MADRID 2017 ESMO

INTEGRATING SCIENCE INTO ONCOLOGY FOR A BETTER PATIENT OUTCOME

DAILY REPORTER

SUNDAY 10 SEPTEMBER 2017

Consolidation immunotherapy offers new hope for patients with stage III locally advanced NSCLC

Pilar Garrido: *Hospital Universitario Ramón y Cajal, CiberOnc, Universidad de Alcalá, Madrid, Spain*

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

Almost 30% of newly-diagnosed non-small-cell lung cancers (NSCLCs) are stage III, with mediastinal lymph node involvement.[1] Prognosis remains poor after chemoradiotherapy, and consolidation chemotherapy does not improve survival in this setting.[2] PD-1 inhibitors effectively unmask cancer cells to the immune system and it is hoped that this contrasting mode of action may improve outcomes.

View the ESMO 2017 Broadcast on the YouTube playlist here.

YouTube

During the Presidential Symposium yesterday, Dr Luis Paz-Ares from Hospital Universitario 12 de Octubre, CiberOnc, Universidad Complutense and CNIO, Madrid, Spain presented potentially practice-changing data from the phase III PACIFIC study of up to 12-month consolidation immunotherapy with PD-L1-targeting durvalumab (Abstract LBA1_PR). In 709 patients with locally advanced unresectable NSCLC without progression after platinum-based treatment and radiotherapy, median progression-free survival (PFS) was 16.8 months with durvalumab versus 5.6 months with placebo hazard ratio 0.52; ($p<0.0001$). Adverse events were comparable in both arms. Although overall survival data were immature at the time of this interim analysis (median follow-up 14.5 months), these impressive results must surely foreshadow maintenance immunotherapy becoming part of standard practice in locally advanced NSCLC.

Dr Pilar Garrido from Hospital Universitario Ramón y Cajal, CiberOnc, Universidad de Alcalá, Madrid, Spain noted that although the goal of treatment for stage III NSCLC is cure, currently less than 25% of patients are long-term survivors.

Dr Stefan Zimmermann, Lausanne University Hospital, Switzerland and Associate Editor of the ESMO 2017 *Daily Reporter*, said that the sheer magnitude of benefit in median PFS is unprecedented in immunotherapy of NSCLC and reinforces the strong rationale for combining it with radiotherapy. Concerns relating to pneumonitis are unfounded, but will be specifically explored in the ETOP 6-14 NICOLAS trial investigating concomitant nivolumab and chemoradiotherapy.

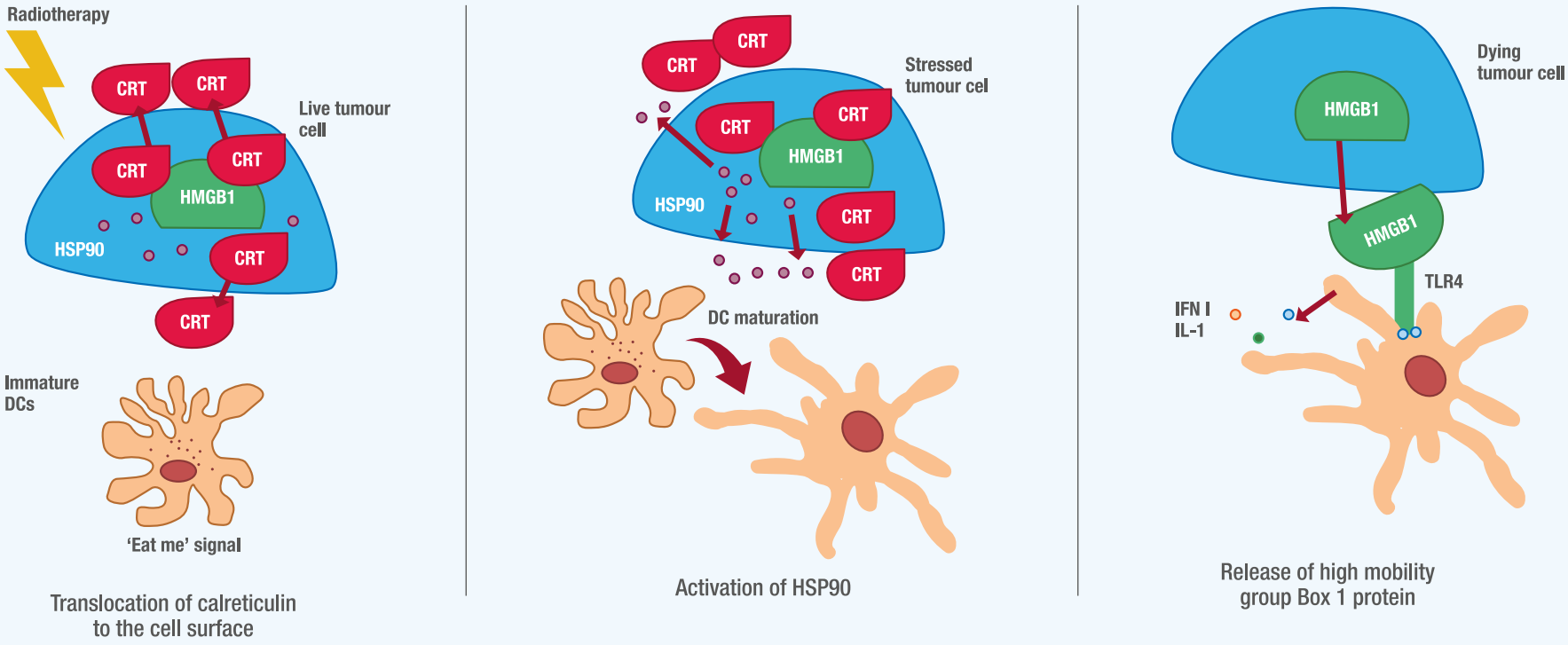
"The results of the PACIFIC study—one of the largest studies ever conducted in stage III NSCLC—will undoubtedly influence our current standard of care. These data are very exciting and clinically relevant, and we hope this will be the first of many studies to help improve cure rates in this setting."

