TESTING TO TARGET IN NON-SMALL CELL LUNG CANCER:

Managed Care Perspectives

Presented by The University of Tennessee College of Pharmacy

University of Tennessee College of Pharmacy

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Supported by an educational grant from AstraZeneca.

Participating Faculty

R. Donald Harvey, PharmD, FCCP, BCOP
Associate Professor
Hematology/Medical Oncology
Director, Phase I Clinical Trials Section
Winship Cancer Institute of Emory University
Atlanta, Georgia

Matthew Farber
Senior Director
Oncology Disease State
Walgreens Specialty Pharmacy
Deerfield, Illinois

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Agenda

Welcome and Goals

State of the Science:
Overview of NSCLC in 2016

Recent Updates on NSCLC Targets and Targeted Therapies:
New Opportunities for Personalized Treatment

Providing Individualized Care for Patients with NSCLC:
Pharmacist Perspectives

Learning Objectives

- **ASSESS** the role of genetic and molecular biomarkers in guiding NSCLC treatment plans.
- **EVALUATE** the safety, efficacy, and therapeutic role of new and emerging targeted therapies.
- **RECOMMEND** pharmacy-driven strategies to facilitate individualized NSCLC management.

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- Q&A
  - Please type in questions at any time during the presentation, using the “Ask a Question” tab located on the left of your screen.
  - The faculty will try to get to all of your questions during Q&A.
  - Slides are available on Event Resource tab
- Post-Test, Evaluation, and Certification

State of the Science: Overview of NSCLC in 2016

R. Donald Harvey, PharmD, FCCP, BCOP

Associate Professor, Hematology/Medical Oncology
Director, Phase I Clinical Trials Section
Winship Cancer Institute of Emory University
Atlanta, Georgia

Lung Cancer Facts and Figures

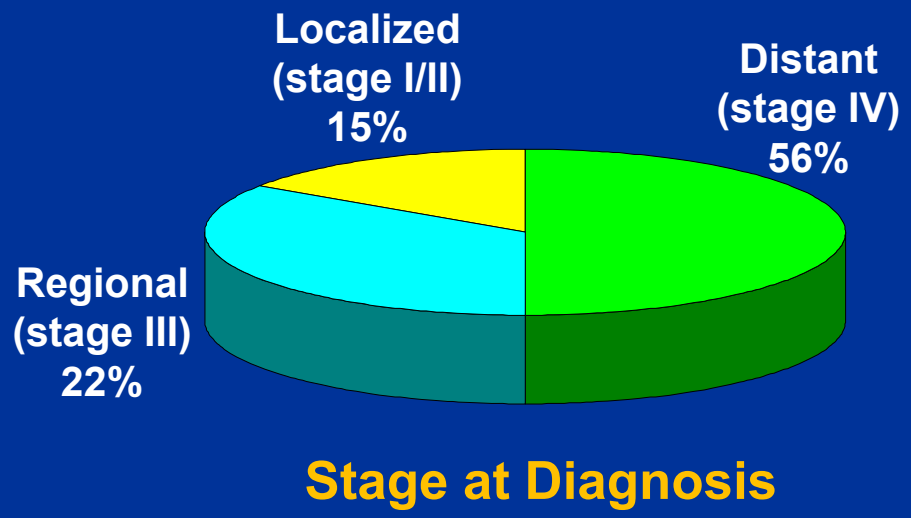
- Second most common cancer and leading cause of cancer-related mortality in the US
  - Estimated 224,390 new cases and 158,080 deaths in 2016
  - Accounts for more deaths than breast, prostate, and colorectal cancers combined
- 25 000 to 30 000 Americans who never smoked will develop lung cancer this year
  - More common than esophageal, gastric, ovarian, testis, Hodgkin lymphoma, myeloma, and CML
- Very heterogeneous histologically and molecularly
- Historically shrouded by therapeutic nihilism

CML = chronic myelogenous leukemia.

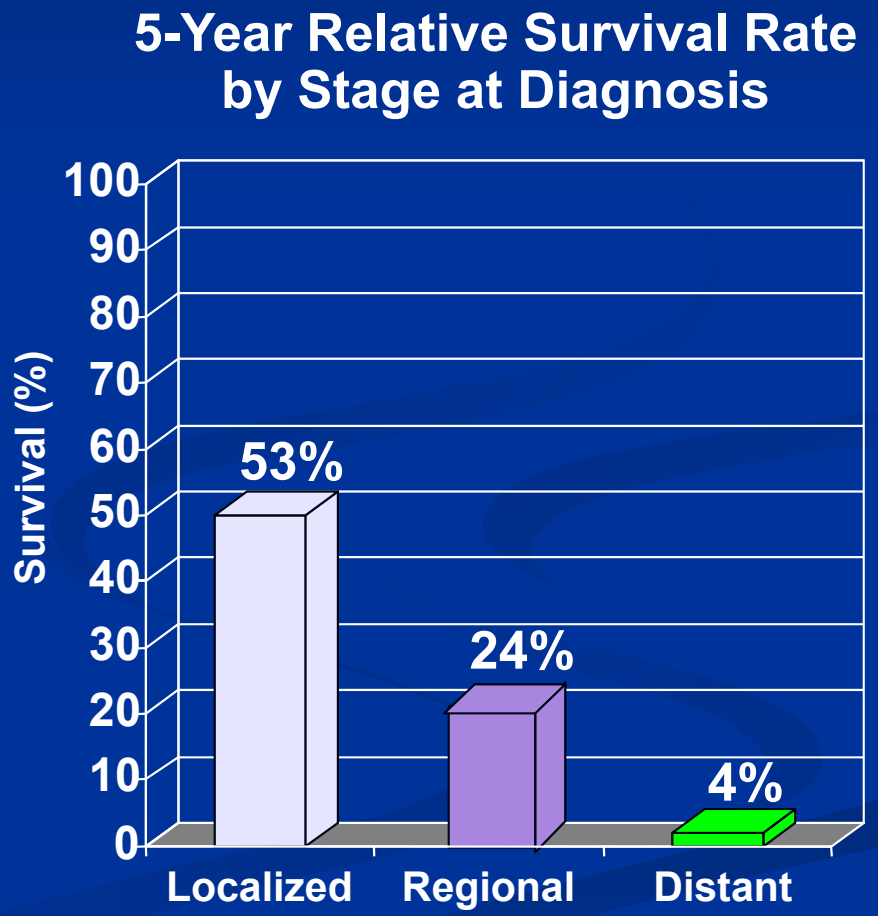
American Cancer Society. Cancer Facts & Figures 2016.

Unfavorable Stage Distribution at Diagnosis

- Screening not routinely practiced



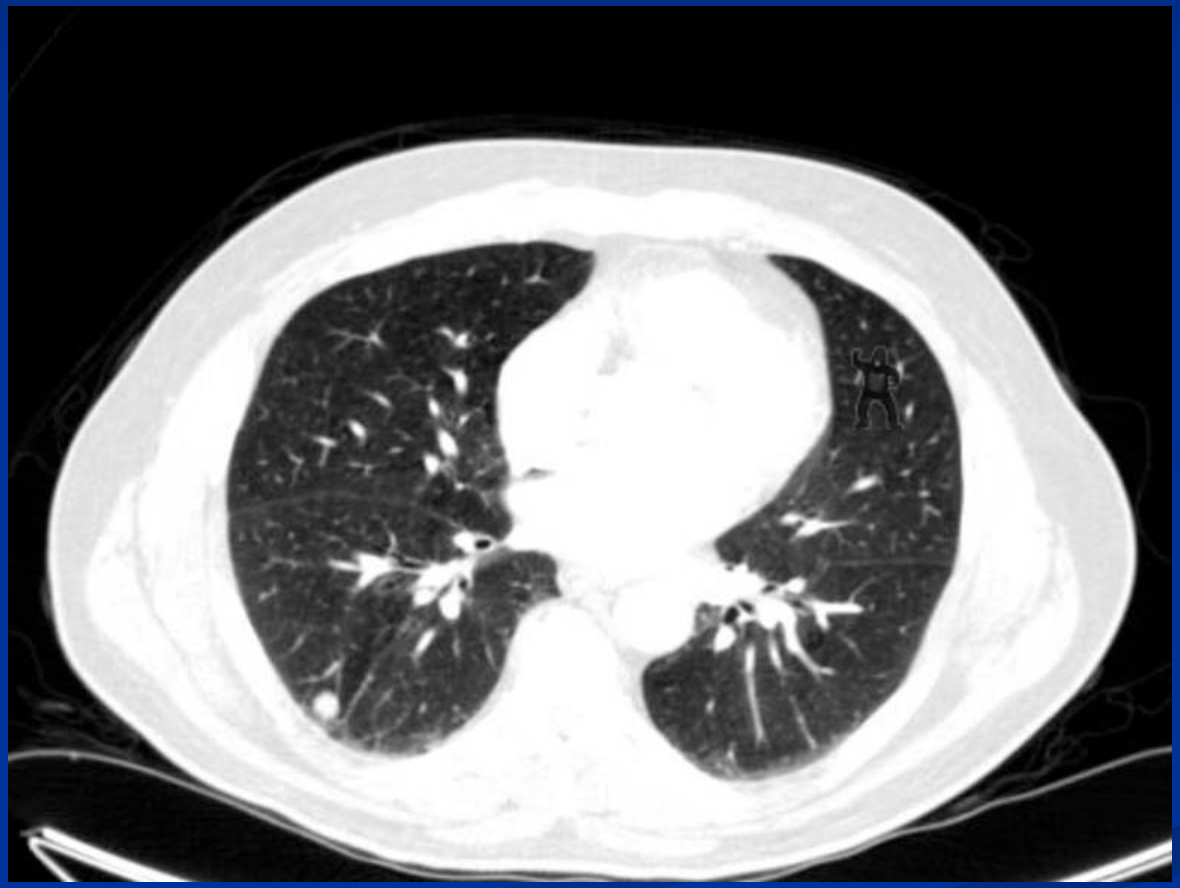
Stage at Diagnosis



American Cancer Society. Cancer Facts & Figures 2016.

Therapies for NSCLC

- Today's treatment approach based on:
  - Histology
  - Molecular selection
  - Performance status (PS)



National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Non-small cell lung cancer. Version 4.2016. Updated January 12, 2016.

Histology

- NSCLC accounts for 85% of all lung cancers.
  - Adenocarcinoma (35% to 40%)
    - Most common in nonsmokers
    - Peripheral location
  - Squamous cell (epidermoid) carcinoma (25% to 30%)
    - Slower growing
    - Clear relationship with smoking
    - Central location
  - Large cell, bronchoalveolar carcinoma

Molina JR, et al. *Mayo Clin Proc*. 2008;83:584-594.

Principles of NSCLC Chemotherapy

Platinum-based doublets are a mainstay of therapy.

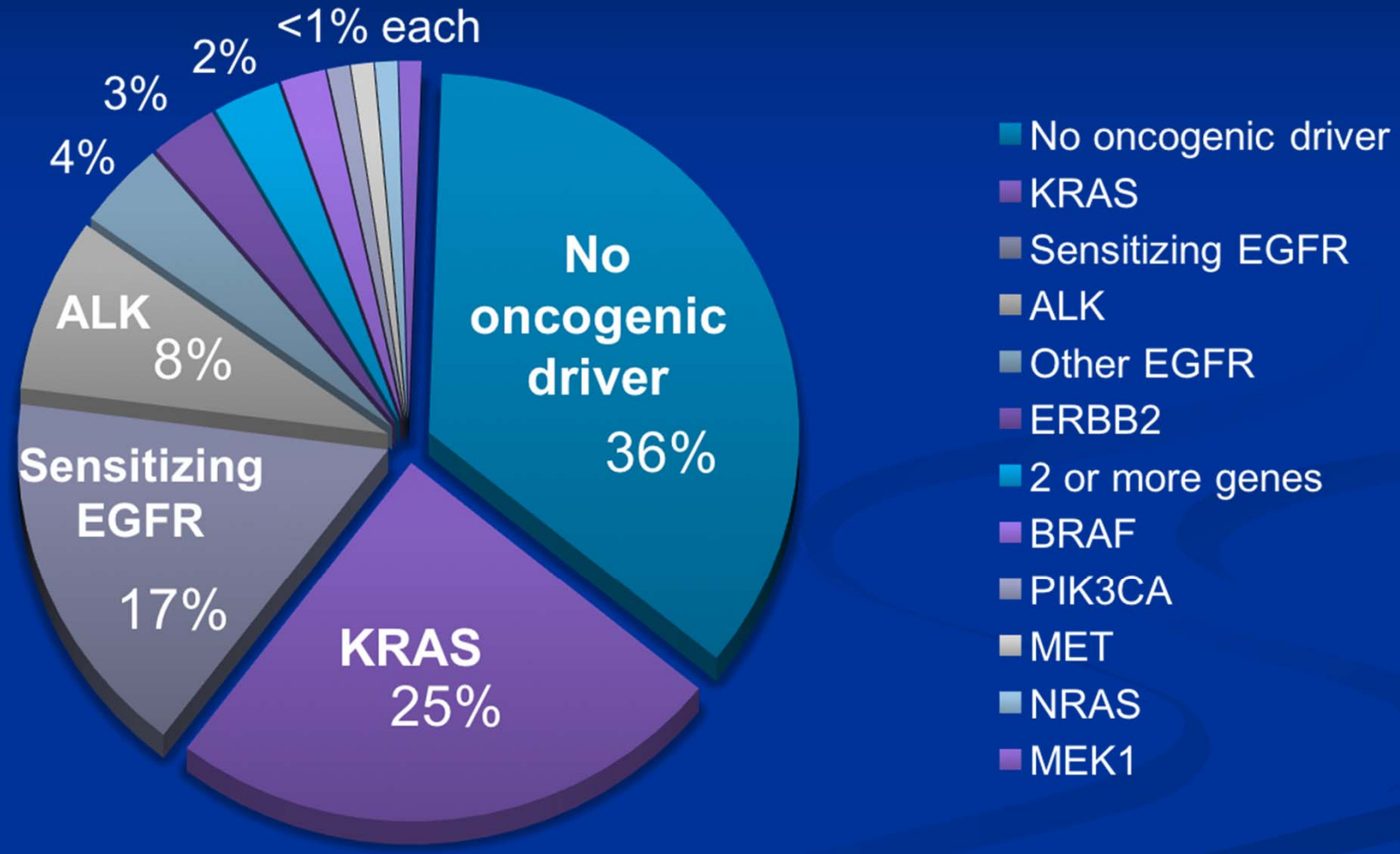
Early Stage (Adjuvant Therapy – Stage II, Selected Stage IB)		
Cisplatin-based (or possibly carboplatin-based) chemotherapy		
Locoregional Disease (Stage III)		
Chemoradiotherapy		
Recurrent or New Diagnosis Metastatic Disease		
First-line	**Maintenance**	**Second, subsequent lines**
Cisplatin- or carboplatin-based chemotherapy ± bevacizumab or pemetrexed in select patients; single-agent EGFR- or ALK-directed therapies in patients with mutations	Continuation vs switch (2B) Bevacizumab, pemetrexed, gemcitabine, docetaxel, or erlotinib	PS 0–2: nivolumab, pembrolizumab (preferred). Pemetrexed, gemcitabine, docetaxel +/- ramucirumab, or erlotinib PS 3–4: best supportive care

ALK = anaplastic lymphoma kinase; EGFR = epidermal growth factor receptor.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Non-small cell lung cancer. Version 4.2016. Updated January 12, 2016.

Lung Cancer Mutation Consortium

Targetable Mutations in 64% of Lung Adenocarcinomas



N = 733

Mutations are found in 64% (466/733) of tumors completely tested.

Kris MG, et al. *JAMA*. 2014;311:1997-2006.

Initial Histology-Based Treatment: Advanced NSCLC

- Nonsquamous
  - Adenocarcinoma, large cell, or NSCLC not otherwise known
  - Molecular testing algorithm
    - EGFR mutation positive → erlotinib, afatinib, or gefitinib
      - PS 0–4 (only therapy to consider in PS 3–4 patients)
    - EGFR mutation negative → send tissue for testing for presence of ALK gene rearrangement
    - EML4-ALK rearrangement positive → crizotinib

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Non-small cell lung cancer. Version 4.2016. Updated January 12, 2016.

Initial Histology-Based Treatment: Advanced NSCLC

- Nonsquamous
- PS 0–1
  - All molecular testing is negative
    - Bevacizumab eligible?
      - Yes → combination with carboplatin and paclitaxel
      - No → consider platinum + pemetrexed
- Squamous
  - Molecular testing not recommended, except in never smokers, small specimens, or mixed histology
  - Platinum-based doublet

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Non-small cell lung cancer. Version 4.2016. Updated January 12, 2016.

