Today's Top Picks

COPENHAGEN 2016 ESMO

MONDAY 10 OCTOBER, 2016

FROM DISEASE TREATMENT TO PATIENT CARE

DAILY REPORTER

The crowds descend on Sunday evening to hear high-profile Late Breaking Abstract data at the hotly anticipated Presidential Session

First-line immunotherapy for advanced NSCLC: A chink in nivolumab's armour? Greater patient selection needed!

Stefan Zimmermann: *ESMO 2016 Daily Reporter Associate Editor. HFR Fribourg-Hôpital Cantonal, Switzerland*

The clinical properties of the anti-programmed death-1 (PD-1) antibody nivolumab continue to be dissected in the expansive CheckMate trial programme across multiple cancer types, disease stages and lines of treatment. Nivolumab is approved in Europe and the USA in previously treated advanced non-small-cell lung cancer (NSCLC) having demonstrated a survival benefit versus docetaxel in CheckMate-017 and -057.[1,2] Furthermore, patients with advanced NSCLC with PD-L1-positive tumours experienced durable responses with first-line nivolumab monotherapy in the phase I CheckMate-012 study.[3]

Yesterday Dr Mark Socinski of the UPMC Cancer Center, Pittsburgh, Philadelphia, USA, presented late-breaking results from CheckMate-026, one of the first studies in chemotherapy-naïve patients with stage IV or recurrent NSCLC to compare immunotherapy with a platinum-based regimen (Abstract LBA7_PR). A total of 541 patients received nivolumab 3 mg/kg every 2 weeks or investigator's choice (IC) of platinum-based doublet chemotherapy every 3 weeks for up to 6 cycles. Despite an enriched population with PD-L1-positive tumours (threshold defined as ≥1%; n= 423), nivolumab did not show superior median progression-free survival compared with IC (4.2 months versus 5.9 months; hazard ratio 1.15, p=0.25).

The low threshold of PD-L1 expression used for patient selection in CheckMate-026 may have accounted for the lack of observed improvement in progression-free survival with nivolumab compared with chemotherapy.

While the threshold of PD-L1 positivity in CheckMate-026 was ≥1%, a similar study comparing first-line pembrolizumab with platinum-doublet chemotherapy in advanced NSCLC, KEYNOTE-024, used a much higher threshold of ≥50% (Abstract LBA8) and showed significant clinical benefit for the anti-PD-1 therapy. Let's see whether the combination of nivolumab and ipilimumab, as in CheckMate-227, will trump chemotherapy in treatment-naïve, low PD-L1 expressors with NSCLC.

1. Brahmer J, et al. N Engl J Med 2015;373:123–35
2. Borghaei H, et al. N Engl J Med 2015;373:1627–39
3. Gettinger S, et al. J Clin Oncol 2016;34:2980–7

View the ESMO 2016 Broadcast on the YouTube playlist here.

Controversy of the Day Biosimilars and bioequivalents: **A wise choice in a demanding treatment landscape?**

Professor Jan H.M. Schellens: *Netherlands Cancer Institute, Amsterdam*

Escalating costs of cancer care have led to a substantial and growing burden on healthcare systems and patients.[1] Consequently, there is a need for biosimilars created after patent expiry of the originator agent.

Two studies of trastuzumab biosimilars for the treatment of patients with HER2-positive metastatic breast cancer were presented yesterday. Dr Hope Rugo (UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, California, USA; Abstract LBA16) described how the biosimilar, MyI-14010, was associated with an equivalent overall response rate (ORR) to trastuzumab at 24 weeks (primary endpoint; 69.6% MyI-14010 versus 64.0% trastuzumab). Other endpoints from this phase III study in 458 randomised patients, such as progression-free and overall survival, also showed no significant difference between the agents. Importantly, safety, pharmacokinetic and immunogenicity findings appeared similar.

A second study presented by Dr Cristina Saura based on a poster by Dr Maria Shustova (JSC "BIOCAD", St Petersburg, Russian Federation; Abstract 224PD) reported how the biosimilar BCD-022 and trastuzumab were statistically equivalent in terms of ORR (53.6% versus 53.7%, respectively), with BCD-022 showing non-inferiority to trastuzumab. Other efficacy parameters (complete and partial responses, stable disease and disease progression) were equivalent between the agents, too. Both medications were associated with comparable safety and immunogenicity findings.

While biosimilars have been available in Europe for more than a decade, they have not been universally accepted and their use varies greatly by product and country.[2] In the Netherlands, for example, adoption of biosimilars has been good and estimated at 40%. However, concerns have been raised over the post-marketing quality and long-term safety of biosimilars.[3] Particular concerns relate to extrapolation of indication. If the reference product is licensed to treat multiple therapeutic indications, extrapolation of the biosimilar for use in these same indications may be possible without the need for comparative clinical trials, but this must be scientifically justified.