Dr Pilar Garrido

1. Price A. Nat Rev Clin Oncol 2012;9:591–8
2. Postmus PE, et al. Ann Oncol 2017;28 (Suppl 4):iv1–21

Radiotherapy and immune checkpoint inhibitors: **A winning new combination?**

‘Priming’ immune system with radiotherapy



CRT, calreticulin; DC, dendritic cell; HMGB1, high-mobility group box 1 protein; HSP90, heat shock protein 90; IFN I, interferon I; IL-1, interleukin-1; TLR4, Toll-like receptor 4

Radiotherapy (RT) is an established cancer modality that has recently emerged as a promising combination strategy with immunotherapy due to its multiple pro-immunogenic effects.[1] Localised, high-dose RT can cause immune-related tumour rejection and immune priming,[2,3] although abscopal effects—tumour shrinkage outside the radiation field—are rare, but well reported.[3] Combining RT with immune checkpoint inhibitors may amplify immunogenicity and the likelihood of abscopal effects. This approach is under investigation in several advanced malignancies.[2]

Pressing questions remain around treatment timing and optimal RT dosing and fractionation. In a mouse model of colon cancer, hypofractionation using 8 Gy x 3 fractions with a PD-1 inhibitor resulted in abscopal effects in the lymph nodes and spleen (Abstract 1205P). Attempts to translate such successes into the clinical setting are promising. The phase II TONIC trial used RT or chemotherapy induction before nivolumab in 50 women with metastatic triple-negative breast cancer (mTNBC) (Abstract LBA14). The overall objective response rate (ORR) was 22% and median response duration was 9 months. Although the trial was not designed to compare the different cohorts, ORR in the RT + nivolumab arm was 10% (1/10 patients) and duration of response was close to 1 year. In a phase II study of RT plus pembrolizumab in mTNBC, only 6/17 women were evaluable and two women had a reduction in tumour burden of ≥75% that lasted for >20 weeks (Abstract 247P).

Dr Silvia Formenti, Weill Cornell Medical College, New York City, NY, USA stated that Abstract 1205P confirms the role of optimal dose/fractionation in achieving preclinical abscopal effects in combination with immune checkpoint blockade, which have been seen previously in a mammary carcinoma model study conducted by her research group.[4] While these findings remain to be confirmed clinically, they support the choice of testing 3–5 sessions of hypofractionated RT in combination with immunotherapy. Abstracts LBA14 and 247P translate preclinical data on the synergy of RT and immune checkpoint inhibitors in TNBC to the clinic by demonstrating enhanced clinical responses with such combinations. “These promising results encourage further investigation of brief courses of localised radiation to enhance the efficacy of available immunotherapies,” commented Dr Formenti.

1. Formenti SC, Demaria S. J Natl Cancer Inst 2013;105:256–65
2. Kang J, et al. J Immunother Cancer 2016;4:51
3. Hu ZI, et al. Curr Breast Cancer Rep 2017;9:45–51
4. Vanpouille-Box C, et al. Nat Commun 2017;8:15618

ESMO YOUNG ONCOLOGISTS

YOUNG ONCOLOGIST EVENTS NOT TO MISS TODAY!

YO Brunch Session
Burn out in young oncologists: How can we combat it?
11.00 – 11.45, Salamanca

YO Masterclass
Young oncologists and excellence in clinical research: ESMO YOC meets Methods in Clinical Cancer Research Workshop – MCCR
14.15 – 17.15, Cartagena

Vesalius Talk
How active participation in ESMO has impacted my career
17.30 – 19.15, Foyer Ibiza

Find out more here!

Casting our NETs for molecular markers in neuroendocrine tumours

Jorge Barriuso: *The Christie NHS Foundation Trust, Manchester, UK*

Neuroendocrine tumours (NETs) consist of a range of neoplasms arising from any (neuro)endocrine tissue throughout the human body. Although considered rare, recent data suggest an almost five-fold increase in the age-adjusted incidence of NETs over the past 30 years.[1] Two biological agents are now approved in this setting, sunitinib for pancreatic NETs, and everolimus for a broader spectrum of non-functioning well-differentiated NETs.[2]

A Proffered Paper Session this afternoon ('Endocrine and neuroendocrine tumours', 16.30 – 18.00, Tarragona) includes fascinating insights into precision medicine for NETs. For example, a high number of immune-related genes associated with chronic infection and T-cell exhaustion have been detected in a previously identified pancreatic NET molecular sub-type, hinting at future opportunities for patient selection for immunotherapy (Abstract 4280). Furthermore, the clinical relevance of genomic profiling in pulmonary large-cell neuroendocrine carcinoma has been demonstrated by reports of differential survival with platinum-based chemotherapy in non-small-cell versus small-cell lung cancer according to *RB1* status (Abstract 4310).

