Today's Top Picks!

Proffered Paper Session
Gastrointestinal tumors, prostate I
10:45 – 12:15 HALL D

Presidential Symposium
Presidential Symposium I
16:00 – 18:00 HALL A

Joint symposium
ESMO-MASCC
Integration between medical oncology and supportive care: Two sides of the same coin
16:15 – 17:45 HALL L-M

ESMO VIENNA 2012

congressdaily

SUNDAY 30 SEPTEMBER 2012

Dual therapy shows potential in melanoma

Two studies presented in the ESMO melanoma session yesterday point to the growing promise of dual blockade strategies in treatment of metastatic melanoma.

The BRAF inhibitor vemurafenib represents a new standard of care for metastatic melanoma patients with BRAF V600 mutations after showing improved progression free and overall survival in comparison with dacarbazine (DTIC). In many cases, however, benefits have proved short-lived as cancer cells develop resistance. Such observations have led to the initiation of new studies exploring treatment strategies targeting multiple signalling pathways at once.

In the first study, Dr Georgina Long and colleagues, from Westmead Hospital, Sydney, Australia, reported on a phase 2 study combining darafenib, an inhibitor of mutated BRAF 600, with trametinib, a selective MEK inhibitor. "The rationale behind adding the MEK inhibitor was that it blocks the same MAP kinase pathway as the BRAF inhibitor, but lower down. We hoped that by combining both drugs we would see significant delays in the emergence of resistance that would impact patients' lives," explained Dr Long.

In the study, 162 melanoma patients with BRAF V600 mutations were randomized 1:1:1 to receive either dabrafenib 150 mg twice daily; dabrafenib 150 mg twice daily plus once-daily 1 mg trametinib; or dabrafenib 150 mg twice daily plus once-daily 2mg trametinib.

Results show progression-free survival (PFS) was 9.4 months for patients receiving dabrafenib plus trametinib 2 mg versus 5.8 months for patients receiving dabrafenib alone (HR 0.39, 95% CI 0.25 – 0.62; p<0.0001). Furthermore, the confirmed response rate was 76% for patients receiving dabrafenib plus trametinib 2 mg versus 54% for dabrafenib monotherapy (p=0.026).

Pyrexia (fever above 38.5°C) and chills were the most common adverse events reported, occurring in 71% and 58% of patients respectively receiving dual therapy. But the fever, she added, can easily be prevented with corticosteroids.

"Importantly, the combination also decreased the rate of the cutaneous toxicities compared with dabrafenib monotherapy, particularly the oncogenic cutaneous toxicity of squamous cell carcinoma," said Dr Long.

In the second study, Dr Rene Gonzalez and colleagues, from the University of Colorada at Denver, Aurora, USA, explored the strategy of combining vemurafenib with the MEK inhibitor, GDC-0973, in patients with unresectable or metastatic BRAF V600 melanoma mutations.

In the phase 1 dose escalation study, patients received vemurafenib 720 mg or 960 mg BID continuously, with GDC-0973 used at doses of 60 mg, 80 mg or 100 mg QD, with a varying regimen of 14 days on / 14 days off; 21 days on and 7 days off and continuously.

Results for individual patients showed decreases in tumor size from baseline ranging from 25% to 60%. The discussant Reinhard Dummer, from Zurich, Switzerland, commented that it was remarkable that every single patient showed a response. He added that he had never seen such striking response rates before in his career.

Dr Georgina Long, Melanoma Institute Australia and Westmead Hospital, University of Sydney, North Sydney, Australia

The most common adverse events were diarrhoea (54.5%), rash (50%), nausea (38.6%), fatigue/ asthenia (34.1%), liver function abnormality (25.0%) and photosensitivity/sunburn (25%). Only one patient developed cutaneous squamous cell carcinoma. "But this particular patient received low levels of the MEK inhibitor," said Dr Gonzalez.

Late-breaking abstracts to be presented during today's Presidential Symposium...see page 3 for details

ESMO survey reveals 'global pandemic' of untreated cancer pain

Findings from an international survey presented in the Special Session yesterday morning concluded that hundreds of millions of cancer patients around the world are suffering needlessly due to government failures to ensure adequate access to pain-relieving drugs.

The 'International Collaborative Project to Evaluate the Availability and Accessibility of Opioids for the Management of Cancer Pain' was conducted by ESMO and the Developing Countries Task Force (DCTF), together with the European Association for Palliative Care (EAPC), the Pain and Policies Study Group (PPSG) at the University of Wisconsin Carbone Cancer Centre, the Union for International Cancer Control (UICC) and the World Health Organization (WHO).

Lead author of the report, Professor Nathan Cherny, from Shaare Zedek Medical Center, Jerusalem, Israel, said, "Unrelieved cancer pain is a cause of major worldwide suffering, not because we don't have the tools necessary to relieve pain, but because most patients don't have access to the essential pain-relieving medications."

Between December 2010 and July 2012, the survey gathered information submitted by experts from 76 countries and 19 Indian states. The results, which collectively represent 58% of all countries, revealed that:

- Very few countries provide all 7 of the opioid medications considered essential for pain relief by the International Association for Hospice and Palliative care
- In many countries, fewer than 3 of the 7 medications are available
- In many countries, the medications that are available are either unsubsidized or weakly subsidized by government, with availability often limited
- Many countries have highly restrictive regulations limiting the entitlement of cancer patients to receive prescriptions, including restrictive limits on the duration of prescriptions, restrictions on dispensing, and bureaucratic burdens in the prescribing and dispensing processes
- The issues were found to be particularly severe in Africa, Asia, the Middle East and Latin and Central America

Findings from this survey highlight the urgent need to examine drug control policies and repeal the excessive restrictions which are impeding a fundamental aspect of cancer care. "The study has provided an unprecedented wealth of knowledge that will be an essential tool in lobbying to reformulate national plans for the treatment of cancer pain," said Professor Cherny.

Novel hypoxia drug shows promise in pancreatic cancer

Combination therapy with the investigational hypoxia targeted drug, TH-302, and gemcitabine improved overall survival (OS) compared to gemcitabine alone in patients with advanced pancreatic cancer, according to results from an open label, Phase 2b study presented in the ESMO Proffered Paper session on Gastrointestinal tumors (non-colorectal) yesterday morning.

Disordered tumor vasculature creates a hypoxic environment, with pancreatic cancer known to be one of the most hypoxic solid tumors. TH-302 is a novel anticancer agent that is converted to bromo-isophosphoramide mustard (Br-IPM), a potent DNA alkylator, under hypoxic conditions, thereby selectively targeting hypoxic tumor cells. In contrast, there is reduced drug-associated toxicity in surrounding healthy tissue since TH-302 remains inactive under normoxic conditions.

In this Phase 2b study, 214 previously untreated patients with locally advanced, unresectable or metastatic pancreatic cancer were randomized 1:1:1 to receive either TH-302 240 mg/m² plus gemcitabine (n=71), TH-302 340 mg/m² plus gemcitabine (n=74) or gemcitabine alone (n=69). All treatments were administered on days 1, 8 and 15 of a 28-day cycle. The study had an 80% power to detect a 50% improvement in progression free survival (PFS) with combination therapy.

Results presented yesterday by Dr Mitesh Borad from the Mayo Clinic, Scottsdale, Arizona, USA, showed that the addition of TH-302 appeared to improve OS compared with gemcitabine alone, although the difference was not significant. The median OS was 9.2 months with TH-302 340 mg/m² plus gemcitabine, 8.7 months with TH-302 240 mg/m² plus gemcitabine and 6.9 months with gemcitabine alone.

Skin and mucosal toxicity and myelosuppression were the most common TH-302-related adverse effects. With TH-302 340 mg/m², rash and stomatitis occurred in 47% and 42% of patients, respectively, although this was rarely severe. However, the amount of hematological toxicity reported with TH-302 340 mg/m² was much higher than that reported with gemcitabine alone: 63% thrombocytopenia (versus 11%) and 60% neutropenia (versus 31%).

Dr Borad commented that although improvements in overall survival did not reach statistical significance in this trial, the results were consistent with the improvement in median progression free survival reported in February this year. The trial, he added, had not been designed to detect a statistically significant improvement in overall survival and had been complicated by a cross-over component, where patients receiving gemcitabine alone could be crossed over to receive gemcitabine plus TH-302 upon disease progression.

Dr Borad informed delegates that the dose of 340 mg has been identified as the way forward for future trials, and that a Phase 3 trial is to be initiated.

