Predicting the Future

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Goals Today

- You will believe and understand the benefit of Therapy for NSCLung cancer
- Develop an understanding of new molecular evaluation of lung cancer
- Recognize that the Fear of cancer does not Predict Response and Outcome.
Lung Cancer Treatment has changed

- Smoking cessation is improving
- Toxicity is less: Neulasta, Procrit, Zofran
- Response is improved
- Survival is increasing
- Staging is more accurate
- Screening is beginning to be accepted

What you say / stays

You set the stage for a successful consult & acceptance of Tx
Toxicity is less

- 5HT<sub>3</sub> (Zofran, Kytril, Anzemet, Aloxi & Sancuso) + Dexamethasone have decreased nausea and vomiting
- Aprepitant (Emend) – neurokinin1 receptor antagonist
- Almost all chemotherapy is outpatient same day tx.

Please Forget the past

- Not everyone throws up
- Be optimistic
- Help prevent anticipatory N/V
- Sedate as necessary if you must rescue and let us know before the next cycle
- Dexamethasone PO a day before and tapered may help

Toxicity is less

- Hospitalized sepsis is less common
- Quinolone antibiotics are broadly effective
- Colony stimulating factors can shorten and decrease severity of neutropenia (G-CSF neupogen, GM-CSF leukine)
- Neulasta increased convenience
- Delayed injection devices for same day application; prevent an extra day travel and loss of time for patients and family.
- Procrit prevents anemia in advanced disease states.
Response is Improved

- Multiple FDA approved agents for NSCL (non small cell lung cancer)
- Medicare approved payment is based upon proven benefit in 1st, 2nd and 3rd line treatments
- Standard of care (no placebo arms in advanced and metastatic investigational protocols for ambulatory patients)

NSCLung
Histology is now everything

- Bevacizumab is contraindicated in Squamous
- Pemetrexed is contraindicated in Adenocarcinoma
- Actionable Mutations are more common in Adenocarcinoma
- Chemo Pre-Approval requires histology & molecular tests
**NSCL lung – HISTOLOGY IS EVERYTHING**

- **Squamous**
- **Adenocarcinoma**

**VS**

- Large Cell Undiff

- Asian, Female, non-smoker
  - EGFR mutation
  - ALK mutation
  - ROS-1

**Squamous Ca Lung**

less common – more resistant

- Lung cancer – is really a collection of distinct tumor types – it is the leading cause of cancer-related deaths in the United States. According to the CDC, rates among U.S. men and women have been on the decline or leveling off in recent years.
- Still, the NCI estimates that in 2014, over 224,000 Americans were diagnosed with lung cancer, and over 159,000 died from it.
- The World Health Organization reports that lung cancer is the most common and lethal tumor worldwide, affecting some 1.8 million men and women, and killing some 1.6 million annually.

**Lung MAster Protocol**

Lung-MAP Trial ($1400)

- Tumor sample analysis
- Sub-strain assignment
- Patients with metastatic squamous and lung cancer after progression on first-line therapy
Lung-MAP Trial

- Is a multi-drug, multi-arm, biomarker driven clinical trial for advanced Squamous Ca of lung.
- Foundation Medicine Profile driven
- Decrease infrastructure burden
- Ability to amend and add/delete molecules
- $150 million invested; Tomorrows care today with no added pt. cost

Something for Everyone

- The trial includes five experimental drugs, as follows: MEDI4736, a monoclonal antibody with immune-stimulating properties (it binds to PD-L1) and is manufactured by MedImmune. (This is the study drug that will be tested in patients whose squamous cell tumors lack otherwise "actionable" mutations in the current protocol); GDC-0032, a PI3K (kinase) inhibitor provided by Genentech; Palbociclib, an oral cyclin-dependent-kinase (CDK) inhibitor (said to selectively inhibit CDK-4 and -6), from Pfizer; AZD4547, an oral Fibroblast Growth Factor Receptor (FGFR) inhibitor, from AstraZeneca; and rilotumumab (an antibody to human Hepatocyte Growth Factor), from Amgen AMGN. This intravenous drug will be given to patients along with erlotinib (Tarceva), an oral chemotherapy that is already FDA-approved for some cancer types.

