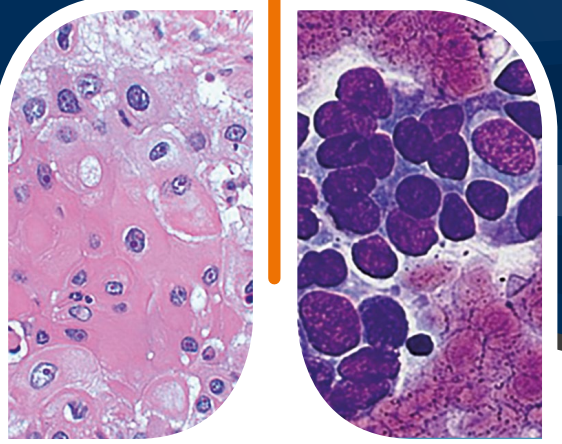

The Treatment Roadmap for Squamous NSCLC

Independent Satellite Symposium at the European Lung Cancer Conference (ELCC)

Geneva, 16th April 2015

Speakers

Solange Peters, Nicholas Thatcher,
Jean-Charles Soria, Enriqueta Felip

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Contents

Dear Colleagues,

This year at the European Lung Cancer Conference (ELCC 2015) in Geneva, I chaired an independent medical education symposium entitled 'The Treatment Roadmap for Squamous NSCLC', which I hope many of you reading this were able to attend.

As healthcare professionals, we are aware just how much the lung cancer landscape is continually evolving. Several new treatment strategies have been developed based on our better understanding of the complexities of the disease process. The molecular characterisation of non-small-cell lung cancer (NSCLC) has opened many new avenues for targeted therapy; however, the majority of these are for non-squamous advanced NSCLC. While immunotherapy will continue to be developed for all histological subtypes, we decided to focus this satellite symposium on the advances to date, and those to come, in the minority subset of squamous NSCLC.

The symposium featured three speakers – Drs Nicholas Thatcher, Jean-Charles Soria and Enriqueta Felip – all of whom gave highly engaging and informative presentations on the current and future treatment options for squamous NSCLC. The symposium ended with a Panel Discussion during which audience members were asked to vote on key questions related to their treatment preferences in specific patient scenarios – it certainly made for a fascinating discussion!

The aim of the symposium was not only to highlight the latest developments in squamous NSCLC, but also to provide insight into how we can use our biological knowledge to both improve treatment pathways and maximise treatment outcomes. If you attended the event, I hope you feel that this symposium met its educational aims and that it will further your understanding of this evolving field and help facilitate your own decision making in the clinic.

For others, I hope this Meeting Report provides an insight into the presentations given and the interesting and provocative discussions that followed.

Yours faithfully,

Solange Peters

Faculty biographies

Solange Peters (Symposium Chair), Head of the Oncology Research Service, University of Lausanne, Switzerland

Dr. Peters is currently in charge of teaching and patient care in the area of thoracic malignancies at the Department of Oncology of Lausanne University. She acts as the local PI of lung trials opened in Lausanne Cancer Centre, focusing on phase I, predictive biomarkers and NSCLC immunotherapy. In addition, she is a co-principal investigator of several other trials. She is co-chair of Swiss Lung Cancer Research group, responsible for trial organisation and coordination, as well as related databases for the ETOP (European Thoracic Oncology Platform) Lungscape project database (member of the Steering Committee), where she is responsible for communication and science coordination.

Dr. Peters is an active member of the educational programme within ESMO (European Society for Medical Oncology). She is Chair of the ESMO Press and Media Affairs Committee, a member of the ESMO Executive Board, ESMO Faculty for Lung and Other Thoracic Cancers and the ESMO E-Learning and CME Committee. She is also Subject Editor for the ESMO Guidelines Working Group. She is in parallel active in IASLC (International Association for the Study of Lung Cancer), where she also acts as a Board Member, and is a member of AACR (American Association for Cancer Research) and EORTC (European Organisation for Research and Treatment of Cancer). Dr. Peters is the president of FOROME (Formation Romande en Oncologie Médicale), Board member of SAMO (Swiss Academy of Multidisciplinary Oncology), and member of SAKK (Swiss Group for Clinical Cancer Research), FMH (Swiss Medical Association) and ASMAC/VSAO (Association of Swiss Interns and Residents).

