

INTEGRATING SCIENCE INTO ONCOLOGY FOR A BETTER PATIENT OUTCOME

DAILY REPORTER

SATURDAY 9 SEPTEMBER 2017

ESMO 2017: Combining science and oncology to benefit patients



In front of a packed auditorium yesterday, Professor Fortunato Ciardiello, ESMO 2017 and Congress President, officially opened the meeting, welcoming delegates to a truly integrated congress combining the expertise of professionals from the worlds of basic science and clinical medicine. Held for the first time in partnership with the European Association for Cancer Research (EACR), Professor Ciardiello was confident that the congress would provide an important forum to stimulate new ideas on disease development and cancer treatment. His views were echoed by the EACR President, Professor Anton Berns, who called it “an exciting partnership.”

“The ESMO–EACR collaboration enriches the whole oncology community by bridging the gap between research innovation and clinical practice.”

Professor Fortunato Ciardiello

Professor Alberto Sobrero, told delegates that such joint ventures are crucial at a time when a comprehensive understanding of the molecular drivers of cancer progression is vital if we are to find new therapeutic options.

Home to the Spanish National Cancer Research Centre (CNIO), which supports both basic and clinical research, Madrid was the ideal venue for ESMO 2017, considered Professor Miguel Martín Jiménez, President of the Spanish Society of Medical Oncology and Local Officer of the ESMO 2017 Congress.

Professor Miguel Martín was also one of three outstanding professionals whose contributions to oncology were recognised with ESMO awards, presented by Chair of the ESMO Fellowship and Award Committee, Professor Christoph Zielinski.

Taking place in a room filled with the brightest and the best from laboratories and clinics around the globe, the Opening Session was a fitting start to this ground-breaking congress.



Clockwise from top right: Fortunato Ciardiello, José Baselga of the Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York City, NY, USA, recipient of the ESMO Lifetime Achievement Award, Christoph Zielinski, Alberto Bardelli of the University of Torino and the Candiolo Cancer Institute-IRCCS, Torino, Italy, recipient of the ESMO Award for Translational Research, Miguel Martín of the Complutense University and the General University Hospital Gregorio Marañón, Madrid, Spain, recipient of the ESMO Award

“Bringing together researchers and clinicians will ultimately lead to better patient outcomes.”

Professor Richard Marais, Scientific Committee Co-Chair



View the ESMO 2017 Broadcast on the YouTube playlist here.

YouTube

Supportive care: More than just a supporting role?

Supportive care is receiving increasing attention due to growing evidence of better outcomes and increased survival when used alongside cancer therapies.¹ However, considerable geographical variation exists in available units providing supportive care.

We asked Dr Andreas Charalambous (Cyprus University of Technology Department of Nursing, Cyprus) and Dr Florian Scotté (Hôpital Foch, Suresnes, France), about the wider context of supportive care.

Patients with advanced cancer and their families experience numerous debilitating physical, psychological and spiritual challenges that often lead to poor quality of life and suboptimal treatment outcomes.² Palliative and supportive care can help relieve symptoms and improve well-being, but there is disparity in the provision of such care. Dr Charalambous said this is due to factors such as a lack of trained professionals, cultural stigma, a paucity of evidence to guide the delivery and dissemination of supportive care services, limited funding and a need

for well-defined metrics.³ Early integration of palliative care services with standard oncology care has been advocated in recent years, with the nurse playing a pivotal role in its successful implementation within the interdisciplinary context.⁴ “There is evidence to indicate that specific nurse- and other healthcare professional-led supportive care interventions can promote the provision of high quality comprehensive care,” Dr Charalambous remarked.

Research indicates that a multidisciplinary approach to cancer care in a supportive care unit can be less expensive than in other oncology departments.⁵ “Moreover, a multidisciplinary approach leads to an improved ability to manage cancer-related complications and adverse events, being better able to provide specific treatment in a time-efficient manner,” says Dr Scotté. Where specific cancer care teams are set up, patients can be monitored closely so that unmet needs are identified quickly and there are fewer (but justified) hospitalisations, leading to reduced healthcare costs. Dr Scotté added that the

development of patient-reported outcome measures could further optimise the cost of patient care on a global level.

Don’t miss tomorrow’s Controversy Session (Sunday 10 September, 09.15 – 10.15, Granada), to hear a debate titled ‘Supportive and palliative care improve patient outcomes and decrease treatment costs.’

1. Scotté F. Oncologist 2012;17(Suppl 1):23–30
2. Charalambous A, et al. Int J Nurs Stud 2016;61:176–86
3. Davis MP, et al. Support Care Cancer 2015;23:2677–85
4. Wells M, et al. Eur J Cancer 2017;72 (Suppl 1):S4
5. Morin S, et al. J Clin Oncol 2017;35(Suppl):Abstract e18326



YOUNG ONCOLOGIST EVENTS NOT TO MISS TODAY!

YO Brunch Session
Communicating with cancer patients in the era of personalised medicine
11.00 – 11.45, Salamanca

Special Session
ESMO for medical students and new physicians 15.00 – 16.00, Room 55

Find out more about ESMO activities for young oncologists at esmo.org/Career-Development/Young-Oncologists-Corner/About-ESMO-for-Young-Oncologists

 **#ESMO17**

Molecular biology of CNS tumours: Applications and implications



Last year, the WHO published a revised classification of CNS tumours—the universal and standard diagnostic system—which, for the first time, incorporates molecular profiling.¹ This follows recent advances in the molecular understanding of CNS tumours, which has enhanced the accuracy with which they are classified and improved the ability to predict outcomes compared with the use of histology alone.²

The use of integrated histopathological and molecular diagnoses will undoubtedly improve treatment selection for patients. In practical terms, pathology laboratories will need to update their range of diagnostic methods and establish standard operating procedures for molecular biology tests. Also, access to molecular testing will vary considerably across different socioeconomic regions and

reimbursement is not yet established for genotypic diagnostic testing.³ Importantly, molecular testing will transform routine practice only if appropriately targeted treatments are identified after demonstration of their activities in scientifically robust studies.

Don’t miss today’s Challenge Your Expert Session, ‘How to use molecular biology in neuro-oncology’, 08.00 – 09.00, Palma

1. Louis DN, et al. Acta Neuropathol 2016;131:803–20
2. van den Bent MJ, et al. Neuro Oncol 2017;19:614–24
3. Reifenberger G. World Federation of Neuro-Oncology Societies Magazine 2017;1:38–42

YOUR KEY TO ACCESS ESMO’S EVENTS

The ESMO Events App

esmo.org





Public health and health policy sessions not to be missed today!

Special Session
Access to novel targeted therapies and clinical trials in Europe
09.15 – 10.45, Tarragona

Special Session
The incoming wave of biosimilars in oncology
14.45 – 16.15, Granada



oncologypro.org

Have you seen the NEW OncologyPRO website structure?

oncology//PRO
Educational Portal for Oncologists

The OncologyPRO knowledge and resources – now organized by Tumour Sites.


 **Visit the ESMO booth S1 for a live demo!**

Major Sponsors



Main Sponsors





WOMEN FOR ONCOLOGY SESSION

**Saturday, 9 September
11.00, Alicante**


Solange Peters
ESMO W40 Committee
and Session Chair, Switzerland

Frances Shepherd
ESMO W40 Session
Co-Chair and 2017 Awardee, Canada

Full programme available
on the ESMO Events App

fb.com/women4onco

esmo.org



Not all small tumours are created equal



Giuseppe Curigliano: Editor-in-Chief of the ESMO 2017 Daily Reporter, European Institute of Oncology, Milan, Italy

The risk of overtreatment with adjuvant therapies, especially chemotherapy, is common in patients with breast cancer as clinicians attempt to eradicate micrometastases. In this setting, overtreatment is defined as adjuvant chemotherapy with a small survival benefit—in the range of 2%—that exposes

the patient to long-term risks such as secondary cancers, secondary leukaemia and congestive heart failure. The MINDACT trial has shown that patients with primary invasive breast cancer at high clinical and low genomic (CH/GL) recurrence risk, or vice versa (CL/GH), do not derive significant distant metastasis-free survival (DMFS) benefit from adjuvant chemotherapy.¹ In a subset analysis of the MINDACT trial, investigators have studied one of the largest series of small breast tumours ever reported to clarify the genomic characteristics of small node-negative breast cancers.

