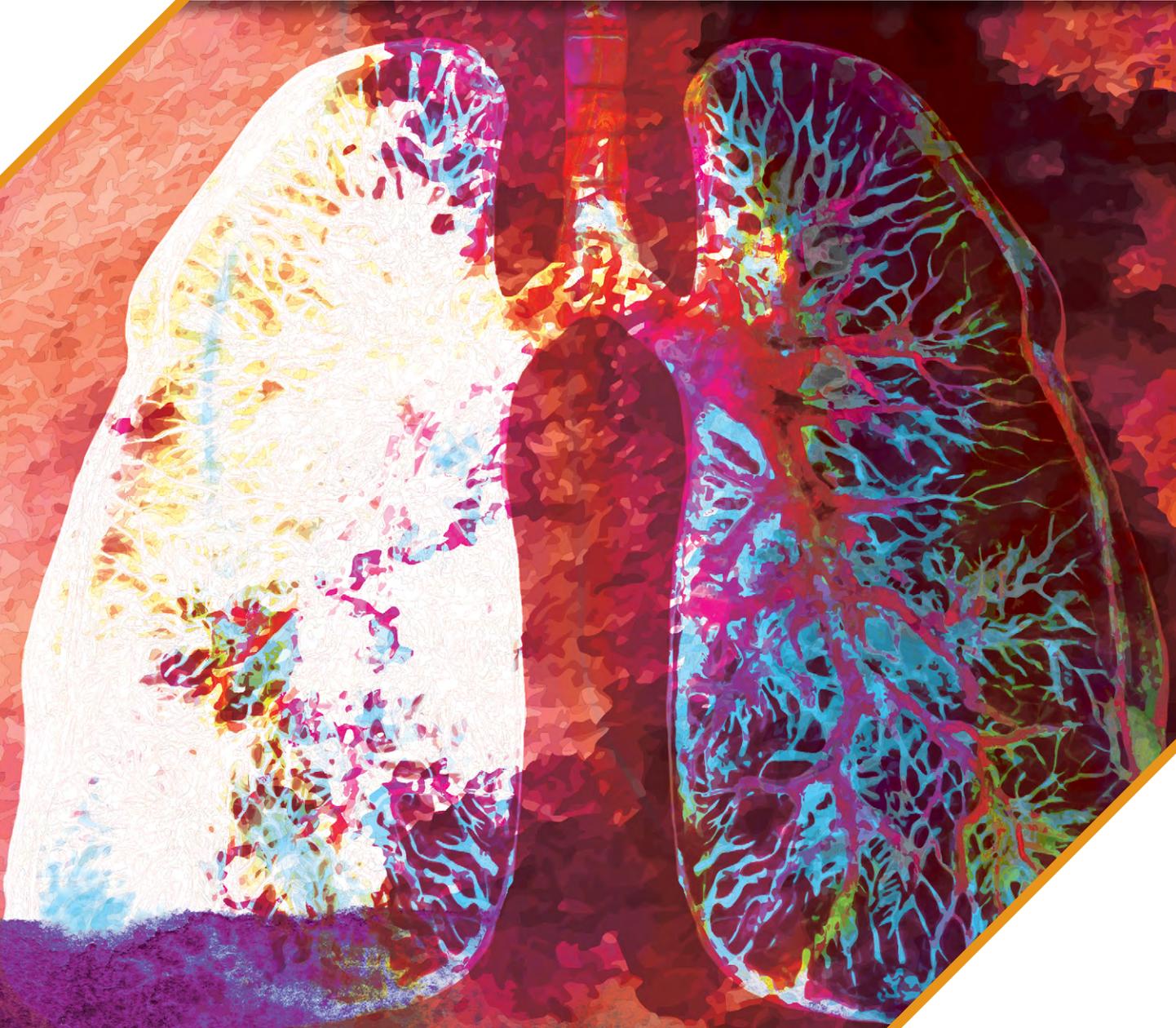


Nursing Clinical Insights Into the Benefits and Challenges of EGFR TKIs in the Treatment of NSCLC

This transcript has been edited for style and clarity and includes all slides from the presentation.



This activity is provided by

Nursing Clinical Insights Into the Benefits and Challenges of EGFR TKIs in the Treatment of NSCLC

Lori McMullen, MSN, RN, OCN®



- ▶ Lori McMullen, MSN, RN, OCN®: Welcome to this educational activity, *Nursing Clinical Insights Into the Benefits and Challenges of EGFR TKIs in the Treatment of Non-Small Cell Lung Cancer*.



Lori McMullen RN, MSN, OCN
Clinical and Program Manager, Cancer
Services
University Medical Center of Princeton,
Edward and Marie Matthews Center
for Cancer Care
Plainsboro, New Jersey

- ▶ I'm Lori McMullen, the Clinical and Program Manager for Cancer Services at the University Medical Center of Plainsboro, Edward and Marie Matthews Center for Cancer Care in Plainsboro, New Jersey.

Agenda

- Introduction
- Overview on biomarkers in NSCLC
- New and emerging EGFR TKIs in NSCLC
- Nursing management strategies of EGFR TKI therapies
- Clinical case challenges

▶ In this activity, I will provide a brief introduction on lung cancer. I'll present an overview on biomarkers in non-small cell lung cancer, and I will briefly discuss new and emerging EGFR tyrosine kinase inhibitors used to treat non-small cell lung cancer.