Dr. Peters was the Associate Editor of *'Lung Cancer'* and became Deputy Editor of the *'Journal of Thoracic Oncology'* (JTO), the official journal of IASLC, in 2013. She is Editor-in-Chief of Cancer Treatment Communications. In addition, she acts as Associate Editor for 'Frontiers in Pharmacology of Anti-Cancer Drugs' and Review Editor for '*Frontiers in Thoracic Oncology'.* She is the author of numerous articles in peer-reviewed publications, as well as book chapters and abstracts, and the co-editor of the book "*Perspectives in Thoracic Oncology*" (UNI-MED), the book series '*Progress in Tumor Research*' and '*New Therapeutic Strategies in Lung Cancers'.*

Nicholas Thatcher, Professor of Oncology, University of Manchester, UK

Professor Thatcher is Professor of Oncology at the University of Manchester, in the School of Cancer and Imaging Sciences at the Christie Hospital NHS Trust and Wythenshawe Hospital. His specialty is clinical and translational research in renal cell cancer, melanoma and lung cancer. He was investigator in key clinical trials into chemotherapy methods and dosages in small-cell lung cancer and non-small-cell lung cancer. He has written several hundred peer-reviewed papers in major scientific medical journals and has directed several PhD theses. He is joint editor of the textbook 'New Perspectives in Lung Cancer'.

Jean-Charles Soria, Professor of Medicine and Medical Oncology, Institut Gustave Roussy, Paris, France

Professor Soria is currently the Chair of Drug Development Department at Gustave Roussy Cancer Center in Paris and is a member of the lung cancer unit with a focus on targeted therapies. Dr. Soria was a member of ESMO Executive Committee from 2008 to 2009, and has served as an ASCO committee member since 2006. He was the scientific chairman of the ECCO-ESMO meeting that was held in Stockholm in 2011. He has contributed to over 340 peer-reviewed publications, including publications in the *New England Journal of Medicine*, the *Journal of the National Cancer Institute* and the *Journal of Clinical Oncology*. He has been appointed as Editor-in-Chief of the *Annals of Oncology* for the period 2014–2018.

Enriqueta Felip, Head of the Thoracic Tumours Group, Vall d'Hebron University Hospital, Barcelona, Spain

Dr. Felip is the Head of Thoracic Cancer Unit and responsible for all lung cancer trials at Vall d'Hebron University Hospital. Research lines of the Lung Cancer Unit include the optimisation of chemotherapy in early-stage disease, evaluation of new drugs, and the use of pharmacogenomic approaches. Dr. Felip is also Associate Professor of Medical Oncology (School of Medicine) at the Autonomous University of Barcelona (UAB). She is member of the Steering Committee of the Spanish Lung Cancer Group, the Spanish Society of Medical Oncology Executive Committee, the European Society for Medical Oncology (ESMO), the American Society of Clinical Oncology (ASCO) and the International Association for the Study of Lung Cancer (IASLC).

Where are we now (and how did we get here)?

Professor Nicholas Thatcher
Christie Hospital, Manchester, UK

Introduction

Nicholas Thatcher opened the symposium by explaining that squamous cell carcinoma (SCC) accounts for approximately one third of non-small-cell lung cancer (NSCLC) cases and represents a "massive economic burden" when considering ill health, disability and premature death alongside the costs of treatment.[1, 2]

The disease is characterised by central tumours involving the main bronchi and the carina area, and these may be cystic and infected. Moreover, SCC patients tend to be male, heavy smokers and older individuals who usually have comorbidity, such as chronic obstructive pulmonary disease, cardiovascular disease and diabetes.[3]

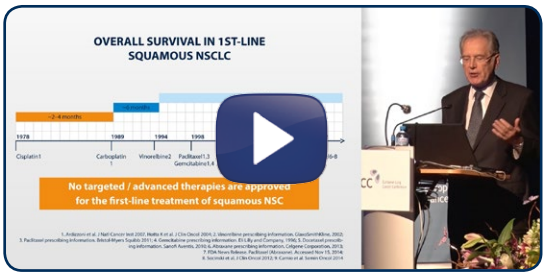
These features, which make SCC "so much more difficult to treat" than other NSCLCs, mean that even relatively small increases in survival can be important to this patient population, he noted.

Proven treatments

The median survival of SCC patients has improved in stepwise 6 to 8 week gains every 10 years with the introduction of chemotherapy agents such as cisplatin, carboplatin, vinorelbine, paclitaxel, gemcitabine, docetaxel and albumin bound (*nab*)-paclitaxel (Figure 1).[4–13]

But median survival plateaued at around 8 to 10 months for patients given one of several different platinum doublet regimens, such as carboplatin plus paclitaxel, cisplatin plus vinorelbine, or cisplatin plus gemcitabine.[14, 15, 16]

And a meta-analysis published in 2005 demonstrated that platinum doublet therapy containing gemcitabine had a small but significant benefit over alternative combinations, amounting to a 3.9% increase in the 1-year overall survival (OS) rate.[17]



SCC – "A treatment challenge"

Gemcitabine is also favoured in Europe because of its ease of use and lack of great toxicity, and good quality of life data, Thatcher added. And although *nab*-paclitaxel has not shown greater survival benefits for SCC, it has favourable toxicity outcomes.