The European Medicines Agency (EMA) has created guidelines for obtaining marketing authorisation of biosimilars.[4] Regulatory approval requires that a biosimilar is characterised analytically and clinically; efficacy and safety (including immunogenicity) should be assessed in the most sensitive patient populations with endpoints that can detect any clinically meaningful differences between the proposed biosimilar and the reference product. This enables manufacturers to develop biological therapies that are broadly accessible within a tailored development programme.

1. Zelenetz AD. Oncology & Hematology Review 2016;12:22–8
2. Siegel JF, Fischer A. www.biologicsblog.com/blog/ten-years-of-biosimilars-in-europe/, 8 December 2015
3. Gascon P. Ther Adv Hematol 2015;6:267–81
4. European Medicines Agency. www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000408.jsp

WHO-ESMO **workforce survey**

Dr Alexandru Eniu: *ESMO Global Policy Committee Chair; Cancer Institute I Chiricuta, Cluj-Napoca, Romania*

It is evident that there are a number of discrepancies between countries in relation to the care received by cancer patients. Among the key differences identified is the workforce, including the number of people with the skills needed to meet the demands of a looming cancer epidemic.

Chaired by Dr Alexandru Eniu (Cancer Institute I Chiricuta, Cluj-Napoca, Romania), the ESMO Global Policy Committee is working closely with the World Health Organization (WHO) Global Health Workforce Alliance to kick off a pilot study in Italy and Spain that will explore the specific requirements of the workforce involved in the management of patients with breast cancer. The aim is to gain a greater insight into the key professionals required and the skills they need to follow evidence-based cancer treatment guidelines and achieve the best possible care for patients.

The aim of the project is to gather data that identify future gaps and needs in the oncology workforce so they can be incorporated in national cancer plans.

Breast cancer was chosen as the first disease to survey because of its high frequency and the need for multidisciplinary management, which will highlight the broad requirements of the oncology workforce and emphasise any gaps in the future needs of breast cancer care. The hope is that the project—led by Dr Eniu together with Dr Giuseppe Curigliano, member of the ESMO Faculty on Breast Cancer (European Institute of Oncology, Milan, Italy)—will enable the current workforce to be optimised and future workforce requirements to be anticipated.

The pilot study will begin in early 2017 with results expected to be available at the ESMO 2017 Congress. It is anticipated that the study will be rolled out in other European countries later next year. A strategic goal from the study's findings is to promote universal healthcare coverage in accordance with the WHO principles.

ESMO 2016 DAILY BROADCASTS

Introducing ESMO 2016 Daily Broadcasts on YouTube!

Visit You Tube daily for an overview of sessions not to be missed. Highlights of the day are also captured in a selection of clips from around the congress, including footage of the experts discussing the day's hot topics. Yesterday, these included key sessions on the latest advances in colorectal cancer and immunotherapy in head and neck and non-small-cell lung cancer.

Highlights are also featured from a Special Symposium on glioblastoma treatments, and the Women for Oncology session.

Female oncologists: Still paying the price for being a woman

ESMO Women for Oncology initiative began in 2013 and was borne from the realisation that female oncologists are under-represented in leadership positions. In an online survey this year, ESMO explored the gender-related challenges faced by oncology professionals. The survey results gave a valuable and unique insight into the perceptions of those working in oncology today.

At the Women for Oncology Session yesterday, Professor Solange Peters from the University of Lausanne, Switzerland, presented key results from the survey. Of the 482 male and female participants, the majority (77%) were female and were medical oncologists (66%). Most respondents (60%) worked in a team in which there were more women than men although the responsible person in the team was male in 64% of cases.

More than one-quarter (27%) of female respondents believed that their gender significantly impacted their career, compared with 14% of male respondents.

In terms of obstacles that respondents had encountered during their career progression, finding a balance between work and family featured prominently (65% of respondents), although the belief that men were perceived as natural leaders and women were team members and supporters was also common (40% of respondents). When questioned about their thoughts on the main barriers that prevented gender equality in the workplace, regardless of gender, respondents said that a lack of work–life balance was a key factor (52% of respondents), and that social pressures were also prominent (31% of respondents).

After the session, Professor Peters commented that some of the additional survey results not presented in yesterday's talk were rather surprising and made for uncomfortable reading. Astonishingly, 41% of surveyed female respondents said that they had encountered unwanted sexual comments, attention or advances by a superior colleague, with 69% of these encountering generalised sexist remarks and behaviours in the workplace.

How can the gender gap in oncology be closed? Half of survey respondents believed that the best approach for the oncology community to take would be to promote work–life balance. Other suggestions considered important were the development and provision of leadership training for women (response: 28.7% of males, 44.2% of females) and the offer and support of flexible working hours (response: 35.1% of males, 41.6% of females).

Full results from the survey will be available from the ESMO website.

Yesterday, Professor Sumitra Thongprasert was presented with the ESMO Women for Oncology Award for her passionate advocacy of female participation and leadership in the oncology workforce.

Professor Peters commented: "Lack of self-esteem was also a major barrier to professional success among women. This is an important finding because self-esteem is subjective, a perception, and you can work on and change perceptions."

