Dear colleague,

Welcome to the 19th Annual Meeting of the BSMO, a unique annual opportunity to gather as a community and exchange ideas and engage in cooperation. These are exciting but also challenging times for the medical oncologist with quickly evolving treatments and getting treatments in a timely fashion to the right patients.

The Friday morning meeting is dedicated to the BSMO Breast Cancer Task Force and in the afternoon to metastatic disease in the central nerve system. The General Assembly of the BSMO is taking place on Friday afternoon, followed by a Satellite symposium and a dinner. On Saturday morning the General Annual Meeting will be held. All BSMO members are welcome at the task force meeting.

On Saturday morning the symposium relates to several aspects of our profession with a balanced clinical and scientific mix. It is these scientific insights combined with compassionate patient care that make the medical oncologist.

On behalf of the board, we would like to wish you a fruitful meeting!

Jacques De Grève,
BSMO President
FRIDAY 24 FEBRUARY 2017

08.30  Registration & coffee

09.00-13.00 Breast cancer Task force
   Chairs: Ahmad Awada and Hans Wildiers
   Biology of young breast cancer and management in pregnant woman
   Matteo Lambertini, Institut J. Bordet, Brussels
   Fertility and breast cancer
   Isabelle Demeestere, ULB, Brussels

10.30-11.00 Coffee break

11.00 Anthracyclines always needed in (neo)adjuvant chemotherapy regimens?
   Hans Wildiers, UZ Leuven

11.30 Genetic variability and risk of neutropenia – related events and cardiac toxicity
   Christof Vulsteke, AZ Maria Middelares, Gent

11.45 Quality control on systemic treatment of Breast Cancer
   Didier Verhoeven, AZ Klina, Antwerpen

12.00 Update on the neoadjuvant trial of BSMO
   Christel Fontaine, UZ Brussel

12.15 Potential projects for the Breast Task Force Cancer of BSMO
   Ahmad Awada, Institut J. Bordet, Brussels
   Oncodistinct network and potential collaboration on projects with the BSMO
   Breast Cancer Task Force

13.00  Registration other delegates & lunch

13.30-15.00 Central Nervous system
   Introduction
   Chair: Luc Dirix, Iridium Kankernetwerk, Antwerpen

13.35 Functional neuroanatomy for the medical oncologist
   David Crosiers, UZ Antwerpen

14.00 CNS imaging
   Bert De Foer, Sint-Augustinus, Antwerpen

14.30 Neurosurgery
   Tony Van Havenbergh, Sint-Augustinus, Antwerpen

15.00-15.30 Coffee Break

15.30 Radiotherapy
   Karen Van Beek, UZ Leuven

16.00 CNS disease and systemic treatment options
   Nicolas Wherham, UCL

16.30 Leptomeningeal disease
   Pierre Freres, CHU Liège

17.00 Conclusion
   Jacques De Grève, UZ Brussel

17.00 General Assembly (members only)

18.00 Drinks

19.00 Pfizer Satellite Symposium and dinner:
   (Separate registration required)
08.30 - 12.50  BSMO 19th Annual Meeting

08.30  Registration and coffee

08.55  Introduction
Jacques De Grève, BSMO President

09.00  Oncology Paper of the year 2016 presentation & award
70-Gene Signature as an Aid to Treatment Decisions in Early-Stage Breast Cancer
Chair: Peter Vuylsteke, CHU UCL Namur
Speaker: Martine Piccart, Institut J. Bordet, Brussels

09.30  Proffered papers by junior members
Chairs: Hans Prenen, University Hospitals Gasthuisberg, Leuven

0.1  Circulating Tumour Cells and Survival in Abiraterone- and Enzalutamide-treated Patients with Castration-Resistant Prostate Cancer
Bram De Laere, University of Antwerp

0.2  Immuno-FIELD: The role of Tumor Infiltrating Lymphocytes and PD-L1 expression in NSCLC adenocarcinoma in little to non-smokers and its relationship with driver mutations and clinical outcome parameters.
Sacha Mignon, Vrije Universiteit Brussel

0.3  Identification of candidate breast cancer predisposition genes by sequencing extended panel of 492 cancer associated genes in BRCA1/2 negative probands
Rajendra Bahadur Shahi, Vrije Universiteit Brussel

0.4  Type II RAF inhibition causes superior ERK suppression compared to type I RAF inhibition in different BRAF mutant types recurrently found in lung cancer
Amir Noeparast, VUB

0.5  Clinical significance of CD73 expression in triple-negative breast cancer from the BIG 02-98 adjuvant phase III clinical trial
Laurence Buisseret, Institut J. Bordet, Brussels

0.7  Mutational Landscaping of Liver Metastases with Desmoplastic and Replacement Growth Patterns
Pieter-Jan Van Dam, University of Antwerp

0.8  Evaluation of HER2 expression and amplification in CTCs using CellSearch immunofluorescence and FISH.
Anja Brouwer, GZA hospitals Sint-Augustinus