Thatcher explained that the development of drugs, such as pemetrexed, has increased the survival of non-mutated patients with non-squamous NSCLC by approximately 30%.[18]

"This is where the division between squamous and non-squamous started", he commented. The divide has continued with the introduction of targeted treatment against *EGFR* and *ALK* mutations that have increased median survival to 2 or 3 years for some patients with mutated non-squamous NSCLC.

The future

Although *EGFR* mutations are relatively rare in patients with SCC, affecting less than 5%, the receptor is expressed in at least 85% of these tumours and the cell surface receptor protein remains an important target for this population.[19]

The FLEX study assessed cisplatin and vinorelbine alone or in combination with the EGFR inhibitor cetuximab in NSCLC patients with EGFR-positive tumours.[20] The primary endpoint of median OS was

significantly higher in cetuximab-treated patients, at 11.3 months versus 10.1 months for controls, giving a hazard ratio (HR) of 0.871.

Toxicity was high, with grade 3 or 4 febrile neutropenia affecting 22% of cetuximab-treated patients versus 15% of controls, and the risk–benefit ratio was found to be unfavourable overall by licensing authorities.

But Thatcher observed that the outcome for the SCC patient subset was "quite reasonable", with an HR for death of 0.80, although it did go up to the upper confidence interval limit of 1.0.

The FLEX trial results informed the design of the SQUIRE trial comparing gemcitabine plus cisplatin alone or alongside the EGFR inhibitor necitumumab in patients with stage IV SCC.[21] The results, reported at the ASCO meeting in 2014, indicated a significant improvement in OS for patients given the necitumumab combination, at 11.5 months versus 9.4 months for controls and an HR of 0.84.

The vascular endothelial growth factor (VEGF) pathway also remains an important target for NSCLC, despite the lack of biomarkers for sensitivity, with both bevacizumab and nintedanib approved in Europe for non-squamous patients, and ramucirumab in the USA for both SCC and non-squamous populations.

Thatcher also touched on the "excitement" on the development of therapies enhancing T-cell proliferation activation, including the complex phase II trial investigating ipilimumab, a monoclonal antibody against cytotoxic T lymphocyte-associated antigen-4, versus placebo, both given in combination with paclitaxel and carboplatin.[22]

The results indicated that phased, but not concurrent, ipilimumab therapy with carboplatin and paclitaxel offers significantly better immune-related progression-free survival (PFS) than chemotherapy with placebo for patients with SCC. But this group had just 57 patients (HR=0.48) and a phase III trial for SCC patients is now underway.

Finally, Thatcher discussed the development of targeted agents against the programmed death ligand-1 (PD-L1) and programmed cell death-1 (PD-1) and their potential role in the treatment of SCC by exposing the tumour to the immune system.[23]

Phase III first-line, second-line, maintenance and safety trials are now underway for pembrolizumab, nivolumab, MEDI4736 and MPDL3280A in SCC and non-squamous NSCLC. In particular, Thatcher highlighted the CHECKMATE 017 randomised study where the second-line PD-1 inhibitor nivolumab is reported to have achieved a 3.2-month gain in survival in SCC patients compared with docetaxel. More details on this "very good result" are now expected.

Future potential targets for SCC include DDR, FGFR, PTEN, DDR, PIK3CA and EGFR vIII.[24, 25, 26]