Commenting after the session, Professor Edith Perez, Vice President and Head of US Medical Affairs, Genentech/Roche BioOncology, and Professor of Medicine, Mayo Clinic, USA, said that gender inequality is an important global issue and one that is currently receiving much attention in science. She said she is pleased to see a good balance of male and female presenters at the ESMO Congress.

Multiple myeloma: New combinations, new optimism

Professor Pieter Sonneveld:
Erasmus Medical Center, Rotterdam, Netherlands

Achieving a good depth of response, addressing symptoms and increasing overall survival are the main treatment goals for incurable diseases, such as multiple myeloma. Rational therapeutic approaches consider individual pathology, transplant eligibility, disease stage, comorbidities, patient age and wider health, quality of life and minimisation of toxicity. Because of these complexities, the optimal sequence of therapies for relapsing refractory multiple myeloma (RRMM) has yet to be established. An enhanced understanding of multiple myeloma disease mechanisms has led to more targeted therapies, and there is now a plethora of treatments available for this disease (Figure) leading to the use of multi-combination treatments becoming common practice.

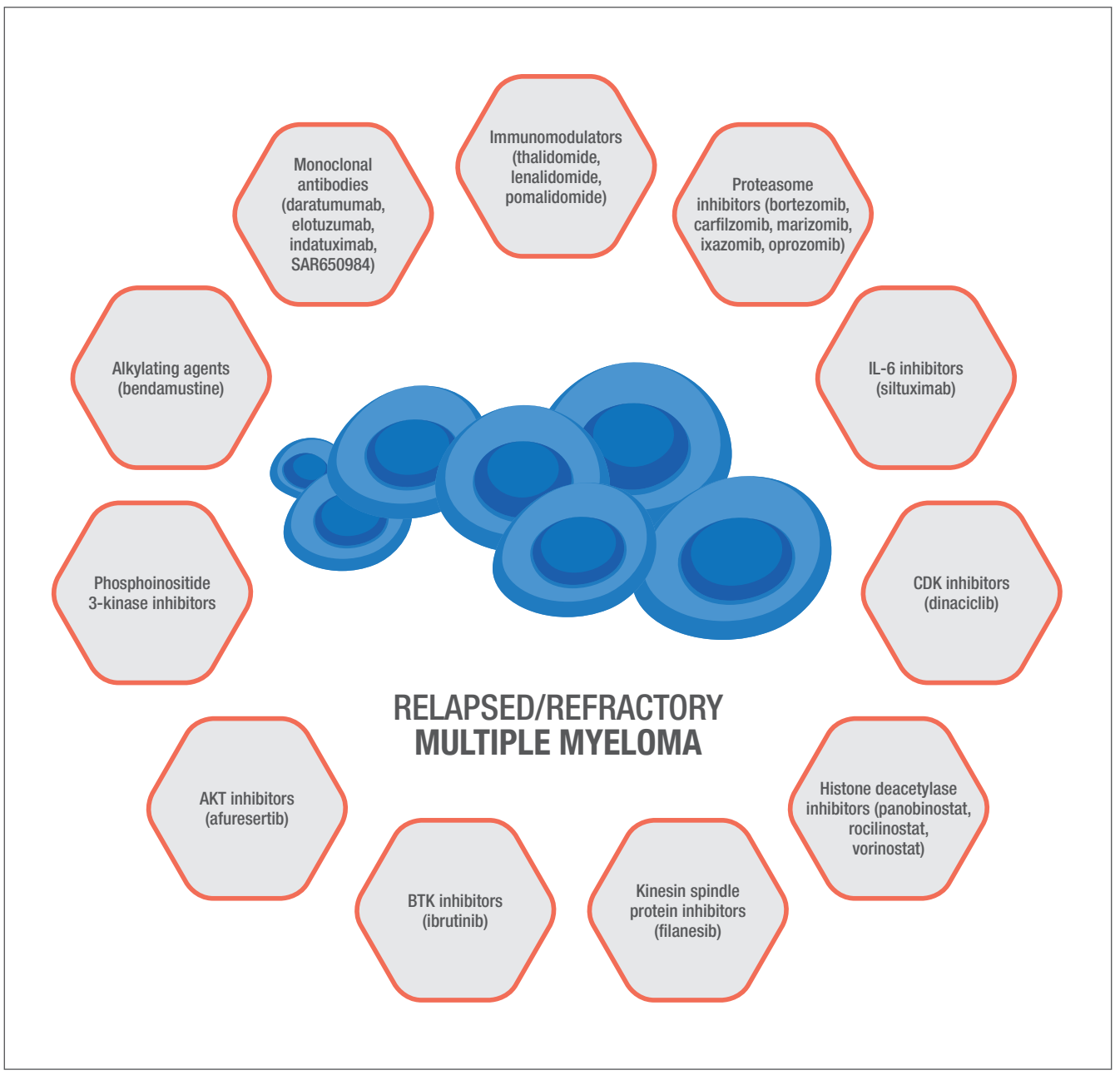
Combination of the proteasome inhibitor bortezomib with dexamethasone is a standard regimen for RRMM treatment. Adding an immunotherapy with a novel mechanism of action to this approach is an intriguing proposition and was the subject of a proffered paper on the daratumumab CASTOR study presented yesterday by Dr Katja Weisel of Tubingen University, Germany (Abstract 9060).