0.9  Geriatric assessment (GA)- guided interventions in older patients (pts) with cancer
Lore Decoster, UZ Brussel

0.10  USP13 as a novel co-target for EGFR targeted therapies in EGFR mutant non-small cell lung cancer.
Philippe Giron, Vrije Universiteit Brussel

10.50 - 11.20  Coffee break and poster viewing

11.00  Heuson memorial Lecture
Chair: Wim Demey, Iridium Kankernetwerk, Antwerpen
“From a nihilistic point of view to some hope in lung cancer management”
Paul Vanhoutte, Institut J. Bordet, Brussels

11.50  Sponsored Awards: MSD Oncology Award + Leo Pharma Grant
Chair: Evandro de Azambuja, Institut J. Bordet, Brussels and Joelle Collignon, CHU Liège

12.20  What you should not have missed in 2016
Luc Dirix, GZA Antwerpen

12.50  Meeting closure & lunch
GENERAL INFORMATION

Accreditation
Pending: erkenningsnummer / N°agréation: 17004329
All delegates will receive an e-mail message as soon as the information is available.

Target audience
Medical oncologists and oncologists in training, other physicians with focus on cancer management are also welcome to join the scientific sessions.

Website
www.bsmo.be

Congress secretariat
Congress Care
PO Box 440
NL-5201 AK ’s-Hertogenbosch
T: +31 (0) 73 690 1415
E: info@congresscare.com
W: www.congresscare.com
ABSTRACTS INVITED SPEAKERS

11:00 Heuson memorial Lecture
From the nihilistic approach to some hope in the management of lung cancer
Paul Vanhoutte, Institut J. Bordet, Brussels

There is a tendency to think the lack of major progress made in the treatment of lung cancer. This is certainly true if we are only looking to the 5 year survival rates over the last years and the only good news is the decline in lung cancer mortality due to the prevention policy and the ban on the tobacco. Comparing to 40 years ago when I started my training in radiation oncology and my involvement in the management of lung cancer, major steps have been made related to the introduction of better imaging procedures (CT, MRI and PET-CT), new technologies in radiation (linacs, dosimetry, IGRT, IMRT...), new drugs (cisplatin, targeted agents), less invasive surgery, better supportive care and of course a better integration of the different modalities leading to a multidisciplinary approach. Some great results have been achieved but also some major disappointments due to the hope generated by some positive results. Several new roads need to be explored in the future: the new checkpoint blockade immunotherapy, the hadrons, the management of the oligometastatic disease... This lecture will review 40 years of lung cancer management outlining the long road to a better future for our patients.

PROFFERED PAPER SESSION

O.01
Circulating Tumour Cells and Survival in Abiraterone- and Enzalutamide-treated Patients with Castration-Resistant Prostate Cancer
Bram De Laere1, Peter Van Oyen2, Christophe Ghysel1, Piet Ost3, Wim Demey4, Lucien Hoeke5, Dirk Schrijvers1, Barbara Brouwers1, Willem Lybaert1, Els Everaert1, Jozef Ampe1, Pieter Van Kerckhove1, Hannelore De Baets1, Michel Strijbos1, Alain Bals1, Karen Franssens1, Stefaan Oeyen1, Valerie Van Dam1, Anja Brouwer1, Gerrit Van den Eynde1, Annemie Rutten1, Jean Van de Vraet2, Steven Van Laere1, Luc Dirix1
1University of Antwerp, Antwerp, Belgium
2Department of Urology, AZ Sint-Jan, Brugge, Belgium
3Department of Radiation Oncology, Ghent University Hospital, Gent, Belgium
4Department of Oncology, AZ KLINa, Brasschaat, Belgium
5Department of Urology, Antwerp University Hospital, Antwerp, Belgium
6Department of Oncology, ZNA Middelheim, Antwerp, Belgium
7Department of Oncology, AZ Sint-Jan, Brugge, Belgium
8Department of Oncology, AZ Nikolaas, Sint-Niklaas, Belgium
9Department of Oncology, AZ Sint-Lucas, Brugge, Belgium
10Center for Oncological Research, University of Antwerp, Antwerp, Belgium
11Department of Pathology, GZA Hospitals Sint-Augustinus, Antwerp, Belgium
12Department of Oncology, GZA Hospitals Sint-Augustinus, Antwerp, Belgium

Introduction: A heterogeneous landscape of patients with metastatic castration-resistant prostate cancer (CRPC) exists in current clinical practice. The enumeration of circulating tumour cells (CTCs) is associated with survival. Here, we investigated the prognostic value of CTC enumeration and dynamics, in the context of second line endocrine therapies (i.e. abiraterone acetate or enzalutamide).