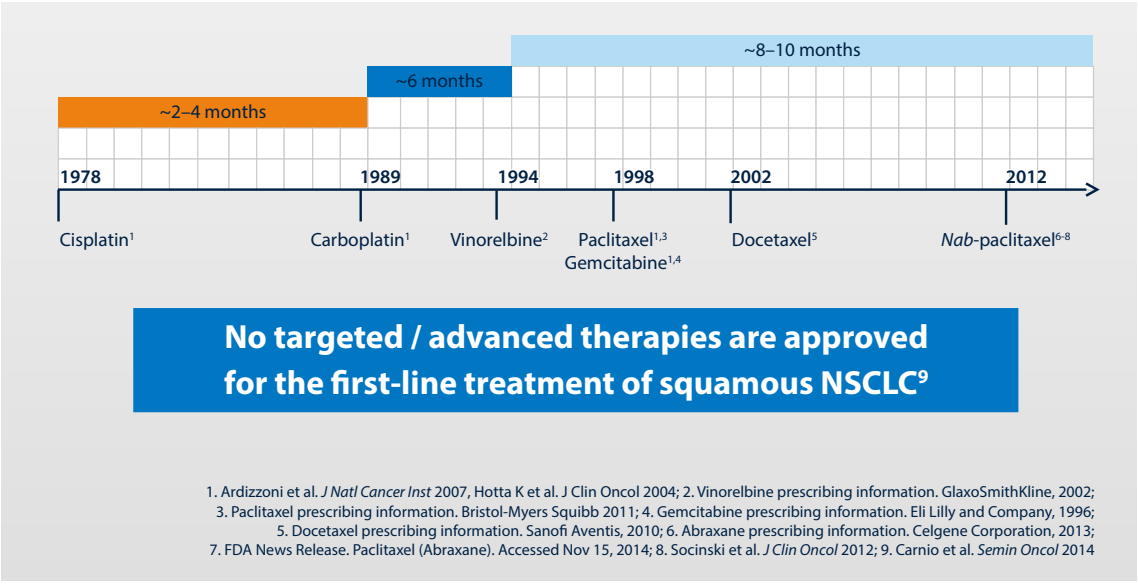


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Figure 1 Overall survival in first-line squamous NSCLC

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Molecular characterisation of lung SCC

Professor Jean-Charles Soria
Institut Gustave Roussy, Paris, France

Introduction

NSCLC is classified as SCC if at least 10% of the tumour bulk has squamous epithelium with keratinisation and/or intercellular bridges; there are two histological variants, papillary and basaloid, the latter of which indicates a poor prognosis. Identification has been aided by immunohistochemistry, with SCC shown to be positive for the biomarker P63 and negative for TTF1.

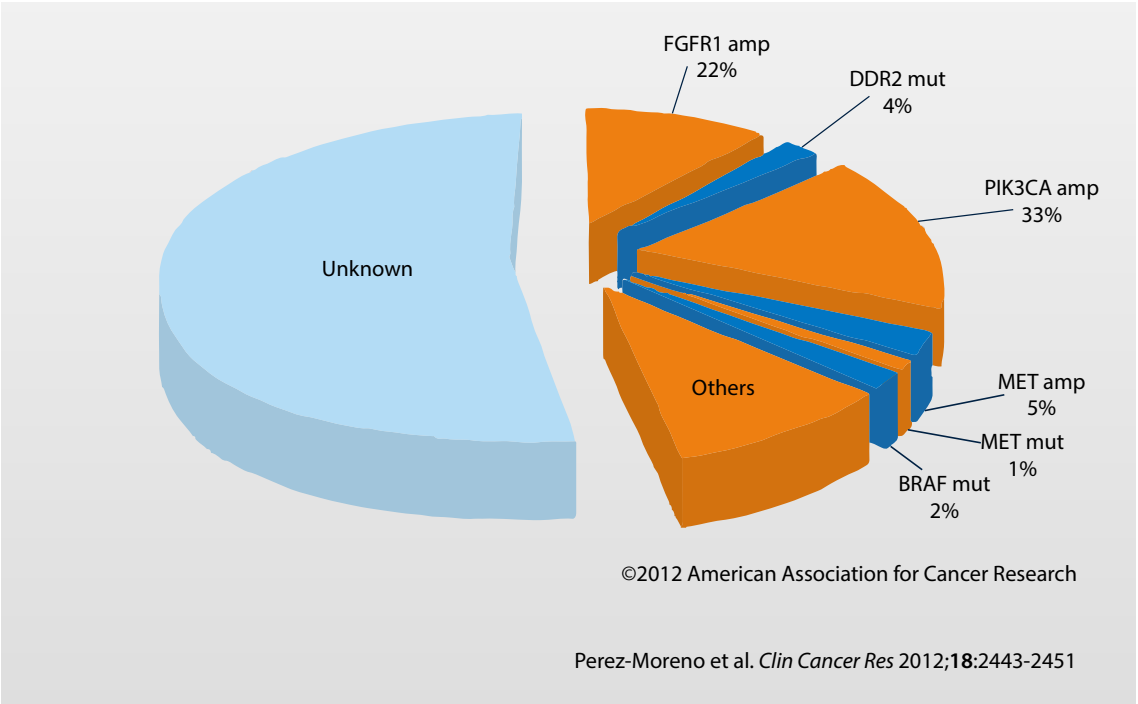
SCC has become less common in France coinciding with the fall in the number of people smoking unfiltered cigarettes, and this mirrors trends in the USA, where SCC has fallen from around 30% of lung cancer diagnoses in 1979 to 20% in 1997.[1]

Unmet needs in SCC NSCLC

Targeted therapies for NSCLC have made greater advances in patients with adenocarcinoma histology than with SCC histology,[2–6] where second-line therapeutic options for SCC recommended by the National Comprehensive Cancer Network include docetaxel, gemcitabine and erlotinib,[7] but there are no ESMO recommended treatments.[8]

Jean-Charles Soria highlighted the large number of known oncogenic drivers for NSCLC adenocarcinoma in 2010 compared with that for SCC, where only PIK3CA and BRAF had been identified.

