Advancing the treatment of sarcoma

Neoadjuvant chemotherapy with three full-dose courses of the anthracycline epirubicin plus ifosfamide has a substantial clinical benefit over “histology-adapted” chemotherapies in patients with localised high-risk soft tissue sarcoma (STS). These were the findings of a prospective randomised study (third futility analysis) reviewed in a Late-Breaking Abstract presentation yesterday by Dr Alessandro Gronchi from Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy (Abstract LBA6 PR). In 286 adult STS patients at high risk of relapse, the probability of relapse-free survival (RFS; primary endpoint) at 46 months (median follow-up 12.34 months) was 62% with epirubicin plus ifosfamide versus 38% with histology-driven treatment (p=0.004). Dr Gronchi noted similar overall survival (OS) data (89% versus 64%; p=0.003), resulting in an increase of >20% in RFS and ≥10% in OS with the anthracycline-containing regimen compared with other chemotherapy regimens.

Subgroup analysis by histologically-tailored regimen suggested that patients with high-grade myxoid liposarcoma derived similar progression-free survival (PFS) and OS benefits from trabectedin compared with epirubicin plus ifosfamide. This patient subgroup will be expanded to further investigate this effect.

An increase in RFS >20% was reported with the anthracycline-containing regimen compared with histology-driven chemotherapy.

Further sarcoma data were reviewed during a Proffered Paper Session on Saturday in two presentations. In the first, trabectedin doubled median PFS (primary endpoint) compared with best supportive care (BSC) in a phase III study of 103 patients with pre-treated advanced STS (3.1 months versus 1.5 months, respectively; hazard ratio [HR] 0.39; 95% confidence interval [CI] 0.24–0.64; p<0.0001). Dr Axel Le Cesne from Institut de Cancérologie Gustave Roussy, Villejuif, France noted that trabectedin had greatest PFS benefit compared with BSC in patients with lipoleiomyosarcoma (5.1 months versus 1.4 months, respectively; HR 0.29; 95% CI 0.15–0.55; p<0.0001; Abstract 1396 O). A similar degree of benefit has been reported with trabectedin in recent trials with similar patient populations.

In the second presentation, analyses of almost 27,000 sarcoma and connective tissue tumour patients from a French database (NETSARC) revealed a significantly lower rate of local relapse in patients who had been presented to a NETSARC multidisciplinary tumour board (NMTB) prior to initial treatment compared with those who had not (p<0.0001 at a median follow-up of 26 months; Abstract 1397 O). Reviewing the data, Professor Jean-Yves Blay from Université Claude Bernard, Lyon, France, noted that a lack of presentation to an NMTB was also an independent unfavourable prognostic factor for relapse on multivariate analysis (HR 1.8; p<0.0001), along with patient age and tumour grade, size and location. These observations provide a strong rationale for multidisciplinary discussion prior to initial treatment of patients with sarcoma. Professor Blay pointed out that a longer follow-up period is needed to evaluate the impact of NMTB presentation on metastasis-free and overall survival.
All good things must come to an end and so we reach the last day of ESMO 2016. In the opening edition of the Daily Reporter, we said our aim was to help you navigate the wealth of data in the packed Congress programme. We hope you feel that we have achieved this!

In this final edition, we wanted to share with you the Editorial Team’s personal picks of the scientific programme. At a time when clinical investigation into targeted agents in oncology is highly active, it will come as no surprise that our selection centres around this type of therapy. Some studies stood out as providing valuable guidance for the clinical community.

Giuseppe Curigliano (Editor-in-Chief): For me, a real breakthrough came in the form of a new proposal for using targeted therapy in the adjuvant setting. That is, instead of adopting a one-size-fits-all approach, we should direct therapy to those patients with clinically and/or pathologically determined high-risk disease. Impressive survival results using this approach were achieved in two placebo-controlled, phase III trials—one investigating ipilimumab following complete resection of melanoma (EORTC 18071; overall survival [OS] hazard ratio [HR] 0.72; p=0.001; Abstract LBA2-PR) and the other looking at sunitinib following nephrectomy in renal cell carcinoma (disease-free survival [DFS] HR 0.761; p=0.03; S-TRAC; Abstract LBA11-PR). These results illustrate how targeted therapies can be most effectively extended into the adjuvant setting, at least at the current time.