Yesterday, Dr Konstantinos Tryfonidis from the European Organisation for Research and Treatment of Cancer (EORTC), Brussels, Belgium, reported on this sub-study that evaluated chemotherapy in 826 patients with small breast tumours (<1 cm), stratified by clinical and genomic recurrence risk (Abstract 1500_PR). Overall, 23.7% of patients were classified as CL/GH risk; 5-year DMFS with and without chemotherapy in this group was 97.3% (95% confidence interval [CI] 89.4–99.3) and

91.4% (95% CI 82.6–95.9), respectively. These results indicate that almost a quarter of patients with node-negative small tumours may derive clinical benefit from adjuvant chemotherapy.

Dr Fatima Cardoso from Champalimaud Clinical Centre, Lisbon, Portugal, co-principal investigator of the MINDACT study, enthused about the latest findings: “Traditionally, small node-negative breast cancers have been considered as low-risk tumours, for which adjuvant chemotherapy is unnecessary. However, recent advances in cancer biology have shown that while tumour burden is still independently prognostic, tumour biology is key for outcome. In this subset analysis of MINDACT, we have clearly shown that about 1 in 4 small node-negative tumours are biologically aggressive and derive a substantial benefit from adjuvant chemotherapy. These findings reinforce the notion that biology and tumour burden must be used together to guide treatment decisions in breast cancer.”

1. Cardoso F, et al. N Engl J Med 2016;375:71–29

Beyond PD-L1: Predictive biomarkers of response to immune checkpoint inhibitors



Ignacio Melero: University of Navarra, Pamplona, Spain

Immune checkpoint inhibitors are associated with remarkable survival benefits in some cancer patients. However, a substantial proportion of patients (50–80%) do not derive benefit. Unfortunately, sufficiently effective patient selection tools are lacking. PD-L1 expression is the most widely studied potential predictive biomarker, but contradictory data have been reported; patients with low or no expression of PD-L1 may also benefit from treatment with these immunotherapy agents.¹ For instance, in a recent exploratory analysis from a

phase III trial (ATTRACTION-02), nivolumab showed a survival benefit compared with placebo regardless of PD-L1 expression in previously treated advanced gastric or gastroesophageal junction cancer (Abstract 6170).

There is growing interest in tumour mutational burden (TMB) as an additional predictive biomarker of response to checkpoint inhibitors, with a statistical association demonstrated between high TMB and improved clinical outcomes in patients with melanoma and non-small-cell lung cancer (NSCLC) treated with anti-PD-L1/PD-1 therapies.² However, analysis of TMB requires tumour tissue, which is often not available, particularly in patients with metastatic disease. Recently, novel assays have been developed and validated analytically to estimate TMB based on circulating tumour DNA in blood (bTMB) (Abstract 102P). One such assay has now been used to correlate bTMB with the clinical activity of atezolizumab as second-line treatment for NSCLC (Abstract 12950). This type of technique is likely to reduce costs compared with whole-exome sequencing of tumour and normal tissue. Although the approaches are technically challenging, accurate quantitative estimation of mutational burden based on analyses of liquid

biopsies would increase the opportunity to personalise immunotherapy.

Tumour mutational burden in blood is showing promise as a predictive biomarker for immune checkpoint inhibition.

From a clinician's perspective, “Any biomarker of response should be easy to use and have high sensitivity and specificity,” comments Professor John Haanen from the Netherlands Cancer Institute, Amsterdam. “The blood-derived biomarker described here, which estimates TMB and is much easier to use than tumour-derived biopsies, could be an important improvement. However, it is unlikely that TMB alone will be sufficient to predict response precisely and biomarkers will need to be multifaceted. Both from a safety and health cost perspective, such a biomarker is needed urgently.”

Multiplex imaging of the tumour microenvironment is attracting much attention and quantitative data regarding the presence of antitumoural and protumoural immune

cell types may offer important information not available from single-parameter immunohistochemistry. A number of imaging platforms are currently in development and RNA expression data can be deconvoluted *in-silico* to estimate the presence of several leucocyte types in the tumour microenvironment.

In all probability, clinically useful predictive biomarkers will be the result of combined algorithms based on a number of parameters.

Biomarker research is also focusing on associations between PD-L1 expression and other potential indicators of response; a relationship between PD-L1, a T-cell inflamed gene expression profile (GEP) and favourable clinical response to pembrolizumab was observed in the KEYNOTE-028 study (Abstract 84PD), while high PD-L1 expression was significantly associated with MET overexpression and expression of PTEN and KRAS mutation in a large cohort of patients with NSCLC (Abstract 1630PD).

1. Sharma P, et al. Lancet Oncol 2016;17:1590–8

2. Rizvi NA, et al. Science 2015;348:124–8

Germline aberrations in prostate cancer

Almost 40% of patients with prostate cancer and pathogenic germline mutations do not qualify for genetic testing according to current guidelines.^{1,2} Germline mutations, particularly those affecting DNA repair, have a more aggressive disease phenotype and substantially curtail life expectancy.² Therefore, early identification has implications for patients and family members, permitting genetic counselling and education about possible outcomes. Importantly, prevention strategies may be initiated in affected family members via lifestyle and diet changes, PSA screening, clinical examination and imaging analysis.

In a Challenge Your Expert Session today ('Germline aberrations and prostate cancer', 08.00 – 09.00, Bilbao), Dr Elena Castro Marcos from the Spanish National Cancer Research Centre, Madrid, Spain, will discuss the broader implications of heritable prostate malignancy. As an investigator in the prospective PROREPAIR-B study of germline mutations in metastatic prostate cancer (see Abstract LBA32), Dr Castro Marcos is ideally placed to comment on the wider implications of DNA aberrations. She said that recent studies found that up to 12% of patients with metastatic prostate cancer had inherited mutations in DNA repair genes. These mutations may have prognostic and therapeutic implications for the patients and their relatives, as they pose an increased risk of other tumours. "Unfortunately, we are currently unable to identify who among these patients could be carrying an inherited mutation in *BRCA2* or other genes, as some carriers have no family history of cancer and no features unique to the tumour unequivocally link to DNA repair defects." She added that, "The number of patients identified as having somatic and germline DNA repair defects is likely to grow because of screening for inherited mutations in patients with lethal prostate cancer, and the use in clinical practice of multi-test panels to detect actionable mutations. It is therefore important that oncologists learn to counsel patients."

Chair of the Challenge Your Expert Session, Professor Ros Eeles from The Institute of Cancer Research and Royal Marsden NHS Foundation Trust, London, UK, noted that, "As costs of genetic sequencing decrease, these new findings will be able to be integrated into the cancer care pathway."

1. Nicolosi PLW, et al. J Clin Oncol 2017;35(Suppl):Abstract 5009
2. Oliva Fernández L, et al, ESMO 2017:Abstract 825P
3. Na R, et al. Eur Urol 2017;71:740–47

No significant PFS benefit with dose-dense chemotherapy in ovarian cancer



Antonio González Martín: Clínica Universidad de Navarra, Madrid, Spain

Standard first-line chemotherapy for epithelial ovarian/fallopian tube/primary peritoneal carcinoma (EOC) consists of 3-weekly (q3w) carboplatin and paclitaxel. However, a Japanese (JGOG3016) study¹ reporting improved progression-free (PFS) and overall survival (OS) with dose-dense, weekly (qw) paclitaxel cast doubt on the optimal administration of the carboplatin/paclitaxel doublet. Conversely, the MITO-7 trial was unable to confirm the superiority

of qw carboplatin/paclitaxel in Italian and French women with EOC, raising questions about the dose-dense strategy.² Now, a phase III trial (ICON8) conducted predominantly in European women with EOC has shown no significant PFS benefit with dose-dense versus standard q3w chemotherapy. The data were presented yesterday by Dr Andrew Clamp from The Christie NHS Foundation Trust and University of Manchester, UK (Abstract 9290_PR).