Twitter (hash tag: #ESMO12)

Diving right into research

In the Breakfast Session yesterday young oncologists were given a 'blue print' for making an impact on clinical research.

Professor Markus Raderer, from the Comprehensive Cancer Center of Vienna, Austria, outlined the three golden rules for success. "Think like a genius, live like a monk and work like a mule," he said.

Advising his audience to be daring and 'think out of the box', he recalled how in his own early career he had successfully published a case report in the New England of Journal of Medicine about treating gemcitabine-induced anal itch with corticosteroids.

Professor Raderer, who is a technical diver, peppered his presentation with diving analogies. The ultimate goal of oncology research, just like that of cave diving he said, is to find and explore unchartered territories. "In oncology as in diving, you are under pressure to publish, with very few colleagues to guide you, and many people find they are largely working in subterranean labs on their own," he said.

Good ways to get started include working on case reports, reviews, and participating in phase 3 studies. But for real success, advised Professor Raderer, oncologists need to focus. In his own career, Professor Raderer found that his publication rates peaked when he focused on his real passion lymphoma, where he has now published nearly 120 papers.

"As I tell my children, if you're an apple you'll always be a second rate banana. Stick to the things you know best, so if you're a clinical researcher you should stick to clinical investigations, and if you are a laboratory researcher stick to bench work. If you try to do both you're not likely to really succeed on an international level," he said.

Young oncologists, he advised, should focus on uncharted areas. "Here you'll not have to compete so much with established laboratories," he said.

But it was also important, he stressed, to network. "Nowadays a lot of people have the impression that you don't have to go to meetings because you can read everything on the internet. But the reality is that meetings are very important for exposing yourself to new ways of thinking about data and for building networks," he said.

But smaller meetings, he stressed, tend to prove more productive. "At specialty meetings, it's often much easier to interact with leaders in the field," he said.

ESMO Young Oncologist, Dr Erika Martinelli, from the Seconda Università delgi Studi, Naples, Italy, said, "This has been a really inspiring talk that got me thinking about all sorts of new approaches to getting going in research. It's given me some idea of how to gain entry into a really exclusive club."

Patient rights and obligations

Yesterday's Patient Symposium reviewing Patient rights and obligations, considered the 'health care financial Tsunami' currently facing European cancer patients and what patients can best do to facilitate good relationships with their doctors.

Ms Kathi Apostolidis, a breast cancer and patients' rights advocate from Greece, reviewed patient rights in 'turbulent' financial times. She quoted the results of a recent Cancer World survey on the impact of public spending cuts on frontline cancer care answered by 90 respondents from 20 European member states – where 10% reported 'no' impact on the quality of cancer care, 40% 'some impact', 35% 'quite an impact' and 15% a 'huge impact'.

"European cancer patients will suffer bitterly in the years to come. The translation of the austerity measures for cancer patients, who mostly use the public health care system, will mean very long waiting times for appointments with surgeons oncologists, and radiotherapists," she said.

Dr Lorenz Jost the Cancer Patient Working Group Chair, from Kantonspital, Bruderholz, Switzerland, gave the 'medical view' of patient's obligations. "Most problems with doctor-patient relationships arise due to poor communication. Communication always involves both partners. So – give your best too!"

Patients, said Dr Jost, need to tell medical staff the truth regarding their medical histories, the actual mediations taken, and any additional/ complementary therapies.

It was also of vital importance, he added, that patients adhere to treatment. "You need to take medications as prescribed. Don't just take half or the double. You need to tell your doctor if you can't and why, and you need to be honest about any side effects," he said.

On the topic of not endangering health care workers patients, he said, you need to tell the truth regarding known communicable diseases, such as tuberculosis, HIV infection and viral hepatitis. Patients need to appreciate that if they expect respect, they should show respect to health care workers, which should facilitate communication and treatment. "But it doesn't mean you shouldn't ask questions, request clarifications, ask for alternative treatment proposals and request a second opinion," said Dr Jost.

Kathi Apostolidis, a breast cancer and patient rights advocate, reviewed patient rights in 'turbulent' financial times. The results of a recent Cancer World Survey on the impact of public spending cuts on frontline cancer care – which was answered by 90 respondents from 20 European member states – showed that 10 % reported 'no' impact on the quality of cancer care, 40% 'some impact', 35% ' quite an impact' and 15% a' huge impact'.

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JOINT SYMPOSIUM

SUNDAY 30 SEPTEMBER

ESMO-EA CR Joint symposium: Targeted therapies: Promises, successes and failures
09:15 – 10:45 Hall B

ESMO-MASCC Joint symposium: Integration between medical oncology and supportive care: Two sides of the same coin
16:15 – 17:45 Hall L-M

MONDAY 1 OCTOBER

ESMO-ASCO Joint symposium: Genomics in breast cancer: Opening new doors
11:00 – 12:30 Hall D

ESMO DCTF-AOR TIC-SLA COM-UICC-WHO Joint Symposium: Independent and publicly funded research: a new global model
11:00 – 12:30 Hall G

ESMO-JSMO Joint symposium: Recent advances in the treatment of GI tract and liver cancer in the EU and Japan
14:00 – 15:30 Hall F1

ESMO-ESP Joint Symposium: Molecular diagnostics for personalized cancer treatment
14:15-15:45 Hall C

Today's Special Sessions for Young Oncologists

Designed for younger researchers and practitioners, the Young Oncologist Breakfast sessions will answer questions specific to the current stage of your career.

YO BREAKFAST

Today's breakfast session on 'How to plan and conduct a successful research fellowship abroad' will feature advice from the highly experienced Professor Wolfgang Köstler, President of the Austrian Society of Oncology, Medical University of Vienna, Austria.

YO BREAKFAST
SUNDAY 30 SEPTEMBER 08:00 – 08:45 HALL K

POSTER PRESENTATION II

During the afternoon poster session, our newly appointed YOC Chair from January 2013, Dr Rafaelle Califarno from The Christie NHS Foundation Trust, Manchester, UK, will present the first scientific findings from a European Survey in incompletely resected (R1) early stage non-small cell lung cancer (NSCLC) conduced by ESMO YOCs.

SUNDAY 30 SEPTEMBER 13:00 – 14:00 HALL X
POSTER: 1183P

PRESIDENTIAL SYMPOSIUM I
SUNDAY 30 SEPTEMBER 16:00 – 18:00 HALL A

Don't miss today's late-breaking abstracts that will be presented during the Presidential Symposium session. These late-breaking abstracts are of significant importance since they provide first reports of important studies with cutting-edge data that could change current clinical practice.

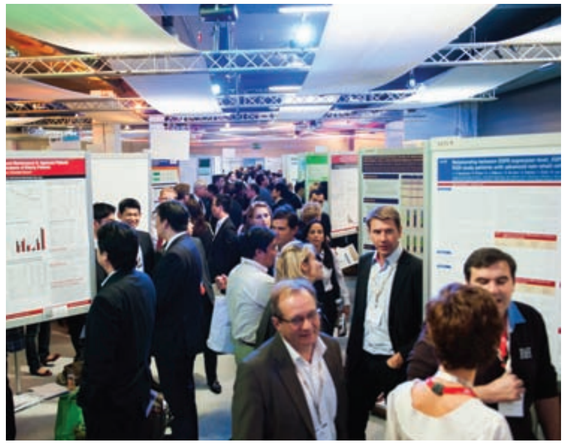
LBA1_PR Dr Alice Shaw from Massachusetts General Hospital, Boston, MA, USA, will present data from PROFILE 1007, a Phase 3 trial of crizotinib versus pemetrexed or docetaxel in patients with advanced ALK-positive non-small cell lung cancer (NSCLC) who had received one prior treatment with a platinum-based chemotherapy regimen. Data for the primary endpoint of progression-free survival (PFS), as well as various secondary endpoints, including objective response rate (ORR), overall survival (OS) and safety, will be presented.

