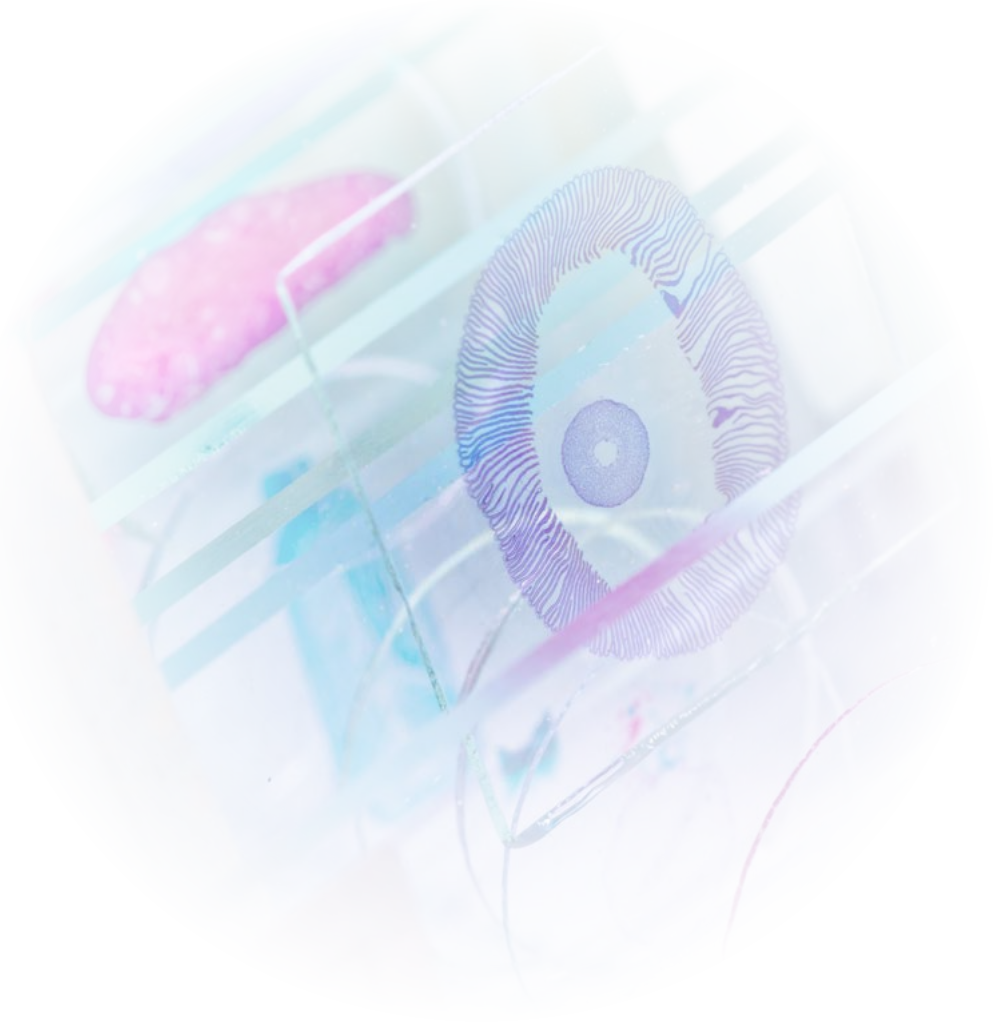
Chairs : Louis LIBBRECHT & Sandrine RORIVE

Clinical management of testicular tumors : from diagnosis to treatment

PROF. THIERRY ROUMEGUERE

Thierry Roumeguere currently is Head of Urology Department at Erasme hospital, Université Libre de Bruxelles. Thierry does research in Urology, Oncology and Andrology.

Skills and Expertise
Urologic oncologiy, Endourology, Laparoscopic urology, robotics & minimally invasive urology



Urologic Pathology : testicular neoplasms

Chairs : Louis LIBBRECHT & Sandrine RORIVE

Handling and Reporting of Orchidectomy Specimens with Testicular Cancer and Updates in the Eighth Edition of the TNM AJCC Cancer Staging Classification

PROF. EVA COMPERAT

Higher Education:

1984-1991	Studies of Medicine in Vienna
1991	Diploma of MD
1995	Diploma of General Practitioner
2000	Graduate of biological and medical science (Maîtrise de sciences biologiques et médicales, Université Paris VI)
2001	Master of biological and medical science (Diplôme des Etudes Approfondies, Université Paris VI)
2002	Diploma of Specialist of Pathology
2005	Assistant Professor
2006	PhD, Université Paris VII
2011	HDR (habilitation à diriger des recherches), Université Paris VI
2017	Full Professor
2016	Head of the Dpt Pathology, Hôpital Tenon, AP-HP, UPMC Paris VI
Since 2003	specialised in uropathology
Since 2010	consulting pathologist in CCAFU (Comité de cancerologie de l'Association Française d'Urologie) for bladder cancer
Since 2011	consulting Pathologist of NMIBC (non muscle invasive bladder cancer) and MIBC (muscle invasive bladder cancer) for EAU Guidelines
Since 2013	consulting Pathologist in penile carcinoma for EAU Guidelines

- Teaching since 2002 at the Université Pierre et Marie Curie (UPMC), Paris VI
- Teaching for the International Academy of Pathology (urinary cytology, bladder and prostate cancer, flat lesions of the bladder, testicular tumours)
- Coauthor of the 4th Ed WHO Tumours of the Urinary System and Male genital organs (Coauthor 4 chapters, responsible of 3 chapters)
- Attached to GRC (Groupe de recherche clinique) - UPMC n°5 ONCOTYPE-URO (Pr Cussenot)

SATURDAY

Urologic Pathology: testicular neoplasms

Chairs: Louis LIBBRECHT & Sandrine RORIVE

Seminoma and spermatocytic tumor

PROF. MAURIZZIO COLLECHIA

Maurizio Colecchia, MD, is Chief of the Uropathology Unit of the Department of Pathology at the Istituto Nazionale dei Tumori in Milan, Italy.

He is Chairman of the Italian Group of Uropathology (GIUP) branch of the Italian Society of Pathology and member of the European Society of Pathology (ESP).

Uropathology is the main field of interest. He has published more than 100 scientific publications and many contributions to textbooks.

He is in the Editorial Board of Pathologica and reviewer for journals including Human Pathology, Virchows Archiv, Histopathology, Analytical and Quantitative Cytology and Histology, Cancer Letter, International Urology and Nephrology, Tumori, Plos One, Pathology Research and Practice, International Journal of Surgical Pathology, The International Journal of Biological Markers

SATURDAY

SUMMARY OF THE PRESENTATION

Seminoma comprises 40–50 % of all GCTs. In white American men, its incidence has increased over the last 20 years by more than 60 %, whereas the incidence of NSGCTs has risen only by 24 % It occurs commonly between the ages of 25–50, with a peak incidence at about 34 years Seminoma is virtually nonexistent before puberty and it is rare in adolescence. About 10 % of seminoma patients have a history of cryptorchidism .

Macroscopically, small seminomas are homogeneous, well-circumscribed tumors, whereas large seminomas cause marked testicular enlargement ; the tunica albuginea is, however, mostly intact and the epididymis uninvolved. On section the tumor bulges above the testicular parenchyma and is lobulated and well circumscribed but without a capsule . The color is white to pinkish white or tan in cases with heavy lymphocytic infiltration. In large tumors, small necrotic areas and small dot-like hemorrhages are present, but large hemorrhagic, firm, or cystic areas are strongly suggestive of an NSGCT component. The typical microscopic pattern of seminoma shows lobules composed of a few dozen to roughly 100 cells, which are separated by thin fibrous septa. The cells resemble immature spermatogonia and are rather monomorphous. The cytoplasm is rich in glycogen and fat and therefore appears water-clear in formalin-fixed material . In well-fixed specimens, mitoses are abundant. More than 80 % of seminomas show lymphocytic infiltration (CD8+ and CD4+ T lymphocytes and some NK cells) ranging in appearance from uniform peppering or clumps scattered in stroma to formation of lymphoid follicles in about 18 % of cases . Macrophages and (in lesser amount) B lymphocytes are also present. Some 10 % of seminomas develop a marked noncaseating granulomatous reaction with epithelioid cells and a few Langhans-type giant cells (granulomatous seminoma.

The reaction is usually patchy but may involve the entire tumor. Beside this "classical" morphology, there are some variants . Because they do not have any prognostic or therapeutic importance, these variants have not been listed in the WHO classification. In pseudoglandular and tubular seminoma, tumor cells form small gland-like clefts. Accumulation of edematous fluid in interstitial tissue gives the tumor a microcystic or cribriform appearance. The name intratubular or interstitial seminoma derives from the predominant way the tumor cells spread . Also seminomas with a high mitotic rate (formerly anaplastic or atypical seminomas) are not considered as an entity in their own right because the high mitotic count does not negatively influence the course of the disease. Seminoma with syncytiotrophoblastic cells is a separate entity in the WHO classification. On H&E-stained slides, multinucleated giant cells are detected in about 7% of seminomas mostly close to vessels . The presenting complaint associated with seminoma is mostly testicular swelling, while about 10% of patients experience local discomfort and pain. Symptoms due to metastases include supraclavicular lymph node swelling and abdominal pain due to enlarged retroperitoneal lymph nodes, which can also obstruct the ureters and cause hydronephrosis.

