Follow-up Care of Lung Cancer Patients

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Medical Oncologist
Vancouver Island Cancer Center
April 18, 2019

Learning Objectives

By the end of this session, participants will be able to:

- Describe the follow-up care of lung cancer patients
- Identify key factors in the seamless transition of care between oncology and primary care
- Cite patient resources to improve the adherence to recommended guidelines

Disclosures

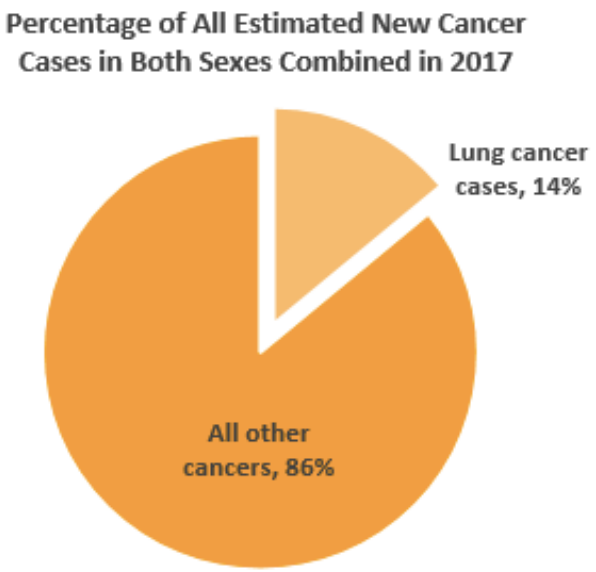
No financial disclosures.

I am a medical oncologist.

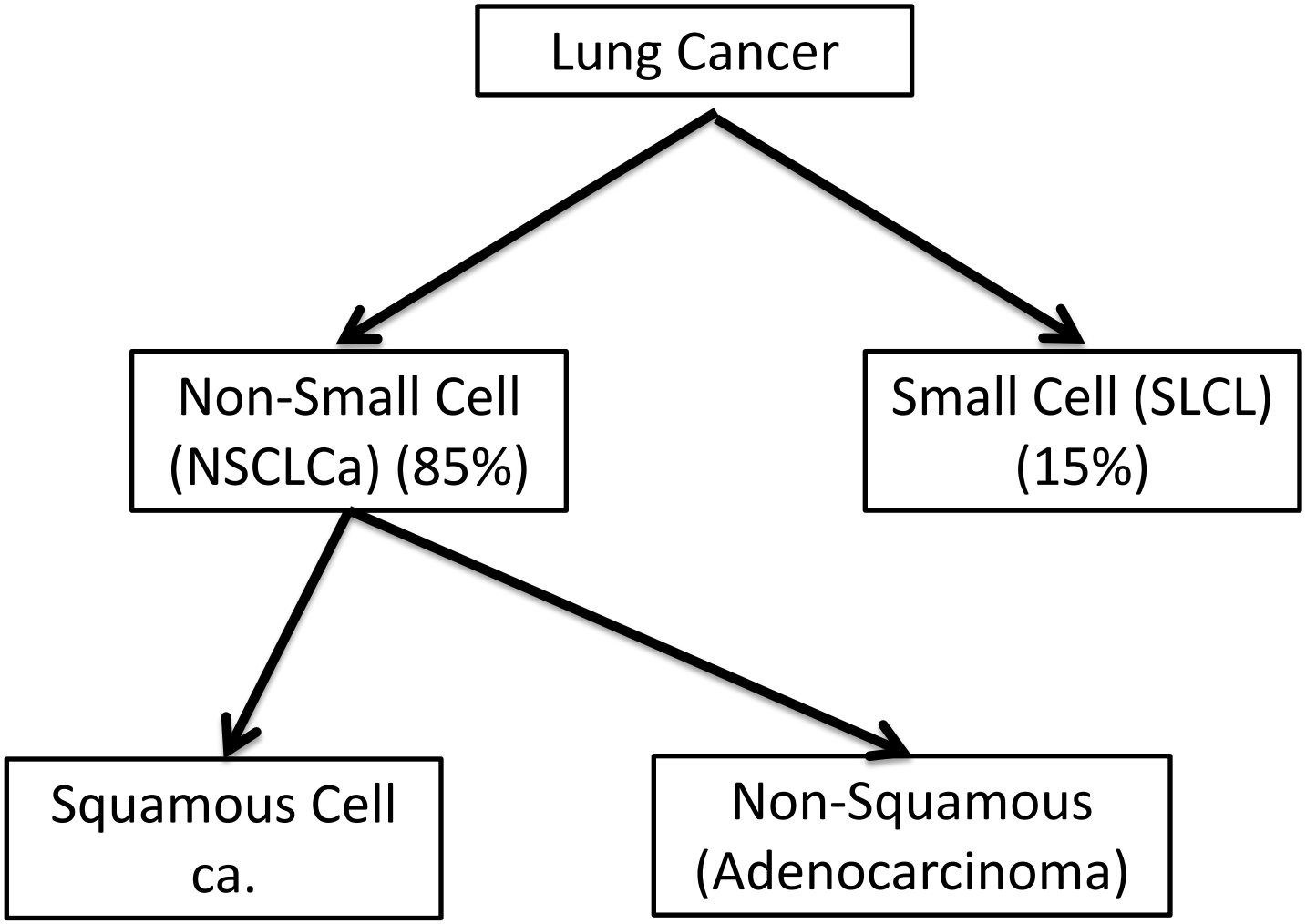
I work in Victoria.

Lung Cancer in Canada

- In 2017:
  - 28,600 Canadians were diagnosed with lung cancer
  - 21,100 Canadians died from lung cancer
- 85% lung cancer associated with smoking
- 5 year survival 15-20%