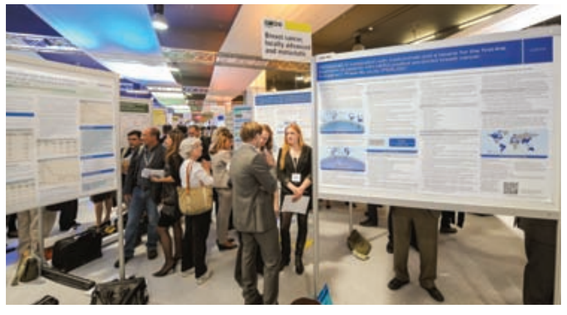
LBA2 Dr Andrew Zhu from Massachusetts General Hospital, Boston, MA, USA, will present data from SEARCH, a Phase 3 trial of erlotinib given in combination with sorafenib in patients with advanced hepatocellular carcinoma (HCC). The aim of this study was to determine whether the addition of erlotinib to sorafenib as standard of care would result in synergistic or additive antitumor activity. Both primary and secondary endpoint data will be presented, which will include OS, time to progression (TTP), disease control rate (DCR) and safety.

LBA3 Professor Florian Lordick from University Clinic Leipzig, Braunschweig, Germany, will present findings from the open-label randomized, controlled Phase 3 EXPAND trial of cetuximab in combination with capecitabine and cisplatin as first-line treatment for advanced gastric cancer. Data for the primary endpoint of PFS will be presented, together with data for key secondary endpoints, including OS, best overall response and safety.

LBA4 Dr Julien Taieb from the Hôpital Européen Georges Pompidou, Paris, France, will present data from the PETACC8 Intergroup Phase 3 trial which evaluated adjuvant therapy with FOLFOX4 with or without cetuximab in patients with resected, stage III, KRAS wild-type (wt) colon cancer. Data for the primary endpoint of disease-free survival (DFS), key secondary endpoints, including OS, treatment compliance and safety, and other pre-planned subgroup analyses, will be presented.

Posters draw crowds at ESMO





Treatment of melanoma makes headway

An educational session held yesterday, which focused on the the diagnosis and management of advanced melanoma, revealed the extraordinary progress made in the past few years.

Professor Boris Bastian from the University of California San Francisco (UCSF), California, USA, provided an overview of the latest insights into melanoma patho-biology. Melanoma gene discovery, he said, has occurred in 'an era of massive parallel sequencing', with over eight genotype phenotypes now identified in primary melanomas.

The susceptibility hypothesis holds that BRAF dependent melanomas develop in younger patients, whereas independent mutations develop in older patients. However, other significant mutations have now been identified, including NRAS, TP53, PTEN, PPP6C, CDKN2A, MAP2KI, SNX31, STK19, RAC1 and TACCC1.

"Melanomas are a genetically and phenotypically diverse group of biologically distinct entities. Integrating molecular and phenotypic features would lead to an improved, more clinically relevant taxomy," said Professor Bastian.

Professor Reinhard Dummer, from the University of Zurich, Switzerland, informed delegates that for over 30 years, the standard of care for patients with advanced melanoma has been single-agent dacarbazine (DTIC) which in trials has displayed response rates of 7 15%. But the discovery of BRAF mutations in 66% of melanomas has resulted in the development of BRAF inhibitors, with vemurafenib leading the way. The Phase 3 trial showed that vemurafenib was associated with a 63% reduction in the risk of death compared to DTIC.

Professor Dirk Schadendorf from the University Hospital Essen, Germany, explored the new approach to immunotherapy. Melanoma immunotherapy, he said, has a ceiling response in the order of 10 – 20% of patients.

"While responses can take time, once there is a response it tends to be durable and some patients are seemingly cured," said Professor Schadendorf. Clinical features associated with increased response rates include skin, in-transit and nodal metastasis, low levels of low-density lipoprotein (LDL), and pre-existing or induced autoimmune phenomenon.

Current immunological approaches include specific immunization and unspecific immunostimulation. Specific approaches have included vaccination of melanoma patients with peptide or tumor lysate-pulsed dendritic cells, while unspecific approaches include iplimumab.

Ipilimumab, he explained, is an antibody that activates the immune system to fight melanoma cells by inhibiting the cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) molecule found on T cells.

Recent studies have shown that in patients with brain metastases, ipilimumab nearly doubled the one and two year survival rates and resulted in prolonged survival. Most strikingly, said Professor Schadendorf, 26% of patients were alive at two years.

In the future, biomarkers will need to be found that identify patients who have the potential to respond, he concluded.

Winning combination for gastric cancer

Findings from the latest analysis of the START trial reported yesterday revealed that adding docetaxel to S-1 significantly improved overall survival in patients with advanced gastric cancer (AGC).

Both S-1 (an orally administered fluoropyrimadine) and docetaxel (a semi synthetic taxane) are known to be active against gastric cancer. In the Phase 3 START trial, the Japanese Clinical Cancer Research Organization (JCCRO) and Korean Cancer Study Group (KCSG) set out to explore whether the addition of docetaxel to standard treatment with S-1 might enhance clinical benefits for patients with AGC.

When the first results from this trial were presented at ASCO GI last year, they showed that this study failed to meet its primary overall survival (OS) endpoint. However, during a subsequent review of the study dataset, an independent biostatistician pointed out that a large number of 'censored' cases had led to an insufficient number of events for proper analysis. As a result, further follow-up for OS was recommended with updated results from this later analysis presented yesterday by Professor Kazuhiro Yoshida, from Hiroshima University, Japan.

In the study, 639 patients from Japan and Korea with unresectable or recurrent gastric cancer were randomly assigned to receive docetaxel (40 mg/m2 q21d) plus S-1 (80 mg/m^2 on days 114 of a 21-day cycle) or S1 alone (80 mg/m^2 on days 1–28 of a 42-day cycle).

Updated results show that OS, progression free survival (PFS) and response rate (RR) were significantly improved with combination therapy: median OS was 12.5 months in the docetaxel plus S-1 group versus 10.8 months in the S-1 group (HR 0.837; 95% CI 0.711 – 0.985, p=0.0319), PFS was 5.3 months in the docetaxel plus S-1 group versus 4.2 months in the S-1 group (HR 0.765; 95% CI 0.653 0.898, p=0.001), and RR was 38.8% in the docetaxel plus S1 arm versus 26.8% in the S-1 arm (p=0.005).

However, Professor Yoshida also explained that the observed benefits of combination treatment in this study were at the expense of increased hematological toxicities – neutropenia was more frequent in the combination arm (29.0% versus 4.2%), with one patient dying from Grade 4 thrombocytopenia.

Daily Editorial

Let's get personal about cancer

It has been a delight to listen to such excellent research presented so far at ESMO. One story particularly stands out: the incredible advances we have made in just a few years in the molecular profiling and genetic subtyping of cancers. Today, the detection and correlation of clinical responses to genetic variation has become a necessary element of almost every clinical trial.

The ongoing search for key mutations and hence molecular targets for therapies fuels the research community. Every tumorigenic mutation offers a potential target for treatment. At the same time, the increase in validated predictive biomarkers will help clinicians to select the most suitable drugs and treatment regimens for their patients. Many patients today are experiencing good response rates and longer survival thanks to detailed genetic subtyping of their tumors.

The 'personalization' of medicine – still not the production of individually tailored therapeutics but at least an informed choice of agents and regimens for every individual – is becoming a reality.

In my area of brain tumors, we heard in the special symposium on molecular neuro-oncology about several genetic mutations and characteristics, which are prognostic, but also predictive for improved treatment outcomes. Studies have shown that testing for isocitrate dehydrogenase (IDH) mutations is not just helpful for the diagnosis of grade II and grade III anaplastic glioma, but also has significant prognostic implications. For glioblastoma, MGMT has been identified as important prognostic and for some patient populations, a predictive marker.

But here is the big question: do molecular biomarkers really help with decision making in the clinical setting? Of course, we know that genetic profiling is standard for some cancers such as HER2 testing for breast cancer, or KRAS mutations testing for colorectal cancer. But for most cancers, molecular profiling is still not clinically validated, although there is plenty of encouraging data emerging, including presentations here at ESMO, to suggest that this could change in the near future.

Can we look forward to a day when tumors are fully profiled for all known biomarkers as standard practice? And if they are, will clinicians know the full extent and implications of the results they receive and the nuances that particular combinations of markers signify in terms of treatment? Or will we continue to stick rigidly to standard therapies – perhaps afraid of the risks and repercussions of following non-standard treatments?

Fortunately, for glioblastoma, a deadly cancer, which we have not understood biologically at all for a long time, promising biomarkers of response to therapy are emerging. Most importantly, MGMT promoter methylation status has been singled out as a predictive marker for response (or non-response) to chemotherapy with temozolomide in elderly glioblastoma patients. Another potential 'druggable' molecular alteration is a specific type of epidermal growth factor receptor mutation, EGFRvIII and this is being explored in randomized clinical trials investigating vaccination strategies.