Daratumumab is a human monoclonal antibody that targets CD38, an antigen located on the surface of myeloma cells. Daratumumab monotherapy recently became the first anti-CD38 to be approved by the EMA for pre-treated patients with RRMM, after open-label studies showed impressive improvements in progression-free survival (PFS) and durable responses.[1,2]

Addition of daratumumab significantly improved median PFS (median not reached versus 7.2 months; 61% risk reduction; hazard ratio 0.39; 95% confidence interval 0.28–0.53; p<0.0001), and overall response rates (83% versus 63%, respectively; p<0.0001) compared with bortezomib plus dexamethasone alone in this highly refractory population. The daratumumab combination had a manageable safety profile that was consistent with the known profiles of the single agents. In light of these findings, Dr Weisel concluded that this triple combination could potentially be considered a new standard of care for patients with RRMM currently receiving the double combination only.

1. Lokhorst HM, et al. N Engl J Med 2015;373:1207–19
2. Lonial S, et al. Lancet 2016;387:1551–60

As one of the CASTOR investigators, I can attest to these striking results that strongly signpost the importance of novel immunotherapies in continuing to improve outcomes for patients with RRMM.



ESMO Focus Talks

Monday 10 October, 12.30
Dr Erika Martinelli (Italy) and
Dr 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.

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Second-generation ALK inhibitor improves outcome in **NSCLC progressing on crizotinib**

Crizotinib changed the face of treatment for ALK-positive non-small-cell lung cancer (NSCLC) but resistance develops almost inevitably within the first year of treatment. Promising phase I/II efficacy findings for the second-generation ALK inhibitor, ceritinib, in NSCLC progressing on crizotinib-based treatment were confirmed by the results of the open-label, phase III ASCEND-5 study, presented in a Proffered Paper Session yesterday by Professor Giorgio Scagliotti from the University of Turin, Italy (Abstract LBA42_PR).

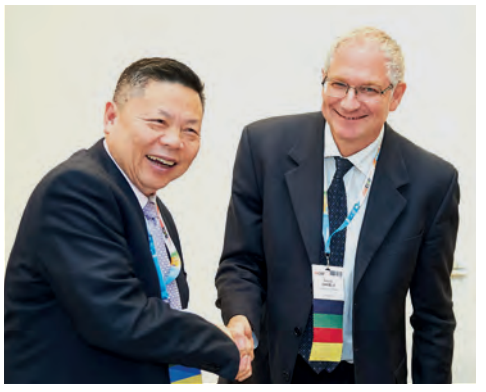
Among 231 patients previously treated with chemotherapy and crizotinib, ceritinib significantly improved progression-free survival (PFS) (median 5.4 months versus 1.6 months, $p<0.001$) and increased response rate (39.1% versus 6.9%) compared with chemotherapy (docetaxel or pemetrexed). The median treatment exposure was 30.3 weeks for ceritinib and 6.3 weeks for chemotherapy. No difference was found between the study arms in relation to overall survival, with most patients crossing over from chemotherapy to ceritinib after progressing. Gastrointestinal adverse events were more common with ceritinib, and fatigue, alopecia and neutropenia were seen more frequently with chemotherapy. Significant improvements in lung cancer-specific symptoms and overall health status were also seen with ceritinib versus chemotherapy ($p<0.05$).

Ceritinib significantly prolonged PFS by nearly 4 months and improved quality of life.

The field of ALK-positive lung cancer is evolving very rapidly, with a wealth of new agents in development. The use of better ALK inhibitors upfront, as demonstrated by the J-ALEX data, is certain to further improve outcomes in crizotinib-naïve patients. In addition, although resistance inevitably develops, their differential activity across ALK-resistance mutations should provide clinicians with new options at progression. Last but not least, the role of immunotherapy in this disease setting has to be defined, and ALK inhibitor-based combinations with PD-L1 inhibitors are already underway in the clinic.

ESMO strengthens **collaboration with CSCO**

On Saturday, the ESMO leadership and the leaders of the Chinese Society of Clinical Oncology (CSCO) signed an agreement to collaborate formally on *ESMO Open*, ESMO's fully open access scientific journal. *ESMO Open* (www.esmoopen.bmj.com) has enjoyed considerable success since its launch in January this year and the collaboration with CSCO is seen as both an exciting and natural development. *ESMO Open* Editor-in-Chief Christoph Zielinski said, "One of the goals of *ESMO Open* has been to reach out to a global oncology audience. ESMO already works with CSCO on a number of activities, most notably the ESMO Asia congress, and involving them in *ESMO Open* seems entirely logical. We are looking forward to CSCO members using the journal's open access format to drive wider visibility of their own research as well as learning about studies undertaken by fellow professionals around the world."