Floriana Morgillo (Associate Editor): I was particularly interested in the insight provided by several studies into treatment sequencing for ALK-rearranged or EGFR mutation-positive NSCLC. In ALK-rearranged disease for which crizotinib is currently the standard first-line treatment, the next-generation ALK inhibitor ceritinib prolonged progression-free survival (PFS) compared with chemotherapy (pemetrexed or docetaxel) following progression on crizotinib (HR 0.49; p=0.001) (ASCEND-5; Abstract LBA42-PR). Durable responses were seen in patients who had received multiple prior therapies, not including ALK inhibitors, with remarkable activity also in patients with brain metastases (ASCEND-3; Abstract 1208PD). In EGFR mutation-positive NSCLC, mature OS data from the LUX-Lung 7 study reported that first-line atezolizumab showed a non-significant trend towards a benefit over gefitinib (HR 0.96; p=0.258) (Abstract LBA43). Updated PFS and response rate (RR) analyses continued to show significant benefits for atezolib, confirming that it remains the preferred first-line choice over gefitinib.

Markus Joerger and Stefan Zimmermann (Associate Editors) both chose results from studies with checkpoint inhibitors in PD-L1-expressing NSCLC among their highlights. Arguably the most important was the phase III trial in which atezolizumab significantly improved OS compared with second- or third-line docetaxel (HR 0.73; p=0.0003) (OAK; Abstract LBA44-PR). We look forward to results from the ongoing CHECKMate-227 (nivolumab and ipilimumab) and MISTIC and NEPTUNE (durvalumab) studies, which are investigating potentially improved first-line immunotherapy options.

Enriqueta de Azambuja (Associate Editor): Amid the excitement surrounding targeted agents, I was very interested to see data urging a note of caution. While the MONALEESA-2 study confirmed the superior efficacy of ribociclib plus hormonal therapy compared with hormonal therapy alone in post-menopausal women with hormone-receptor-positive breast cancer (PFS, HR 0.596; p=0.0000329) (Abstract LBA14-PR), the FALCON study reminded us that a substantial proportion of these patients will experience a long median PFS (16.6 months) with hormonal therapy alone (Abstract LBA14-PR). There is an urgent need to identify biomarkers predicting the lack of efficacy of these targeted agents, thus avoiding unnecessary costs and toxicities. No less important is the worrying underreporting of adverse events with targeted agents (Abstract 320P) and the poor access to them in some parts of Europe (Abstract 1389O-PR). Also, we cannot forget that some patients will do extremely well with standard treatments and it remains our duty to identify these.

So that’s all from us for ESMO 2016! I would like to thank the Daily Reporter Editorial Team and all article contributors for their hard work in helping to put together what I think have been informative and stimulating newspaper editions. And I would like to thank you, the delegates, for taking the time to read the Daily Reporter.

We hope to see you all next year at ESMO 2017 in Madrid, Spain (8–12 September)!
ESMO and ASCO working together to take better care of our patients

“...This has been an incredible meeting. As President of ASCO, I am actually envious of the amount of really terrific science. Several game changers were presented here—there were six New England Journal of Medicine papers over the five days, and that’s unprecedented. The really great thing here is not that ESMO did a good job, or that ASCO does a good job, it’s that we’re doing a better job taking care of our patients and that’s what we’re seeing here this week. We’re seeing a reduction in mortality in metastatic melanoma, metastatic non-small-cell lung cancer and ovarian cancer, non-small-cell lung cancer. Who thought we would ever see that? And it’s not just the immunotherapy that’s exciting—although I think it’s the most exciting thing in oncology—it’s also the PARP inhibitors, the CDK4/6 inhibitors and the mTOR inhibitors. There is so much going on, it’s just unbelievable. I’m fond of saying I wish I was 30 years old again, for many reasons, not just for the science, but boy this is a great time to be an oncologist and it’s a great time to be in the field. And the really great thing is the way that ESMO and ASCO are working together, not just to make these advances but also to apply them. Medicine doesn’t work if it doesn’t get to the patient and we have a number of challenges in this respect. We have to get the cost of these drugs down so that everyone can receive them. It’s bad enough that any patient dies of metastatic cancer because we don’t understand the cancer and we don’t have the therapies, but it’s even worse if a patient dies who could have been cured. And we have to fix that. ASCO’s trying, ESMO’s trying; we’re working together. Let’s face it, most of our fathers and grandfathers were fighting a war and trying to kill each other and now we’re sitting around a table and trying to save lives. That’s what we’re supposed to do. And ESMO, this meeting, really shows that we can do that.”

