Evolution of the individualized treatment landscape for advanced NSCLC

Chaired by Tony Mok

Friday 13th May 11:00 – 12:00
Empress Grand Hall, 3rd floor, Empress Convention Center

Scientific summary
Contents

3  Welcome message

4  Faculty biographies

6  How best to manage patients with nonsquamous cell NSCLC without EGFR/ALK mutations
   Dr Ross Soo

11 Therapeutic options for patients with advanced squamous NSCLC
    Professor Giorgio Scagliotti
Dear Colleagues,

Thank you for attending the satellite symposium entitled ‘Evolution of the individualized treatment landscape for advanced NSCLC’ at the IASLC Asia Pacific Lung Cancer Conference (APLCC 2016).

Chiang Mai, Thailand’s northern capital, provided a historic and culturally vibrant host city for this conference that brought together a unique community of medical professionals from across the Asia–Pacific region. The aim of the symposium was to facilitate the management of squamous and nonsquamous NSCLC, and the implementation of new discoveries in clinical practice. It also addressed the challenges facing clinicians in the Asia–Pacific region in an increasingly complex treatment landscape.

During the session, the expert Faculty guided us through this complexity by placing the latest developments in advanced NSCLC into the context of treatment. They provided their insights into how we can use our biological knowledge not only to improve treatment pathways, but also to maximize treatment outcomes by understanding different approaches.

We hope that you found the symposium educational and that it has furthered your understanding of this evolving field.

Yours faithfully,

Tony Mok

Tony Mok
Chair
Faculty biographies

Tony Mok  
(Symposium Chair)  
The Chinese University of Hong Kong, Hong Kong

Tony Mok was trained at the University of Alberta and subsequently completed a fellowship in medical oncology at the Princess Margaret Hospital. After working as a community oncologist in Toronto for seven years, he returned to Hong Kong in 1996 to pursue an academic career.

Professor Mok is the Li Shu Fan Medical Foundation Named Professor of Clinical Oncology and Chairman of Clinical Oncology at The Chinese University of Hong Kong. His main research interest focuses on biomarker and molecular-targeted therapy in lung cancer. He co-founded the Lung Cancer Research Group, and has led a number of important multinational clinical trials, which include the IPASS (IRESSA Pan-Asia Study), a landmark study that established the role of first-line gefitinib in patients with EGFR mutations.

Professor Mok has contributed to over 200 articles in international peer-reviewed journals, including The New England Journal of Medicine, Science, The Lancet and Journal of Clinical Oncology, and has also contributed to multiple editorials and textbooks. He is also active and experienced in serving academic societies. He is the Past President of the International Association for the Study of Lung Cancer (IASLC), Past Chair of the American Society of Clinical Oncology (ASCO) International Affairs Committee, a member of the ASCO Publications Committee and Vice Secretary of the Chinese Society of Clinical Oncology (CSCO).

He is closely affiliated with the oncology community in China and has received an Honorary Professorship at Guang Dong Province People's Hospital, Guest Professorship at Peking University School of Oncology, Visiting Professorship at Shanghai Jiao Tong University and West China School of Medicine/West China Hospital, Sichuan University. He is an Editor on thoracic oncology for the Journal of Clinical Oncology. He has also authored eight books in Chinese and hosted three television series in Hong Kong.
Ross Soo
National University Cancer Institute, Singapore

Ross Soo is a Senior Consultant for the Department of Hematology–Oncology at the National University Cancer Institute, Singapore (NCIS), where he specializes in lung cancer and head and neck cancer, and leads the Lung Tumor Group. Additionally, he is an Adjunct Principal Investigator for the Cancer Science Institute of Singapore and belongs to several professional societies and associations, such as the American Society of Clinical Oncology (ASCO), the International Association for the Study of Lung Cancer (IASLC), and the Singapore Society of Oncology.

