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Today's Top Picks

COPENHAGEN 2016 ESMO

SATURDAY 8 OCTOBER, 2016

FROM DISEASE TREATMENT TO PATIENT CARE

DAILY REPORTER

ESMO 2016: A practice-changing congress

Yesterday, Professor Fortunato Ciardiello, ESMO President and President of this year's Congress officially opened the meeting and welcomed delegates to Copenhagen. Professor Ciardiello spoke enthusiastically during his address about his aspirations for the meeting. Acknowledging the growing burden of cancer in Europe and worldwide, he said that ESMO is continually evolving to meet the challenges that this brings. Professor Ciardiello added that as part of this, ESMO provides a platform for sharing knowledge, educating colleagues, forging new collaborations and, ultimately, finding the best possible outcomes for cancer patients.

Oncology, Professor Ulrik Lassen was pleased that Denmark—and his home city of Copenhagen—played host to the ESMO 2016 Congress. He felt it was very fitting, considering the important role that Danish oncologists had played in the advancement of oncology research. Passionate speeches were a theme of the Opening Session. Professor Andrés Cervantes, ESMO 2016 Scientific Chair, encouraged everyone to make the most of the Congress.

Also present at the Opening Session was the Prime Minister of Denmark, Lars Løkke Rasmussen who gave a very personal account of losing his father to cancer. Mr Rasmussen described a national programme to have the first smoking-free generation in Denmark by 2030, stating that we owe it to future generations to be ambitious in combating cancer. He also emphasised that one of the best weapons in our armamentarium is international co-operation, calling on the elite 'troops' at ESMO to continue to demonstrate their incredible determination and tireless work ethic.

The Opening Session was also an opportunity to celebrate award recipients, who were introduced by Professor Christoph Zielinski, Chair of the ESMO Fellowship and Award Committee. These awardees represent truly inspirational and international clinicians and researchers from a broad spectrum of cancer disciplines.

By encompassing exceptional oncologists and ardent speeches, the Opening Session of ESMO 2016 enthused delegates and may even help to foster new working relationships to create the award winners of the future.

"I am certain that ESMO 2016 will be remembered as an important practice-changing congress," said Professor Ciardiello.

In answer to the rapid pace of progress in the field, he said that from now, ESMO will hold an annual congress.

As ESMO National Representative for Denmark and President of the Danish Society of Clinical

Left to right: ***Professor Alberto Sobrero,*** IRCCS San Martino IST, Genova, Italy, recipient of the ESMO Award; ***Professor Carlos Caldas,*** Cancer Research UK Cambridge Institute, University of Cambridge, UK, recipient of the Hamilton Fairley Award; ***Professor Sir Richard Peto,*** University of Oxford's Nuffield Department of Population Health, UK, recipient of the ESMO Lifetime Achievement Award

View the ESMO 2016 Broadcast on the youtube playlist here. YouTube

Our record-breaking **Congress!**

Giuseppe Curigliano: Editor-in-Chief of the ESMO 2016 Daily Reporter
European Institute of Oncology, Milan, Italy

Copenhagen is the fitting location for the ESMO 2016 Congress, being the home of one of the Society's founders, Heine H. Hansen, who was instrumental in the evolution of ESMO into an international organisation. The city also boasts several other alumni notable for their contribution to oncology, including Niels Kaj Jerne, with his Nobel Prize-winning work on the immune system and the principles of monoclonal antibody production, and Niels Bohr, who first proposed the potential use of electron energy levels in cancer treatment.

The Congress has had a record-breaking start, with just over 20,239 registered delegates who now have the opportunity to experience around 730 presentations from >500 speakers and to get first-hand information on the latest treatments and technologies from the 75 pharmaceutical companies and publishers taking part in the exhibition.

First-class SCIENCE

Several of the Late-Breaking Abstract presentations at ESMO 2016 have the potential to change clinical practice. New targeted agents show exciting data in the treatment of stage 3 melanoma. We will hear about the final, 5-year efficacy data from the EORTC 18071 study in which adjuvant ipilimumab administered after complete resection was compared to placebo (Abstract LBA2_PR) and the results in the neoadjuvant setting of ipilimumab–nivolumab combination in the OpACIN trial (Abstract LBA39). Interim results from the MONALEESA-2 study of the CDK 4/6 inhibitor ribociclib plus letrozole are much anticipated, and are expected to provide a valuable insight into the potential role of this combination in patients with hormone receptor-positive, HER2-negative advanced breast cancer (Abstract LBA1_PR). We will also hear the results from the S-TRAC study comparing sunitinib to placebo after nephrectomy in patients with high-risk renal cell carcinoma (Abstract LBA11_PR).

As Editor-in-Chief, I recommend ESMO 2016's Daily Reporter as a really useful source of information on the latest data presentations, along with other news and reports from the Congress.

First-class EDUCATION

Talks and educational sessions at ESMO 2016 will focus on accelerating the transition of novel treatments from the laboratory to the bedside, based on the discovery and better understanding of cancer genomic and immunology targets, and new predictive and prognostic biomarkers. Even recently, many experts and opinion leaders have bemoaned the shortage of trained medical oncologists with a working knowledge of laboratory terminology, creating a translational gap between physicians and their scientific colleagues. ESMO 2016 addresses this gap head-on with high-quality presentations and posters, and also dedicated sessions facilitating closer collaboration between medical oncologists and basic scientists **(Young Oncologist Vesalius Talk; Sunday 9 October; 17.30 – 18.45).**

ESMO has also identified and emphasised a second translational gap, namely, getting best practice and improved methodologies into all medical oncologists' clinics. So please, look carefully at the excellent educational sessions at this meeting. At least I think they're excellent, but I'm an academic! Let us know if you find them interesting and useful as we really value your feedback in developing the programmes for future Congresses.