Gynecomastia can be a symptom in patients affected by seminoma with syncytiotrophoblastic giant cells. The main unfavorable morphologic prognostic factors are a tumor diameter >3 cm and tumor pagetoid infiltration of the epithelium of the rete testis or the rete testis stromal infiltration, whereas vascular invasion is prognostically not as important as in NSGCTs . Following inguinal orchiectomy, the management options for patients with stage I seminoma are initial surveillance or adjuvant treatment. The recommendation for patients with two risk factors (tumor size and rete testis invasion) is treatment with carboplatin, while for patients with 0–1 risk factor, surveillance is recommended. Orchiectomy alone cures 80% of seminomas and 70% of non-seminomas, and standard care has increasingly shifted to active surveillance. Stage I seminomas have a 13–19% rate of relapse. Adjuvant radiation to the retroperitoneal lymph nodes was standard care, but has been largely abandoned.

Spermatocytic tumor

In 1946 the renowned French-Canadian pathologist Pierre Masson described a novel GCT composed of tumor cells with filamentous nuclear chromatin resembling spermatocytes and therefore named it "spermatocytic seminoma". In the 2016 WHO classification, the name has been changed to "spermatocytic tumor" (ST) to stress the fact that this tumor is not a variant of seminoma . However, it does not originate from spermatocytes but from spermatogonia. The pathogenesis seems to be quite different from that of the other GCTs because ST does not develop from the CIS precursor and the common chromosomal aberration i(12p) is missing. Moreover, it is the only GCT that does not occur in the ovary . ST is an extremely rare tumor and accounts for only 0.61% of all GCTs. The incidence is 0.3/1 million in men younger than 55 years of age and 0.8/1 million in older men . With an average age of 55 years, patients are older than those with seminoma. Young age, even under 30 years, is therefore not an exclusion criterion for this diagnosis. There are no known risk factors for ST, not even cryptorchidism. There are also no differences in incidence between races.

Because of the gelatinous and mucinous cut surface and/or the presence of small mucoid unique and would permit a diagnosis "at first glance." The tumors are usually rather large with a mean diameter of 4–5 cm, but sizes up to 15 cm have been reported. ST is microscopically composed of three distinct cell types : medium-sized cells (diameter, 15–20 μm) with a rather regular, round nucleus ; small cells (diameter, 6–8 μm) resembling lymphocytes ; and scattered single mono- or multinucleated giant cells (diameter, 50–150 μm) whose nuclei have coarse chromatin similar to the spireme of spermatocytes in meiotic division.

The main part of the tumor shows an expansive growth pattern, and the surrounding tubules are greatly extended and filled with neoplastic cells . In contrast to other GCTs, no CIS can be detected in the adjacent tubules ; they may show completely normal spermatogenesis with m ture spermatozoa. The stroma is inconspicuous and there are no lymphocytic infiltrates. Large edematous areas similar to those of microcystic seminomas are also often observed. So far 18 cases of ST combined with sarcoma have been described. In contrast to ST, ASS contains only the medium sized cell type characterized by large nucleoli, causing the cells to resemble those of an EC. Moreover, mitotic activity is brisk and areas of necrosis are frequently observed, and there are usually many apoptotic tumor cell.

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Prof. Dr. W. Glenn McCluggage, Belfast, UK

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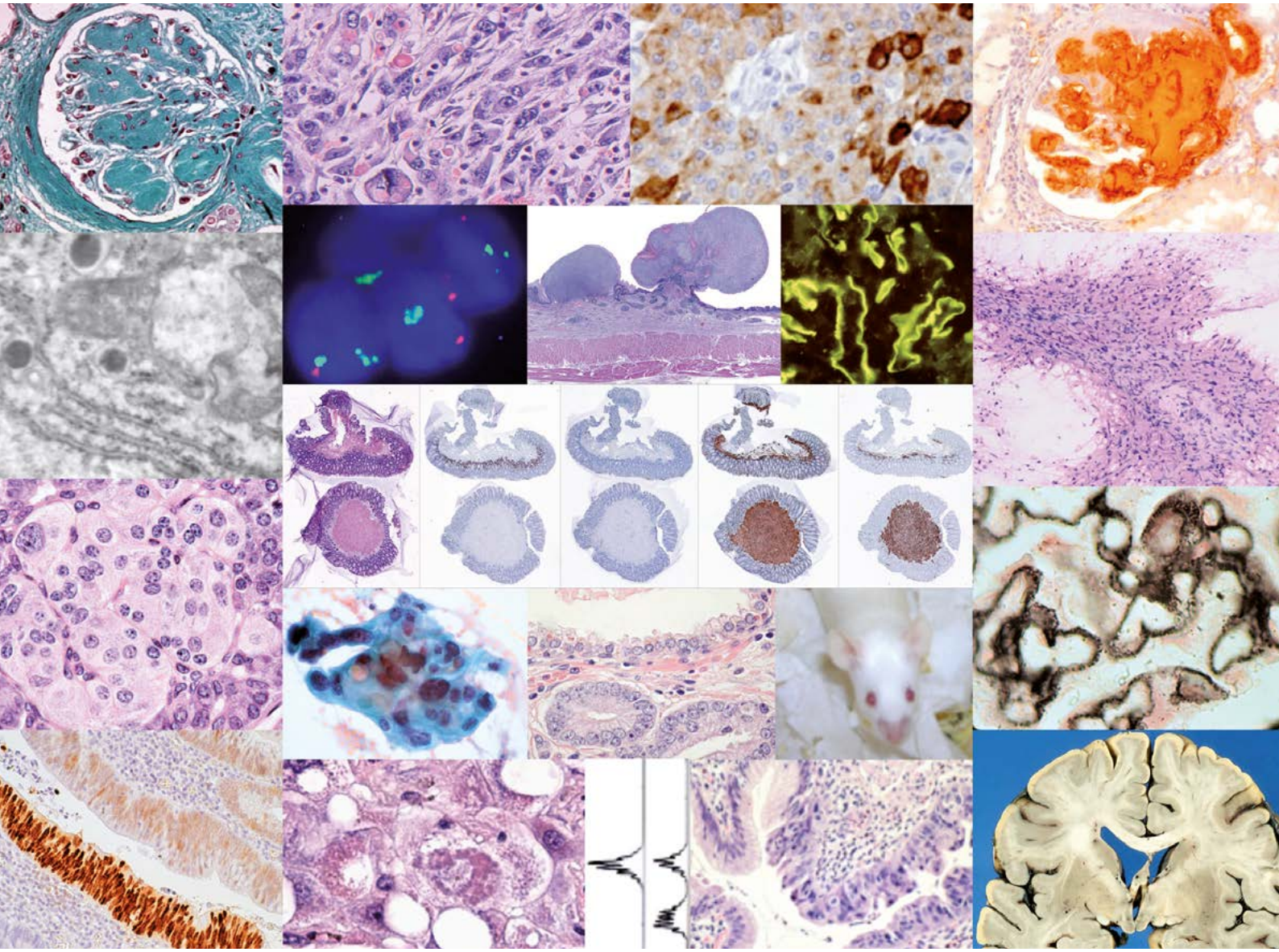

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Molecular Pathology

Chairs: Nicky D'HAENE and Isabelle VAN DEN BEMPT

DNA repair in cancer: a new target

PROF. DIETHER LAMBRECHTS

Bio-Ir.: Univ. of Leuven, Leuven, Belgium, 1999
PhD: Univ. of Leuven, Leuven, Belgium, 2003
Postdoc.: Vesalius Research Center, Univ. of Leuven, Leuven, Belgium, 2003-07
Postdoc.: Wellcome Trust Center, Oxford, UK, 2007
VIB Group leader since January 2008
VIB Acting director 2015-2016
VIB Science Director since 2017

Laboratory of Translational Genetics (LTG) at the VIB-KU Leuven Center for Cancer Biology headed by Prof. Diether Lambrechts is interested in the discovery of genetic or epigenetic markers, either as susceptibility factors for cancer development, as prognostic markers to improve the molecular genetic annotation of cancer or as predictive markers for targeted cancer therapies. In particular, our main interest lies in understanding which (epi)-genetic factors modulate hypoxia-driven tumorigenesis or predict response to therapies targeting hypoxia-driven oncogenesis, such as anti-angiogenic therapies.

One of our main research topics is to investigate how hypoxia influences the cancer epigenome, possibly by regulating TET hydroxylase activity and affecting DNA demethylation. Notably, TET hydroxylases belong to the same family of dioxygenases as the PHDs, which target hypoxia-inducible factors for degradation and are considered key mediators of the hypoxic response.

Dermatopathology : Melanocytic tumors

Chairs : Sofie DE SCHEPPER and David CREYTENS

Biphenotypic naevi: tumour progression that does not indicate malignancy

PROF. WOLTER MOOI

EDUCATION & RELATED TRAINING EXPERIENCES

W.J. (Wolter) Mooi was born in Groningen, 1956. After studying medicine at the University of Leiden, and pathology at the Universities of Amsterdam and London, Wolter obtained his registration as consultant pathologist and his PhD degree (University of Amsterdam) in 1986. He joined the Netherlands Cancer Institute as research fellow, consultant pathologist and head of the Department of Pathology. Professorships at the VU University Amsterdam (1991) and the Erasmus University of Rotterdam (1996) followed. After a period of four years as head of department at Erasmus University Rotterdam, Wolter went back to Amsterdam, where is was appointed professor of pathology at the University of Amsterdam and, for the second time, at the VU University of Amsterdam, where he is now stationed and divides his time between surgical pathology, undergraduate teaching and research.

Wolter is (co-) author of 184 peer-reviewed articles, 3 monographs and numerous chapters on various topics of melanocytic and pulmonary pathology. He is laureate of various pathological societies, and in 2011 he was chosen, among 2000 competitors, as teacher of the year of VU University Amsterdam.