I will also provide important information regarding management strategies for these therapies. I will end the activity with a case to help provide some clinical context to the information I'm presenting.

EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; TKIs, tyrosine kinase inhibitors.

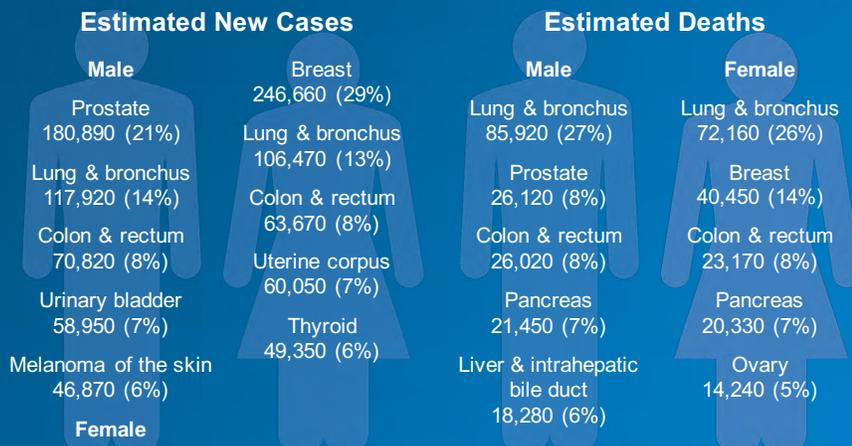
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Introduction

▶ We're going to start with an overview of lung cancer facts and figures.

Leading Sites of New Cancer Cases and Deaths: 2016 Estimates



Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

American Cancer Society. Cancer facts & figures, 2016.
National Cancer Institute. SEER Stat Fact Sheets: Lung and Bronchus Cancer.

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▶ Lung cancer is the second most commonly diagnosed cancer for both men and women, and accounts for about 14% of new cases per year. It's the leading cause of cancer-related deaths for both men and women.

For those diagnosed with localized disease, the survival rate is about 55%; however based on 2006 to 2012 data, the National Cancer Institute reports that only 17.7% of all patients diagnosed with lung cancer survive past 5 years.

There is good news: the incident rates trends are falling since 1990 due to changes in smoking habits, with subsequent drop in death rates from the disease.

The median age for diagnosis is 70, and it's more prevalent in African-American men.

Risk Factors for Lung Cancer

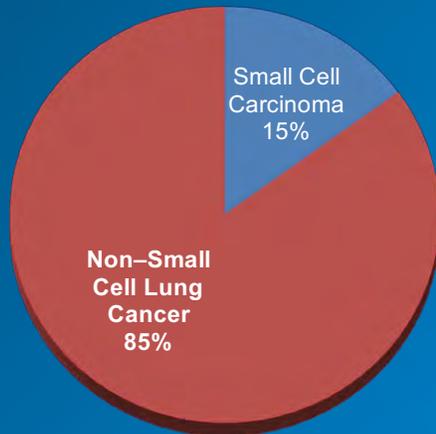
- Smoking
- Exposure to radon gas
- Occupational or environmental exposure to secondhand smoke
- Asbestos
- Certain metals
- Organic chemicals
- Radiation
- Air pollution
- Diesel exhaust

American Cancer Society. Cancer facts & figures, 2016.

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▶ There are several risk factors that most of us know for lung cancer, but we're going to take a minute to review them. Smoking is related to 80% of lung cancer deaths, and radon, coming from soil or building materials, is the second leading cause. Second-hand smoke is another cause of lung cancer, as well as chemicals such as chromium, cadmium, and arsenic. Rubber manufacturing, paving, roofing, painting, chimney sweeping, radiation, air pollution, and diesel exhaust are other causes, and then genetic susceptibility is a risk factor.

Types of Lung Cancer



Lungevity, 2016.
US Library of Medicine, Medline, 2015.

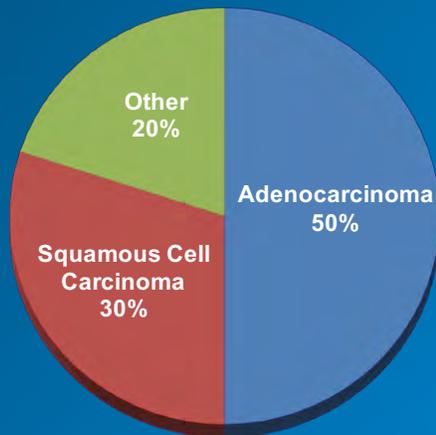
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- ▶ There are two types of lung cancers; 15% is small cell lung cancer and 85% is non-small cell lung cancer.

Small cell lung cancer is known as an aggressive cancer with early metastasis to distant organs. Surgery is not likely to cure the disease, but the good news is it's more sensitive to chemotherapy and to radiation therapy.

Non-small cell cancer is localized to the thorax if it's caught early, making surgery cure an option.

NSCLC by Histology



NSCLC, non-small cell lung cancer.
Chan and Hughes. *Transl Lung Cancer Res*. 2015;4:36-54.