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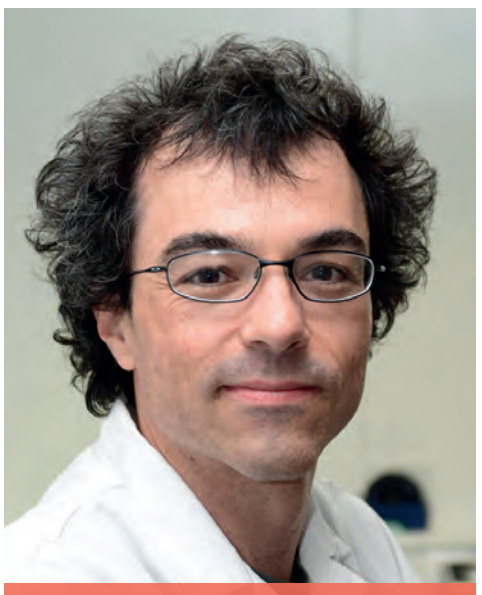
Precision medicine: Evolving trial design for targeted treatment

Physicians can now analyse tumours for the presence of multiple genes and proteins, but there are currently no guidelines to determine which molecular assays are suitable for metastatic cancers.



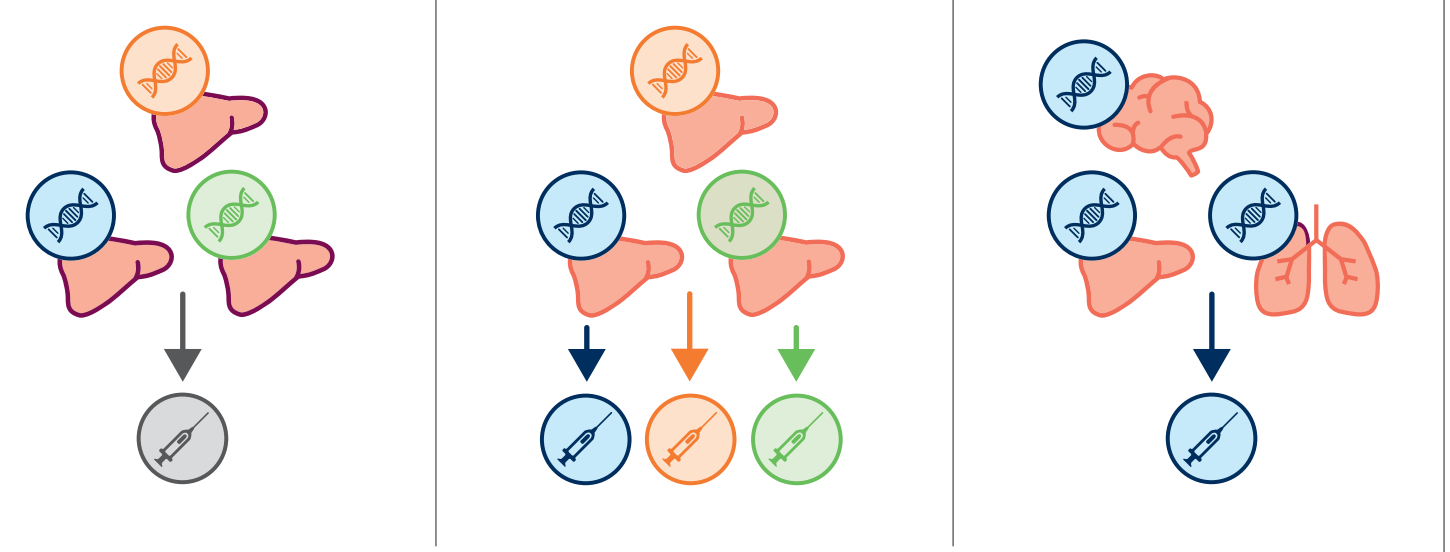
Professor Fabrice André: *Institut Gustave Roussy, France*

Last year, the first Molecular Analyses for Personalized (MAP) Medicine conference explored the use of genomics to help improve therapy selection in this setting.[1] New technologies, including next-generation sequencing of tumours, have been validated but the conference concluded that precision medicine trials should be stratified according to the level of evidence available for the identified genomic alterations.[1]

A number of oncology trials have begun to address the complexities of tumour pathology by identifying drugs that may be highly effective in patients with particular mutations, regardless of their cancer type. Umbrella trials allow testing of multiple treatments targeted to specific tumour pathways in patients grouped according to an identified molecular alteration. Umbrella trials therefore eliminate the need for numerous regulatory and ethical approvals and give drug sponsors access to an existing network of study centres and/or a central pool of patients screened for specific mutations.