In this study, 1,566 patients were randomised 1:1:1 to standard carboplatin + paclitaxel (arm 1), standard carboplatin + qw paclitaxel (arm 2) or qw carboplatin + qw paclitaxel (arm 3). Unlike the Japanese JGOG3016 trial, there was no significant increase in PFS in either of the dose-dense arms; median PFS was 17.9, 20.6 and 21.1 months in arms 1, 2 and 3, respectively (hazard ratio [HR] 0.92 [arm 2 versus arm 1]; HR 0.94 [arm 3 versus arm 1]). No substantial increase in toxicity was observed with weekly treatment.

Other than dose-dense chemotherapy, alternative first-line therapies for EOC include augmentation of q3w carboplatin/paclitaxel with bevacizumab, or administration via a different

route to the usual peritoneal infusion. ICON8 was designed to be a validating trial for two dose-dense regimens in Caucasian women with EOC. However, the results presented at ESMO 2017 clearly show that q3w carboplatin/paclitaxel should remain the standard-of-care first-line chemotherapy in this population. Furthermore, the GOG-262 trial showed that dose-dense qw paclitaxel plus q3 carboplatin did not prolong PFS compared with q3w doublet therapy when either regimen was combined with bevacizumab.³ As a consequence, dose-dense administration should be abandoned in daily clinical practice, at least among Caucasian women.

The European phase III trial reports no significant PFS benefit with dose-dense chemotherapy versus a standard q3w regimen as first-line treatment for EOC.

1. Katsumata N, et al. Lancet Oncol 2013;14:1020–6
2. Pignata S, et al. Lancet Oncol 2014;15:396–405
3. Chan JK, et al. N Engl J Med 2016;374:738–48

Are oncolytic viruses the next big thing in cancer therapy?



Christophe Massard: Gustave Roussy Institute, Villejuif, France

Several new therapeutic strategies are currently on the horizon for the treatment of cancer—in particular, new immunotherapy drugs. Immune checkpoint-targeted monoclonal antibodies (anti-PD-1, -PD-L1 and -CTLA-4) have shown impressive

results in different tumour types and clearly represent the new paradigm of treatment for advanced cancers. However, few patients achieve a long-term objective response and some can develop severe auto-immune toxicities. Intratumoural immunotherapy is a strategy that aims to use the tumour as its own vaccine.¹ Approaches include the use of double-stranded RNA that induces a robust immune response against cancer cells,² small therapeutic peptides selectively designed to target cancer cells without damaging healthy tissue³ and oncolytic viruses.

Oncolytic virus therapy has been heralded as the next major breakthrough in cancer treatment.

A genetically engineered herpes simplex virus (T-VEC) has recently received US FDA and EMA approval for melanoma.⁴ In a phase I/IIa trial of an oncolytic herpes simplex virus (HSV1716), anti-tumour immunogenicity was observed in patients with inoperable, malignant pleural mesothelioma. Notably, patients who showed evidence of a pleural cytokine response experienced numerically longer median survival than those without (18 months versus 15 months, respectively; Abstract 366PD). Data from this study will be presented later today at the Poster Discussion Session 'Developmental therapeutics' (16.30 – 18.00, Alicante).

1. Marabelle A, et al. Clin Cancer Res 2014;20:1747–56
2. Jin B, Yeo AET. Austin J Gastroenterol 2014;1:1005
3. Marqus S, et al. J Biomed Sci 2017;24:21
4. Fukuhara H, et al. Cancer Sci 2016;107:1373–9

SINGAPORE 2017 **ESMO** ASIA

Are you a Young Oncologist based in Asia and an ESMO Member?

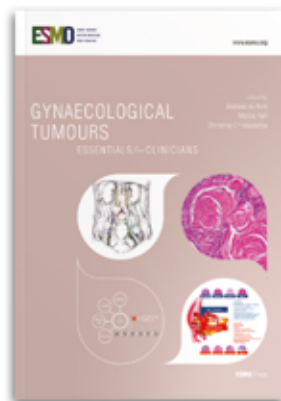
Win free registration to ESMO Asia 2017

Visit the ESMO booth for your chance to win!

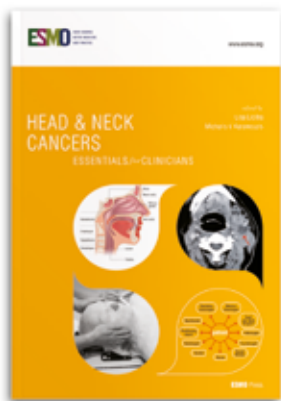
EDUCATIONAL PUBLICATIONS AVAILABLE NOW!

NEW FOR ESMO MEMBERS

Essentials for Clinicians
reserved for ESMO members – collect from the ESMO booth



Gynaecological Tumours

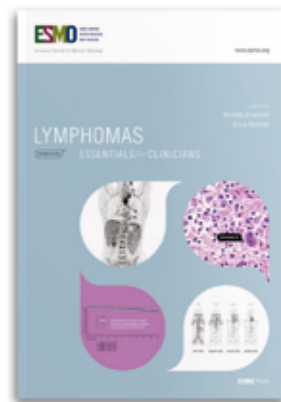


Head and Neck Cancers

AVAILABLE TO CONGRESS ATTENDEES



Gastrointestinal Tract Tumours
Servier booth 204



Lymphomas
Servier booth 204



Nutrition and Cancer
Nutricia booth 126

Also available to ESMO Members from the ESMO booth: **Essentials for Clinicians: Genitourinary Tract Tumours**
ESMO Handbooks: Oncological Emergencies, Translational Research, Rehabilitation Issues during Cancer Treatment and Follow-up

Medscape's ESMO 2017 Live Blog

Expert updates in real time
from the most important
sessions in Madrid

Read Now:
Medscape.com/esmo-live

Immunotherapy resistance: Addressing the elephant in the room

With the meteoric rise in the use of PD-1/PD-L1 and CTLA-4 inhibitors, the frequency of immunotherapy resistance is often overlooked. Innate resistance to anti-PD-1 agents occurs in 60–70% of patients with metastatic melanoma¹ and resistance can be acquired after initially successful treatment, leading to relapse.² To be susceptible to immunotherapy, tumours must express antigens differentiating them from surrounding non-transformed cells. Poor immunogenicity, disruption of antigen presentation and T-cell exhaustion are a number of mechanisms responsible for PD-1 inhibitor resistance.³

In tomorrow's 'Immunotherapy in head and neck cancer' Educational Session (Sunday 10 September, 14.45 – 16.15, Tarragona), Dr Robert Ferris from University of Pittsburgh, PA, USA, will address resistance to PD-1 inhibitors and discuss options for patients who do not

respond to immunotherapy. By highlighting ways that immunotherapies can be made effective for a broader spectrum of patients, this talk promises to be informative and thought provoking. On Monday, much-awaited mature overall survival data will be presented from KEYNOTE-040, showing whether pembrolizumab is superior to chemotherapy in the second-line treatment of patients with head and neck cancer (Abstract LBA45_PR).

Dr Antoni Ribas from University of California, Los Angeles Jonsson Comprehensive Cancer Center, CA, USA, commented, "To continue to improve outcomes with cancer immunotherapy we need better understanding of the mechanisms that lead to resistance."

1. Hugo W, et al. Cell 2016;165:35–44
2. Sharma P, et al. Cell 2017;168:707–23
3. O'Donnell, JS et al. Cancer Treat Rev 2017;52:71–81

Don't miss today's Special Symposium, 'Mechanisms of intrinsic and acquired resistance to current treatment strategies', (11.00 – 12.30, Cordoba).

Addition of a PI3K inhibitor to neoadjuvant letrozole improves response rate in post-menopausal early breast cancer patients

Letrozole is effective in post-menopausal patients with hormone receptor-positive (HR+) breast cancer; patients frequently develop resistance to treatment, with PI3K being a significant mediator of endocrine resistance, since it is activated in about 30–40% of HR+ breast cancers.¹ A Late-Breaking Abstract presentation yesterday reported that adding the beta-sparing PI3K inhibitor taselisib, which has antitumour activity against PIK3CA mutant cancer cells, to neoadjuvant letrozole improved the objective response rate (ORR) in post-menopausal patients with oestrogen receptor (ER)-positive/HER2-negative early breast cancer (Abstract LBA10).