ESMO 2016: Reflections and aspirations

This ESMO Congress has been really spectacular. The scientific content has been focused on patient care, especially with a clinical and a translational approach. Importantly, we were able to secure an outstanding scientific programme. The programme included 47 Late-Breaking Abstracts, 11 of which were featured in the three Presidential Sessions. We have seen innovations in different diseases, among which are melanoma, non-small-cell lung cancer and ovarian cancer; giving very good news for patients. At the same time, several sessions discussed how we can make these drugs—these innovations—available to all patients. This is very important: ESMO initiatives that policy makers can consider to help make these drugs available on a wider scale. For example, ESMO has established the Cancer Medicines Working Group that works very closely with the ESMO Magnitude of Clinical Benefit Scale Working Group in putting the efficacy and safety of drugs into perspective with the actual value they offer to the patient and, ultimately, value-based reimbursement. This is a crucial aspect because the only way to favour availability and dissemination is to address it in relation to different reimbursement policies. ESMO is working to secure the co-operation of all stakeholders, including reimbursing bodies, representatives of national health systems and national cancer plans, patients, specialists, health economists and the pharma companies. Our ultimate goal is to provide models that will enhance the availability of information worldwide.

You can visit us online at www.esmo.org. Follow us on Twitter @myesmo. Find us on Facebook www.facebook.com/esmo.org
Immune checkpoint inhibitors for urothelial cancer: New hope with new options

Platinum-based chemotherapy has been the mainstay of treatment for urothelial cancer; however, targeted biologics are now gaining prominence in this setting. Programmed death-1 (PD-1/PD-L1) checkpoint inhibitors facilitate tumour infiltration by T cells, resulting in targeted destruction by the immune system.

Earlier this year, the PD-L1 inhibitor atezolizumab was approved by the US FDA for the treatment of locally advanced/metastatic urothelial cancer. Late-breaking results for other PD-1/PD-L1 inhibitors in urothelial cancer offer hope for the future treatment of metastatic urothelial cancer in the post-chemotherapy setting.

Pembrolizumab has been investigated as a first-line treatment for metastatic urothelial cancer in 374 patients enrolled in the open-label phase II KEYNOTE-052 study as reported on Saturday by Dr Arjun Balar of the NYU Langone Medical Center, New York, USA (Abstract LBA32_PR). Preliminary results were very promising, with objective and complete response rates of 24% and 6%, respectively, in the overall population. Notably, in a subpopulation of 30 patients with combined tumour and immune cell PD-L1 expression of ≥10%—the cut-off point determined to identify those patients most likely to respond to pembrolizumab—11 patients (objective response rate 37%) responded to treatment. At a median 8-month follow-up, the median duration of response is yet to be reached in any patient subgroup in this study and toxicity was manageable.

The PD-1 inhibitor nivolumab is approved for the treatment of a number of advanced cancers. Results from CheckMate 275—to date, the largest phase II trial of nivolumab in locally advanced urothelial cancer—were presented on Saturday by Professor Matthew Galsky from Mount Sinai School of Medicine, New York, USA (Abstract LBA31_PR). While objective and complete responses were seen in 19.6% and 2.3%, respectively,

Commenting on his results, Dr Balar said, “These findings, together with results from a previous study with atezolizumab, suggest that in the very near future immunotherapy will become a potential standard of care in the first-line setting for these patients.”

Optimal duration of adjuvant capecitabine for stage III colon cancer still equivocal

Final results from a phase III study of adjuvant capecitabine therapy in stage III colon cancer indicate a lack of superiority in disease-free survival (DFS) with treatment extension to 48 weeks compared with the standard of 24 weeks. These findings were revealed yesterday in a poster by Dr Shigeki Yamaguchi from Saitama Medical University International Medical Center, Hidaka, Japan (Abstract 469PD).

At a median follow-up of 60 months, 3-year DFS was 75.3% versus 70.0% and 5-year DFS 68.7% versus 65.3%, in the 48-week and 24-week treatment arms, respectively (hazard ratio 0.866; 95% confidence interval 0.717–1.046; p=0.068).