First-class NETWORKING

ESMO 2016 offers delegates the chance to share their ideas with the global oncology community and international companies at the forefront of drug development.

We are aiming to bridge the gap between the Congress and daily practice by providing a platform for high-level scientific content, with improved educational sessions and paradigm-changing Late-Breaking Abstract data. ESMO is constantly working on providing more solutions and innovations for your day-to-day clinical practice!

Science, education and networking are the key elements of the ESMO Congress.

ESMO **Educational Survey**

Have you taken the ESMO Educational Survey?

Please complete online:

https://esmoeducation.formstack.com/forms/survey2016

The hope of novel antibody constructs **and antibody drug conjugates in cancer treatment**

Markus Joerger: *Associate Editor of the ESMO 2016 Daily Reporter. Cantonal Hospital, St. Gallen, Switzerland*

Hot on the heels of the success of monoclonal antibodies for cancer therapy[1] are novel antibody constructs. Among the promising agents are designed ankyrin repeat proteins (DARPins®), which are synthetic scaffolds or antibody mimetics that can be engineered to bind to specific targets with high precision and affinity. Owing to their small size, DARPins have greater tissue penetration than antibodies and may reach targets beyond the bloodstream, such as the brain.[2,3] DARPins targeting HER2 have been examined in mouse xenograft models, while other DARPins could deliver toxins to tumours.[3]

In a Developmental Therapeutics Poster Discussion Session tomorrow (Abstract 361PD, 15.00 – 16.00, Berlin), interim results will be presented from a phase I, first-in-human study of MP0250 for the treatment of advanced solid tumours. MP0250 is a first-in-class, multi-DARPin that targets HGF and VEGF, and binds to human serum albumin to increase plasma half-life and potentially enhance tumour penetration. Efficacy findings include significant reductions in tumour volume (including one confirmed partial response) in 2/24 patients, and prolonged stable disease (22–60 weeks) in four patients. Dose-limiting toxicities were consistent with VEGF inhibition, such as gastrointestinal haemorrhage, nephrotic syndrome and hypertension. A phase II study is due to recruit patients by the end of this year.

Encouraging clinical activity has been shown with PF-06647020, an antibody-drug conjugate comprising a humanised monoclonal antibody directed against PTK7, linked to an auristatin microtubule inhibitor payload. PTK7 is a catalytically inactive receptor tyrosine kinase that is often over-expressed in many tumour types and therefore represents a promising target for new innovative antibody–drug conjugates. In xenograft model studies of triple-negative breast cancer (TNBC), non-small-cell lung cancer and ovarian cancer (OVCA), PF-06647020 induced tumour regression. Initial phase I data provide evidence of PF-06647020's activity in patients with heavily pre-treated or platinum resistant OVCA. In a Poster Discussion Session today (Gynaecological cancers, 09.30 – 10.30, Bern, Abstract LBA35), updated safety and efficacy data are expected.

Innovative antibody–drug conjugates may overcome pharmacological barriers and issues of non-specificity that hamper the clinical activity of some classical monoclonal antibodies and cytotoxic agents. Presentations on MP0250 (Abstract 361PD) and PF-06647020 (Abstract LBA35) show very promising new avenues of antibody–drug conjugates with a good safety profile and convincing early activity data, and both new agents are being further developed.

1. Scott AM, et al. Nat Rev Cancer 2012;12:278–87
2. Hanenberg M, et al. J Biol Chem 2014;289:27080–9
3. Toporkiewicz M, et al. Int J Nanomedicine 2015;10:1399–4

ONO-7643/anamorelin associated with significant improvements in **cachexia symptoms in Japanese patients with advanced NSCLC**

Most (~70%) patients with advanced cancer suffer from the distressing symptoms of cancer cachexia. Characterised by weight loss—primarily lean body mass (LBM)—and anorexia, cancer cachexia is associated with a poor prognosis and poor quality of life (QoL).[1] Today, Dr Junji Uchino from Fukuoka University School of Medicine, Japan, will report the findings of a phase II double-blind study of the first-in-class selective ghrelin receptor agonist, ONO-7643/anamorelin, for the treatment of cachexia in Japanese patients with non-small-cell lung cancer (NSCLC; Abstract 1434O). Anamorelin is a mimetic of ghrelin; the so-called 'hunger hormone' secreted by the stomach. The binding of anamorelin to ghrelin receptors stimulates the release of the growth hormone, resulting in enhanced appetite, increased food intake and anabolic effects.

In this confirmatory study of 173 patients with advanced NSCLC (63% stage IV) randomised to 100 mg anamorelin or placebo orally once daily for 12 weeks, anamorelin significantly increased LBM versus placebo ($p<0.0001$). Significant improvements in body weight ($p<0.0001$) and anorexia symptoms ($p<0.05$) were also noted with anamorelin versus placebo, and the treatment was well tolerated over the 12-week study period.