Matthias Preusser, Associate Editor
Medical University of Vienna, Vienna, Austria

The number of validated biomarkers for virtually every cancer is set to explode and there are important advances not only in adult, but also in pediatric neurooncology. Yesterday's symposium heard about the molecular heterogeneitiy of medulloblastoma. Beside known alterations (CTNNB1, PTCH1, MLL2, SMARCA4), an integrative deep-sequencing analysis has revealed that several genes not previously implicated in the disease (DDX3X, CTDNEP1, KDM6A) are recurrently mutated, often in subgroup-specific patterns; many of these genes are involved in chromatin remodeling. Hopefully, these advances will soon lead to the development of targeted agents for pedriatic brain cancer subtypes, for example sonic hedgehog inhibitors in medulloblastoma patients.

But even as the pool of biomarkers expands, we observe that most treatment decisions for brain tumor patients are still based on age and performance status today, even though biomarkers with validated clinical performance have been identified. Indeed, this pattern is replicated across many therapy areas.

In my opinion, one major obstacle to bringing new biomarkers into use in everyday clinical work and for the benefit of patients is the lack of studies validating our laboratory assays. It is important to understand that assays that can separate patient populations in large studies often turn out not to be sensitive and specific enough to be used for treatment decisions in the individual patient sitting in front of you today. We need more high quality studies on the analytical performance of test methods to identify the best assays for a given biomarker. At present we are missing a selection process for biomarkers, which is similar to the process novel drugs have to go through, i.e. phase 1, 2, 3 trials. Clinical and tissue-based researchers need to come together to solve this problem in an interdisciplinary effort.

As a young oncologist I am thrilled about the speed at which oncology is moving forward at the moment and that becomes clear once again here at the ESMO 2012 meeting. Attending this meeting incredibly motivates me to continue being part and research in oncology to help develop this fascinating field so that we can ultimately defeat cancer some day. I hope many of my colleagues share this feeling and enjoy the congress here in the beautiful city of Vienna!

Treatment advances in head and neck cancer

Treatment choices based on risk factors in locally advanced head and neck cancers were considered in an educational session yesterday afternoon.

Dr Boudewijn Braakhuis from the University Medical Centre, Amsterdam, The Netherlands, advised that improvements in therapy are desperately needed for this field, because only 40 50% of patients currently survive five years. Biomarkers, said Dr Braakhuis, are essential to develop new targeted treatments and improve survival through personalized therapy.

Potential biomarkers for head and neck cancers include loss of heterozygosity (LOH) and TP53 mutations. Furthermore, high EGFR expression and the emergence of skin rash are also believed to be predictive markers of cetuximab efficacy.

Validation of putative biomarkers in clinical trials should now be mandatory, said Dr Braakhuis. "But the idea of 'one-mutation-one-treatment' is probably too simplistic. Information on all possible gene alterations in a given pathway and parallel pathways is likely to be needed to predict responses to a targeted therapy," she said.

Optimization of drug prescriptions for head and neck cancers were considered by Dr Lillian Siu from the Princess Margaret Hospital, Toronto, Ontario, Canada.

Current treatments include sequential therapy (induction chemotherapy and concurrent chemo-radiotherapy), chemo-additive (adding another agent to standard chemotherapy), chemo-sparing (using another agent to replace or reduce chemotherapy), and radio-sparing (using an alternative treatment to reduce radiation doses).

There is a need to achieve a balance between preserving high cure rates while reducing acute and late toxicities. "We need to understand the biology of head and neck cancers so that patients who relapse despite having low risk can be identified early," said Dr Siu. Research, she added, should be targeted at primary and acquired resistance mechanisms.

Professor Jordi Giralt, from Vall d'Hebron University Hospital, Barcelona, Spain, advised that dose painting is a new strategy that can be used for optimal dose intensification. The technology involves the integration of multimodal imaging to optimize target volumes and prescription doses in head and neck cancers.

The value, said Professor Giralt, is reductions in toxicity that should deliver quality of life advantages, including recovery of saliva flow and improvements in swallowing.

Controlled trials have shown dose painting to be feasible, with clinical trials now required to validate this strategy. Such approaches, said Professor Giralt, should pave the way for more effective and individualized treatments in head and neck cancers.

VIP treatment at the Membership Lounge

TODAY'S EDUCATIONAL SESSIONS

Decision making & management of glioma: Practical considerations
09:15 – 10:45 Hall G

Diagnosis and management issues in colorectal cancer (Repetition)
11:00 – 12:30 Hall C

Diagnosis and management issues in lymphoma
14:15 – 15:45 Hall L-M

Diagnosis and management issues in melanoma (Repetition)
16:15 – 17:45 Hall F1

Issues in sarcoma (Repetition)
14:15 – 15:45 Hall C

Locally advanced disease: Treatment choice based on risk factors in head and neck cancer (Repetition)
11:00 – 12:30 Hall F1

Molecular tools for decision making in breast cancers (Repetition)
09:15 – 10:45 Hall C

Towards integrated management of patients with carcinoma of an unknown primary site (CUP)
16:15 – 17:45 Hall C

Updates in supportive and palliative care
14:15 – 15:45 Hall F1

Image of the day

Case for including patients with brain metastases in clinical trials

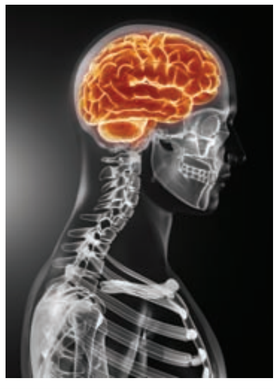
The presence of brain metastases should not preclude patients from being entered into clinical trials, delegates heard in the Molecular Neuro-Oncology Special Symposium yesterday. However, Professor Michael Brada, from the Royal Marsden Hospital, London, UK, told the audience that there was a need for subgroup analyses where patients with brain metastases are analyzed separately from those with systemic extracranial disease only.

Professor Brada advised that this will be especially important in clinical trials testing new anti-metastatic agents, otherwise it will be impossible to provide proof-of-principal for the therapeutic efficacy of these agents in the brain.

Traditionally, investigators have shied away from recruiting patients with brain metastases into clinical trials since chemotherapy agents are of limited efficacy due to their inability to cross the blood brain barrier. However, tumor vasculature tends to be relatively permeable, as evidenced by enhancement of lesions with contrast agents. Therefore, many chemotherapeutic agents, although unable to penetrate the blood-brain barrier, may still achieve therapeutic levels where brain metastases have disrupted the blood brain barrier.

Professor Brada stressed that future clinical trials exploring agents in brain metastases should focus on patients in whom brain metastases are likely to be the main determinants of outcome and who have inactive systemic disease. The issue has been that many previous trials treating patients with solitary brain metastases with chemotherapy have not influenced survival, suggesting that brain disease is not the principal determinant of life expectancy when patients have disseminated disease.

Professor Brada concluded that for future studies to have any chance of success, appropriate patient selection using enrichment with predictive biomarkers will also be needed.



ESMO holds first session dedicated to Community Oncologists

Issues regarding the tailoring of chemotherapy dosing in specific situations, awareness of drug-drug interactions with chemotherapy and concurrent medications and defining quality indicators for oncology practice, were all raised and discussed during the first ESMO Special Session yesterday.

The ESMO Community Oncology Working Group was created in 2010 with the aim of representing professionals working outside academic institutions or comprehensive cancer centers who treat patients with a wide range of tumors.

"This working group believes that cancer care ought to be of the same quality if delivered in an academic institution or by an ESMO member oncologist practising in a community setting. The group therefore works with ESMO to support practising oncologists in delivering the best available care to their patients," explained Dr Robert Eckert, Chair of the ESMO Community Oncology Working Group.

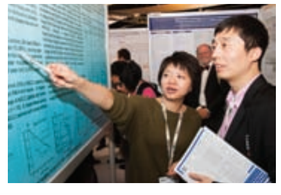
Dr Eckert from Weindlingen, Germany, explained that yesterday's special session 'Excellence in Care and Chemotherapy: Goals and Challenges for the Oncology Team' had been devised in direct response to results from a European survey which showed that community oncologists would like ESMO conferences to provide education relevant to their every day practice. Already, ESMO has implemented a number of measures for community oncologists, including OncologyPRO, ESMO's online education portal, ESMO Clinical Practice Guidelines and additions to the ESMO web pages to ensure the efficient delivery of relevant information to oncologists everywhere.

