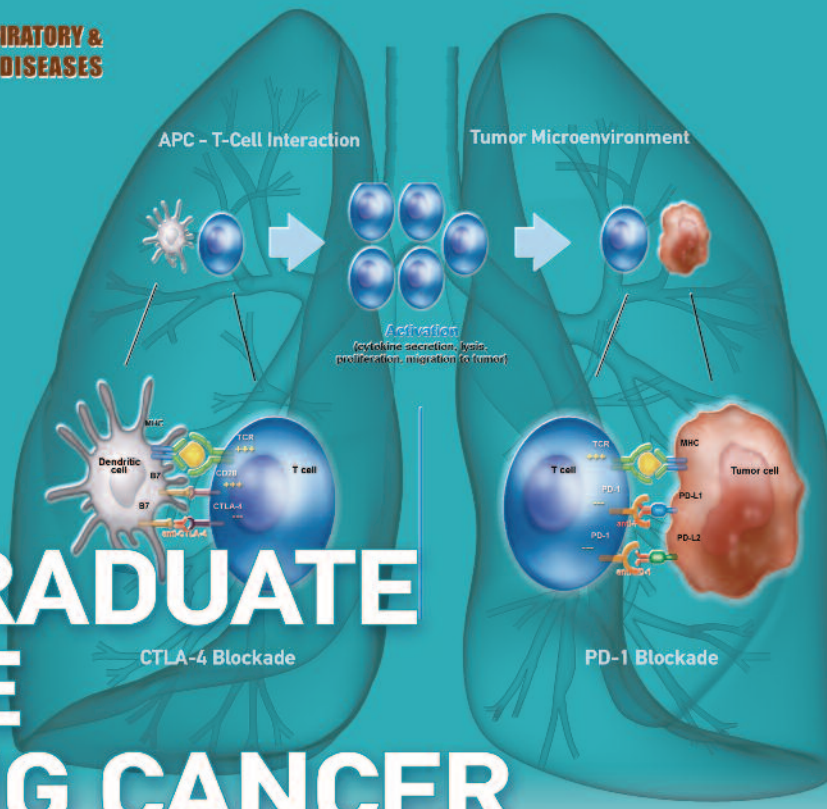
HELLENIC SOCIETY OF RESPIRATORY & OCCUPATIONAL CHEST DISEASES



POSTGRADUATE COURSE ON LUNG CANCER

28/9-1/10/2017 CHALKIDIKI - ATHOS PALINI

PROGRAM

FORUM Congress & Travel

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UNDER THE AUSPICES OF

ERS EUROPEAN RESPIRATORY SOCIETY

HELLENIC SOCIETY OF RESPIRATORY & OCCUPATIONAL CHEST DISEASES

POSTGRADUATE COURSE ON LUNG CANCER

Athos Palace and Pallini Beach, Chalkidiki, Greece

28/9/-1/10 2017

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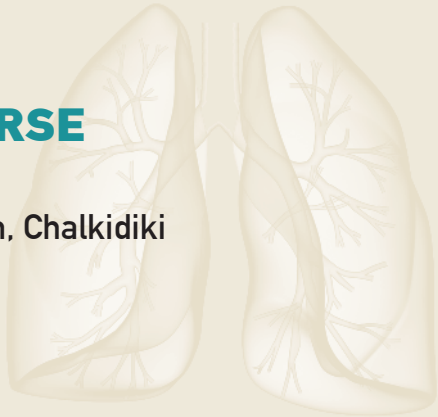
POSTGRADUATE COURSE ON LUNG CANCER

in Athos Palace and Pallini Beach, Chalkidiki

28/9/-1/10 2017



Dear Colleagues

Recent advances in the diagnosis and management of Lung Cancer have brought an optimistic view in the improvement of the therapeutic outcomes. International scientific meetings offer opportunities for communication between experienced and junior scientists and clinicians in this area of research for exchanging experiences, ideas and information. For these reasons, the Hellenic Society of Respiratory and Occupational Chest Diseases is organizing an International Postgraduate Symposium on Lung Cancer on 28-30 September 2017 in Chalkidiki at Athos Pallini Resorts.

The above Symposium will be under the auspices of the European Respiratory Society.

In this educational course, the participants will have the opportunity to obtain practical information regarding the clinical significance from the translation of the histological and molecular profile of the tumor and how this integrate in the therapeutic algorithm changes in the clinical practice.