Anamorelin significantly increased lean body mass, body weight and anorexia symptoms compared with placebo.

Importantly, these data reflect those from an exploratory phase II Japanese study of NSCLC patients that also reported improvements in QoL with anamorelin versus placebo,[2] and two multinational phase III trials (ROMANA 1 and 2) conducted in the USA, Europe and Australia.[3]

Cachexia may affect the majority of patients with advanced cancer. It is a multifactorial syndrome that impacts many organs and is often irreversible. While nutritional counselling and physical training may delay or prevent cachexia from developing, these interventions have limited effect. Notably, there are no definitive pharmacological treatments to target the relevant elements of cachexia. Anamorelin represents a new drug class and the first effective agent in this patient group, whose therapeutic options are currently limited. Anamorelin is presently under review for potential marketing authorisation in Europe.

Dr Uchino will give a full presentation of these data this evening during the Proffered Papers Session **'Supportive and palliative care' (16.30 – 18.00, Oslo).**

1. von Haehling S, Anker SD. J Cachex Sarcopenia Muscle 2010;1:1–5
2. Takayama K, et al. Support Care Cancer 2016;24:3495–505
3. Temel SA, et al. J Clin Oncol 2015;33 (Suppl 15):9500

Neoadjuvant bevacizumab and nintedanib enhance surgical outcomes in ovarian cancer

Angiogenesis is fundamental to normal ovarian physiology and key to the progression of ovarian cancer. Consequently, there are well-defined recommendations on the inclusion of the anti-angiogenesis agent bevacizumab for the treatment of ovarian cancer. Other anti-angiogenic agents and combinations of agents, such as those targeting Angiopoietin-1 and -2, PARP inhibitors and immune checkpoint inhibitors are in development, with the potential of broadening the choice of treatments in the future. Importantly, while the majority of ovarian cancer patients will receive anti-angiogenic treatment, the incidence of cures is not increased and toxicities can be severe. Biomarkers predictive of response with these agents would be desirable so that treatment can be tailored to those more likely to benefit.

"The addition of bevacizumab to neoadjuvant chemotherapy resulted in a complete resection rate of 58.6% … significantly exceeding a previous reference rate of 45% with chemotherapy alone..."

The addition of bevacizumab to neoadjuvant chemotherapy was well tolerated and resulted in a complete resection rate (CRR) of 58.6% at interval debulking surgery (IDS), significantly exceeding a previously reported reference CRR of 45% with chemotherapy alone, and meeting the primary study objective.[1] This was an encouraging finding of the phase II ANTHALYA trial—an open-label, randomised study in 95 patients with initially unresectable FIGO stage IIIc/IV ovarian, tubal or peritoneal adenocarcinoma. The data will be presented today by Dr Roman Rouzier from Institut Curie, St Cloud, France (Abstract 860PD).

While bevacizumab-containing neoadjuvant chemotherapy was previously associated with a good safety profile in the ANTHALYA trial,[2] alternative neoadjuvant treatment combinations have also been explored. Dr Gwenaël Ferron from Institut Claudius Régaud, Toulouse, France presented safety data from a randomised, double-blind, phase II trial of the multi-tyrosine kinase inhibitor nintedanib or placebo added to neoadjuvant chemotherapy in 188 patients with unresectable ovarian cancer (Abstract 859PD). Compared with placebo, nintedanib did not increase the incidence of IDS-related peri- (18% versus 13%, respectively) or post-operative complications (53% versus 47% with at least one complication, respectively).

Both studies will be presented this morning at the Poster Discussion Session 'Gynaecological cancers' (09.30 – 10.30, Bern).

1. Vergote I, et al. N Engl J Med 2010; 363:943–53
2. Selle F, et al. Eur J Cancer 2015;51 (Suppl 3):S553

Controversy of the Day Biomarkers in immunotherapy: Where are we now?

Professor John Haanen:
Netherlands Cancer Institute, Amsterdam, Netherlands

Since the first immune checkpoint inhibitor was approved to treat advanced melanoma in 2011, impressive improvements in clinical outcomes have continued to be demonstrated across several cancer types. However, not all patients benefit from these agents and many studies have focused on identifying predictive and prognostic biomarkers in an attempt to better inform and guide treatment decisions.

Several studies investigating established and novel biomarkers of response to immunotherapy will be presented at this year's Congress (see Table).

Programmed death ligand-1 (PD-L1) expression has been one of the most hotly debated biomarkers in immuno-oncology since the introduction of PD-1/PD-L1 immune checkpoint inhibitors. There are currently multiple assays under investigation or approved as companion or complementary diagnostic tests for PD-L1 expression. It is a concern that the US FDA approval of an assay on the basis of its performance appears to have become more important than the accurate and reproducible measurement of the target. As a result, at least four separate antibodies have been included in assays that are part of separate FDA submissions, creating a challenge for pathologists who may need to perform four different assays rather than simply assess PD-L1 expression. Indeed, a recent comparative study found that differences reported in PD-L1 expression in lung cancer tissue arose from tumour heterogeneity or the assay or platform used, rather than the choice of antibody.[1] Imagine a situation where a pathologist was required to use separate assays to assess the dozen or so drugs that target the oestrogen receptor in breast cancer.