In a Poster Discussion Session tomorrow ('Endocrine and neuroendocrine tumours', Monday 11 September, 11.00 – 12.00, Alicante), I will present results from an integrated analysis of differentially expressed microRNA and methylated DNA regions, which allowed our group to identify regions within chromosomes 1 and 2 with variable epigenetic regulation that correlate with relapse and non-relapse in patients with entero-pancreatic NETs (Abstract 437PD). To validate our preliminary data, we are now determining whether the expression of genes related to these genomic regions are in fact different and can be used as markers of poor prognosis.

Trials of peptide receptor radionuclide therapies (PRRTs) have reported positive results in NETs (Abstracts 438PD and 439PD). Notably, efficacy outcomes appear to be dependent on tumour grade, location and choice of PRRT, suggesting that patient selection will remain at the forefront of NET research for the foreseeable future.

We are beginning to understand the biology that could lead to a precision medicine approach for NETs, but collaboration will be needed to ensure new biomarker candidates are incorporated within clinical trials.

1. Yao JC, et al. J Clin Oncol 2008;26:3063–72
2. Liu IH, Kunz PL. J Gastrointest Oncol 2017;8:457–65

#ESMO17

EACR funding opportunities: Apply for support to attend a conference

EACR European Association for Cancer Research

The European Association for Cancer Research (EACR) is continuously working to support cancer researchers in their activities. One of the biggest challenge for early-career researchers is securing funding.

The EACR provides bursaries of up to €500 plus a free registration to help members who have difficulty securing the necessary funding to participate in its Conference Series.

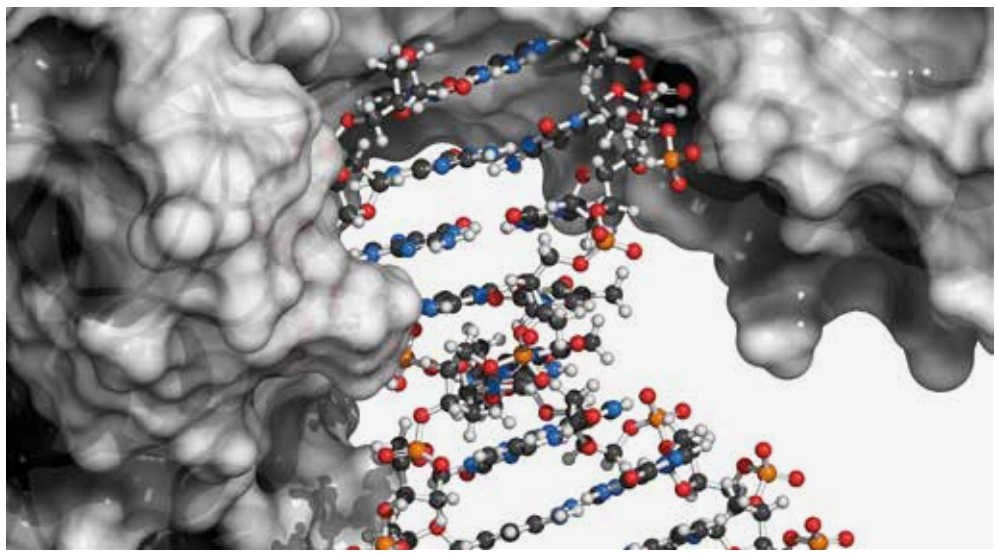
Eligibility - in order to apply, you should:
- have been a member of the EACR for at least 3 months prior to the application
- have less than four years post-doctoral experience
- have difficulty in securing the necessary funding to participate in the conference

In 2016, the EACR supported 24 Conference Series participants from 27 countries, as well as 53 Congress participants and 10 bursaries to attend a partnered meeting.

The EACR provided 14 meeting bursaries to support its members to attend the ESMO Congress and wishes to congratulate bursary winners:

Ali Memarian (Iran)
Nitin Shivappa (USA)
Fara Brasó-Maristany (UK)
Prahlad Raninga (Australia)
Mariana Seke (Serbia)
Debottam Sinha (Australia)
Hajrah Khawaja (Ireland)
Pinelopi Samara (Greece)
Ivan Zaporozhchenko (Russia)
Rossella Loria (Italy)
Maria Morlan Mairal (UK)
Ece Akhan Guzelcan (Turkey)
Ana Podolski-Renić (Serbia)
Meera Chauhan (UK)
Cristina Amaral (Portugal)
Mümin Alper Erdoğan (Turkey)
Martín Arturo Gallardo (Mexico)

Bursaries for the next EACR Biennial Congress, EACR25
The EACR is pleased to be able to offer meeting bursaries to assist student and early-career EACR members to attend the next EACR Congress, EACR25, in Amsterdam, Netherlands, from 30 June to 03 July 2018. The bursaries provide funds of up to €1,300 to support early rate registration, travel and accommodation. More details are available on the Congress website: **www.eacr25.org**.



PARP inhibitors in aggressive breast and ovarian cancers

PARP enzymes play a central role in DNA repair pathways. PARP inhibition converts single-strand DNA breaks to double-strand breaks—repairable by homologous recombination[1]—meaning that malignancies with homologous recombination deficiency (HRD) are acutely susceptible to PARP inhibitors.

In OlympiAD, monotherapy with olaparib demonstrated a greater reduction in lesion size versus physician's choice of standard single chemotherapy in 302 patients with HER2-negative metastatic breast cancer (mBC) and germline *BRCA* mutations (*BRCA*m) (median best percent change from baseline -45.1% versus -14.8%, respectively; Abstract 243PD). These improvements were accompanied by less and later deterioration in quality of life in olaparib-treated patients (Abstract 290P). Combination of olaparib with the mitotic inhibitor eribulin has shown promise in 24 patients with triple-negative BC, with an overall response rate of 29.2% by central review (Abstract 251P); response was higher in patients with versus without HRD (Abstract 282P).