Dermatopathology

Chairs: Sofie DE SCHEPPER and David CREYTENS

Biphenotypic naevi: tumour progression that does not indicate malignancy

Wolter J. Mooi

A sudden change of a previously stable naevus it a clinical warning sign that may point to malignant transformation, and usually leads to the removal of the naevus for histology.

In some instances the cause is immediately apparent: it may be a folliculitis within or below the naevus, or there may be a halo response (Sutton naevus) or spongiotic dermatitis (Meyerson naevus) - that generally affects the entire naevus. In some instances however, there is a morphologically divergent melanocytic population within the naevus, which raises concern on histological grounds as well. In any melanocytic lesion, the conclusion that the least atypical part is an entirely banal naevus, does not mean that another part may not in fact be melanoma.

In recent decades, it has become obvious that malignant transformation is never a one-step phenomenon. Rather, it results from the presence of multiple mutations affecting key regulatory systems of the cell that impact on, amongst others, cell cycle regulation, induction of apoptosis and the senescence response, and a number of other key features of cellular behaviour (Hanahan and Weinberg, Cell 2011). It is self-evident that within a neoplastic cell population in which ultimately, such a fully malignant subpopulation has emerged, there must be many other cell populations that have acquired some, but not all, required driver mutations that result in the malignant phenotype. In addition, one can expect that such populations show a morphological phenotype that diverges in some aspects from the 'parent' population that harbours less mutations.

In sum, one would expect that some features of tumour progression, all within a lesion that in its entirety is not biologically malignant, would result in a phenotypically divergent part. The emergence of the new subclone may indeed be noted clinically, in the way mentioned above.

In melanocyte pathology, a few examples of this phenomenon have now been identified. These include the combined naevus (with deep penetrating naevus-component) and the 'BAPoma' / MBAIR (melanocytic BAP1-assiated intradermal tumour), both of which feature an entirely banal naevus component, often but not always pushed to the side of the naevus, and a divergent component that is a little more of a struggle to diagnose: deep penetration with retention of pigment production, a large cell type and some mitotic activity in deep penetrating naevus; large cell type in all levels associated with occasional mitotic figures, and similar absence of 'maturation' in MBAIT. Both lesions have now been shown to be associated with additional mutations leading to β-catenin increase in DPN and BAP1 function loss in MBAIT. A third example is the – often multiple – emergence of proliferative nodules in some congenital naevi.

It is likely that many more melanocytic naevi that show some architectural or cytological irregularities that pathologists have difficulty with, but ultimately consider to be benign, fall into similar, as yet unspecified, categories of biological benign melanocytic neoplasms with a limited set of mutations that exceeds that of the entirely banal melanocytic naevus, and is benign nonetheless.

Dermatopathology : Melanocytic tumors

Chairs : Sofie DE SCHEPPER and David CREYTENS

Signatures in melanoma

PROF. JOOST VAN DEN OORD

Anatomo-Pathologist in UZ Leuven
Specialized in Dermatopathology and Ocular Pathology

SATURDAY

Dermatopathology : Melanocytic tumors

Chairs : Sofie DE SCHEPPER and David CREYTENS

Melanocytic tumours : on the MAPKinase road again !

DR. INGRID FERREIRA

Anatomo-Pathologist in Clinique Notre-Dame de Grâce,
Gosselies, Belgium

Dermatopathology : Melanocytic tumors

Chairs : Sofie DE SCHEPPER and David CREYTENS

Bridging genetics, dermoscopy and pathology (new WHO classification)

DR. MARC HASPESLAGH

Dr. M. Haspeslagh is founder and director of the private dermatopathology lab 'Dermpat' in Ghent. He also works as a consultant dermatopathologist in the department of Dermatology of the University Hospital of Ghent.

Dr. Haspeslagh finished his education in general medicine, pathology and clinical genetics at the University Hospital of Louvain. After working for more than 20 years as a general surgical pathologist in the city hospital of Roeselare, he developed a specific interest in dermatopathology and obtained the International Dermatopathology Board certification in 2005. Since 2011, he works as a full time dermatopathologist in Dermpat.

In 2018, Dr Haspeslagh defended his PhD thesis on a new method of processing skin biopsies with 'ex vivo dermoscopy and derm dotting'. His main interests are syndromic skin disease and pigment lesions of skin, with specific interest for the correlation between dermoscopy and morphology. His current research is focused on the dermoscopic-pathologic subclassification of flat nevi.

NOTES

ORAL PRESENTATIONS

P 01	De Brabander I, Denolf P, Lambein K, Fabri V, Van Damme N, Floris G, Colpaert C, Neven P (On behalf of the Belgian Working Group for Breast Pathology)	Management of breast lesions of uncertain malignant potential: a Belgian retrospective study.
P 02	Kuijpers CJH, van den Heuvel MM, Overbeek LIH, van Lindert ASR, Damhuis RAM, Willems SM	Laboratory variation of molecular testing in metastatic lung cancer in the Netherlands.
P 03	Ramman L, Van der Eecken K, Van der Linden M, Surmont V, Vermaelen K, Demedts I, Himpe U, Dedeurwaerdere F, Lievens Y, Ferdinande L, Dheedene A, Menten B, Van Dorpe J	Copy number alterations derived from liquid biopsies support lung cancer subtyping.
P 04	Lemaire E, Schmidt C, Delbecque K, Dubois N, Denooz R, Charlier C, Delvenne P	Combination of postmortem redistribution aspects with pathological findings in drugs-related deaths.

P 01

MANAGEMENT OF BREAST LESIONS OF UNCERTAIN MALIGNANT POTENTIAL: A BELGIAN RETROSPECTIVE STUDY

De Brabander I[1], Denolf P[1], Lambein K[2], Fabri V[3], Van Damme N[1], Floris G[4], Colpaert C[5], Neven P[6] (on behalf of the Belgian Working Group for Breast Pathology)

1. Belgian Cancer Registry, Brussels, Belgium 2. AZ St Lucas Hospital Ghent, Department of Pathology, Ghent, Belgium 3. Intermutualistic Agency, Brussels, Belgium 4. KU Leuven, University Hospitals Leuven; Department of Imaging and Pathology; Laboratory of Translational Cell & Tissue Research; Department of Pathology, Leuven, Belgium 5. Laboratory for Pathological Anatomy PA[2], Antwerp, Belgium 6. KU Leuven, University Hospitals Leuven; Department of Oncology; Department of Obstetrics and Gynaecology, Leuven, Belgium

Background and objective

A more conservative approach for the management of breast lesions of uncertain malignant potential (B3-lesions), diagnosed on core needle (CNB) or vacuum assisted biopsy (VAB), is recommended according to recent international guidelines. Instead of open surgical excision, therapeutic excision by vacuum-assisted biopsy, followed by surveillance imaging is stated to be sufficient for most B3-lesions. We evaluated the current practice in Belgium by calculating surgical open excision rates and upgrade risks after a B3-lesion diagnosis.

Methods

The Belgian Cancer Registry collects the pathology results of all breast specimens in the Cyto-histopathological data base. These data are completed with reimbursement data from the Health Insurance Companies, related to diagnostic and therapeutic procedures. We selected all B3-lesions diagnosed on CNBs and VABs from 2013 and 2014 in Belgian women aged 48-72 years. We calculated the open surgical excision rate within 6 months after diagnosis and the upgrade risk to ductal carcinoma in situ (DCIS) or invasive breast cancer.

Results

A high open surgical excision rate of 50% for all B3-lesions diagnosed on CNB (n=686) and 45% for those diagnosed on VAB (n=414), was observed. The overall upgrade rate was 21% (10% to DCIS, 11% to invasive carcinoma) for B3-lesions diagnosed on CNB and 17% (12% to DCIS and 5% to invasive carcinoma) after diagnosis on VAB. Upgrade rates for each different B3-lesion morphology diagnosed on CNB ranged from 10% to 52% while it varied from 0% to 24% for VAB lesions.

Conclusions

Open surgical excision is commonly used as a therapeutic intervention for B3-lesions in Belgium. More data are necessary to assess upgrade rates for different B3-lesion morphologies in order to evaluate guidelines for management of B3-lesions. A pathological review of upgraded lesions next to further follow-up of the study cohort may reveal additional predictors for upgrade risk.

L 02

LABORATORY VARIATION OF MOLECULAR TESTING IN METASTATIC LUNG CANCER IN THE NETHERLANDS

Kuijpers CJH[1,2], van den Heuvel MM[3], Overbeek LIH[2], van Lindert ASR[4], Damhuis RAM[5], Willems SM[4,2]

1. University Medical Centre Utrecht, Utrecht 2. Foundation PALGA, Houten, the Netherlands 3. Radboud UMC, Nijmegen, the Netherlands 4. University Medical Centre Utrecht, Utrecht, the Netherlands 5. Netherlands Comprehensive Cancer Organisation, Utrecht, the Netherlands

Background and objective

Adequate and timely testing for molecular alterations in non-small cell lung cancer (NSCLC) is necessary for the best possible treatment, to enable treatment with tyrosine kinase inhibitors (TKI) when a certain mutation/rearrangement is present. We aimed to assess the performance of molecular testing for EGFR and/or KRAS mutation, ALK and ROS rearrangement in a Dutch cohort of metastatic non-squamous (ns)-NSCLC on a nationwide basis.

Methods

All stage IV ns-NSCLC from 2013 and 2015 were identified from the Netherlands Cancer Registry, and matched to the Dutch Pathology Registry (PALGA). Using information extracted from pathology reports, proportions of tumors tested for EGFR and/or KRAS and ALK, and in 2015 also for ROS, within 3 months after diagnosis, were determined, and variation between 48 laboratories was assessed.