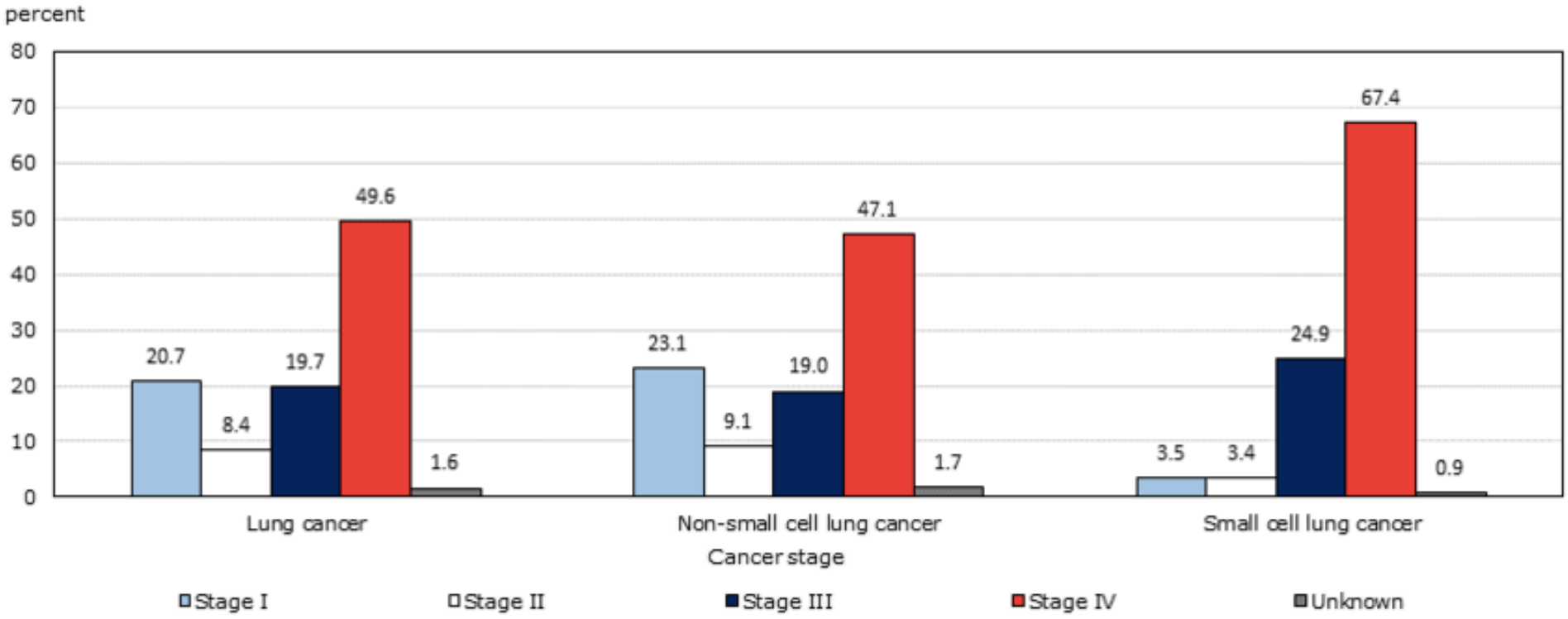


http://www.cancer.ca/en/cancer-information/cancer-type/lung/statistics/?region=on


Lung Cancer
Non-Small Cell (NSCLCa) (85%)
Small Cell (SLCL) (15%)
Squamous Cell ca.
Non-Squamous (Adenocarcinoma)

Stage at Diagnosis

Figure 1
Distribution of lung cancer cases by type of lung cancer and stage at diagnosis for the population aged 18 to 79, Canada excluding Quebec, 2011-2015



Source: Canadian Cancer Registry database, 2011-2015, combined.

Lung Cancer Screening

2016 Canadian Task Force on Preventative Healthcare

Annual low dose computed tomography (LDCT) for three consecutive years for people age 55-74 years with ≥ 30 pack-year* smoking history who currently smoke or quit less than 15 years ago

NOTE: ONLY do screening in health care settings with expertise in early diagnosis and treatment of lung cancer.

*pack-year = avg. # of cigarette packs smoked daily x # yrs smoking

http://canadiantaskforce.ca/ctfphc-guidelines/overview/

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Initial Lung Cancer Investigations

Typically can be done as an outpatient but consider admission if respiratory failure, significant hemoptysis, debilitating metastases (brain or bone)

- History and physical exam
- CXR
- Labs (CBC, electrolytes, Ca, Cr, ALK P, LET, Alb, LDH)
- CT Chest/upper abdomen
- If localized disease: CT Head, PET/CT scan and PFTs
- Additional investigations based of symptoms (ie. CT Abdo/pelvis, bone scan…)
- Biopsy (CT guided, Bronchoscopy +/- EBUS, Mediastinoscopy)
- Referral to Respirology and Thoracic surgery or Radiation/Medical Oncology (un-resectable disease)

BC CANCER

Simplified NSCLCa Staging

Stage I: Tumor up to 4 cm, No LN involved

Stage II: 4-7 cm or ipsilateral peribronchial, hilar or intrapulmonary LNs (N1).

Stage IIIa: Greater than 7 cm or 4-7cm and N1 or up to 5cm and ipsilateral mediastinal +/or subcarinal LN (N2)

Stage IIIb/c: Greater than 5cm and N2 or contralateral mediastinal and hilar, scalene or supraclavicular (N3)

Stage IV: Metastatic disease

AJCC TNM Staging 8th Edition

BC CANCER

IASLC

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

Conquering Thoracic Cancers Worldwide

8th Edition Lung Cancer TNM Staging Summary

T – Primary Tumor

TX		Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
T0		No evidence of primary tumor
Tis		Carcinoma in situ
T1		Tumor 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus)[1]
	T1mi	Minimally invasive adenocarcinoma[2]
	T1a	Tumor 1 cm or less in greatest dimension[3]
	T1b	Tumor more than 1 cm but not more than 2 cm in greatest dimension[3]
	T1c	Tumor more than 2 cm but not more than 3 cm in greatest dimension[3]
T2		Tumor more than 3 cm but not more than 5 cm; or tumor with any of the following features:[3] • Involves main bronchus regardless of distance to the carina, but without involving the carina • Invades visceral pleura • Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, either involving part of the lung or the entire lung
	T2a	Tumor more than 3 cm but not more than 4 cm in greatest dimension
	T2b	Tumor more than 4 cm but not more than 5 cm in greatest dimension
T3		Tumor more than 5 cm but not more than 7 cm in greatest dimension or one that directly invades any of the following: chest wall (including superior sulcus tumors), phrenic nerve, parietal pericardium; or associated separate tumor nodule(s) in the same lobe as the primary
T4		Tumors more than 7 cm or one that invades any of the following: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina; separate tumor nodule(s) in a different ipsilateral lobe to that of the primary

N – Regional Lymph Nodes

NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2		Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3		Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral, or contralateral scalene, or supraclavicular lymph node(s)

M- Distant Metastasis

M0		No distant metastasis
M1		Distant metastasis
	M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural or pericardial nodules or malignant pleural or pericardial effusion[4]
	M1b	Single extrathoracic metastasis in a single organ[5]
	M1c	Multiple extrathoracic metastases in one or several organs

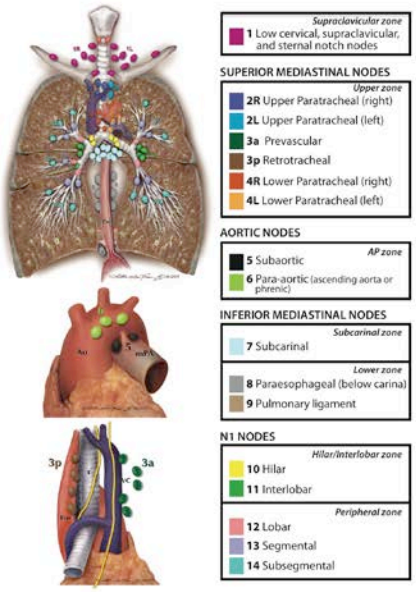
[1]The uncommon superficial spreading tumor of any size with its invasive component limited to the bronchial wall, which may extend proximal to the main bronchus, is also classified as T1a.