Dr Soo received his medical degree from Monash University and underwent specialist training in Melbourne and Sydney. He subsequently became a fellow of the Royal Australasian College of Physicians and the Academy of Medicine in Singapore. Dr Soo maintains an international presence in oncology, as he has been invited to speak and present his research findings at many international meetings and has published more than 90 papers in scientific journals including *Cell*, *Nature Medicine*, *Cancer Research* and *Science Translational Medicine*.

Dr Soo’s research interests are in lung cancer and nasopharyngeal cancer. Dr Soo also sits on various committees, including the IASLC Communications Committee, National Healthcare Group Domain-Specific Ethics Review Board, the Ministry of Health Drug Advisory Committee, and the Medical Oncology Specialist Training Committee.

Giorgio Scagliotti
University of Torino, Italy

Giorgio Scagliotti is currently Head of the Department of Oncology and Professor of Oncology at the University of Torino. He is also Chief of the Medical Oncology Division at the S. Luigi Hospital. He earned his medical degree and completed his postgraduate training in Respiratory Medicine, Internal Medicine and Medical Oncology at the University of Torino.

Professor Scagliotti is a member of several scientific societies, including the Italian Society of Respiratory Medicine, the European Respiratory Society, the American Society of Clinical Oncology (ASCO), and the International Association for the Study of Lung Cancer (IASLC). From 2003–2007 he was an Executive Board member of the IASLC. He is also Associate Editor for the *Journal of Thoracic Oncology*, International Editor for *Clinical Lung Cancer* and the author or co-author of more than 280 publications in peer-reviewed journals. Alongside this, he is the International Editor of the 4th Edition of ‘Lung Cancer: Principles and Practice’ and co-editor of the IASLC textbook ‘Multidisciplinary Approach to Thoracic Oncology’.
Here we provide a scientific summary of not only the presentations and associated discussion, but also of the questions put to the audience by the Chair Professor Tony Mok, from The Chinese University of Hong Kong – look out for the blue boxes below.

How best to manage patients with nonsquamous cell NSCLC without EGFR/ALK mutations

Dr Ross Soo used the case of a 58-year-old male heavy smoker to discuss the treatment options for patients with nonsquamous non-small-cell lung cancer (NSCLC) lacking targetable mutations.

The patient presented with a persistent cough, but no haemoptysis, and was otherwise asymptomatic, with an ECOG performance status of 0. Chest x-ray showed a right hilar mass and bronchoscopy identified the presence of a poorly differentiated adenocarcinoma.

When asked how they would manage this patient, the vast majority (84.6%) of attendees said that they would wait for the results of the EGFR and ALK tests, while the remaining 15.4% said they would test for the alterations, but initiate cytotoxic chemotherapy while awaiting results.

Tony Mok: How long does it take for the results of EGFR testing to become available?

Audience Member: Approximately 10 days in Thailand.

Tony Mok: Ross, is that an acceptable time to wait before starting treatment?

Ross Soo: For this patient, it would be. The patient was asymptomatic apart from cough and had a low tumour burden – for such a patient, it would be acceptable to wait for 10 days.

Tony Mok: One of the downfalls of starting cytotoxic chemotherapy without knowing the mutation status is of course toxicity, so how do you explain your decision to the patient?

Audience Member: I would tell the patient that we can switch to a tyrosine kinase inhibitor (TKI), if appropriate, once the mutation results become available.
Dr Ross Soo noted that the main question is when should \( \text{EGFR/ALK} \) testing be performed? The guidelines from the College of American Pathologists, International Association for the Study of Lung Cancer and Association for Molecular Pathology recommend testing for adenocarcinoma patients, and for those where an adenocarcinoma component cannot be completely excluded. In the latter scenario, the guidelines suggest using clinical criteria – such as, young age and non-smoking history – to select patients for testing.

The speaker highlighted the importance of testing for \( \text{EGFR} \) mutations in Asian adenocarcinoma patients, citing a study that found \( \text{EGFR} \) mutations in nearly a third (28%) of the 262 men who were heavy smokers (>30 pack-years).