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- ▶ Non-small cell lung cancer is divided into subtypes of adenocarcinoma, which is cancer that begins in the cells that line the alveoli; squamous cell carcinoma, which is epidermoid carcinoma; and large cell carcinoma, which may begin in several types of cells, and on this graphic it's related as the "other" on the chart.

Overview on Biomarkers of Non-Small Cell Lung Cancer

▶ Advances in research have given birth to targeted or personalized treatment with the identification of driver mutations. Driver mutations are responsible for uncontrolled growth, proliferation, and survival of cancer cells.

Frequency of Mutations in NSCLC

Gene	Alteration	Frequency in NSCLC
<i>AKT1</i>	Mutation	1%
<i>ALK</i>	Rearrangement	3%-7%
<i>BRAF</i>	Mutation	1%-3%
<i>DDR2</i>	Mutation	~4%
<i>EGFR</i>	Mutation	10%-35%
<i>FGFR1</i>	Amplification	20%
<i>HER2</i>	Mutation	2%-4%
<i>KRAS</i>	Mutation	15%-25%

- Drugs approved in NSCLC
- Drugs approved in other cancer
- Drugs approved in NSCLC but for other molecular subtype
- Drugs in clinical development

▶ Research has shown that up to 60% of lung adenocarcinomas have oncogenic driver mutations.

Discovery of driver mutations had led the National Comprehensive Cancer Network® Clinical Practice Guideline in Oncology (NCCN Guidelines®) to suggest that mutational testing is done on all non-small cell lung cancers.

On the next 2 slides, there's a list of 15 known mutations found in non-small cell lung cancer.

EGFR and *KRAS* are the 2 most frequently seen mutations in non-small cell lung cancer. The mutations listed on these slides are color-coded to delineate drugs that are approved or in clinical development to treat the various mutations. You'll see that there are 3 drugs highlighted in green; these are specifically approved for non-small cell lung cancer.

NSCLC, non-small cell lung cancer. Lovly et al. My Cancer Genome. 2016.

Frequency of Mutations in NSCLC (cont)

Gene	Alteration	Frequency in NSCLC
MEK1	Mutation	1%
MET	Amplification	2%-4%
NRAS	Mutation	1%
PIK3CA	Mutation	1%-3%
PTEN	Mutation	4%-8%
RET	Rearrangement	1%
ROS1	Rearrangement	1%

- Drugs approved in NSCLC
- Drugs approved in NSCLC but for other molecular subtype
- Drugs approved in other cancer
- Drugs in clinical development

NSCLC, non-small cell lung cancer.
Lovly et al. My Cancer Genome. 2016.

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► There are 5 drugs approved for use in other cancers. There is 1 drug approved for MET amplification in non-small cell lung cancer, and currently there are 6 drugs in clinical development. We'll touch on those later in the presentation.

It's important to note that usually only 1 mutation is found in each tumor, and never-smokers have the highest incidence of *EGFR*, *HER2*, *ALK*, *RET*, and *ROS1* mutations.

EGFR Mutations

- Expressed on cell surface
- Nonmutated = wild-type
- Mutated
 - Most commonly occur at exons 19 (deletion) and 21 (substitution)
 - Women
 - Never smokers
 - Asian population (up to 50%) compared to white population (10%-15%)
- Predict sensitivity/response to TKIs

TKIs, tyrosine kinase inhibitors.
Chan and Hughes. *Transl Lung Cancer Res*. 2015;4:36-54.
Wang et al. *J Hematol Oncol*. 2016;9:34.

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► So let's look briefly at the pathobiology of *EGFR* mutations. *EGFR* mutations occur in about 16% of non-small cell lung cancer cases. *EGFR* mutations are expressed on the cell surface and occur at exon 19 and exon 21. An exon is the portion of a gene that codes for amino acids.

Terminology is important. *EGFR* is either mutated or non-mutated; non-mutated is referred to as wild-type.

EGFR mutation is more common in women, never-smokers, and the Asian population, in up to 50% of those with non-small cell lung cancer. It's important to qualify that the CDC defines a never-smoker as someone who has smoked less than 100 cigarettes in a lifetime.

Tyrosine kinase inhibitors, or TKIs, are the class of drugs that are most commonly associated with treatment

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EGFR Mutations

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of *EGFR* mutations and do just that; they inhibit *EGFR*, resulting in a blockade of downstream signaling. *EGFR* mutation predicts sensitivity and response to TKIs. This is based on data from the Iressa Pan-Asia Study (IPASS) and from the First-SIGNAL study (first-line single agent Iressa versus gemcitabine and cisplatin trial in never smokers with adenocarcinoma of the lung). Both studies confirmed that *EGFR* mutation predicts improved response and progression-free survival with TKIs over chemotherapy in never-smokers.

Most tumors are *EGFR* wild-type or non-mutated, meaning there is no indication for TKIs in the treatment of these patients, and these patients should be considered for chemotherapy.