[2]Solitary adenocarcinoma (</= 3 cm), with a predominantly lepidic pattern and </= 5 mm invasion in greatest dimension.

[3]T2 tumors with these features are classified T2a if 4 cm or less, or if size cannot be determined and T2b if greater than 4 cm but not larger than 5 cm.

[4]Most pleural (pericardial) effusions with lung cancer are due to tumor. In a few patients, however, multiple microscopic examinations of pleural (pericardial) fluid are negative for tumor, and the fluid is non-bloody and is not an exudate. Where these elements and clinical judgement dictate that the effusion is not related to the tumor, the effusion should be excluded as a staging descriptor.

[5]This includes involvement of a single distant (non-regional) node.



Supraclavicular zone
- **1** Low cervical, supraclavicular, and sternal notch nodes

SUPERIOR MEDIASTINAL NODES

Upper zone
- **2R** Upper Paratracheal (right)
- **2L** Upper Paratracheal (left)
- **3a** Prevascular
- **3p** Retrotracheal
- **4R** Lower Paratracheal (right)
- **4L** Lower Paratracheal (left)

AORTIC NODES

AP zone
- **5** Subaortic
- **6** Para-aortic (ascending aorta or phrenic)

INFERIOR MEDIASTINAL NODES

Subcarinal zone
- **7** Subcarinal

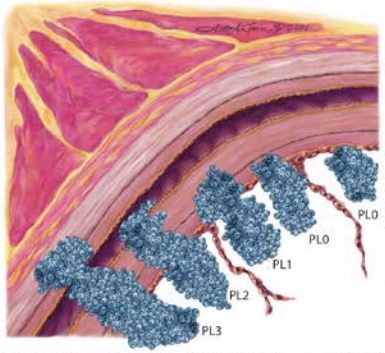
Lower zone
- **8** Paraesophageal (below carina)
- **9** Pulmonary ligament

N1 NODES

Hilar/interlobar zone
- **10** Hilar
- **11** Interlobar

Peripheral zone
- **12** Lobar
- **13** Segmental
- **14** Subsegmental

IASLC Nodal Chart with Stations and Zones



Visceral Pleural Invasion. PL0 indicates tumor within the subpleural lung parenchyma or invading superficially into the pleural connective tissue; PL1, tumor invades beyond the elastic layer; PL2, tumor invades the pleural surface; PL3, tumor invades any component of the parietal pleura. PL1 & PL2 = T2 and PL3 = T3. *Copyright ©2016 Aletta Ann Frasier, MD.*

N1a: involvement of a single N1 nodal station;

N1b: involvement of multiple N1 nodal stations;

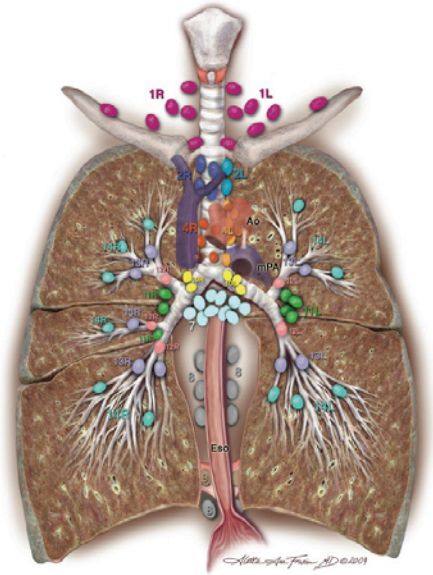
N2a1: involvement of a single N2 nodal station without N1 involvement;

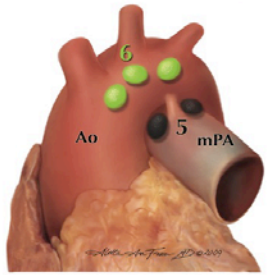
N2a2: involvement of a single N2 nodal station with N1 involvement; and

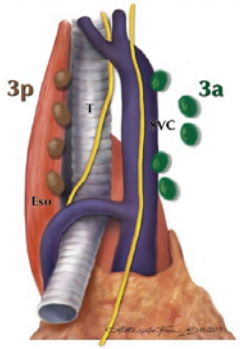
N2b: involvement of multiple N2 nodal stations.

International Association for the Study of Lung Cancer,
13100 East Colfax Avenue, Unit 10, Aurora, Colorado 80011 USA.

BC CANCER







Supraclavicular zone

1 Low cervical, supraclavicular, and sternal notch nodes

SUPERIOR MEDIASTINAL NODES

Upper zone

2R Upper Paratracheal (right)

2L Upper Paratracheal (left)

3a Prevascular

3p Retrotracheal

4R Lower Paratracheal (right)

4L Lower Paratracheal (left)

AORTIC NODES

AP zone

5 Subaortic

6 Para-aortic (ascending aorta or phrenic)

INFERIOR MEDIASTINAL NODES

Subcarinal zone

7 Subcarinal

Lower zone

8 Paraesophageal (below carina)

9 Pulmonary ligament

N1 NODES

Hilar/Interlobar zone

10 Hilar

11 Interlobar

Peripheral zone

12 Lobar

13 Segmental

14 Subsegmental

IASLC Nodal Chart with Stations and Zones

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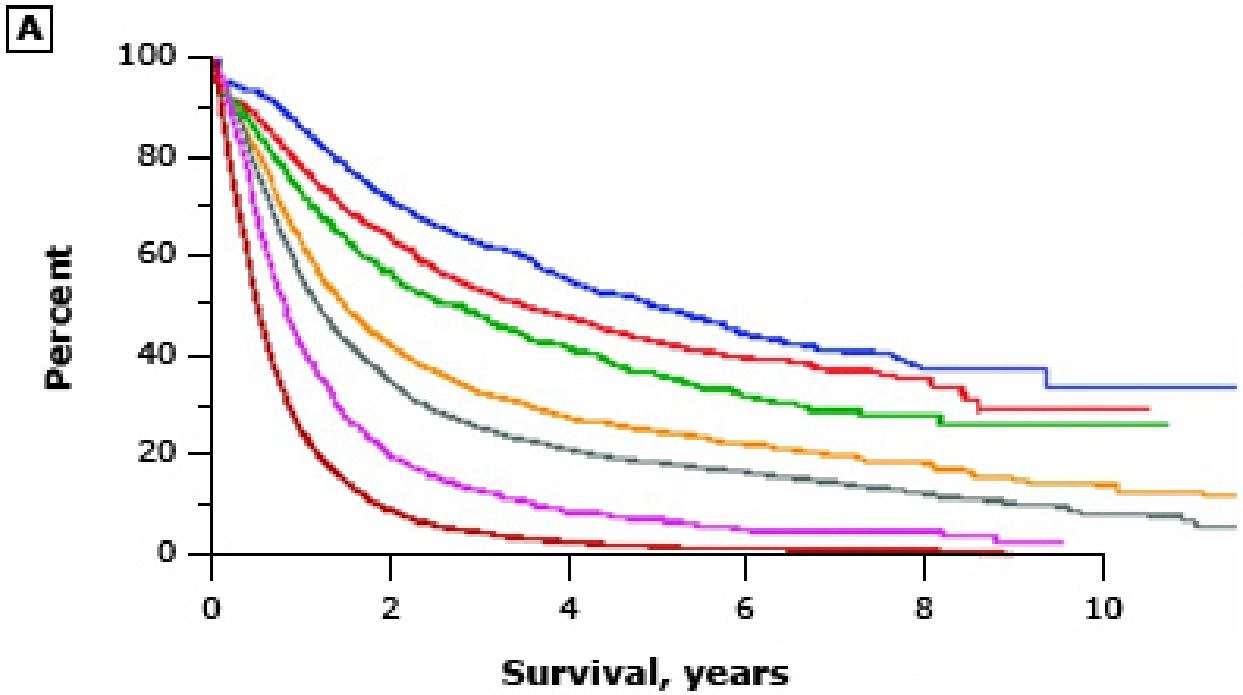
NSCLCa Curative Intent Treatment