Two Late-Breaking Abstract presentations will describe efficacy data in advanced non-small-cell lung cancer (NSCLC) by PD-L1 expression status. In the first, overall survival data will be presented from the first phase III study of atezolizumab versus docetaxel (Abstract LBA44_PR), while in the second, preliminary efficacy data will be presented from the first study to combine anti-VEGF (ramucirumab) and anti-PD-1 (pembrolizumab) antibody treatments (Abstract LBA38). The value of PD-L1 expression as a biomarker of response in melanoma is also considered in a pooled analysis of phase II (CheckMate 069) and phase III (CheckMate 066 and 067) trials comparing nivolumab plus ipilimumab versus nivolumab alone. Data in advanced melanoma appear to be far from clear-cut and PD-L1 expression does not seem to predict response to immune-targeting drugs (Abstract 1112PD).

Multiple diagnostic assays are available for determining PD-L1 expression status and have been used in clinical trials of different immunotherapies. Data from a study comparing three PD-L1 diagnostic assays from biopsies of squamous cell carcinoma of the head and neck (SCCHN) show a strong correlation between the assays, suggesting that it may be feasible to compare data derived from different PD-L1 diagnostic tests (Abstract 955PD).

To date, a number of regulatory approvals for PD-(L)1-targeting agents are linked to companion diagnostic assays and there are potential risks associated with cross-matching agents to assays in the absence of established clinical and analytical concordance, according to Dr Jorge Martinalbo from the European Medicines Agency, London, UK. Further confusion comes from different scoring criteria and thresholds for defining PD-L1 positivity, which vary by agent and tumour type. Acknowledging that harmonisation of assays is probably unrealistic, a blueprint proposal initiative was started in 2015 with the remit to 'agree and deliver, via cross-industry collaboration, a package of information/data upon which analytic comparison of the various diagnostic assays may be conducted, potentially paving the way for post-market standardisation and/or practice guideline development, as appropriate'.[2]

In patients with advanced cancer, the relationship between tumour mutational burden and microsatellite instability both appear to be of value in identifying patients most likely to derive benefit from immunotherapy (Abstract 520). However so far, there is no single reliable, validated biomarker for selecting patients who are likely to benefit from immunotherapies. At the moment PD-L1 expression, CD8+ T-cell infiltrates and 'foreignness' of the tumour, despite all being correlated with response or survival to immunotherapy with checkpoint inhibitors, are not sufficiently robust to discriminate with high specificity and sensitivity between those patients who would and would not benefit. The reason for this could be that different treatment-evasive mechanisms may play a role across tumour types. This is quite different for targeted agents that require a specific gene mutation or translocation in order to be active. In particular, because the overall response rate to immunotherapy for many tumour types is modest, improved selection criteria are becoming more urgent as we expose our patients to sometimes highly toxic drugs. Establishing predictive biomarkers is also becoming increasingly important from a health economic perspective. The cost of immunotherapies is such that it impacts ever more on the total healthcare budget, which in turn affects the availability of these drugs in different European countries. We at the Netherlands Cancer Institute have developed the 'cancer immunogram', an initial framework of seven parameter classes describing cancer–immune interactions for individual patients.[3] This may become a tool to help oncologists assess the likelihood of benefit from immunotherapy in the future.

Biomarkers and exploratory translational endpoints under investigation as potential predictors of response to immunotherapy

BIOMARKER/ EXPLORATORY ENDPOINT	RELATED INVESTIGATIONS	ABSTRACT/PRESENTATION DETAILS
PD-L1	NSCLC: Phase III study of atezolizumab versus docetaxel; overall survival by PD-L1 expression level on tumour cells and tumour-infiltrating immune cells	LBA44_PR, Proffered Paper Session 'NSCLC, metastatic 2', Sunday 9 October, 16.25 – 18.20, Copenhagen
	NSCLC: Phase I study of combined anti-VEGF (ramucirumab) and anti-PD-1 (pembrolizumab) treatment; efficacy by PD-L1 expression level	LBA38, Poster Discussion Session 'Immunotherapy of cancer', Monday 10 October, 9.30 – 10.30, Berlin
	Melanoma: Pooled analysis of phase II and III trials of nivolumab plus ipilimumab versus nivolumab alone; efficacy by high PD-L1 expression level	1112PD, Poster Discussion Session 'Melanoma and other skin tumours', Monday 10 October, 11.00 – 12.00, Rome
	SCCHN: Comparative study of three diagnostic PD-L1 assays	955PD, Poster Discussion Session 'Head and neck cancers', today, 15.00 – 16.00, Bern
Tumour mutational burden (TMB) and microsatellite instability (MSI)	Advanced cancers: Assessment of the relationship between TMB and MSI with comprehensive genomic profiling, and value as predictive biomarkers for response to immunotherapy	520, Proffered Paper Session 'Basic science and translational research', today, 11.00 – 12.30, Madrid
	Advanced cancers: Assessment of the relationship between TMB and MSI with comprehensive genomic profiling, and value as predictive biomarkers for response to immunotherapy	

1. Gaule P, et al. JAMA Oncol 2016. Aug 18. Epub ahead of print
2. www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM439440.pdf
3. Blank CU, et al. Science 2016;352:658–60

ESMO 2017

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Selfies will be entered into a draw and a winner will be chosen at random

Mouse 'avatars' may hold the key to better targeted cancer therapies and the future of personalised medicine