Results

In total, 6,619 tumors were included (2013: N=3,195; 2015: N=3,424). EGFR and/or KRAS testing was performed for 73.1% of the tumors in 2013 (variation between laboratories 30.6-91.7%) and was significantly higher in 2015: 78.9% (40.0-91.0%). Of the tumors without EGFR and KRAS mutations (EGFR/KRASwt), 49.5% underwent ALK testing in 2013 (6.3-100%) and 77.4% in 2015 (32.5-100%), which was significantly higher. ROS testing was performed for 50.9% (0-100%) of the EGFR/KRASwt tumors from 2015. In 2015, 6, 7 and 13 laboratories tested significantly less often for EGFR/KRAS, ALK and ROS, respectively, than the national proportion. Insufficient tissue was the most stated reason for not testing.

Conclusions

Although the proportions of EGFR and ALK tested tumors were significantly higher in 2015, still in some laboratories/hospitals improvement remains possible, as part of the patients were denied the possibility and advantages of TKI. In a planned "sharing best practice session" with laboratories with highest testing proportions, we aim to identify a process for the best possible flow (in turnaround times) and the highest possible testing proportions.

L 03

COPY NUMBER ALTERATIONS DERIVED FROM LIQUID BIOPSIES SUPPORT LUNG CANCER SUBTYPING

Ramman L[1], Van der Eecken K[1], Van der Linden M[1], Surmont V[2], Vermaelen K[2], Demedts I[3], Himpe U[3], Dedeurwaerdere F[4], Lievens Y[5], Ferdinande L[1], Dheedene A[6], Menten B[6], Van Dorpe J[1]

1. Department of Pathology, Ghent University, Ghent University Hospital, Ghent, Belgium 2. Department of Respiratory Medicine, Ghent University, Ghent University Hospital, Ghent, Belgium 3. Department of Respiratory Medicine, AZ Delta, Roeselare, Belgium 4. Department of Pathology, AZ Delta, Roeselare, Belgium 5. Department of Radiation Oncology, Ghent University, Ghent University Hospital, Ghent, Belgium 6. Center for Medical Genetics Ghent, Ghent University, Ghent University Hospital, Ghent, Belgium

Background and objective

Recent advances in personalized medicine have made it crucial to distinguish lung cancer subtypes prior to treatment. As the necessity of tumor tissue is intrinsically associated with possible procedural complications, the use of liquid biopsies could form an attractive alternative for the latter invasive approach.

Copy number alterations are known to correlate with cancer histology to at least some level. Concerning adenocarcinoma, squamous cell carcinoma and small-cell carcinoma, our study investigates the predictive potential of liquid biopsy derived aberrations for lung cancer subtyping across 31 high stage patients.

Methods

Low-depth whole-genome sequencing of cell-free (tumor) DNA enables copy number alteration prediction in an economic feasible manner. Novel bioinformatics pipelines and established statistical and predictive modeling techniques essentially enable the analyses in this study.

Results

We demonstrate that copy number profiles from formalin-fixed paraffin-embedded tumor biopsies are often well-represented by their liquid counterpart. Plasma genomic abnormality analysis reveals less abnormalities in adenocarcinomas compared to squamous cell and small-cell carcinomas. Importantly, aberrant liquid biopsies exhibit multiple typical deviations reflecting the original classification. This could be confirmed by regression modeling, using public training data and previously published prognostic features, which realizes an accuracy of 95% for lung cancer subtyping on samples with detectable tumor content.

Conclusions

Investigating the potential of cell-free copy number alterations for lung cancer subtyping, which is to our knowledge never evaluated on liquid biopsies until now, proves to be promising. Additional larger studies are necessary and could contribute to improved statistical and clinically useful models.

L 04

COMBINATION OF POSTMORTEM REDISTRIBUTION ASPECTS WITH PATHOLOGICAL FINDINGS IN DRUGS-RELATED DEATHS.

Lemaire E[1], Schmidt C[2], Delbecque K[1], Dubois N[3], Denooz R[3], Charlier C[3], Delvenne P[1]

1. Department of Pathology, University Hospital - CHU Sart Tilman, Liège, Belgium 2. Department of Pathology, University of Michigan, Ann Arbor, Mi, USA 3. Medico-legal Toxicology Laboratory, University Hospital - CHU Sart Tilman, Liège, Belgium

Background and objective

Postmortem redistribution (PMR) of drugs contributes to blood concentration variations after death, and combination of toxicological with pathological findings is required to determine cause of death (COD). Femoral vein is the gold standard postmortem sampling site; however, popliteal vein had never been explored so far. Drugs-related pathological findings may be specific or not. The goal is to demonstrate that a multi-sites approach of PMR in combination with pathological findings is useful in assessing COD.

Methods

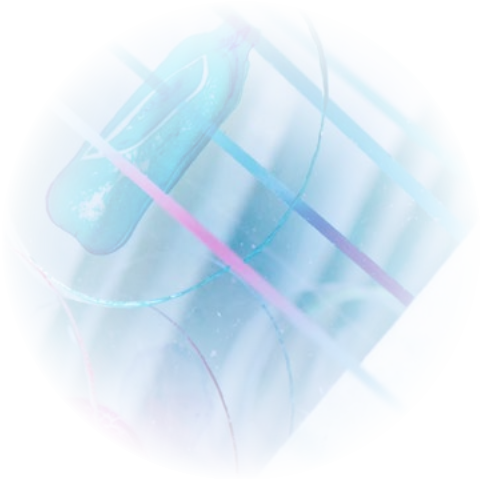
There were 24 autopsied cases, sampled as follows: intracardiac blood (ICB), subclavian blood (SCB), femoral blood (FB) and popliteal blood (PB). Selected substances (diazepam, methadone and morphine) were sampled in all sites whereas a complete drug screening was concomitantly performed on FB. Microscopic exam was systematically done on heart, lungs, liver, and kidneys; other organs were analyzed depending on macroscopic findings. PMR of selected substances was assessed according following mean concentrations ratios: ICB/FB, ICB/PB, SCB/FB, SCB/PB, and FB/PB; the greater the ratio, the greater the extent of PMR. Pathological and toxicological findings were combined to determine COD.

Results

Toxicological results indicate that popliteal site is less subject to PMR according to mean FB/PB ratios. Pathological findings are mostly nonspecific in 16 cases where toxicological results suggest obvious intoxication. In 4 cases with equivocal toxicological findings, nonspecific pathological findings are observed, but considering PB instead of FB concentrations allows clarifying COD. In 4 cases, COD is natural according to both findings, but PB concentrations still allows helping to confirm COD.

Conclusions

Our study is the first to suggest a multi-sites PMR assessment, including popliteal site, in combination with pathological findings in order to establish COD in drug-related fatalities, and shows that the interpretation of toxicological findings alone, especially with FB instead of PB concentrations, may lead to confusion in determining COD.



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L05

MASS SPECTROMETRY IMAGING OF NEUROPEPTIDES IN FFPE MATERIAL. A PROMISING APPROACH TO PATHOLOGY?

Ramael M[1], Sciot R[2], Porta T[3], Paine M[3], Verhaert MA[2], Ramael M[1], Verhaert PD[3,4]

1. University of Antwerp, Antwerp, Belgium 2. Gasthuisberg University Hospital, Leuven, Belgium 3. Maastricht Multi-Modal Molecular Imaging (M4i) Institute, Maastricht University, Maastricht, Netherlands 4. ProteoFormiX, Beerse, Belgium

To analyze secretory peptides in formalin-fixed, paraffin-embedded (FFPE) tissues, we applied an innovative mass spectrometry imaging (MSI) method. We designate this method Mass Spectrometry Histochemistry (MSHC) in analogy to immunohistochemistry (IHC). We will present data illustrating [1] MSHC validation in human clinical tissue and [2] the potential of MSHC for discovery of candidate biomarkers on histopathological sections of carcinoids.

Originally developed on tissues of a model organism, using a linear ion trap (IT)-orbitrap system custom fitted with a MALDI source, we further evaluated MSHC on genuine human clinical material, using commercial highly sensitive MALDI MS systems, including TOF(TOF), FTICR, and IT-TOF. Validation experiments were performed on FFPE blocks of human pituitary by IHC as well as tandem MS.

A small tissue microarray was constructed, including 5 cores of colon carcinoids and 2 cores representing non-cancerous colon mucosa, for preliminary MSHC screening. Sections (10 μm) were produced with a microtome and processed for top-down (i.e. trypsin-free) MSI, by deparaffinization and coating with dihydroxybenzoic acid (DHB, MALDI matrix). MSHC analysis was performed at a spatial resolution of, depending on the tissue size, between 5 and 25 μm.

MSHC data representing the neuropeptides oxytocin (OT) and vasopressin (AVP) were clearly confined to the neurohypophysis parts of the pituitary sections, as confirmed by H&E examination. IHC with anti-OT and anti-AVP antibodies perfectly agreed with the specific MSHC localization of OT and AVP mass peaks. Furthermore, tandem MS fragmentation analysis by collision-induced dissociation confirmed the peptides' sequences.

Preliminary data on carcinoids seem to suggest that several peptide-like MS peaks correlate with the tissue microarray cores representing cancer, whereas others appear more abundant in the 'healthy' gut.

We conclude that MSHC has exciting potential to unveil secretory peptide molecular information locked in the countless materials stored in FFPE biobanks of hospitals worldwide.

L 06

MACHINE LEARNING-BASED EXTRACTION OF EGFR RESULTS FROM PATHOLOGY REPORTS.

Van Damme N[1], Macq G[1], Pironet A[1], Henau K[1], Van Eycken L[1]

1. Belgian Cancer Registry, Brussels, Belgium

Background and objective

The Belgian Cancer Registry (BCR) annually receives over 250,000 pathology protocols describing results of (pre-)malignant specimens. In the case of non-small cell lung cancer, these protocols can contain information concerning the assessment of epidermal growth factor receptor (EGFR) expression and mutation. To expand the standard data already available at the BCR, the present work explores the possibility to automatically extract the results for EGFR expression and mutation from those protocols.