Patients and methods: In a prospective, multicentre study baseline peripheral blood samples for CTC enumeration were collected from patients with CRPC (n=147). Follow-up sampling was performed in 95/147 (64.6%) patients. At baseline, patients were stratified in favourable (i.e. <5 CTCs/7.5mL) and unfavourable (i.e. ≥5 CTCs/7.5mL) groups, whereas at follow-up, in those demonstrating a stable, in- or decreasing CTC count. Progression-free survival (PFS) and overall survival (OS) were compared between defined groups. Additionally, PSA changes at 10-12 weeks were evaluated in 83 patients.

Results: Patients with ≥5 CTCs/7.5 mL (n=59) at baseline had a shorter PFS (3.9 vs. 11.3 months, p<0.0001) and OS (9.34 months vs. not reached, p<0.0001). Patients demonstrating increasing CTCs (n=21) during therapy had a shorter PFS (4.03 vs. 10.36 vs. 13.08 months, p<0.0001) and OS (11.2 months vs. not reached, p=0.0003), compared to patients with decreasing (n=41) and stable (n=33) CTCs, respectively. Multivariate Cox proportional-hazards regression showed that the number of CTCs (HR (95%CI): 1.0054 (1.0006–1.010), p=0.0260) and an having an increasing follow-up CTC count (HR (95%CI): 2.8987 (1.2856–6.536), p=0.0103) were independent predictors of PFS. Increasing CTCs was the sole independent predictor for OS (HR (95%CI): 7.3512 (1.7953–30.101), p=0.0054). At 10-12 weeks, a PSA response of ≥30% and ≥50% was achieved in 46/83 (55.4%) and 33/83 (39.8%) patients, respectively. PSA responses were statistically different between chemo-naive or -pretreated patients (≥30%: p=0.0395), patients with increasing, stable or decreasing CTC counts (≥30%: p=0.00324) and patients with increasing or stable/decreasing CTC counts (≥30%: p=0.000671; ≥50%: p=0.001397).

Conclusion: Baseline CTC levels are associated with PFS and OS in patients with metastatic CRPC, starting a new line of endocrine therapy. However, follow-up CTC enumeration is associated with PSA response and its dynamics is an independent predictor of PFS and OS, thereby demonstrating the pharmacodynamics properties of CTCs.
Identification of candidate breast cancer predisposition genes by sequencing extended panel of 492 cancer associated genes in BRCA1/2 negative probands

Rajendra Bahadur Shahi, Ben Caljon, Sylvia De Brakelere, Lore Decoster, Christel Fontaine, Leen Vanacker, Marian Vanhoeij, Ingrid Pauwels, Mary-Louise Bonduelle, Sonia Van Dooren, Didier Croes, Erik Teugels, Jacques De Grève

1Vrije Universiteit Brussel, BRUSSEL, Belgium
2Universitair Ziekenhuis Brussel, BRUSSEL, Belgium

Even after examining an array of current known breast cancer predisposition genes, 60-80% of hereditary breast cancer remains unresolved. To bring this missing heritability to light, in the present study we have analyzed 492 genes known to be associated with different types of cancer/syndromes in 67 probands from BRCA1/2-negative high risk BC families (BRCAX).

In total, 26 of 64 probands (~41%) were found with 33 protein truncating and splice site variants, of which 12 variants were novel. These variants were found in 1) PALB2, BARD1, CHEK2, RAD51C, FANCI, FANCA, RECQL4, RINT1 and ABCC11; genes already been proven to be associated with BC predisposition, 2) EXO1, ALKBH2, CCNH, MUS81, TDP1, DCLRE1A, DCLRE1C and PDE11A; genes already reported to be associated with other cancers but not with BC predisposition yet and in 3) BBS10, CD96, CYP1A1, DNAH11, ESCO2, FLT4, HPSE, MYH8, NME8 and TTC8 genes associated with different hereditary syndromes but vaguely related with BC/cancer syndromes.

Similarly, three in-frame deletions and 353 missense substitutions were also detected. Among missense substitutions, 242 were of ‘probably damaging’ and 111 were of ‘possibly damaging’ according to PolyPhene-2 prediction. The mutations detected were further clinically validated by examining other affected and non-affected family members and mining the literature. Some of the mutations in known cancer predisposing genes were considered for prudent application in clinical counseling. Genotype-phenotype correlations were being examined.

Massively parallel sequencing of 492 cancer associated genes in 64 probands from BRCAX families enabled us to detect protein truncating and splice site variants, of which 12 variants were novel. These variants were found in 1) PALB2, BARD1, CHEK2, RAD51C, FANCI, FANCA, RECQL4, RINT1 and ABCC11; genes already been proven to be associated with BC predisposition, 2) EXO1, ALKBH2, CCNH, MUS81, TDP1, DCLRE1A, DCLRE1C and PDE11A; genes already reported to be associated with other cancers but not with BC predisposition yet and in 3) BBS10, CD96, CYP1A1, DNAH11, ESCO2, FLT4, HPSE, MYH8, NME8 and TTC8 genes associated with different hereditary syndromes but vaguely related with BC/cancer syndromes. Similarly, three in-frame deletions and 353 missense substitutions were also detected. Among missense substitutions, 242 were of ‘probably damaging’ and 111 were of ‘possibly damaging’ according to PolyPhene-2 prediction. The mutations detected were further clinically validated by examining other affected and non-affected family members and mining the literature. Some of the mutations in known cancer predisposing genes were considered for prudent application in clinical counseling. Genotype-phenotype correlations were being examined.