Like umbrella trials, basket trials treat by causative mutation, rather than tumour histology. Patients with identified tumour alterations, regardless of cancer type, are matched to a medication targeting that specific mutation or pathway, allowing investigation of multiple, often rare, tumour pathologies (Figure). Although basket trials have resulted in notable successes, including vemurafenib in *BRAF V600E*-mutated lung cancers, effectively blocking an identified mutation does not necessarily ensure clinical tumour response, and success in one cancer cannot be assumed across other tumour types, as illustrated by a lack of response to vemurafenib in *BRAF V600E*-mutated colorectal cancer.[2] Combination treatment is a rational approach in precision medicine as tumours may exploit alternative biological pathways for survival, although in the aforementioned vemurafenib study, addition of the anti-EGFR antibody cetuximab did not improve outcomes in patients with colon cancer.[2]

The uncertainties of precision medicine were starkly emphasised in a presentation concerning olaparib in advanced gastric cancer given on Saturday by Dr Yung-Jue Bang of the Seoul National University Hospital, South Korea (Abstract LBA25). Originally, a basket trial of olaparib in patients with recurrent solid tumours who all had *BRCA1/2* mutations showed encouraging results in ovarian cancer.[3] This finding allowed more targeted investigation, and olaparib maintenance treatment was recently approved for patients with *BRCA1/2*-mutated ovarian cancer after responding to platinum-based second-line chemotherapy. A phase II trial of olaparib plus paclitaxel in metastatic/recurrent gastric cancer yielded a promising increase in overall survival versus paclitaxel alone, particularly in patients with low levels of *ataxia-telangiectasia* mutation *(ATM)*, a key activator of DNA damage response,[4] suggesting that precision medicine with olaparib may also be a possibility in gastric cancer. Despite these early signals, the phase III GOLD trial failed to show a significant increase in OS for patients with advanced gastric cancer treated with olaparib plus paclitaxel in either the total population or in *ATM*-negative patients. Pooling resources and patients using novel approaches, like umbrella trials, are vital in identifying new and effective anti-cancer drugs.



ONCOLOGY TRIAL DESIGNS.
Unlike histology-based trials, umbrella and basket trials treat patients according to tumour mutations.

1. Swanton C, et al. Ann Oncol 2016;27:1443–8
2. Hyman DM, et al. N Engl J Med 2015;373:726–36
3. Kaufman B, et al. J Clin Oncol 2015;33:244–50
4. Bang YJ, et al. J Clin Oncol 2015;33:3858–65

Combined targeted therapy shows promise for *BRAF V600E*-mutated metastatic CRC

Combined targeted treatment appears to have therapeutic potential in *BRAF V600E*-mutated colorectal cancer (*BRAFm* mCRC) according to latest data from an ongoing study presented yesterday by Dr Ryan Corcoran from Massachusetts General Hospital, Boston, USA (Abstract 4550). These are important findings given that *BRAFm* mCRC is notoriously difficult to treat and is associated with poor prognosis; targeted therapies (BRAF and MEK inhibitors) have previously had minimal activity, although preclinical data have provided a rationale for investigating combined inhibition.[1]

This study of 134 patients with *BRAFm* mCRC assessed the BRAF inhibitor dabrafenib (D), the MEK inhibitor trametinib (T), and the anti-EGFR antibody panitumumab (P) across three treatment arms (DP, TP and DTP) and reported clinical responses (Table) and evidence of downstream target inhibition. DTP had an acceptable tolerability profile with the most common adverse events being rash, diarrhoea, fatigue and nausea.

Serial circulating tumour DNA (ctDNA) analysis revealed >70% reduction in *BRAF V600E* mutant fraction (MF) in 12 of 14 (86%) DTP-treated patients by week 4, with six of the 12 patients achieving partial response by week 6. *RAS* mutations that were not detectable at baseline were detected in ctDNA at progression in seven of 12 (58%) patients who achieved complete/partial response or stable disease, indicating a potential resistance mechanism. "These data suggest that ctDNA analysis may have value in monitoring disease response and progression in *BRAFm* mCRC," noted Dr Corcoran.

"…ctDNA analysis may have value in monitoring disease response and progression in *BRAFm* mCRC."

Despite clinically relevant data emerging from this study, consideration should be given to the potential toxicities arising from combination therapies targeting multiple pathways.

1. Corcoran RB, et al. Cancer Discov 2012;2:227–35

ENDPOINT	COMBINATION		
	DP (N=20)	TP (N=31)	DTP (N=83)
Complete/partial response, % patients	10	0	18
Stable disease, % patients	80	53	67
Median progression-free survival, months	3.4	2.8	NYM

NYM, not yet mature

Encouraging results for nivolumab in advanced hepatocellular carcinoma

Therapeutic options for patients with advanced hepatocellular carcinoma (aHCC) failing first-line sorafenib are limited and best supportive care is associated with a survival time of only around 7–8 months. Immunotherapy with the anti-PD-1 monoclonal antibody nivolumab is a potential new approach to improve patient outcomes.

In a Proffered Paper Session yesterday, Dr Ignacio Melero from Universidad de Navarra, Pamplona, Spain, presented results from an interim analysis of the phase I/II CheckMate 040 study (Abstract 6150). Patients with aHCC were treated with nivolumab 0.1–10 mg/kg in three dose escalation cohorts: hepatitis B virus (HBV)-infected; hepatitis C virus (HCV)-infected; and uninfected. This was followed by nivolumab 3 mg/kg in an expansion phase comprising four cohorts: uninfected sorafenib-naïve/-intolerant; uninfected sorafenib progressors; HBV-infected; and HCV-infected. In the expansion cohorts, grade 3–4 adverse events were reported in 19% of patients, the most common being increases in aspartate and alanine aminotransferases, lipase and amylase. Responses were observed in 35 of 214 patients in this cohort (16%), including two complete responses. Response was not dependent on PD-L1 expression or tumour aetiology.

