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."

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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.

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"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."

This newspaper contains advertisements for prescription-only medicines for healthcare professionals qualified to prescribe medicinal products.
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. 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 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. 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. “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. “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.’

Molecular biology of CNS tumours: Applications and implications

Molecular biology of CNS tumours—the universal and standard diagnostic system—which, for the first time, incorporates molecular profiling. 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.

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. 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

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

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. 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 8170).

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. 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). 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 antitumoral 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 84P), while high PD-L1 expression was significantly associated with MET overexpression and expression of PTEN and KRA5 mutation in a large cohort of patients with NSCLC (Abstract 1630PD).

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. Germline mutations, particularly those affecting DNA repair, have a more aggressive disease phenotype and substantially curtail life expectancy. 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-8 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.’


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

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] study 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. Now, a phase III trial (ICON9) conducted predominantly in European women with EOC has shown no significant PFS benefit with dose-dense versus standard qw chemotherapy. The data were presented yesterday by Dr Andrew Climp 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 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 qw carboplatin/paclitaxel with bevacizumab, or administration via a different route to the usual peritoneal infusion. ICON9 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 qw 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 q3w carboplatin did not prolong PFS compared with qw doublet therapy when either regimen was combined with bevacizumab. 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 qw regimen as first-line treatment for EOC.


Are oncolytic viruses the next big thing in cancer therapy?

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. 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, Aicardi).


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-PO-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. Approaches include the use of double-stranded RNA that induces a robust immune response against cancer cells, small therapeutic peptides selectively designed to target cancer cells without damaging healthy tissue and oncolytic viruses.

Oncolytic virus therapy has been heralded as the next major breakthrough in cancer treatment.
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. Inborn resistance to anti-PD-1 agents occurs in 60–70% of patients with metastatic melanoma\(^1\) and resistance can be acquired after initially successful treatment, leading to relapse.\(^2\) To be susceptible to immunotherapy, tumors 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.”

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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. 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 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.


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

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.  Omitted 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, 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. However, nivolumab is associated with immune-related adverse events and weights 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 1297O).

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 blockades in NSCLC therapy should be continued, at least until progression or limiting toxicity.


EACR funding opportunities: experience a new lab

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 Fellowship 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 Clara Reader at the Barts Cancer Institute (BCI), UK.

“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.
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!
Automatic biosimilar substitution: Putting patients first

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, 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).


**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 inhibitors 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. 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. 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 2017 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).**


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**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

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**13:00-14:30**

**SEVILLA AUDITORIUM**

**HALL 9**

**MADRID SPAIN**

**Co-Chairs**

Jean-Luc Raoul, France
André Vögel, Germany

This educational activity is provided by ESMO and supported by Bristol-Myers Squibb.
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. 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. Currently, AYAs have different attitudes towards clinical trials, and impact of burnout.

AYA-focused education and research are an emerging priority for ESMO and the European Society for Paediatric Oncology (SIOP). European results from a global survey will report that two-thirds of ESMO and SIOP respondents have no access to specialised AYA cancer care centres, with poorest service provision in Eastern and South Eastern European countries (Abstract 143802).

The AYA patient perspective has been explored in a follow-up survey, which strongly suggests there is an unmet need for greater psychological and pastoral support (Abstract 111062). 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 154102), emphasising a sub-group of AYA patients who may need specific support and counselling.

Research on BRCA-positive patients (Abstract 154102) showed that up to half

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%. In retrospective studies, these mutations predicted a more aggressive disease course and mortality at an earlier age. 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, but these agents are not currently approved in this indication.

A proffered paper on Friday (Abstract 154102) 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 versus 36.0 months, respectively; 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 mutations and 12% had germline DNA repair mutations, meaning that up to half of patients with this type of cancer may benefit from agents such as PARP inhibitors.

Today’s ESMO-International Psychosocial 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.”

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. 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 unmutated IDH (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.1 In the randomised exploratory phase II REGOMA trial in 119 patients with recurrent GBM, the multikinase inhibitor, regorafenib, showed improved OS compared with temozolomide (6.5 months versus 5.5 months, respectively, hazard ratio 0.64, p=0.029) and a significantly higher disease control rate (44.1% versus 21.1%, p=0.008) (Abstract LBA18).

The presence of intratumoural PD-1-positive tumour-infiltrating lymphocytes and strong membranous PD-L1 staining were identified as favourable prognostic factors in 95 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 3329). 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 American/European (63–57%) (Abstract 3270). The translational GLIOCAT study used immunohistochemistry to analyse sample points from 272 patients with newly diagnosed GBM for expression of the β-galactosidase binding protein Gal-1. Gal-1 was an independent prognostic factor, with high cytopenias/nuclear expression correlating with worse OS (Abstract 3309). Low-grade gliomas (LGG) with IDH mutation and 1p19q co-deletion have a protected 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 3309). The same team also demonstrated a similar correlation for patients with IDH-mutated tumours without 1p19q co-deletion (n=108) (Abstract 3299).

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.

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