Additionally, the participants will gain knowledge for the early diagnosis of Lung Cancer and the influence on the final prognosis.

International faculty members will present the latest clinical data regarding the implementation of targeted therapies on Lung Cancer.

Finally, a hands-on session will be programmed for a practical view of the new therapeutic options.

On behalf of the Organizing Committee we cordially welcome you all in Chalkidiki, at Athos Pallini Resorts for our innovative and educational meeting!

The chairmen of the meeting

Jean-Paul Sculier Arnaud Scherpereel Konstantinos Zarogoulidis

Thursday 28/9/2017

15.00-19.30 **Registration**

15.50-16.50 Screening in lung cancer: Present and Future
M. Gaga

16.50-18.20 Chairs: **W-H Schmidt – Th. Kontakiotis**
Diagnostic techniques for Lung cancer

The role of PET/CT in the management of lung cancer
G. Arsos

The evolving role of EBUS in LC staging
W-H Schmidt

EBUS: pros and cons
P. Zarogoulidis

The role of thoracoscopy under local anesthesia in the management of lung cancer
R. Heine

18.20-18.30 **Coffee Break**

18.30-19.30 Chairs: **J. Chorostowska – K. Zarogoulidis**
Histological classification of Lung Cancer: The role of immunohistochemical assessment

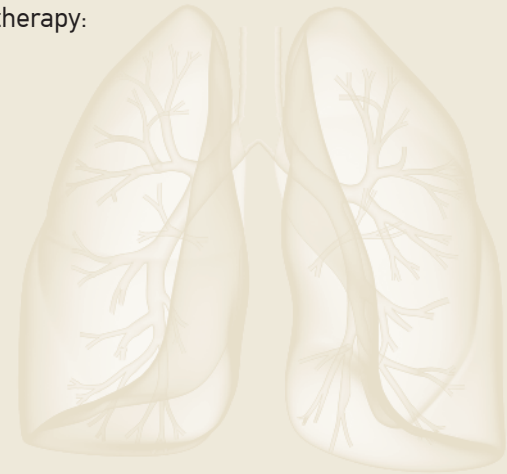
Molecular signature of Non-Small Cell Lung Cancer
J. Moldvay

Preselecting candidates for immunotherapy: current challenges in testing
J. Chorostowska

Liquid Biosies
E. Kosmidis

19.30-20.00 Chair: **R. Pirker – P. Zarogoulidis**
Lecture
Are all anti-PD-L1 agents the same? Opportunities for Differentiation
N. Peled

20.30 **Opening Ceremony**



Friday 29/9/2017

08.45-09.45 Chairs: **N. Barbetakis – G. Drosos**
Early Stage NSCLC

Surgery approach for I-II stage NSCLC
K. Tsakiridis

Radiotherapy-recent developments (ablation included)
D. Misailidou

Induction/adjuvant NSCLC treatment
B. Perin

09.45-10.45 Chairs: **A. Rapti – P. Papakotoulas**
Locally advanced NSCLC

The place of surgery for N2 disease
Th. Karaiskos

The role of chemoradiotherapy vs trimodality treatment
J. VanMeerbeeck

10.45-11.45 Chairs: **J-P Sculier – K. Syrigos**
Personalized treatment of advanced IIIB-IV NSCLC

According to performance status, histology and the extent of the disease
B. Perin

Personalized treatment of advanced IIIB-IV NSCLC" according to predictive genetic biomarkers and immunohistochemical assessment of the tumor
R. Pirker

11.45-12.30 Chairs: **K. Zarogoulidis – Th. Tsiouda**
Lecture
Optimal treatment of neuroendocrine tumors of the Lung
E. Boutsikou

12.30-12.45 **Coffee Break**

12.45-14.15 Chairs: **I. Giozos – N. Secen**
Perspective targeted therapies in NSCLC

Therapeutic algorithm for EGFR-mutated patients
A. Rapti

Treatment options after Progression in advanced EGFR-Mutated NSCLC
I. Giozos

14.15 **Lunch Break**

16.00-17.30 Chairs: **B. Perin – A. Scherpereel**
Emerging Targeted therapies for Lung Cancer (I)

Targeting the BRAF/MEK pathways
R. Pirker

Targeting the MET pathway in the management of NSCLC
G. Lazaridis

Management of ALK+ROS1+ NSCLC: what is the evidence?
V. Karavasilis

17.30-19.00 Chairs: **Ch. Andreadis – J. VanMeerbeeck**
Emerging therapies for Lung Cancer (II)