PD-L1 expression on tumor cells and TILs did not influence survival. However, PD-L1 expression on tumor stromal cells indicates a worse prognosis, leading to the hypothesis that stromal cells can supress the anti-tumor immune response.
O.04
Type II RAF inhibition causes superior ERK suppression compared to type I RAF inhibition in different BRAF mutant types recurrently found in lung cancer

Amir Noeparast, Philippe Giron, Sylvia De Brakeleer, Ulrike De Ridder, Erik Teugels, Jacques De Grève
VUB, BRUSSELS, Belgium

Background: Somatic driver BRAF mutations account for 6-8% of lung cancers. As opposed to melanoma in which V600E mutant BRAF predominates, the majority of lung cancer-derived BRAF mutations are non-V600. Yet, the efficacy of RAF-inhibitors and the possible resistance mechanisms in non-V600 BRAF mutant cells remain to be uncovered. Recently, we have shown that non-V600 BRAF mutations recurrently found in lung cancer predict sensitivity to the combination of type I RAF inhibitor Dabrafenib and a MEK inhibitor Trametinib. Yet, Dabrafenib as a single agent shows only weak suppression of mutant BRAF-induced ERK signaling; moreover it can induce ERK paradoxical activation in CRAF overexpressing cells.

Methods: We generated several recombinant BRAF expression vectors by performing site-directed mutagenesis. We compared the effects of Dabrafenib and a type II RAF inhibitor (AZD628) at clinically relevant dose on ERK activity, in HEK293T cells expressing several tumor-derived BRAF mutants and a non-V600 BRAF mutant lung cancer cell line (H1666).

Results: In contrast to Dabrafenib, AZD628 does not induce paradoxical ERK activation in CRAF expressing cells. Increased CRAF expression desensitizes mutant BRAF expressing cells to Dabrafenib but not to AZD628. Notably, AZD-628 has superior ERK-inhibitory effect in HEK293T cells co-expressing several different BRAF-mutants with CRAF and in H1666 cells. Combination of Trametinib and AZD-628 has superior MEK-inhibitory and pro-apoptotic effects in H1666 cells compared to combined Trametinib/Dabrafenib.

Conclusions: In our in vitro model, we obtained strong indications that at clinically relevant dose, type II RAF-inhibitor AZD628 is superior to type I RAF-inhibitor Dabrafenib, both as single agent and combined with MEK inhibition (Trametinib) for the treatment of non-V600 BRAF mutant lung cancer.

O.05
Clinical significance of CD73 expression in triple-negative breast cancer from the BIG 02-98 adjuvant phase III clinical trial

Laurence Buisseret, Sandra Pomme, Bertrand Allard, Soizic Garaud, Marjorie-Allison Bergeron, Isabelle Cousineau, Lieveke Ameye, Guillaume Chouinard, Hugues Duvillier, Marianne Paesmans, Martine Piccart-Gebhart, Karen Willard-Gallo, Christos Sotiriou, John Stagg
1Institut Jules Bordet, BRUSSELS, Belgium
2Centre de Recherche du Centre Hospitalier de l’Université de Montréal, MONTREAL, Canada
3Institut Jules Bordet, Université Libre de Bruxelles, BRUSSELS, Belgium