NSCLC Treatment Landscape:
First-line Treatment by Histologic Subtype

Nonsquamous cell (70%)

Adenocarcinoma
Large cell
NSCLC NOS

- *EGFR* mutation testing
- ALK testing

EGFR mutation or *ALK* (-), or unknown

- PS 0-1
- PS 2
- PS 3-4

Ctx (doublet or single agent)

BSC

EGFR mutation (+) (15%)

Erlotinib, afatinib, or gefitinib

ALK (+) (4%)

Crizotinib

Platinum doublet Ctx*

- Carbo/paclitaxel +/- bevacizumab (if no recent hemoptysis)
- Cis/pemetrexed
- Cis/docetaxel
- Others

Response or SD (4–6 cycles total)

Maintenance therapy

- Continue current regimen until PD
- Continuation maintenance
  - Bevacizumab, cetuximab, pemetrexed, or gemcitabine
- Switch maintenance
  - Pemetrexed or erlotinib
- Observation

Squamous cell (30%)

- *EGFR* mutation and *ALK* testing not routinely recommended

- PS 0-1
- PS 2
- PS 3-4

Platinum doublet*

- Cis/gemcitabine
- Cis/docetaxel
- Carbo/paclitaxel

Ctx (doublet or single agent)

BSC

Response or SD (4–6 cycles total)

Maintenance therapy

- Continue current regimen until PD
- Continuation maintenance preferred
- Switch maintenance
- Observation

*Cisplatin or carboplatin have been proven effective in combination with any of the following agents: paclitaxel, docetaxel, gemcitabine, vinorelbine, irinotecan, etoposide, vinblastine, pemetrexed. If cisplatin-intolerant, carboplatin doublets are used.

BSC = best supportive care; Carbo = carboplatin; Cis = cisplatin; Ctx = chemotherapy; NOS = not otherwise specified; PD = progressive disease; SD = stable disease.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Non-small cell lung cancer. Version 4.2016. Updated

Recent Updates on NSCLC Targets and Targeted Therapies: *New Opportunities for Personalized Treatment*

R. Donald Harvey, PharmD, FCCP, BCOP

Associate Professor, Hematology/Medical Oncology
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Winship Cancer Institute of Emory University
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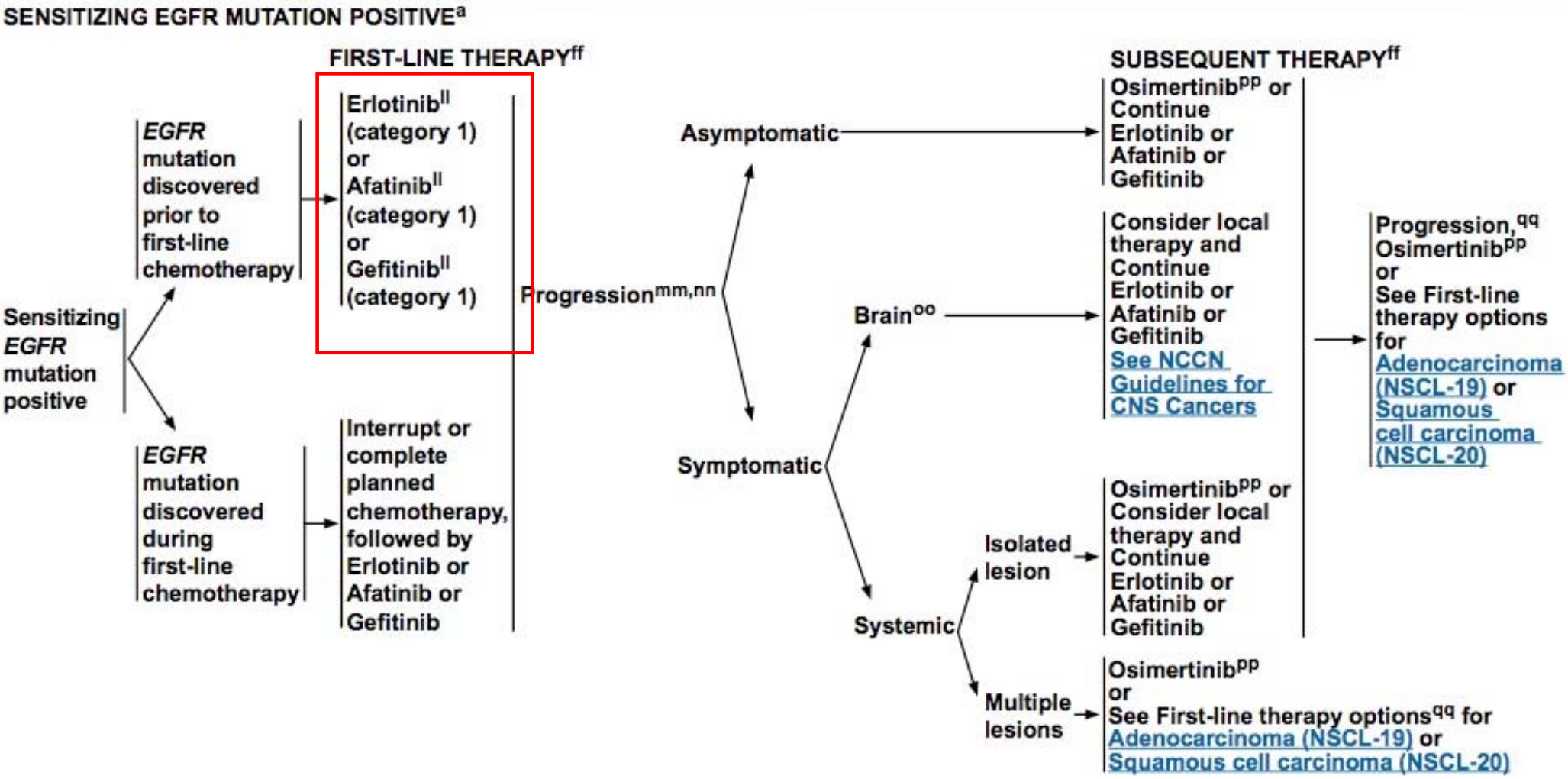
EGFR-Mutated NSCLC

EGFR-Mutated NSCLC

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2016
Non-Small Cell Lung Cancer



National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology.
Non-small cell lung cancer. Version 4.2016. Updated January 12, 2016. For educational purposes only.

Which of the following MOST accurately describes the adverse effects of EGFR tyrosine kinase inhibitors (TKIs)?

A. Each approved EGFR TKI has a unique side effect profile
B. Common class effects of the EGFR TKIs include fatigue and elevated transaminases
C. Common class effects of the EGFR TKIs include diarrhea and rash
D. The AEs depend on route of administration (oral vs. parenteral)
E. I'm not sure

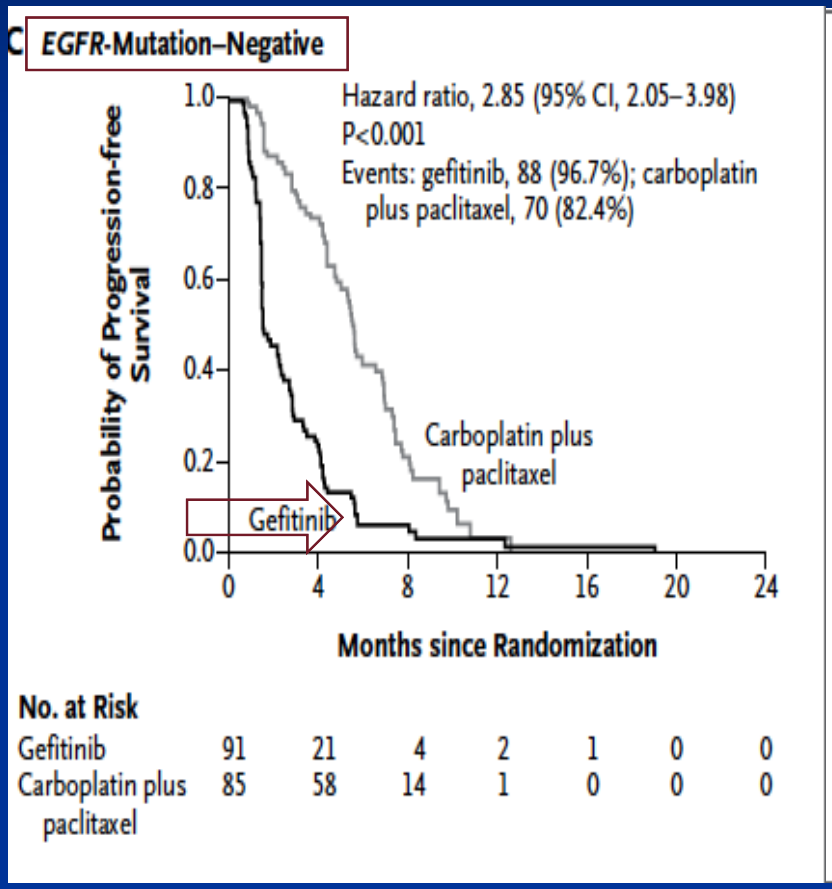
EGFR Tyrosine Kinase Inhibitors: Clinical Pharmacology Points

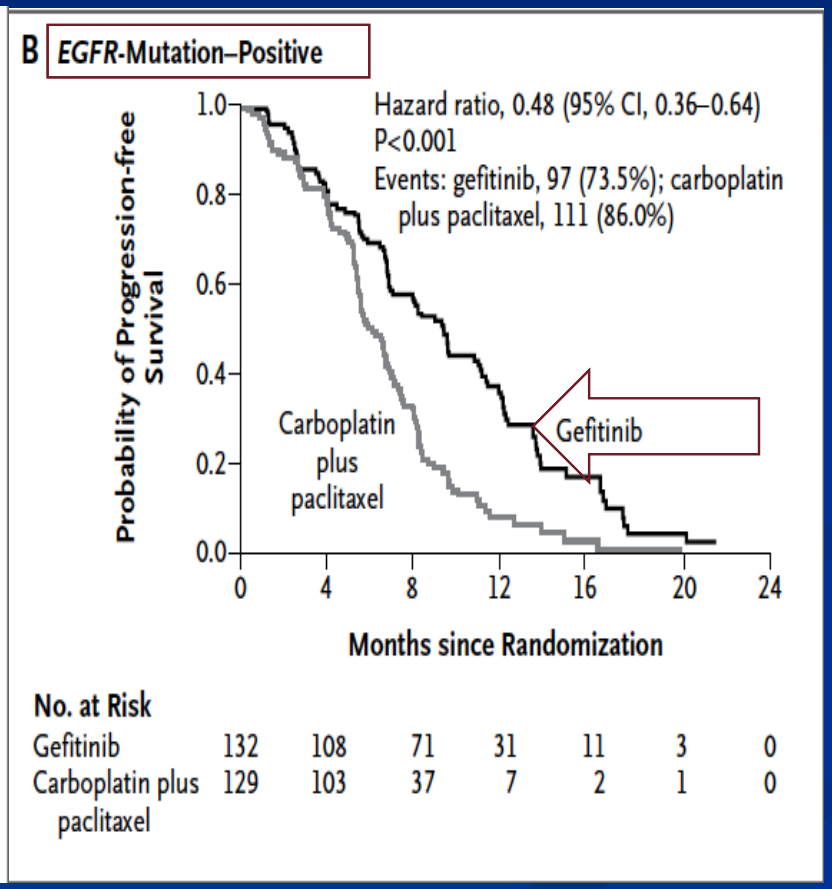
	Erlotinib	Afatinib	Gefitinib
Dose	150 mg po daily	40 mg po daily	250 mg po daily
Interactions	CYP3A4 inducers, inhibitors, smoking (induces CYP1A2 goal = 300 mg po daily)	High-fat meal decreases exposure by 39% compared with fasted state	Systemic exposure may be increased in CYP2D6 poor metabolizers
Common AEs	Rash, diarrhea, weakness	Rash, weight loss, diarrhea	Rash, diarrhea, weakness
Administration	Empty stomach, avoid PPIs, H2 antagonists	Take at least 1 hour before or 2 hours after meals	No food effect
Strengths	25-, 100-, 150-mg tablets	20-, 30-, 40-mg tablets	250-mg tablet

AE, adverse event; po, by mouth; PPI, proton-pump inhibitor.

EGFR-Sensitizing Mutations Predict Response to EGFR TKI Therapy

IPASS Gefitinib Study





Incidence of *EGFR* mutation: 261/437 = 59.7%
Most common: *EGFR* exon 21 L858R and exon 19 deletion
Treatment by subgroup interaction test, *P* < .0001

CI = confidence interval; IPASS = Iressa Pan-Asia Study; TKI = tyrosine kinase inhibitor

Mok TS, et al. IPASS. *N Engl J Med*. 2009;361:947-957.

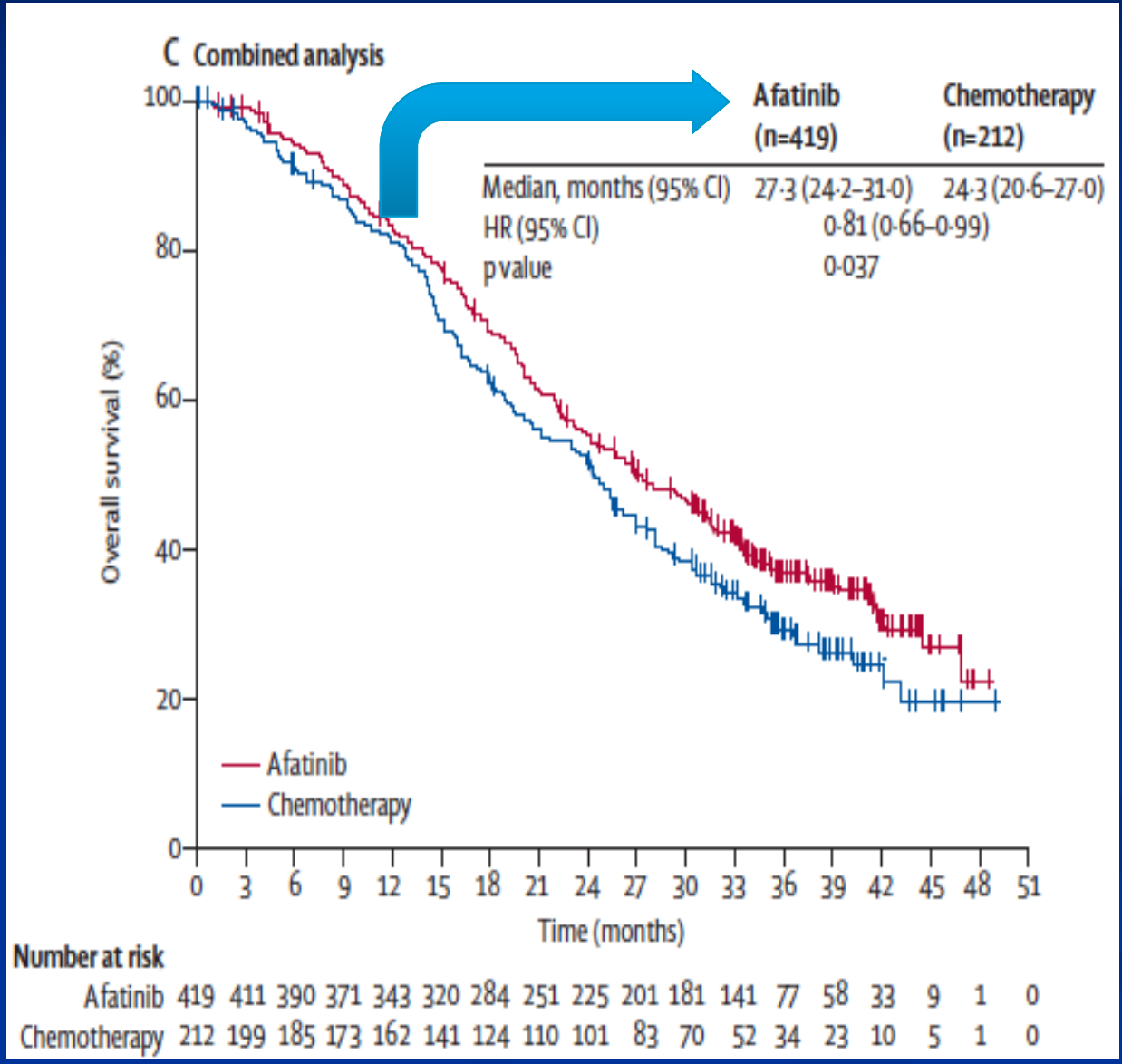
Treatment-Naive *EGFR*-Mutated Lung Cancer: EGFR TKIs Beat Chemotherapy

Study	Treatment	*N*	Median PFS, mo	Median OS, mo
NEJ002	Gefitinib vs carboplatin/paclitaxel	230	10.8 vs 5.4 (*P* <.001)	27.7 vs 26.6 (*P* = .48)
WJTOG-3405	Gefitinib vs cisplatin/docetaxel	172	9.2 vs 6.3 (*P* <.0001)	34.8 vs 37.3 (HR: 1.25)
OPTIMAL	Erlotinib vs carboplatin/gemcitabine	165	13.1 vs 4.6 (*P* <.0001)	22.7 vs 28.9 (*P* = .69)
EURTAC	Erlotinib vs platinum-based chemotherapy	174	10.4 vs 5.2 (*P* <.0001)	22.9 vs 19.6 (*P* = .68)
LUX-Lung 3	Afatinib vs cisplatin/pemetrexed	345	11.1 vs 6.9 (*P* =.001)	28.2 vs 28.2 (*P* = .38)
LUX-Lung 6	Afatinib vs cisplatin/gemcitabine	364	11.0 vs 5.6 (*P* <.0001)	23.1 vs 23.5 (*P* = .61)

HR = hazard ratio; OS = overall survival; PFS = progression-free survival.