First-line therapy

Mutation testing showed that the tumour was wild-type for \( \text{EGFR} \) and did not harbour \( \text{ALK} \) or \( \text{ROS1} \) gene rearrangements – what first-line treatment would you offer, asked Soo?

Over half (55.6%) of the audience opted for cisplatin plus pemetrexed, a third (33.3%) chose the combination of carboplatin, paclitaxel and bevacizumab, and the remaining (11.1%) chose cisplatin plus gemcitabine. There were no takers for the cisplatin, vinorelbine plus cetuximab or platinum-based triplet options.

Discussing first-line options for this patient population in more detail, Soo pointed out it is important to consider histology when choosing a cytotoxic regimen. For instance, in a study comparing pemetrexed with gemcitabine, both given alongside platinum-based chemotherapy, the benefits of pemetrexed were restricted to patients with nonsquamous histology.

Tony Mok:
OK, so the patient responds to chemotherapy, the tumour shrinks, but then the mutation tests come back positive for an \( \text{EGFR} \) mutation, what would you do?

Audience Member:
I would continue the chemotherapy because according to the IPASS study, in \( \text{EGFR} \)-mutation positive patients, the overall survival (OS) and objective response rate (ORR) were comparable for first-line TKI and chemotherapy. Thus, as I cannot be sure if a TKI would be feasible and effective in this patient, I would continue with chemotherapy if it is working.

Giorgio Scagliotti:
I believe a good choice would be to continue for four courses of chemotherapy and then switch to an \( \text{EGFR} \) TKI for maintenance.

Tony Mok:
Why not continue with Alimta as maintenance?

Giorgio Scagliotti:
If I believe the INFORM study, even though it has been conducted in a non-selected population, maintenance with gefitinib showed a benefit in progression-free survival in that population.
The addition of bevacizumab to carboplatin plus paclitaxel improves OS as shown by the ECOG4599 trial, but this is not the case for the addition of an anti-EGFR monoclonal antibody to platinum doublet, at least not in adenocarcinoma patients, said Soo. In the phase III FLEX, BMS099 and INSPIRE trials that added either cetuximab or necitumumab to platinum-based chemotherapy, OS and progression-free survival (PFS) were comparable between treatment arms for the subset of adenocarcinoma patients.

Additionally, triplet therapy is no longer given since a meta-analysis showed no difference in OS between triplet and doublet chemotherapy, but increased toxicity with the triplet.

At this stage, the majority (66.7%) of the audience voted to continue with single-agent monotherapy, while 15.2% said they would stop treatment and observe. The remaining three options – continue with pemetrexed plus bevacizumab or switch to single-agent immunotherapy or gefitinib – were each chosen by 6.1% of the attendees.

Soo explained that there is evidence to support the most popular option – continuation maintenance with pemetrexed. In the randomised PARAMOUNT trial, OS was significantly prolonged in patients who received pemetrexed after four cycles of cisplatin plus pemetrexed compared with those given placebo, at a median of 13.9 versus 11.0 months.

However, the findings are more mixed for other maintenance options. Trials evaluating switch maintenance – ie, when an agent not used in the first-line is introduced at the maintenance stage – generally show an improvement in PFS, but not OS, with the agent versus observation or placebo. One exception is the SATURN study, which also shows a significant improvement in OS with erlotinib versus placebo, a result mainly driven by EGFR mutation-positive patients, the presenter believes.

Soo added that the benefits of switching to an EGFR TKI remain unestablished for patients with nonmutated NSCLC. The WJTOG and INFORM trials found that PFS was significantly better with maintenance gefitinib versus observation and placebo, respectively, but the treatment arms were comparable with respect to OS.