However, molecular characterisation of SCC is now much better understood thanks to advances in



Perez-Moreno et al. *Clin Cancer Res* 2012;**18**:2443-2451

Figure 2 Frequencies of potentially actionable / targetable genetic abnormatlities present in SCC of the lung

DNA sequencing methodologies, moving from gel-based systems to capillary sequencing and parallel sequencing,[9] as well as the substantial reduction in the cost of next generation sequencing from around 2008 onwards.[10]

Histology is increasingly guiding clinical decisions, using tumour samples taken from resected tissue, from computed tomography (CT)-guided biopsy, and from endobronchial ultrasound or pleural fluid.

"With a simple 18-gauge needle and a CT-guided biopsy, you have more than enough material to perform a full next generation sequencing of a patient, even exome sequencing", Soria said.

The Cancer Genome Atlas (TCGA) initiative has accelerated the molecular characterisation of SCC (Figure 2), publishing data in 2012 for samples taken from 178 patients, including whole genome sequencing for 19 samples and microRNA sequencing for 159 samples.[11]

This has allowed identification of structural DNA changes including chromosomal arm gains of 3q and 5p. Focal copy number alteration analysis for each chromosome has identified amplification targets, including *EGFR*, *SOX2* and *FGFR1*. Other opportunities may include *MCL1* and *MDM2*. Deletions that may become actionable include loss of *CDKN2A* or *PTEN*.

FGFR1 amplification in chromosome 8p12 is more frequent in SCC than in adenocarcinoma or non-squamous carcinomas, affecting around 10% of patients,[12] and further research is now ongoing to find out if *FGFR1* is a truly actionable disease target and a true oncogenic driver, Soria said.

The TCGA also revealed that SCC is the NSCLC with the highest mutational load, associated with exposure to carcinogens.[11] It has been speculated that there may be a correlation between mutational load and the level of cell response to PD-1 blockade and anti-PD-L1 agents that goes across different tumour types.[13]

Indeed a recent paper in *Science* demonstrated "very clearly" that the overall mutational load in lung cancer is a "good predictor" of the activity of anti-PD-1,[14] he commented.

Commercial reports in the future will say not only if a patient is positive for specific mutations but whether a patient's mutational load index is high, medium or low, and this could help to decide whether or not to use immunotherapy, Soria explained.

The TCGA identified SCC gene alterations in the oxidative stress response pathway in 34% of patients, and in up to 62% of patients with the classical subtype. These include *KEAP1*, *CUL3* and *NFE2L2*. SCC also shows alterations in genes that are involved in squamous differentiation in 44% of patients, affecting *SOX2*, *TP63*, and *NOTCH1*, *NOTCH2*, *ASCL4* and *FOXP1*.[11]

While there are not yet drugs targeting TP63 – "the day we have one will change our lives" – Soria noted that NOTCH inhibitors are now being explored in the phase I setting. Anti-NOTCH therapy is hindered by the presence of both activating and inactivating mutations but he commented "NOTCH alteration and inhibition is going to be an interesting story in future years."

Whole genome sequencing has also revealed the complexity across SCC samples, with significant variation in the number of translocations, raising the question whether the level of genomic complexity correlates with number of mutations.

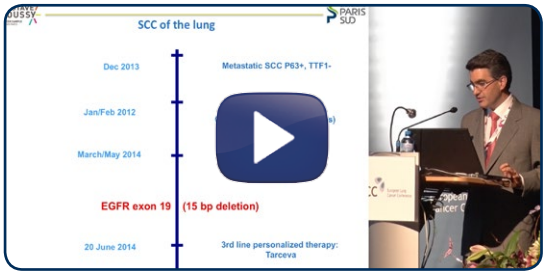
Patient management

A frequent debate in the clinic is whether *EGFR* genetic testing should be performed in patients with SCC who are not heavy smokers. Yes, said Soria, because some patients do test positive.