According to Dr Cristina Saura, principal investigator in the study, from Vall d'Hebron University Hospital, Barcelona, Spain, the randomised, phase II LORELEI trial in 334 patients with stage I–III operable disease met its primary endpoint; ORR was significantly higher with the addition of taselisib versus placebo, both in all randomised patients (50.0% versus 39.3%; odds ratio [OR] 1.55; $p=0.049$) and in 152 patients with PIK3CA mutant disease (56.2% versus 38.0%; OR 2.03; $p=0.033$). There was no significant difference between treatment arms in terms of

pathological complete response rate at surgery in both cohorts. Also, toxicity was manageable and as expected for this class of drug.

Commenting on the results, Dr Evandro de Azambuja from Jules Bordet Institute, Brussels, Belgium and co-principal investigator in the LORELEI study said that this trial showed a significant increase in ORR with the combination of taselisib and letrozole using centrally-assessed MRI in this patient population. He added, "As expected, pathologic complete response was not shown to be a good endpoint for this patient population and alternative endpoints may be considered for future trials."

LORELEI is the first randomised study to demonstrate a significant increase in ORR with the addition of a selective PI3K inhibitor to endocrine therapy in ER+/HER2-early breast cancer.

1. Hoefflich KP, et al. *Genes Cancer* 2016;7:73–85



EACR funding opportunities: experience a new lab

EACR
Travel
Fellowships

From its early days the European Association for Cancer Research (EACR) recognised the importance of promoting collaboration between cancer researchers and so some 40 years ago it established the EACR Travel Fellowships Programme. The Fellowships provide funding for students and early career researchers to develop their cancer research careers by visiting a laboratory in a different country to learn new skills and work alongside senior researchers.

"It is an essential component of modern research that you interact with multiple laboratories around the world and share ideas," said John Marshall, supervisor of Travel Fellowship recipient Claire Reader at the Barts Cancer Institute (BCI), UK.

The Programme is co-sponsored by Worldwide Cancer Research, which has enabled the EACR to increase the number of researchers supported each year. In 2016 alone, Travel Fellowships were awarded to 20 researchers from nine different countries.

- 100% of winners would recommend the EACR Travel Fellowship Programme to a colleague
- 74% said that the programme had a very positive impact on their career

The EACR has also developed other types of awards over the years, such as a bursary scheme to provide financial support to enable members to attend its conferences and scientific meetings. Find more information on the EACR website: www.eacr.org.

"Experiencing [a new] culture and community was invaluable for my professional development and as well as facilitating the valuable collaboration with the Weksberg lab, my visit ultimately led to an offer of a postdoctoral position at SickKids in the Tabori lab working in paediatric brain tumour research, which I will begin in early 2017. I'd like to thank the EACR once again for funding my travel fellowship and supporting me at a very exciting and pivotal stage of my career,"

Vicky Forster, 2016 Travel Fellowship Award.

How long is enough? Optimal treatment duration with PD-1 inhibitors in NSCLC



Stefan Zimmermann: Associate Editor of the ESMO 2017 Daily Reporter. Lausanne University Hospital, Switzerland

PD-1 inhibitors have transformed the treatment of a number of cancers, including advanced non-small-cell lung cancer (NSCLC), melanoma and bladder cancers. PD-1 inhibitors have durable clinical activity owing to downstream infiltration of memory T-cells into the tumour

microenvironment.¹ Optimal treatment duration with checkpoint inhibitors in advanced NSCLC has not yet been clarified and currently, therapy is continued until disease progression or unacceptable toxicity occurs. While the characteristics and outcomes of patients at the tail-end of the survival curve are becoming clearer,² we still do not know how long is really long enough in relation to checkpoint inhibitor therapy. Nivolumab was approved in Europe in 2015 as second-line monotherapy for locally advanced or metastatic NSCLC.³ However, nivolumab is associated with immune-related adverse events⁴ and weighs heavily on scarce healthcare financial resources, thus identifying a treatment duration that provides the best benefit/risk profile is clearly highly desirable.

A proffered paper presented yesterday by Dr David Spigel from Sarah Cannon Research Institute, Nashville, TN, USA reported follow-up data (median 14.9 months) from the

CheckMate 153 trial. This long-term study in advanced NSCLC randomised patients on second-line nivolumab for 1 year to either continue or stop treatment (Abstract 12970). Overall survival (OS) data showed a trend favouring continuous nivolumab (hazard ratio [HR] 0.63, 95% confidence interval [CI] 0.33–1.20). Also, progression-free survival (PFS) was significantly improved for those receiving continuous treatment compared with those who stopped: HR 0.42 (95% CI 0.25–0.71). Treatment-related adverse events—including grade 3–4 events—were numerically more frequent in patients who continued to receive nivolumab after 1 year, but there were few new-onset events after 1 year.

Despite PFS and OS being exploratory endpoints, it is noteworthy that this trial should be industry-sponsored at a time when 'de-escalation' studies are almost exclusively academically-driven. While de-escalation

trials have proved impossible to set up in melanoma patients, CheckMate 153 demonstrates that most patients progressing after a planned treatment interruption cannot be successfully salvaged with re-treatment with anti-PD-1. This strongly suggests that immune checkpoint blockade in NSCLC therapy should be continued, at least until progression or limiting toxicity.

1. Ribas A, et al. *Cancer Immunol Res* 2016;4:194–203
2. Herbst RS, et al. *World Conference on Lung Cancer*, 2016: Abstract OA03.07
3. www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/003985/WC500189768.pdf
4. Feld E, Horn L. *Onco Targets Ther* 2017;10:3697–708

The Society Village

Visit the Society Village in Hall 8!

The Society Village is the area where most of the non-profit societies, National Societies and Patient Advocates active in the field of oncology are looking forward to meeting participants.

Drop by to find out about current projects, identify new partners for your work and explore opportunities provided by ESMO's reciprocal membership agreements with many national societies!

Reportage – Day one



NOW APPROVED

CABOMETYX[®]
(cabozantinib) tablets
60 mg | 40 mg | 20 mg

✓ PFS¹
✓ OS¹
✓ ORR¹

“CABOMETYX[®] is indicated for the treatment of advanced RCC in adults following prior vascular endothelial growth factor (VEGF)-targeted therapy”.¹

CABOMETYX[®] Abbreviated prescribing information (Before prescribing please consult the full Summary of Product Characteristics (SmPC)). CABOMETYX[®] 20mg, 40mg and 60mg film-coated tablets Pack size: one plastic bottle with 30 tablets. **Active ingredient:** Cabozantinib (S)-malate 20mg, 40mg and 60mg. **Other components:** Lactose. **Indications:** CABOMETYX[®] is indicated for the treatment of advanced renal cell carcinoma (RCC) in adults following prior vascular endothelial growth factor (VEGF)-targeted therapy. **Dosage and Administration:** The recommended dose of CABOMETYX[®] is 60 mg once daily. Treatment should continue until the patient is no longer clinically benefiting from therapy or until unacceptable toxicity occurs. Management of suspected adverse drug reactions may require temporary interruption and/or dose reduction of CABOMETYX[®] therapy. For dose modification, please refer to full SmPC. CABOMETYX[®] is for oral use. The tablets should be swallowed whole and not crushed. Patients should be instructed to not eat anything for at least 2 hours before through 1 hour after taking CABOMETYX[®]. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients listed in the SmPC. **Special warnings and precautions for use:** As most events can occur early in the course of treatment, the physician should evaluate the patient closely during the first eight weeks of treatment to determine if dose modifications are warranted. Events that generally have early onset include hypocalcaemia, hypokalaemia, thrombocytopenia, hypertension, palmarplantar erythrodysesthesia syndrome (PPES), proteinuria, and gastrointestinal (GI) events (abdominal pain, mucosal inflammation, constipation, diarrhoea, vomiting). Dose reductions and dose interruptions due to an AE occurred in 59.8% and 70%, respectively, of cabozantinib-treated patients in the pivotal clinical trial. Two dose reductions were required in 19.3% of patients. The median time to first dose reduction was 55 days, and to first dose interruption was 38 days. **Perforations and fistulas:** Serious gastrointestinal perforations and fistulas, sometimes fatal, have been observed with cabozantinib. Patients who have inflammatory bowel disease (e.g., Crohn's disease, ulcerative colitis, peritonitis, diverticulitis, or appendicitis), have tumour infiltration in the GI tract, or have complications from prior GI surgery (particularly when associated with delayed or incomplete healing) should be carefully evaluated before initiating cabozantinib therapy and subsequently they should be monitored closely for symptoms of perforations and fistulas including abscesses. Persistent or recurring diarrhoea while on treatment may be a risk factor for the development of anal fistula. Cabozantinib should be discontinued in patients who experience a GI perforation or a fistula that cannot be adequately managed. **Thromboembolic events:** Events of venous thromboembolism, including pulmonary embolism, and events of arterial thromboembolism have been observed with cabozantinib. Cabozantinib should be used with caution in patients who are at risk for, or who have a history of, these events. Cabozantinib should be discontinued in patients who develop an acute myocardial infarction or any other clinically significant arterial thromboembolic complication. **Haemorrhage:** Severe haemorrhage has been observed with cabozantinib. Patients who have a history of severe bleeding prior to treatment initiation should be carefully evaluated before initiating cabozantinib therapy. Cabozantinib should not be administered to