- Stage I: Surgery alone (or SBRT)
- Stage II: Surgery and adjuvant chemotherapy
- Stage IIIa: Surgery and adjuvant chemotherapy (+/- adjuvant radiation).

  If un-resectable manage like stage IIIb/c
- Stage IIIb/c: Chemoradiation +/- Durvalumab

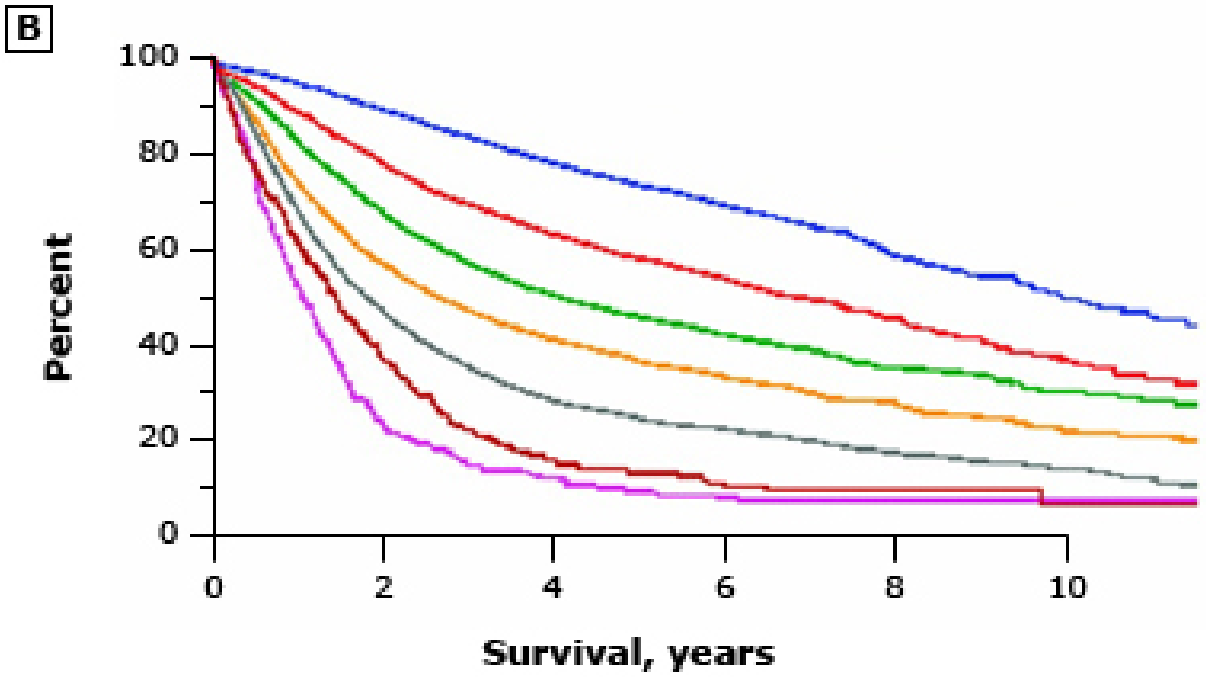
5-year Survival of NSCLCa Based on Clinical Stage



	Deaths/N	MST	5-year (percent)
IA	443/831	60	50
IB	750/1284	43	43
IIA	318/483	34	36
IIB	1652/2248	18	25
IIIA	2528/3175	14	19
IIIB	676/758	10	7
IV	2627/2757	6	2

www.uptodate.com

5-year Survival of NSCLCa Based on Pathologic Stage



	Deaths/N	MST	5-year (percent)
IA	1168/3666	119	73
IB	1450/3100	81	58
IIA	1485/2579	49	46
IIB	1502/2252	31	36
IIIA	2896/3792	22	24
IIIB	263/297	13	9
IV	224/266	17	13

www.uptodate.com

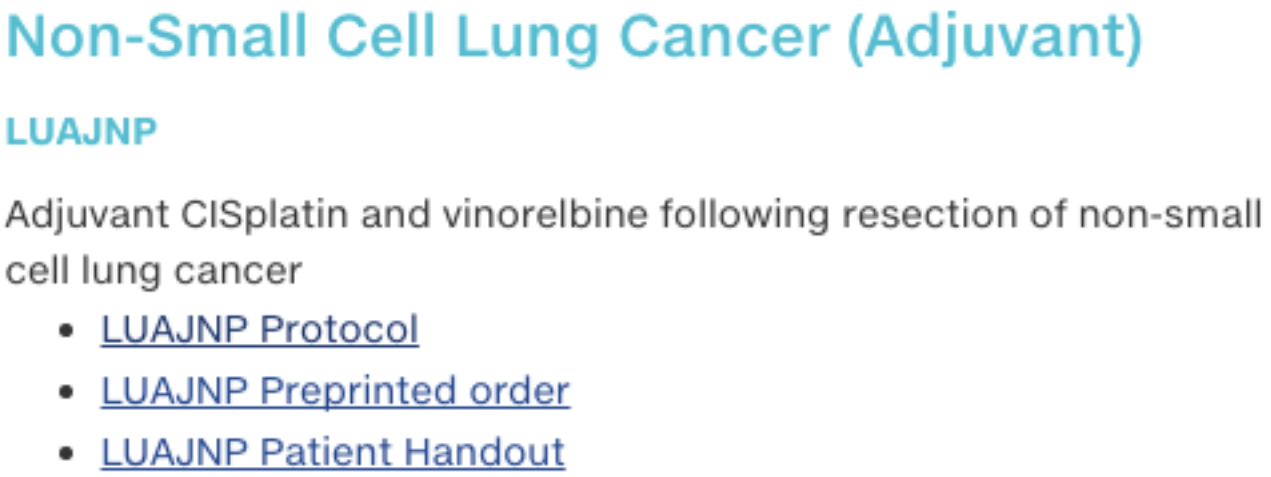
Adjuvant Chemotherapy

- Adjuvant chemotherapy should be offered to patients with resected stage II and III NSCLC
- LACE meta-analysis: 5.4% absolute benefit in 5 year survival (stage I-III), HR for death 0.89
- 4 cycles of cisplatin and vinorelbine
  - Cisplatin 80 mg/m2 day 1, Vinorelbine 30mg/m2 Day 1, 8 and 15 Q21D
  - Side effects: Fatigue, mucositis, nausea/vomiting, allergic reactions, extravasation, neuropathy, tinnitus/hearing dysfunction, nephrotoxicity, neutropenia/infections, thrombocytopenia/bleeding, thrombosis.