Similarly, the evidence for combination maintenance is also mixed. For instance, the ATLAS trial that investigated maintenance bevacizumab plus either erlotinib or placebo found a significant improvement in PFS, but not OS. By contrast, in the PointBreak study, neither PFS nor OS were significantly improved with the addition of maintenance pemetrexed to bevacizumab.

**Tony Mok:**
How do you choose between paclitaxel, carboplatin plus bevacizumab and pemetrexed plus cisplatin? What is the key factor?

**Audience Member:**
I would choose pemetrexed plus cisplatin because the other option is more expensive in my country (Vietnam).

**Tony Mok:**
Who are the patients to whom you would not give bevacizumab? Those with brain metastases? Elderly patients?

**Audience Member:**
Research has shown that bevacizumab can be given to patients with brain metastases, especially if they are small and treated. Thus, brain metastases are not an absolute contraindication for bevacizumab, and I also do not have an issue with giving it to older patients.

**Maintenance therapy**

Going back to the case, the presenter explained that the patient received four cycles of carboplatin and pemetrexed, which resulted in tumour shrinkage and stable disease. The patient remained asymptomatic and the performance status did not worsen.
Tony Mok:
How do you select a patient for maintenance therapy versus observation?

Audience Member:
I generally give all my patients maintenance therapy unless there are cost concerns, if the patient can’t afford the drugs anymore. The other situation in which I may withhold maintenance is if the patient is relatively well (say, performance status of 0) and wants to stop chemotherapy.

Tony Mok:
How would the level of response influence your decision?

Audience Member:
If the patient has very good partial response, I would encourage maintenance therapy, while if the best response is stable disease then it would be a matter of choice.

Tony Mok:
Is there any occasion when you would add bevacizumab to the maintenance regimen?

Audience Member:
Bevacizumab is quite expensive in Malaysia so cost is usually a concern for my patients. I do not have sufficient experience with maintenance bevacizumab.

Tony Mok:
Ross, you said that there is not sufficient data for giving TKIs as maintenance – is there any situation where you would use an EGFR TKI in an EGFR wild-type patient?

Ross Soo:
If you suspect the patient is EGFR mutation-positive, based on clinical features, but couldn’t prove it.

Tony Mok:
Giorgio, do you agree with giving an EGFR TKI as maintenance to a patient with unknown mutation status?

Giorgio Scagliotti:
In principle, no, as I would like the patient to be tested again to be sure that the patient is EGFR wild-type, and if so, I would choose cytotoxic chemotherapy maintenance. However, if the patient has an EGFR mutation, then I would prefer to go with an EGFR TKI maintenance treatment. Remember that in the SATURN and INFORM studies, the benefit was limited to patients with EGFR mutations.

Second-line therapy
Soo told the audience that the patient progressed after four cycles of maintenance pemetrexed, and their performance status changed to 1. PD-L1 testing could not be performed as a tumour sample was not available.

When asked their opinion on the next step, over a third (38.7%) of the attendees chose second-line docetaxel, over a quarter (29.0%) chose immunotherapy (either nivolumab or pembrolizumab), with smaller proportions choosing erlotinib (16.1%), docetaxel plus ramucirumab (12.9%) and docetaxel plus nintedanib (3.2%).

Docetaxel has been the second-line treatment of choice for “a long, long time”, commented Soo. The Shepherd et al trial showed that OS was significantly longer for the 55 patients given docetaxel than for the 49 treated with best supportive care, at a median of 7.5 versus 4.6 months17.

Moving onto the issue of second-line EGFR TKIs in patients with wild-type EGFR, he added that the results are “quite conflicting”. Although there have been many trials, the primary endpoints are different and the findings are controversial. “And when there is a controversy, do a meta-analysis”, said Soo. In the Lee et al meta-analysis, subgroup analysis results favour chemotherapy in patients with nonmutated EGFR at second- or later-line, and of note, also when a more sensitive platform is used for EGFR mutation analysis18. “So if you have a more sensitive platform and the tumour is proven to be wild-type, you would be better off giving docetaxel.”