PD-L1 Immune therapy

- Cancer can evade detection
- Histocompatibility antigens can become covered over, or have a ligand (PD1) that inhibits CD4 Helper Binding at its immune site
- Blocking PD1/PD-L1 Stimulates the immune system
Immunologic Tx is associated with Auto Immune diseases

- Hypo and Hyperthyroid
- Adrenal insufficiency – Addison’s
- Rheumatoid & Lupus
- Chron’s and Colitis
- Auto-immune Hepatitis, nephritis, pneumonitis

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Hx Survival from start of 2nd line Sq Ca

![Graph showing survival rate over time]

22%

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Nivolumab (OPD1VO)
CheckMate trial 017 AFTER Platinum

Note the significant shoulder – Durable response effect

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Remember: Immune Awakening is Not Tumor Specific

- Hypo and Hyperthyroid
- Adrenal insufficiency – Addison’s disease
- Rheumatoid & Lupus
- Chron’s and Colitis
- Auto-immune Hepatitis, Nephritis, Pneumonitis

Adenocarcinoma is the most common 40% of all lung

Robert a 76 y/o

- Presented in 5/2009 as a previous smoker (off for 15yrs) and underwent a thoracotomy with resection of a node (+) Adenocarcinoma. Stage IIIB; T2 (11cm), N0/8 (6 hilar, 2 mediastinal),Mo
- He accepted 4 cycles of cisplatin based adjuvant chemotherapy
- He remained disease free for 2 1/2 years
Robert becomes symptomatic

- He comes to you with a non-productive cough, No fever or weight loss.
- You offer a CXR with his prior history of cancer
- It shows diffuse bilateral pulmonary infiltrates and nodules.

2 ½ year later he has recurrent, metastatic and symptomatic adenocarcinoma of the lung

- What is the prognosis you present to this 77y/o & his wife?

Adeno Ca Lung

- Asian, Female and NonSmokers have a 70% chance of driver mutation
- Smokers have a 3-7% chance of mutation or Driver gene
- EGFR, ALK and ROS-1 have “Actionable Approved Treatments”, others pending
2 wks Post Erlotinib (Tarceva)
- Cough and symptoms have completely resolved
- CXR has normalized
- CT is nearly undetectable by 1mo
- 2.5 yrs later small nodules developed; he has a second response to Gilotrif (Axitinib) an irreversible binder to the EGFR receptor; with less toxicity.

Survival is Improved
- Chronic disease state
- Periods or significant and occasional complete remissions
- Symptoms are decreased
- Levels of independent care and functional improvement.
- We avoid hospitalization with response management, supportive care and transitions

Robert is now 81
last month new evaluation began
- He underwent a CT Image guided navigational bronchoscopy; multiple turns predicted a path to a small nodule.
- Biopsy was non-diagnostic for cancer
- We will Look for NEW Actionable mutations; when ever growth occurs in an accessible area
Molecular Analysis of Adenocarcinoma of Lung

- EGFR wild vs Mutated (Exon 19 del & L858R)
- EGFR T790M resistance (clinical trial open at TCI)
- ALK Mutations
- ROS1
- KRAS
- Other biomarker driven protocols S1700 trial

Adenocarcinoma of Lung

- IF a Driver Mutation is present !!!
- 1st Line Molecular driven therapy has a higher response rate and less toxicity and improved quality and quantity of life (diarrhea and acne rash)
- Cytologic Dx is rarely adequate; core tissue for testing is needed
- I recommend 2-3 core bx in separate containers. We use one for Diagnosis and preserve tissue for testing
- Re-biopsy is indicated at progression

Bio/Molecular Agents

- Bevacizumab (Avastin) IV anti-angiogenesis (VEGF inhibitor)
- Erlotinib (Tarceva) – oral Epidermoid Growth Factor Receptor inhibitor
- Afatinib (Gilotrif) – irreversible
- CO-1686-008 – T790M resistant
- Crizotinib (Xalkori) – ALK mutation (+) & ROS-1
- Ceritinib (Zykadia) for Crizotinib resistant
Chemotherapy of Adeno Ca of Lung

- Adenocarcinoma: Platinum doublet has standard response in Mutated or Wild genotypes + Avastin if metastatic.
- Treatment is expected to have the same benefit after Driver gene therapy.