patients that have or are at risk for severe haemorrhage. **Wound complications:** Wound complications have been observed with cabozantinib. Cabozantinib treatment should be stopped at least 28 days prior to scheduled surgery, including dental surgery, if possible. The decision to resume cabozantinib therapy after surgery should be based on clinical judgment of adequate wound healing. Cabozantinib should be discontinued in patients with wound healing complications requiring medical intervention. **Hypertension:** Hypertension has been observed with cabozantinib. Blood pressure should be well-controlled prior to initiating cabozantinib. During treatment with cabozantinib, all patients should be monitored for hypertension and treated as needed with standard anti-hypertensive therapy. In the case of persistent hypertension despite use of anti-hypertensives, the cabozantinib dose should be reduced. Cabozantinib should be discontinued if hypertension is severe and persistent despite anti-hypertensive therapy and dose reduction of cabozantinib. In case of hypertensive crisis, cabozantinib should be discontinued. **Palmar-plantar erythrodysesthesia syndrome:** Palmar-plantar erythrodysesthesia syndrome (PPES) has been observed with cabozantinib. When PPES is severe, interruption of treatment with cabozantinib should be considered. Cabozantinib should be restarted with a lower dose when PPES has been resolved to grade 1. **Proteinuria:** Proteinuria has been observed with cabozantinib. Urine protein should be monitored regularly during cabozantinib treatment. Cabozantinib should be discontinued in patients who develop nephrotic syndrome. **Reversible posterior leukoencephalopathy syndrome:** Reversible Posterior Leukoencephalopathy Syndrome (RPLS), also known as Posterior Reversible Encephalopathy Syndrome (PRES), has been observed with cabozantinib. This syndrome should be considered in any patient presenting with multiple symptoms, including seizures, headache, visual disturbances, confusion or altered mental function. Cabozantinib treatment should be discontinued in patients with RPLS. **Prolongation of QT interval:** Cabozantinib should be used with caution in patients with a history of QT interval prolongation, patients who are taking antiarrhythmics, or patients with relevant pre-existing cardiac disease, bradycardia, or electrolyte disturbances. When using cabozantinib, periodic monitoring with on-treatment ECGs and electrolytes (serum calcium, potassium, and magnesium) should be considered. **Interactions:** CYP3A4 inducers and inhibitors: Cabozantinib is a CYP3A4 substrate. Concurrent administration of cabozantinib with the strong CYP3A4 inhibitor ketoconazole resulted in an increase in cabozantinib plasma exposure. Caution is required when administering cabozantinib with agents that are strong CYP3A4 inhibitors. Concurrent administration of cabozantinib with the strong CYP3A4 inducer rifampicin resulted in a decrease in cabozantinib plasma exposure. Therefore, chronic administration of agents that are strong CYP3A4 inducers with cabozantinib should be avoided. **P-glycoprotein substrates:** Cabozantinib was an inhibitor but not a substrate, of P-glycoprotein (P-gp) transport activities in a bi-directional assay system using MDCK-MDR1 cells. Therefore, cabozantinib may have the potential to increase plasma concentrations of co-administered substrates of P-gp. Subjects should be cautioned regarding taking a P-gp substrate while receiving cabozantinib. **MRP2 inhibitors:** Administration of MRP2 inhibitors may result in increases

in cabozantinib plasma concentrations. Therefore, concomitant use of MRP2 inhibitors should be approached with caution. **Bile salt-sequestering agents:** Bile salt-sequestering agents may interact with cabozantinib and may impact absorption (or reabsorption) resulting in potentially decreased exposure. The clinical significance of these potential interactions is unknown. **Excipient related warnings:** Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. **Pregnancy and lactation:** Avoid pregnancy, use effective methods of contraception and discontinue breast-feeding during treatment with cabozantinib, and for at least 4 months after completing therapy. **Drive and use machines:** Caution is recommended. **Undesirable effects:** The most common serious adverse reactions associated with cabozantinib are abdominal pain (3%), pleural effusion (3%), diarrhoea (2%), and nausea (2%). The most frequent adverse reactions of any grade (experienced by at least 25% of patients) included diarrhoea (74%), fatigue (56%), nausea (50%), decreased appetite (46%), palmar-plantar erythrodysesthesia syndrome (PPES) (42%), hypertension (37%), vomiting (32%), weight decreased (31%), and constipation (25%). Other very common adverse reactions: anemia, hypophosphataemia, hypoalbuminaemia, hypomagnesaemia, hyponatraemia, hypokalaemia, hyperkalaemia, hypocalcaemia, hyperbilirubinemia, dysgeusia, headache, dizziness, dysphonia, dyspnea, cough, stomatitis, abdominal pain, dyspepsia, rash, dry skin, muscle spasms, arthralgia, proteinuria, mucosal inflammation, serum ALT, AST, and ALP increased, creatinine increased, triglycerides increased, hyperglycaemia, hypoglycaemia, lymphopenia, neutropenia, thrombocytopenia, GGT increased, amylase increased, blood cholesterol increased, lipase increased. For all common and uncommon adverse reactions, please refer to full SmPC. **Ipsen Pharma 65, Quai Georges Gorse, 92100 Boulogne-Billancourt, France.** For more information, see the regularly updated registered product information on the European Medicine Agency www.ema.europa.eu

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.
Este medicamento está sujeto a seguimiento adicional, es prioritaria la notificación de sospechas de reacciones adversas asociadas a este medicamento.
Reference: 1. CABOMETYX[®] (cabozantinib) Summary of Product Characteristics 2016.

CBZ-ES-000016 – June 2017



Automatic biosimilar substitution: Putting patients first



Javier Cortes: Ramon y Cajal University Hospital, Madrid and Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain

With the escalating costs of anticancer medicines, biosimilars show promise in positively impacting on the financial sustainability of healthcare systems. While switching generic medicines should not be of concern to physicians,¹ any decision regarding substitution should be taken by well-informed physicians and patients,

taking into consideration all aspects, including, but not limited to, label information and healthcare sustainability.

According to a global survey conducted by the Alliance for Safe Biologic Medicines (ASBM) among biologics prescribers, most oncologists believe it is important for them to have the ability to control which biologic—original product or biosimilar—they prescribe for their patients (Abstract 1463P). The majority of oncologists (75%) considered that it was critically/very important to have sole decision-making authority regarding the suitability of a biologic agent, very few (6%) oncologists viewed pharmacy-level substitution to be totally acceptable and most (76%) felt it to be critically/very important to be notified of such a substitution. These results might at first appear somewhat surprising, since biosimilars are approved according to rigorous trials demonstrating equivalence of the new agent with respect to the originator biologic; any biosimilar approved by a regulatory agency should be analytically similar to the originator in terms of activity and safety. However, small but real differences between the drugs highlight that

they are not completely equal and so it seems reasonable that prescribers should be able to decide which agent to use.

The survey data will be further reviewed by Dr Michael Reilly, ASBM, Washington, DC, USA, in a Poster Display Session tomorrow (Sunday 10 September, 'Public health, biosimilars', 13.15 – 14.15, Hall 8; Abstract 1463P).

Don't miss the Special Session today 'The incoming wave of biosimilars in oncology', 14.45 – 16.15, Granada.