N Engl J Med. 2010;362:2380-2388; *Ann Oncol*. 2013;24:54-59; *Lancet Oncol*. 2010;11:121-128; *J Clin Oncol*. 2014;32:abstract 8117; *Lancet Oncol*. 2011;12:735-742; *J Clin Oncol*. 2012;30:abstract 7520; *Lancet Oncol*. 2012;13:239-246; *Ann Oncol*. 2014;25:iv426-iv470; *J Clin Oncol*. 2013;31:3327-3334; *Lancet Oncol*. 2014;15:213-222; *Lancet Oncol*. 2015;16:141-151.

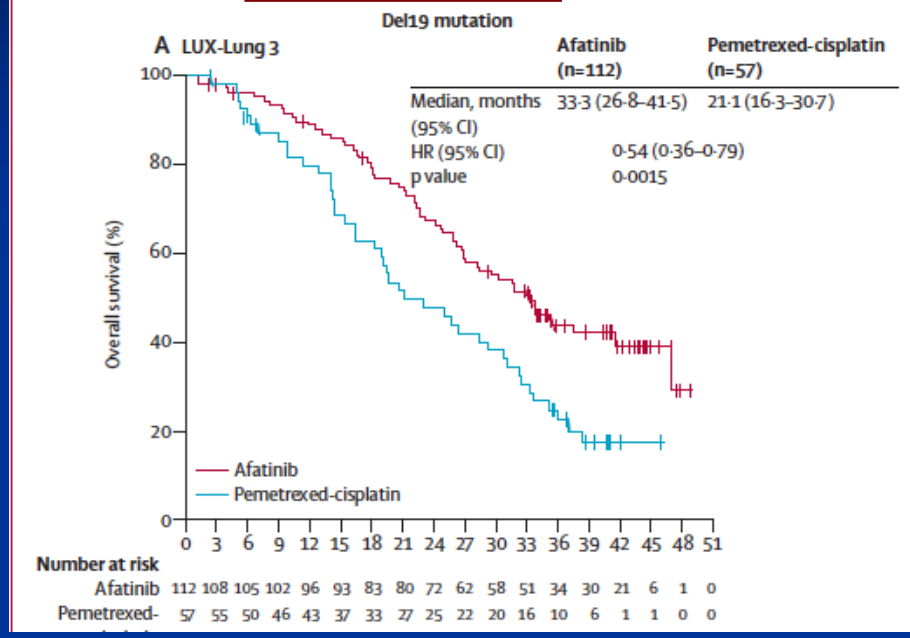
Combined LUX-Lung 3 and 6 Afatinib Data: Overall Survival Benefit with EGFR TKI Therapy



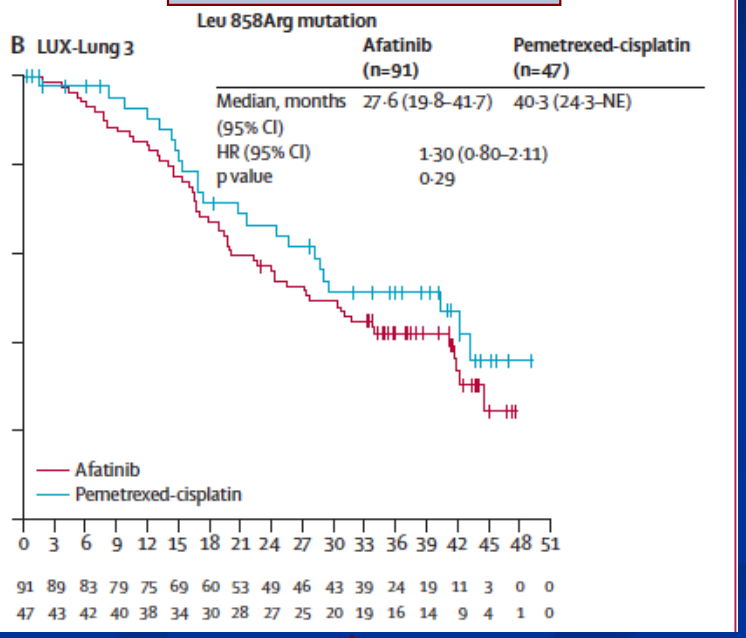
Yang JC, et al. *Lancet Oncol*. 2015;16:141-151. For educational purposes only.

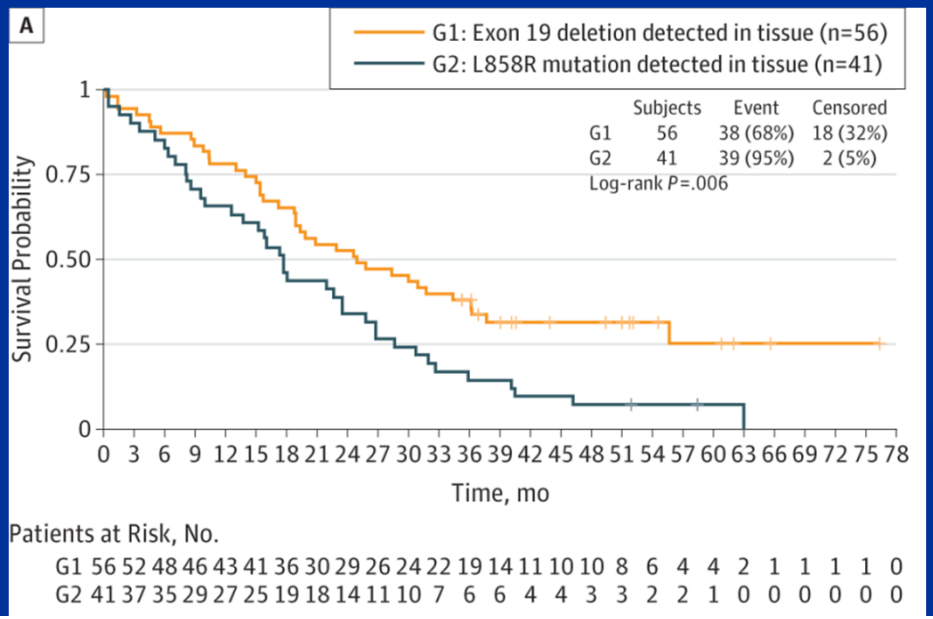
Mutation Subtype Predicts Response to Anti-EGFR: Exon19del > Exon21 L858R

Exon19Del



Exon21L858R





AFATINIB

ERLOTINIB

Yang JC, et al. *Lancet Oncol*. 2015;16:141-151; Karachaliou N, et al. *JAMA Oncol.* 2015;1:149-157. For educational purposes only.

Case 1

- 65-year-old woman with EGFR-mutation-positive NSCLC starts erlotinib 150 mg oral daily dosing.
- Her cough resolves within 2 weeks.
- She develops a bothersome acneiform rash on her face, chest, and back and grade 2 diarrhea.
- She is started on oral doxycycline and topical steroids, which improves the rash.
- The diarrhea is controlled after the initiation of loperamide.

Case 1 (cont'd)

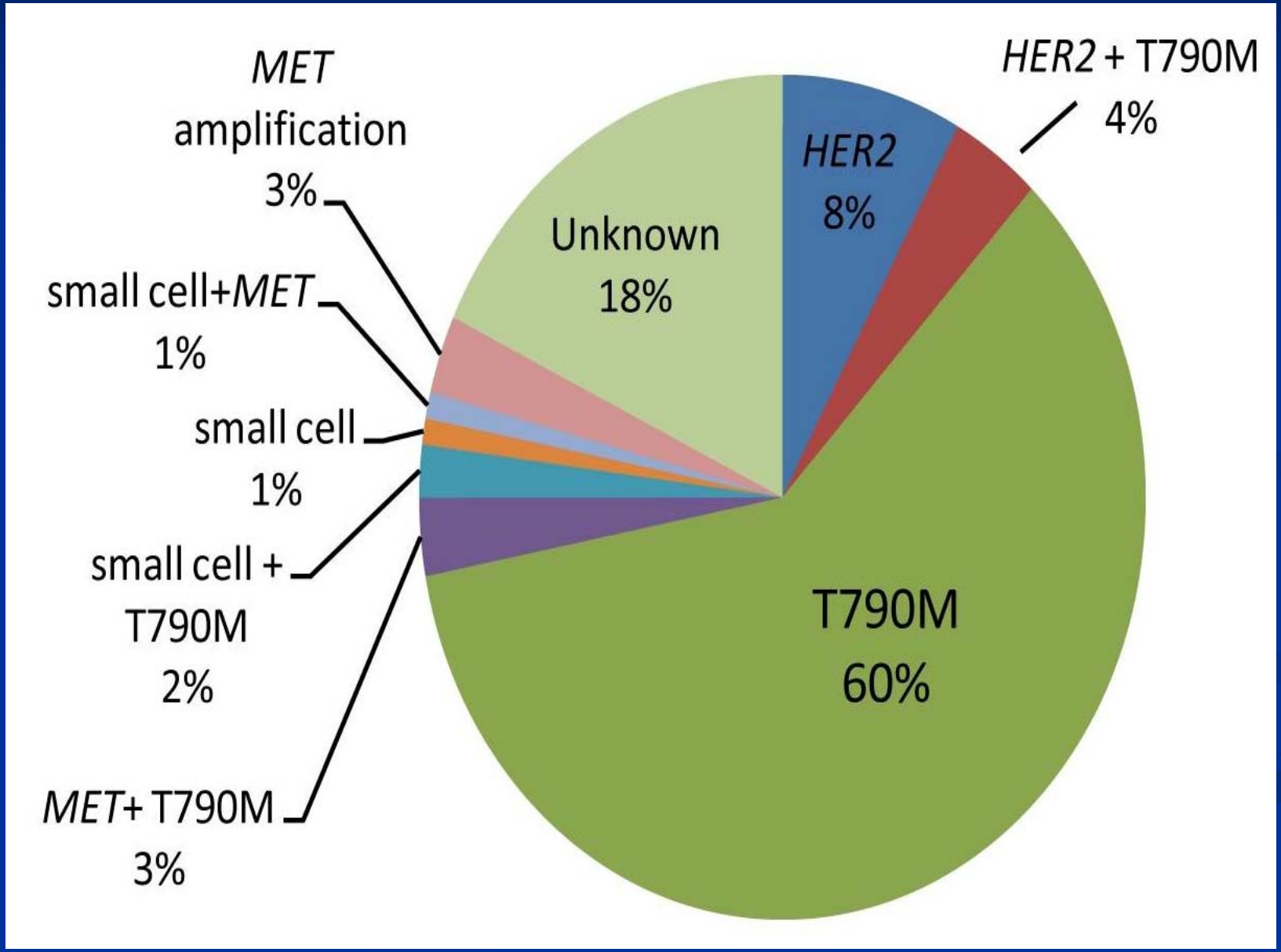
- She does well on therapy for ~8 months before she has progressive disease.
  - Diffuse new metastases
- She is symptomatic with fatigue and cough.
- Brain MRI is stable.

MRI = magnetic resonance imaging.

What Do You Do Next?

A. Repeat biopsy of an accessible tumor lesion
B. Switch to carboplatin, pemetrexed, bevacizumab
C. Begin osimertinib
D. Start afatinib and cetuximab
E. Add platinum-based chemotherapy to erlotinib
F. Liquid biopsy with circulating tumor DNA

Mechanisms of Resistance to EGFR TKI Therapy: T790M Gatekeeper Mutation in 60%



Yu HA, et al. *Clin Cancer Res*. 2013;19:2240-2247. For educational purposes only.

Plasma Genotyping for T790M:
"Good Sensitivity and Likely Good Specificity"

		Tissue*			Total
		Positive	Negative	Inadequate tissue	
Plasma*	Positive	155	23	12	190
	Negative	37	12	8	57
Total		192	35	20	247

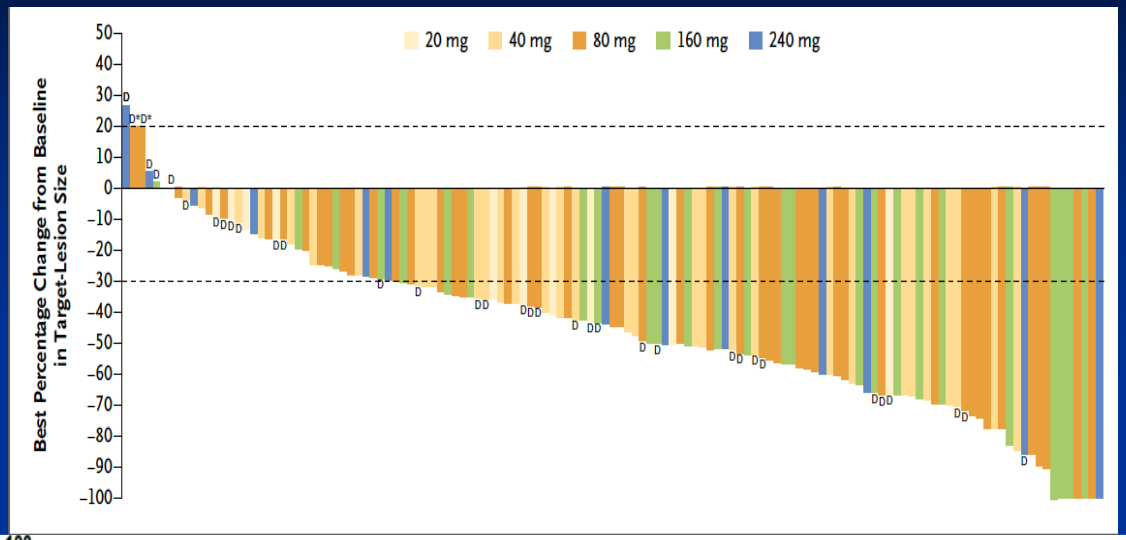
*Patients at all doses.

