18th Multidisciplinary Management of Cancers: A Case-based Approach

Multidisciplinary Management of Cancers
Thoracic Oncology Tumor Board

18th Multidisciplinary Management of Cancers: A Case-based Approach

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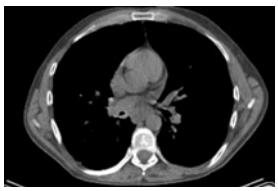
Case 1

A 62 year old man, with a history of tobacco use, presents with cough, found to have a 4.5 cm right lower lobe mass, with right paratracheal and right hilar lymphadenopathy.

EBUS with biopsy of a 4R LN returned positive for pulmonary adenocarcinoma.

PET/CT and MRI brain confirm FDG-avid primary lesion and single R paratracheal and R hilar node, without distant metastases.



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Case 1

How does the staging of this patient change using AJCC 8th edition criteria?

(1) T2b instead of T2a
(2) T3 instead of T2 disease
(3) T1c instead of T2a

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Case 1

Question 3: What initial treatment strategy would you offer this patient with T2bN2 pulmonary adenocarcinoma

A) Induction chemotherapy, followed by re-evaluation for surgical resection
B) Induction chemoradiation, followed by re-evaluation for surgical resection
B) Definitive chemoradiation with weekly carboplatin/paclitaxel
C) Definitive chemoradiation with weekly carboplatin/paclitaxel, followed by two full dose cycles
D) Definitive chemoradiation with cisplatin/etoposide
E) Definitive chemoradiation with cisplatin/pemetrexed

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Case 1

The patient completes chemoradiation with good tolerance to therapy, PS1 at completion, with expected treatment effect without evidence of new or progressive disease at initial imaging.

Question 4: What do you recommend?
A) Begin surveillance with CT chest every 3-6 months for the first 3 years, followed by less frequent surveillance intervals
B) Begin surveillance with CT chest/abdomen/pelvis every 3-6 months for the first 3 years, followed by less frequent surveillance
C) Offer consolidation therapy with durvalumab (every two weeks) for up to one year
D) Offer molecular and PDL1 testing on diagnostic biopsy specimen to guide selection of consolidation therapy

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Case 1

What if the 4R LN initially returned negative on pathology. Right hilar LN sampling positive. PFTs demonstrate a mild obstructive defect.

How would you initially manage this T2bN1M0 pulmonary adenocarcinoma?

A) Additional mediastinoscopy for mediastinal LN staging
B) VATs resection of RUL with mediastinal LN dissection
C) Induction chemotherapy with carboplatin/pemetrexed prior to consideration for resection

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Case 1

The patient undergoes a VATS right upper lobe lobectomy and mediastinal LN dissection.

Pathology reveals a 3.9 cm pulmonary adenocarcinoma
+right hilar LN (1/10)
+LVI and PNI
Margins positive (microscopic)

What subsequent management would you offer to this patient with pT2aN1 adenocarcinoma.
A) Surveillance every 3-6 months with CT chest for the first year, then with decreasing frequency
B) Concurrent chemoradiation
C) Platinum doublet followed by radiation
D) Offer re-resection, followed by platinum doublet
E) Chemoradiation, followed by consolidation with durvalumab

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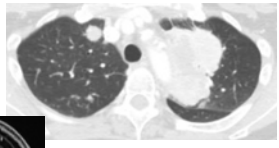
Case 1 Take Away Points

Consider consolidation durvalumab for patients with unresectable stage III NSCLC, following response to definitive chemoradiation

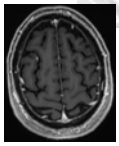
The 8th edition of the AJCC guideline updates criteria for T and M staging.

Case 2

A 52 year old woman without co-morbidities presents with a 7 cm left upper lobe lung mass, with mediastinal lymphadenopathy and bilateral pulmonary lesions up to 3 cm in size.



Staging PET/CT and MRI brain also demonstrate 3 frontal lobe metastases up to 5 mm in size.



Biopsy of the left upper lobe lesion shows pulmonary adenocarcinoma.

Molecular testing is positive for EGFR L858R.

PD-L1 IHC (22C3): 60% positive tumor cells

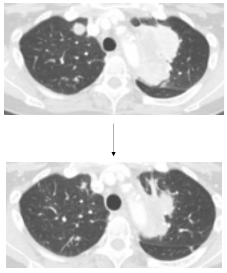
Case 2

How would you treat this 52F with new diagnosis of stage IV, EGFR L858R+ adenocarcinoma with CNS involvement.