1. Tabernero J, et al. ESMO Open 2016;1:e000142



FREE Wi-Fi
Network Name
ESMO2017



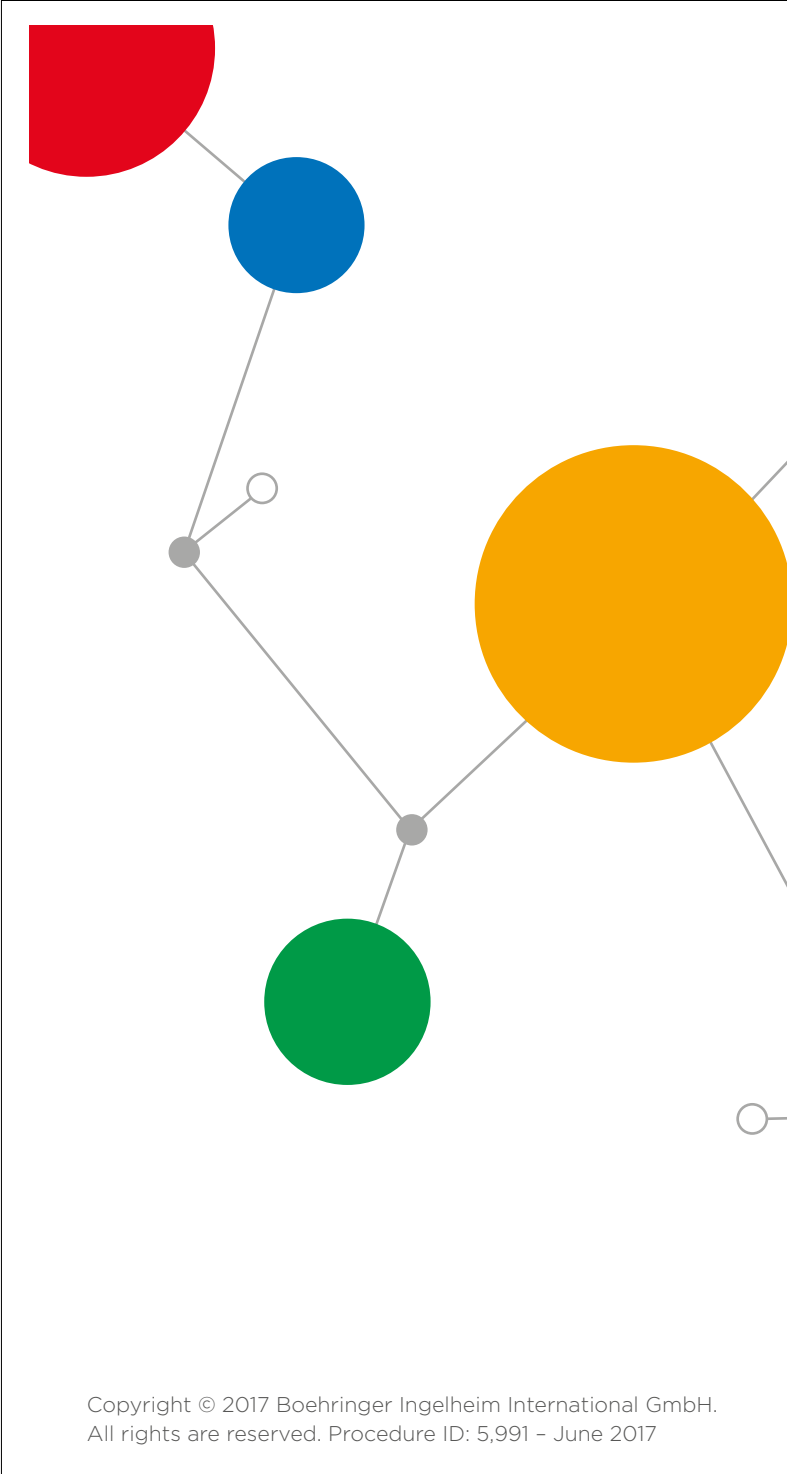
Opening hours:
Friday 8 September to
Monday 11 September: 08.30 – 18.00
Tuesday 12 September: 08.00 – 12.00

Located in Hall 10, the exclusive ESMO 'members only' lounge provides a range of facilities, including a working area with laptops, printers and phone charging stations, a literature area stocked with ESMO publications, and refreshments.




A programme of short talks about ESMO committees, activities and products will take place in the lounge from Saturday to Monday. For further details visit the 'Discover ESMO Programme'.

You can also register at the lounge today (10.00 – 14.00) to sit the ESMO Examination!




DISCOVER BRIGHT IDEAS

Visit Boehringer Ingelheim at **Booth 203, Hall 7** to find out more about how we're making the future brighter for people with cancer.



Copyright © 2017 Boehringer Ingelheim International GmbH.
All rights are reserved. Procedure ID: 5,991 – June 2017

LET'S COLLABORATE
ONCOLOGY FROM BOEHRINGER INGELHEIM



MUNICH
2018

ESMO

congress



REGISTER NOW!

Special onsite
registration offer

MUNICH GERMANY
19-23 OCTOBER 2018

The first 100 people to register for
the ESMO 2018 Congress onsite in Madrid
can benefit from reduced registration fees.

esmo.org

Molecular taxonomy of genitourinary cancer

Recent advances in sequencing technology and computational biology are enabling detailed analysis and interpretation of genomic data. Molecular taxonomy is now being used to guide clinical care in oncology through identification of biological sub-groups that are amenable to therapeutic targeting. This approach may be particularly advantageous in identifying tumours with high genomic instability that are more likely to respond to immune checkpoint inhibitors¹ and to adequately stratify patients for selected targeted therapies or approaches making ‘personalised therapy’ a reality for urothelial cancers.

Bladder cancer is a molecularly heterogeneous disease with a high mutational burden.² A consensus meeting held at the Spanish National Cancer Research Center brought together a number of groups proposing genome-based sub-classification of urothelial bladder cancer and outlined multiple potential opportunities for therapeutic intervention.³ Dr Joaquim Bellmunt from Dana Farber Cancer Institute, Boston, MA, USA will be discussing the potential implications of collaborative genomic classification in bladder cancer at the Special Symposium ‘Impact of tumour heterogeneity on precision medicine in kidney and bladder cancers’ on Monday (11.00 – 12.30, Barcelona).

A new report from The Cancer Genome Atlas project based on a comprehensive analysis of 412 muscle-invasive bladder cancers characterised by multiple analytical platforms has been completed. Some preliminary data were presented during the ASCO Congress in May 2017⁴ and will be updated during ESMO 2017. Amongst the new findings are newly-described sub-types that may stratify response to different treatments and allow for enrichment selection in basket trials.

When asked for comment Dr Bellmunt said: “Bladder cancer is a prime candidate for precision medicine based on genomic classification.”

Discover the latest data exploring genomic alterations in urothelial cancer in tomorrow’s Poster Discussion (14.45 – 16.15, Cordoba; Abstract 849PD) and Poster Display Sessions (13.15 – 14.15, Hall 8; Abstracts 859P and 857P).

1. Bellmunt J, et al. Eur Urol 2015;68:547–9
2. Nandagopal L, Sonpavde G. Bladder Cancer 2016;2:369–79
3. Lerner SP, et al. Bladder Cancer 2016;2:37–47
4. Lerner SP, et al. J Clin Oncol 2017;15(Suppl):4500

Please join us for this
Satellite Symposium.

REFRESHMENTS WILL
BE PROVIDED



Daiichi-Sankyo
cancerenterprise

Saturday 9th September
18:30–20:00

Valencia Auditorium, Hall 4, IFEMA,
Feria de Madrid

Care. Compassion. Science.
It's Our Obligation.

ESMO 2017 Industry Satellite Symposium

BREAST CANCER BRAIN METASTASES:
An integrated approach

18:30

Welcome and introduction
Professor Volkmar Müller (Germany) - Chairperson

18:40

Therapy of breast cancer brain metastases: Challenges,
new therapies and the potential role of etirinotecan pegol
Professor Ahmad Awada (Belgium) - Chairperson

19:00

The BEACON trial: Results from pre-defined subgroups
Professor Chris Twelves (UK)

19:20

Breast cancer with brain metastases: Patient case studies
Professor Nadia Harbeck (Germany)

19:40

Panel discussion
All

19:55

Meeting summary and close
Professor Ahmad Awada



ESMO 2017 Industry Satellite Symposium organised and funded by Daiichi Sankyo Oncology Europe GmbH

MADRID
2017

ESMO

congress

ESMO
COLLOQUIA

SYSTEMIC TREATMENT
OF UNRESECTABLE
HEPATOCELLULAR CARCINOMA

WE INVITE YOU TO JOIN US!