- When inadequate tissue specimens are factored in, plasma testing identifies as many patients as T790M+ as tissue testing
- T790M tissue^{-} plasma^{+} are not false-positives – T790M confirmed in plasma on subsequent testing in 5/7 samples

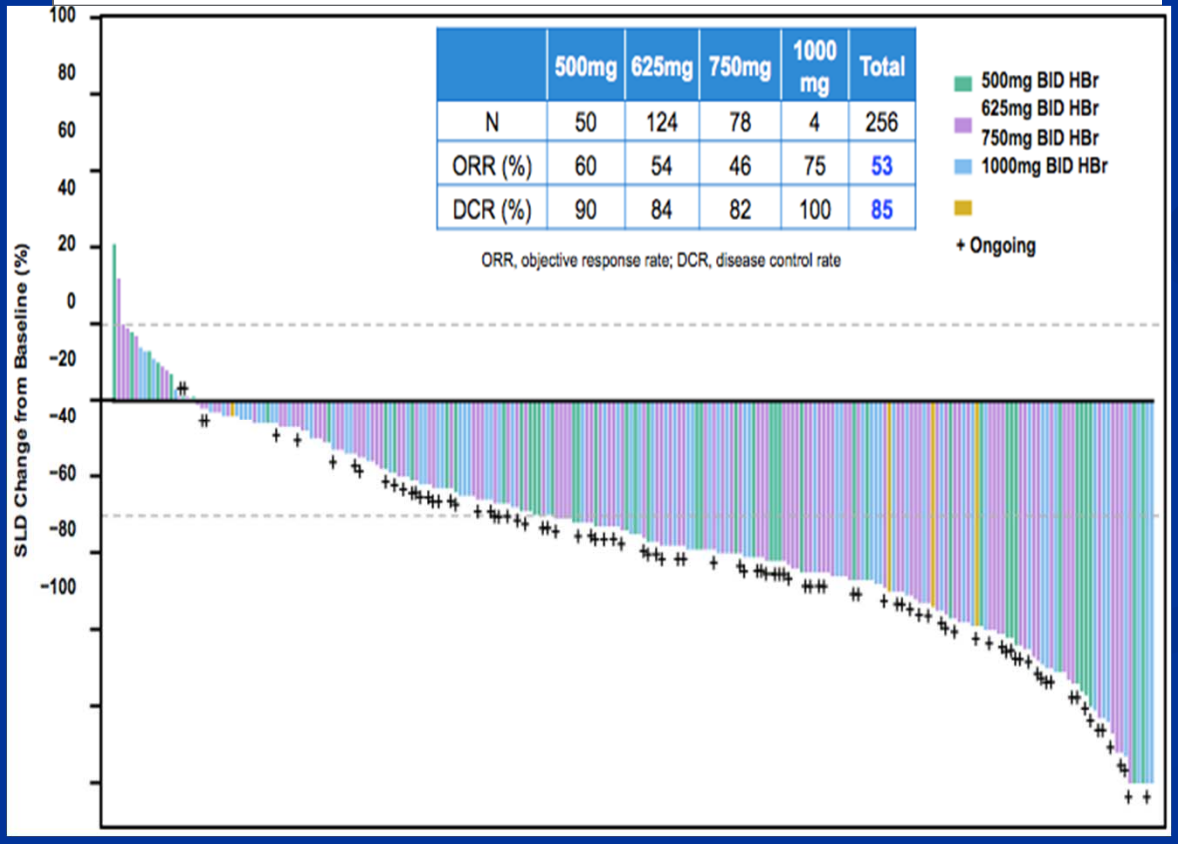
Tissue as reference: Positive percent agreement	T790M	Activating mutations
	81% (155/192)	87% (193/221)

Sequist LV, et al. *J Clin Oncol*. 2015;33:abstract 8001.

Third-Generation EGFR TKIs Have Activity at Time of Acquired Resistance (eg, osimertinib and CO-1686)



AZD-9291/osimertinib ORR
- **EGFR T790M+ 61%**
- **EGFR T790M- 21%**



	500mg	625mg	750mg	1000 mg	Total
N	50	124	78	4	256
ORR (%)	60	54	46	75	53
DCR (%)	90	84	82	100	85

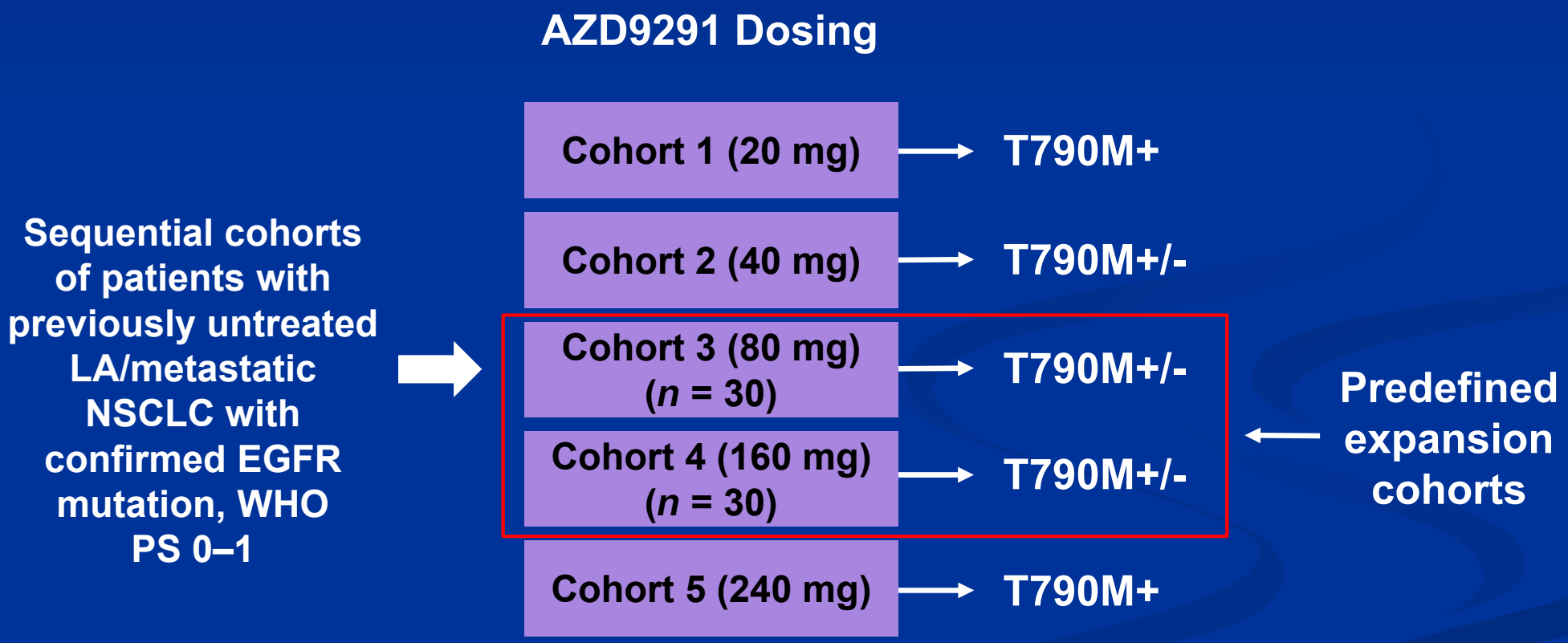
ORR, objective response rate; DCR, disease control rate

CO-1686/rociletinib ORR
- **EGFR T790M+ 53%**
- **EGFR T790M- 35%**

HBr = hydrogen bromide; ORR = objective response rate.

Janne PA, et al. *N Engl J Med*. 2015;372:1689-1699; Sequist LV, et al. *N Engl J Med*. 2015;372:1700-1709; Sequist LV, et al. *J Clin Oncol.* 2015;33:abstract 8001; Wakelee HA. MINI03.10. WCLC 2015. For educational purposes only.

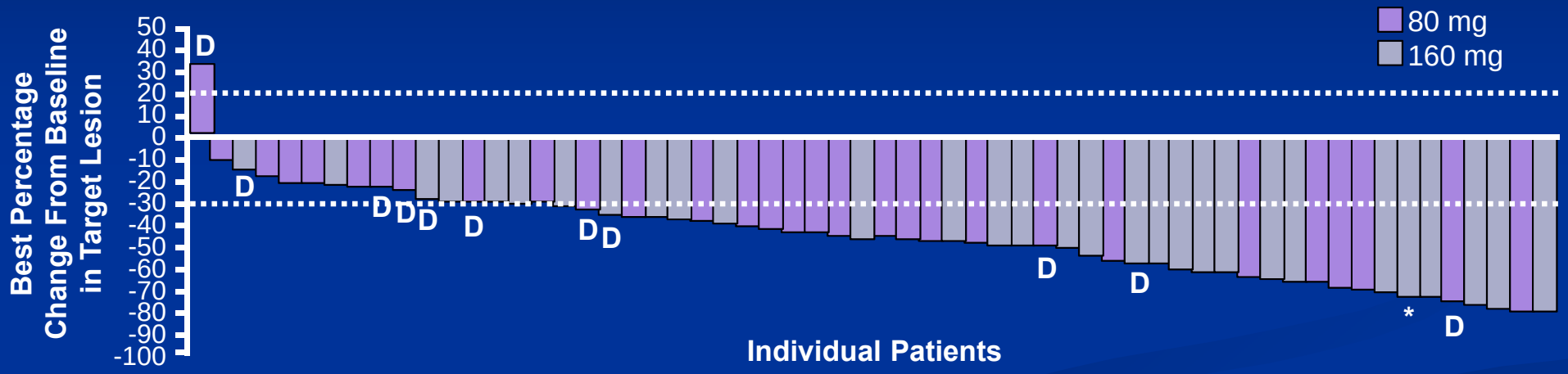
AURA: Osimertinib in First-Line EGFR-Mutant NSCLC



LA = locally advanced; WHO = World Health Organization.

Ramalingam SS, et al. ASCO 2015. Abstract 8000.

AURA: Tumor Response and PFS



Outcome	80 mg (*n* = 30)	160 mg (*n* = 30)	Total (*N* = 60)
Maximum DOR, months	**13.8***	**9.7***	
PFS, % (95% CI)			
▪3 months	90 (72–97)	97 (79–100)	93 (83–97)
▪6 months	83 (64–93)	90 (72–97)	87 (75–93)
▪9 months	83 (64–93)	78 (57–89)	81 (68–89)
▪12 months	73 (51–87)	NC	72 (55–64)

*Ongoing.

DOR = duration of response; NC = not calculable.

Ramalingam SS, et al. ASCO 2015. Abstract 8000.

AURA: Safety

- Most common toxicities: skin rash, diarrhea, dry skin, stomatitis; mostly grade 1
- No grade ≥3 hyperglycemia, QT prolongation, or ILD-like events

AE, %	80 mg (*n* = 30)	160 mg (*n* = 30)	Total (*N* = 60)
Any event grade ≥3	33	43	38
Treatment-related AE	97	100	98
Treatment-related AE grade ≥3	10	20	15
Treatment-related AE leading to discontinuation	7	3	5
Treatment-related serious AE	10	3	7

ILD = interstitial lung disease.

Ramalingam SS, et al. ASCO 2015. Abstract 8000.

Summary: Third-Generation EGFR TKIs

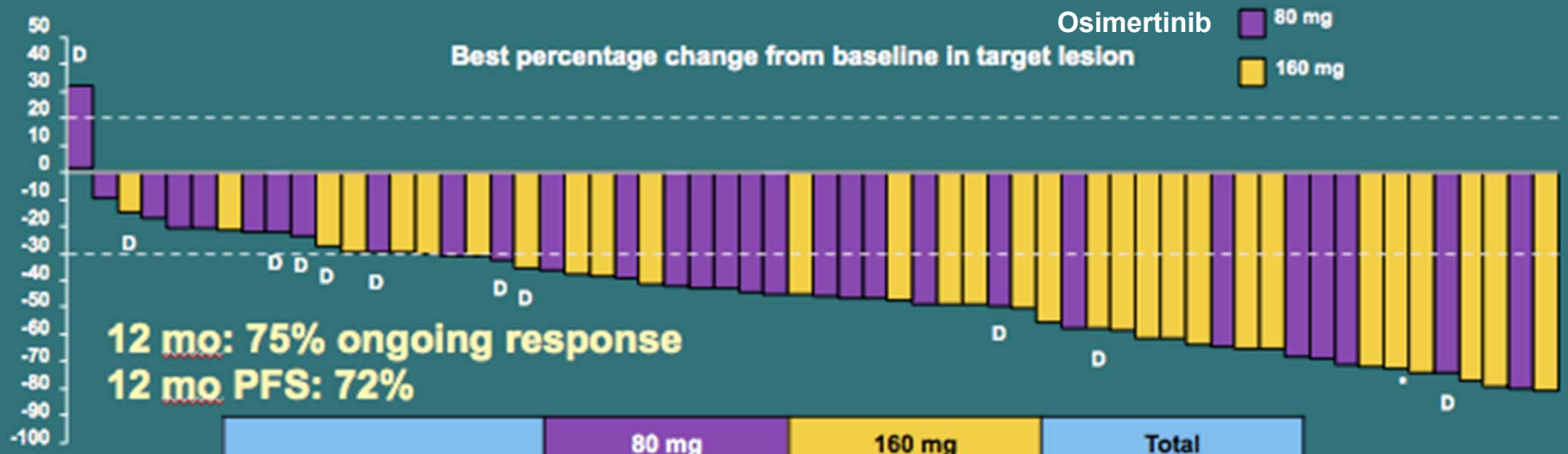
"Third" Gen	*N*	RR* T790M-	RR T790M+	PFS	Adverse Events
Rociletinib (CO-1686)	256	35%	53%	~8.0 mo	Hyperglycemia
Osimertinib (AZD-9291)	253	21%	61%	~8.2 mo	Diarrhea/rash
HM61713 (800 mg)	62	29%† (300 mg)	55%	NR	Diarrhea/rash
EGF816X*	53	–	60%	NR	Rash
ASP8273*	47	~33%	67%	NR	Hyponatremia/ diarrhea

*T790M- subgroups are very small; †12% T790M+.
Multiple other agents earlier in development

NR = not reached.
Modified slide courtesy of Heather A. Wakelee, ASCO 2015 discussant.
Sequist L. PASCO 2015:8001; Janne P, et al. *N Engl J Med*. 2015;372:1689-1699; Park. PASCO 2015:8084; Tan. PASCO 2015; Goto. PASCO 2015; Wakelee HA. MINI03.10, WCLC2015.

Third-Generation EGFR TKIs Being Tested in the First-Line Setting

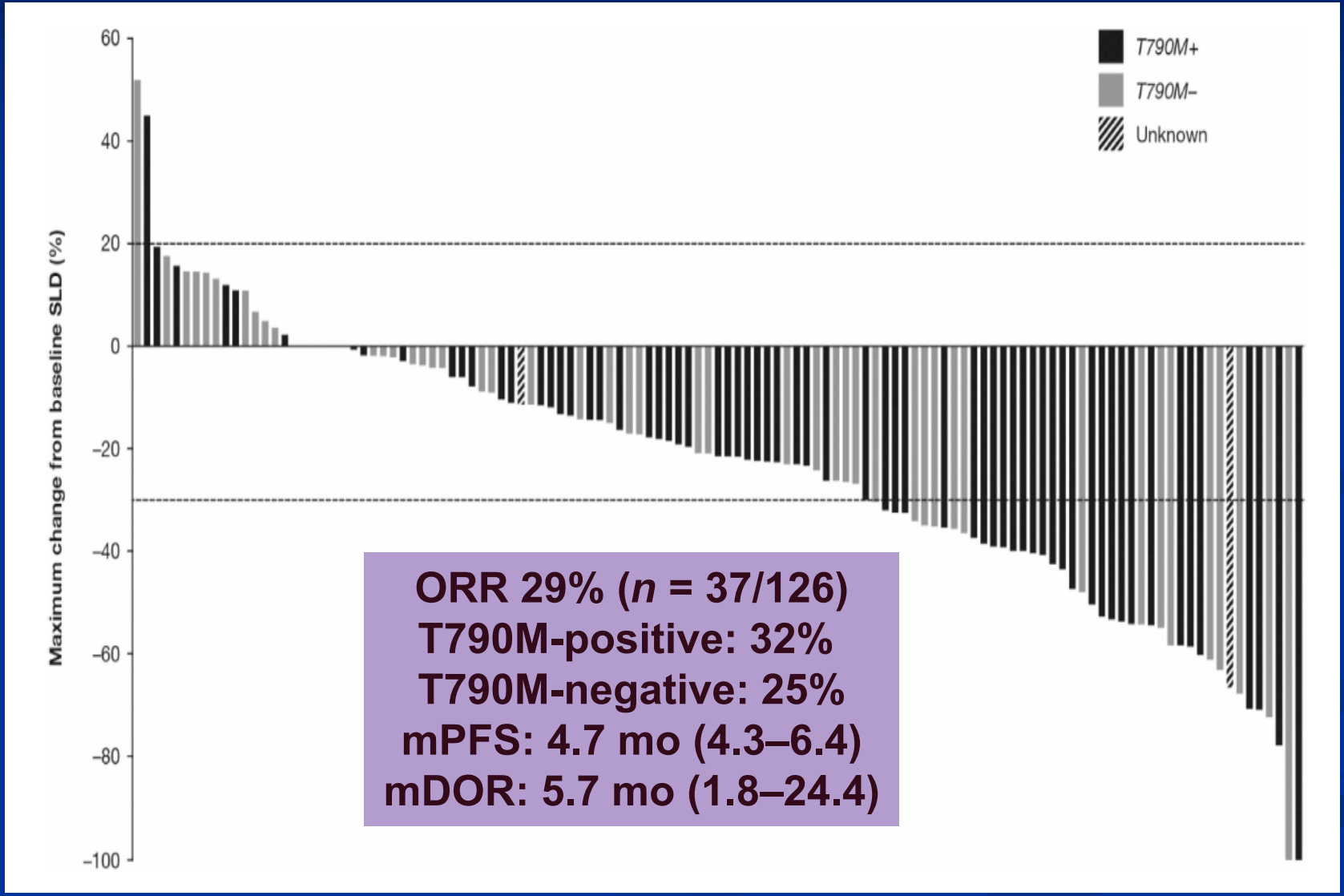
Response Rate in First-line Cohorts by Dose



	80 mg N=30	160 mg N=30	Total N=60
Objective response rate[a]	63% (95% CI 44, 80)	83% (95% CI 65, 94)	73% (95% CI 60, 84)
Disease control rate	93% (95% CI, 78, 99)	100% (95% CI 88, 100)	97% (95% CI 89, 100)
Best objective response			
Complete response[a]	0	1	1
Partial response[a]	19	24	43
Stable disease	9	5	14
Progressive disease	2	0	2

Ramalingam SS, et al. ASCO 2015. Abstract 8000. For educational purposes only.