1) Begin treatment with a 1st/2nd generation EGFR TKI (erlotinib, afatinib, gefitnib)
2) Begin treatment with osimertinib at 80 mg once daily
3) Begin treatment with osimertinib at 160 mg once daily
4) Refer for consideration for SBRT to CNS lesions, then start an oral agent

Case 2

The patient begins first-line treatment with osimertinib at the usual 80 mg po daily dosing. She tolerates therapy well with minimal toxicity.



CT chest/abdomen/pelvis obtained after the initial 2 months of treatment show a partial response, with approximately 50% decrease in pulmonary lesions and mediastinal adenopathy.

MRI brain shows decrease in previously seen 3 frontal lobe lesions, largest 2 mm in size.

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Case 2

After 12 months treatment with osimertinib, scans show the following compared to imaging 3 months prior:
-1-2 mm increase in a subcarinal LN and a 1-2 mm increase in left upper lobe mass, currently 2 cm, other pulmonary nodule and lymph nodes remain stable.
-In the CNS, one frontal lesion has increased in size from 2 mm to 1 cm with mild surrounding edema.

The patient continues to feel well, without new pulmonary or neurologic symptoms.

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Case 2

What is your treatment recommendation for this patient with EGFR-mutant NSCLC with both systemic and CNS disease progression during treatment with osimertinib?

1) Continue osimertinib, refer for consideration for SBRT, with plan for reimaging of systemic disease in 2-3 months
2) Refer for consideration for SBRT. Refer for biopsy of a progressing chest lesion for molecular testing.
3) Refer for consideration for SBRT and plan to change systemic therapy to platinum-based chemotherapy
4) Change systemic therapy to platinum-based chemotherapy

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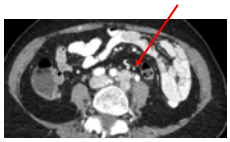
Case 2

After completing SBRT to three CNS lesions, the patient continues on osimertinib.

Subsequent scans over the next six months show stability versus slow increase in her LUL mass and mediastinal adenopathy.

Her most recent scans show a 1.5 cm increase in her LUL mass (now 3.5 cm in size) with newly enlarged left-side retroperitoneal and left common iliac LN, up to approximately 3 cm in size. MRI brain without new or progressive disease.

She is more fatigued and has begun to lose weight, ECOG PS 1.



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Case 2

What is your treatment recommendation for this patient with EGFR-mutant NSCLC with symptomatic systemic progression during treatment with osimertinib, with PD-L1 60%?

1) Continue osimertinib and increase imaging interval to every 6-8 weeks
2) Obtain biopsy of an enlarging abdominal LN with molecular and PD-L1 testing
3) Discuss beginning treatment with pembrolizumab as next line of therapy
4) Discuss beginning treatment with carboplatin/pemetrexed/bevacizumab as next line of therapy
5) Answer 2 and 3
6) Answer 3 and 4

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Case 2

What if this 52F with new diagnosis of stage IV EGFR L858R adenocarcinoma, without CNS involvement, had already begun first-line treatment with erlotinib. She is tolerating treatment well, with response as of 6 months treatment.

She asks if she should be taking osimertinib instead of erlotinib.

(1) Continue treatment with erlotinib. At progression, transition to osimertinib if EGFR T790M present.
(2) Continue treatment with erlotinib. At progression transition to osimertinib without evaluation for T790M.
(3) Switch to treatment with osimertinib now
(4) Switch to osimertinib prior to progression only if intolerance to erlotinib.

Case 2 Take Away Points

Osimertinib is now approved for first-line treatment of NSCLC with a sensitizing EGFR mutation

Osimertinib has better CNS activity than earlier generation EGFR TKIs and a trial of treatment can be considered in lieu of radiation for small/asymptomatic CNS lesions.

EGFR-mutant NSCLC has a very poor response rate to checkpoint inhibitor therapy. Where permitted by co-morbidities EGFR TKI therapy and platinum-based therapy should be attempted prior to trial of immunotherapy .