BC CANCER

BC Cancer Chemotherapy Protocols

http://www.bccancer.bc.ca/health-professionals/clinical-resources/chemotherapy-protocols



Non-Small Cell Lung Cancer (Adjuvant)

LUAJNP

Adjuvant CISplatin and vinorelbine following resection of non-small cell lung cancer

- LUAJNP Protocol
- LUAJNP Preprinted order
- LUAJNP Patient Handout

BC Cancer Drug Manual

http://www.bccancer.bc.ca/health-professionals/clinical-resources/cancer-drug-manual/drug-index

DRUG NAME: Cisplatin

SIDE EFFECTS:

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials, and/or determined to be clinically important.[19]

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
allergy/immunology	hypersensitivity (rare); see paragraph following **Side Effects** table
auditory/hearing	***ototoxicity*** (31%); see paragraph following **Side Effects** table
	audiogram abnormalities (24%)
	tinnitus (9%)
	vestibular toxicity (rare)
blood/bone marrow/ febrile neutropenia	***myelosuppression*** (25-30%); WBC nadir 18-23 days (range 7.5-45), platelet nadir 18-23 days (range 7.5-45), recovery 39 days (range 13-62)
	anemia (25-30)%; see paragraph following **Side Effects** table

Chemoradiation

- Concurrent chemoradiation
  - Radiation 60 Gy in 30#
    - Side effects: Fatigue, skin irritation, SOB, cough, esophagitis, pneumonitis, pericarditis, fibrosis, decline in lung function, esophageal stricture, cardiac events, second malignancy
  - Platinum and Etoposide (or carboplatin and paclitaxel)
    - Cisplatin 25 mg/m2 Day 1-3 and Etoposide 100 mg/m2 Day 1-3 Q21D x 2-4 cycles
    - Side effects: Alopecia, Fatigue, mucositis, nausea/vomiting, allergic reactions, extravasation, neuropathy, tinnitus/hearing dysfunction, nephrotoxicity, neutropenia/infections, thrombocytopenia, thrombosis.
- 5 year survival 15-25%

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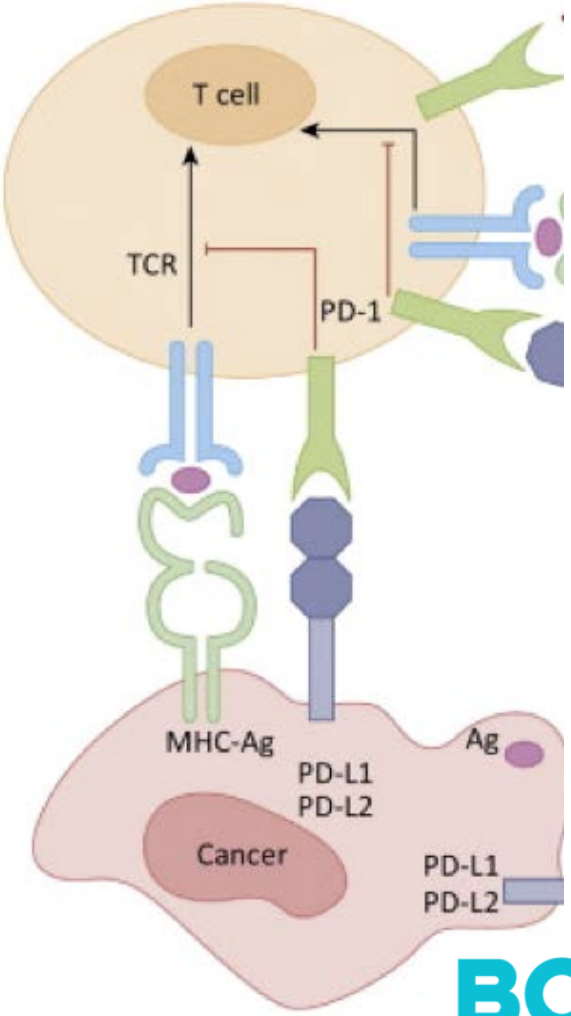
Durvalumab

- Durvalumab (PDL1 antibody)
  - NEJM PACIFIC Trial
  - 10mg/kg Q2W x 12 months
  - 10% improvement in 2 year overall survival
  - Not provincially funded, currently drug access program available



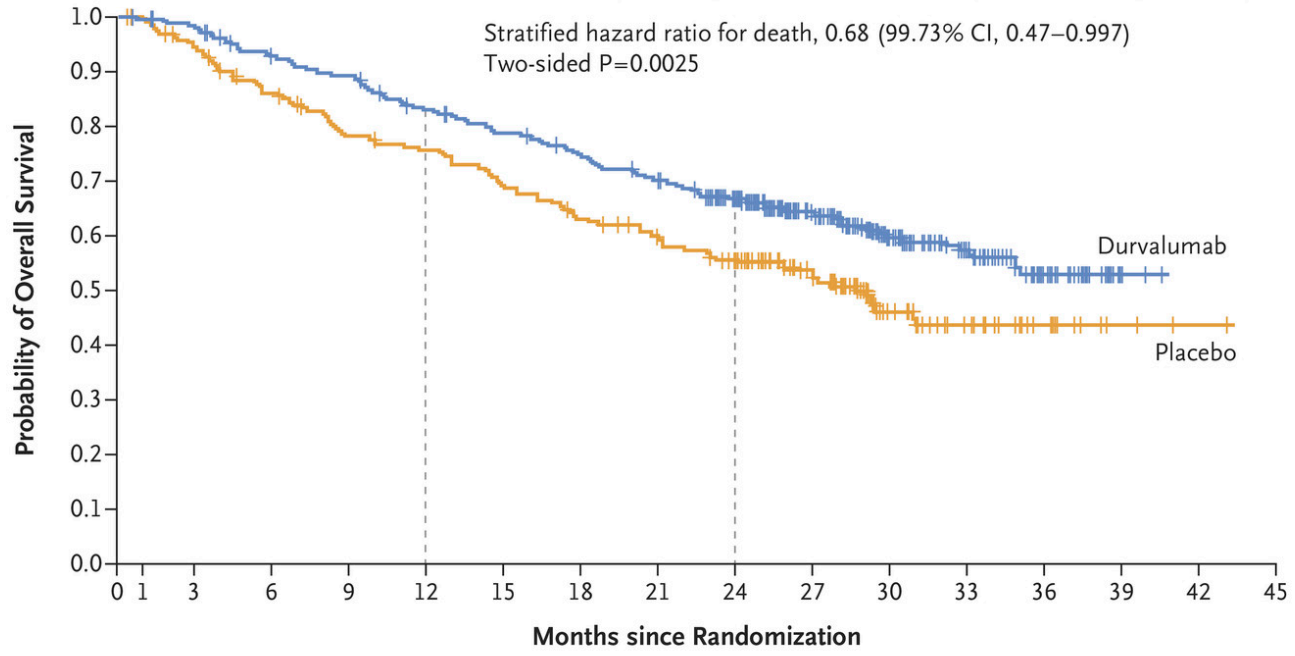
http://www.cell.com/trends/molecular-medicine/fulltext/S1471-4914(14)00183-X