The role of angiogenesis in the management of advanced lung cancer neovasculature in the oncogenic metastatic potential-therapeutic options
Ch. Emmanouilides

Harmonizing patient outcames by selecting the right treatment for the right patient at the right time
A. Charpidou

19.00-19.30 **Satellite Lecture**
Sponsored by Bristol - Myers Squibb

Immunotherapy in Non-Small Cell Lung Cancer:
From Monotherapy to Combinations

A. Rapti

Saturday 30/9/2017

09.00-10.30 Chairs: **J. Moldvay – J-P Sculier**
Perspectives in the systemic treatment of Small Cell Lung Cancer

Multimodality approaches for limited stage SCLC (including PCI)
J.-P. Sculier

Systemic treatment of metastatic SCLC
N. Secen

SCLC treatment in the era of biological agents
Ch. Tolis

SCLC surgery: for whom and with which strategy
Ch. Foroulis

10.30-11.30 Chairs: **G. Lazaridis – D. Spyratos**
Special issues in everyday practice

Influence of age, comorbidities and performance ptatus (PS) in the outcome of lung cancer treatment
K. Zarogoulidis

Palliative care for the lung cancer patient; Management of Lung Cancer pain
S. Lampaki

11.30-12.00 **Coffee Break**

12.00-13.30 Chairs: **V. Karavasilis – J. Chorostowska**
Immunotherapy

Assessment of Biomarkers in Immune Checkpoint Inhibitors
D. Hatzibougias

The best choice of immunotherapy in Lung Cancer treatment
K. Syrigos

Anti PD-1/L1 combined with other agents in NSCLC
J. VanMeerbeeck

13.30-15.00 **Chairs: A. Scherpeereel – Ch. Tolis**
Special Issues

Current and future perspectives in the treatment of mesothelioma
A. Scherpereel

Management of malignant pleural effusion
D. Spyratos

15.00 **Lunch Break**

17.00-18.30 **5. Case study presentations, A. Scherpereel, D. Spyratos, P. Zarogoulidis, S. Lampaki**

18.30-19.00 Chair: **D. Spyratos**
Lecture
Obesity and cancer
K. Pazaitou

Sunday 1/10/2017

Only for speakers and chairmen

09.00-13.00 Highlights and future directions of Lung Cancer treatment in the new era
Conclusions

GENERAL INFORMATION

VENUE AND DATES

ATHOS-PALINI HOTEL • Chalkidiki • Greece • 28/9-1/10/201

CONGRESS FEE

	UNTIL 10/08 /2017	FROM 11/08/2017
Global Fee	150€	180€
ERS Members	120€	150€
Trainees	80€	100€

In the above prices is not included VAT 24%

HOTEL	ATHOS PALACE	PALINI BEACH
SGL	90 €	90 €
DBL	110 €	110 €

Breakfast and all taxes are included

Important: Congress fee covers attendance of the conference, congress bag and participation to the Scientific Program.

In all participants will be given a certificate of participation with credits in the framework and continuing medical education (CMC/ CPD) provided only under the condition that fulfill all participation requirements.

CANCELLATION POLICY

Written Cancellation up to August 10, 2017: full refund minus bank charges and 20 Euros handling fees. From 11th of August will be no refund.

CONGRESS SECRETARIAT

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Bristol-Myers Squibb
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LECTURES

The evolving role of EBUS in Lung Cancer staging

Bronchoscopy allows the pulmonologist to directly visualize the central airways until the 5th-6th generation of the bronchial tree which is less than 1% of all divisions with 2^{20-23} branches. Looking beyond mucosa or finding consolidations along a bronchus sign raised enormously the potential of bronchoscopic techniques. As radial EBUS is clearly linked to one of the main issues in interventional pulmonology, the diagnosis of an incidental solitary pulmonary nodule (iSPN), the longitudinal EBUS has gained its leading place in decision of lymph node (LN) involvement in N2 or N3 malignant disease substituting nowadays 70% of all mediastinoscopies. Both techniques have even more broadened the potential in combination with other technology like Electromagnetic Navigation or (Cone Beam) CT. New development is added for these above mentioned two key situations: The announced INOD system based on radial EBUS technology allowing to see via US real time the peripheral transbronchial needle access into a nodule and Elastography to further discriminate non-invasively LN architecture in case of longitudinal EBUS. Furthermore beside the exploration of the above mentioned classical fields the EBUS-technology allows the interventional pulmonologist to enter into new organs with percardial sac puncture or infiltration of sympathicus nerve. Even though invented as a diagnostic tool EBUS-TBNA has shown its value in special therapeutic lung cancer situations. The variety of systems and tools has grown over time which made EBUS a story of success the last 2 decades.