Methods

6,157 protocols received from 78 Belgian pathology laboratories in 2013 and 2014 were selected, based on the presence of "EGFR" in the text. All protocols were read and EGFR expression and mutation results were manually extracted. As a second step, a machine learning algorithm was built to reproduce the human decision-making process from the protocol content and its accuracy was calculated.

Results

For the 2 years, a clear EGFR expression test result was available in 3,359/6,157 protocols (84% positive, 16% negative) and in 2,956 protocols a clear EGFR mutation test result was mentioned (9% mutated, 91% non-mutated). The automatic extraction of EGFR expression and mutation status by the machine learning algorithm achieved 86% and 95% accuracy, respectively.

Conclusions

This work presents a machine learning-based algorithm able to automatically extract the test results of EGFR expression and mutation from pathology protocols. The algorithm will be applied to all protocols received by the BCR, allowing estimation of the frequency of EGFR testing in Belgium and per individual laboratory. The algorithm also provides information about the outcome of these tests (positive or negative). Subsequently, this work opens new perspectives for other biomarkers and the obtained information will substantially enrich the data available at BCR. Machine learning-based extraction results will be used in descriptive epidemiology as well as in projects on quality of care.

L 07

PECOMAS: FROM BENIGN CLEAR CELL "SUGAR" TUMOR OF THE LUNG TO MALIGNANT RETROPERITONEAL MASS.

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1. Department of Pathology, University Hospital - CHU Sart Tilman; Liège, Belgium

Background and objective

Perivascular Epithelioid Cell tumors (PEComas) are a rare family of related mesenchymal neoplasms that include angiomyolipoma (AML), lymphangiomyomatosis (LAM), clear cell 'sugar' tumour (CCST), and morphologically and immunophenotypically similar lesions arising at a variety of visceral and soft tissue sites. PEComas are composed of distinctive epithelioid and/or spindle cells, with reactivity for melanocytic and smooth muscle markers. 3 clinical cases are presented, accounting for the variable behavior of PEComas, ranging from benign lesions to aggressive, high-grade sarcomas. Morphologic and immunohistochemical spectrum, malignant potential criteria as well as recent genetic findings about PEComas, are also discussed.

Methods

3 cases were analyzed for morphologic and immunohistochemical characteristics established for PEComas; clinical and outcome data were obtained for all cases. In addition, a large review of reported cases of PEComas was realized, with emphasis on the anatomical region concerned.

Results

Case #1 concerned a well-delimited 2.6cm nodule of the left lung. Case #2 dealt with a circumscribed 4.0cm tumor of the transverse colon. Case #3 considered a large retroperitoneal invasive mass. Morphology and immunochemistry were in accordance with: #1 benign CCST; #2 benign PEComa; #3 malignant PEComa. Clinical outcome showed no recurrence for cases #1 and #2; case #3 developed distant metastases, followed by death of the patient 8 months after surgery. According to literature, PEComas show a spectrum of histologic appearances and clinical behaviors, in a wide variety of anatomical sites. Criteria are also proposed for predicting malignant behavior.

Conclusions

PEComas are rare tumors which may arise in almost any location and characterized by distinctive overlapping morphology and immunophenotype, supporting the view that they are variants of a single entity. Challenges frequently arise as a result of the myriad names assigned to them, spectrum of histologic appearance, ubiquity and clinical behavior that can be difficult to predict.

L 08

KRAS MUTATION IN SEROUS BORDERLINE TUMOUR OF THE TESTIS: REPORT OF A CASE AND REVIEW OF THE LITERATURE.

Bouri S[1], Noël JC[1,3], Catteau X[1,3], Al Hajj Obeid W[2], Roumeguère T[2], Nicky D'Haene N[1,3], RORIVE

1. Department of Pathology, Erasme University Hospital, Université Libre de Bruxelles, Brussels, Belgium 2. Department of Urology, Erasme University Hospital, Université Libre de Bruxelles, Brussels, Belgium 3. Centre Universitaire Inter Regional d'Expertise en Anatomie Pathologique Hospitalière (CurePath)

Ovarian-like epithelial tumours of the testis, including serous borderline tumours, are rare entities. We report here the case of a 60 year-old man with a left intratesticular mass who was subjected to radical orchidectomy. Histologically, the tumour was identical to the ovarian counterpart showing a well delineated cystic lesion characterized by intramuminal papillae. The papillae are lined by atypical cuboidal or ciliated cells and are associated with psammoma bodies. Immunohistochemically, the tumour cells express cytokeratin 7 (CK7), cytokeratin 5-6 (CK5-6), cancer antigen 125 (CA125), estrogen (ER), progesteron (PR), Wilm's tumour gene (WT1), paired box gene 8 (PAX8), Ber-EP4, epithelial membrane antigen (EMA). There was no positivity for cytokeratin 20 (CK20), CDX2 gene, Sal-like protein 4 (SALL4), human chorionic gonadotropin (beta-HCG), alpha foeto protein (AFP), podoplanin (D2-40), and calretinin. The diagnostic of serous borderline tumour of the testis was proposed. Mutation testing using next-generation-sequencing showed a Q61K KRAS gene mutation. To the best of our knowledge, this is the second reported case of a serous borderline tumour of the testis with a Q61K KRAS gene mutation.

A review of the literature and the putative differential diagnoses are discussed to complete the description of this case report.

This work was supported by the Fonds Yvonne Boel (Brussels, Belgium)

L 09

CLEAR CELL RENAL CELL CARCINOMA INTRAOCULAR METASTASIS.

Koufopoulos N[1], Pigadioti E[1], Antoniadou F[1], Kokkali S[2], Nasi D[2], Khaldi L[1]

1. Department of Pathology, Anticancer Oncologic Hospital "St.Savvas", Athens, Greece 2. 1st Department of Medical Oncology, Anticancer Oncologic Hospital "St. Savvas", Athens, Greece

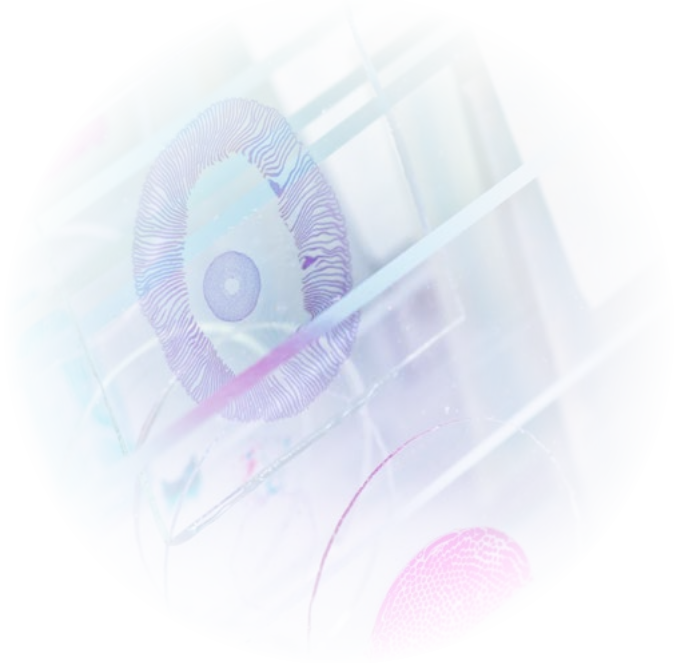
Background and objective

Clear cell renal cell carcinoma (ccRCC) intraocular metastasis occurs very rarely with less than 100 cases described in the English literature. We report a case of intraocular ccRCC metastasis.

Methods

A 67 year-old man was admitted to the department of ophthalmology because of gradual, painless reduction in vision of the right eye. There was no previous history of malignancy. On physical examination, proptosis was found. A computed tomography (CT) scan and an ocular ultrasound examination revealed a retrobulbar mass lateral to the optical nerve.

An enucleation of the right eye was performed. Grossly the tumour was well circumscribed, solid, yellowish-white measuring 1.5cm.



Results

On microscopic examination the neoplasm consisted of small nests, glands and follicles separated by a prominent thin walled vascular network. The cells displayed moderately atypical nuclei with abundant clear cytoplasm. Necrosis was not observed.

The differential diagnosis included clear cell melanoma, ccRCC and other malignant clear cell neoplasms.

Tumour cells stained positive for AE-1/AE-3, Vimentin, CD-10, EMA, RCCma, and negative for S-100, HMB-45 and Melan-A.

The morphological features as well as immunohistochemical results were consistent with metastatic ccRCC. Abdominal CT scan revealed a mass in the upper pole of the right kidney, highly suggestive of a ccRCC. The patient refused further treatment and was lost to follow-up.

Conclusions

ccRCC accounts for 85% of primary renal neoplasms. Patients present with metastatic disease in about 40% of cases. ccRCC usually metastasizes to lungs, lymph nodes, bones, brain and liver. Intraocular metastasis is rare. Metastatic ccRCC prognosis is poor. Treatment in patients with metastatic disease consists in nephrectomy in selected patients and adjuvant therapy.

L 10

IGG4-RELATED DISEASE IN PTERYGOPALATINE FOSSA. A RARE CASE MIMICKING AN INFLAMMATORY PSEUDOTUMOUR.

Koufopoulos N[1], Kokkali S[2], Nasi D[2], Khaldi L[1]

1. Department of Pathology, Anticancer Oncologic Hospital "St.Savvas", Athens, Greece 2. 1st Department of Medical Oncology, Anticancer Oncologic Hospital "St. Savvas", Athens, Greece

Background and objective

IgG4-related disease (IgG4-RD) is a fibroinflammatory condition which may involve a wide range of organs. Isolated head and neck region localisation is very rare with few cases described in the literature. We report a case of this rare entity.