Dr Walter Baumann, from the Scientific institute of office-based Hematologists and Oncologists, Cologne, Germany, outlined the issue of quality assurance in oncology and provided an overview of the WINHO (Wissenschaftliches Institut der Niedergelassenen Hämatologen und Onkologen GmbH) project, that aims to enhance ongoing quality reporting, ensure fair assessment of every outpatient care unit, consider peer-to-peer benchmarking and incorporate systematic support of practice quality improvement. Dr Baumann described how 46 quality measures for oncology practices have been defined from 67 measures selected from the literature concerning medical oncology treatment in general and treatment of breast and colorectal cancer in particular, with 6 measures used to pilot data collection. Dr Baumann advised that the first experience in Germany showed that many oncologists are willing to participate. However, there are still a number of challenges ahead for this initiative, including the need to ensure uniform data collection in a way that does not enlarge bureaucracy and that can be translated into quality improvements in everyday practice

Professor Carsten Bokeymer from University Cancer Center, Hamburg, Germany, reviewed the challenge of identifying the right chemotherapy dose for the right patient. During his talk, he highlighted several key patient groups where these issues are particularly relevant, including patients with obesity, those with renal insufficiency and dialysis patients, and those with liver dysfunction, and stressed that although safety data for dose modifications are limited, careful action is always required.

Professor David Kerr, from the Universities of Oxford and Cornell, addressed the serious issue of drug-drug interactions. During his talk, he highlighted key factors predisposing patients to drug interactions, multiple medications, advancing age, compromised liver or kidney function, more than one prescriber and comorbidities. He warned that drug interactions can often be overlooked or even explained as poor compliance or progressing disease, and advised that an improved knowledge of the drug interaction process, possibly by the development of a dedicated web-based service, could aid diagnosis of many cases of unexplained or unexpected responses to drug therapy.

Finally, Dr Elizabeth Schnoy, from Regensburg, Germany, outlined the principle goals of process safety in chemotherapy and explored processes that could be put in place to improve safety in terms of both the prescription and administration of chemotherapy.



Heat shock protein inhibitor shows potential in NSCLC

Ganetespib is a potent inhibitor of heat shock protein 90 (HSP90), a molecular chaperone required for the proper folding and activation of many cancer-promoting proteins, that has already demonstrated single-agent activity in pre-treated patients with advanced NSCLC harboring the ELM4-ALK rearrangement and KRAS mutations.

Although severe liver or ocular toxicities have been observed previously with HSP90 inhibitors, investigators believe that the physicochemical properties of ganetespib - including its smaller molecular weight, greater potency and lipophilicity, and the absence of the benzoquinone moiety - contribute to its improved safety profile.

The GALAXY (Ganetespib Assessment in Lung CANCER with docetaXel) trial has been designed with two distinct stages. The first stage was a randomized, open-label, Phase 2b trial that enrolled 300 patients with Stage IIIB/IV NSCLC who had progressed following one prior line of therapy; the goal of this stage of the trail was to determine biomarkers predictive of ganetespib activity. Results from the phase 2b part of the trial reported here at ESMO will be used to guide the choice of patient populations for the subsequent Phase 3 stage of the trial.

In addition to NSCLC, ganetespib is currently being evaluated in clinical trials in a broad range of tumor types, including breast, colorectal, gastric, prostate, pancreatic, melanoma and hematologic cancers.

Joint ESMO-ESTRO symposium tackles brain metastases

The joint ESMO-ESTRO symposium yesterday explored innovative approaches to the treatment of brain metastases, including prevention in patients with primary cancers, treating patients with human epidermal growth factor 2 (HER2)-positive metastatic breast cancer (MBC) and brain metastases with the combination of lapatinib and capecitabine, and the potential for radiation dose escalation.

The symposium heard that as chemotherapies improve and result in better systemic disease control, the number of patients with brain metastases is likely to increase.

Preventing the development of brain metastasis in patients with primary cancers represents a feasible goal, argued Dr Brunilde Gril, from the National Institutes of Health, Bethesda, M D, USA.

Brain metastases outnumber primary brain tumors by 10 to 1, with the most common primary sites being lung (50 60%), breast (15 20%), melanoma (5 10%) and GI tract (4 6%). Traditional drug therapies are ineffective for brain metastasis, with the blood-brain barrier remaining an obstacle for brain metastasis therapy. "Brain permeable drugs are needed," said Dr Gril.

Reporting on a study that had recently been undertaken to test the efficacy of 18 compounds, including traditional chemotherapeutics and small molecule inhibitors, in an experimental model of brain metastasis, Dr Gril said that vorinostat, lapatinib, pazopanib, TPI-287, gemcitabine and irinotecan have all been shown to prevent the development of brain metastases. But no drug, he added, has been found to effectively shrink already-established brain metastases.

The next step, said Dr Gil, should be to launch Phase 2 prevention trials in which patients with aggressive primary tumors and limited brain metastases (who have not undergone whole brain radiotherapy) would be randomized to receive a preventive agent or placebo. The endpoint of the trial, Dr Gil added, should be time to development of new metastases.

Brain metastases occur in 3 40% of patients with MBCs that overexpress HER2, explained Dr Thomas Bachelot, from the Centre Leon Berard, Lyon, France. Treating HER-positive breast cancer patients with brain metastasis with a combination of lapatinib and capecitabine prior to local treatment, he said, represented a potential new approach.

Presenting the results of the LANDSCAPE study, Dr Bachelot said that between April 2009 and August 2010, 45 patients with HER2-positive MBC and brain metastases (who had not previously undergone whole brain radiotherapy) received lapatinib 1.250 mg once daily and oral capecitabine 2.000 mg/m² from day 1 to day 14 every 21 days. Results showed that 86% of patients experienced reductions in tumor volume; the median time to progression was 5.5 months, median time to radiotherapy was 8.3 months, and the median overall survival was 17 months. The most common adverse events were diarrhea, hand foot syndrome, and nausea.

"Our data suggests this strategy could help delay whole brain radiotherapy associated neurological toxicity," said Dr Bachelot. The strategy, he added, now deserves further evaluation to confirm the clinical benefits in terms of survival, cognitive function and quality of life.

Professor Claus Belka, from the Ludwig Maximilian University, Munich, Germany, explored the potential role for intensity modulated radiotherapy (IMRT), Intensity-modulated arc therapy (IMAT) and tomotherapy to reduce the neurotoxicity of whole brain radiotherapy. Radiation, he said, has the potential to depopulate neural stem cells and impair neurogenesis through inflammatory processes. Irradiation increases hippocampal apoptosis and decreases hippocampal proliferation, leading to deficits in learning, memory, attention and spatial processing due to radiation-induced hippocampal injury. The late toxicity effect of dementia occurs in more than 11% of patients following radiotherapy, with early toxicity effects including problems with verbal and short term memory recall.

"But only 3% of brain metastases are actually situated within the hippocampus leading to the possibility of introducing strategies to reduce neurotoxicity in whole brain radiotherapy," said Dr Belka.

IMRT, IMAT and tomotherapy, he said, all seem to have a role in sparing hippocampus structures. "But no date is available on improved neurological outcomes or tumor control," he said.

Dr Frank Lagerwaard, from the University Medical Center, Amsterdam, The Netherlands, explored the potential role for radiation dose escalation in patients with brain metastases. While the majority of patients with brain metastases from solid tumors have a prognosis of only a few months based on extracranial tumor activity and performance status, said Dr Lagerwaard, a subset exist who may be able to achieve long term survival if brain metastases are treated aggressively.

Radiosurgery, involving high precision delivery of a single fraction of approximately 20 Gy directed to the lesion results in local control rates of 60 to 90 %, depending on the size and position of the lesion.

The question of whether whole brain radiotherapy (WBRT) should be added to radiotherapy has been a long standing unresolved issue. Proponents of the combination approach highlight the opportunity for better intracranial control; while opponents point out increased neuro cognitive toxicity.

Techniques such as volumetric intensity modulated arc therapy (VMAT, Rapid Arc), or tomography, which allow fast and accurate delivery of fractionated stereotactic integrated boosts to multiple brain metastases might be used in combination with whole brain radiotherapy. Such integrated approaches, said Dr Lagerwaard, have the advantage of allowing steep dose gradients outside the brain metastases thereby minimizing toxicity.