Case 3

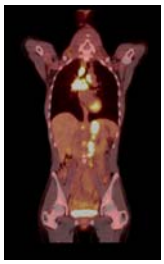
A 60 year old woman presents with progressive cough. Found to have extensive right hilar and mediastinal lymphadenopathy.

Biopsy of a subcarinal lymph node showed pulmonary adenocarcinoma.

Staging PET/CT confirmed hypermetabolic mediastinal lymphadenopathy, right hilar lymphadenopathy, a RUL nodule, a hypermetabolic left adrenal nodule, as well as multiple retroperitoneal lymph nodes. MRI brain without metastases

Broad molecular testing is negative for EGFR, ALK, ROS1, and BRAF alterations. PD-L1 IHC (22C3) is 30%, and TMB is high.

ECOG PS is 1. She has hypertension and type II diabetes with good medical control.



Case 3

How would you treat this 60 year-old woman, with a new diagnosis of stage IV lung adenocarcinoma, without targetable mutation, PD-L1 40% and TMB high.

(1) Carboplatin/pemetrexed +/- bevacizumab
(2) Carboplatin/paclitaxel +/- bevacizumab
(3) Pembrolizumab
(4) Carboplatin/pemetrexed/pembrolizumab
(5) Carboplatin/paclitaxel/atezolizumab +/- bevacizumab
(6) Nivolumab/ipilumumab

Case 3

If this patient with stage IV adenocarcinoma, without targetable mutation, had instead presented with PD-L1 IHC (22C3) of 90%, what would you recommend for management.

(1) Carboplatin/pemetrexed +/- bevacizumab
(2) Carboplatin/paclitaxel +/- bevacizumab
(3) Pembrolizumab
(4) Carboplatin/pemetrexed/pembrolizumab
(5) Carboplatin/paclitaxel/atezolizumab +/- bevacizumab
(6) Nivolumab/ipilumumab

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Case 3

If this patient with stage IV adenocarcinoma, without targetable mutation and PD-L1 90% reported a history of rheumatoid arthritis, not currently on active immunosuppressive therapy, how would you proceed?

(1) Carboplatin/pemetrexed +/- bevacizumab
(2) Consultation with rheumatology
(3) Proceed with pembrolizumab monotherapy
(4) Carboplatin/pemetrexed/pembrolizumab
(5) Answers 2 and 3.

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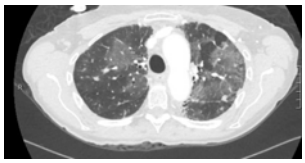
Case 3

Your patient with stage IV adenocarcinoma with 90% PD-L1 expression begins monotherapy with pembrolizumab with an excellent partial response.

After 6 months of treatment, she reports a new progressive dry cough and increased dyspnea with exertion. O2 saturation is 95% RA.

Chest CT is as follows:



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Case 3

How would you manage this patient with new dyspnea/cough and bilateral ground glass opacities during treatment with pembrolizumab?

1) Obtain induced sputum for cultures and begin antibiotic therapy for CAP
2) Refer for bronchoscopy with lung biopsy
3) Continue pembrolizumab and initiate steroid treatment at 1 mg/kg
4) Hold pembrolizumab and initiate steroid treatment at 1 mg/kg

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Case 3

Pembrolizumab is held and the patients symptoms improve with prednisone at 1 mg/kg daily.

Steroids are tapered to off over the next month without recurrence of symptoms and a follow up CT chest shows resolution of previously seen infiltrates.

The patient asks whether they should resume their pembrolizumab.

Case 3

What would you recommend to this patient with PD-L1 90% and partial response to first-line pembrolizumab monotherapy, currently held for pneumonitis.

1) Continue to hold checkpoint inhibitor therapy, initiate surveillance off therapy and reconsider initiation at subsequent disease progression
2) Hold checkpoint inhibitor therapy indefinitely given significant immune-related AE
3) Resume treatment with pembrolizumab now with monitoring for recurrent pneumonitis
4) Attempt to obtain off label nivolumab or atezolizumab
5) Resume treatment with carboplatin/pemetrexed +/- bevacizumab given intolerance to pembrolizumab.