Methods

A 66 year-old man with chronic headache was admitted to the ENT department with a suspicious mass lesion located in the left pterygopalatine fossa. The clinical impression was that the mass was malignant. However, imaging studies were consistent with a benign lesion. An endonasal endoscopic sinus surgery for the excision of the lesion was performed. There were no postoperative complications.

Results

On microscopic examination the lesion consisted of fibrous tissue with diffuse lymphoplasmacytic infiltration and obliterative phlebitis. The majority of plasma cells showed positive staining for IgG4.

Morphological and immunohistochemical findings were consistent with IgG4-RD. Postoperatively all necessary exams were performed excluding any other manifestation of IgG4-RD apart from this tumour. Nine months after diagnosis the patient is symptom free with no evidence of disease.

Conclusions

IgG4-RD is a recently discovered entity. In the head and neck region it is most frequently encountered in the salivary and lacrimal glands, orbits and thyroid gland. Clinically IgG4-RD may mimic malignancy or other autoimmune disease. Preoperative evaluation may be very difficult. Treatment consists in glucocorticoid administration. Prognosis is generally favourable. Our literature review revealed only 13 cases of IgG4-RD with pterygopalatine fossa involvement. However, the case we present is unique due to the isolated involvement of this anatomical location. earunt lit restrunture, il iuntotatiur sitassequo cus doluptatquis ant, consequis rem quo cum volupti onsende nissimp erumet as qui consequas et volorempor sitatum qui volecus deritat enditi quam restruptae pa aria aut oditate molore dioritasit quiaecumque ped mincium num que pratquae vendionesto es pla iditi utatendusam dit, tenducia quoditat omnimilis auditist, earupti berenissi reperest, enet quidi des prerchilit, comnis estrum nonsed ut eumquibernam expelit volorro restrum quis cusdam dolore, sandunt iniet earcipid moluptibus aut mo con endeni rati conessi vollent oritatemEt ipiet que nobis sim latiant.

L 11

SARCOMATOID CARCINOMA OF THE URINARY BLADDER WITH A LARGE CELL NEUROENDOCRINE CARCINOMA COMPONENT.

Koufopoulos N[1], Lazaris A[2], Liapis G[2].

1. Department of Pathology, Anticancer Oncologic Hospital "St.Savvas", Athens, Greece 2. 1st Department of Pathology Medical School, National and Kapodistrian University of Athens, Greece

Background and objective

Sarcomatoid carcinoma (SC) of the urinary bladder is an uncommon malignant tumour composed of carcinomatous and sarcomatous components. We present a rare case of urinary bladder SC with a large cell neuroendocrine carcinoma component.

Methods

An 80 year-old man was admitted to the department of urology due to gross hematuria, dysuria and lower abdominal pain. Ultrasound examination, revealed a large bladder mass arising from the left lateral wall, expanding to the posterior wall. At cystoscopy the tumour was polypoid, tightly adherent to the bladder wall. Transurethral resection biopsy was performed. The overall volume of the biopsy specimen was 60 cc.

Results

On microscopic examination the tumour showed biphenotypic morphology consisting of areas of sarcomatoid and large cell neuroendocrine carcinoma. Focal areas of squamous and glandular differentiation were also present. The neuroendocrine component formed islands and nests of medium to large sized cells with granular chromatin, while the sarcomatous areas consisted of high grade spindle cells with abundant mitoses.

Immunohistochemical study showed positivity for vimentin and focally for CK-7 and P-63. The neuroendocrine carcinoma stained positively for chromogranin and synaptophysin.
The morphological features as well as immunohistochemical results were consistent with SC of the urinary bladder with a large cell neuroendocrine carcinoma component.

Conclusions

SC is an aggressive neoplasm presenting at an advanced stage and having a poorer prognosis in comparison with conventional urothelial carcinoma. Median survival for SC is 14 months. Due to small number of cases optimal treatment has not been defined. The co-existence of SC with neuroendocrine carcinoma is extremely rare.

L 12

DIFFERENTIATED-TYPE INTRAEPITHELIAL NEOPLASIA ASSOCIATED WITH SQUAMOUS CELL CARCINOMA OF THE ANUS: A CASE REPORT WITH MOLECULAR PROFILE.

Koopmansch C[1], Maris C[1], Demetter P[2], Van de Stadt J[1], Hendlisz A[3], D'Haene N[1], Noël JC[1]

1. Department of Pathology, Erasme University Hospital, Free University of Brussels (ULB), Brussels, Belgium 2. Department of Pathology, Jules Bordet Institute, Free University of Brussels (ULB), Brussels, Belgium 3. Digestive Oncology Unit, Medicine Department, Jules Bordet Institute, Free University of Brussels (ULB), Brussels, Belgium

Introduction

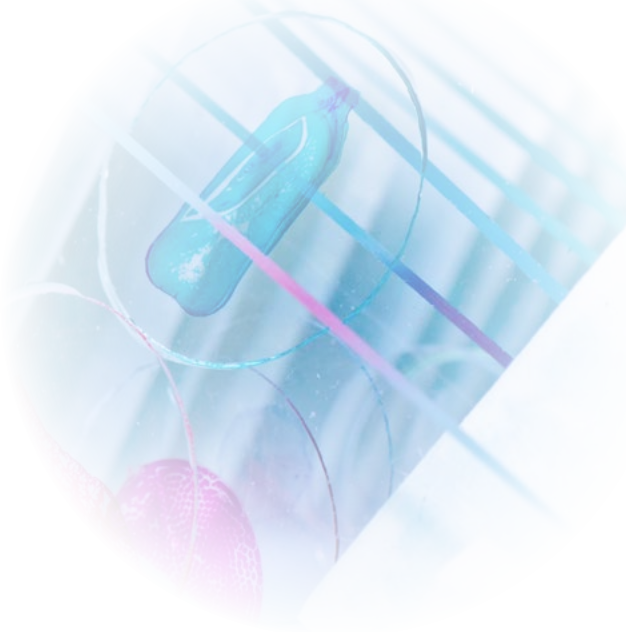
Differentiated-type Intraepithelial Neoplasia (DIN) is defined as HPV-negative squamous intraepithelial proliferation with abnormal keratinocyte differentiation and basal cell atypia, originally described in the vulva, with following descriptions in the oral cavity. In the vulva, DIN is, with few exceptions, associated with TP53 mutations. To the best of our knowledge, only one author reported DIN in the anus. This report describes the clinicopathological and the molecular features of this entity in anal margin.

Case report

A 59-year-old man presented moderately differentiated squamous cell carcinoma (SCC) of the anal margin, classified cT1 and treated by radiotherapy. After a period of complete response, the patient noted recurrence and underwent a first excision. The diagnosis of moderately differentiated SCC of the anal margin was made, classified rpT2Nx. Lateral margins were positive. TP53 mutation (indel) was found in this invasive component but the detection of High Risk-HPV was negative. Second resection showed DIN without TP53 mutation.

Discussion

In the present study, we analyzed for the first time molecular profile of both DIN and associated SCC in the anus. Such analysis has already been done in the vulva. Tumors of the anus and perianal skin are rare. After treatment, locoregional failure rates vary between 16% to 33%. Several studies indicated that HPV-/P16- anal cancers had significant worsed prognosis. Moreover, loss of p53 function has been linked to resistance to radiotherapy in head and neck SCC. In conclusion, we described a precursor lesion of SCC in the anus analogous to DIN in the oral cavity and vulva. The recognition of such a precursor should lead to a careful analysis of the HPV status and the molecular profile of cancer to detect the presence of TP53 mutations.



L 13

CEREBRAL LYMPHOPROLIFERATIVE DISORDER IN A MULTIPLE SCLEROSIS PATIENT UNDER AUBAGIO®: A CASE REPORT.

Wilgenhof K[1], Michotte A[1], De Raeve H[1], Deprijck B[2], Bureau M[3], Born J[4], Sartenaer D[5], Lefesvre P[1]

1. UZ Brussel 2. CHU de Liège 3. Clinique Astrid Malmedy 4. Hôpital du Valdor Liège 5. IPG Charleroi, Belgium

Immunodeficiency-associated lymphoproliferative disorders (IA-LPDs) have variable outcome ranging from benign lymphoid proliferations resolving without chemotherapy to very aggressive lymphomas. The diagnostic criteria between those entities are not well established mostly because they represent a continuum. The pathogenesis of IA-LPDs usually combines an immunodeficiency and a viral agent (e.g. EBV or HHV-8). The WHO separates the entities depending on the immunodeficiency (post-transplant - HIV - iatrogenic - primary immunodeficiency). However, there is evidence that shared pathogenic mechanisms underlie IA-LPDs among various immunodeficiency settings. The Society for Hematopathology and the European Association for Haematopathology (SH/EAHP) proposed a three-part nomenclature consisting of (1) the name of the lesion, (2) the associated virus, if any and (3) the specific immunodeficiency. This way, LPDs with similar morphologic, immunophenotypic and genetic features can be classified together.