Despite the lack of superiority in DFS (the primary endpoint), differences in favour of longer-term treatment were observed in 5-year overall survival (87.6% versus 83.2%; p=0.0159) and 5-year relapse-free survival (74.1% versus 69.3%; p=0.0207), suggesting that further investigation of optimal treatment duration may be warranted.

Discussing the results, Dr Richard Adams from Cardiff University, UK, noted that caution would need to be used in the application of the results from this non-US-, non-European-based population.


Prolonging adjuvant capecitabine treatment does not significantly improve disease-free survival.

The trial was conducted to investigate the optimal duration of adjuvant capecitabine treatment following observations of a peak in risk of recurrence of curatively resected colon cancer at 12–18 months post-surgery in patients who received the conventional 24 weeks, but not in those who received 48 weeks, of capecitabine therapy.

ESMO Educational Survey

Have you taken the ESMO Educational Survey?
Please complete online: https://esmoeducation.formstack.com/forms/survey2016
At AbbVie, we build bonds with oncologists, patients, payers, advocacy groups, health authorities, and other pharmaceutical companies, because we know that advancing the science of this devastating disease is not something that one person, or even one company, can do alone.

Together we can conduct research that deepens our understanding of the disease and its pathways, to ultimately develop new molecules that make a transformational improvement in cancer care.

LEARN MORE ABOUT THE BONDS WE’RE BUILDING AT BOOTH 316.
SPECTAcolor: The first prospective genetic screening platform for patients with advanced colorectal cancer

As discussed in the Daily Reporter yesterday, oncology trials are focusing increasingly on precision medicine, by assessing treatments that target pathways specifically activated in an individual patient in order to give the best chance of positive outcomes. The Screening Platform for Efficient Clinical Trial Access in advanced colorectal cancer (SPECTAcolor) is an EORTC initiative that co-ordinates gene-panel sequencing of patient tissue samples from 32 centres in 11 countries to identify causative genetic alterations and, if feasible, match patients with recruiting trials of targeted therapies.

The results of the first SPECTAcolor cohort of approximately 400 patients were presented yesterday by the project’s co-ordinating oncologist, Dr Gunnar Folprecht of the University Hospital Carl Gustav Carus, Dresden, Germany (Abstract 458O). Among the patients screened to date, approximately 10% had potentially actionable mutations making them possible candidates for enrollment into studies with mutated gene-specific inclusion criteria.

In addition to SPECTAcolor, SPECTAmel, SPECTAlung, SPECTAbrain and SPECTAprostate are related ongoing screening platforms for patients with melanoma, thoracic, neurological and prostate cancers. These initiatives promise to increase the efficiency of patient recruitment in precision-medicine trials and, it is hoped, improve the likelihood of better treatment responses as a result.

Commenting on the SPECTA initiative, Dr Fabrice André from Institut Gustave Roussy, France, said that, “When discussing molecular screening programmes, it’s important to define how they will be evaluated. The number of patients presenting with potentially actionable alterations can no longer be regarded as evaluation criteria.” He added that four criteria define successful programmes: 1. the number of patients who receive a matched therapy; 2. the number of new targets/drugs identified from the programme; 3. improvement in progression-free and overall survival; and; 4. the quality of translational research performed in the context of the programme.

Many molecular screening programmes are now in their mature phases and some scepticism has arisen about their utility. Dr André believes it is important for leaders in the field to ensure programmes are robust and will have real-world value.

By screening patients for biomarkers relevant to targeted clinical studies, SPECTAcolor increases opportunities for patients with colorectal cancer to access studies with new, molecularly defined approaches.

科学转变癌症治疗

#ESMO16
Annual Congress
October 7 - October 11
Copenhagen

Visit
www.astrazeneca.com

科学转变癌症治疗

科学转变癌症治疗

科学转变癌症治疗

科学转变癌症治疗
New data on anti-PD-1 therapy in patients with brain metastases

Brain metastases are a common complication of melanoma and are associated with poor prognosis. The pressing need for effective management is in part due to the extended survival times afforded by improved primary tumour treatments, particularly targeted therapies. While survival is prolonged, unfortunately there is a greater frequency of brain metastases. Reduced blood–brain barrier penetration and resistance development may limit the brain activity of some targeted agents that show excellent extracranial activity, such as the ALK inhibitor crizotinib in lung cancer. The activity of other agents, such as immunotherapies, remains unclear because patients with brain metastases are often excluded from clinical trials.