A high *EGFR* copy number and protein overexpression is observed in SCC.[15, 16] Across the whole of the ErbB pathway, around 1% of patients will test positive for a mutation in the *EGFR* tyrosine kinase domain and between 5% and 8% for the *EGFR* variant III mutation,[16] with a further 1% testing positive for mutations in ErbB3[17] and 2% to 3% for ErB4 mutations.[18]

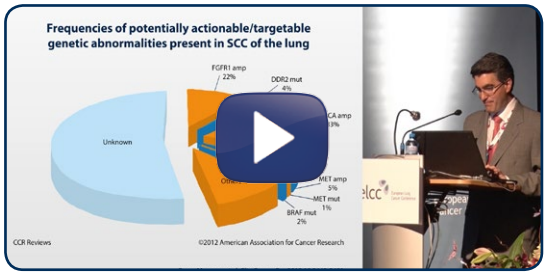
The EGFR tyrosine kinase inhibitor erlotinib is a second-line option for SCC,[7] with a phase III clinical trial, LUX-Lung 8, now underway comparing afatinib versus erlotinib after first-line platinum-based chemotherapy.[19]

Soria described a case study of a metastatic SCC patient who experienced disease progression after both first-line cisplatin and vinorelbine and second-line docetaxel. On finding the patient smoked less than 5 packs of cigarettes per year, she underwent genetic testing and this revealed a 15 base-pair deletion in *EGFR* exon 19. Erlotinib therapy shrunk her brain metastases and the patient has had 1.5 years without disease progression.



EGFR mutation in SCC – a case study

Soria therefore concluded that in 2015 there are increasing genetic and molecular opportunities for SCC therapy, as well as the possibility of immune modulation in SCC,[15] with PD-1 and PD-L1 being important targets.[8, 20]



Molecular advances in SCC and the need for tissue samples

It is therefore key for SCC management to get enough tissue for *EGFR* analysis where possible. In the future, tumour biopsies and blood draws will improve cancer diagnosis, define prognosis, determine sensitivity to chemotherapy and targeted therapies, and identify opportunities for treatments targeting oncogene addiction and immunotherapy.

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Current route and future directions

Dr. Enriqueta Felip
Vall d'Hebron University Hospital, Barcelona, Spain

Introduction

As explained by Professor Nicholas Thatcher, treatment options for patients with SCC have been limited to platinum-based doublet therapy in combination with gemcitabine, taxane or vinorelbine, the only first-line option, and either docetaxel or erlotinib available as second-line therapy.

Recently, however, developments have been made in the treatment of SCC, both in the first-line and second-line setting, some of which Enriqueta Felip outlined in her presentation.

First-line treatment of SCC

Nab-paclitaxel was the focus of a phase III trial with 1052 patients who were randomly assigned to receive carboplatin together with either *nab*-paclitaxel or paclitaxel. The primary endpoint, the objective response rate (ORR), significantly favoured the *nab*-paclitaxel treatment arm, both in the overall study population (33 vs 25%) and in the subgroup of patients with squamous histology (41 vs 24%). However, median OS did not vary significantly between the *nab*-paclitaxel and paclitaxel groups in patients with SCC.[1]

The benefit of *nab*-paclitaxel in SCC may be further elucidated in an ongoing phase III trial in which patients are initially given four cycles of *nab*-paclitaxel and carboplatin. Patients who achieve a response are then randomly assigned to continue with *nab*-paclitaxel or to receive best supportive care. The primary endpoint of the trial is PFS.[2]

Anti-EGFR strategies are also being considered in this patient population as a vast majority of patients have high EGFR expression as assessed by immunohistochemistry and a number of patients have an increased copy number of the *EGFR* gene.