Accurate Staging

- Matches appropriate treatment options
- Avoids toxicity and morbidities when possible
- A good plan is more important than a fast plan
- Don't let shortened length of stay drive you to hospital decisions
Localized NSCLung
Stage I; T1-2, No, Mo

- Less than 3cm
- Node negative
- Does have a potential for disease free survival with surgery (65-80% 5yr DFS)
- ANY MEDIASTINAL NODES = POOR PROGNOSIS BY SURGERY = Stage III
- Absence of detectable metastasis by PET (Bx prove any suspicious areas)

How do you find Stage I

- Incidentally at CXR or CT
- Low Dose Screening CT (without contrast)
- 55-80 years old
- 30 pack year or quit in last 15yrs
- Do Not Biopsy or consult unless recommended, follow - repeat as recommended – like Mammography

Regional NSCLung

- Hilar N1 or Mediastinal N2 nodes = Stage II or III
- Frequently these stages of ds have microscopic disease that is not resectable
- Combined Modality Chemo + XRT can be curative for a subset of patients
- If nodal ds is found at resection Adjuvant Chemo can decrease risks
Regional NSCLung
Mediastinal Node Evaluation

- CT Scan has poor specificity unless massive nodal size
- Mediastinoscopy has been the gold standard of “Pre-Op” evaluation of resectability
- EUS and EBUS now offer alternative evaluations

PET
Positron Emission Tomography

- Works by increased glucose metabolism by malignant vs normal tissue in a resting state
- FDG (fluorodeoxyglucose)
- Differentiates viable tumor from scar in post treatment evaluations
- Identifies viable tumor vs necrotic or atelectatic for biopsy direction

60 y/o female
Fused PET-CT Study
No visualized Malignancy - Normal PET Scan
75 y/o Female
Fused PET-CT Study
Large Left Lung Mass,
Normal Kidney,
And L5 met.

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75 y/o Female
Fused PET-CT Study
Axial View
Large Left Lung Mass

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52 y/o Male
Fused PET-CT Study
Positive
Pulmonary Nodule
w/ bone met to right hip

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Lung Carcinoma with treatment

Pre-treatment  Post-treatment

Best Supportive Care

- That Global Osteopathic “Holistic Approach” is proven to benefit.
- Treatment of the cancer alone is not enough. You need a Dr. or a group of Drs. That will seek out other reliefs of pain, suffering, fatigue and depression and supportive care
- Palliative Care + Treatment is superior

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A daily fight –
Deserves to be in a Day facility
Solitary Pulmonary Nodule

- 40% are Malignant
- 60% are Benign
- PET
  - Sensitivity of 95%
  - Specificity of 81%
- Cost savings of $1200-$2200 per patient
  - J Clin Oncol 1998;16:2113-2125
  - Nucl Med Biol 1996;23:737-743
- Predictive accuracy of PET was 94% and TTFA was 86%
Solitary Pulmonary Nodule

- False Positive
  - Vary by region
  - Granulomatous processes
    - TB, fungus (Histoplasmosis), sarcoid, plasma cell granuloma
- False Negative
  - Bronchoalveolar carcinoma, carcinoid, and well-differentiated adenocarcinomas with high fibrous content (scar carcinoma)
  - Small lesions less than 8 – 10 mm
  - Increased serum glucose

Smoking cessation

- 1-800-QUITNOW; 866*PITCH-EM
- Ask
- Advise
- Assess Willingness
- Assist referral
- Arrange follow-up

Medicare payment for cessation counseling

- 99046 Smoking and tobacco use cessation counseling visit; greater than 3 minutes up to 10 minutes
- 99047 Smoking and tobacco use cessation counseling visit; greater than 10 minutes
Medicare payment for cessation counseling

- A cessation attempt includes up to 4 sessions
- Two attempts per year are allowable
- Up to a total of 8 sessions per year are billable
- Standard E&M may be billed

Medicare payment for cessation counseling

- Ask about tobacco use
- Advise to quit
- Assess willingness to make an attempt to quit
- Assist in an attempt to quit
- Arrange a follow-up

Toxicity is less

- Anemic Symptoms are less
- Procrit/Aranesp is approved for Hb less than 10
- Fatigue is less severe
- Hospital transfusion is less likely (avoiding admit, avoids nosocomial complications)