Expanding PARP inhibitor targets in ovarian cancer (OC) is a recurring theme at ESMO 2017. ARIEL3 investigated rucaparib maintenance after platinum response in 564 patients with recurrent OC, demonstrating significantly improved progression-free survival (PFS) versus placebo across all patient sub-groups, including those with *BRCA* wild-type tumours with or without HRD (loss of heterozygosity) (Abstract LBA40). Patients with epithelial OC with *BRCA*m or wild-type tumours with *TP53* mutations disrupting DNA repair experienced a significant overall survival benefit of 39.5 months with olaparib maintenance versus 24.0 months with placebo (Abstract LBA42). Importantly, further results from the SOLO2 trial indicate that in relapsed OC olaparib maintenance prolongs PFS and demonstrates antitumour activity shown by investigator-assessed objective response rates of 41.1% versus 17.1% for placebo (odds ratio 3.52, 95% confidence interval 1.34–10.59; Abstract 965P).

These findings represent part of an impressive body of work to identify new targets in resistant gynaecological cancers.

1. Dockery LE, et al. OncoTargets Ther 2017;10:3029–37

ESMO member lounge

Opening hours:
Sunday 10 September and
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 on Sunday and Monday. For further details visit the 'Discover ESMO Programme'.

Slides available!

Slides available from Special Session on cancer prevention

In a Special Session on Friday ('Primary and secondary prevention of cancer: Where do we stand?'), experts reviewed the important topic of cancer prevention, with a focus on therapeutic aspects (including the role of aspirin), and the impact of tobacco cessation on cancer incidence and recurrence. For delegates who missed the session or who would like a copy of the presentations, slides are now available!

Tumour agnostics: The future for cancer drug development?

Markus Joerger: *Associate Editor of the ESMO 2017 Daily Reporter; Cantonal Hospital, St. Gallen, Switzerland*

Ever since the introduction of tumour molecular profiling and the identification of common markers across different tumour types, support for treating cancers according to their molecular aberration rather than their anatomical origin has grown steadily.

In May 2017, the US FDA gave its first tissue/site-agnostic approval to pembrolizumab for the management of unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumours progressing on treatment.[1] At ESMO 2017, two abstracts illustrate the complexity of tissue agnostics. Yesterday, Dr Chiara Ambrogio from the Dana Farber Cancer Institute, Boston, MA, USA, reported results from studies on *KRAS*—the most frequent *RAS* alteration in human cancers—in lung adenocarcinoma models, in which wild-type *KRAS* allele was shown to mediate growth inhibition and resistance to MEK inhibitors through a mechanism dependent on dimerisation with mutated *KRAS* allele (Abstract 10). In a Poster Discussion Session today ('Basic science', 16.30 – 17.45, Bilbao; Abstract 1703PD), Dr Yolla El Dakdouki from Institut Gustave Roussy, Villejuif, France, will describe how DNA damage response (DDR) gene alterations are common in solid tumours, with 156 alterations occurring in almost 10% of 1,092 patients and 30 DDR genes investigated. Aberration of MMR was found in 11 different primary tumour types.

Tumour agnostics will undoubtedly influence the way that new drugs are tested and approved, but primary site still plays an important part in treatment decisions and the efficacy of drugs,[2] suggesting that a greater understanding of the interplay between molecular alterations and tumour location is needed.

1. www.fda.gov/drugs/informationondrugs/approveddrugs/ucm560040.htm
2. www.nature.com/news/tissue-independent-cancer-drug-gets-fast-track-approval-from-us-regulator-1.22054

Osimertinib: A new first-line option for *EGFR* mutated NSCLC

EGFR T790M-mediated resistance to first-line standard of care (SoC) EGFR tyrosine kinase inhibitors (TKIs) is a major problem in the treatment of non-small-cell lung cancer (NSCLC). A late-breaking abstract presentation yesterday on the phase III FLAURA trial, reported that the third-generation EGFR TKI, osimertinib—which prolonged progression-free survival (PFS) compared with platinum-pemetrexed in patients with _T790M_-positive NSCLC failing EGFR TKI therapy[1]—was effective in the first-line treatment of _EGFR_ mutated disease (Abstract LBA2_PR).

According to Dr Suresh Ramalingam from the Winship Cancer Institute, Atlanta, GA, USA, the median PFS (primary endpoint) among 556 patients was 18.9 months with osimertinib versus 10.2 months with SoC EGFR TKIs (hazard ratio 0.46; 95% confidence interval 0.37–0.57; p<0.0001).