SUNDAY, 10 SEPTEMBER 2017
13:00-14:30

SEVILLA AUDITORIUM
HALL 9
MADRID SPAIN

Co-Chairs
Jean-Luc Raoul, France
Arndt Vögel, Germany

This educational activity is
provided by ESMO and
supported by Eisai.





Adolescents and young adults with cancer: Under-represented and underserved?

Since the early 1990s, incidence rates of cancer in adolescents and young adults (AYAs) have increased by more than 25% in many countries.^{1,2} Special considerations for AYAs with cancer include scheduling treatments around their work and social activities, and collaborative decision-making in light of potential treatment effects on fertility.^{3,4} Currently, AYAs have different attitudes towards clinical trials, suggesting that tailored approaches may be warranted.⁵

AYA-focused education and research are an emerging priority for ESMO and the European Society for Paediatric Oncology (SIOPE). European results from a global survey will report that two-thirds of ESMO and SIOPE respondents have no access to specialised AYA cancer care centres, with poorest service provision in Eastern and South Eastern European countries (Abstract 1438O_PR).

The AYA patient perspective has been explored in a follow-up survey of 1,198 young adult cancer survivors in Norway, which strongly suggests there is an unmet need for greater psychological and pastoral support (Abstract 1110PD). The long-term ability of survivors to work was impacted by somatic disorders and psychosocial features, such as a fear of recurrence and lower education levels rather than treatment burden and survivorship.

Research on fertility outcomes in young adults with breast cancer will also be presented at ESMO 2017. Women positive for germline *BRCA* mutation had reduced reproductive potential and

poorer oocyte and ovarian tissue cryopreservation outcomes than *BRCA*-negative patients (Abstract 1541O), emphasising a sub-group of AYA patients who may need specific support and counselling.

Ana Kogan Wais from Madrid, Spain, was 16 when she was treated for Ewing’s Sarcoma. “After I was diagnosed, I had lots of contact with children or adults, but barely any with other teenagers. A specific AYA ward would have made a massive difference to my treatment. The medical team did their best to give me age-appropriate information, but there is little specifically targeted to teenagers and young adults. Being treated in both paediatric and adult hospitals made it all the more confusing; I received either sugar-coated information suitable for children or more harsh and realistic adult information and support.” Now 25, she struggles with chronic pain on a daily basis. “The issue of side effects has been the hardest to cope with. The focus of information is on getting you through treatment. No-one mentions what will happen later.”

- 1. www.cancerresearchuk.org/health-professional/cancer-statistics/teenagers-and-young-adults-cancers/incidence
- 2. Moon EK, et al. PloS One 2014;9:e96088
- 3. Levine J, et al. J Clin Oncol 2010;28:4831–41
- 4. Zebrack BJ, et al. J Cancer Surviv 2007;1:137–45
- 5. Ferrari A, et al. Pediatr Blood Cancer 2008;50(5 Suppl):1101–4

ESMO-IPOS: Working together for the benefit of oncology professionals and patients

In the field of oncology, psychological support is vital not only for patients but also for professionals. In recent years, burnout among oncologists, particularly young oncologists, has become recognised as a significant problem, with potentially important consequences both for clinicians and their patients.¹ Raising awareness of the issue on personal and professional levels and promoting a range of different self-care strategies—including improving work–life balance and having adequate vacation time—will go a long way towards reducing the incidence and impact of burnout.¹

Today’s ESMO-International Psycho-Oncology Society Joint Symposium (‘ESMO-IPOS: Working together to prevent professional burnout and improve patient care’, 11.00 – 12.30, Bilbao) will discuss practical ways to avoid burnout and to help patients’ cancer treatment journey.

According to the session’s Co-Chair and ESMO Executive Board member, Dr Susana Banerjee from The Royal Marsden NHS Foundation Trust, London, UK, “Working together, ESMO and IPOS can further address burnout in oncology. I am confident that this first joint session during ESMO 2017 will lead to measures to tackle burnout for the benefit of oncology professionals and patients.”

- 1. Banerjee S, et al. Ann Oncol 2017;28:1590–6

3 FOR 2

ESMO MEMBERSHIP OFFER

3 YEARS FOR THE PRICE OF 2!

Renew or join onsite to benefit and gain access to the ESMO Member Lounge.

Visit us at the ESMO Booth S1 to learn more.

esmo.org

Could harmful mutations become helpful markers in metastatic prostate cancer patients?

Men with metastatic prostate cancer (mPC) are a population enriched with germline DNA repair mutations, with a reported incidence of 12%.¹ In retrospective studies, these mutations predicted a more aggressive disease course and mortality at an earlier age.² Sustained responses to PARP inhibitors and platinum-based chemotherapy after progression on previous treatment have been reported in men with mPC who carry these mutations^{3,4} but these agents are not currently approved in this indication.

A proffered paper on Friday (Abstract LBA32) described the results from a fascinating prospective study that followed 419 patients with newly diagnosed castrate-resistant mPC to investigate the effect of germline DNA repair mutations on survival. Twenty-six patients had known mutations. While cause-specific survival (CSS) was not significantly shorter in mutation carriers versus non-carriers (28.5 months versus 36.0 months, respectively; *p*=0.49), patients with *BRCA2* germline mutations had significantly shorter CSS: 17.4 months (*p*=0.02). Also, there was a trend to a better response to first taxane and worse response to first androgen receptor-targeted therapy among mutation carriers than non-carriers, particularly those with *BRCA2* mutations. Moreover, the duration of responses was shorter for mutation carriers than non-carriers.

These results add valuable information to the growing body of evidence on germline and somatic DNA repair mutations in patients with mPC. Previous findings showed that 33% of castrate-resistant mPC patients had somatic DNA repair mutations³ and 12% had germline DNA repair mutations,¹ meaning that up to half of patients with this type of cancer may benefit from agents such as PARP inhibitors.

- 1. Pritchard CC, et al. N Engl J Med 2016;375:443–53
- 2. Na R, et al. Eur Urol 2017;71:740–47
- 3. Mateo J, et al. N Engl J Med 2015;373:1697–708
- 4. Cheng HH, et al. Eur Urol 2016;69:992–5

What's new in brain tumours?



Despite advances in genomic sequencing for gliomas, new effective treatments remain elusive and are hampered by the molecular complexity and heterogeneity of these tumours.¹ The move towards a precision medicine approach was discussed in a Proffered Paper Session yesterday and will be addressed further in a Poster Discussion Session today.

Hear more about the latest findings in CNS tumours in today's Poster Discussion Session (16.30 – 17.30, Bilbao).

Results from exploratory cohorts of CheckMate 143 reported that nivolumab + radiotherapy ± temozolomide was well tolerated in 113

patients with newly diagnosed glioblastoma (GBM), most of whom had unmethylated *MGMT* (Abstract 3250). The most common treatment-emergent neurological adverse events were headaches (up to 47%) and seizures (up to 31%). Results of ongoing randomised trials of this regimen in newly diagnosed GBM are eagerly awaited, although primary results from the phase III monotherapy cohort of CheckMate 143 presented at the World Federation of Neuro-Oncology meeting in May 2017 reported that nivolumab in recurrent GBM failed to improve overall survival (OS) compared with bevacizumab.² In the randomised exploratory phase II REGOMA trial in 119 patients with recurrent GBM, the multikinase inhibitor, regorafenib, showed improved OS compared with lomustine (6.5 months versus 5.5 months, respectively, hazard ratio 0.64, $p=0.028$) and a significantly higher disease control rate (44.1% versus 21.1%, $p=0.008$) (Abstract LBA16).