The role of thoracoscopy under local anesthesia in the management of lung cancer

R. Heine

The assessment of the prognosis and the initiation of an adequate therapy for lung cancer are dependent on an exact staging. In cases of pleural effusions in early or local advanced lung cancer the dignity of pleural effusion is important to exclude or to prove stage 4 (M1a or M0).

The first step to clarify the dignity of effusion is the puncture and the cytological examination. In own investigations the sensitivity of cytological examination is 88%, the specificity is 98% and the negative predictive value 85%. When malignant cells are detected no further investigations are necessary.

In negative cases malignancy is not excluded and thoracoscopy should be performed. If resection of the tumor is possible the surgeon can perform VATS and exclude the pleural metastasis before resection.

Thoracoscopy under local anesthesia is indicated when the lung cancer is local advanced (resection is not indicated) or if the cytological result in the effusion is suspicious. This strategy is also appropriate if the patient is functionally not operable.

Thoracoscopy under local anesthesia is a very simple method with a low rate of complications. We use a thoracoscop (30A view) with a diameter of 4 mm. The diameter of trocar is 6mm. With this single port technique you can clarify the reason of pleural effusion in nearly 100%. If pleural metastases are found talc poudrage is possible in one session.

Liquid Biopsies

Efstratios K. Kosmidis

Tissue biopsies have been used by clinicians to diagnose and manage disease for more than 1,000 years. In oncology, biopsies allow the histological definition of the disease and, lately, its genetic profiling. However, recent advances in cancer research regarding tumor heterogeneity have highlighted tumor biopsy limitations. In light of these limitations, new ways to observe tumor genetics and dynamics have evolved. The specific detection of cell-free tumor DNA (cftDNA) in plasma has been shown to correlate with tumor burden, to a change in response to treatment or surgery, and to indicate that subpopulations of tumor cells that are resistant to treatment can proliferate in response to therapy. Another valuable source of tumor related information is Circulating Tumor Cells (CTCs). They have been detected in various carcinomas but are extremely rare in healthy subjects and patients with nonmalignant diseases. A third tumor related source of genetic material is actively released vesicles (carrying RNA, DNA and protein), termed exosomes. It has been shown that tumor exosomes stimulate tumor cell growth, suppress the immune response and induce angiogenesis and even be part of the metastatic process. ëLiquid biopsies£ is an evolving field which shows great potential for early prognosis, prediction and prognosis, resistance emergence and disease monitoring in our fight against cancer. Nevertheless, key challenges lie ahead and not all results consistently support their application in the clinic. Clinical applications of liquid biopsies, perspectives and limitations will be discussed during the course with an emphasis on lung cancer.

OPTIMAL TREATMENT OF LUNG NEUROENDOCRINE (CARCINOID) TUMORS

Neuroendocrine tumors (NETs) comprise a heterogeneous group of malignancies that arise from neuroendocrine cells throughout the body, most commonly originating from the lungs and gastrointestinal tract. Lung NETs can be classified as well differentiated (low-grade typical carcinoids [TCs] and intermediate-grade atypical carcinoids [ACs]) and poorly differentiated (high-grade large cell neuroendocrine carcinoma or SCLC)

Lung neuroendocrine tumors (NETs) are neoplasms that are characterized by neuroendocrine differentiation and often by indolent clinical behavior. Typical lung NETs seldom metastasize and have an excellent prognosis, even when regional lymph nodes are involved; atypical lung NETs have a higher likelihood of metastases and a worse prognosis, particularly if mediastinal nodes are involved.

Surgery remains the only curative option for TCs/ACs, but there is a lack of consensus between lung NET management guidelines regarding optimal treatment approaches in the unresectable/metastatic setting on account of the limited availability of high-level clinical evidence. As a result, a multidisciplinary approach to management of lung NETs is required to ensure a consistent and optimal level of care. Systemic treatment options for advanced NETs of all primary tumor sites include SSAs (octreotide and lanreotide), targeted therapy (everolimus, sunitinib, and bevacizumab), interferon, chemotherapy, and PRRT (for SSTR-expressing NETs).