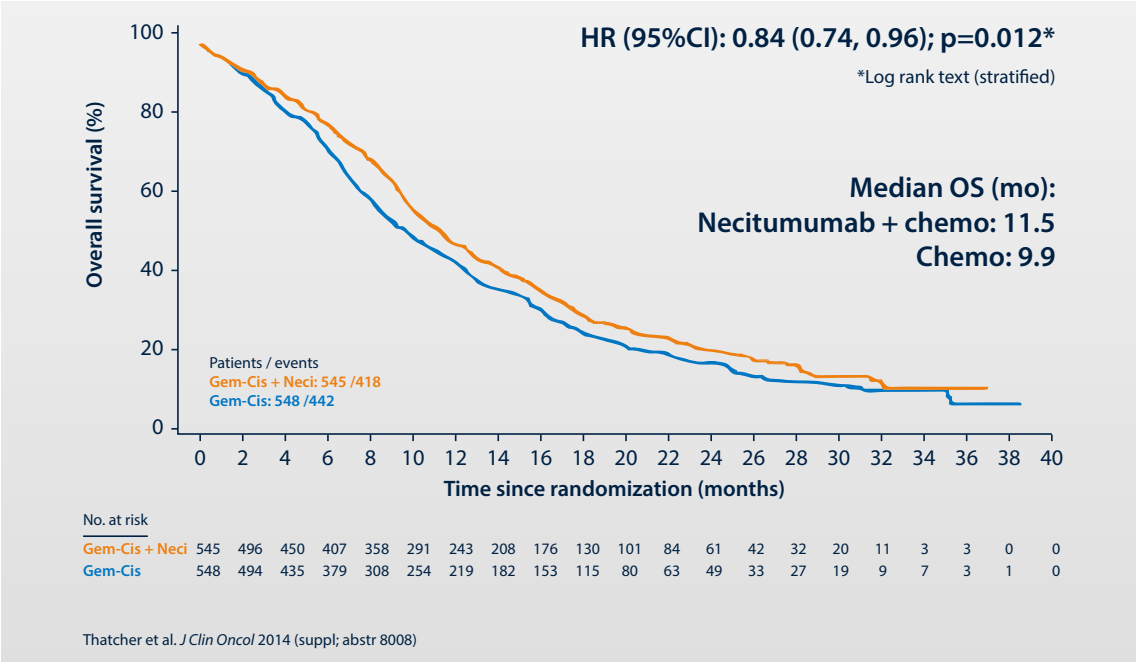


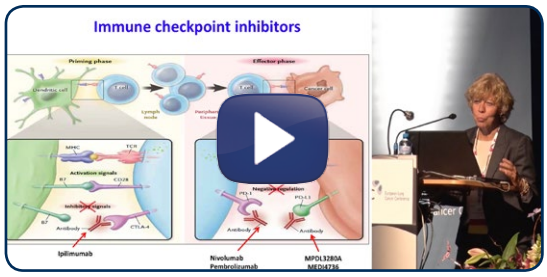
Figure 3 SQUIRE: Overall survival

In the phase III randomised SQUIRE trial of SCC patients, treatment with the second-generation EGFR inhibitor necitumumab together with gemcitabine plus cisplatin (n=545) led to a significantly prolonged OS compared with gemcitabine and cisplatin (n=548), at a median of 11.5 versus 9.9 months. Median PFS was also improved at 5.7 and 5.5 months, respectively (Figure 3).[3]

Second- and third-line treatment of SCC

Anti-EGFR agents have also been explored in second-line therapy. The LUX-Lung 8 trial compared the anti-EGFR tyrosine kinase inhibitors afatinib and erlotinib in patients with advanced SCC who had failed platinum-based chemotherapy. Median PFS was 2.5 months in the 335 patients in the afatinib group and 1.9 months in the 334 erlotinib-treated patients, a statistically significant difference. The final OS survival results of this trial are awaited.[4]

Although positive results have been obtained with other approaches, the immune checkpoint inhibitors, such as the anti-CTLA-4 antibody ipilimumab, are the class of drugs that "probably will change the treatment algorithm for patients with [SCC] histology", said Felip.



Immune checkpoint inhibitors and SCC

A phase II trial in which participants were randomly assigned to receive paclitaxel plus carboplatin either with phased (n=68) or concurrent (n=70) ipilimumab or with placebo (n=66) favoured the phased ipilimumab regimen in terms of OS for patients with squamous histology, at a median of 10.9, 6.2 and 7.9 months, respectively.[5] Despite the "very small" number of patients, these findings have led to a phase III trial in SCC patients, the results of which are awaited, Felip commented.

The PD-1 inhibitor nivolumab was evaluated in CHECKMATE-063, a phase II trial comprising 117 SCC patients who had previously been treated with at least two systemic therapies. The ORR, disease control rate and 1-year OS was 14.5%, 40.0% and 40.8%, respectively, but Felip noted that "importantly" the median duration of response was not reached. Moreover, at the time of data analysis, there were 77 patients with an ongoing response.[6]

Furthermore, Felip noted that the CHECKMATE-017 trial showed that in patients with SCC, nivolumab (n=135) resulted in "clearly better survival" compared with docetaxel (n=137), the standard second-line treatment for this patient population, with median OS of 9.2 versus 6.0 months, a significant difference.[7]

Nivolumab has since been approved by the US Food and Drug Administration (FDA) for the treatment of patients with metastatic squamous NSCLC who have progressed on or after platinum-based chemotherapy.[8] And several trials of nivolumab and other anti-PD1 and anti-PDL1 agents, such as pembrolizumab and MEDI-4736, are ongoing.[9]