The 9-month overall survival rate in this interim analysis was 71%.

Discussing the results, Dr Ian Chau from the Royal Marsden Hospital, London and Surrey, UK, observed, "Overall survival is promising for nivolumab ≥2-line in a single-arm, uncontrolled setting."

Delegate **voices**

"As a young oncologist, I want to hear interesting data and find out about new clinical trials. Tomorrow, I am going to the Young Oncologist Mentorship Session."

Nassima Kouadri, Medical Oncologist, Annaba, Algeria

"This is my first ESMO congress and I'm already considering changing the way I treat metastatic renal cell carcinoma after learning about cabozantinib."

Vijith Shetty, Medical Oncologist, Chennai, India

"I have enjoyed the Young Oncologist's sessions and attended the meeting yesterday. I also regularly participate in the Young Oncologist's online discussions. I would certainly recommend membership to my colleagues."

Oridiu Bochis, Medical Oncologist, Cluj-Napoca, Romania

"I've come to ESMO to improve my knowledge not only about oncology treatments but also about my relationships with patients."

Aldo Iop, Medical Oncologist, Latisana, Italy

A renaissance in the treatment and management of ovarian cancer?

Professor Nicoletta Colombo: *European Institute of Oncology and University of Milan-Bicocca, Milan, Italy*

High-grade ovarian cancer currently has a poor prognosis; however, a number of tumour subtypes have been recognised that could lead to targeted treatments and perhaps, better outcomes. A number of presentations at ESMO 2016 highlight important developments in ovarian cancer.

Poly ADP ribose polymerase (PARP) family proteins are involved in DNA repair. *BRCA1/2* genes code for PARP-independent DNA repair enzymes, meaning that *BRCA* mutation-positive tumours are particularly susceptible to PARP inhibition. On the basis of improvements in progression-free survival (PFS) in phase II trials,[1,2] the PARP inhibitor olaparib received accelerated US FDA and EMA approval in 2014 as a maintenance monotherapy for germline *BRCA* mutant (*gBRCAm*), platinum-sensitive relapsing ovarian cancer responding to platinum therapy (EMA) or for relapse after ≥3 lines of previous therapy (US FDA).

On Saturday, Dr Mansoor Raza Mirza of the NSGO & Rigshospitalet-Copenhagen University Hospital, Copenhagen, Denmark, reported data from the first completed phase III trial of a PARP inhibitor in 553 ovarian cancer patients (Abstract LBA3_PR). Maintenance therapy with niraparib significantly improved PFS compared with placebo in patients with *gBRCAm* ovarian cancer (21.0 months versus 5.5 months, respectively; $p<0.0001$) and in *gBRCAm*-negative patients who were later identified as homologous recombination (HR) DNA-repair deficient (12.9 months versus 3.8 months, respectively; $p<0.0001$). HR DNA-repair deficiency is an important target in ovarian cancer and is present in ≥50% of patients. Intriguingly, niraparib also significantly improved PFS in patients who did not harbour *BRCA* mutations or HR DNA-repair deficiency (9.3 months versus 3.9 months with placebo; $p<0.0001$). Patient-reported outcomes were similar for niraparib and placebo. The mechanism responsible for the effect of niraparib in patients negative for *BRCA* mutation and HR DNA-repair deficiency is currently unknown. These exciting results were further bolstered by data from a pooled analysis of two phase II studies of the PARP inhibitor rucaparib in patients with high-grade ovarian carcinoma and *gBRCAm* or somatic *BRCAm* previously treated with ≥2 lines of chemotherapy (Abstract 8560). Rucaparib has a breakthrough therapy designation in the USA in this indication and Dr Rebecca Kristeleit of the University College London, Cancer Institute, UK, reported that the median confirmed response duration with rucaparib was 9.2 months in these two trials. Phase III trials are ongoing.

Not only do these data confirm the positive results achieved with PARP inhibition for patients with relapsing *gBRCAm* ovarian cancer, but they also give new hope for all ovarian cancer patients. A major challenge, however, is the identification of patients who may benefit from PARP-inhibitor therapy, but who lack *BRCA* mutations. Although adopting different identification methods, the above studies detected patients lacking *BRCA* mutations or HR DNA-repair deficiency. The intriguing data for niraparib showing a benefit in these patients may reflect the fact that the methods used are not definitive and that some patients harbour a DNA-repair deficiency not detectable with current tests.