ORIGINAL ARTICLE

Overall Survival with Durvalumab after Chemoradiotherapy in Stage III NSCLC

Scott J. Antonia, M.D., Ph.D., Augusto Villegas, M.D., Davey Daniel, M.D., David Vicente, M.D., Shuji Murakami, M.D., Rina Hui, Ph.D., Takayasu Kurata, M.D., Ph.D., Alberto Chiappori, M.D., Ki H. Lee, M.D., Ph.D., Maike de Wit, M.D., Ph.D., Byoung C. Cho, M.D., Ph.D., Maryam Bourhaba, M.D., et al., for the PACIFIC Investigators*

	No. of Events/ Total No. of Patients	Median Overall Survival (95% CI)	12-Mo Overall Survival Rate (95% CI)	24-Mo Overall Survival Rate (95% CI)
		mo	%	%
Durvalumab	183/476	NR (34.7–NR)	83.1 (79.4–86.2)	66.3 (61.7–70.4)
Placebo	116/237	28.7 (22.9–NR)	75.3 (69.2–80.4)	55.6 (48.9–61.8)



No. at Risk															
Durvalumab	476	464	431	415	385	364	343	319	274	210	115	57	23	2	0	0
Placebo	237	220	198	178	170	155	141	130	117	78	42	21	9	3	1	0

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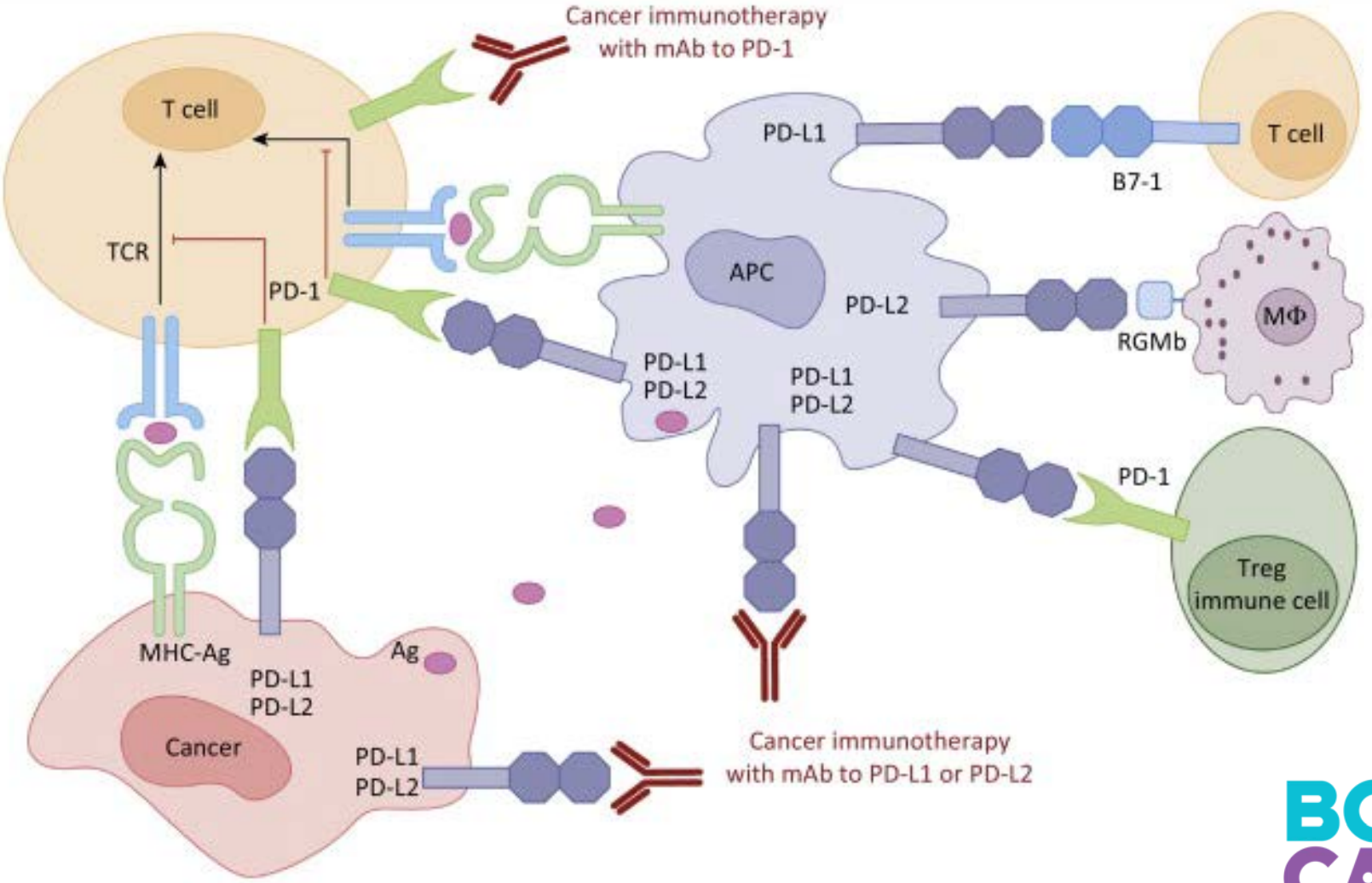
Immunotherapy: PD-1/PD-L1



http://www.cell.com/trends/molecular-medicine/fulltext/S1471-4914(14)00183-X

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Side Effects of PD1/PDL1 Inhibitors

Non- Immune

Fatigue

Pyrexia

Nausea

Decreased appetite

Diarrhea

Anemia

Immune-mediated

(Can involve any organ)