Testing

- Testing techniques vary by institution
- Finding *EGFR* mutations depends on type of testing done on tumor
 - Test for single mutation vs. whole genome sequencing
- Tumor sample (tissue) biopsy versus cytology
- Plasma testing

Ellison et al. *J Clin Pathol.* 2013;66:79-89.
Wang et al. *Transl Lung Cancer Res.* 2015;4:119-125.
Lovly et al. *My Cancer Genome.* 2016.

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- ▶ Because the presence or absence of *EGFR* mutation is important when determining treatment, it is essential to assess the mutation status at the time of diagnosis. Not all tests are the same; be sure that you know exactly what mutations are tested when the results state no mutation detected, or wild-type. Results should state exactly what sequencing is tested. Did the testing include only sequencing of *EGFR* exons 19 and 21? If so, the results should read no mutation detected on exon 19 and 21, or *EGFR* status is wild-type exons on 19 and 21. It's also important to look at what your tumor sample is—biopsy or cytology—including a fine-needle aspirate or pleural effusion.

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Testing

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Ellison et al. *J Clin Pathol*. 2013;66:79-89.
Wang et al. *Transl Lung Cancer Res*. 2015;4:119-125.
Lovly et al. *My Cancer Genome*. 2016.

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Some thoughts to consider: that *EGFR* is higher in lung resection sample specimens, advanced disease tumor sample may not be possible, no statistical significance exists between small biopsy and cytology, and it's important for the testing laboratory to know its expertise and equipment.

Another option for testing is plasma testing, and defined *EGFR* mutations are detected using DNA isolated from formalin-fixed paraffin-embedded tumor tissue or circulating-free tumor DNA from plasma, which is taken from anticoagulated peripheral whole blood.

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New and Emerging *EGFR* TKIs in NSCLC

- ▶ Next we'll discuss some new and emerging *EGFR* TKIs being used in the treatment of NSCLC.

First-Line Treatment

○ EGFR TKIs (exon 19 deletion and *L858R* substitution)

- Erlotinib (vs platinum-based doublet)
 - Median PFS = 10.4 mo (vs 5.2 mo)
- Gefitinib (vs carboplatin/paclitaxel)
 - Median PFS = 10.9 mo (vs 7.4 mo)
- Afatinib (vs pemetrexed/cisplatin)
 - Median PFS = 11.1 mo (vs 6.9 mo)

EGFR, epidermal growth factor receptor; PFS, progression-free survival; TKIs, tyrosine kinase inhibitors.
Tarceva [package insert]. 2016.
Gilotrif [package insert]. 2016.
Iressa [package insert]. 2015.

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▶ Erlotinib and gefitinib and afatinib are all approved as first-line therapy in metastatic non-small cell lung tumors with *EGFR* exon 19 deletions or exon 21, and that's the *L858R* substitution—in mutations detected by an FDA-approved test. And it's important to note that the safety and efficacy have not been evaluated in tumors with *EGFR* mutations other than exon 19 and deletion or exon 21 substitution.

The statistics on this slide represent progression-free survival compared to a platinum-based chemotherapy.

Additional Indications

○ Erlotinib

- Maintenance
- Metastatic NSCLC with exon 19 deletion or 21 substitution, second or greater line therapy, after progression, following at least 1 prior chemotherapy regimen
- Not recommended for use in combination with platinum-based chemotherapy

○ Afatinib

- Metastatic, squamous NSCLC, progressing after platinum-based chemotherapy

NSCLC, non-small cell lung cancer.
Tarceva [package insert]. 2016.
Gilotrif [package insert]. 2016.

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▶ Additional indications for erlotinib are for maintenance, and in advanced non-small cell lung cancer after 4 cycles of platinum-based first-line chemotherapy, and a second- or third-line therapy in advanced non-small cell lung cancer. Erlotinib is not recommended for use in combination with platinum-based chemotherapy.

Afatinib is also indicated in metastatic squamous non-small cell lung cancer progressing after a platinum-based chemotherapy.

Disease Progression

○ Resistance to TKIs

– Primary

- Exon 20 insertion

– Acquired-

- Resistance develops after 7-12 months
- *T790M* mutation in exon 20 (50%-65% of acquired resistance to EGFR TKIs)

○ Always re-biopsy to assess for new tumor biology

EGFR, epidermal growth factor receptor; TKIs, tyrosine kinase inhibitors.
Ogunleye et al. *Am J Hematol Oncol*. 2015;11:16-25.
Chan and Hughes. *Transl Lung Cancer Res*. 2015;4:36-54.

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▶ Disease progression in non-small cell lung cancer is not unexpected. In patients with *EGFR* mutations treated with TKIs, 2 types of resistance have been identified. Primary resistance is suspected when tumors do not respond in patients never treated previously with EGFR TKI.

In less than 5% of patients, tumors have demonstrated exon 20 insertion, which is thought to be insensitive to EGFR TKI. More common is an acquired resistance, which occurs in most patients treated with EGFR TKIs after 7 to 12 months of treatment, from secondary *EGFR* mutations or activation of a new EGFR pathway.

The most common mutation, *T790M* in exon 20, is responsible for 50% to 65% of acquired resistance. This still leaves about 30% of patients who develop resistance mediated by an unknown mechanism. For these patients, the treatment of choice is cytotoxic chemotherapy.

Therefore, rebiopsy should always be considered in progression to identify possible new cell biology to guide appropriate next course of treatment.