CD73 is an ecto-enzyme involved in the mechanism of tumor immune escape through the production of extracellular adenosine in the tumor microenvironment. Adenosine has multiple immunosuppressive functions and has recently emerged as a new cancer target. CD73 gene expression is associated with a worse clinical outcome in various malignancies, including triple negative breast cancer (TNBC). Using multiplex immunofluorescence in combination with digital image analysis on whole tumor tissue sections, we quantitatively assessed CD73 expression and CD45+ tumor-infiltrating leukocytes (TIL) area in 122 TNBC samples from the BIG 02-98 adjuvant phase III clinical trial comparing the addition of docetaxel to doxorubicin with doxorubicin-based chemotherapy in node-positive breast cancer. Our results demonstrated that high levels of CD73 on epithelial tumor were significantly associated with reduced disease-free (DFS) and overall survival (OS) in patients with TNBC. Using the median as a threshold between low and high levels of CD73 on epithelial cells, hazard ratios (HR) adjusted for grade, number of positive lymph nodes and tumor size, were of 2.21 (95% confidence interval (CI): 1.15-4.25); p= 0.02 for DFS and of 2.47 (95%CI: 1.21-5.07); p=0.01 for OS. We also demonstrated that high levels of epithelial CD73 were negatively correlated with CD45+ tumor-infiltrating leukocytes (TIL) area in 122 TNBC samples from the BIG 02-98 adjuvant phase III clinical trial comparing the addition of docetaxel to doxorubicin-based chemotherapy in node-positive breast cancer. Our results demonstrated that high levels of CD73 on epithelial tumor were significantly associated with reduced disease-free (DFS) and overall survival (OS) in patients with TNBC. Using the median as a threshold between low and high levels of CD73 on epithelial cells, hazard ratios (HR) adjusted for grade, number of positive lymph nodes and tumor size, were of 2.21 (95% confidence interval (CI): 1.15-4.25); p= 0.02 for DFS and of 2.47 (95%CI: 1.21-5.07); p=0.01 for OS. We also demonstrated that high levels of epithelial CD73 were negatively correlated with CD45+ tumor-infiltrating leukocytes (TIL) area in 122 TNBC samples from the BIG 02-98 adjuvant phase III clinical trial comparing the addition of docetaxel to doxorubicin-based chemotherapy in node-positive breast cancer. Our results demonstrated that high levels of CD73 on epithelial tumor were significantly associated with reduced disease-free (DFS) and overall survival (OS) in patients with TNBC. Using the median as a threshold between low and high levels of CD73 on epithelial cells, hazard ratios (HR) adjusted for grade, number of positive lymph nodes and tumor size, were of 2.21 (95% confidence interval (CI): 1.15-4.25); p= 0.02 for DFS and of 2.47 (95%CI: 1.21-5.07); p=0.01 for OS. We also demonstrated that high levels of epithelial CD73 were negatively correlated with CD45+ tumor-infiltrating leukocytes (TIL) area in 122 TNBC samples from the BIG 02-98 adjuvant phase III clinical trial comparing the addition of docetaxel to doxorubicin-based chemotherapy in node-positive breast cancer. Our results demonstrated that high levels of CD73 on epithelial tumor were significantly associated with reduced disease-free (DFS) and overall survival (OS) in patients with TNBC. Using the median as a threshold between low and high levels of CD73 on epithelial cells, hazard ratios (HR) adjusted for grade, number of positive lymph nodes and tumor size, were of 2.21 (95% confidence interval (CI): 1.15-4.25); p= 0.02 for DFS and of 2.47 (95%CI: 1.21-5.07); p=0.01 for OS. We also demonstrated that high levels of epithelial CD73 were negatively correlated with CD45+ tumor-infiltrating leukocytes (TIL) area in 122 TNBC samples from the BIG 02-98 adjuvant phase III clinical trial comparing the addition of docetaxel to doxorubicin-based chemotherapy in node-positive breast cancer.
Further integration of gene expression data and neo-antigen profiling will be performed. In CMS4 group, whereas TP53 and APC mutations were observed more in the CMS2 group. Gene expression data of the same LM was used to infer the consensus molecular subtype (CMS) subtype: 7 LM were CMS4, 6 CMS2 and 1 CMS1. KRAS mutations were observed more concordant in 6/7 (85%). None of the mutations are shared between LM with distinct HGP. KRAS status of the primary tumor or metastasis was known in 7 LM and results were 22 samples (range 0 – 3). These SNV's occurred in the APC, KRAS, PIK3CA, SMAD4 and TP53 replacement HGP LM. A total of 20 pathogenic significant mutations were picked up in 14 of two metastatic samples with no significant differences between the desmoplastic and replacement HGP. A mean of 40020 (range 9573-53150) variants were picked up in the twenty-variants with a total depth of ≥ 20 and a variant read support ≥ 3 were kept.

Results:

Background: Different histological growth patterns (HGP) have been described and reflect the biological heterogeneity of liver metastases (LM). In the desmoplastic HGP tumor cells are separated from the liver parenchyma by a layer of desmoplastic stroma containing new blood vessels resulting from sprouting angiogenesis. In the replacement HGP, the tumor cells replace the hepatocytes in the liver cell plates thereby co-opting sinusoidal blood vessels as a means of blood supply. Recent research has confirmed that vessel co-option mediates resistance to anti-angiogenic therapy in LM2. To get an insight in the differences between the two distinct HGP, molecular characterization is needed.

Methods: Twenty-two colorectal LM (ten desmoplastic and twelve replacement) and adjacent normal liver tissue were sampled at the tumour-liver interface. Extracted RNA was converted in cDNA libraries and sequenced on a HiSeq 1500 using 2x100bp paired-end sequencing. After quality trimming, sequencing reads were aligned with STAR. Variant calling was performed using Varscan2 and annotated using Annovar. Only exonic, non-synonymous mutations that were not present in 1000Genomes, that were present in COSMIC and that were pathogenic were included. Variants with a total depth of ≥ 20 and a variant read support ≥ 3 were kept.