Evandro de Azambuja:
Associate Editor of the ESMO 2016 Daily Reporter. Jules Bordet Institute, Brussels, Belgium

The use of mouse models to mimic human cancer has become increasing popular over recent decades.[1] Several presentations at the Congress describe the use of such models, for example to evaluate a novel agent chemotherapy combination for ovarian cancer (Abstract 382P) and novel peptide nucleic acid oligonucleotide analogues for BRAF V600E mutant melanoma (Abstract 368P). However, while contributing to a greater understanding of disease, traditional mouse models have a limited capacity to assist in the development of therapies for human cancers; crucially, they lack the heterogeneity of human tumours and are unable to mimic inter-patient variability in response to treatment.[1]

Patient-derived tumour xenograft (PDX) models, or mouse 'avatars' have been developed in an attempt to overcome these limitations and enable mouse models to be used in the study of personalised medicine.[1,2] This will ultimately reduce the number of preclinical drugs that fail when tested in humans. A mouse avatar encyclopaedia has been compiled containing more than 1,000 PDX models of common solid tumours to aid in the selection of the most appropriate therapy for individual patients.[2] Initial findings in ovarian cancer are encouraging, with correlation demonstrated between patients and their mouse avatars in response to platinum-based therapy.[3] Interestingly, in a PDX clinical trial, each mouse will receive the therapy of interest taking into account tumours from an individual patient.

Patient-derived tumour xenograft models, or mouse 'avatars' have been developed to benefit personalised medicine.

The use of mouse models to facilitate the development of better targeted therapies was the topic of an ESMO-EACR joint symposium yesterday chaired by Professor Anton Berns (Amsterdam, Netherlands) and Professor Fortunato Ciardiello (Naples, Italy). Delegates learnt about the clinical evolution of mouse models, including developments in thoracic cancer models, and the utility of mouse models in deciphering mechanisms of resistance and integrating immunotherapy with molecular targeted treatments.

1. Malaney P, et al. Cancer Lett 2014;344:1–12
2. Poh A. Cancer Discov 2016;6:5–6
3. Zayed AA, et al. Chinese Clin Oncol 2015;4:30

#ESMO16

Final OS results from phase III IMPRESS study confirm detrimental effect of **continuing gefitinib plus chemotherapy beyond progression in NSCLC**

Patients with acquired resistance to first-line gefitinib should not continue to receive gefitinib plus doublet chemotherapy beyond progression due to a detrimental effect on overall survival (OS). This guidance is based on the final OS analysis from the phase III IMPRESS study in 265 patients with *EGFR* mutation-positive non-small-cell lung cancer (NSCLC). The data, which are consistent with the primary progression-free survival analysis[1] and preliminary OS findings,[2] will be presented by Professor Jean-Charles Soria from Institut Gustave Roussy, Villejuif, France (Abstract 12010).

Median OS in the gefitinib plus chemotherapy (cisplatin/pemetrexed) arm was 13.4 months versus 19.5 months with placebo plus chemotherapy (hazard ratio 1.44; p=0.016).

While these data verify earlier reports from the IMPRESS trial, the final OS analysis also suggests that the detrimental effect of continuing gefitinib plus chemotherapy may be driven by *T790M*-positive mutation status.

The presence of the *T790M* mutation is known to be associated with resistance to EGFR tyrosine kinase inhibitors (TKIs), and a new class of EGFR inhibitors that target *T790M*-mediated drug resistance have recently demonstrated efficacy in NSCLC; AZD9291 was approved by the US FDA in November 2015 following an accelerated development programme to meet this important unmet need. While the findings of the IMPRESS study may remain relevant to NSCLC patients undergoing later lines of therapy and those lacking the *T790M* mutation, these results are arguably less relevant to a large proportion of patients currently requiring treatment. In the NSCLC setting, acquired *T790M* mutation is estimated to be present in around 50% of patients with TKI-resistant, *EGFR*-mutated disease.[3] While AZD9291 is now standard of care for NSCLC patients with *EGFR* mutations who have failed EGFR TKI therapy and whose disease harbours the *T790M* mutation, it is also being tested in treatment-naïve patients in the ongoing FLAURA study.

Patients with acquired resistance to first-line gefitinib should not continue to receive gefitinib plus doublet chemotherapy beyond progression.

Professor Soria will give a full presentation of these data tomorrow in the Proffered Papers Session **'NSCLC, metastatic 1' (11.00 – 12.30, Copenhagen).**

1. Soria JC, et al. Lancet Oncol 2015;16:990–8
2. Mok TSK, et al. Ann Oncol 2014;25 (Suppl 4):LBA2_PR
3. Maione P, et al. Ther Adv Med Oncol 2015;7:263–73

ESMO **Focus Talks**

Saturday 8 October, 12.30
Professor Alberto Sobrero (Italy) and Professor Carlos Caldas (UK)
Integrating science into oncology for better patient outcomes: the need for collaboration between researchers and oncologists

Sunday 9 October, 10.45
Professor Rossana Berardi (Italy) and Professor Ulrik Lassen (Denmark)
Setting standards in medical oncology training: the 2016 edition of the ESMO/ASCO Global Curriculum

Monday 10 October, 12.30
Dr Erika Martinelli (Italy) and Antonio D'Alessio (Italy)
Your career in oncology, with ESMO by your side

All sessions will take place at the ESMO Booth in the Society Village.