"But with the exception of a few randomized radio surgery trials, the clinical benefit of dose escalation remains to be defined," said Dr Langerwaard.

PRESIDENTIAL SYMPOSIUM II MONDAY 1 OCTOBER **16:00 – 17:45 HALL A**

Don't miss the second Presidential Symposium, taking place tomorrow, which will comprise presentations of the very best late-breaking abstracts, findings from which could change current clinical practice.

Abstract: LBA5_PR PHARE Trial results comparing 6 to 12 months of trastuzumab in adjuvant early breast cancer

Presenter: Professor Xavier Pivot, Hôpital Jean Minjoz, Besancon, France

Abstract: LBA6_PR HERA TRIAL: 2 years versus 1 year of trastuzumab after adjuvant chemotherapy in women with HER2-positive early breast cancer at 8 years of median follow up

Presenter: Professor Richard Gelber, Dana-Farber Cancer Institute, Boston, USA

Abstract: LBA7 Results of a randomised phase 3 trial (EORTC 62012) of single agent doxorubicin versus doxorubicin plus ifosfamide as first line chemotherapy for patients with advanced or metastatic soft tissue sarcoma: a survival study by the EORTC Soft Tissue and Bone Sarcoma Group

Presenter: Professor Winette van der Graff, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

Abstract: LBA8_PR Randomized, open label, phase 3 trial of pazopanib versus sunitinib in first-line treatment of patients with metastatic renal cell carcinoma (mRCC); Results of the COMPARZ trial

Presenter: Professor Robert Motzer, Memorial Sloan-Kettering Cancer Center, New York, USA

The road towards stratified care for patients with glioblastoma

Extensive efforts are currently underway to define biological markers as the basis for treatment selection for patients with glioblastomas, delegates heard yesterday in a symposium dedicated to exploring new avenues in molecular neuro-oncology diagnosis and treatment.

Dr Michael Weller, from University Hospital, Zurich, Switzerland, advised that a recent clinical issue has been the growing population of elderly patients with glioblastoma, where the combination of radiochemotherapy doesn't appear to be superior to monotherapy and may be less well tolerated than either radiotherapy or chemotherapy alone. Given this situation, Dr Weller highlighted the need to identify biomarkers to help stratify patient care.

It has already been shown that glioblastoma patients with promoter methylation of the 06-methylguanine methyltransferase (MGMT) gene derive greater benefits from alkylating agent chemotherapy. MGMT promoter methylation may therefore assume a particularly important role as a predictive biomarker among elderly glioblastoma patients.

Although results from registration trials for two anti-angiogenic compounds are still awaited, biomarkers to indicate which patients might derive most benefit from anti-vascular endothelial growth factor (VEGF) therapies have not been introduced into the clinic. However, it may be possible to use positron emission tomography (PET) for the detection of avb3/5 integrins in order to select patients for anti-integrin/anti-angiogenic therapy.

Screening for the epidermal growth factor receptor mutation, EGFRvIII, is also being explored as a biomarker for selecting patients for vaccination in two randomized clinical trials. "It's to be hoped that these and other ongoing clinical trials may enrich the repertoire of criteria for clinical decision making in the very near future," concluded Dr Weller.

Family cancer histories prove challenging

Identifying individuals with inherited mutations conferring high risks of cancer before they develop tumors may be our best strategy for cancer prevention. But in a special symposium yesterday exploring how medical oncologists are dealing with the new wave of genetic information, Dr Ephrat Levy Lahad from Shaare Zedek Medical Center, Jerusalem, Israel, advised that real challenges exist for the widespread implementation of such approaches.

Currently, carriers are most often identified after they have been diagnosed with cancer, or through a family history of cancer. The utilization of family history, however, is limited by a lack of communication both about cancer diagnoses and the results of genetic testing.

Dr Levy Lahad presented data from his recent study on BRCA1/ BRCA2 testing that he had undertaken in the general Ashkenazi (European) Jewish population. Two mutations in BRCA1 and one in BRACA2 are common in the Ashkenazi Jewish population, placing them at increased risk of ovarian and breast cancer. Findings from his study revealed that half of the families included did not possess sufficient information on their family histories, suggesting that many carriers of BRCA1/ BRCA2 mutations could not be readily identified without the implementation of a general screening program. However, Dr Levy-Lahad warned that there are both technical and ethical challenges to such an approach.

SPECIAL SYMPOSIA SUNDAY 30 SEPTEMBER

Re-inventing the medical treatment of advanced prostate cancer
09:00 – 10:30 **Hall F1**

Optimizing treatment in luminal breast cancer
11:15 – 12:45 **Hall E**

How to integrate new drugs in the current therapeutic landscape of metastatic triple negative breast cancer
16:15 – 17:45 **Hall D**

Imaging biomarkers in the era of targeted therapies

A variety of imaging techniques and technologies are helping clinicians to evaluate treatment success as well as to determine the stage and spread of disease in patients. Yesterday, ESMO joined forces with the European Association of Nuclear Medicine (EANM) and the European Society of Radiology (ESR) for a joint symposium entitled 'Imaging biomarkers in the era of targeted therapies'.

Professor Elisabeth de Vries from the University Medical Center Groningen, Groningen, the Netherlands, opened the session with an overview of imaging approaches in cancer, where she outlined the important role of imaging in oncology and emphasized the need for oncologists and radiologists to work together in order to maximize the potential of imaging biomarkers in oncology, particularly in the current era of targeted therapy.

Dr Jan Bogaerts from the EORTC, Brussels, Belgium, discussed the basis of Response Evaluation Criteria in Solid Tumors (RECIST), a widely applied method to assess solid tumor response and progression. He outlined the technique's strengths, weaknesses and ongoing efforts to improve this methodology. For example, in 2009 RECIST v1.1 was published, which included a host of modifications and additional specifications and clarifications, including a restriction in the number of target lesions to a maximum of five and special considerations for lymph nodes.

However, work on the existing EORTC RECIST database is ongoing, which includes efforts to collect FDG-PET data for evaluation and potential inclusion into the methodology.

Dr Yves Menu from Saint Antoine Hospital, Paris, France, continued the discussion on RECIST, as he described the advantages of standardizing assessment processes and the technical requirements that practitioners need to consider when using RECIST. Dr Menu argued that standardization also has limitations since certain tumors, such as GIST and HCC, may also need adapted criteria. "Morphology does not summarize tumor biology," he remarked, "so adding structural, metabolic and/or functional information is desirable."

New developments in oncologic imaging, including how functional imaging influences treatment decisions in patients with malignancy, were discussed by Dr Anno Graser from the University of Munich in Germany. In his talk, he presented results of studies using functional CT and MRI in humans and animals treated with antiangiogenic drugs. Based on his findings, he concluded that advanced imaging, including functional imaging tests, can detect early response to treatment and can be used to aid treatment decisions.

Professor Stefano Fanti from the University of Bologna, Italy, talked about the molecular imaging techniques, particularly Positron Emission Tomography (PET), that are complementary to conventional imaging methods. Hybrid PET-CT scanners combine functional data with anatomic details to increase diagnostic accuracy. Professor Fanti also introduced a wide range of alternative tracers to FDG for PET scans. "Some malignancies do not show an increase in glucose consumption and are almost invisible with FDG," he said, "therefore other tracers have been developed to study alternative metabolic pathways." Indeed, tracers already in clinical use include choline (labeled with 11C or 18F), a marker of cell membrane metabolism particularly useful for prostate cancer detection; 18F-tyrosine and 11C-methionine, markers of protein metabolism that are successfully employed for CNS neoplastic diseases; and 18F-DOPA and 68Ga-DOTA-NOC, which are both useful in neuroendocrine tumors.

Finally, Professor Wim Oyen from the Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands, ended the symposium with his perspective on how clinicians are using advanced imaging techniques to address a variety of challenges. He highlighted how molecular imaging with radiopharmaceuticals is aiding patient evaluation before targeted therapy is initiated. "The ability of FDG-PET to predict response of metastatic GIST to imatinib became the role model for the potential of molecular imaging to provide clinically relevant answers within days after the start of treatment," he said.

In his talk, Professor Oyen also gave an overview of clinical studies that have incorporated the use radiolabelled therapeutics, for example to visualize monoclonal antibody drug targets. "The time has come to systematically position advanced imaging for treatment selection in clinical trials," he concluded.