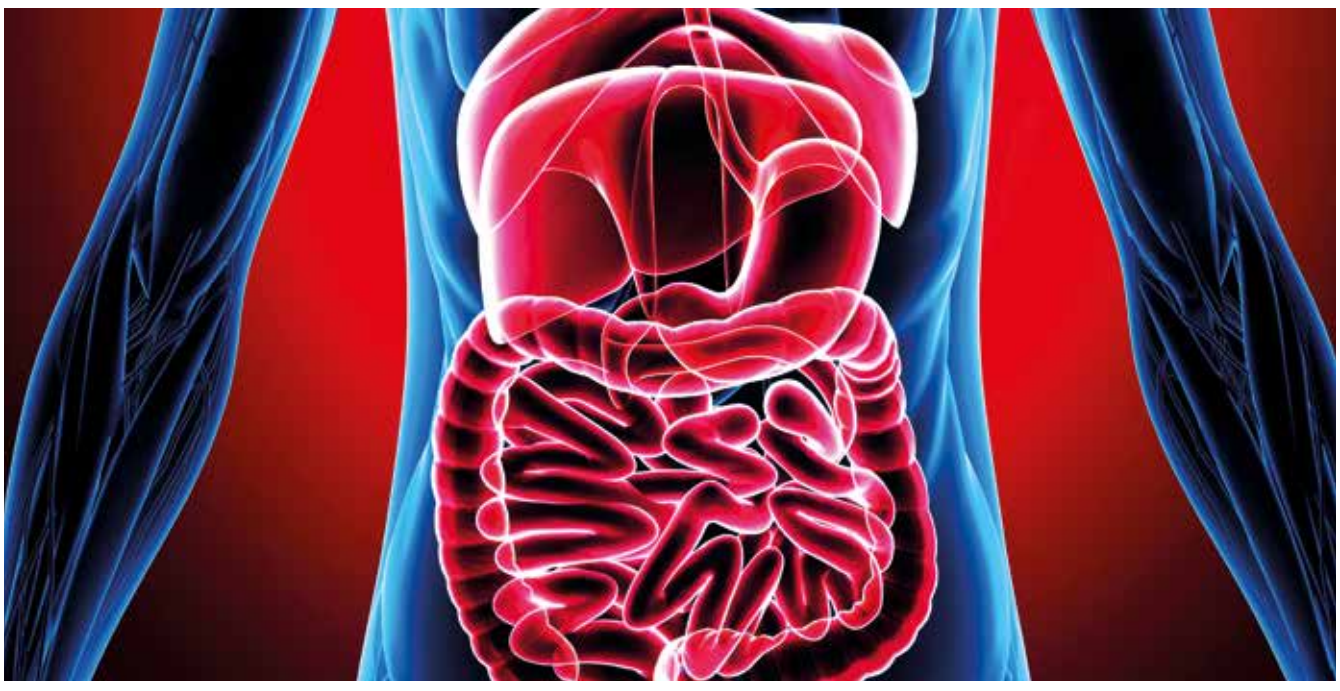
Osimertinib significantly reduced the risk of progression by 54% (p<0.0001).

Benefit was consistent across sub-groups, including those with/without CNS metastases and osimertinib was at least as well tolerated as SoC EGFR TKIs.

"There is little doubt that FLAURA is a positive study demonstrating superiority in PFS with first-line osimertinib," said Professor Tony Mok from the Chinese University of Hong Kong, China. "However, the question remains whether all *EGFR* mutation-positive patients should receive first-line osimertinib. I have confidence that patients with CNS metastases at presentation would benefit the most considering osimertinib's higher CNS penetration, but the optimal sequence for overall survival benefit is still controversial. Current overall survival data are immature and the final total number of patients able to cross over from SoC to osimertinib is uncertain. The other uncertainty is the mechanism and management of osimertinib resistance upon disease progression. Thus, the real paradigm change will have to wait until the eventual maturity of the data."

Lung cancer patient Dyanne Søraas from Oslo, Norway, commented, "Osimertinib is in many ways a great drug, but these results were somewhat disappointing. It seems unlikely that these data will change treatment for many patients. What we need are trials that aim to cure patients, not only prolong survival by a bit."

1. Mok TS, et al. N Engl J Med 2017;376:629–40



Conclusive data on the place of adjuvant imatinib in GIST

Approximately 60% of gastrointestinal stromal tumours (GISTs) are cured with surgery,[1] although metastases are common and 3 years of adjuvant treatment with the tyrosine kinase inhibitor imatinib is recommended for high-risk patients.[2]

An ambitious collaboration between international and national trial bodies was launched in 2004 to evaluate 2 years of adjuvant imatinib 400 mg daily versus no further treatment in intermediate/high-risk GIST.[3] Five-year interim data were encouraging, showing a trend toward improvement in imatinib failure-free survival (IFFS) in the active arm.[3] Final study results reported yesterday were perhaps less positive (Abstract LBA55). Compared with the control arm, imatinib treatment was associated with equivalent 10-year IFFS rate (hazard ratio [HR] 0.87; 95% confidence interval [CI] 0.65–1.15; p=0.31) but improved relapse-free survival (RFS, HR 0.71; 95% CI 0.57–0.89; p=0.002). Adjuvant imatinib was more effective in a high-risk sub-group, with 10-year IFFS of 69.3% (95.7% CI 61.6–75.7) and 62.4% (95.7% CI 54.1–69.6) and RFS of 48% and 43% in the active and control arms, respectively. These results concur with current ESMO treatment recommendations and do not support extension of adjuvant imatinib to the broader GIST population, particularly those at low risk.

Professor Paolo Casali from Istituto Nazionale Tumori, Milan, Italy, who was a study chair for this trial, commented that, "adjuvant imatinib is a standard of care for high-risk GIST."

1. Joenssu H, et al. Lancet 2013;382:973–83
2. ESMO/European Sarcoma Network Working Group. Ann Oncol 2014;25(Suppl 3):iii21–6
3. Casali PG, et al. J Clin Oncol 2015;33:4276–83

Be sure to attend today's Special Session
on the Integrated Oncology & Palliative Care Community

Special Session
4th ESMO Integrated Oncology & Palliative Care Community Session and Awards
16.30 – 18.30, Salamanca

Key features of this Special Session will be a discussion of some of the ESMO 2017 abstracts from the ESMO Designated Centres of Integrated Oncology & Palliative Care as well as presentation of the Fellowship awards to 8 new Designated Centres and a presentation from André Ilbawi from the WHO.