Results: A mean of 40020 (range 9573-53150) variants were picked up in the twenty-two metastatic samples with no significant differences between the desmoplastic and replacement HGP LM. A total of 20 pathogenic significant mutations were picked up in 14 of 22 samples (range 0 – 3). These SNV's occurred in the APC, KRAS, PIK3CA, SMAD4 and TP53 genes. KRAS status of the primary tumor or metastasis was known in 7 LM and results were concordant in 6/7 (85%). None of the mutations are shared between LM with distinct HGP. Gene expression data of the same LM was used to infer the consensus molecular subtype (CMS) subtype: 7 LM were CMS4, 6 CMS2 and 1 CMS1. KRAS mutations were observed more in CMS4 group, whereas TP53 and APC mutations were observed more in the CMS2 group. Further integration of gene expression data and neo-antigen profiling will be performed.
O.09 Geriatric assessment (GA)- guided interventions in older patients (pts) with cancer


1AZ Brussels, BRUSSELS, Belgium
2UZ Brussels, BRUSSELS, Belgium
3AZ Groeninge, KORTRIJK, Belgium
4Iridium Cancer Network, St Augustinus, WILRIJK, Belgium
5Clinique St Joseph, CHG LIEGE Hospital Group, LIEGE, Belgium
6Cliniques Universitaires St Luc, BRUXELLES, Belgium
7GHDC Grand Hôpital de Charleroi, CHARLEROI, Belgium
8AZ St Lucas, GENT, Belgium
9ULB Institut Jules Bordet, BRUXELLES, Belgium
10University Hospital Erasme, BRUXELLES, Belgium
11Centre Hospitalier de Mouscron, MOUSCRON, Belgium
12Imelda hospital, BONHEIDEN, Belgium
13Clinique et Maternité Sainte-Elisabeth, NAMUR, Belgium
14UZ Brussel, BRUSSELS, Belgium
15Wildiers


O.10 USP13 as a novel co-target for EGFR targeted therapies in EGFR mutant non-small cell lung cancer

Philippe Girou, Carolien Eggermont, Erik Teugels, Gustavo Gutierrez, Jacques De Grève

Vrije Universiteit Brussel, BRUSSELS, Belgium

Lung cancer is one of the most common human cancers in terms of incidence and mortality worldwide. Non-small cell lung carcinomas (NSCLCs) represent 85% of all lung cancer cases. Approximately 15-30% of NSCLCs are driven by mutations in the Epidermal Growth Factor Receptor (EGFR), leading to a strongly increased receptor activity stimulating cancer cell survival, proliferation and metastasis. Targeted therapies aimed to inhibit EGFR have been clinically approved and are now first line therapy for patients harbouring EGFR mutant NSCLC. The strongest clinically available EGFR inhibitor used as first-line therapy is the pan-HER inhibitor Afatinib. Despite a promising increased clinical outcome compared with conventional therapies, patients often relapse due to limited treatment efficacy and the emergence of resistance mechanisms. We postulate that early functional insensitivity mechanisms prevent optimal function of EGFR inhibitors upon initial treatment, and that these mechanisms can be co-targeted to improve overall treatment efficacy. In this study we aimed to identify and characterize proteins involved in early functional insensitivity against EGFR inhibitors in NSCLCs harbouring mutant EGFR. In order to discover these co-targets, we have performed an siRNA high-throughput screen targeting ubiquitin libraries in the presence of sub-lethal doses of afatinib using EGFR mutant NSCLC cell lines. We found that downregulation of the Ubiquitin Specific Peptidase 13 (USP13) strongly enhances the effect of afatinib to reduce the viability of NSCLCs in vitro. The combination of USP13 siRNA or inhibitor (spautin-1) with 5nM afatinib led to respectively 71±1,2% and 11±0,7% viability compared to vehicle control in PC9 (EGFR mutant NSCLC). We observe that co-targeting of EGFR and USP13 strongly enhanced the apoptotic rate in both caspase-3 cleavage analysis in western blot analysis and annexin-V/7-AAD signal in flow cytometry analysis. The decreased viability and increased apoptotic signalling is correlated to a decreased EGFR phosphorylation and downstream signalling. Moreover, in PC-9 both spautin-1 as USP13 siRNA leads to a decrease in total levels of EGFR.

In conclusion, we have identified USP13 as a potential co-target for afatinib as it is involved in EGFR signalling by controlling EGFR total and phosphorylation levels, thereby strongly enhancing afatinib efficacy in vitro.
P.01 Targeting Polo-like kinase 1 and TRAIL enhances apoptosis in non-small cell lung cancer (NSCLC) cells
Alfiah Noor1, Umele Adaku Ijeoma2, Peter Kronenberger3, Erik Teugels4, Jacques De Grève5
1Vrije Universiteit of Brussels, JETTE, Belgium
2Erasmusmushogeschool Brussel, BRUSSEL, Belgium

P.02 Polymorphisms in the Von Hippel Lindau gene are associated with poor overall survival in metastatic clear-cell renal cell carcinoma patients treated with VEGF tyrosine kinase inhibitors.
Annelies Verbiest6, Jessica Zucman-Rossi7, Dieter Lambrechts7, Benoît Beuselinck8
1KU Leuven, LEUVEN, Belgium
2INSERM UMR-1162, PARIS, France
3VIB, LEUVEN, Belgium