We present a MS patient treated by teriflunomide (Aubagio®) who developed a brain lesion that fulfilled all the usual criteria for a primary cerebral classical Hodgkin Lymphoma (cHL). Reed-Sternberg (RS) cells showed a typical immunohistochemical profile with CD45 and CD20 negativity and PAX5, CD30, MUM1 and PD-L1 positivity. CD15 was, however, negative. The inflammatory infiltrate consisted of T-cells (CD3+/CD4+), eosinophils and plasmocytes. EBV in situ hybridization was positive. FISH identified genomic gains (9p24, 7p and 11q) in the RS-cells. Following the SH/EAHP nomenclature, this lesion should be named a cHL, EBV associated, iatrogenic induced. The patient was almost asymptomatic and underwent surgical ablation of the lesion. Adjuvant therapy, after diagnosis, consisted of replacement of teriflunomide by glatiramer acetate combined with rituximab. Six months later the progression of the patient is favorable. Retrospectively, should we reclassify this lesion as a polymorphic LPD, EBV associated, iatrogenic induced? Discussion on the significance of the genomic alterations will be presented on the poster.

L 14

PRIMARY CEREBRAL ALK-1+ ANAPLASTIC LARGE CELL LYMPHOMA AS A RARE CAUSE OF BITEMPORAL HEMIANOPIA.

De Froidmont S[1], Bianchi E[1], Delvenne P[1], Martin D[2], Bonnet C[3], Beckers A[4], Somja J[1]

1. Sevice d'Anatomie et Cytologie Pathologiques, CHU de Liège. Liège, Belgium 2. Service de neurochirurgie, CHU de Liège. Liège, Belgium 3. Service d'hématologie clinique, CHU de Liège. Liège, Belgium 4. Service d'endocrinologie, CHU de Liège. Liège, Belgium

We report a case of primary central nervous system ALK-1 positive anaplastic large cell lymphoma (ALCL) in a 34-years-old man presenting with bitemporal hemianopia, tetraparesis and headache. Medical laboratory tests highlighted a panhypopituitarism. CT scan and MRI demonstrated the presence of multiple enhancing expansive processes in the pituitary gland, epiphysis, cerebellum and cervical spinal cord associated with spinal meningeal tumoral infiltration. Endoscopic transphenoïdal pituitary biopsy showed a diffuse infiltrate composed of large atypical lymphoid cells, with a moderate amount of cytoplasm, irregular ovoid, twisted, nuclei and conspicuous small nucleoli. The cells were positive for CD30, CD2, CD7, CD4, Perforin, Granzyme-B and ALK-1, supporting a diagnosis of ALK-1 + ALCL. Further investigations showed no evidence of systemic disease. The patient was successfully treated with systemic chemotherapy and last follow-up, 6 months later, showed complete regression of the lesions.

The association of hemianopia and panhypopituitarism reliably directs to an optic chiasma compression. The most common cause of this syndrome is a non-secreting pituitary adenoma. Other benign causes are craniopharyngioma, sellar meningioma, pituicytoma, pituitary abscess and hypophyisitis. Primary malignant tumors include germ cell tumor, chordoma, chondrosarcoma and primary central nervous system lymphoma (PCNSL). Metastases to the hypothalamus and pituitary gland account for approximately 1 to 2% of sellar masses.

PCNSL accounts for 1-2% of non-Hodgkin lymphomas and represents 5% of primary brain tumors. PCNSL of T-cell origin is less frequent accounting for 2 to 8,5% of PCNSL. To our knowledge, less than 85 cases of PCNS ALK-1 positive ALCL have been reported and we present the first case of hemianopia and panhypopituitarism resulting from ALK-1+ ALCL into the pituitary gland. Recognition of this rare presentation needs a biopsy of the lesion for pathological confirmation and is important as an adequate therapy greatly improves patient survival.

L 15

FISH ON EXTRACTED NUCLEI FROM FORMALIN FIXED AND PARAFFIN EMBEDDED TISSUES FOR THE DIAGNOSIS OF CHROMOSOMAL ANEUPLOIDIES IN MALFORMED FETUSES.

Yacoubi MT[1] , Mougou S[2]

1. Department of anatomic pathology, F.Hached University Hospital, Sousse, Tunisia 2. Departement of cytogenetics, F.Hached university Hospital, Sousse, Tunisia

Background and objectives

The most frequent chromosomal anomalies in human pathology are aneuploidies especially the trisomy 13, 18 and 21 and the monosomy X since they are compatible with a postnatal life. Theses anomalies generally produce severe malformations that could terminate the pregnancy without any prenatal Karyotype. The use of fluorescent in situ hybridization (FISH) to detect and characterize theses chromosomal anomalies is largely applied in lymphocytes and amniocytes but its use on formalin- fixed and paraffin-embedded tissues is not routinely made. The aim of this study is to detect above mentioned anomalies using FISH technique.

Methods

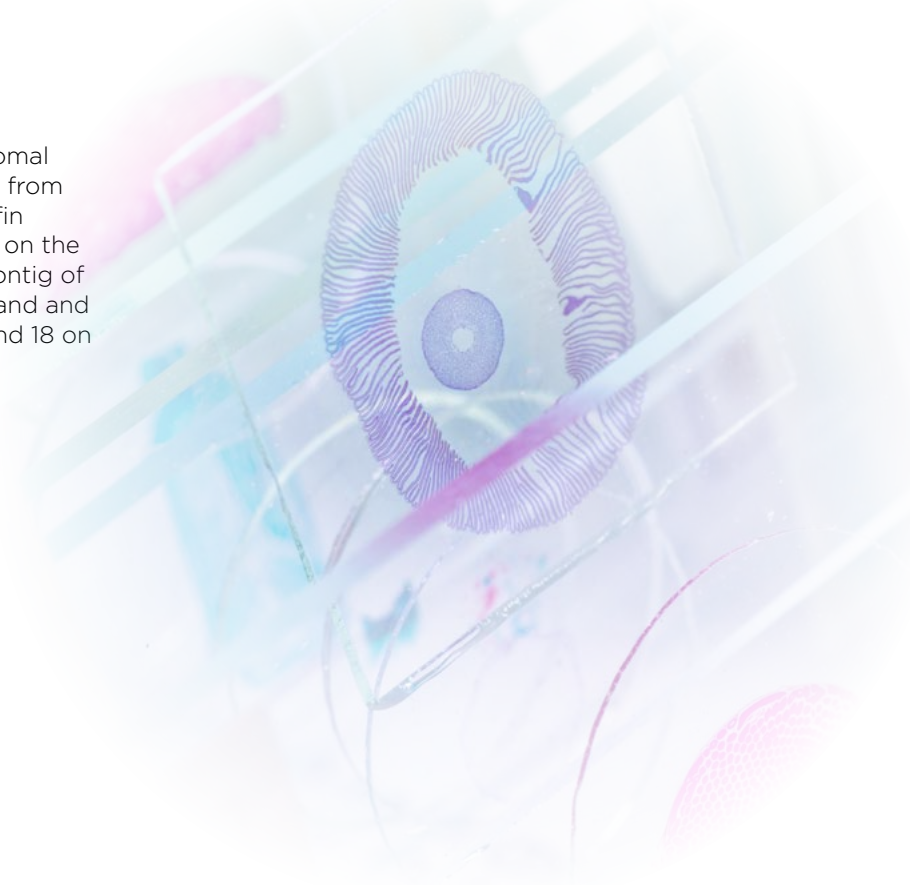
20 foetuses have been screened for the specific malformations of these chromosomal aneuploidies. Nuclei have been extracted from kidney and liver formalin- fixed and paraffin embedded tissues. FISH then was tested on the extracted nuclei by a combination of a contig of probes from chromosome 21, 13 on one hand and centromeric probes of chromosomes X and 18 on the other hand.

Results

Trisomy 21 was detected in one case, trisomy 18 was confirmed in 4 cases, trisomy13 in 4 cases and monosomy X in 2 cases.

Conclusions

The application of FISH on fetal tissues is very useful in detecting chromosomal anomalies in embryofetopathology. FISH can so, straighten (strengthen may be better to use confirm) the diagnosis what constitutes a help to the genetic counselling for the related couples or in the cases where a differential diagnosis exists.



L 16
NEURO-AXONAL DYSTROPHY CAUSING AKINESIA : A RARE FETAL ONSET.

Yacoubi MT[1], Chaeib S[1]

1. Unit of fetal and placental pathology, Department of anatomic pathology, University hospital of Sousse, Sousse, Tunisia

Background and objective

Fetal akinesia deformation sequence (FADS) is the result of decreased fetal movement. It may be caused by defects along the motor system from the central and peripheral nervous system to the neuromuscular junction or the muscle cell itself.

In the Central nervous system (CNS), the common lesion is the involvement of the anterior horn of the spinal cord which can be either isolated with its usual mode of expression that is arthrogryposis, or integrated in a diffuse central nervous system pathology whose clinical expression is a sequence of complete fetal akinesia.

We report here a new case of FADS due to neuroaxonal dystrophy (NAD) with overviewing the neurogenic causes, focusing on NAD and its diagnostic tools.

Methods

A female fetus with multiple congenital abnormalities was delivered by a 29 years old Tunisian mother. Fetal ultrasound at 22 weeks of gestation demonstrated arthrogryposis, anamnios and subcutaneous edema. Medical termination of pregnancy was indicated. A full feto-placental examination was performed.

Results

Autopsy examination showed a 411 g female fetus with Potter's face. Limbs examination showed arthrogryposis, clubfoot and popliteal pterygium knee. Internal examination showed hypoplastic lungs. Brain sectioning showed dilated ventricles and hypoplastic corpus callosum. All sections of the brain and spinal cord, demonstrated axonal swelling and prominent eosinophilic, inclusion-like of the axons (axonal spheroids), positive for neurofilaments.

Conclusions

Investigation of FADS, should cover all the spectrum, especially the examination of the CNS including the spine.

NAD is an extremely rare cause of this FADS, an inherited degenerative disorder of the nervous system, characterized by abnormalities of nerve endings within the central and peripheral nervous system. NAD is autosomal recessive, begins usually at 6th month of life. Fetal onset is extremely rare.

the PLA2G6 gene on chromosome 22q13.1 encoding for the calcium-independent phospholipase iPLA2-VI, is the causative.