Center	City	Country
St. Hedwig Krankenhaus Berlin, Integratives Zentrum für Hämatologie, Onkologie und Palliative Care	Berlin	Germany
Azienda Ospedaliero Universitaria Maggiore della Carità di Novara	Novara	Italy
Beacon International Specialist Hospital	Petaling Jaya, Selangor	Malaysia
Acharya Tulsi Regional Cancer Treatment & Research Institute	Bikaner, Rajasthan	India
Hospital Alemão Oswaldo Cruz	São Paulo	Brazil
Bhagwan Mahaveer Cancer Hospital & Research Centre	Jaipur	India
Instituto Português de Oncologia do Porto Francisco Gentil, EPE	Porto	Portugal
Hacettepe Oncology Hospital	Ankara	Turkey

Meeting the demands of treating cancer: Balancing cost and innovation

At a time when the number of patients with cancer is growing globally, providing equal access to new, effective treatments is an increasing challenge. However, inequity across the EU in the availability of innovative medicines is well recognised[1] and the community is faced with improving patient access to such medicines while managing costs.

The lack of a common EU healthcare system, together with different levels of economic standards and evaluation processes for individual anticancer medicines, represent formidable challenges for a harmonised attempt at controlling increasing costs. "The utmost aim of the oncology community must be to ensure that high costs do not deter future innovation," said Dr Markus Joerger from Cantonal Hospital, St. Gallen, Switzerland, and Associate Editor of the ESMO 2017 *Daily Reporter*.

Don't miss today's Keynote Lecture 'Coping with escalating healthcare costs in 2017 and beyond' by ESMO President-Elect, Professor Josep Tabernero from Vall d´Hebron Institute of Oncology, Barcelona, Spain (08.15 – 09.00, Barcelona).

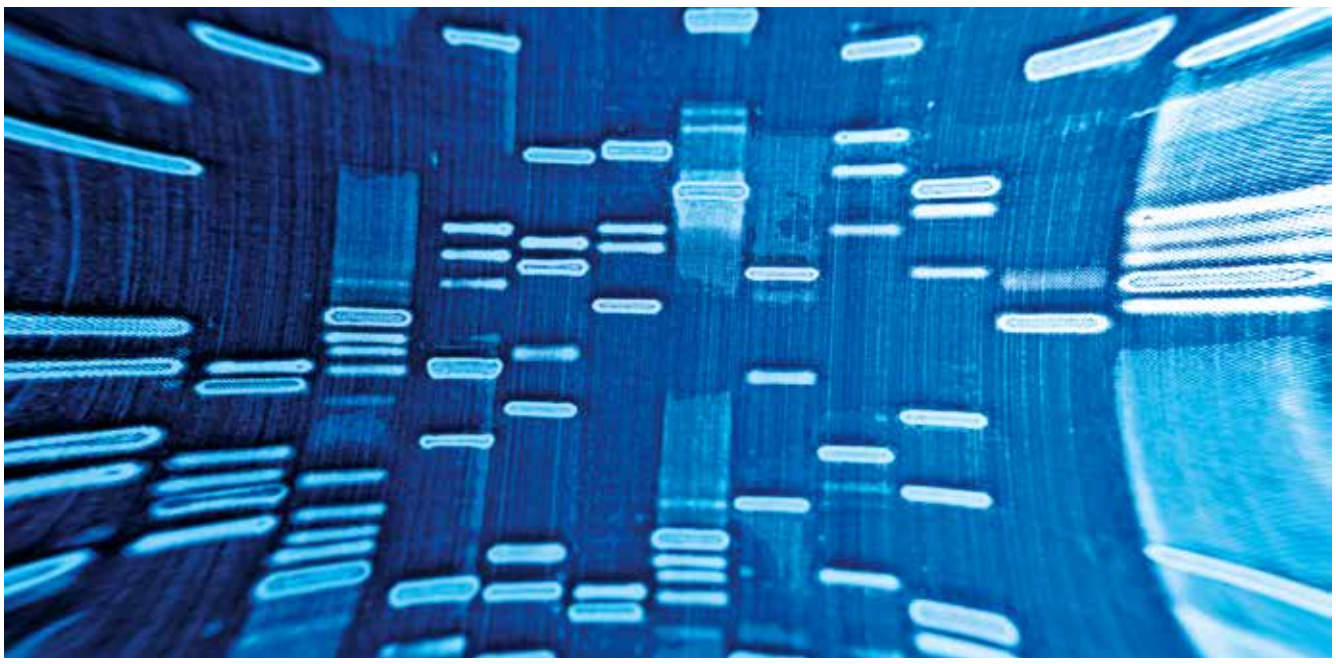
The discussion will continue in tomorrow's Special Symposium 'Access to innovative drugs in the EU' (Monday 11 September, 11.00 – 12.30, Tarragona).

1. Bergmann L, et al. Ann Oncol 2016;27:353–6

Don't miss!

What is a good outcome?
Patient Outcomes Research
Sunday, 10 September,
12:00 - 14:30, Room Palma

View the latest edition of ESMO Perspectives



Next-generation sequencing: **Our best weapon in identifying shifting targets?**

Oncogenic drivers both initiate and maintain tumour growth. Next-generation sequencing (NGS) of tumour-derived DNA can identify oncogenic drivers and potentially match patients with appropriately targeted therapies.[1,2] Newly acquired resistance variants may also be identified through NGS in patients who relapse.[1] Only with large databases can we discover rare alterations in common cancer types or identify relevant targets in rare malignancies.