Treatment implications of genomic testing in early breast cancer

Fatima Cardoso: *Breast Unit, Champalimaud Clinical Center, Lisbon, Portugal*

As oncologists, our first instinct is often to offer early and aggressive treatment to minimise the likelihood of recurrence (such as adjuvant chemotherapy after surgery for early breast cancer); however, not all patients really do need aggressive treatments and they will, ultimately, experience acute and long-term side effects. There is therefore a need to minimise over-treatment in adjuvant approaches in early breast cancer. Genomic testing of tumours involves analysing panels of genes that have the potential to affect cancer prognosis and treatment response to give a score denoting the likely recurrence of breast cancer. Low risk scores indicate a lower risk of recurrence, in which case the balance between the potential benefit and potential harms of adjuvant chemotherapy may not be in favour of prescribing this treatment.

A number of commercially developed prognostic and predictive gene signatures have been validated in early breast cancer and ductal carcinoma in situ.[1–3] The phase III MINDACT (Microarray In Node – negative and 1 to 3 positive lymph node Disease may Avoid ChemoTherapy) trial investigated the clinical utility of the 70-gene signature MammaPrint in conjunction with traditional clinical-pathological prognostic factors. Of the 6,600 patients enrolled, all of whom had undergone surgery for early breast cancer, 23% had discordant risk assessment arising from high clinical but low genomic recurrence risk. After randomisation to a clinical or genomic prognostic-based approach, the 5-year distant metastases-free-survival (DMFS) was 94.7% in the group who did not receive adjuvant treatment: well above the hypothesised 92%. In this high clinical but low genomic recurrence risk group, those who received chemotherapy had a DMFS 1.5 percentage points higher, albeit not statistically significant since the trial was not powered to assess this difference. MINDACT provides the highest level of evidence for the use of the MammaPrint genomic test for the selection of patients who may avoid adjuvant chemotherapy. Importantly, the final decision about this treatment lies with the patient, who would be adequately informed of the potential risks and benefits.

As the weight of evidence for its utility becomes ever greater, it is likely that genomic testing will become more commonplace, providing patients and clinicians with a very important additional tool when making potentially life-altering decisions.

The MINDACT findings emphasise the potential for positive outcomes using genomic testing as the basis for treatment decisions; a number of proffered papers at the ESMO Congress this year will further delineate the utility of this approach. Dr Cristina Truica of Penn State Hershey Medical Center, Pennsylvania, USA will report that the rate of recurrence scores denoting candidacy for adjuvant treatment differs widely between breast cancer types. Less than 7% of patients with invasive lobular carcinoma had recurrence scores above the cut-off for chemotherapy, a rate far lower than that seen in invasive ductal carcinoma (today, 15.00 – 16.00, Poster Discussion; Abstract 148PD). Dr Maria Toribio of H.U. ARABA, Vitoria, Spain will report that basing treatment decisions on genomic recurrence scores partially offsets the cost of testing by lowering associated short-term expenditure on chemotherapy **(Monday 10 October, 13.00 – 14.00, Poster Display; Abstract 181P).**

Recurrence assays are incorporated into many international oncology guidelines; however, reimbursement for their use is still uncommon.

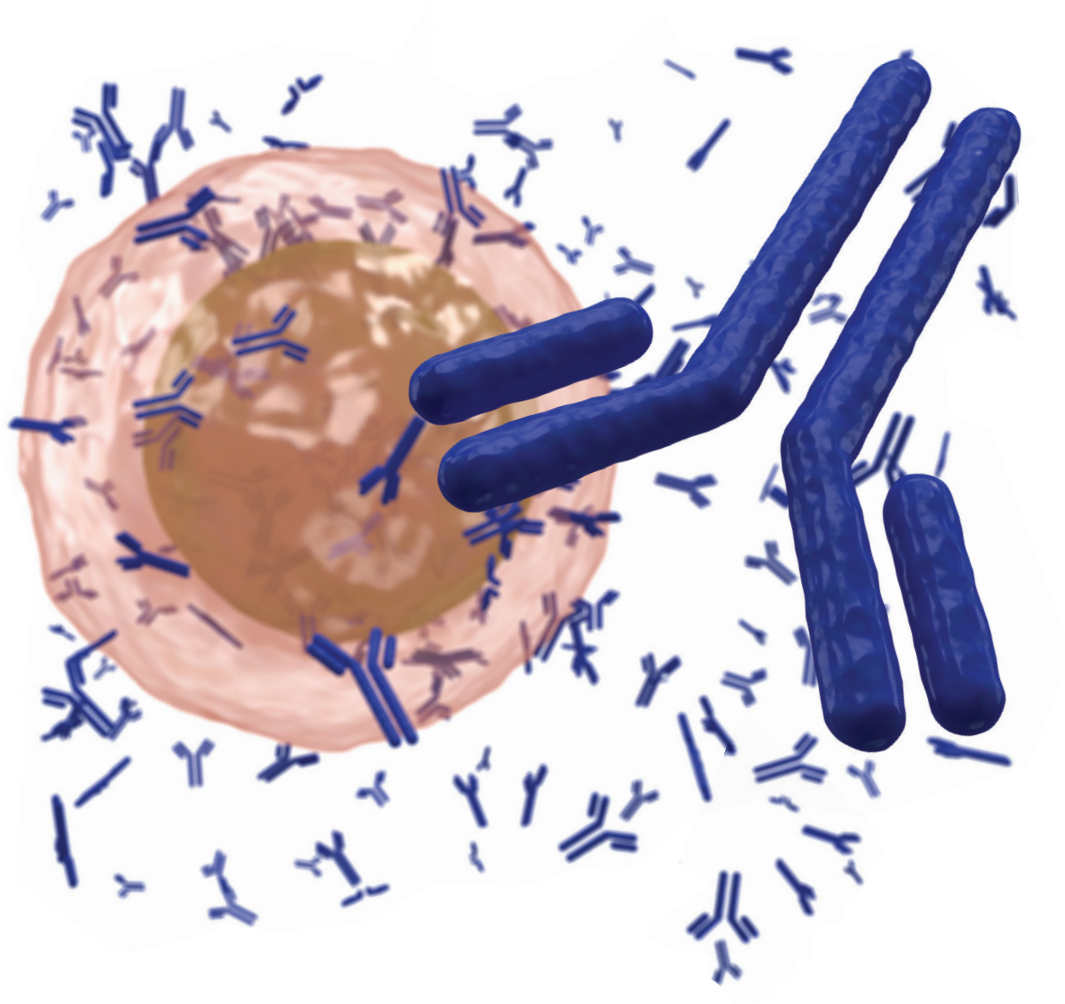
Therefore, there is a need for governments to negotiate prices with the companies developing such approaches in order to render them more cost-effective and widely available.