L 17

EXPRESSION OF ONCOPROTEINS AND TUMOUR SUPPRESSOR GENES IN NON MOLAR HYDROPIC ABORTIONS, PARTIAL AND COMPLETE HYDATIDIFORM MOLES.

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Background and objective

Hydatidiform moles (HM) are characterized by an abnormal proliferating trophoblastic tissue and carry a potential of malignant transformation. Similar to other human cancers, malignant transformation in gestational trophoblastic tumours is likely a multistep process and involves multiple genetic alterations including activation of oncogenes and inactivation of tumour suppressor genes.

Methods

We investigate the expression of bcl-2 and mdm-2 oncoproteins and p53, p21 and Rb tumour suppressor genes, in non-molar hydropic abortions (HA), partial HM (PHM) and complete HM (CHM). This expression was determined immunohistochemically by specific antibodies for these proteins on formalin-fixed paraffin sections of 38 HA, 49 PHM and 133 CHM.

Results

Positive staining for bcl-2 and mdm-2 oncoproteins and of p21 was significantly higher in CHM and PHM than in HA ($p<0.05$) but there was no significant difference for the expression of these proteins between CHM and PHM. The expression of p53 and Rb was significantly higher in CHM than PHM and HA ($p<0.05$).

Conclusions

Altered expression of oncoproteins and tumour suppressor genes may be important in the pathogenesis of HM. A possible role of the over-expression of p53 and Rb in CHM is an attempt to modulate the excessive proliferative activity in trophoblastic cells.

L 18
SPINDLE CELL LIPOMA OF THE BREAST.

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Background and objective

Spindle cell lipoma (SCL) is a rare lipoma variant usually occuring in the upper back, posterior neck and shoulders. It also been reported in other sites including the oral cavity, extremities and deep skeletal muscle. Few cases of mammary SCL have been reported in the English literature. We report a case of mammary SCL.

Methods

A 46 year-old woman with no previous history was admitted to the department of surgery due to a breast mass discovered recently during self examination. The lesion was solitary, painless, well circumscribed, freely movable with a maximum diameter of 2.4 cm. A lumpectomy with wide margins was performed.

On gross examination the tumour was well circumscribed, solid, yellowish-white in colour.

On microscopic examination, the neoplasm consisted of a mixture of mature adipocytes arranged in lobules and uniform, bland spindle cells arranged in short fascicles. The spindle cells were uniform, wavy, with pale eosinophilic cytoplasm in a fibrous background.

Cellular atypia, lipoblasts, necrosis or mitotic figures were not observed.

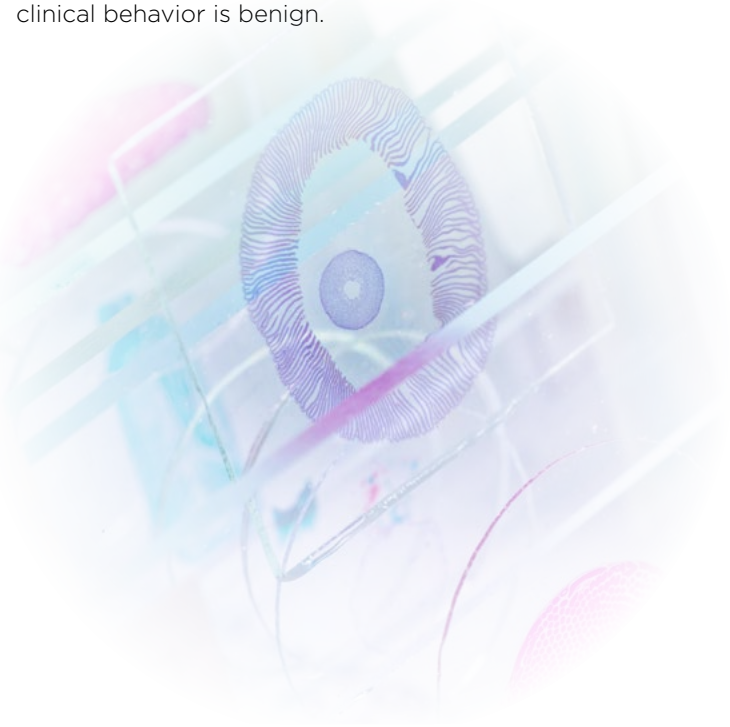
Spindle cells stained positive for CD-34 and adipocytes for S-100. Tumour cells were negative for beta-catenin.

Results

The morphological features as well as immunohistochemical results were consistent with mammary SCL. On postoperative evaluation, three months after surgery, the patient shows no evidence of recurrence.

Conclusions

SCL is a rare lipoma variant. It commonly presents as a solitary mass but multifocality has been reported. It appears as a well-circumscribed mass on X-ray and as a homogeneous hyperechoic nodule ultrasonographically. Wide local excision is the recommended treatment. Its clinical behavior is benign.



L 19

INTRAMUSCULAR GRANULAR CELL TUMOR OF THE GLUTEAL REGION. REPORT OF A CASE.

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Background and objective

Granular cell tumours (GCT) are uncommon benign neoplasms accounting for approximately 0.5% of soft tissue tumours. They are usually located in the head and neck region, the chest wall and the upper extremities. Less frequently they may be encountered in the larynx, breast, gastrointestinal and genital tracts. We present a case of a rapidly growing GCT mimicking clinically a malignant neoplasm.

Methods

A 79 year-old man was referred to the department of plastic surgery with a 6 month medical history of a rapidly growing mass in the left gluteal region. Rapid growth gave the clinical impression of malignancy. Imaging studies demonstrated a 7x4.4 cm sized soft-tissue mass in the left gluteal region and were negative for metastasis. Computed tomography guided fine needle biopsy was non diagnostic. A wide local excision was performed. On gross examination, the tumour was poorly defined, pale yellow on cut surface with a maximum diameter of 7.6 cm.

Microscopically, the tumour was poorly circumscribed and diffusely infiltrating. Neoplastic cells were large, polygonal with eosinophilic granular cytoplasm and small round to ovoid nuclei separated by sclerotic collagenous tissue. Atypia, spindling, high nuclear to cytoplasmic ratio, pleomorphism, or areas of necrosis were not identified. Mitotic figures were rarely noticed.

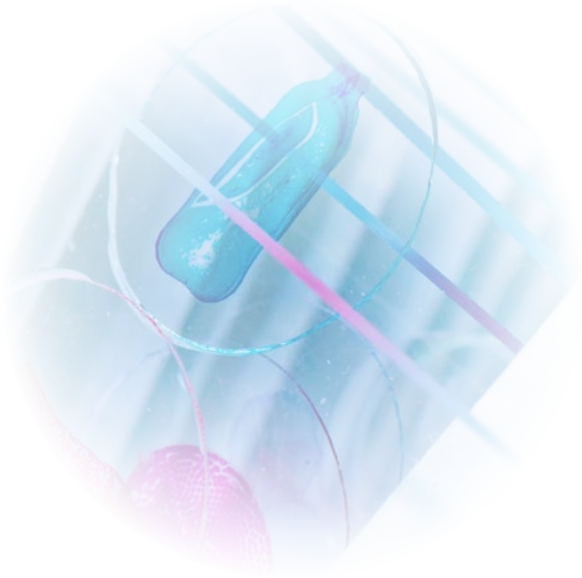
Immunohistochemical study was positive for S-100, CD-68, inhibin-A, calretinin, CD-57, NSE and negative for AE-1/AE-3 and desmin.

Results

Morphological features as well as immunohistochemical results were consistent with GCT. On postoperative evaluation, six months after surgery, there were no signs of local recurrence or distant metastasis.

Conclusions

GCT should be considered in the differential diagnosis of rapidly growing intramuscular tumours. Wide local surgical excision with tumor free margins is the treatment of choice. Recurrence occurs in 21–50% of cases.



L 20
LEIOMYOADENOMATOID TUMOR OF THE UTERUS.

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Background and objective

Adenomatoid tumour (AT) is an uncommon benign tumour of mesothelial origin. It is most commonly encountered in the male and female genital tracts. Leiomyoadenomatoid tumour (LMAT) is a rare variant of AT with a prominent smooth muscle component. We present a case of LMAT.

Methods

A 79 year-old woman without previous history was admitted to the department of gynaecology due to lower abdominal pain. Transvaginal ultrasonography revealed a 7.2 cm fibroid in the anterior wall of the uterine cervix. Hysterectomy and bilateral salpingo-oophorectomy was performed.

On gross examination, besides the large leiomyoma of the uterine cervix a second intramural leiomyoma located in the antero-lateral wall of the corpus uteri was observed measuring 2.5 cm.

On microscopic examination, both tumours consisted of smooth muscle bundles arranged in a fascicular pattern. In the smaller one, smooth muscle bundles were separated by slit-like and tubular structures lined by cuboidal epithelioid cells with small, uniform nuclei and scanty, pale, eosinophilic cytoplasm. Mitotic figures were not observed.

Tumour cells were positive for AE-1/AE-3, CK-8/18, CK-7, Calretinin and negative for CD-31 and CD-34. SMA and Desmin highlighted smooth muscle cells. Ki-67 stained less than 1% of tumour nuclei.

Results

The morphological features as well as immunohistochemical results were consistent with LMAT of the uterus. On postoperative evaluation, three months after surgery, the patient shows no evidence of recurrence.

Conclusions

LMAT is a rare variant of AT with a prominent smooth muscle component. It was first described in 1992. Our literature review revealed 13 reported cases. Awareness of this rare entity is important in order to avoid misdiagnosis as adenocarcinoma.

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