Third-Generation EGFR Inhibitors

- Target *T790M* mutation
 - Approved
 - Osimertinib (aka, AZD9291)
 - ORR: 51%; median duration of response: 12.4 months
 - Ongoing Trials
 - HM61713 (BI 1482694, olmutinib)
 - ASP8273
 - EGF816
 - PF-06747775
 - No longer in development
 - CO-1686 (rocicentiniib)

EGFR, epidermal growth factor receptor; ORR, objective response rate.
Wang et al. *J Hematol Oncol*. 2016;9:1-7.
Tagrisso [package insert]. 2015.
Broderick. <http://www.onclive.com/web-exclusives/clovis-ends-development-of-rocicentiniib-in-lung-cancer>.



- ▶ For patients who have progressed on a first-line TKI and have a *T790M* mutation, there's 1 approved drug and several in clinical trials. Osimertinib is a third-generation EGFR TKI with an overall response rate of 51% and a median duration of response of 12.4 months. Osimertinib is recommended in the NCCN Guidelines® for disease that has progressed on erlotinib, gefitinib, and afatinib. If you recall I had mentioned that there are several EGFR TKIs currently in clinical trials. HM61713 has been approved in South Korea only. Another promising drug, CO-1686, is no longer in development as of May 2016. Most recently, new resistance to osimertinib EGFR TKI C797S mutation has been identified.

Common EGFR Inhibitor Adverse Effects

- Cutaneous reactions
- Diarrhea
- Nausea/vomiting
- Stomatitis
- Liver toxicity
- Cardiotoxicity
- Interstitial lung disease

EGFR, epidermal growth factor receptor.
Hirsh. *Curr Oncol*. 2011;18:126-138.
Gilotrif [package insert]. 2016
Tagrisso [package insert]. 2016



- ▶ In the world of oncology, no treatment is without adverse effects. There are several associated with EGFR inhibitors, and this is a list of the most common. Cutaneous reactions in the form of acneiform eruptions, xerosis, trichomegaly and alopecia, diarrhea, nausea, vomiting, stomatitis, cardiac, and liver toxicity. And, lastly, interstitial lung disease, which is rare but occurs with a rapid onset and usually presents with a dry, nagging cough. Treatment includes stopping the drug and dosing with steroids.

Cutaneous Adverse Effects



Typical EGFR Rash



Xerosis

EGFR, epidermal growth factor receptor.

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▶ Here are a couple of patient examples of cutaneous adverse events seen with the use of EGFR TKIs. The one on the left is typical EGFR rash. Cutaneous adverse effects are common with EGFR TKI because EGFR is normally expressed in skin, sebaceous glands, and hair follicle epithelium. Using TKIs as inhibition for EGFR causes follicular occlusion and rupture.

Nonbacterial eruptions of follicular papules and pustules present in an acneiform distribution. Approximately 45% to 100% of patients usually develop rash within 2 to 4 weeks in areas of high density of sebaceous glands—the scalp, face, upper chest, and back.

Cutaneous Adverse Effects (cont)



Trichomegaly



Paronychia

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▶ On this slide, we have pictures of trichomegaly, which is increased length, curling, pigmentation, or thickness of the eyelashes, and paronychia, which is fissures on the tips of the fingers and toes, which can lead to infection and certainly affects the quality of life.

Nursing Management Strategies of EGFR TKI Therapies

► So how do we manage these adverse events?

Managing Adverse Effects

- Rash develops in 45%-100% of patients in first 2-4 weeks; diminishes in 4-6 weeks
- Educate patient about expected adverse effects before starting treatment
- Adverse events are graded according to Common Terminology Criteria for Adverse Events from the National Cancer Institute
- Developing rash is associated with improved outcomes and clinical benefit

► For cutaneous adverse events, the management is for the acneiform eruptions—again, this is seen in between 45% and 100% of patients—and is based on educating the patient and the caregiver so they are aware of what to be expected and how to be proactive and prepared.

Managing Adverse Effects Cutaneous

- Rash
 - Gentle soaps, moisturizers without fragrance or dyes
 - Sunscreen SPF 15, protective clothing
 - MASCC or NCCN recommendations for prevention and management of EGFR rash
- Paronychia
 - Can lead to infection, affects function
 - Warm soaks, topical antifungal, gloves, avoid pressure on toes
- Trichomegaly
 - Risk for corneal abrasion
 - Ophthalmology consult if indicated

EGFR, epidermal growth factor receptor; MASCC, Multinational Association of Supportive Care in Cancer; NCCN, National Comprehensive Cancer Network.
Hirsh. *Curr Oncol*. 2011;18:126-138.
Polovich et al. In: *Chemotherapy and Biotherapy Guidelines and Recommendations for Practice*. 4th ed. Pittsburgh, Pennsylvania: Oncology Nursing Society; 2014:171-435.



- ▶ Gentle soaps, dermatology-approved makeup, shaving with caution, avoiding excessive beard growth, avoiding skin products with alcohol, cotton instead of synthetic garments, patting dry instead of rubbing with a towel, and not using acne creams are all interventions the nurses can teach the patient to help him or her manage their adverse effects.