16 NEW CENTERS...
27 CENTERS RE-ACCREDITING FOR 1ST TIME...
8 CENTERS RE-ACCREDITING FOR 2ND TIME.

ESMO Pocket guidelines delivered directly to your smart phone

ESMO goes mobile! Embracing the latest in 21st century communications, ESMO offers you the possibility to download condensed versions of the ESMO Clinical Practice Guidelines (CPG) wherever you are. Launched for the first time at ESMO 2012 you'll be able to download the pocket guidelines directly onto your Smartphone, iPhone or iPad free from Google Play and iTunes stores.

ESMO pocket guidelines were developed to provide oncologists with a concise summary of the main recommendations included in the parent CPG and consensus reports in an easily accessible format. Each guideline contains the most important information on incidence rates, diagnostic criteria, staging and risk assessment, treatment and follow-up, making them an invaluable quick reference guide to access the latest recommendations for the best standards of care in oncology.

The latest development takes that accessibility one step further.

Pick up your printed copy of the ESMO Pocket Guidelines from the Exhibition Hall – details below – or download a copy from: www.esmo.org/pocket-guidelines. Guidelines are also available from the Annals of Oncology Website: www.annonc.oxfordjournals.org and OncologyPRO.

ESMO thanks the sponsors who have supported the distribution of the Pocket Guidelines. You can pick them up at the Congress Exhibition Hall.

Breast Cancer
Celgene, Hall X, Booth 131

Supportive Care
Grünenthal, ESMO Booth 29, Society Village

Urogenital Cancer
Janssen, Hall Z, Booth 109,110

Lung Cancer
Lilly Oncology, Hall Y, Booth 125

NETs & GIST
Novartis Oncology, Hall X, Booth 125

Sarcoma
PharmaMar, Hall X, Booth 128

DESIGNATED CENTERS AWARD COCKTAIL SUNDAY 30 SEPTEMBER **18:00 – 19:00**

Recognizing centers of excellence

A total of 16 cancer centers will be formally recognized for their commitment to providing the highest standard of palliative care during a private cocktail this evening.

ESMO is committed to promoting excellence in all aspects of oncology care, and this unique accreditation program serves to raise the visibility of palliative care across Europe and the rest of the world.

CENTER	COUNTRY
Campus Bio Medico, Rome	Italy
Cancer Center, Ospedale San Pietro Fatenbenefratelli, Rome	Italy
Centre Léon Bérard, Lyon	France
Consorci Sanitari de Terrassa, Barcelona	Spain
El-Qabbary Specialized Oncology and Palliative Care Center, Alexandria	Egypt
Instituto Oncologico Veneto - I.R.C.C.S., Medical Oncology 1, Padova	Italy
Oncologia Medica Policlinico Universitario Tor Vergata (Roma) & San Raffaele Hospices (Rocca di Papa - Montecompatri), Rocca di Papa	Italy
Oncology Center GZA Sint Augustinus, Wilrijk	Belgium
Radboud University Nijmegen Medical Center, Nijmegen	The Netherlands
Raffles Cancer Center	Singapore
Saroj Gupta Cancer Centre & Research Insitute (SGCC&RI), Kolkata	India
St. George's Hospital NHS Trust, London	United Kingdom
Struttura Complessa di Oncologia, Macroattività di Cure Palliative, Fondazione I.R.C.C.S. Policlinico San Matteo, Pavia	Italy
Tumor Zentrum, Hirslanden Medical Center, Aarau	Switzerland
U.O.C. Oncologia Medica, Azienda Ospedaliera Sant' Andrea, Sapienza Universita' Di Roma, Rome	Italy
UOC Oncologia & Breast Unit - OSP. "A.Perrino", Brindisi	Italy

The list of 27 DC´s re-accreditating first time and the 8 DC´s re-accrediting 2nd time can be found on the ESMO website under the Education & Research section.

ESMO Fellows, host institutes and industry are being awarded certificates of recognition at the end of the YO Special Session on Monday 1 October 14:00 – 15:45.

ESMO Spotlights Now Available

ESMO Spotlights "A Selection of Important Studies" is an essential educational resource for oncologists. Based on the most significant oncology information presented over the last 12 months, the publication includes concise presentations that have been reviewed, interpreted and distilled by leading experts within each field. This year's ESMO Spotlights covers several major tumor types including a new chapter on rare cancers, as well as supportive and palliative care.

"The ESMO spotlights comprise topic overviews of study reports, which could or even should alter the current therapy standard. But the reimbursement issue cannot be ignored." comments Dr Henk van Halteren, ESMO Spotlights Editor,

"I always look forward to receiving the latest issue of ESMO Spotlights because it helps me put the latest studies in context, and to know what I should be incorporating into my practice. With targeted therapies it's more important than ever before to have an overview of the entire field," says Dr Henk van Halteren

Pick up your copy of the ESMO Spotlights from the Lilly Booth, situated in Hall Y, booth Y102.

Molecular characteristics critical to improve sarcoma treatments

Recent studies in soft tissue sarcomas and locally aggressive connective tissue tumors have identified six molecular subgroups of connective tissue tumors. However, these classifications are rapidly evolving, and the identification of the 'driver' mutation in some diseases appears to be paving the way for the selection of efficient targeted therapies.

In yesterday's special symposium entitled 'Subtyping soft tissue sarcomas for treatment approaches,' Professor Jean-Yves Blay from the University Claude Bernard Lyon I, Lyon, France, reminded delegates of how the identification of mutations in KIT and alpha-type platelet-derived growth factor receptor (PDGFRA), and subsequently in Raf, neurofibromatosis type 1 (NF1) and succinate dehydrogenase (SDH) in GIST led to the rapid development of imatinib, sunitinib and regorafenib. Today, however, it is recognized that GIST can be subtyped, with around 10 different molecular entities that may influence the therapeutic approach and prognosis in localized and advanced stages of disease.

Professor Blay highlighted a recent study which showed that targeting MdM2/p53 interaction in sarcomas with MDM2 amplification can lead to an efficient reactivation of p53 and biological response in tumor cells. In Ewing sarcoma, whose fusion gene product regulates IGFBP3, treatment with an anti-IGF1R antibody has yielded responses in several Phase 1 and 2 trials, but only in a small proportion of patents. However, more studies are demonstrating the efficacy of antiangiogenics (pazopanib) and mTOR inhibitors (ridaforolimus) in Phase 3 trials in a broader group of sarcoma subtypes.

"Treating sarcoma subtypes according to their molecular characteristics is vital for the effective development of new treatments, and will also be essential to understand the biological mechanisms of response and resistance" Professor Blay concluded.

PERFORMANCE SUNDAY 30 SEPTEMBER

Crime to seek cure for cancer

An updated version of a play by a leading oncologist exploring how unnecessary screening results in the diagnosis of "pseudo-cancers" will be staged at lunch time today. The satirical drama will be performed by a cast of eminent oncologists.

The play '2084', envisages the hero of Orwell's novel as a medical oncologist in the year 2084. The drama shows how Winston Smith's attempts to carry out clinical research lead him into confrontations with the authorities and end with him being hauled before the Ministry of Truth and Health accused of the ultimate crime of 'not being politically correct'.

For ESMO 2012 Professor Baum has updated the play with a new third Act addressing the problems of over diagnosis. "In today's performance ESMO President Martine Piccart takes the role of Martine Kwik-Fix, the senior data manager at Republican Marsden Hospital. The cast list, which reads like a Who's Who of European oncology, also features Kamal Saini (Brussels), Mario Dicato (Luxembourg), John Crown (Dublin), Angelo Di Leo (Prato, Italy), Elisabeth de Vries (Groningen, Netherlands), Michael Gnant (Vienna), Nadia Harbeck (Munich), Cristiana Sessa (Bellinzona, Switzerland) and David Cameron (Edinburgh).

For a thought provoking lunch break, don't miss the performance which takes place between 13:15 – 14:00 in Hall D.

Molecular imaging of NETs is a requirement for personalized medicine

The growth of tailored therapy has led to a need for accurate and non-invasive molecular imaging.

Speaking at yesterday's Special Symposium 'Integrating targeted treatments with tumor biology and molecular imaging in the current and future management of neuroendocrine gastrointestinal tumors, Professor Andreas Kjaer from the University of Copenhagen, Denmark, discussed the practice of neuroendocrine tumor (NET) molecular imaging. He presented results to show that high sensitivity Positron Emission Tomography (PET) enables the non-invasive visualization of tumor-specific receptors and tissue characteristics. "Molecular imaging will play an important role for implementing the new paradigm of personalized medicine," he concluded.