The addition of the TKI nintedanib or the anti-angiogenesis agent ramucirumab to docetaxel has been shown to extend OS in patients with adenocarcinoma...
and nonsquamous NSCLC, respectively\textsuperscript{19-20}. Nintedanib has a “manageable” adverse event profile, with increased diarrhoea and a slight increase in transaminases, said Soo, while the most common toxicities with ramucirumab were stomatitis and mucositis. Ramucirumab treatment also resulted in an increase in haematological side effects and hypertension, a class effect.

The immune checkpoint inhibitors – nivolumab, pembrolizumab and atezolizumab – also show promise in the second-line setting. In head-to-head comparisons with docetaxel, each of these agents significantly improved OS in patients with nonsquamous NSCLC\textsuperscript{21-23}. And toxicities were less frequent among immunotherapy-treated patients than those given docetaxel.

The presenter said that the patient received six cycles of docetaxel with stable disease as the best response, following which he relapsed. A repeat biopsy for an immune checkpoint inhibitor trial revealed that the tumour was PD-L1-negative, and “unfortunately, he was randomised to chemotherapy”, the presenter continued.

The Chair queried the use of the term ‘unfortunately’, to which Soo replied that firstly, phase I trials confirm the benefits of immune checkpoint inhibitors in later lines, while there is no information on third- or fourth-line chemotherapy. Second, even if the patient is PD-L1-negative, there is a chance the patient would respond to immunotherapy. And Mok responded: “Unfortunately, I actually agree with you.”

**Concluding remarks**

To conclude, Soo highlighted the importance of basing the choice of the first-line cytotoxic agent on a patient’s tumour histology.

He noted that there are several available options for second-line therapy in this patient population, but that the optimal second-line treatment is unknown. Immune checkpoint inhibitors confer durable survival and have manageable toxicity at second-line, but the data for their use in the first-line setting are awaited.

What is important is to maybe revisit the options by repeating the biopsy to look for old targets and new targets, and if a rebiopsy is not possible then to perhaps consider a liquid biopsy, Soo concluded.

**References**

Therapeutic options for patients with advanced squamous NSCLC

Professor Giorgio Scagliotti presented the case of a 69-year-old man diagnosed with stage IV squamous NSCLC with diffuse bone metastases. The patient was a heavy smoker, with a performance status of 1 and several comorbidities including mild chronic obstructive pulmonary disease. The tumour lacked EGFR, ALK and K-RAS mutations, and had low PD-L1 expression.

Most (65.6%) of the audience believed that the appropriate first-line treatment for this patient was a platinum doublet – cisplatin or carboplatin alongside either vinorelbine or taxanes or gemcitabine. An identical proportion (12.5%) chose cisplatin plus pemetrexed, which Scagliotti said was “probably not the best choice based on what the previous presenter showed you”, and any chemotherapy plus denosumab, in addition to a few other scattered choices.

Tony Mok:
Twelve percent of the audience chose pemetrexed plus platinum – is it wrong to give this combination to a squamous NSCLC patient?

Audience Member:
Based on the available data, this combination should not be used, so I am not sure why some people do.

Tony Mok:
Giorgio, the subgroup analysis of your study showed that pemetrexed was inferior to gemcitabine in squamous NSCLC patients, but some patients do respond – is it wrong to want to use this option in light of the lower toxicity?

Giorgio Scagliotti:
Well, we need to follow the rules, and I follow the guidance of the regulatory agencies. But looking at the major phase III trials, despite the inferiority of pemetrexed in terms of outcomes, some patients were responsive in terms of tumour shrinkage – it is just that the proportion was inferior to that in the gemcitabine group. My investigational brain is telling me that probably some biological and molecular determinants need to be explored, which may explain the response.