Both the Multinational Association of Supportive Cancer in Cancer and the NCCN® have recommended topical hydrocortisone and systemic doxycycline for prevention and management of EGFR TKI adverse effects for weeks 1 to 6.

For paronychia, which can lead to infection because of the sores on the ends of the fingers, warm soaks, topical antifungals, gloves, and avoiding pressure on the toes are good ways to avoid problems.

For trichomegaly, there's a risk for corneal abrasion because of the length of the eyelashes, although nothing should be done unless there's a problem, and then the ophthalmologist should be consulted, if indicated.

Managing Adverse Effects Diarrhea

- 18%-95% experience diarrhea
 - Occurs within first 4 weeks of treatment (with afatinib, usually occurs within first 7 days)
- Always rule out infection (*C. difficile*)
- Monitor for fluid/electrolyte imbalance
 - Daily fluid intake 3-4 liters
 - Fluids should contain salt and sugar
- Diet modifications; BRAT diet
- Antidiarrheal
 - Loperamide

BRAT, bananas, rice, applesauce, and toast.

Hirsh. *Curr Oncol*. 2011;18:126-138.

Polovich et al. In: *Chemotherapy and Biotherapy Guidelines and Recommendations for Practice*. 4th ed. Pittsburgh, Pennsylvania: Oncology Nursing Society; 2014:171-435.

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▶ Managing adverse effects of diarrhea for patients taking EGFR TKIs involves same treatment as diarrhea induced by chemotherapy. Approximately 18% to 95% of patients experience diarrhea on these agents, and it is usually seen within the first 4 weeks of treatment; with afatinib, it is usually seen in the first 7 days. You should always rule out *Clostridium difficile* infection, monitor for fluid and electrolyte imbalance—make sure the patient has a daily fluid intake of 3 to 4 liters—and fluids should contain salt and sugar. For diet modifications, a BRAT diet is suggested, and antidiarrheal drugs such as loperamide are suggested.

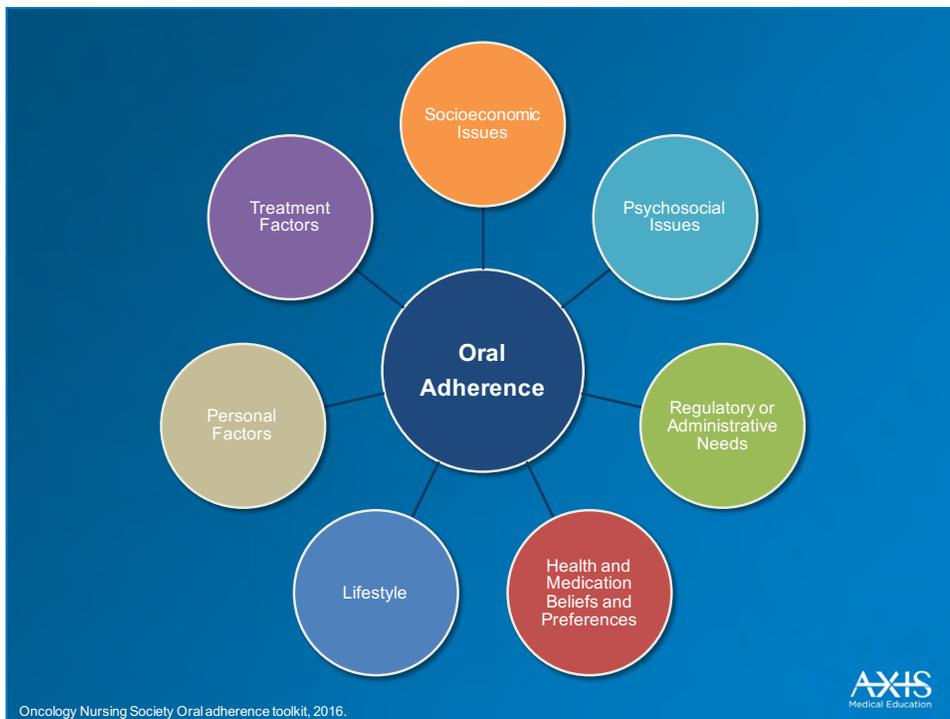
Treatment Adherence Issues

- Adherence rates to oral anticancer medication (OAM) often <80%
- 10% of patients do not refill OAM prescription
- Half do not take oral agents as prescribed
- Start with a patient assessment
 - Can the patient obtain and administer the regimen?

Atkinson et al. *Oncol Nurs Forum* 2016;43:576-582.
Oncology Nursing Society Oral adherence toolkit, 2016.

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▶ With the adverse events for oral anticancer medications comes added challenge for treatment adherence. Adherence rates in oral anticancer medications often are less than 80%. About 10% of patients do not refill oral anticancer medication prescriptions, and half do not take oral agents as prescribed. The best way to intervene with patients starting an oral anticancer medication is to have a good patient assessment; can the patient obtain and administer the regimen? It's more than just sending the patient home with a prescription.



▶ Two organizations have put a great deal of work into combating adherence issues. The Oncology Nursing Society and the Multinational Association of Supportive Care in Cancer have both designed tools to be used to help with adherence issues for patients.