Data from a retrospective analysis provide important new information on this issue.

Yesterday, Dr Christian Blank presented a poster by Dr John Park (Crown Princess Mary Cancer Centre, Westmead Hospital, Sydney, Australia; Abstract 1114PD) on the efficacy of anti-programmed death-1 (PD-1) therapies in treating brain metastases from melanoma. In a retrospective analysis of 66 patients with intracranial metastases (38% had ≥5) and relatively poor prognostic features (elevated lactate dehydrogenase [50%] and/or performance status ≥2 [32%]), an intracranial response rate (ICRR) of 20% was reported with anti-PD-1 therapy (nivolumab or pembrolizumab); ICRR was lower for patients with symptomatic lesions (11%) and those receiving steroids for brain metastases (14%). With a median follow-up of 7 months, median intracranial progression-free survival (PFS) and overall survival were 5.3 months and 9.9 months, respectively. Symptoms and steroid treatment for brain metastases were associated with significantly shorter PFS.

Concluding, Dr Christian Blank said that on the basis of these results, anti-PD-1 therapy may not be the best option for the treatment of brain metastases; combinations of checkpoint inhibitors or checkpoint inhibitors with the appropriate targeted therapy may be required in addition to radiotherapy. He added that treatment should be given upfront in this population with such a high unmet medical need.

Is an intracranial response rate of 20% good enough for patients with brain metastases from melanoma?
Positive new phase III data for sunitinib as adjuvant therapy in high-risk RCC

The first trial of a tyrosine kinase inhibitor to show prolonged disease-free survival (DFS) following adjuvant treatment for renal cell carcinoma (RCC) was reviewed yesterday by Dr Alain Ravaud from CHU Bordeaux Hôpital St André, Bordeaux, France, in a Late-Breaking Abstract presentation (Abstract LBA11_PR).

Results of the S-TRAC trial suggest that sunitinib may be of benefit to a broader range of patients in the future.

The double-blind, phase III S-TRAC trial randomised 615 treatment-naive patients at high risk of recurrent RCC post-nephrectomy to sunitinib (50 mg/day) or placebo for 1 year. DFS by blinded independent central review (primary endpoint) was significantly longer with sunitinib compared with placebo (median DFS 6.8 months versus 5.6 months; hazard ratio [HR] 0.761; p=0.030). These potentially practice-changing data were confirmed in secondary DFS analyses that included a higher risk patient subgroup (HR 0.737; p=0.044).

“These data show that sunitinib has the potential to become a first-line standard treatment for mRCC,” concluded Dr Choueiri.

Positive new phase III data for sunitinib as adjuvant therapy in high-risk RCC

Compared with sunitinib, first-line cabozantinib significantly improved progression-free survival (PFS) and objective response rate (ORR) in patients with metastatic renal cell carcinoma (mRCC). These were the conclusions of a randomised, multicentre phase II trial reported in a Late-Breaking Abstract presentation yesterday by Dr Toni Choueiri from the Dana-Farber Cancer Institute and Brigham and Women’s Hospital, Boston, Massachusetts, USA (Abstract LBA30_PR).

Cabozantinib has recently shown superior PFS, overall survival and ORR compared with everolimus in previously treated patients with mRCC, while sunitinib is considered the reference standard of care for the first-line treatment of mRCC.

In the phase II ALLIANCE study, 157 intermediate- or poor-risk patients who had not received prior systemic therapy were randomised to cabozantinib (60 mg once daily [qd]) or sunitinib (50 mg qd, 4 weeks on/2 weeks off). Median PFS (primary endpoint) was considerably prolonged with cabozantinib compared with sunitinib (8.2 months versus 5.6 months, respectively), equivalent to a 31% reduction in median rate of progression or death with cabozantinib (hazard ratio 0.69; 95% confidence interval 0.48–0.98; p=0.012) at a median follow-up of 20.8 months. ORR was also markedly and significantly higher with cabozantinib (46%) versus sunitinib (18%). Adverse events (AEs) were reported at a similar incidence in the cabozantinib and sunitinib treatment arms (70.5% and 72.2% of patients, respectively, experienced grade ≥3 AEs).

“This data show that cabozantinib has the potential to become a first-line standard treatment for mRCC,” concluded Dr Choueiri.