While point mutations are the focus of routine searches, kinase domain duplications—which constitute a new type of genetic alteration amenable to targeted therapy—are not. In a study of >100,000 advanced-stage solid tumours (Abstract 17000), diverse kinase domain duplications, identified in almost 600 cases (0.62%), appeared to be a mechanism of acquired resistance to targeted therapy. *ROS1* fusions were found in 0.9% of non-small-cell lung cancer (NSCLC) and 0.1% of non-NSCLC tumours, including brain gliomas, soft tissue sarcomas and colorectal carcinomas. Non-NSCLC tumours harbouring these mutations respond vigorously to kinase inhibitors. Genomic profiling was also used to refine tumour sub-types in a study of 174 cases of metastatic thymic gland carcinoma (Abstract 17010). Clinically relevant genomic alterations could be identified, with an average of 0.9 alterations/case.

Circulating tumour DNA (ctDNA) for NGS can be obtained non-invasively by liquid biopsy. Plasma samples from >30,000 patients with advanced cancer revealed ctDNA alterations in 86% of cases. Importantly, 19% of patients had ≥1 ctDNA alteration targetable with a US FDA-approved treatment (Abstract 17020).

Finally, two studies reported potential novel therapeutic targets: CUB domain-containing protein 1 was identified as a novel oncogenic driver in high-grade prostate cancer (Abstract 20), while wild-type *KRAS* allele was discovered to have a complex role in both tumour suppression and MEK inhibitor resistance in *KRAS*-mutated lung adenocarcinoma (Abstract 10).

Professor Carlos Caldas from Cancer Research UK Cambridge Institute, University of Cambridge, UK, an expert in translational genomics, had this to say about these exciting new data: "These abstracts offer clear evidence for the power of genomics. Whether using tissue or liquid biopsies, NGS identifies potentially targetable mutations in a significant fraction of human cancers. Gathering and interpreting these data is not a trivial exercise and requires the expertise of multidisciplinary cancer centres. Patients seen in smaller units and private offices should have access to this expertise so that their care can continue locally."

1. Cummings CA, et al. Clin Transl Sci 2016;9:283–92
2. Rizvi NA, et al. Science 2015;348:124–8

Sessions not to miss!

ESMO Clinical Practice Guidelines sessions today
Two Clinical Practice Guidelines sessions will be held today, each featuring several clinical case presentations with questions to the audience. The cases will subsequently be reviewed, with focus on the relevant guidelines recommendations.

ESMO Clinical Practice Guidelines 1
ESMO Clinical Practice Guidelines Session
10.45 – 12.45, Granada

ESMO Clinical Practice Guidelines 2
ESMO Clinical Practice Guidelines Session
14.30 – 16.30, Granada

Public health and health policy session

Keynote Lecture
Coping with escalating healthcare costs in 2017 and beyond *08.15 – 09.00, Barcelona*

Look out today for a Special Session to include the updated version of the ESMO-MCBS v1.1

Special Session
Cost, value and assessment tools of therapies in modern oncology *16.30 – 18.00, Alicante*

Next-generation targeted combination therapies

Early trial data on new innovative anticancer compounds are a theme of ESMO 2017, particularly new immunotherapy combinations and novel treatment targets for malignancies with poor response or high rates of primary or secondary resistance.

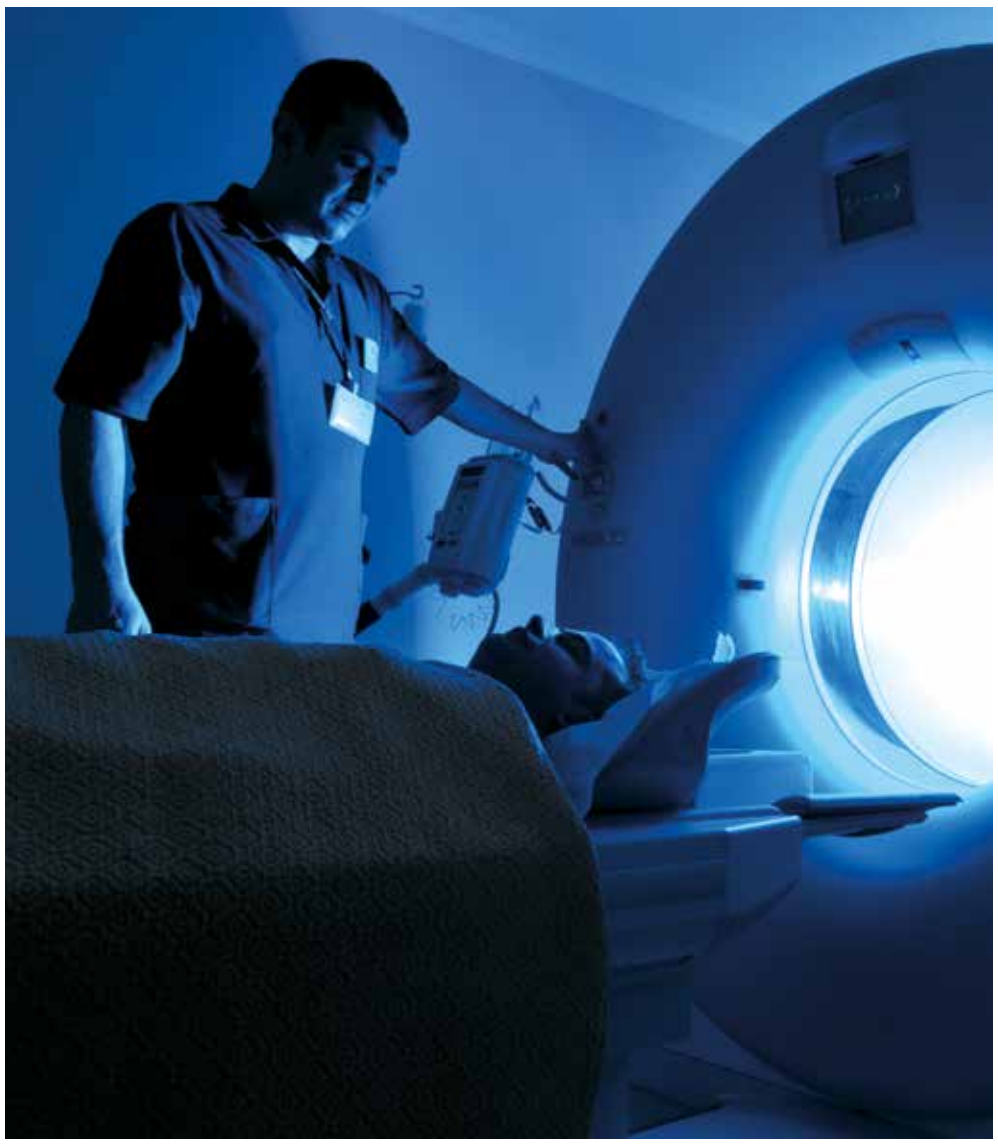
A Proffered Paper Session today ('Developmental therapeutics', 16.30 – 18.00, Cordoba) will take a closer look at some of the most exciting work-in-progress therapies.