Thyroid

Hypophysitis

Pneumonitis

Colitis

Pancreatitis

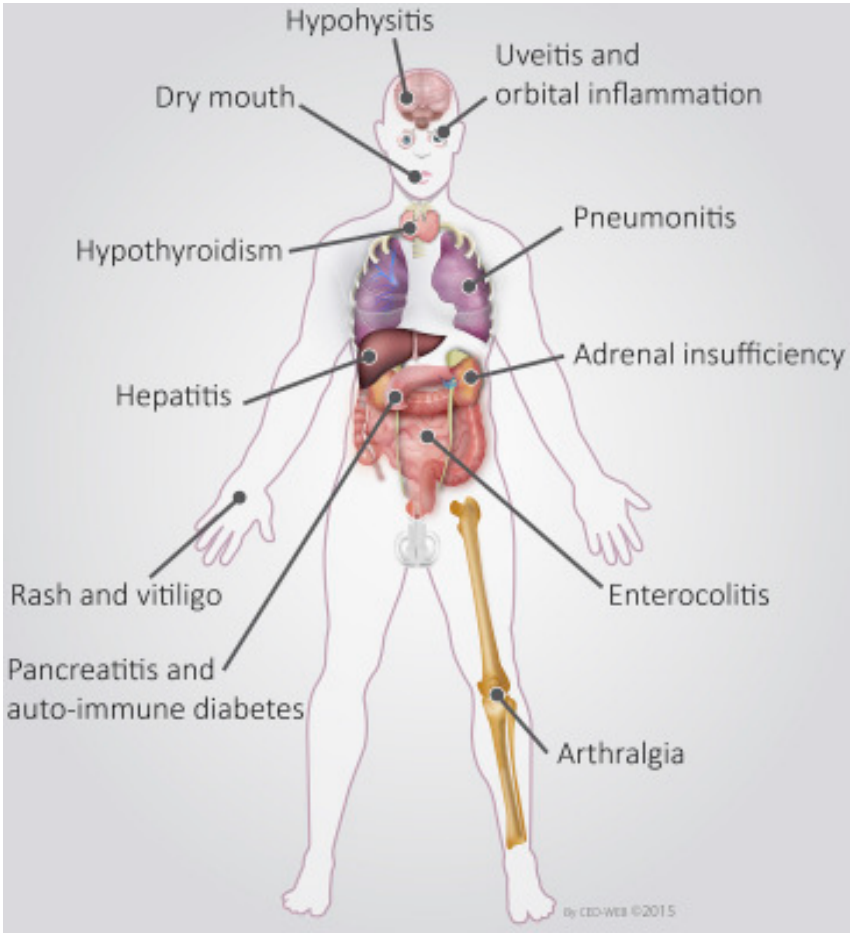
Myositis

Nephritis

Rash

Infusion reactions

Immune-mediated Side Effects of PD1/PDL1 Inhibitors



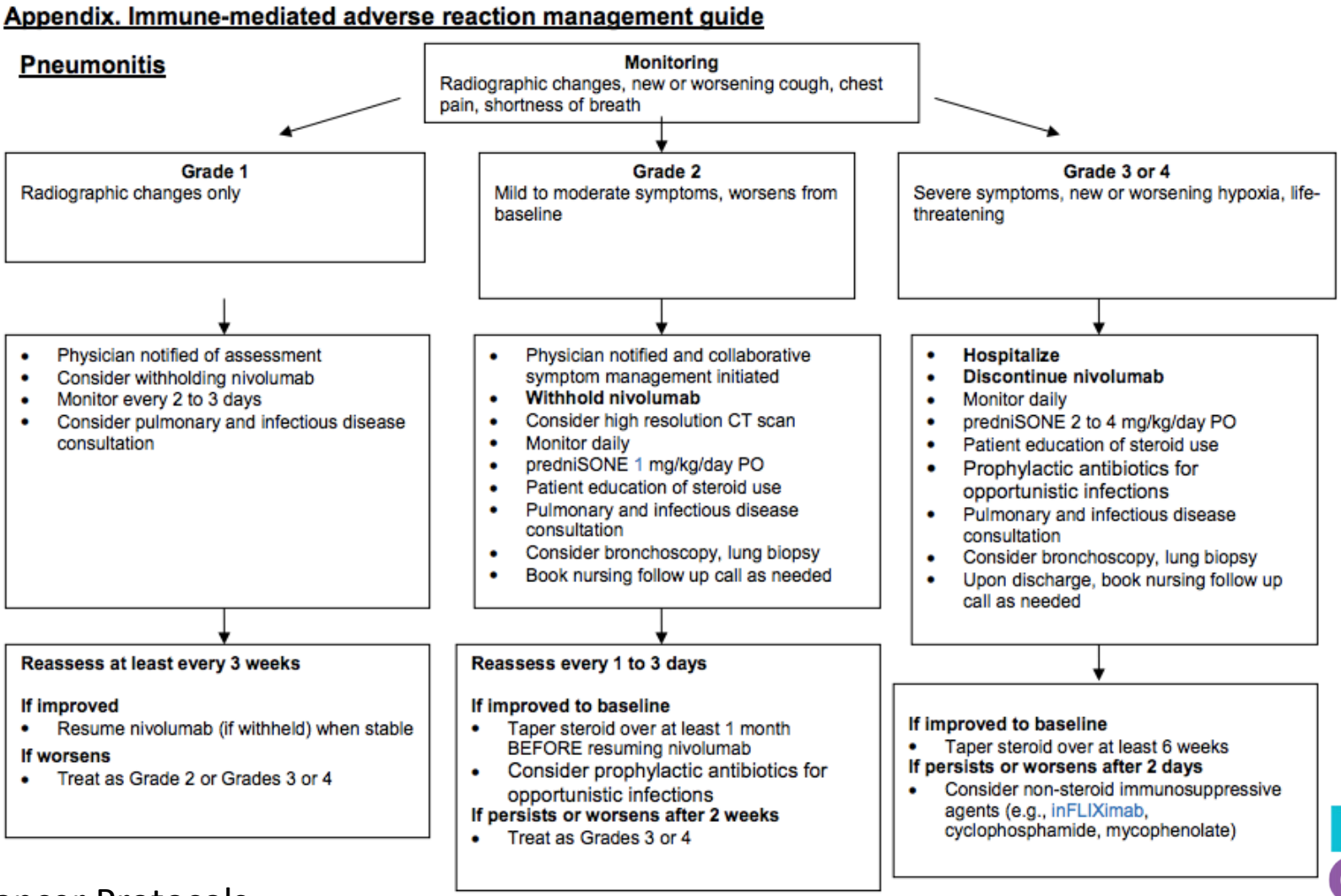
Toxicity can develop at **ANY time** during or following treatment

http://www.sciencedirect.com/science/article/pii/S0959804915011120

Management of Immune-mediated Toxicity

- Contact medical oncology
- Hold PD1/PDL1 inhibitor
- Grade 2+: Prednisone 1mg/kg with taper over 6w+
  - Watch for complications of prolonged prednisone use
- Severe cases may need additional immunosuppressive medications
- Ability to restart treatment depends on toxicity and grade

Management of Autoimmune Side effects



BC Cancer Protocols

Small Cell Lung Cancer

- Limited stage disease treated with concurrent chemoradiation
  - Radiation (45 Gy in 30# BID or 40Gy in 15# daily)
  - 4 cycles Platinum and Etoposide
- Consider prophylactic cranial irradiation (PCI)
- 5 year survival 15-20%