This randomised, phase II trial has demonstrated for the first time superior activity of a new therapy compared with sunitinib in previously untreated patients with RCC.


#ESMO16

Tuesday 11 October 2016 – ESMO European Society for Medical Oncology
A novel prognostic biomarker of poor overall survival in advanced CRC

Colorectal cancer (CRC) can have highly variable prognoses and treatment outcomes and, as a result, assessment of molecular markers has become a major factor in therapeutic decision-making for this disease. Yesterday, Professor Frédérique Penault-Llorca of the Centre Jean Perrin, Clermont-Ferrand, France, presented on the discovery of a novel genetic prognostic factor in stage III CRC (Abstract 459O), identified using prospectively collected tissue samples from an interventional study, PETACC8, a phase III, open-label, randomised study of FOLFIRI-4 plus cetuximab versus FOLFOX-4 alone for patients with resected stage III colon cancer,1 was used to assess the prognostic effects of a number of gene mutations.

A previous post-hoc analysis of this dataset revealed that the presence of BRAF and KRAS mutations predicted shorter durations of disease-free and overall survival.2 The present analysis showed that alterations (mutations or amplifications) of ERBB2, a key tumourigenesis driver, were detected in 3.9% of 1,795 patients in PETACC8 and predicted a significantly shortened duration of recurrence-free and overall survival. Professor Penault-Llorca concluded by advocating the use of next-generation sequencing and fluorescence in situ hybridisation (FISH) to analyse this rare but potentially useful prognostic biomarker and facilitate the use of targeted CRC therapies in the adjuvant setting.


Nintedanib shows clinical activity in a phase III study of refractory CRC

The oral multiple angiokinase inhibitor nintedanib appears to have activity in refractory metastatic colorectal cancer (CRC) according to the findings of the phase III LUME-Colon 1 study. Reviewing the data in a Late-Breaking Abstract presentation on Sunday (Abstract LBA20: PB), Professor Eric Van Cutsem from University Hospitals Leuven, Belgium, noted the statistically significant improvement in progression-free survival (PFS) observed with nintedanib (hazard ratio 0.58; 95% confidence interval 0.49–0.69; p<0.0001) versus best supportive care (BSC), but cautioned that this did not translate into an overall survival (OS) advantage (co-primary endpoint). Nintedanib is a new compound that appears to have activity in refractory metastatic CRC according to the findings of the phase III LUME-Colon 1 study. Reviewing the data in a Late-Breaking Abstract presentation on Sunday (Abstract LBA20: PB), Professor Eric Van Cutsem from University Hospitals Leuven, Belgium, noted the statistically significant improvement in progression-free survival (PFS) observed with nintedanib (hazard ratio 0.58; 95% confidence interval 0.49–0.69; p<0.0001) versus best supportive care (BSC), but cautioned that this did not translate into an overall survival (OS) advantage (co-primary endpoint).

Nintedanib is a new compound that appears to have activity in a patient population with limited treatment options. This study was conducted after an earlier phase III study suggested the agent had similar efficacy to bevacizumab when given as first-line treatment in combination with mFOLFOX6.1 Consistent with the phase III findings, nintedanib appeared to be well tolerated; grade ≥3 adverse events occurring more frequently in the nintedanib than placebo arm were liver-related investigations (16% versus 8%) and fatigue (9% versus 6%).

Nintedanib is a new compound that appears to have activity in a patient population with limited treatment options, and further analyses of the phase III data are ongoing. The agent is currently approved in the EU for the treatment of idiopathic pulmonary fibrosis and for non-small-cell lung cancer after first-line chemotherapy, based on the LUME-Lung 1 trial, which demonstrated significantly extended median OS (approximately 25% of patients survived for ≥2 years) with nintedanib plus docetaxel versus docetaxel alone.2


Delegate voices

“Great variety—how do you choose what to go to?! And it’s a good social networking space for meeting colleagues and opinion leaders.”
Sarah Payne, Honorary Consultant at Guy’s and St Thomas’, London, UK

“I’ve heard a lot of interesting data – significant advances are clearly being made across many tumour types, although we still have much work to do.”
Theo Smalberger, Medical Oncologist, South Africa

“I’ve really enjoyed the congress this year – it has been well organised and the scientific content has been great, particularly the breast and lung cancer data. I’m looking to join the Young Oncologist initiative and will be back next year!”
Thais Abreu de Almeida, Oncologist, Brazil