1. Cardoso F, et al. N Engl J Med 2016;375:717–29
2. Albanell J, et al. Eur J Cancer 2016;66:104–13
3. Rakovitch E, et al. Breast Cancer Res Treat 2015;152:389–98

Neoadjuvant nivolumab in early NSCLC: **Flexing its therapeutic muscles beyond advanced cancer treatment**

Programmed death-1 (PD-1) is a checkpoint cell-surface protein receptor that protects against lymphocyte-mediated autoimmunity and inflammation in the normal state, but can facilitate immune evasion by tumour cells. Nivolumab is an anti-PD-1 monoclonal antibody approved in 2015 for the treatment of metastatic non-small-cell lung cancer (NSCLC) that has progressed after platinum-based therapy. Nivolumab is also indicated for the treatment of advanced melanoma, advanced renal cell carcinoma and relapsed/progressed classical Hodgkin lymphoma, highlighting its broad clinical utility.

Yesterday, Dr Patrick Forde of Johns Hopkins University, Baltimore, Maryland, USA reported potentially ground-breaking results from a study of neoadjuvant nivolumab in patients with early NSCLC (resectable stage I–IIIA) the first instance of its use outside advanced cancer treatment (Abstract LBA41_PR). Two doses of nivolumab were administered to 18 patients prior to lung surgery: seven patients demonstrated a major pathologic response (<10% residual tumour evident), one patient had complete pathologic response and 13 patients had stable disease. Importantly, nivolumab treatment was well tolerated with no significant safety concerns. Grade 3–4 treatment-emergent adverse events were reported in one patient and led to nivolumab discontinuation. There was no delay in surgery in any patient, indicating that the benefits of this neoadjuvant therapy outweighed the potential risks. This proof-of-concept study is a breakthrough, hinting at the very real possibility of substantially improved outcomes in early NSCLC; however, whether tumour shrinkage will ultimately translate into better survival is still to be proven.



Dr Forde added that, "Following these initial results we are expanding the study. One cohort will receive a third dose of nivolumab pre-operatively and the other will receive the combination of nivolumab and ipilimumab pre-operatively."

ESMO W40: **Giving a voice to women in oncology**

Undoubtedly, there is recognition of the crucial role that female oncologists play in healthcare systems, but there is also awareness that few women become leaders in the field.

ESMO aims to support women oncologists looking to achieve leadership positions by giving prominence to female leaders considered role models of excellence. ESMO also functions as a platform for initiatives that endorse the role of women in oncology. ESMO acknowledges that engaging young female oncologists to strive for prominent positions is key to balancing the future gender gap.

But why are women under-represented in leadership positions in oncology? In an effort to find out, earlier this year, ESMO commissioned an online survey to discover your opinions on issues pertinent to women, such as fellow employees' perceptions of successful women in oncology and women who worked part-time. The results of this survey will be revealed at the ESMO Women for Oncology Session.

Come along to the ESMO Women for Oncology Session on Sunday 9 October 2016 (09.00 – 10.30, Bern), chaired by Professor Solange Peters (Switzerland)

New developments in **castrate-resistant prostate cancer**

A Poster Discussion Session tomorrow focuses on hot topics in castrate-resistant prostate cancer (CRPC). The androgen receptor (AR) isoform AR-V7 is a major theme of this session; AR-V7 is functionally active but lacks the binding target for the AR signalling inhibitors (ARSi) enzalutamide and abiraterone. The presence of AR-V7 in circulating tumour cells (CTCs) in pre-treated patients with CRPC has been shown to be predictive of tumour resistance to ARSi.[1] Currently there is no valid assay for AR-V7 but its usefulness in predicting response in CRPC has made it a worthy subject for further study.