This graphic represents 7 issues of areas to assess for the nurse when an oral anticancer medication is started. Starting with socioeconomic issues: How will the patient fill the prescription; does the patient have insurance; what copays and out-of-pocket costs are associated with the patient's insurance?

Psychosocial issues: What is the patient's mental status; does the patient have social support? Regulatory or administrative needs: Is the drug on formulary; is the drug approved by the FDA? Health and medication beliefs and preferences: Is the patient ready to accept the necessity of treatment, is the patient prepared for safety and adherence concerns, have the patient's expectations about treatment been managed?

Lifestyle: Where does the patient live in proximity to the clinic or pharmacy, is the treatment regimen a good fit for the patient, will a family member or caregiver be available to help with treatment and patient care?

Personal factors: How does the patient learn best; does the patient have any cognitive impairment, does the patient have the ability to take medications as prescribed, does the patient have comorbidities that could affect the treatment regimen

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or adherence, and does the patient use alcohol or drugs? And, lastly, treatment factors: How complex is the patient's treatment regimen? Is there a pill burden associated with the treatment regimen? What is the treatment duration?

Performing this comprehensive needs assessment will also help care coordination as barriers are identified and appropriate referrals are made to support services. Always keep in mind that pharmaceutical companies offer patient support programs for both medication and financial assistance.

Best Practices to Ensure Adherence

- Calendar or daily medication checklist
- Pill diaries
- Patient and family education
- Establishing routine, which includes drug administration
- Home psychological support

► Some best practices to ensure adherence include a calendar or daily medication checklist; a pill diary; patient and family education; establishing a routine, which includes drug administration; and home psychological support.

Oncology Nursing Society Oral adherence toolkit, 2016.

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Best Practices to Ensure Adherence

- Pillboxes with multiple compartments (as packaging form and storage needs permit)
- Electronic reminders
 - Alarms on clocks, timers and cell phones
 - Smartphone applications
 - Glowing or electronic pillboxes
 - Text message reminder
 - Automated voice recording (phone call) reminder
- Medication-dispensing machines

- ▶ Others include pillboxes with multiple compartments as packaging form and storage needs permit; electronic reminders—alarms on clocks, timers, or cell phones, smartphone applications, glowing or electronic pillboxes, text message reminders, or automated voice recording or a phone call reminder; and, lastly, medication-dispensing machines.

Oncology Nursing Society Oral adherence toolkit, 2016.

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Resources

- Oncology Nursing Society (ONS) Oral Adherence Toolkit:
www.ons.org
- Multinational Association of Supportive Care in Cancer (MASCC) Oral Agent Teaching Tool:
www.mascc.org/moatt



- ▶ These are the 2 examples of the tools I was referring to, the Oncology Nursing Society Oral Adherence Toolkit, and the Multinational Association of Supportive Care in Cancer Oral Agent Teaching Tool. Both are available online, and the websites are there for you.

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- ▶ We're going to move into a clinical case challenge to try to drive some of these points home.

Clinical Case Challenge

Clinical Case Challenge



- 56-year-old woman presents with cough and SOB, 10-pound weight loss, back pain
- Single mother, executive for international company, telecommuter, social alcohol, never-smoker, avid tennis player

- ▶ This is a 56-year-old woman who presents with a cough, shortness of breath, and a 10-pound weight loss and back pain. She's a single mother, an executive for an international company, a telecommuter, drinks alcohol only socially, is a never-smoker, and an avid tennis player.

SOB, shortness of breath.

Clinical Case Challenge (cont)



- Diagnostic imaging studies reveal hilar mass and T2 bone metastasis
- Endobronchial ultrasound is done
- Biopsy shows NSCLC, adenocarcinoma, molecular diagnostic testing shows *EGFR* exon 19 mutation

NSCLC, non-small cell lung cancer.

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- ▶ Diagnostic imaging studies reveal a hilar mass and T2 bone metastasis. Endobronchial ultrasound is done. Biopsy shows non-small cell lung cancer, adenocarcinoma. Molecular diagnostic testing shows *EGFR* exon 19 mutation.

Clinical Case Challenge

- The medical oncologist prescribes afatinib 40 mg orally once daily.

What should the oncology nurse do next to ensure that patient has the best chance of medication adherence?

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- ▶ The medical oncologist prescribes afatinib, 40 mg orally once daily.
So what should the oncology nurse do next to ensure that patient has the best chance of medication adherence?

Oncology Nursing Intervention

1. Assess for barriers/issues that would prevent adherence.
2. Provide the patient with information to access the pharmaceutical website to investigate patient support and assistance programs.
3. Reinforce the education the medical oncologist provided regarding the diagnosis and prescription.
4. Review side effect profile, discuss proactive strategies to prevent toxicities.



- ▶ One, assess for barriers/issues that would prevent adherence. Two, provide the patient with information to access the pharmaceutical website to investigate patient support and assistance programs. Three, reinforce the education the medical oncologist provided regarding the diagnosis and prescription. Or, four, review side effect profile, discuss proactive strategies to prevent toxicities.

And the answer is all the above.