Other Methods to Overcome Resistance: Afatinib + Cetuximab (T790M+/-)

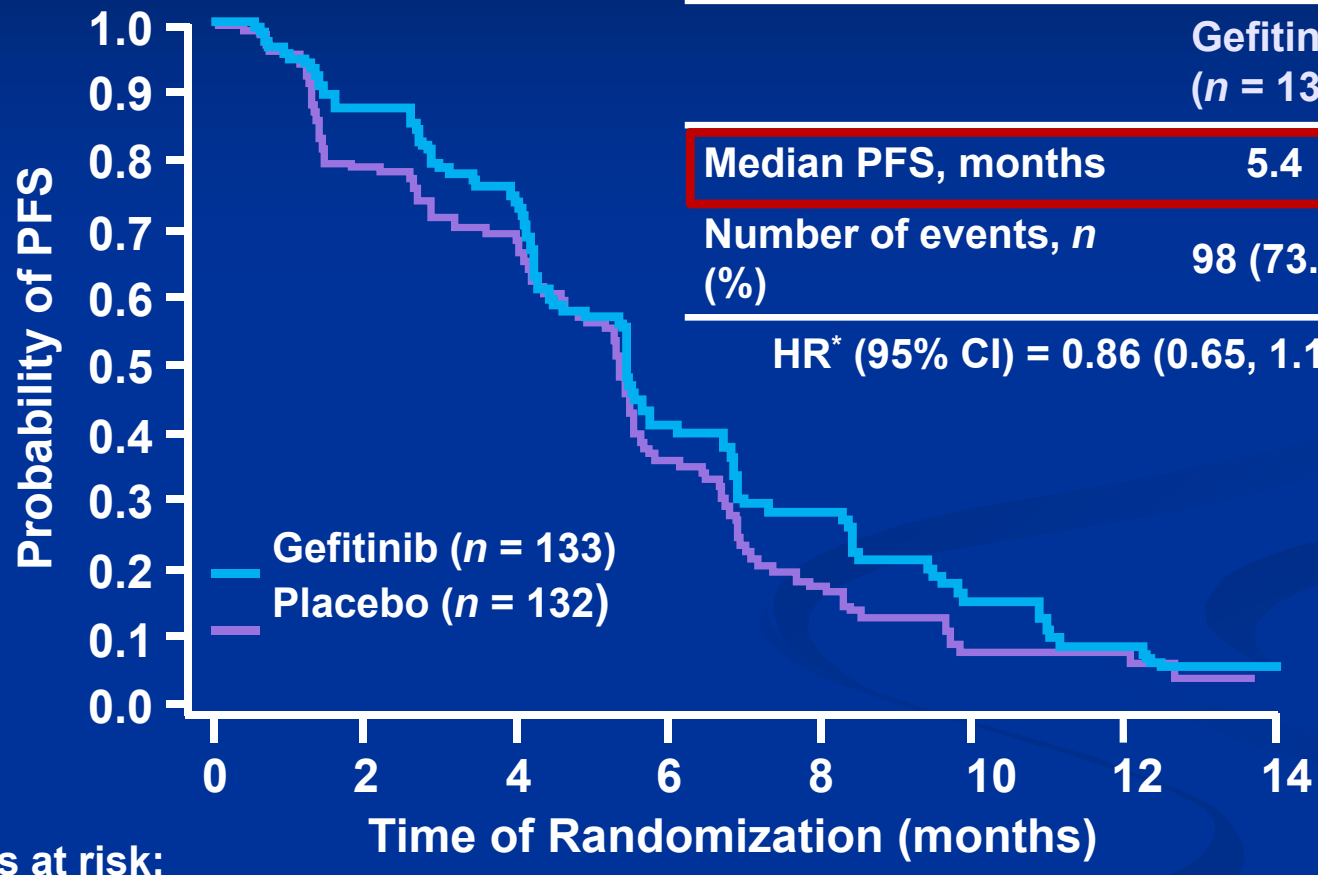


mDOR = median duration of confirmed objective response; mPFS = median progression-free survival.

Janjigian YY, et al. *Cancer Discov*. 2014;4:1036-1045.

Other Methods to Overcome Resistance

IMPRESS: Continue EGFR TKI Beyond Progression and Add Chemotherapy



	Gefitinib (*n* = 133)	Placebo (*n* = 132)
Median PFS, months	5.4	5.4
Number of events, *n* (%)	98 (73.7)	107 (81.1)

HR* (95% CI) = 0.86 (0.65, 1.13); *P* = .273

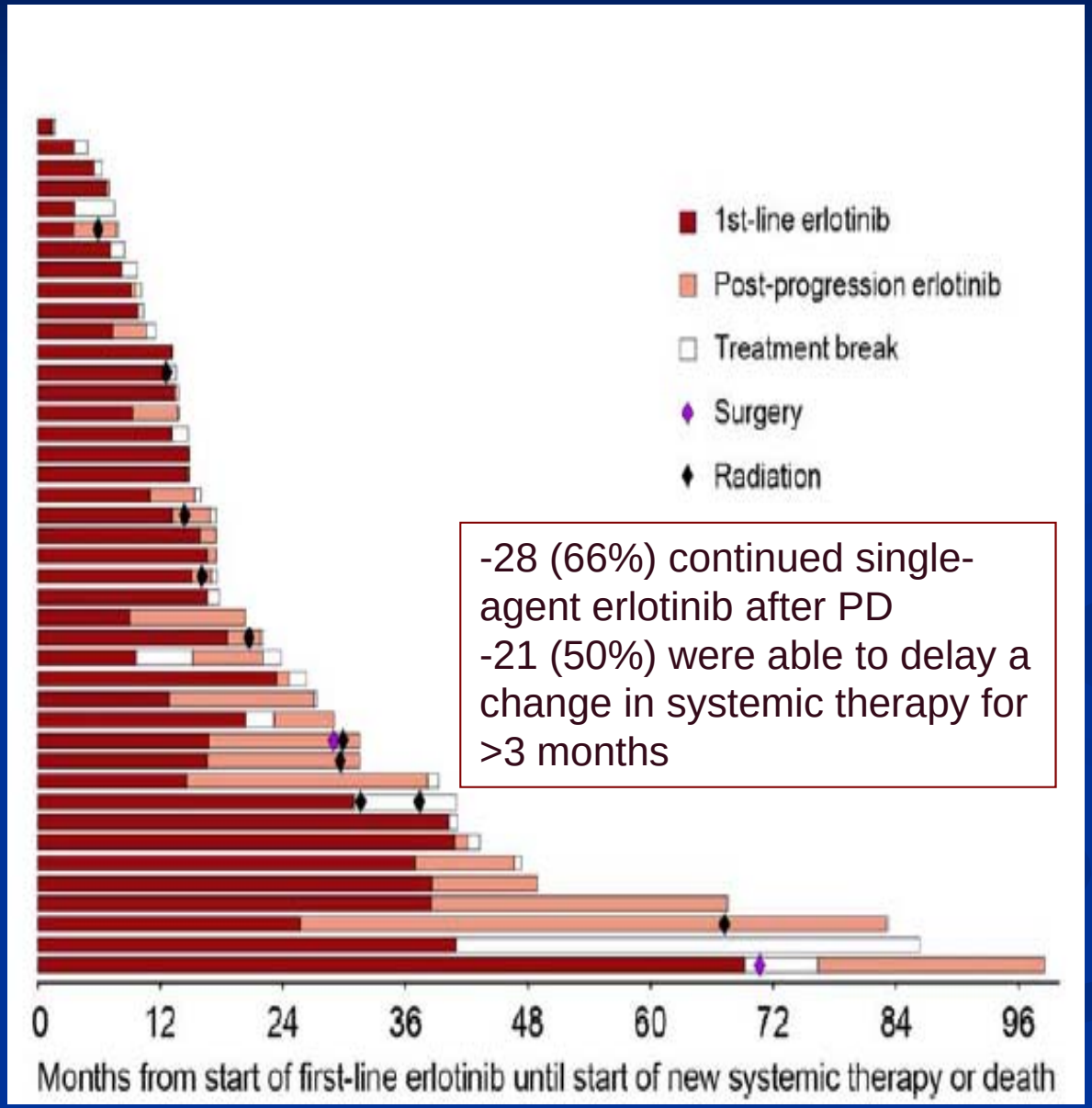
Patients at risk:

Gefitinib	133	110	88	40	25	12	6	0
Placebo	132	100	85	39	17	5	4	0

*Primary Cox analysis with covariates.
An HR <1 implies a lower risk of progression with gefitinib.
Mok T, et al. ESMO 2014:abstract LBA2.

Med OS: 14.8 months (G) vs 17.2 months (P)
HR 1.62, *P* = .029 but 33% of events

Continuing EGFR TKI Therapy Post Progression to Delay Second-Line Therapy



Lo PC, et al. *Cancer*. 2015;121:2570-2577. For educational purposes only.

AURA3: Osimertinib in Second-Line EGFR T790M-Mutant NSCLC

- AURA3: Phase III trial of 419 patients with EGFR-T790M-mutant locally advanced or metastatic NSCLC who progressed on a frontline EGFR TKI
  - Patients randomized 2:1 to osimertinib or standard platinum-based chemotherapy doublet
- On July 18th, it was announced that AURA3 met the primary endpoint of improved PFS with osimertinib
  - Full trial data to be presented at a future congress
  - Confirms benefits of phase II AURA/AURA2 trial showing activity of osimertinib in 2nd-line EGFR-mutant NSCLC

Inman S. OncLine. July 18, 2016; Yang J. ESMO 2016. Abstract LBA2.

Case 1 (cont'd)

- The patient has a repeat bronchoscopic endobronchial tumor biopsy, which demonstrates a T790M mutation.
- She begins osimertinib and has a deep response, with significant improvement in symptoms.

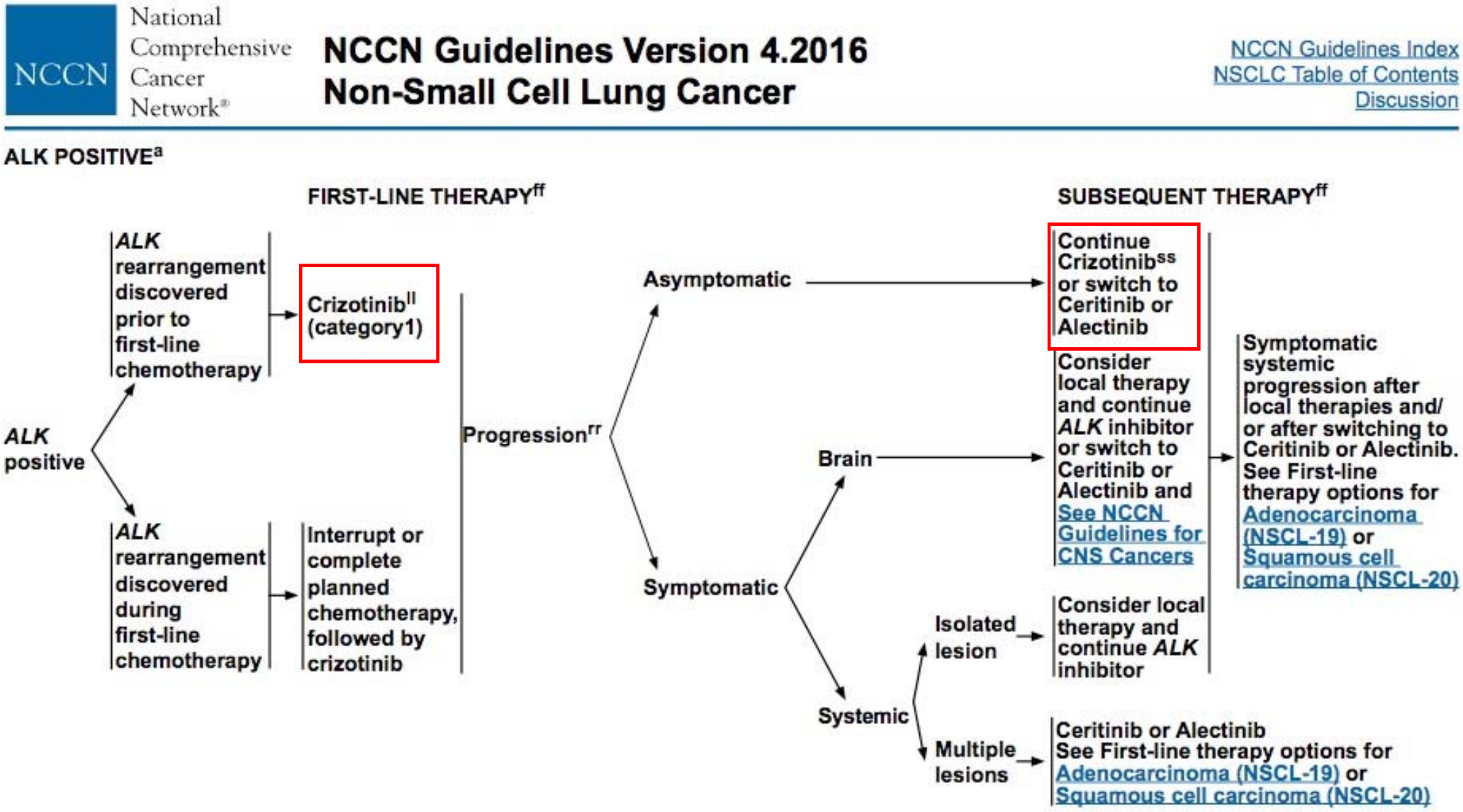
Summary
EGFR-Mutated NSCLC

- **Three options for first-line treatment of EGFR-mutated NSCLC: afatinib, erlotinib, or gefitinib**
  - **All individual trials comparing EGFR TKI to chemotherapy showed no improvement in OS (only PFS and RR).**
  - **EGFR exon 19 del associated with better response to EGFR TKI therapy than EGFR exon 21 L858R**
- **Most patients develop resistance to EGFR TKI at a median of ~9 to 12 months.**
  - **EGFR T790M gatekeeper mutation most common mechanism of resistance**
  - **Plasma genotyping emerging**
  - **Osimertinib FDA approved**
  - **Additional clinical trials with 3rd-generation EGFR TKIs (target T790M) show significant promise.**

FDA = US Food and Drug Administration; RR = response rate.

ALK-Rearranged NSCLC

ALK-Rearranged NSCLC



National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology.
Non-small cell lung cancer. Version 4.2016. Updated January 12, 2016. For educational purposes only.

Which of the following MOST accurately describes the potential for drug-drug interactions with ALK inhibitors?