Case 3 Take Away Points

Patients with PD-L1 > 50% can be treated with first-line pembrolizumab monotherapy

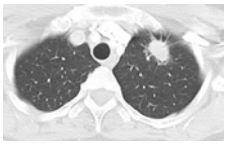
Consider first-line combination platinum-chemotherapy with pembrolizumab at any PD-L1 expression level

Depending on the clinical context, prior auto-immune disease is not a definite contraindication to checkpoint inhibitor therapy

Patients with an irAE can be considered for repeat trial of checkpoint inhibitor therapy, however their risk of recurrent irAE is higher than the general population

Case 4

41 year-old woman without history of tobacco use presents with incidental finding of a spiculated 2.3 cm LUL lung nodule. PET/CT without hypermetabolic lymphadenopathy.



How would you proceed?
1)Biopsy for pathologic diagnosis
2)Surgical resection
3)Close interval surveillance imaging
4)Consideration for SBRT following biopsy

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Case 4

She undergoes a VATS LUL lobectomy with mediastinal lymph node dissection.

Pathology shows a pT2aN0 pulmonary adenocarcinoma, 2.3 cm in size, well differentiated. Acinar predominant. No pleural or visceral invasion. No vascular invasion or visceral pleural involvement. Margins negative

What would you recommend as subsequent therapy:

(1) Mutational testing to guide adjuvant therapy
(2) Adjuvant carboplatin/pemetrexed x 4
(3) Adjuvant cisplatin/pemtrexed x 4
(4) Durvalumab for 1 year
(5) Surveillance every 6 months for the first 2-3 years, then annually

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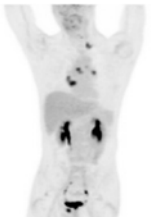
Case 4

Surveillance imaging one year after resection demonstrates mediastinal, hilar, and left supraclavicular lymphadenopathy. MRI brain shows no metastatic lesions.

Biopsy of a left supraclavicular lesion shows pulmonary adenocarcinoma

PD-L1 IHC (22C3) 10%

FISH positive for ALK fusion



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Case 4

What do you recommend for initial treatment for this patient with newly diagnosed, metastatic recurrence of ALK+ NSCLC?

1) Crizotinib
2) Ceritinib
3) Alectinib
4) Brigatinib

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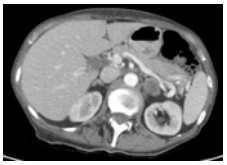
Case 4

The patient receives alectinib with partial response lasting 14 months. Surveillance imaging then demonstrates progression in the mediastinal lymph nodes, with approximately 1 cm growth, and a new 2 cm left adrenal metastasis.

1) Transition to crizotinib
2) Transition to ceritinib
3) Transition to brigatinib
4) Change to carboplatin/pemetrexed +/- bevacizumab
5) Biopsy of a progressing lesion for ALK mutational analysis



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Case 4

What if this 41 year old woman with newly diagnosed stage IV adenocarcinoma were found to have a ROS1 rearrangement rather than an ALK rearrangement.

What would you NOT recommend as initial treatment?

1) Crizotinib
2) Ceritinib
3) Alectinib
4) Brigatinib

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Case 4

What if this 41 year old woman with newly diagnosed stage IV adenocarcinoma were found to have a MET exon 14 skipping mutation rather than an ALK rearrangement.

What would you recommend as initial treatment?

1) Crizotinib
2) Ceritinib
3) Alectinib
4) Carboplatin/pemetrexed +/- bevacizumab

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Case 4

What if this 41 year old woman with newly diagnosed stage IV adenocarcinoma were found to have a BRAF V600E mutation rather than an ALK rearrangement.

What would you recommend as initial treatment?

1) Dabrafenib
2) Dabrafenib/trametinib
3) Vemurafenib
4) Carboplatin/pemetrexed +/- bevacizumab

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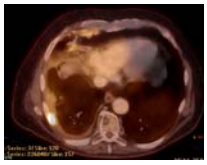
Case 4

A similar 41 year old woman without history of tobacco use presents with right-sided chest pain, found to have right pleural nodularity and a small right-sided pleural effusion.

Pleural fluid cytology returns with pulmonary adenocarcinoma, however there is insufficient tissue for molecular testing.

The patients remaining pleural lesions are found not to be accessible for biopsy.



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Case 4

How would you treat this 41F with stage IV adenocarcinoma with insufficient available tissue for molecular/PD-L1 testing?