Oncology Nursing Intervention (cont)

- The oncology nurse knows that there are multiple barriers/issues that affect the patient's ability to maintain adherence, so she uses the ONS Oral Adherence Toolkit to perform a patient assessment.
- Because afatinib is an oral chemotherapy and billed differently than chemotherapy, the nurse ensures that the patient is aware of patient assistance and support programs.



- ▶ The oncology nurse knows that there are multiple barriers and issues that affect the patient's ability to maintain adherence, so she uses the Oncology Nursing Society Oral Adherence Toolkit to perform a patient assessment. Because afatinib is an oral chemotherapy and in some instances billed differently than chemotherapy, the nurse ensures that the patient is aware of patient assistance and support programs.

Oncology Nursing Intervention (cont)

- She assess/reinforces the patient's understanding of her disease and treatment regimen
 - She knows that afatinib should be taken on an empty stomach and that disease in most patients started on a first-line tyrosine kinase inhibitor will progress within 1 year
- She informs the patient that diarrhea develops in most patients, and tells her how to manage the diarrhea and when to notify the physician



- ▶ She assesses and reinforces the patient's understanding of her disease and treatment regimen. She knows that afatinib should be taken on an empty stomach and that the disease in most patients started on a first-line TKI will progress within 1 year. She informs the patient that diarrhea develops in most patients and tells her how to manage the diarrhea and when to notify the physician.

Oncology Nursing Intervention (cont)

- Skin reactions are common, so she reinforces the MASCC rash prevention protocol and recommends moisturizers, sunscreen SPF 15 or higher, and protective clothing when outdoors



MASCC, Multinational Association of Supportive Care in Cancer.

- ▶ Skin reactions are common, so she reinforces the MASCC rash prevention protocol and recommends moisturizers, sunscreen with SPF 15 or higher, and protective clothing when outdoors.

Clinical Case Challenge



- A 9-month follow up CT scan shows disease progression
- A biopsy confirms metastatic adenocarcinoma, NSCLC

Should this specimen be sent for molecular diagnostic testing?

- ▶ So now it's 9 months later and this patient goes for her follow-up CT scan, which shows progression of disease, and biopsy results confirm metastatic adenocarcinoma, non-small cell lung cancer. Should this specimen be sent for molecular testing?

CT, computed tomography; NSCLC, non-small cell lung cancer.

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Rebiopsy

- Acquired resistance to EGFR TKIs eventually develops in all patients with *EGFR* mutation-positive lung cancers
- Repeat biopsy is essential to determine appropriate treatment
- Secondary mutations have been identified
 - *T790M*
 - *MET*
 - Histologic transformation to small cell lung cancer

- ▶ The answer is yes. *EGFR* mutation *T790M* is reported in approximately half of adenocarcinomas with acquired resistance to EGFR inhibitors, and is a potential prognostic, predictive biomarker. Acquired resistance to EGFR TKIs develops after a median of 7 to 12 months in patients with *EGFR* mutation-positive lung adenocarcinoma.

Jekunen. *J Oncol*. 2015;2015:1-11.

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Clinical Case Challenge



- Molecular testing identifies *T790M* mutation in exon 20
- Afatinib is discontinued and osimertinib 80 mg once daily is started

How should the nurse help to educate the patient about the potential side effects of osimertinib?



- ▶ Molecular testing identifies the *T790M* mutation in exon 20. Afatinib is discontinued and osimertinib 80 mg once daily is started.

How should the nurse help to educate the patient about the potential side effects of osimertinib?

Oncology Nursing Intervention: Adverse Effects Education

- Because osimertinib has a side effect profile similar to that of afatinib, the nurse reinforces the education concerning diarrhea and skin care.



- ▶ Because osimertinib has a side effect profile similar to that of afatinib, the nurse reinforces the education concerning diarrhea and skin care.

Key Takeaways

- Lung cancer is the second most commonly diagnosed cancer
- Up to 60% of lung adenocarcinomas have an oncogenic driver mutation
- Determination of *EGFR* status drives appropriate treatment choices



- ▶ So, as we finish this slide deck, there are several key takeaways I'd like you to remember. Lung cancer is the second most commonly diagnosed cancer; up to 60% of lung adenocarcinomas have an oncogenic driver mutation; the determination of *EGFR* status drives appropriate treatment choices.

Key Takeaways (cont)

- Disease in most patients progresses within 1 year of starting a tyrosine kinase inhibitor and acquires a *T790M* mutation
- Oncology nurses are key in providing education on adherence with oral oncolytics and preventing/moderating side effects from tyrosine kinase inhibitors



- ▶ Disease in most patients progresses within 1 year of starting a TKI and acquires a *T790M* mutation.

Oncology nurses are key in providing education on adherence with oral oncolytics and preventing and moderating side effects from tyrosine kinase inhibitors.

**Nursing Clinical Insights Into the
Benefits and Challenges of EGFR
TKIs in the Treatment of NSCLC**



- ▶ Thank you for participating in this activity. If you're interested in receiving credit for your participation, please proceed to the post-test and evaluation.

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The executive leadership of AXIS combines 75 years of experience in adult learning theory, curriculum design/implementation/assessment, continuing education accreditation standards, and medical meeting planning and logistics. Our team has a deep understanding of the governing guidelines overseeing the medical education industry to ensure compliant delivery of all activities.

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