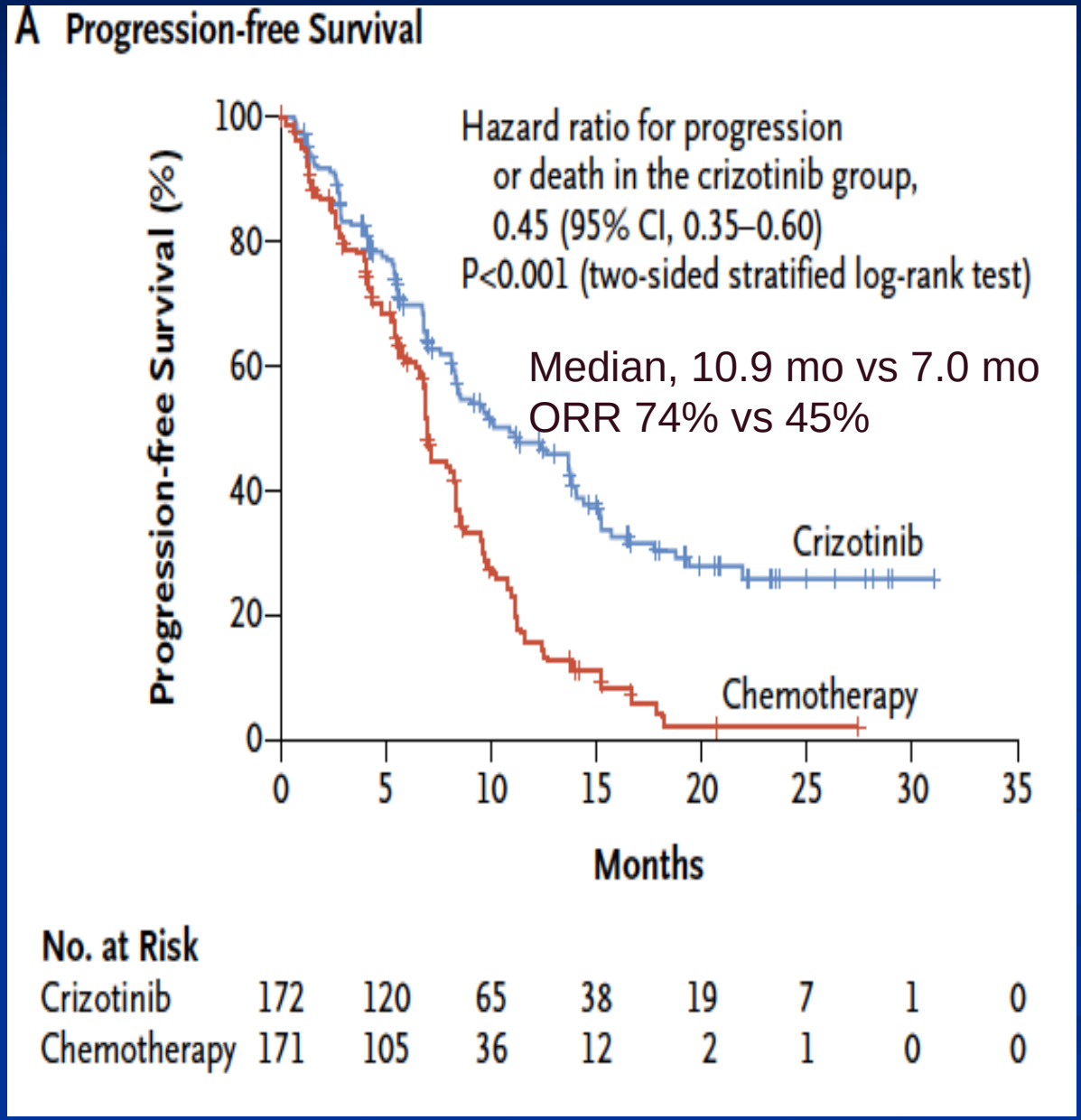
A. ALK inhibitors may interact with CYP3A4 inducers only
B. ALK inhibitors may interact with CYP3A4 inhibitors only
C. ALK inhibitors may interact with CYP3A4 substrates only
D. ALK inhibitors may interact with CYP3A4 inducers and CYP3A4 inhibitors
E. I'm not sure

ALK Inhibitors: Clinical Pharmacology Points

	Crizotinib	Ceritinib	Alectinib
Dose	250 mg po bid	750 mg po daily	600 mg po bid
Interactions	CYP3A4 inducers, inhibitors	CYP3A4 inducers, inhibitors	CYP3A4 inducers, inhibitors. High-fat, high-calorie meal increases exposure by 3-fold compared to fasted state.
Common AEs	Vision disorders, edema, elevated transaminases, nausea, diarrhea	Diarrhea, nausea, vomiting, elevated transaminases, fatigue	Fatigue, constipation, edema, myalgia, rash. Monitor liver function tests every 2 weeks for first 2 months.
Administration	No food effect (avoid grapefruit)	Take on an empty stomach (2 hours before or after a meal). Fat significantly increases exposure	Take with food
Tablet options	200-, 250-mg tablets	150-mg tablet	150-mg capsule
Hepatic dysfunction	Study ongoing (NCT01576406)	Study ongoing (NCT01950481)	Study ongoing (NCT02621047)

Bid = twice a day.
Derived from product prescribing information.

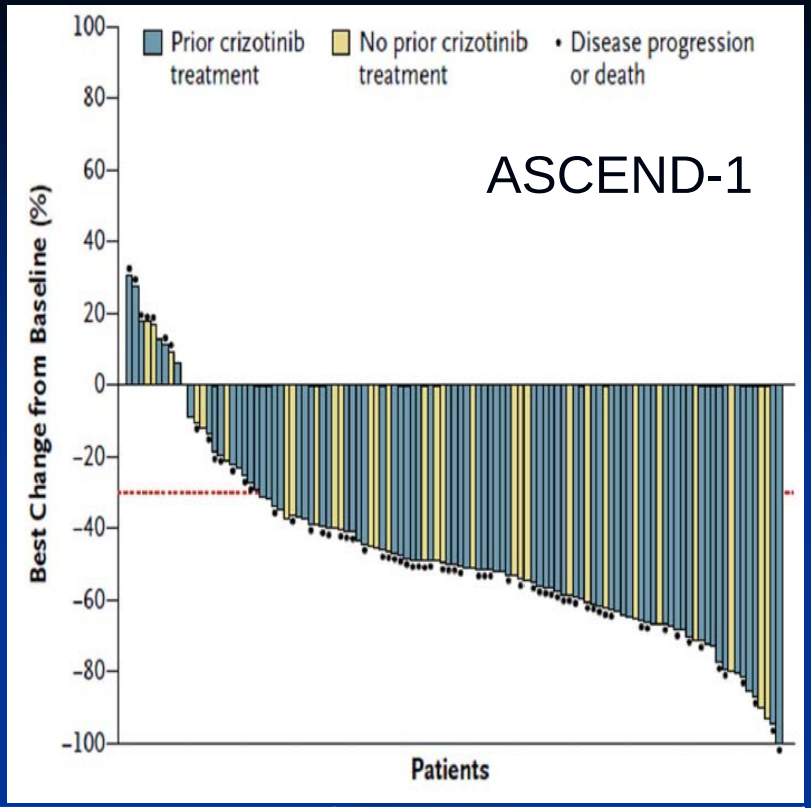
First-Line Crizotinib Prolongs PFS Compared with Pt-Pemetrexed-Based Chemotherapy (PROFILE1014)



Pt = platinum.

Solomon BJ, et al. *N Engl J Med*. 2014;371:2167-2177. For educational purposes only.

Ceritinib Trials

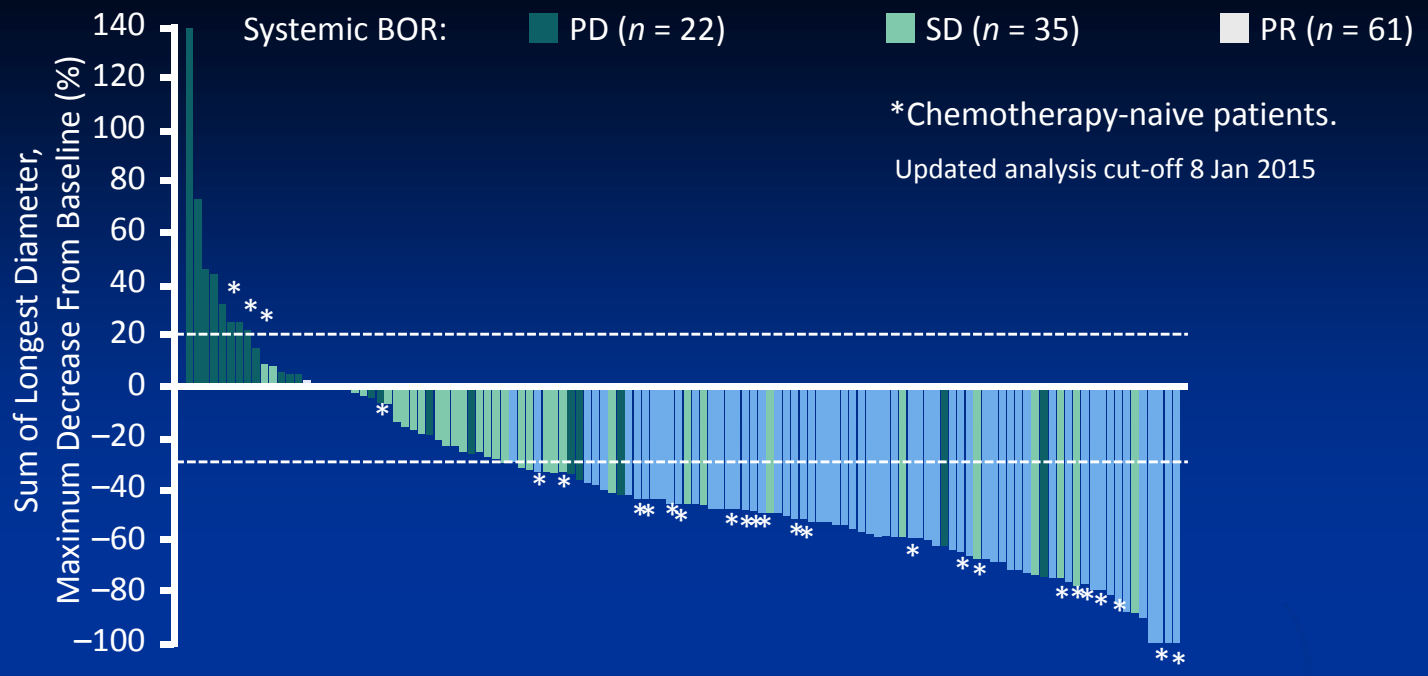


Trial	Patients	ORR	mDOR	mPFS
ASCEND-1 Ph I, *n* = 114	Both crizo-naive and prior crizo	**58%** (48–67) (56% prior crizo)	**8.2 months** (6.9–11.4)	**7.0 months** (5.6–9.5)
ASCEND-2 Ph II, *n* = 140	**Chemo and ALKi refractory**	**38.6%** (30.5–47.2)	**9.7 months** (7–11.1)	**5.7 months** (5.4–7.6)
ASCEND-3 Ph II, *n* = 124	**ALKi naive** (prior chemo)	**63.7%** (54.6–72.2)	**9.3 months** (9.1–NE)	**11.1 months** (9.3–NE)

ALKI = anaplastic lymphoma kinase inhibitor; NE = not estimable; Ph = phase.

Shaw AT, et al. *N Engl J Med*. 2014;370:1189-1197; Mok T, et al. *J Clin Oncol*. 2015;33:abstract 8059; Felip E. *J Clin Oncol*. 2015;33:abstract 8060. For educational purposes only.

Alectinib Trials



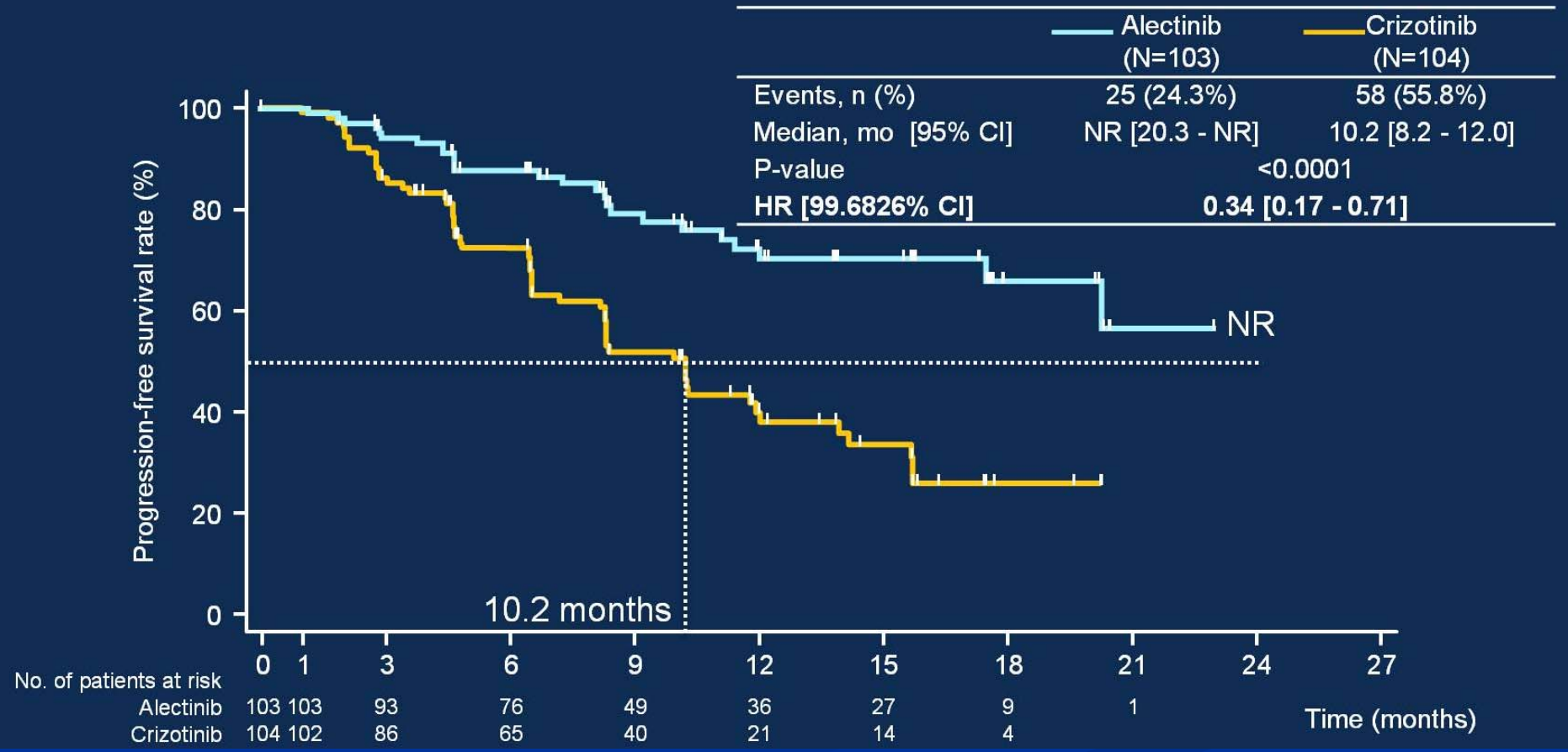
Trial	Patients	ORR	mDOR	mPFS
AF-001JP Ph I/II, *n* = 46	ALKi naive but not treatment naive	93.5% (82–98.6)	NA	NR estimated >29 months
NP28673 Ph II, *n* = 122	ALKi resistant (chemo naive and resistant)	50.0% (40.8–59.1) prior chemo: 44.8% vs none: 69.2%	11.2 months (9.6–NE)	8.9 months (5.6–11.3)
NP28761 Ph II, *n* = 67	ALKi resistant (chemo naive and resistant)	52.2% (39.7–64.6)	13.5 months (6.7–NE)	8.1 months

BOR = best overall response; NA = not available; PR = partial response.

Ohe Y. *J Clin Oncol*. 2015;33:abstract 8061; Ou SI. *J Clin Oncol*. 2015;33:abstract 8008; Shaw AT, et al. ORAL33.03. WCLC 2015; Hotta K, et al. P301.020. WCLC 2015.

J-ALEX: Alectinib vs Crizotinib in ALK-Inhibitor Naïve ALK-Positive NSCLC

Primary Endpoint: PFS by IRF (ITT Population)



IRF = independent review facility; ITT = intent to treat; PFS = progression-free survival.

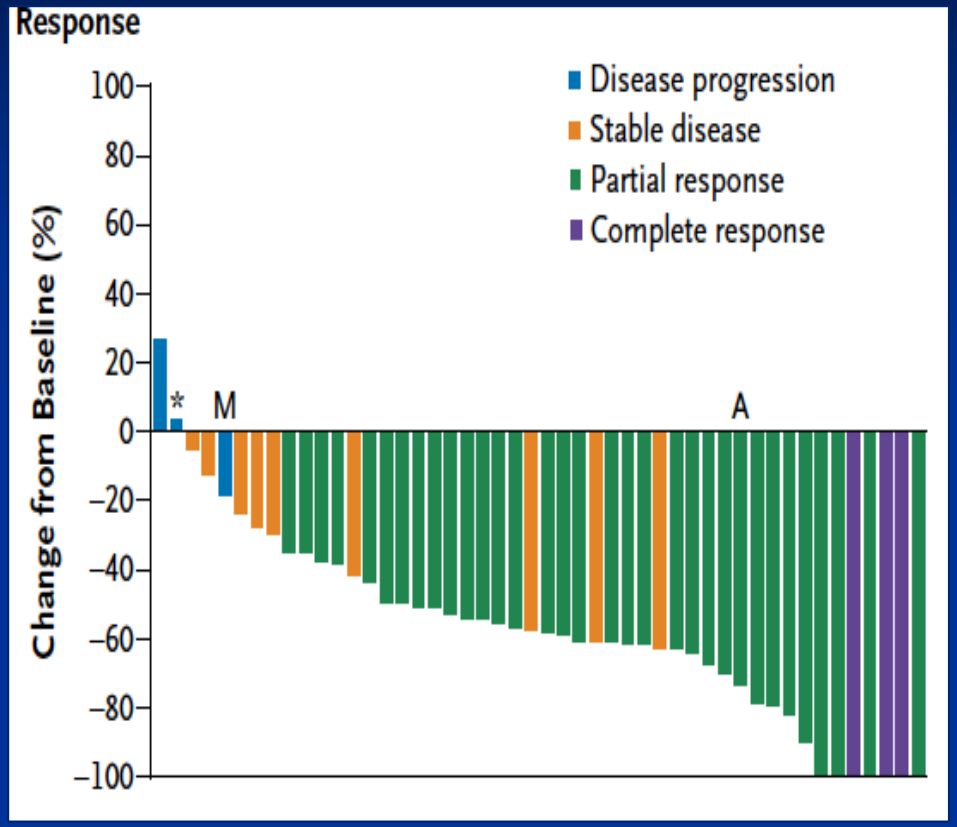
Nokihara H, et al. ASCO 2016. Abstract 9008. For educational purposes only.