First-line therapy

Expanding on the first-line options in the squamous NSCLC setting, the presenter noted that probably the “largest study conducted in recent times” was the phase III trial in which advanced NSCLC patients were randomly assigned to receive carboplatin alongside either albumin-bound (nab) or solvent-bound paclitaxel. Treatment with nab-paclitaxel significantly improved the primary endpoint of ORR in the squamous subgroup, but not in the nonsquamous subgroup. But OS and PFS did not differ between the experimental and control arms, either in the overall population or among patients with squamous histology¹.

Nonetheless, nab-paclitaxel, in combination with carboplatin, was approved by the US Food and Drug Administration for the first-line treatment of locally advanced or metastatic NSCLC in 2012². And two trials are currently underway investigating the safety and efficacy of maintenance nab-paclitaxel in late-stage squamous NSCLC and the safety and efficacy of nab-paclitaxel plus carboplatin in elderly patients³-⁴.

Nedaplatin, a second-generation platinum compound with lower rates of nausea, vomiting and nephrotoxicity...
Tony Mok: Cisplatin and carboplatin have been around for decades – is nedaplatin going to be better? If so, what are the potential advantages of nedaplatin?

Audience Member: Nedaplatin is a very cheap drug and has mild toxicity compared with cisplatin.

He continued: “Just to lower the enthusiasm for immunotherapy a little, let me remind you of a study from 5 years ago that looked into the role of ipilimumab in combination with chemotherapy. This phase II trial found no difference between treatment with concurrent or phased ipilimumab plus chemotherapy compared with chemotherapy alone in patients with advanced NSCLC. But the squamous NSCLC subset derived a “quite impressive” PFS and OS benefit with phased ipilimumab. This study formed the basis for a phase III randomised clinical trial, the findings of which are “eagerly awaited”.

The SQUIRE trial evaluated the addition of the anti-EGFR antibody necitumumab to cisplatin plus gemcitabine in patients with advanced squamous disease, and found that the triplet imparted a survival benefit in the range of 1.4 months, with marginal improvement in 1- and 2-year OS rates. Noting that the FLEX trial identified a nonsignificant OS benefit for squamous NSCLC patients treated with the anti-EGFR antibody cetuximab, the presenter wondered whether SQUIRE is essentially a Re-FLEX? Moreover, given that “we are talking about two extremely similar agents with extremely similar results, should we make a distinction between statistical and clinical significance of this data?” he questioned.

The speaker wound up the discussion on first-line therapies by mentioning denosumab. He explained that an analysis of registration studies of the bone targeting agent showed a survival advantage relative to zoledronic acid in advanced lung cancer patients with bone metastases. However, the results need to be approached with caution as the database “lacked critical prognostic parameters that are, in my opinion, critical to isolate the cytotoxic effects of one specific agent”, said Scagliotti.

Continuing with the case, the presenter said that the patient was given first-line cisplatin plus gemcitabine followed by four cycles of maintenance gemcitabine.

Tony Mok: Giorgio, if I remember correctly, there are two studies on gemcitabine maintenance that were negative so what is the data to support the its use?

Giorgio Scagliotti: There is only one study in Europe that showed that continuation with gemcitabine was giving some PFS advantage. I tend to agree with you, but this is not a typical case and not the typical treatment that we are delivering to every patient with squamous NSCLC, I chose this case as a matter of discussion.

Tony Mok: Would you ever consider maintenance nab-paclitaxel as a single agent, after a good response to nab-paclitaxel plus platinum?

Ross Soo: Yes, I would consider it, although there is no data to support it.

Giorgio Scagliotti: No, I would not.

Tony Mok: And then I say, I do not know.
Second-line therapy and beyond

After initially achieving stable disease, the patient relapsed locally and systematically after 9 months. Analysis of a hepatic biopsy confirmed the low levels of PD-L1 and next-generation sequencing revealed the presence of a \textit{PI3K} mutation.