Follow-up care:
Goals of Surveillance

1. To detect early recurrence

2. To identify a second lung primary

To improve survival +/or quality of life

To Detect Early Recurrence

- Majority recur within 2 years
- 75-85% present as distant recurrence
- Stage III cancers more likely to present with symptoms then stage I/II (40% vs. 30%)

(Lou F. Ann Thorac Surg. 2014)

To Identify a Second Lung Primary

- “Field carcinogenesis”
- Hazard rate for second primary cancer is 1-3% per patient per year
- Continuing smoking has been associated with an increased risk of second primary lung cancers

(Boyle et al. Cancer. 2015)

Surveillance Guidelines

- There are a variety of different guidelines regarding surveillance
- No strong data to demonstrate survival benefit with routine surveillance/imaging
- Large discrepancy between frequency of imaging between guidelines
- Potential risks with surveillance (radiation exposure, false-positive results, anxiety)
- Evolving area because is influenced by changes in management of recurrent disease

Evidence for surveillance: IFCT-0302 trial

- Phase III 1775 pts with early or locally advanced NSCLC
- Postoperative surveillance
  - Q6M x 2yrs then Q1Y x 3 yrs
  - Clinical exam + CXR
  - Clinical exam + CXR + CT chest/abdo +/- bronchoscopy
- Follow-up 8.7 years
- mOS 8.2 vs. 10.3 years but not significant (HR 0.92, 95% CI 0.8-1.07)

Lung Cancer Surveillance Guidelines

	BC Cancer	CC Ontario	ESMO	NCCN stage I/II	NCCN stage III
History + Physical	Q3M x 2 yrs then Q6M x 3 yrs then Q12M	Q3M x 2yrs then Q6M x 1 yr then Q12M	Q6M x 2-3 yrs then Q12M	Q6M x 2-3 yrs then Q1Y	Q3-6M x 3 yrs then Q6M x 2 yrs then Q1Y
Imaging	No routine imaging. Consider CXR.	CT chest Q3M x 2yrs then Q6M x 1 yr then Q12M	CT chest Q12M If treated with SBRT: CT chest Q6M x3 yrs then Q12M	CT chest +/- contrast Q6M x 2-3 yrs then LDCT Q1Y	CT chest +/- contrast Q3-6M x 3 yrs then Q6M x 2 yrs then LDCT Q1Y

No guidelines recommend the use of PET scan as part of routine surveillance as no data demonstrating improvement in survival.

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My Approach to Surveillance

- For surgical patients involve surgeon in decision (typically discharge to surgeon for surveillance)
- History and Physical exam Q3M x 2 years then Q6M x 3 years then Q1Y
- CT chest/adrenals Q6M x 3 years then Q12M x 2 years*

(* Can vary based on stage, treatment, patient comorbidities and patient preference)

Surveillance: Symptoms to Investigate

Constitutional symptoms:

- Dysphagia
- Fatigue (new onset)
- Nausea or vomiting (unexplained)
- New finger clubbing
- Suspicious lymphadenopathy
- Sweats (unexplained)
- Thrombosis
- Weight loss or loss of appetite

Pain:

- Bone pain
- Chest pain
- Caveat shoulder pain not related to trauma

Neurological symptoms:

- Headaches (if persistent)
- New neurological signs suggestive of brain metastasis or cord compression such as leg weakness or speech changes
- Headache or focal neurological symptoms

Respiratory symptoms:

- Cough (despite use of antibiotics)
- Dyspnea
- Hemoptysis
- Hoarseness
- Signs of superior vena cava obstruction
- Stridor

Cancer Care Ontario Guidelines

Surveillance: Symptoms to Investigate

Constitutional symptoms:

- Dysphagia
- Fatigue (new onset)
- Nausea or vomiting (unexplained)

Neurological symptoms:

- Headaches (if persistent)
- New neurological signs suggestive of brain metastasis or cord compression such as leg weakness

Think of cancer if patient has persistent symptoms

Pain:

- Bone pain
- Chest pain
- Caveat shoulder pain not related to trauma

- Hemoptysis
- Hoarseness
- Signs of superior vena cava obstruction
- Stridor

Cancer Care Ontario Guidelines

BC CANCER

Smoking Cessation

- Counseling and interventions that involve behavioral and pharmacotherapy support
- Multiple systemic reviews show smoking cessation associated with improved clinical outcomes including QOL

Complications of Treatments and Late Effects

Constitutional Issues:

- Anxiety/Depression
- SOB/Cough
- Decline in appetite
- Decrease in general health
- Dysphagia/Esophageal stricture
- Fatigue
- Pain
- Physical ability restrictions
- Reduced sleep quality
- Sexual dysfunction
- Stigma
- Financial/employment issues
- Family stress

Long-Term Chemotherapy Effects:

- Hearing loss
- Neuropathies
- Renal impairment

Long-Term Radiation Effects:

- Breathing complications
- Esophageal stricture
- Cardiac events
- Second malignancy

Long-Term Surgery Effects:

- Post-thoracotomy pain syndrome
- Reduced exercise tolerance or activity limitations
- Empyema
- Oxygen dependence

BC CANCER

Exercise and Lung Cancer

- Lung cancer patients are often sedentary
- Preoperative exercise programs may improve surgical outcomes and decrease length of hospital admissions
- Lung cancer survivors who are active have better QOL
- Increased challenges due to patient comorbidities and treatment effects
- Important to encourage patients to exercise

Steffens D. Br J Sports Med. 2018
Up To Date. Overview of approach to lung cancer survivors. 2019

Keys to Improve Transition of Care

Family physician:

- Stay involved throughout patient's treatment with regular follow-up visits
- Be informed of treatments received and potential complications/long term impacts
- Call patient's oncologist if any questions

Oncologist:

- Clearly outline treatment and discharge plan in dictations and who is responsible for each task
- In person handover for complicated cases

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COMMUNICATION IS KEY

Oncologist:

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Patient Resources

- BC Cancer Library
- Coping with Cancer http://www.bccancer.bc.ca/health-info/coping-with-cancer
- BC Cancer Patient and Family Counseling
- Lung Cancer Canada www.lungcancercanada.ca
- Cancer Grace: cancergrace.org/
- Inspire Health

Physician Resources

- BC Cancer Guidelines

http://www.bccancer.bc.ca/health-professionals/clinical-resources/cancer-management-guidelines

- BC Cancer Lung Cancer Protocols

http://www.bccancer.bc.ca/health-professionals/clinical-resources/chemotherapy-protocols/lung

- BC Cancer Drug Manual

http://www.bccancer.bc.ca/health-professionals/clinical-resources/cancer-drug-manual

- Cancer Care Ontario Guidelines

https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/lung

- ESMO guidelines

https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours

- ASCO guidelines

https://www.asco.org/practice-guidelines/cancer-care-initiatives/geriatric-oncology/specific-cancer-types/

BC CANCER

Thank you.

Questions?