P.03 Selective internal radiotherapy: a 5-year single-center experience.
Tom Van den Mooter, Stijn Van Hecke, Ivan Huyghe, Thiery Chapelle, Marc Peeters
UZ Antwerpen, ANTWERP, Belgium

P.04 Osteonecrosis of the Jaw Incidence in Patients Treated Sequentially with Bisphosphonates and Denosumab
Tine Lysøe9, Thomas Van Cann10, Constantinus Politis11, Benoît Beuselinck12
1KU Leuven, LEUVEN, Belgium
2Department of Oral and Maxillofacial Surgery, University Hospitals Leuven, LEUVEN, Belgium

P.05 Incidence of osteonecrosis of the jaw in patients both treated with bone resorption inhibitors and vascular endothelial growth factor receptor tyrosine kinase inhibitors
Thomas Van Cann9, Tine Lysøe10, Constantinus Politis11, Philip Debruyne13, Benoît Beuselinck12
1KU Leuven, LEUVEN, Belgium
2Department of Oral and Maxillofacial Surgery, University Hospitals Leuven, LEUVEN, Belgium
3Department of Medical Oncology, AZ Groeninge, KORTRIJK, Belgium

P.06 A Nursing Intervention for Reducing Symptom Burden during Chemotherapy (CHEMO-SUPPORT): Results of a Quasi-Experimental Study
Annemarie Coolbrandt14, Hans Wildiers15, Anouschka Loenen16, Bert Aertgeerts17, Bernadette Dierickx de Casterlé18, The Van Achterberg19, Koen Milisen20
1KU Leuven, LEUVEN, Belgium
2University Hospitals Leuven - Department of General Medical Oncology, UZ Leuven, LEUVEN, Belgium

P.07 The role of CD70 in oropharyngeal squamous cell carcinoma and effect on survival
Astrid De Meulenaere21, Tijl Vermassen, Liesbeth Ferdinande, Sylvie Rottey
UZ Gent, GENT, Belgium

P.08 A prospective study on the impact of a NET specific multidisciplinary tumor board on individual treatment plans
1AZ Nikolaas, SINT-NIKLAAS, Belgium
2University of Antwerp, ANTWERP, Belgium
3Ziekenhuis Netwerk Antwerpen (ZNA), ANTWERP, Belgium
4GZA Ziekenhuizen, WILRIJK, Belgium
5AZ KLINA, BRASSCHAAT, Belgium
6Sint-Jozef Kliniek Bornem, BORNEM, Belgium
7University Hospital Antwerp, EDEGEM, Belgium
8NETwerk, EDEGEM, Belgium

P.09 Tamoxifen metabolism and breast cancer efficacy in the neo-adjuvant or metastatic setting - a prospective multicenter trial.
1KU Leuven, LEUVEN, Belgium
2University Hospitals Leuven - Department of Gynecology and Obstetrics, LEUVEN, Belgium
3Algemeen Ziekenhuis Sint-Blasius, DENDERMONDE, Belgium
4Algemeen Ziekenhuis Sint-Maarten, DUFFEL, Belgium
5University Hospitals Leuven - Department of Clinical Pharmacology & Pharmacoth, LEUVEN, Belgium
6Cantonal Hospital, ST. GALLEN, Switzerland
7Université catholique de Louvain, Centre hospitalier universitaire, Namur site S, NAMUR, Belgium
8Imelda Ziekenhuis, BONHEIDEN, Belgium
9KU Leuven, Department of Electrical Engineering, iMinds Medical Information, LEUVEN, Belgium
10KU Leuven, Department of Development and Regeneration, LEUVEN, Belgium
11Department of General Medical Oncology, UZ Leuven, LEUVEN, Belgium
12Department of Clinical Pharmacy and Toxicology, LEIDEN, Netherlands
13LUMC, Department of Clinical Pharmacy and Toxicology, LEIDEN, Netherlands

P.10 Systematic treatment preferences for patients with advanced desmoid-type fibromatosis (DF) in Europe
Thomas Van Cann38, Annelies Requilé39, Patrick Schönfee40
1Lab of Exp. Oncology, KU Leuven and Dept. of General Medical Oncology, UZ Leuven, LEUVEN, Belgium
2Department of General Medical Oncology, University Hospitals Leuven, LEUVEN, Belgium

P.11 Outcome and relapse pattern between squamous cell and adenocarcinoma of the cervix
Karen Couveure, Katrien Vandecasteele, Philippe Tummers, Amin Makar, Rudy Van den Broecke, Hannelore Denys
UZ Gent, GENT, Belgium
**P12**