Dr Enrique Grande from Ramón y Cajal University Hospital, Madrid, Spain, will report on evidence suggesting that AR-V7 is not a reliable predictive factor for treatment resistance in chemotherapy-naïve patients with CRPC. While this finding defines more clearly the utility of AR-V7 as a biomarker, it also serves to highlight stark differences in disease pathology at varying stages (Abstract 726PD). Dr Howard Scher from Memorial Sloan-Kettering Cancer Center, New York, USA, will focus on AR-V7 localisation in CTCs as a predictor of treatment response (Abstract 728PD). Intriguingly, it appears that AR-V7 protein localised to the CTC nucleus is a better indicator of overall survival outcomes with ARSi than AR-V7 localised to the cytoplasm. The results of a third proffered paper describe a simpler approach to measuring AR-V7 in patients with CRPC. Dr Marzia Del Re from the University of Pisa, Italy, will report on assaying AR-V7 in plasma-derived exosomal RNA (Abstract 729PD). Preliminary reports indicate exosomal RNA that AR-V7 is also predictive of ARSi treatment outcomes and may be a more convenient and sensitive test than AR-V7 sourced from CTCs. Overall, the results from these studies suggest that before AR-V7 can become a tool for use in daily clinical practice, its role as a biomarker at different stages of disease and treatment needs to be established and there should be agreement on the most effective and reliable assays.

Hear more on prostate cancer in tomorrow's Poster Discussion Session: 09.30 – 10.30, Brussels.

In light of these treatment resistance studies in CRPC, are there data on novel medications for these patients? In the same session, Dr Aaron Hansen from the Princess Margaret Hospital, Toronto, Canada, reports on promising early results with pembrolizumab for heavily pre-treated patients with PD-L1-expressing advanced prostate cancer (Abstract 725PD). The overall response and 6-month progression-free survival rates were 13% and 39%, respectively, and side-effects were manageable. As we continue to shape the use of current treatments by using predictive biomarkers, it is important that therapies with novel mechanisms of action are developed to expand the available options in precision medicine.

1. Antonarakis ES, et al. N Engl J Med 2014;371:1028–38

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VARGATEF® Abbreviated European Prescribing information. Please refer to local prescribing information as it may vary between countries. Different brand names are used in some countries. **Presentations:** Soft capsules; each containing 100 mg or 150 mg nintedanib (as esilate). **Indication:** VARGATEF® is indicated in combination with docetaxel for the treatment of adult patients with locally advanced, metastatic or locally recurrent non-small cell lung cancer (NSCLC) of adenocarcinoma tumour histology after first-line chemotherapy. **Posology and method of administration:** 200 mg twice daily administered approximately 12 hours apart, on days 2 to 21 of a standard 21-day docetaxel treatment cycle. VARGATEF® must not be taken on the same day of docetaxel. Adverse reactions may be managed by temporary treatment interruption, dose reductions or permanent treatment discontinuation. **Contraindications:** Hypersensitivity to nintedanib, peanut or soya, or to any of the excipients. **Special warnings and precautions:** Patients should be closely monitored for: gastrointestinal disorders, neutropenia and sepsis, hepatic impairment, haemorrhage, venous and arterial thromboembolic events, QTc prolongation. VARGATEF® is not recommended in patients with predisposition to bleeding, anti-coagulant treatment, active brain metastases, and gastrointestinal perforation. **Fertility, pregnancy and lactation:** There are no data on the potential effects of VARGATEF® on female fertility. Women of childbearing potential should be advised to avoid becoming pregnant and to use adequate contraception during and at least 3 months after the last dose of VARGATEF®. There is no information on the use of VARGATEF® in pregnant women. Breast-feeding should be discontinued during treatment with VARGATEF®. **Effects on ability to drive and use machines:** Minor influence. **Undesirable effects:** Very common: neutropenia (including febrile neutropenia), decreased appetite, electrolyte imbalance, peripheral neuropathy, bleeding, diarrhoea, vomiting, nausea, abdominal pain, ALT increase, AST increase, blood alkaline phosphatase increase, mucositis (including stomatitis), rash. Common: febrile neutropenia, abscesses, sepsis, dehydration, venous thromboembolism, hypertension, hyperbilirubinaemia. Uncommon: perforation. Overdose: increased liver enzymes and gastrointestinal symptoms. Marketing Authorisation Number(s): EU/1/14/954/001 to EU/1/14/954/004. **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, Binger Strasse 173, 55216 Ingelheim am Rhein, Germany. **Date of product information preparation:** April 2015. (ALT = alanine aminotransferase; AST = aspartate aminotransferase).

*** Indication and usage:** Nintedanib is approved in the European Union (EU) under the brand name VARGATEF® for use in combination with docetaxel in adult patients with locally advanced, metastatic or locally recurrent NSCLC of adenocarcinoma tumour histology after fi rst-line chemotherapy. Registration conditions differ internationally, please refer to locally approved prescribing information. Nintedanib is not approved in other oncology indications. The compulsory product information is freely available at the booth.

Note: The information presented here is intended for NON-US, NON-UK, NON-Canadian healthcare professionals only. To allow quick identification of new safety information, please report any suspected adverse reactions. Please refer to the Summary of Product Characteristics (SmPC) for detailed information.

1. Reck M et al. Lancet Oncol. 2014;15:143-55. **2.** Reck M, Mellemgaard A. Biologics. 2015; 9:47-56.

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