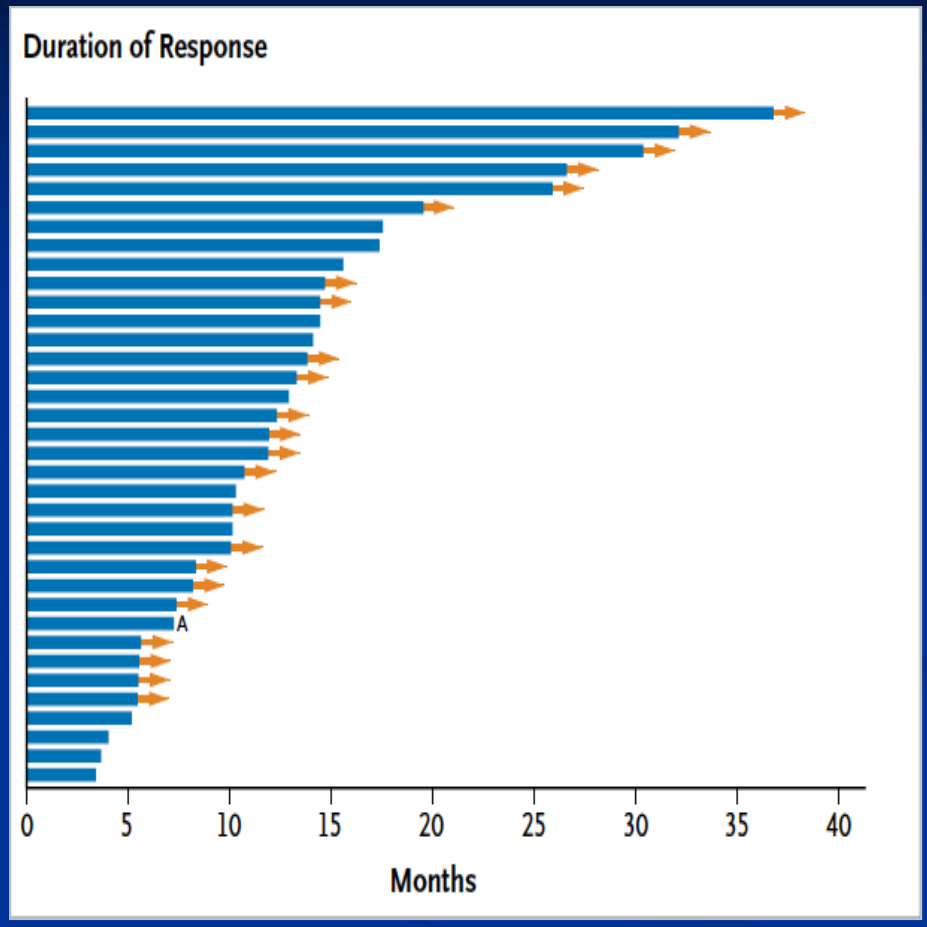
Summary
ALK-Rearranged NSCLC

- **Approved therapies**
  - **Crizotinib: 1st-line treatment**
  - **Ceritinib: 2nd-line treatment after crizotinib**
  - **Alectinib: 2nd-line treatment after crizotinib**
  - **Many other ALK inhibitors in clinical trials**

ROS1 and Other Genomic Targets

Crizotinib Activity in ROS1





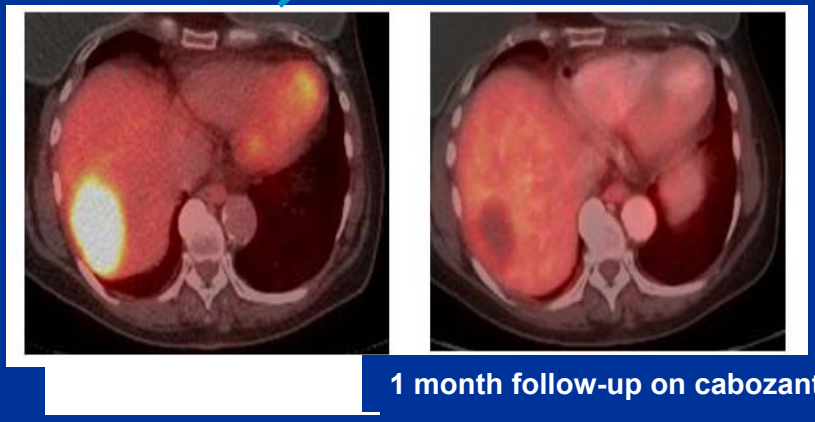
- **72% ORR** (95% CI, 58%–84%; 3 CRs)
- 64% (23/36) ongoing responses
- **Median DOR 17.6 months** (95% CI, 14.5–not reached [NR])
- **mPFS of 19.2 months** (95% CI, 14.4–NR)

CR = complete response.

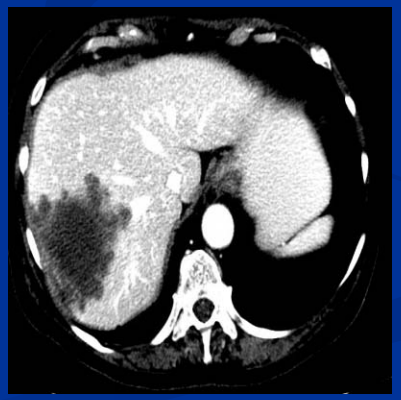
Shaw AT, et al. *N Engl J Med*. 2014;371:1963-1971. For educational purposes only.

Other Genomic Targets

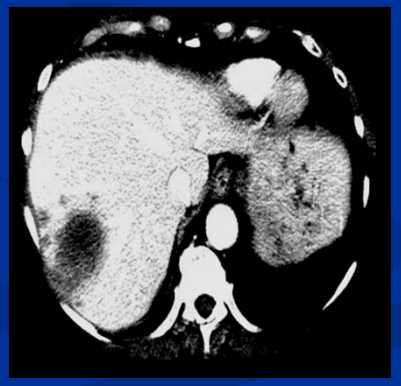
Mutation	Drug(s)	References
BRAF V600E	**Dabrafenib** **Dabrafenib + trametinib**	Planchard D. *Lancet Oncol*. 2016; Planchard D. ASCO 2016. Abstract 107.
RET fusion	**Cabozantinib or vandetanib**	Drilon AE. ASCO 2015. Abstract 8007; Seto T. ASCO 2016. Abstract 9012.
MET exon 14 splice mutation	**Cabozantinib or crizotinib**	Paik PK. ASCO 2015. Abstract 8021; Drillon AE. ASCO 2016. Abstract 108.



1 month follow-up on cabozantinib



Baseline



1 month follow-up on crizotinib

Example of response of MET splice from Paik P, et al. ORAL03.07. WCLC 2015.

Providing Individualized Care for Patients with NSCLC: *Pharmacist Perspectives*

Matthew Farber

Senior Director
Oncology Disease State
Walgreens Specialty Pharmacy
Deerfield, Illinois

Understanding the Role of Specialty Pharmacy

History of Rx: IV therapy

- Care delivered in the practice/hospital setting
- Buy-and-bill model
- Adherence easy to monitor

Today: advent of oral therapies

- Combination of oral and IV Rx
- More time spent on PAP, PA
- Adherence more challenging
- Delivery models changing

Tomorrow: 40% of all drugs in oncology pipeline are oral.

- Restricted access
- PBM involvement

IV = intravenous; PA = prior authorization; PAP = patient assistance program; PBM = pharmacy benefit manager.

What Is a Specialty Pharmacy?

- National SP affiliated with PBM
- National SP not affiliated with PBM
- National SP with a disease focus
- Local SP or independent; hospital
- Affiliated with insurance company

SP = specialty pharmacy.

Role of Specialty Pharmacy

Access to therapy

- Adherence
- Patient assistance
- Insurance verification
- MTM
- Drug interactions

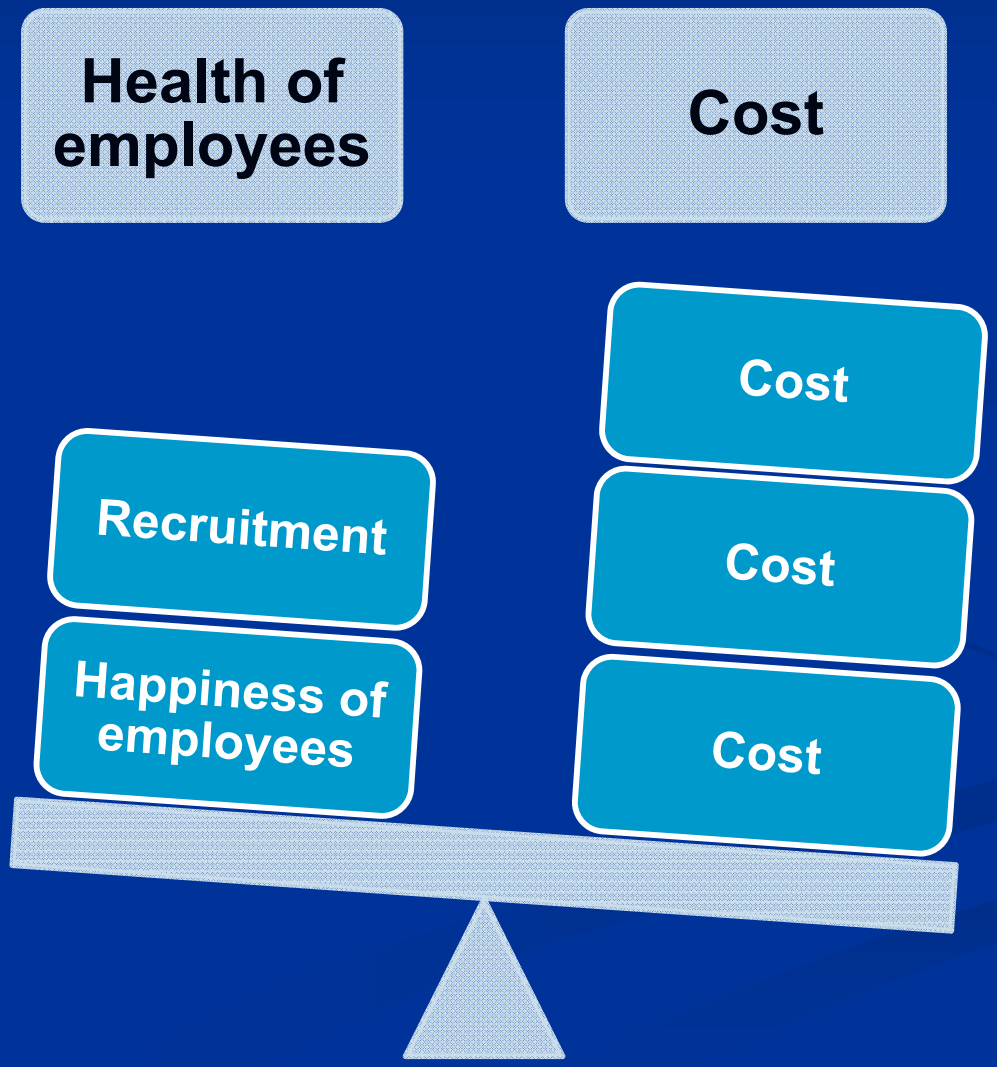
MTM = medication therapy management.

How common is "financial toxicity" within the patient population you serve?

A. Rare: most of my patients are insured
B. Somewhat common: patients occasionally express concerns about cost
C. Common: treatment costs are among the top 5 concerns I hear from patients
D. Widespread: treatment cost is the most common question I hear
E. I don't know what you mean by "financial toxicity"

The Forgotten Actor: Employer

One in 3 cancer patients with insurance still experience significant debt or bankruptcy.



Cancer Benefit Design

Reduce Overall Cost

- Limit in-network providers
- Limit access to therapies through PBM/formulary/SP

Keep Patients Healthy

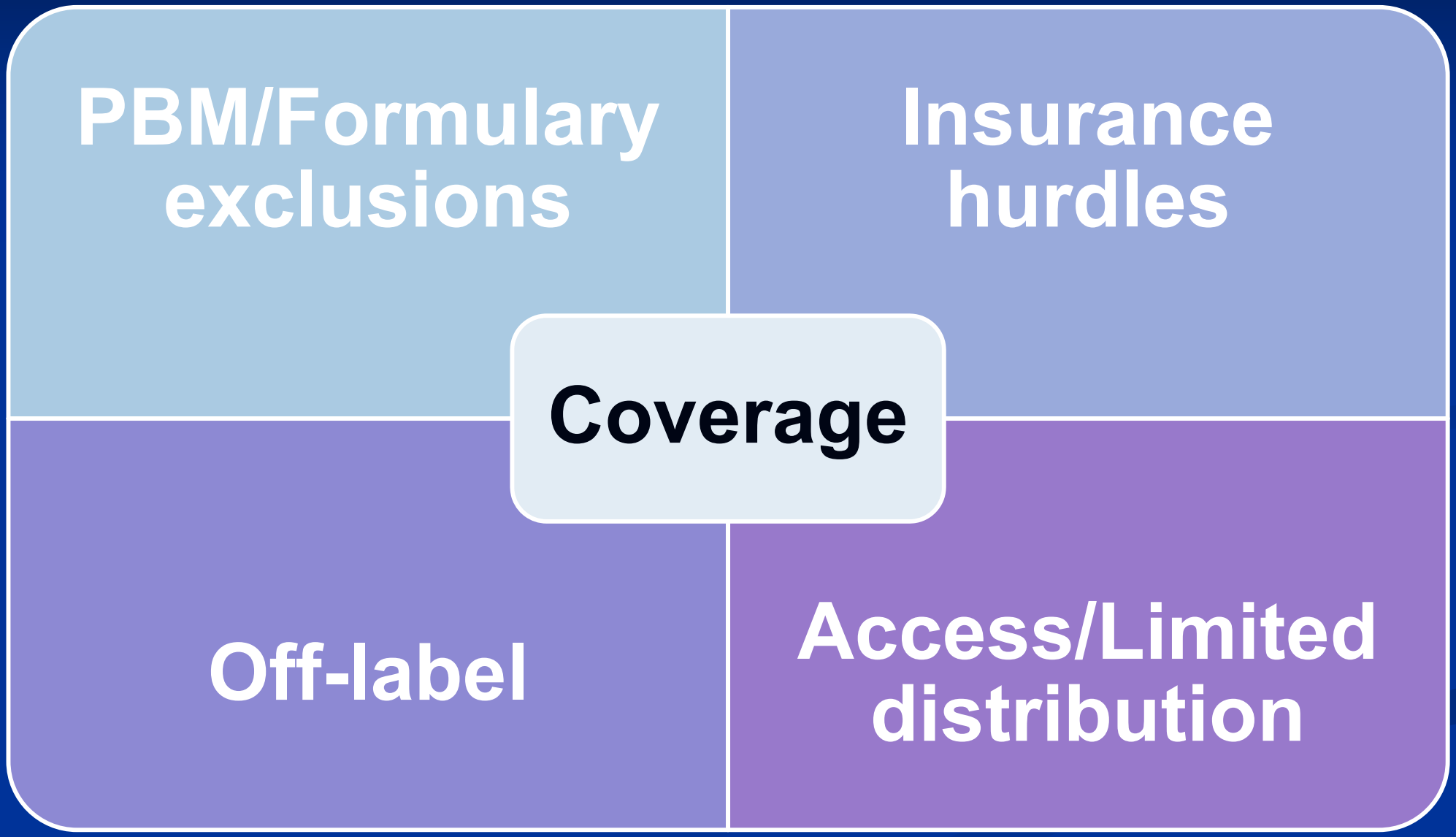
- Reward healthy decisions
- Encourage care planning/knowing when to go to ED