During this session, Dr Noboru Yamamoto from National Cancer Center Hospital, Tokyo, Japan, will present phase I data from 90 patients with advanced or metastatic solid tumours treated with a combination of the anti-CC-chemokine receptor 4 (CCR4) antibody mogamulizumab and the PD-1 inhibitor nivolumab. This complementary pairing offers a rational approach, blocking multiple mechanisms involved in the suppression of anti-tumour immunity. Early data reported objective tumour shrinkage in 4/14 patients with hepatocellular carcinoma and partial responses in 3/15 patients with pancreatic adenocarcinoma, alongside acceptable safety (Abstract LBA17).

Professor George Coukos from Ludwig Cancer Research at the University of Lausanne, Switzerland, enthused, "This is an exciting combination. CCR4 neutralising antibodies seek to reduce T regulatory (Treg) cells in tumours. Combining Treg reduction with PD-1 blockade makes great sense since Treg cells are powerful suppressors of tumour infiltrating effector cells and could mediate resistance to PD-1 checkpoint therapy. Treg cells likely play an important role in heavily immunosuppressed cancers (such as gastrointestinal and ovarian) that traditionally do not respond to immune checkpoint blockade, and this paves the way for new immuno-oncology combinations to treat patients."

Encouraging results have also been reported in earlier sessions. A phase IIa study of the antibody–drug conjugate tisotumab vedotin in relapsed/recurrent/metastatic cervical cancer reported clinical benefit (disease control) in 17/34 patients (50%) after 12 weeks and objective responses in 11/34 patients (32%)—exceptional results in a population with high unmet treatment needs (Abstract 9310). DCC-2618 is a tyrosine kinase inhibitor with broad activity on PDGFRα and KIT growth factor receptor mutations that resulted in partial metabolic responses at doses ≥100 mg/day in 22/32 patients (69%) with pre-treated imatinib-resistant gastrointestinal stromal tumours. A decreased frequency of resistance mutations was observed with DCC-2618, supporting its investigation in an imatinib-refractory setting (Abstract 14730).

Reportage – Day two



Post-resection follow-up in NSCLC: **Should we move away from CT scans?**

Post-operative follow-up in non-small-cell lung cancer (NSCLC) aims to detect disease recurrence; however, optimal techniques and monitoring frequency have not been established.[1] The case for intensive follow-up—including computed tomography (CT) scans—has strong support in this setting,[2,3] but remains controversial.[1]

During a Presidential Symposium yesterday, Dr Virginie Westeel from CHRU Jean Minjoz, Besançon, France, reported that after ~9 years, overall survival (OS) was not significantly different in patients with resected NSCLC who received minimal follow-up (clinical examination and chest X-ray) versus minimal follow-up plus CT scanning (hazard ratio 0.92; 95% confidence interval 0.8–1.07; p=0.27), although median OS was shorter in the minimal follow-up arm (Abstract 12730). Dr Westeel emphasised that these results were not conclusive and that longer follow-up is needed to evaluate a potential long-term survival benefit with CT scan monitoring. Elimination of post-resection CT scans from routine follow-up in NSCLC may shorten the time needed for visits and lower costs as well as reduce patients' exposure to radiation.

Dr Floriana Morgillo from the University "Luigi Vanvitelli" Naples, Italy, and Associate Editor of the ESMO 2017 *Daily Reporter*, agrees with the need for longer follow-up, given the 2-year median survival benefit trend favouring CT scanning (10.3 years versus 8.2 years). "Also, clinicians may be cautious about rejecting CT scanning because it can detect post-resection recurrence when the patient is still asymptomatic, allowing early intervention. However, doctors must explain the radiation implications of CT scans to their patients."

1. Van Schil PE. Eur Respir J 2013;42:1178–9
2. Aberle DR, et al. N Engl J Med 2011;365:395–409
3. Gourcerol D, et al. Eur Respir J 2013;42:1357–64

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G.MKT.SM.ON.07.2017.2194
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