Androgens may also have a role in the aetiology of epithelial ovarian cancer and androgen receptors are frequently expressed in this tumour type. Abiraterone inhibits androgen biosynthesis and is commonly used for the treatment of prostate cancer. On Friday, Dr Susana Banerjee of The Royal Marsden NHS Foundation Trust, London, UK, reported the results of the phase II abiraterone CORAL study in 42 patients with hormone therapy-naïve epithelial ovarian cancer (Abstract LBA33_PR). Sustained efficacy was seen in a patient with low-grade serous disease but low overall efficacy led to early trial closure. While hormone receptor expression is relatively common in ovarian cancer, it has not been extensively investigated as a target in phase III trials; despite the CORAL data, further exploration may still be warranted.

While these results allow us to make positive projections for better outcomes in the treatment of ovarian cancer, it is important that patient management and support evolve alongside molecular medicine. On Saturday, I reported interim results from ENGAGE, an oncologist-led model of *gBRCAm* testing and genetic counselling for patients with ovarian cancer being enrolled across 26 centres internationally (Abstract LBA34). Routine *BRCA* testing in ovarian cancer patients is advocated by several scientific societies and is part of current clinical guideline recommendations. However, the classical model of genetic counselling may not enable the systematic testing of all ovarian cancer patients and could lead to substantial delays in testing turnaround time. This new model proposed in the ENGAGE study could help overcome these barriers and lead to efficient resource use, while providing the opportunity to test most patients. Moreover, the use of effective prevention procedures in as-yet unaffected family members has the potential to greatly impact the incidence and mortality of this deadly disease.

It appears that treatment and management of ovarian cancer are currently going through somewhat of a renaissance and future advancements are eagerly anticipated.

1. Ledermann J, et al. Lancet Oncol 2014;15:852–61
2. Kaufman B, et al. J Clin Oncol 2015;33:244–50

Intensive follow-up beneficial in detecting treatable recurrence in **curatively treated colon cancer**

Intensive follow-up of patients with curatively treated colorectal cancer (CRC) for 5 years using carcinoembryonic antigen (CEA) and/or computed tomography (CT) analysis increases the detection of treatable recurrence, but only in colon cancer. Furthermore, a survival advantage is only observed in patients with recurrence from a left-sided colon cancer. These were the conclusions of a mature overall survival (OS) analysis from the FACS trial (a randomised clinical trial conducted in 39 UK hospitals)[1] presented yesterday by Dr Siân Pugh from the University of Southampton, UK (Abstract 4530).

In the study, 1,202 patients who received curative-intent treatment for primary stage I–III CRC were followed up with intensive (either CEA alone, CT scan alone or both modalities) or minimum (symptomatic ± single CT scan) strategies. At 12-years' follow-up, intensive monitoring by CEA and/or CT scan significantly increased the detection of surgically treatable recurrence compared with minimum monitoring (7.0% versus 2.7%, respectively; p=0.008). Treatable colon, but not rectal, tumour recurrences were more commonly detected by intensive follow-up, although this translated into a survival advantage only in those with recurrence from a left-sided colon cancer (median OS: 4.4 years versus 3.1 years, respectively; p=0.03).

Intensive follow-up by either CEA or CT scan significantly increased the detection of treatable colon cancer recurrence compared with minimum follow-up.

This small but positive signal for improved OS with increased detection of recurrence (at least in a subpopulation) in the FACS follow-up study contrasts with the findings of a recent meta-analysis. This evaluated trials of CEA and/or CT monitoring for early detection of asymptomatic metastatic disease after potentially curative resection of primary CRC and included 16 randomised comparisons, 11 with published survival data.[2] More intensive monitoring brought forward the diagnosis of recurrence by a median of 10 (interquartile range 5–24) months. In 10 of 11 studies, the authors reported no demonstrable difference in OS. Seven randomised, controlled trials, published from 1995 to 2016, assigned 3,325 patients to a monitoring protocol intensified by the introduction of new methods or increasing the frequency of existing follow-up protocols compared with less invasive monitoring. More intensive monitoring protocols were not associated with a detectable difference in OS (hazard ratio 0.98; 95% confidence interval 0.87–1.11).

While intensive follow-up after surgery for CRC is common practice, it is based on limited evidence, and there is no general guidance regarding surveillance across Europe. Given the large patient population and extended follow-up of the FACS trial, these important data may be used to inform clinical practice and guide future monitoring of CRC patients.

Commenting on the results of the analysis, Professor Dirk Arnold from CUF Hospitals in Lisbon, Portugal, cautions that they must be viewed in the context of the treatment options available, which may differ for earlier or later detection of relapse. At the time most of these analyses were conducted, including the FACS follow-up, treatment options were often very limited and life expectancy/OS was poor. Today's treatment landscape includes (potentially) curative approaches for oligometastatic disease and localised metastasation, making the detection of early relapse crucial. This is an essential part of the ESMO Clinical Practice Guidelines and is in agreement with most national treatment recommendations, which advocate the use of follow-up with CT scans/ultrasound and CEA evaluations to detect early relapsing disease.[3]

1. Primrose JN, et al. JAMA 2014;311:263–70
2. Mokhles S, et al. Br J Surg 2016;103: 1259–68
3. Van Cutsem E, et al. Ann Oncol 2014;25(Suppl 3):iii1–iii9

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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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