RADIANT-4 is the first phase III trial involving a large subpopulation of patients with advanced well-differentiated lung NETs to report reductions in the risk for disease progression and death with everolimus over placebo. This led to the recent FDA/EMA approval of everolimus½the first agent approved for advanced lung TCs/ACs. To further improve evidence-based care, additional randomized controlled trials in patients with lung carcinoids are needed.

Treatment Options after Progression in advanced EGFR-Mutated NSCLC

The landscape of treatment for advanced stage NSCLC has changed dramatically the last decade with the discovery of EGFR mutations and their prognostic and predictive role.

In our days the first systemic treatment for an EGFR mutated patient is a 1st or 2nd generation EGFR-TKInhibitor, but unfortunately in almost 1 year later acquired resistance to treatment will develop. The vast majority 50%-60% of this resistance refers to T790M mutation on exon 20 and is overcoming with an 3rd generation EGFR-TKI which is Osimertinib. Osimertinib in AURA 3 Study presented significantly better efficacy than the combination of Platinum-Pemetrexed therapy in advanced stage NSCLC patients EGFR-mutated who failed in EGFR-TKI as 1rst line treatment.

The acquired resistance to TKI s has to be confirmed via plasma or tissue sample and then to decide the treatment approach upon the type of resistance e.g. histological transformation to SCLC, bypass signaling, target modification and other mechanisms.

So, the main options after failure of 1rst line TKI£ s for EGFR mutated patients are the confirmation or not for T790M presence in order to start Osimertinib or discover transformation to Small Cell Lung Cancer for conventional chemotherapy or find other mutation according to the re-biopsy in order the patient to participate in a clinical trial.

Managing Resistance to EFGR- and ALK-Targeted Therapies

Harmonizing patient outcomes by selecting the right treatment for the right patient at the right time

Andriani Charpidou Md, PhD, FCCP

Lung Cancer is the leading cause of cancer death worldwide. Non-Small Cell Lung Cancer (NSCLC) accounts for approximately 85% to 90% of all lung cancer with 5-year survival rate of 22.1%. Fifty-seven percent (57%) of NSCLC patients are diagnosed with advanced (stage IIIB or IV) NSCLC. Furthermore, recurrence rates after complete surgical resection range from 30% to 75% among patients initially diagnosed with stage I, II, or III, with the majority experiencing metastatic recurrence.

For un-resectable NSCLC the first line treatment approach is based on histology and molecular profile. Patients with driven mutations of EGFR, ALK, and ROS-1 should be initially treated with the appropriate TKIs. All patients with NSCLC should be tested for PD-1 receptor expression levels, and for those with PL-L1≥50% in TC, Pembrolizumab is the recommended first treatment choice. All the others are candidates for platinum based chemotherapy based on histology.

When disease progress or recurred, further treatment will depend on the first line regimen, the location and extent of the cancer, as well as the new molecular profile. It£s important to understand the goal of any further treatment. For patients which chemotherapy was the first line, immunotherapy with Nivolumab, Atezolizumab or Pemrolizumab for PD-L1≥ 1% expressors is a reasonable option. For patients with driven mutations new generation TKIs are recommended. Patients no longer responding to immune-therapy or TKIs platinum based chemotherapy according to histology is the proposed choice.

Systemic treatment of metastatic small cell lung cancer (SCLC)

Prof. Dr sci Nevena Secen

Treatment of stage IV SCLC is palliative and combination chemotherapy has been the main treatment option for more than three decades. Despite response rates (RRs) close to 70%, outcomes remain poor with a median progression-free survival (PFS) of only 5.5 months and a median OS of <10 months.OS in patients with SCLC has changed little since the late 70s. Platinum-based chemotherapy remains the cornerstone of treatment with the aim of palliation of symptoms and increase survival.

The standard treatment of Extensive Disease (ED) is chemotherapy as cisplatin or carboplatin plus etoposide for up to six cycles, followed by active surveillance. A meta-analysis of 19 randomised trials with a total of 4054 patients demonstrated prolonged OS of patients receiving a cisplatin-containing regimen compared with older chemotherapy combinations.