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- Treatment-naïve patients: 11.1 months vs. 2.8 months[1]
- Cytokine-pretreated patients: 7.4 months vs. 4.2 months[1]
- Combined population: 9.2 months vs. 4.2 months[1]

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(Please refer to full SmPC before prescribing)
Votrient® (pazopanib) 200mg and 400mg film-coated tablets. Each tablet contains pazopanib hydrochloride, equivalent to 200mg and 400mg of pazopanib, respectively. **Indication:** In adults for first-line treatment of advanced renal cell carcinoma (RCC) and those with prior cytokine therapy. **Dosage and administration:** Only to be initiated by physician experienced in use of anti-cancer agents. 800mg once daily. Take without food (≤1 hour before or ≥2 hours after a meal). Take tablets whole; do not break or crush. *Dose modification:* In 200mg steps based on individual tolerability to manage ADRs. Not to exceed 800mg. *Renal impairment:* No dose adjustment required in patients with CrCl >30ml/min. Caution advised in patients with CrCl <30ml/min. *Hepatic impairment:* Severe hepatic impairment - Not recommended. Undertake with caution and close monitoring in mild/moderate impairment. Mild impairment - 800mg once daily; Moderate impairment - 200mg once daily. *Elderly:* Limited data in patients ≥65 yrs. *Paediatrics:* Not to be used in children <2 yrs. Safety & efficacy not established in children 2-18 yrs; no data available. **Contra-indications:** Hypersensitivity to active substance or excipients. **Special warnings and precautions:** *Hepatic effects:* Hepatic failure reported during pazopanib use; Increases in serum transaminases (ALT, AST) and bilirubin also observed. Monitor liver function before initiation of treatment and ≥once every 4 weeks for first 4 months, and periodically thereafter. If transaminases ≤8xULN, continue pazopanib with weekly monitoring until they return to ≤Grade 1. If transaminases >8xULN, interrupt pazopanib until they return to ≤Grade 1. If transaminases >3xULN occur following re-introduction, discontinue pazopanib. If transaminases >3xULN occur concurrently with bilirubin >2xULN, perform bilirubin fractionation. If direct (conjugated) bilirubin is >35% of total, discontinue pazopanib. Concomitant use of pazopanib and simvastatin increases risk of ALT elevations: Undertake with caution and close monitoring. *Hypertension:* Events of hypertension, including hypertensive crisis, have occurred in pazopanib studies. Control BP prior to initiating pazopanib. Monitor for hypertension early (≤1 week after starting treatment) and frequently thereafter. Manage elevated BP with anti-hypertensive therapy and pazopanib dose modification. Discontinue pazopanib if BP is persistently elevated (140/90 mmHg) or if arterial hypertension is severe and persists despite anti-hypertensive therapy and dose reduction. *Cardiac dysfunction/heart failure:* Consider risks/benefits of pazopanib in patients with pre-existing cardiac dysfunction. Safety and pharmacokinetics of pazopanib not studied in patients with moderate to severe heart failure or those with below normal LVEF. Events of cardiac dysfunction (e.g. CHF and LVEF decline) have occurred in pazopanib trials. Monitor patients for signs and symptoms of CHF. Baseline and periodic LVEF evaluation recommended. *QT prolongation and Torsade de Pointes:* Use with caution in patients (i) with history of QT interval prolongation, (ii) taking antiarrythmics or other medications that may prolong QT interval or (iii) with relevant pre-existing cardiac disease. Baseline and periodic ECGs, and maintenance of electrolytes within normal range recommended. *Arterial thrombotic events:* Use with caution in patients at increased risk for these events. Base treatment decision on individual patient's benefit/risk assessment. *Venous thromboembolic events (VTEs):* VTEs including venous thrombosis and fatal PE have occurred in pazopanib trials. *Haemorrhagic events:* Not recommended in patients with history of haemoptysis, cerebral, or significant GI haemorrhage in past 6 months. Use with caution in patients with significant risk of haemorrhage. *GI perforations and fistula:* Use with caution in patients at risk for GI perforation or fistula. *Wound healing:* Stop treatment ≥7 days prior to surgery. Resume after surgery based on clinical judgement of adequate wound healing. Discontinue pazopanib in patients with wound dehiscence. *Hypothyroidism:* Baseline measurement of thyroid function recommended prior to start of pazopanib treatment; Monitor periodically during treatment. Monitor patients for signs and symptoms of thyroid dysfunction and manage as per standard medical practice. *Proteinuria:* Baseline and periodic urinalysis recommended. Monitor patients for worsening proteinuria. Discontinue pazopanib if Grade 4 proteinuria develops. *Pneumothorax:* Observe patients closely for signs and symptoms of pneumothorax. *Infections:* Cases of serious infection (with/without neutropenia) reported. **Interactions:** Avoid concomitant use with strong inhibitors of CYP3A4, p-glycoprotein (P-gp) or breast cancer resistance protein (BCRP) and CYP3A4 inducers. Hyperglycaemia observed during concomitant administration with ketoconazole. Undertake concomitant administration with uridine diphosphate glucuronosyl transferase 1A1 (UGT1A1) substrates and simvastatin (and other statins) with caution. Avoid grapefruit juice during pazopanib treatment. **Pregnancy and lactation:** No adequate data on use in pregnant women. Not to be used unless clearly necessary; Appropriate contraception advised. Not known whether pazopanib excreted in human milk; Breastfeeding should be discontinued. Animal studies indicate fertility may be affected. **Effects on ability to drive and use machines:** No studies conducted. Avoid driving or using machines if affected. **Undesirable effects:** Most important serious ADRs associated with pazopanib in clinical studies were: TIA, ischaemic stroke, myocardial ischaemia, myocardial and cerebral infarction, cardiac dysfunction, GI perforation and fistula, QT prolongation; Pulmonary/GI/cerebral haemorrhage. All events occurred in <1% of patients. Fatal events possibly related to pazopanib included: GI haemorrhage, pulmonary haemorrhage/haemoptysis, abnormal hepatic function, intestinal perforation, ischaemic stroke. Treatment-related events reported with pazopanib in advanced RCC patients with following frequencies: *Very common*: Decreased appetite; Dysgeusia; Hypertension; Diarrhoea, nausea, vomiting, abdominal pain; Hair colour changes; Fatigue; Increased ALT and AST. *Common:* Thrombocytopenia, neutropenia, leucopenia; Hypothyroidism; Headache, dizziness, lethargy, paraesthesia; Hot flush; Epistaxis, dysphonia; Dyspepsia, stomatitis, flatulence, abdominal distension; Abnormal hepatic function, hyperbilirubinaemia; Rash, alopecia, PPE, skin hypo/de-pigmentation, erythema, pruritus, dry skin, hyperhidrosis; Myalgia, muscle spasms; Proteinuria; Asthenia, mucosal inflammation, oedema, chest pain; Decreased weight/WBC, Increased creatinine/bilirubin/lipase/BP/TSH/GGT. *Uncommon events include:* Hypophosphataemia; Hypomagnesaemia; Peripheral sensory neuropathy; Hypoaesthesia; Eyelash discolouration; CVA, myocardial infarction, bradycardia; Flushing, hypertensive crisis; Mouth ulceration, frequent bowel movements; Pancreatitis, peritonitis; Hepatotoxicity, hepatic failure, hepatitis; Jaundice; Photosensitivity reaction, skin exfoliation; Menorrhagia, metrorrhagia, retroperitoneal/urinary tract/vaginal haemorrhage; Mucous membrane disorder; Increased blood urea/amylase, decreased blood glucose, abnormal thyroid function test; Infections (with/without neutropenia). **Overdose:** No specific antidote. Treatment should consist of general supportive measures. **Marketing authorisation (MA) nos:** EU/1/10/628/001-4. **MA holder:** Glaxo Group Limited, Berkeley Avenue, Greenford, Middlesex UB6 ONN. **Legal category:** POM. Votrient is a trademark of the GlaxoSmithKline group of companies.

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Reference: 1. Sternberg CN, *et al*. Pazopanib in locally advanced and/or metastatic renal cell carcinoma: results of a randomized Phase III trial. *J Clin Oncol* 2010; **28**: 1061–1068.
Code: ONCE/PAZ/0079c/12. Date of preparation: July 2012.

Votrient® pazopanib