Highlight Prevention

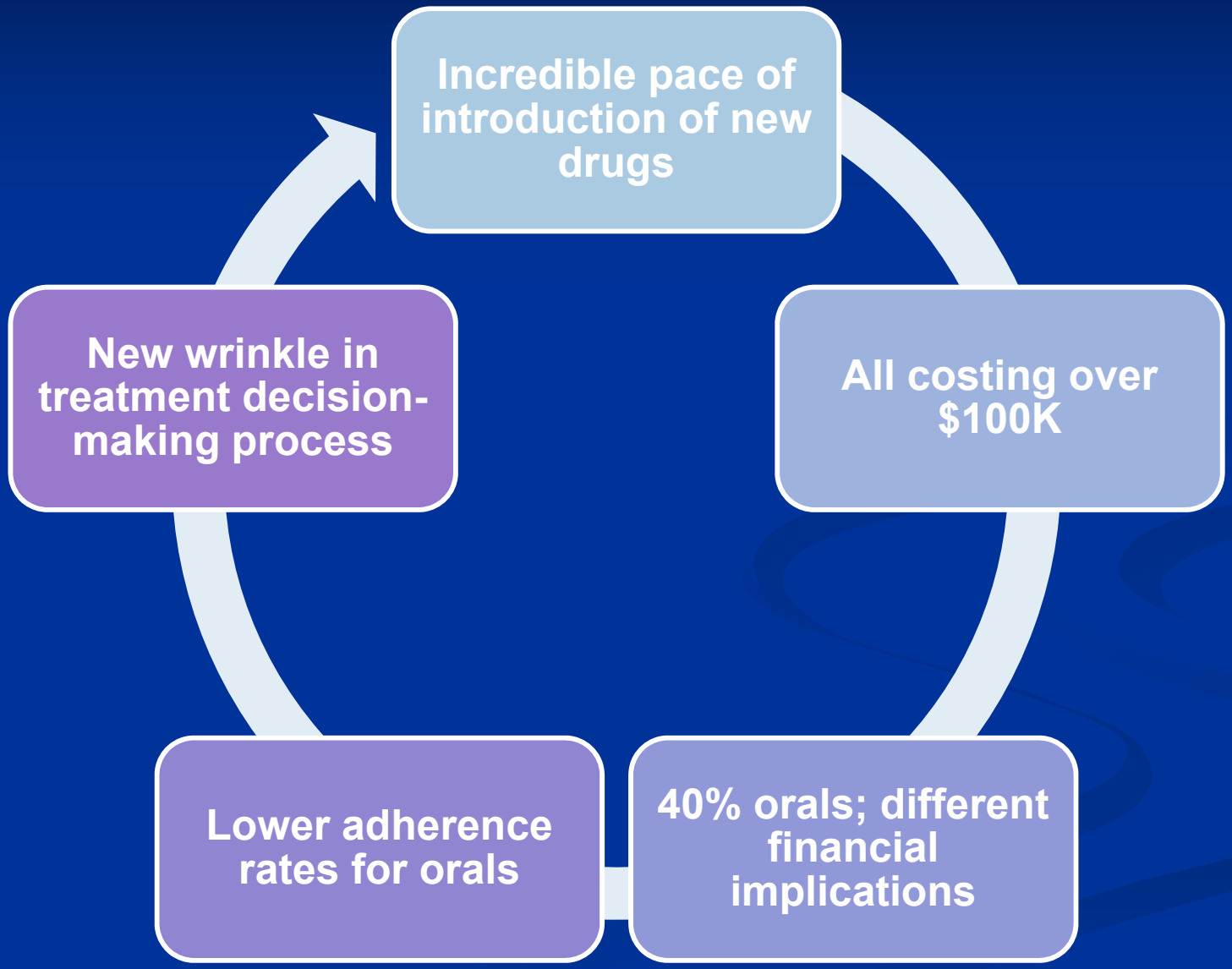
- Educate employees on importance of cancer screening

ED = emergency department.

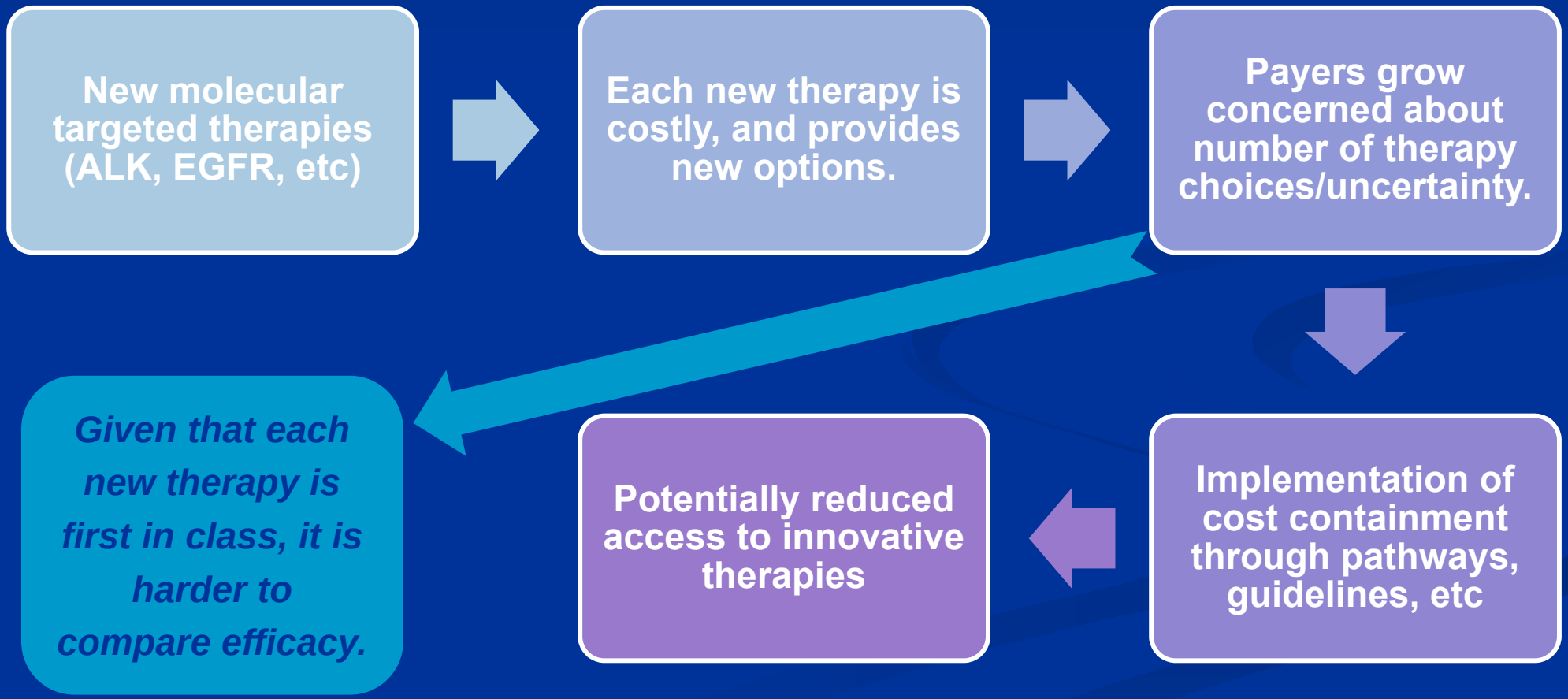
New Drugs


PBM/Formulary exclusions
Insurance hurdles
Coverage
Off-label
Access/Limited distribution

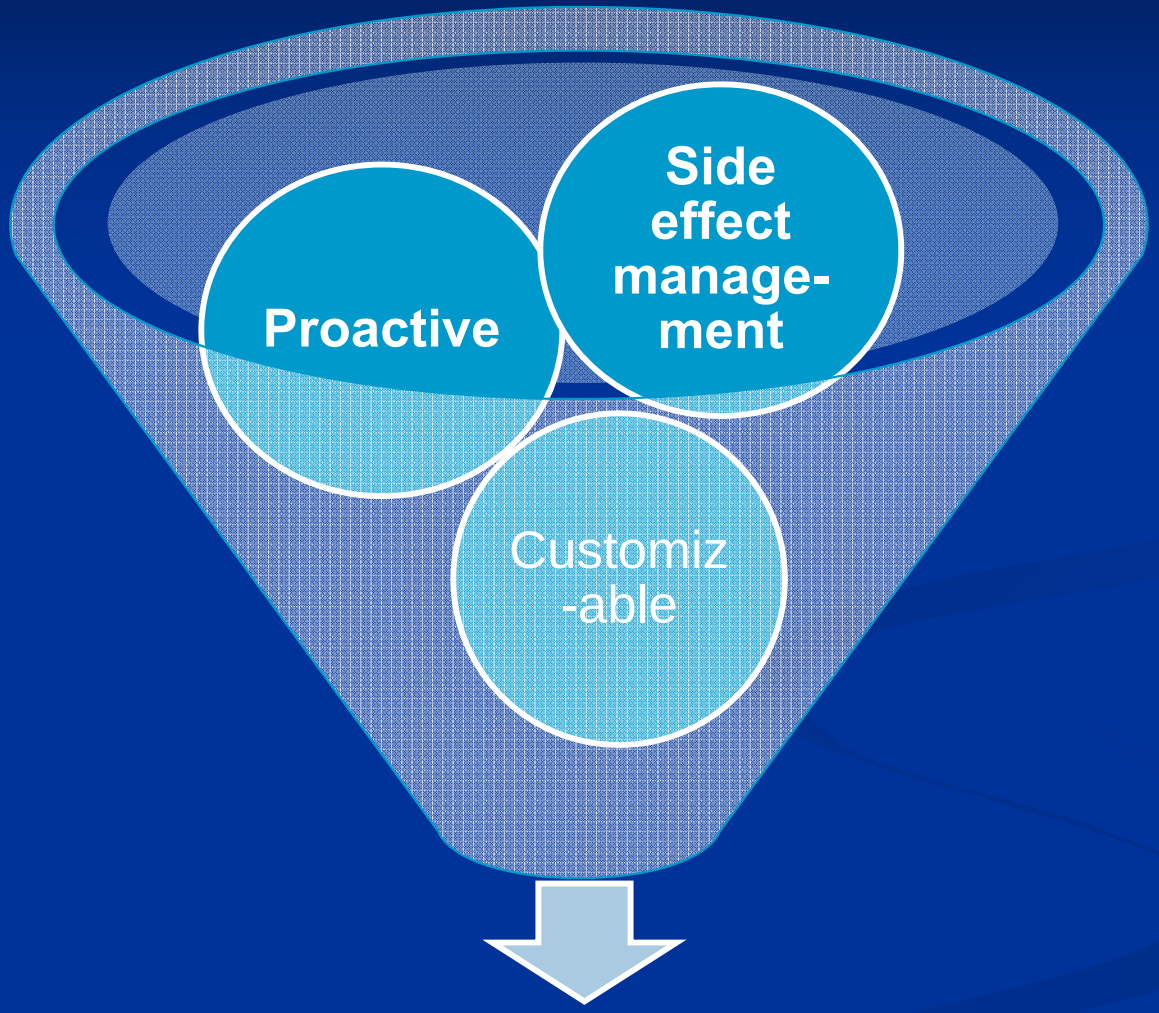
Importance of Cost



How the Pharmacoeconomics of Molecular-Based Therapies Fits into the Process (NSCLC)



Importance of Adherence



Improved Outcomes

Common Reasons for Nonadherence

- Adverse events
- Financial toxicity
- Feeling good
- Confusion

Importance of Navigation

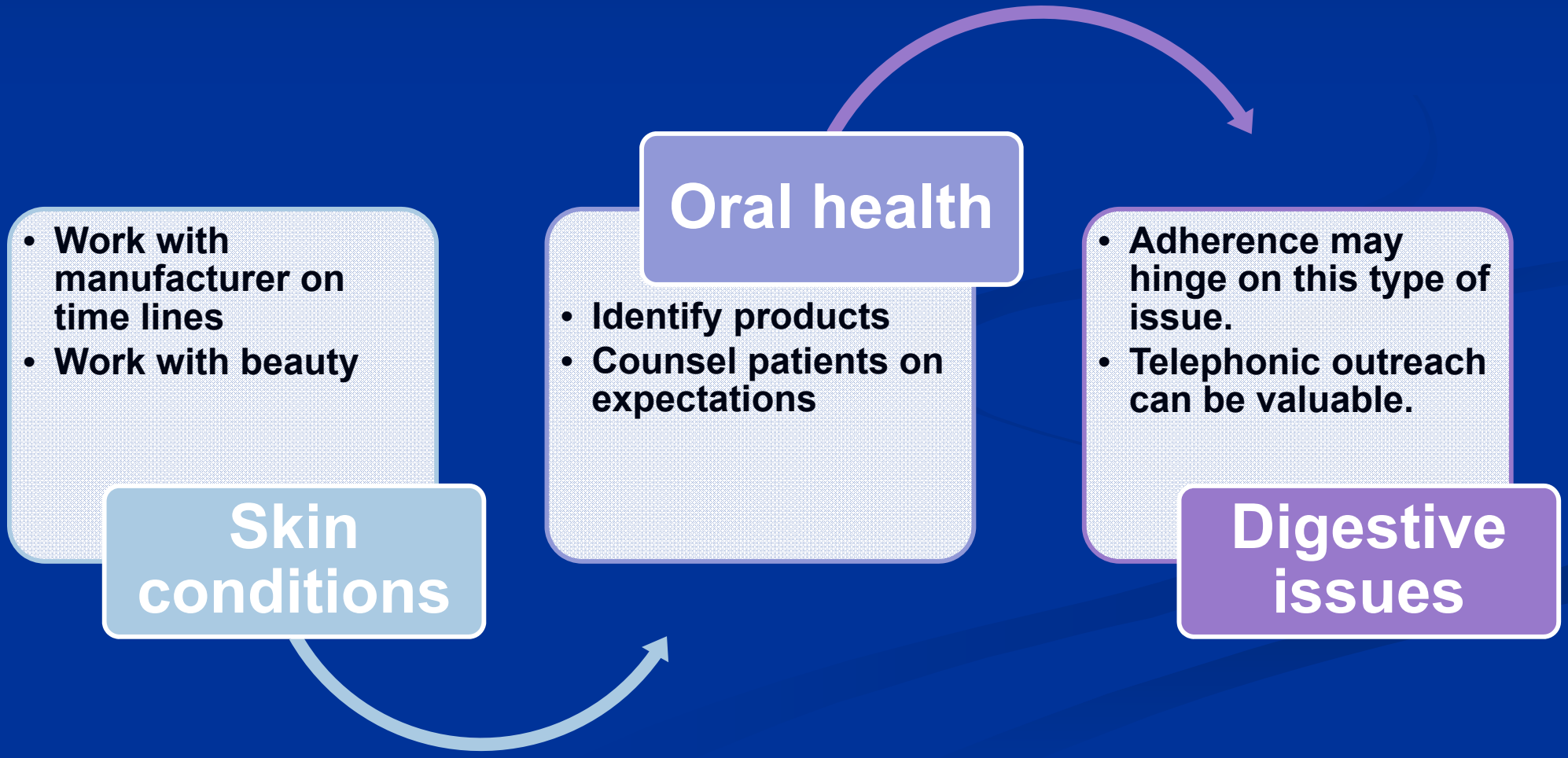
Given the cost implications, additional conversations needed to determine best Rx decision (financial toxicity).

Cancer Center staff is instrumental in key conversations with patients and caregivers.

Specialty Pharmacies can play a role as an extension of the care team.

Tracking and Proactively Managing Common Side Effects

Many of the new treatments have similar side effect profiles.



New Role for Pharmacists?

More and more molecularly based treatments and tests, some now blood-based

Additional tests create strains on labs, pathologists.

Can pharmacists play a more active role in blood-based testing?

Pharmacists Managing Targeted Therapies

Drug Development; Manufacturer Education Internal

During clinical trials, pharma is compiling info for internal teams.

Education of Providers

As drug progresses, focus shifts to prescribers.

Pharmacists

Pharma should look to pharmacists to manage personalized therapies, drug/drug interactions.

Q&A

To submit a question, please use the "Ask a Question" tab located on the left side of your screen.

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COMPLIMENTARY LIVE INTERACTIVE CPE WEBCASTS

TESTING TO TARGET IN NON-SMALL CELL LUNG CANCER:

Managed Care Perspectives

Presented by The University of Tennessee College of Pharmacy

University of Tennessee College of Pharmacy

Advanced Studies *in* Pharmacy®

Supported by an educational grant from AstraZeneca.