In 2007, the pivotal study published by EORTC clearly demonstrated the utility of PCI in ED SCLC. This group showed that PCI reduced risk of CNS metastases at 1 year by 25% (40% of brain metastases in the control group *vs.* 15% in the PCI group) in patients who responded to chemotherapy.

SCLC remarkably responds to initial treatment, most patients will relapse with relatively resistant disease. Tumor cells at progression are less sensitive to treatment with cytotoxics, therefore treatment selection will depend on the time of relapse or progression. Clinical studies and basic research should continue to identify better treatment strategies that help increase the duration and effectiveness of treatment of patients with SCLC.

INFLUENCE OF AGE, COMORBIDITIES AND PERFORMANCE STATUS (PS) IN THE OUTCOME OF NON SMALL CELL LUNG CANCER TREATMENT

Konstantinos Zarogoulidis MD, PhD, FCCP

Non Small Cell Lung Cancer frequently is a disease of less robust as well as a disease of the elderly. Nowadays, expansion of the aging population, especially in developed countries, elderly lung cancer cases show an increasing trend. Surveillance Epidemiology and End Results (SEER) program data show that patients ≥ 70 years and older account for 47% of all lung cancer[1]. According to National Institute on Aging (NIA) and NCI SEER Collaborative Study on Comorbidity and Cancer in the Elderly, in the USA in 2030, 1 in 5 Americans will be aged ≥ 65 years[2].

Men and women aged ≥ 65 years have a risk and mortality of 11 and 15 times greater than persons aged < 65 years to experience a cancer, respectively. Additionally, an elderly patient may already have concurrent health problems. Although, aging is a highly individualized process, however all the changes involved cannot be predicted safely on the basis of chronological age. In an analysis by the SEER database, about 50% of lung cancer cases diagnosed in persons aged more than 70 years, 15% of whom aged more than 80 years. The loss of organ function reserve (e.g. declining marrow and renal function) and the existence of chronic disease comorbidities (e.g. COPD, cardiac risk, use of polypharmacy etc) lead to tolerance differences on treatment[3].

There is no agreement on the definition of ™elderlyî (65-70-75 years?) and many believe that “biological age” rather than “chronological age” should guide medical decision. The absence of criteria and the lack of adequate laboratory tests and tools prevent the establishment of “biological age”. “Chronological age” is the only indicator in defining the elderly and the age ≥ 70 years appears as the most appropriate threshold because the incidence of age-related changes start to increase after this cut-off age. Of course calendar age is not sufficient to encompass various individuals, life style, health status, status education and social support[3,4].

Limitations to the treatment of the elderly are: a) physicians and doctors hesitate to treat or treat aggressively (undertreatment), b) elderly cannot tolerate aggressive therapy, c) elderly have different wishes with respect to the prolongation of life. Socio-economic possible limitations are: the cost of treatment, the dependence on others, and the belief of relatives/doctors that “treatment is worse than the disease”.

The Canadian Study of Health and Aging (CSHA) developed 7-point clinical rules based on the definition of frailty (very fit, well, well with treated comorbid disease, apparently vulnerable, mildly frail, moderately frail, severely frail)[5].

On the other hand, the Italian Association of Thoracic Oncology through an International Experts Panel Meeting with the intent to review the evidence base regarding

the treatment of elderly patients with NSCLC provide instruments allowing the estimation of individual risk of mortality and treatment toxicity: the Comprehensive Geriatric Assessment (CGA) and the Chemotherapy Risk Assessment Scale for High-Age Patients Score[6].

Single-agent cytotoxic third generation monotherapies: Elderly Lung Cancer Vinorelbine Italian group Study (ELVIS) (1999), randomly assigned 154 patients to vinorelbine 30mg/m2 (d1, d8) vs BSC. Vinorelbine improved Overall Survival (OS) (p=0.03) and QoL. In the WJT06 (2006) randomised phase III trial, 180 patients administered docetaxel at 60mg/m^2 every 21 days or vinorelbine 25mg/m^2 (d1, d8). Docetaxel improved Progression Free Survival (PFS) (p<0.001) and RR (p=0.019) but not OS and was associated with grade 3-4 neutropenia. Thus docetaxel considered as a reasonable agent for monotherapy in the elderly[6].

Monotherapy vs doublets treatment: In the Multicenter Italian Lung cancer in the Elderly Study (MILES) (2003) phase III trial including 698 patients compared either vinorelbine 30mg/m^2 (d1, d8) or gemcitabine (1200 mg/m^2, d1, d8) to a vinorelbine/gemcitabine doublet. Overall Survival was similar among arms but combination regimen was more toxic[6].