The presence of intratumoural PD-1-positive tumour-infiltrating lymphocytes and strong membranous PD-L1 staining were identified as favourable prognostic factors in 90 patients with newly diagnosed GBM (Abstract 3260). A study of 29 paired samples of newly diagnosed and recurrent high-grade glial tumours showed conserved PD-L1 expression at baseline and after therapy in 17/29 patients, while PD-L1 expression was lost in 6 patients and gained in 6 patients. Thus, evaluation of biomarkers at

recurrence may be important to select appropriate immunotherapy (Abstract 332PD). EGFR remains a key potential treatment target in GBM. In an analysis of two randomised trials in 2,077 patients with newly diagnosed or recurrent GBM, *EGFR* amplification rate was found to be lower in patients from Asia (34%) compared with those from the Americas/Europe (53–57%) (Abstract 3270). The translational GLIOCAT study used immunohistochemistry to analyse samples from 272 patients with newly diagnosed GBM for expression of the β -galactoside binding protein Gal-1. Gal-1 was an independent prognostic factor, with high cytoplasmic/nuclear expression correlating with worse OS (Abstract 330PD).

Low-grade gliomas (LGG) with *IDH* mutation and 1p19q co-deletion have a protracted natural history and a more favourable prognosis. A retrospective multivariate analysis of 93 consecutive LGG patients with these mutations (90% of cases considered high-risk) who underwent surgery showed that progression-free survival (PFS) correlated with the extent of surgery ($p=0.043$) and the type of post-surgical treatment (Abstract 3280). The same team also demonstrated a similar correlation for patients with *IDH*-mutated tumours without 1p19q co-deletion ($n=198$) (Abstract 329PD).

Slow but steady progress has been made over the last decade in the management of glioma. Early use of chemotherapy has been shown to

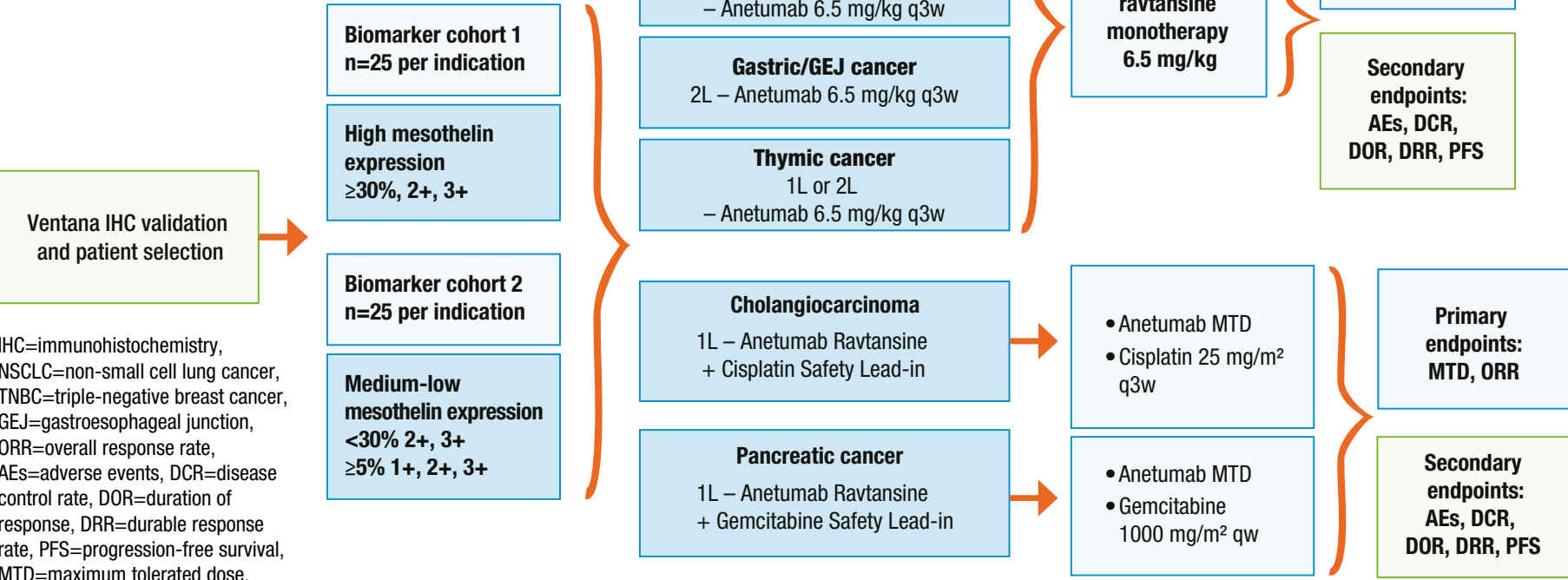
improve outcomes not only in GBM—including in elderly patients—but also in lower-grade tumours. Tumour-treating fields prolong both PFS and OS in GBM. Immunotherapy and EGFR-targeting treatments are being investigated in newly diagnosed GBM as we have learned that innovative therapies are best investigated in the upfront setting. At ESMO 2017, the REGOMA trial investigators presented data suggesting improved outcomes when patients were treated with regorafenib. However, OS was much worse than would be expected in this population and critical analysis and further investigation are required. Several preclinical reports at ESMO 2017 provide the basis for additional research of immunotherapy in malignant glioma. However, we still lack adequate biomarkers for patient selection, and combination strategies may be warranted. EGFR-targeting treatments are undergoing phase III investigation in both recurrent and newly diagnosed GBM and the observation described above of substantial variation in *EGFR* amplification between Asian and Caucasian patients with GBM raises questions about assays, methodology and analytical cut-offs.

- 1. Prados M, et al. Neuro Oncol 2015;17:1051–63
- 2. www.news.bms.com/press-release/bmy/bristol-myers-squibb-announces-results-checkmate-143-phase-3-study-opdivo-nivoluma

NOW ENROLLING: Phase 1b Multi-indication Study of Anetumab Ravtansine (BAY 94-9343) in Patients With Mesothelin Expressing Advanced or Recurrent Malignancies (ARCS-Multi Tumor)



Estimated Enrollment: 348
Study Start Date: May 2017
FPFV: May 2017
Estimated Study Completion Date: February 11, 2020



Anetumab ravtansine es un fármaco en investigación que no está aprobado por la FDA, ni por la EMA ni por otras autoridades sanitarias. Anetumab ravtansine is an investigational agent currently in clinical trials and is not approved by the EMA, FDA, or other health authorities. The efficacy and safety of anetumab ravtansine has not been established. This information is being provided only for the purpose of providing an overview of clinical trials for recruitment and should not be construed as a recommendation for use.

To see patient inclusion and exclusion criteria, visit: <http://www.clinicaltrials.gov/ct2/show/NCT03102320>

© 2017 Bayer. All rights reserved.
Bayer and the Bayer Cross are registered trademarks of Bayer. G.MA.SM.ON.06.2017.2154 L.ES.MKT.06.2017.2894 06/17

Trial Sponsor: Bayer
100 Bayer Boulevard
Whippany, NJ 07981 USA





JOINING FORCES, CHANGING THE OUTLOOK

As a **1st line therapy** for mBC, IBRANCE® + letrozole has demonstrated **>2 years mPFS**.^{*1} IBRANCE has also demonstrated a **consistent** and **manageable safety profile**,¹⁻⁴ without exerting clinically relevant effects on the QTc interval.^{3,5}

Visit our booth to learn more about IBRANCE for the treatment of mBC

This drug is centrally authorised in the EU but not yet marketed in Spain pending pricing and reimbursement approval.

Este medicamento está autorizado centralmente en la UE, pero aún no se comercializa en España a la espera de la aprobación de precio y reembolso.

*Based on results from a Phase III RCT.

mBC = metastatic breast cancer; **mPFS** = median progression-free survival; **QTc** = QT interval corrected for heart rate; **RCT** = randomised controlled trial.

1. Finn RS, et al. N Engl J Med. 2016;375(20):1925-1936. **2.** Cristofanilli M, et al. Lancet Oncol. 2016;17(4):425-439. **3.** IBRANCE® Summary of Product Characteristics. Available at: <http://www.ema.europa.eu>. Accessed May 2017. **4.** Verma S, et al. Oncologist. 2016;21:1165-1175. **5.** Ruiz-Garcia A, et al. SABCS 2016; poster P4-22-10.

PP-PLB-ESP-0014

© 2017 Pfizer Pharma GmbH PP-PLB-ESP-0013. Date of preparation: June 2017

▼ This medicinal product is subject to additional monitoring. Any suspected side effects associated with this medicine should be reported.
Este medicamento está sujeto a seguimiento adicional, es prioritaria la notificación de sospechas de reacciones adversas asociadas a este medicamento.