“I’ve been most interested in the breast cancer track – the MONALEESA 2 data might mean a change in the standard of care and makes treatment sequencing less certain especially in light of the FALCON study results. It will be interesting to see how this story evolves at future congresses.”
Simon Oliver, Researcher, UK
Controversy of the Day: Tailoring treatment in elderly cancer patients

Two posters reported the designs of ongoing trials using GAs to tailor treatment strategies to older patients. The GrantPax multicentre, interventional trial in patients ≥75 years with pancreatic cancer is basing treatment—nab-paclitaxel/gemcitabine, gemcitabine alone or best supportive care—on baseline CGA scores (Abstract 7141P). In the NORDICO trial (Abstract 601TIP), associations between outcome and GAs, biomarkers and pre-treatment characteristics in elderly patients with metastatic CRC are being investigated.

Several studies reported relationships between outcome and a variety of measures. Our study in metastatic CRC (Abstract 549F) and another in metastatic gastric cancer (Abstract 650F) confirm Eastern Cooperative Oncology Group (ECOG) performance score as a prognostic tool for patients ≥70 years old, but specific parameters such as nutritional status, measured by Mini Nutritional Assessment (MNA), provide additional information. In metastatic breast cancer, the Charlson Comorbidity Index score was a significant prognostic indicator for survival in patients ≥65 years who received either primary tumour removal or no surgery (Abstract 252P). A phase II trial in 102 patients receiving chemotherapy ± bevacizumab for metastatic CRC reported that baseline scores for the Spitzer quality of life index and Kühne prognostic group criteria were prognostic for overall and progression-free survival (Abstract 583P).

The importance of cognitive function for compliance with oral anticancer treatment was also stressed (Abstract 1497P). Among 126 patients receiving oral anticancer therapy, working memory disorders were significantly associated with treatment non-adherence (HR 1.38; p=0.0326) and were significantly worse with increasing age. Depression was also significantly associated with treatment non-adherence (HR 4.67; p=0.0352).

The GrantPax trial is one of the first to assign anticancer treatment to elderly patients strictly according to baseline CGA scores.

Selumetinib plus docetaxel fails to show significant benefits over docetaxel alone in KRAS-mutant NSCLC

The eagerly awaited first prospective phase III trial in KRAS-mutant non-small-cell lung cancer (NSCLC; N=510), evaluating selumetinib plus docetaxel versus docetaxel alone as second-line treatment (“SELECT-1”), has failed to meet its primary endpoint of improvement in progression-free survival (PFS).

Dr Pasi Jänne from Dana-Farber Cancer Institute, Boston, Massachusetts, USA, presented the findings in a Late-Breaking Abstract presentation yesterday (Abstract LBA47_PR). He noted that despite observing a significant improvement in PFS and response with the MEK1/2 inhibitor combination in an earlier phase II study, “the phase III data was disappointing in this KRAS-mutant population that is associated with a particularly poor prognosis and is notoriously difficult to treat. Median PFS was 3.9 months with selumetinib plus docetaxel and 2.8 months with placebo plus docetaxel (hazard ratio 0.95; 95% confidence interval 0.77–1.22; p=0.44). Similarly, the combination did not show a significant effect on overall survival, while a trend towards a higher objective response rate was observed with selumetinib compared with placebo (20.1% versus 13.7%; odds ratio 1.61; p=0.051). The selumetinib plus docetaxel combination was associated with a higher incidence of grade ≥3 adverse events (AEs), serious AEs, and AEs leading to hospitalisation compared with the docetaxel arm.

Selumetinib was granted Orphan Drug Designation by the US FDA in May 2016 for the adjuvant treatment of thyroid cancer and is being further investigated as an adjuvant treatment option for high-risk thyroid cancer (for its capacity to re-sensitise tumour cells to radioactive iodine) and other tumour types. 1. Jänne PA, et al. Lancet Oncol 2013; 14:38–47
ESMO 2016

NAME OUR NEW DIGITAL MAGAZINE...

IT’S YOUR CHOICE!
ESMO Pulse
ESMO Pathways
myESMO

Visit the ESMO booth to record your choice and help us to name our new magazine.