Single agent vs platinum-based doublet: The GALGB 9730 phase III randomised trial compared paclitaxel vs combination paclitaxel + carboplatin in elderly advanced NSCLC patients. The results showed an improvement in Response Rate (RR) and PFS when treated with the combination[7]. Outcomes regarding RR, PFS and OS from a number of phase III retrospective age-specific subgroup analyses showed no significant differences between age groups[8]. On the other hand, a high incidence of toxicity (grade ≥ 3) in elderly patients was reported. In the Hellenic Oncology Research Group pooled analysis, elderly patients with NSCLC, were treated with front-line docetaxel/gemcitabine. Chemotherapy was well tolerated but the incidence of grade 3-4 mucositis and diarrhea was significantly higher in elderly patients compared to younger patients. Multivariate analysis revealed that PS (p=0.0001) and Stage (p= 0.0001) but not the age were significant independent factors in the hazard of death[9].

In the IFCT-0501 phase III Study 451 patients with advanced NSCLC, PS 0-2, randomized to receive weekly paclitaxel combined with monthly carboplatin vs single agent therapy (vinorelbine or gemcitabine). The combination produced better OS compared with single - agent with the cost of increased toxicity (especially neutropenia). Patients in both arms received erlotinib at the Time of Progression[10].

Nab-paclitaxel alone chemotherapy showed beneficial results as far as median OS is concerned with manageable toxicities[11].

Targeted Therapies: All available evidence showed that TKIs are well tolerated compared with platinum - based chemotherapy.

Elderly patients with advanced non-squamous NSCLC should be tested for EGFR mutation and ALK rearrangement for ALK positive[9,12].

The addition of bevacizumab in the paclitaxel/carboplatin doublet in the elderly population did not result in a significant prolongation of median OS. On the other hand, the addition of bevacizumab resulted in significantly higher grade ≥ 3 toxic effects compared with the paclitaxel/carboplatin doublet[6].

Conclusions

The elderly patients are a specific population where data from younger population cannot be applied. Specifically designed clinical trials with adequate CGA are needed. Single third generation agent is a reasonable choice.

Platinum-based regimen with attenuated dose or weekly schedule could be considered for good PS elderly patients without significant comorbidities. Age, PS and Stage influence survival but PS and the extent of the disease is of greater importance.

Biological agents are well tolerated and they have to be considered as first choice for EGFR-mutated patients or with ALK positive patients.

Other targeted therapies, i.e. bevacizumab, still require further prospective evaluations.

Tailored treatment is required in many cases according to age, comorbidities and health function.

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Immunotherapy as first line treatment for NSCLC

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Lung cancer is the leading cause of cancer related deaths throughout the world. Diagnosis is made in most cases after lung cancer has given metastases to other areas of the body, thus making treatment more difficult. Up to now, a chemotherapy doublet has been the standard of care as well as the targeted therapy for patients with EGFR activating mutations and ALK translocations. Recently, immunotherapy treatment is providing new hope.

Better understanding of interactions between tumor and immune system led to the development of immune modulating therapies. In order to overcome T-cell tolerance and to boost cellular immune response, the application of monoclonal antibodies targeting CTLA-4 or the PD-1/PD-L1 axis enlarged the therapeutic options for advanced cancer patients. Immune checkpoint inhibitors are increasingly being used to treat NSCLC. The major immunotherapy drugs are nivolumab and pembrolizumab that target PD-1 and there are trials ongoing for atezolizumab that target PD-L1.

Pembrolizumab was approved as a first-line treatment for patients with metastatic NSCLC who have PD-L1 expression more than 50% of tumor cells and in addition it was approved as a second-line treatment for patients with metastatic NSCLC that have progressed after platinum-based chemotherapy and with PD-L1 expression on at least 1% of tumor cells. Results from clinical trials showed that pembrolizumab was associated with a higher overall response rate compared to chemotherapy, a longer duration of response and lower incidences of serious adverse events. Recently, approval of pembrolizumab was expanded as a first-line treatment with pemetrexed and carboplatin for patients with advanced non-squamous NSCLC

regardless of whether their tumors express the protein PD-L1. Clinical trials are expected to explore more the role of immunotherapy, chemotherapy and the combination of the two.