What would you do next, Scagliotti asked the attendees? The most popular option was nivolumab (42.4%), followed by enrolling the patient in a PI3K inhibitor trial (30.3%) and docetaxel either alone (12.1%) or with ramucirumab (12.1%). A very small proportion (3.0%) opted for erlotinib, while no one chose afatinib.

Second- and later-line therapy is dictated by histology, tumour phenotype and components of the first-line regimen, commented Scagliotti. And currently, there are several options available for patients lacking actionable mutations, “let us review the evidence”, he said.

In the phase III REVEL trial, OS was significantly better with the addition of ramucirumab to docetaxel in NSCLC patients regardless of histology. Of note, PFS, ORR and DCR were also significantly improved when ramucirumab, rather than placebo, was given alongside docetaxel\textsuperscript{10}. By contrast, investigations of other antiangiogenesis agents have been positive for some, but not all, outcomes, said Scagliotti, adding that “even if the amount of improvement for each efficacy outcome is irrelevant, if there is consistency amongst the efficacy endpoints, it makes me personally more comfortable.”

He continued: “The introduction of immune checkpoint inhibitors has dramatically changed the landscape of squamous NSCLC therapy.” The key study was the phase III CheckMate 017 trial that showed the superiority of nivolumab over docetaxel in patients with late-stage squamous NSCLC\textsuperscript{11}. Although acknowledging the “dramatic” OS improvement in nivolumab-treated patients, the speaker admitted to reservations regarding the study, specifically with the performance of the control arm, which with a median OS of 6.0 months was “probably the worst control arm” he had seen in over a decade. He added that while it is true that immunotherapy generates long-term benefits and nivolumab was favoured consistently across most prespecified subgroups, “we need to be careful in drawing definitive conclusions from one single study”. Scagliotti drew attention to the fact that almost 50% of treated patients did not get any benefit, a point also raised by Professor Johan Vansteenkiste at the SpringHcalthcare IME symposium at ELCC earlier this year\textsuperscript{12}.

Finally the presenter briefly mentioned the LUX-Lung 8 trial\textsuperscript{13}, which showed that in squamous NSCLC patients OS was significantly longer with afatinib than erlotinib. But is a 1.1 month improvement enough to make a choice in this setting where EGFR TKIs are not frontline choices, he asked?

Future directions

The majority of mutations in squamous NSCLC tumours tend to be in tumour suppressor genes, which is not fertile ground for intervention. However, there are a few genes that have interventional potential – \textit{PIK3CA} is one such target; the gene is mutated in 8–10% of squamous NSCLC cancers and some patients with \textit{PIK3CA} mutation-positive NSCLC have shown responses to GDC-0032, a potent, small molecule inhibitor of PI3K, in a phase I trial\textsuperscript{14}.

Additionally, \textit{CDK4} amplification has been detected in approximately 1% of squamous NSCLC neoplasms and \textit{FGFR} amplification in 15–20%\textsuperscript{15-16}. Agents that target...
these genes are available – palbociclib and AZD4547, respectively – and these, along with GDC-0032, are currently being tested in the previously treated squamous NSCLC setting in the Lung-MAP trial.

Concluding remarks

As we have seen, there are various choices for this patient population, ranging from new platinum agents, such as nedaplatin, to targeted therapies, such as necitumumab, Scagliotti said. He added a note of caution that not all targeted therapies are a success story – for instance, trials of motesanib were stopped by the independent data monitoring committee for toxicity.

Immune checkpoint inhibitors, such as nivolumab, are being actively studied in squamous NSCLC, as are other agents targeting other genes, such as PIK3CA and the CDK4/6 pathway.

References

3. ClinicalTrials.gov.
   https://clinicaltrials.gov/ct2/show/NCT02027428
   https://clinicaltrials.gov/ct2/show/NCT02151149
5. Shukuya T et al. J Clin Oncol 2015; 33 (suppl; abstr 8004)
17. ClinicalTrials.gov.
   https://clinicaltrials.gov/ct2/show/NCT02154490