#NAMEOURMAG
GIOTRIF®
Proven efficacy vs gefitinib (PFS and TTF) and vs chemotherapy in 1st-line EGFR M+ NSCLC1-4*

Efficacy
PFS1-4 OS1-3 TTF2

TREAT

40mg

DIAGNOSE

GEME

LET’S WORK
ONCOLOGY FROM BOEHRINGER INGELHEIM

GEOXONTRIF (afatinib) tablets
RAISING EXPECTATIONS

NOW APPROVED in Squamous NSCLC

* LUX_Lung 3 (in premature/patients); and LUX_Lung 8 (premature/patients); PFS (overall survival) and superior OS; in CAF subgroup (Cox endpoint); LUX_Lung 7 (vs gefitinib); superior PFS (vs chemotherapy).

GIOTRIF®: Abbreviated European Prescribing Information. Please refer to local prescribing information as they vary between countries. Different trade names are used in some countries. Presentations: Film-coated tablets: each containing 20 mg, 30 mg, 40 mg or 80 mg (immediate). Indications: GIOTRIF® as monotherapy is indicated for the treatment of Epidermal Growth Factor Receptor (EGFR) TKI-naïve adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating EGFR mutations; locally advanced or metastatic NSCLC of squamous histology progressing on or after platinum-based chemotherapy. Pooled and method of administration: GIOTRIF® mutation status should be established prior to initiation of GIOTRIF®. Recommended dose is 40 mg once daily if able to be taken without food. Dose escalation to a maximum of 80 mg/day may be considered in patients who tolerate 40 mg/day. Symptomatic adverse reactions may be successfully managed by treatment interruption and dose reduction or treatment discontinuation. No starting dose adjustment necessary in patients with mild or moderate renal or hepatic impairment. Not recommended in patients with severely impaired renal function (CrCl ≤ 30 mL/min), severe hepatic impairment, children or adolescents. Contraindications: Hypersensitivity to afatinib or any of its excipients. Special warnings and precautions for use. Diarrhea, including severe diarrhea, and rash/cramp may require interruption and dose reduction or discontinuation of therapy. Higher exposure to afatinib has been observed in female patients. Patients with lower body weight and those with underlying renal impairment. Intestinal Long Disease (ILD) or Grade 4 adverse reactions, including fatalities, have been reported in patients receiving GIOTRIF®. ILD is diagnosed, permanently discontinue GIOTRIF®. Uncommon GIOTRIF® in patients who develop severe hepatic impairment. If ILD is diagnosed, the benefits and risks of continuing treatment should be carefully considered. Cardiac monitoring, including an ECG assessment, should be considered in patients with cardiac risk factors and patients who develop novel cardiac biomarkers during treatment. GIOTRIF® contains lactose: patients who are lactose intolerant should be advised that CGIOTRIF® contains lactose and may contain trace amounts of milk protein. Adverse reactions: The most common adverse reactions include diarrhea (21%), rash/cramp (19%), elevation in liver enzymes (ALT and/or AST) (13%), dry skin (12%), weight gain, paronychia, headache and hypothyroidism in ≥ 10% of patients. Overall, fatal adverse reactions in ≥ 1% patients were: urinary tract obstruction, pulmonary embolism, myocardial infarction, liver failure, diarrhea, rash/cramp, pancreatitis, deep venous thrombosis, pulmonary embolism, pneumonia, bone fracture, arrhythmia, heart failure, ventricular tachycardia, pericarditis, pleural effusion, cough, respiratory tract infection, herpes zoster, lymphoma, nasopharyngitis, infection and sepsis, peritonitis, diarrhea, pyrexia, vomiting, abdominal pain, cellulitis, hypoglycemia, hypothyroidism, hypophosphatemia, metabolic acidosis, hypokalemia, hypertension, hyperglycemia, hyperuricemia, neutropenia, thrombocytopenia, anemia, leukopenia, neutropenia, lymphopenia, increased creatine kinase, increased lipase, increased aspartate aminotransferase (AST) levels, increased alanine aminotransferase (ALT) levels, increased alkaline phosphatase levels, increased gamma glutamyl transpeptidase (GGT) levels, increased total bilirubin. 1. Yang JC et al. Lancet Oncol. 2015;16:e26-e37. 2. Sequist LV et al. J Clin Oncol. 2013;31:273-283. 3. Wang Y et al. Lancet Oncol. 2016;17:e23-e32. 4. Park K et al. Lancet Oncol. 2016;17:e57-e69.