Angiogenesis is a hallmark of cancer, and anti-angiogenic approaches have been active in various solid tumours, including NSCLC. However, this strategy has thus far largely not been successful in SCC patients, and agents such as bevacizumab, sorafenib and motesanib have not been approved for SCC treatment, "probably due to toxicity issues", observed Felip.[10, 11, 12]

However, the anti-VEGFR2 antibody ramucirumab has shown promise in NSCLC. In the phase III REVEL trial, patients with stage IV NSCLC were randomly assigned to receive docetaxel in combination with either ramucirumab (n=628) or placebo (n=625). Ramucirumab-treated patients had a significantly improved OS and PFS compared with those given placebo.

When just patients with squamous histology were considered, median OS in the ramucirumab (n=157) group was numerically higher than that in the placebo (n=171) group, but the difference was not significant, which could be because of the small sample size. By contrast, ramucirumab significantly prolonged median PFS, at 4.2 versus 2.7 months.[13]

Conclusion

For patients with SCC, although treatment options have been limited, positive results have been obtained in the first-line setting and various approaches have led to improvements in survival in the second-line setting.

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Panel Discussion report

The first question put to the panel – what percentage of SCC patients carry mutations to *EGFR*? – was correctly answered by 63.2% of the audience as less than 5%, and this explains why patients are not systematically screened for the mutation.

The panel Chair, Dr. Solange Peters, asked Professor Jean-Charles Soria whether there was any indication that the epidemiology of *EGFR* mutations in SCC patients varies according to ethnicity.

Soria explained that some unpublished data indicates that mutation rates are higher in Asians than Caucasians, with mutations occurring in perhaps up to 15% of Asian patients. Reflex testing is prevented by budget costs so it is important to consider patients for testing using clinical features such as ethnicity, he suggested.

Soria also stated that he thought there was no evidence to suggest that EGFR targeted therapy differs in SCC and non-squamous patients and, in response to Professor Nicholas Thatcher's question, noted that there are no data to support the hypothesis that the efficacy of targeted therapy may be linked to the proportion of tumour cells affected by the mutation.

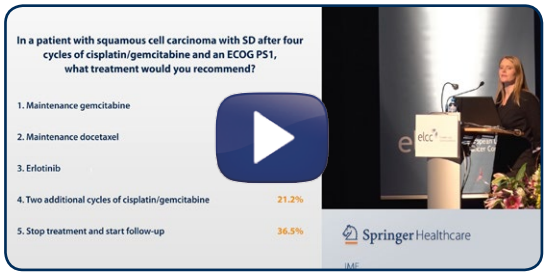
The panellists discussed their treatment recommendations for SCC patients with stable disease after four cycles of cisplatin/gemcitabine and an Eastern Coopoerative Oncology Group performance status of 1.

Treatment options for SCC patients with stable disease after first-line therapy

There are no "right answers" to this question, Peters explained. Over a third (36.5%) of the audience stated they would stop treatment and begin follow-up, while 17.1% choose erlotinib, an option associated with a small survival benefit. Maintenance docetaxel or gemcitabine have not proven to be active and adding a further two additional cycles of chemotherapy has not shown to improve outcomes.

Peters stated she occasionally uses maintenance gemcitabine in this situation, whereas Thatcher emphasised that, in his opinion, erlotinib is the only option with a sufficient evidence base for treatment. Both Dr. Enriqueta Felip and Soria said they consider additional cycles of chemotherapy if the patient has no toxicity, with Soria also using maintenance gemcitabine for highly symptomatic patients who are at risk of rapid progression.

The panellists also considered their recommendations for the second-line treatment of a patient with stage IV SCC after progression with a platinum doublet and a chemotherapy-free interval of 3 months.



Second-line preferences for stage IV SCC and disease progression

The majority, at 57.1%, of the audience, preferred to go to clinical trial for an anti-PD1 or anti-PD-L1 agent if feasible, while 20.1% chose docetaxel plus ramucirumab where available, and smaller numbers indicated they would recommend docetaxel, erlotinib or afatinib where possible.

Most people at this meeting have been convinced that there is room for immunotherapy in SCC, Peters commented, noting that regulatory authorities are now reviewing the efficacy of docetaxel plus ramucirumab.

Thatcher said all options were reasonable, with the exception of docetaxel alone as the REVEL trial data indicate there is "no reason" not to give the drug alongside ramucirumab. And he suggested that the comparator for anti-PD1 or anti-PD-L1 trials should now be docetaxel plus ramucirumab.