(1) Begin treatment with carboplatin/pemetrexed
(2) Begin treatment with carboplatin/gemcitabine
(3) Obtain ctDNA testing as a secondary evaluation for targetable mutation
(4) Monitor off treatment, with plan for future biopsy at progression
(5) VATS or mini-thoracotomy for pleural sampling

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Case 4 Take Away Points

Alectinib is now the preferred first-line treatment for ALK-rearranged metastatic NSCLC

While ceritinib, crizotinib, and brigatinib have activity against ROS1, alectinib does not have activity against this target

ctDNA may provide an supplementary approach to mutational testing in patients for whom tissue cannot be obtained.

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Case 5

A 56 year old man with 70 pack-year smoking history presents with progressive exertional dyspnea. Found on CT chest to have a 2.5 cm RUL mass.

Biopsy of RUL mass: Small cell lung cancer, Ki67 95%

PET/CT and MRI brain do not show evidence of distant metastatic disease.

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Case 5

How would you treat this 56M with radiographically staged limited-stage small cell lung cancer (assuming no additional nodes found on pathologic analysis)?

1) Mediastinoscopy → surgery → chemo
2) Mediastinoscopy → surgery → chemo+radiation (sequential or concurrent)
3) Surgery → chemo
4) Surgery → chemo+radiation (sequential or concurrent)

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Case 5

After initial definitive treatment of this limited stage SCLC, what would be your approach to the brain?

1) Prophylactic cranial irradiation
2) Brain surveillance with MRI brain

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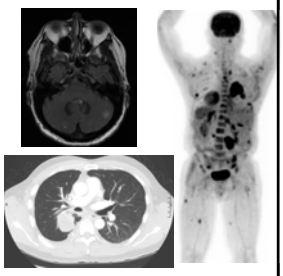
Case 5

The patient has definitive treatment of his limited stage SCLC.

9 months after surgery, restaging CT chest demonstrates rapid progression at his right upper lobe mass. A PET/CT confirmed progression at the RUL and pleura, as well as identified multiple soft tissue implants in the chest wall and right psoas muscle, a new right adrenal nodule, omental involvement, and bone lesions.

MRI brain shows three new cerebellar lesions, up to 4 mm in size.

The patient reported increased fatigue and right-sided chest discomfort. No new neurological symptoms.



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Case 5

How would you proceed in this patient with widespread recurrence of his SCLC?

1) Rebiopsy for histopathological analysis
2) Rebiopsy for histopathologic and molecular testing
3) Switch to carboplatin/pemetrexed +/- bevacizumab
4) Consider pembrolizumab, based on prior PD-L1 60%
5) Refer for SBRT to new CNS lesions

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Case 5

He now has widespread recurrence of his SCLC. ECOG PS is 1, and he is motivated for treatment.

What systemic treatment would you recommend?

(1) Carboplatin/paclitaxel
(2) Carboplatin/etoposide
(3) Cisplatin/etoposide
(4) Nivolumab
(5) Nivolumab/ipilimumab

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Case 5

Imaging shows a partial response following treatment with six cycles carboplatin/etoposide. MRI brain shows slight decrease in three previously seen CNS lesions.

What treatment would your recommend following completion of carboplatin/etoposide

(1) Surveillance with CT c/a/p and MRI brain every 3 months
(2) Referral to radiation oncology to discuss thoracic radiation and whole-brain radiation therapy
(3) Referral to radiation oncology to discuss thoracic radiation and SBRT to known CNS lesions
(4) Referral to radiation oncology to discuss CNS radiation, without thoracic radiation.

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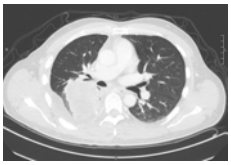
Case 5

The patient completes thoracic radiation and whole brain radiation. Imaging at four months following completion of treatment shows disease progression in the RUL, pleura and lymph nodes. ECOG PS 1.



How would you treat this 59M with recurrent SCLC following initial response to platinum-based chemotherapy?

1) Repeat treatment with carboplatin/etoposide
2) Begin treatment with topotecan
3) Recommend treatment with nivolumab
4) Recommend treatment with nivolumab/ipilimumab

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18th Multidisciplinary Management of Cancers: A Case-based Approach

Case 5 Take Away Points

MRI brain surveillance may be a reasonable choice instead of PCI in selected patients.

Consolidation thoracic radiation can be considered after systemic treatment of ES-SCLC.

Consider checkpoint inhibitor therapy for patients with SCLC who progress after initial platinum-based chemotherapy.

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