**Oncological Home-Hospitalization in Belgium - Concept for optimizing ambulant cancer care**

Lieslent Cool, Jana Misljenova, Denise Vincken, Stefania Fugate, Marc Desmedt, Michelle Lycke, Tessa Lefebre, Hans Pottel, Veerle Foulen, Philip Debruyne, Direkta Van den Eyken

Koen Van Eygen

AZ Groeninge, KORTRIJK, Belgium

AZ Sint-Lucia, KORTRIJK, Belgium

Kulak, Catholic University Leuven Kulak, KORTRIJK, Belgium

KU Leuven, LEUVEN, Belgium

Ghent University, GHENT, Belgium

**P13**

**Tumour Databanking in Belgium: a central role for the BTV, the nationwide Belgian Virtual Tumourbank**

Kim Vande Voorde, Eva Van der Stock, Annelies Debucquoy, Mia Slaabberdt, Karen Ves, Katia Emmercamps, Lieselent Van Eyken, Vincent Grégoire

1Stichting Kankerregister, BRUSSELS, Belgium

2St-Luc University Hospital, BRUSSELS, Belgium

3Kulak, Catholic University Leuven Kulak, KORTRIJK, Belgium

4Hasselt University, HASSELT, Belgium

Lieselot Cool, Jana Missiaen, Dominique Vandeghinste, Sofie Degraeve, Melissa Desmedt, Marijke Ulenaers, Greetje Vanhoutte, Marc Peeters

**P14**

**Launching NE'Werk: diagnosis and treatment of neuroendocrine tumours within a multi-institutional collaboration in the region of Antwerp-Waasland in Belgium.**

Willem Lybaert, Timon Vanromunde, Marc Simons, Pascale Abram, Wim Demey, Tjou Mouperin, Marije Uilenbroek, Grethe Vanhoutte, Marc Peeters, NE'twerk Steering Committee

AZ Nikolaos, SINT-NIKLAAS, Belgium

University of Antwerp, ANTWERP, Belgium

Ziekenhuis Network Antwerpen (ZNA), ANTWERP, Belgium

GZA Ziekenhuisen, WILRIJK, Belgium

AZ KLINIKA, BRASSCHAAT, Belgium

Sint-Jozef Kliniek Borem, BORNEM, Belgium

AZ Heilige Familie Rums, RUMST, Belgium

University Hospital Antwerp, EDEGEM, BELGIUM

NE'twerk, EDEGEM, BELGIUM

**P15**

**Abiraterone acetate associated rhabdomyolysis**

Bert Van Den Heuvel, Hanomele Celen, Lieve Van de Heyning, Anne Rutten

Rdium kankernetwerk - campus Sint-Augustinus, WILRIJK, Belgium

**P16**

**Pharmacological and methodological aspects of the registration of side effects in clinical trials with abiraterone acetate.**

Georges El Hachem, Ziad El Ali

Jules Bordet, BRUSSELS, BELGIUM

---

**NAAM VAN HET GENEESMIDDEL:** ZYTIGA 250 mg tabletten.

**KWALITATIEVE EN KWANTITATIEVE SAMENSTELLING:**

Elke tablet bevat 250 mg abirateronacetaat. Hulpstoffen met bekend effect: Elke tablet bevat 189 mg lactose en 6,8 mg natrium.

**FARMACEUTISCHE VORM:** Ronde witte HDPE flessen met een polypropyleen kindveilige dop, met 120 tabletten. Elke verpakking bevat 1 fles.

**AFLEVERINGSWIJZE:**

– Over gevoeligheid voor de werkzame stof of voor één van de hulpstoffen.
– Vrouwen die zwanger zijn of die zwanger zouden kunnen zijn.
– Ernstige nierinsufficiëntie (crude creatinine nierfunctie < 60 ml/min of eGFR < 60 ml/min). Bij deze patiënten is voorzichtigheid geboden. Gelijktijdig gebruik van een corticosteroïd verlaagt de incidentie en de ernst van deze bijwerkingen. Lijst van bijwerkingen: In studies bij patiënten met gemetselde geassocieerde prostaatkanker was de overledenrate bij patiënten die werden behandeld met abirateronacetaat (15%) lager dan bij patiënten die geen of een lager dosering kregen en die werden behandeld met placebo (26%). Abirateronacetaat moet niet worden gebruikt bij patiënten met gemetselde geassocieerde prostaatkanker die ongecontroleerde hypertensie hebben, of bij patiënten die al vóór de start van de studie een gemetselde geassocieerde prostaatkanker hadden. voor de verandering van de dosis of bij het onderbreken of hernieuwen van de behandeling.
In the COU-AA-302 study, in which asymptomatic or mildly symptomatic patients with mCRPC post-ADT were treated with ZYTIGA® plus prednisone/prednisolone vs. placebo plus prednisone/prednisolone, 4.4 months median survival benefit was reported in the overall population (P=0.0033); in a post-hoc analysis, patients with BPI-SF 0–1, PSA <80 ng/ml and GS <8 showed 11.8 months median survival benefit (P=0.0055).2,3