Global Lung Cancer Academy

Global Lung Cancer Academy

Sharing Best Practices to Optimize Patient Care

24 October 2022

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Sponsor: Sanofi Oncology & Regeneron

Global Lung Cancer Academy

Welcome and Meeting Overview

Corey Langer, MD, and Carlos Barrios, MD

Meet the faculty

CO-CHAIRS

Corey J. Langer, MD, FACP
University of Pennsylvania, PA, USA

Carlos H. Barrios, MD
Center at Hospital São Lucas, Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Porto Alegre, Brazil

FACULTY

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Ignacio I. Wistuba, MD
MD Anderson Cancer Center, Houston, TX, USA

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Objectives of the program

- Discuss current evidence-based practices in the diagnosis and treatment of lung cancer
- Learn about current genomic testing practices and how these results inform treatment decisions
- Understand advances made in immunotherapy for lung cancer and how these agents are being used in clinical practice
- Gain insights into the latest developments in targeted therapies used for lung cancer
- Promote best practice cancer care via the review of clinical patient cases
- Recognize the major clinical trials underway to further develop treatment in lung cancer
- Learn about the regional challenges and differences in lung cancer treatment patterns in Latin America and Canada

Day 2: Plenary Sessions

Monday, 24 October 2022 from 4.00 PM – 7.00 PM EDT

Time (EDT)	Title	Speaker
4.00 PM – 4.10 PM (10 min)	**Session Open** • ARS questions	Corey Langer and Carlos Barrios
4.10 PM – 4.40 PM (30 min)	**Interactive Discussion: Regional Challenges in NSCLC Management** • Interactive discussion and Q&A	Moderator: Carlos Barrios All faculty
4.40 PM – 5.00 PM (20 min)	**Current Diagnostic Options and Initial Management of Early-Stage NSCLC in Latin America** • Overview of currently available diagnostic methods and treatment options for early-stage NSCLC (resectable vs unresectable)	William William
5.00 PM – 5.20 PM (20 min)	**Current Treatment Options for Metastatic NSCLC in Latin America** • Overview of currently available treatment options for metastatic NSCLC	Carlos Barrios
5.20 PM – 5.50 PM (30 min)	**Tumor Board Discussion** • Patient case 1 (10 min) • Patient case 2 (10 min) • Discussion and Q&A (10 min)	Moderator: Carlos Barrios Caio Abner Leite Alvaro Guimaraes Paula All faculty
5.50 PM – 6.00 PM (10 min)	***Break***	
6.00 PM – 6.20 PM (20 min)	**Monitoring and Managing Immunotherapy-Related AEs** • Optimal monitoring and managing of the most common AEs associated with immunotherapy	Edgardo S. Santos
6.20 PM – 6.50 PM (30 min)	**Tumor Board Discussion** • Patient case (10 min) • Discussion and Q&A (20 min)	Moderator: Corey Langer Barbara Melosky All faculty
6.50 PM – 7.00 PM (10 min)	**Session Close** • ARS questions	Carlos Barrios

Introduction to Voting

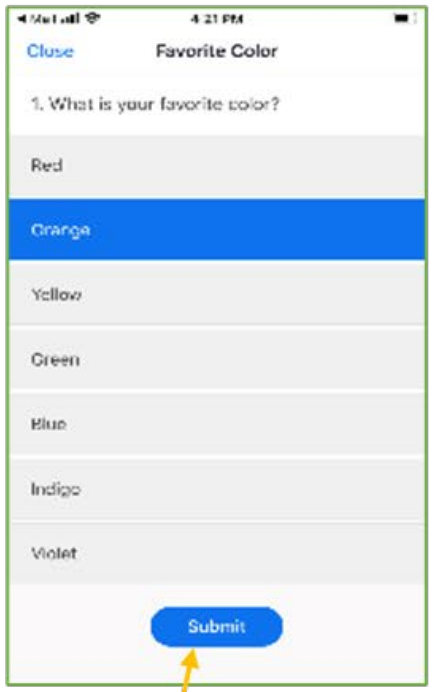
Desktop View

Choose Your Answer
Click on the answer (or answers if multiple choice)

Select Submit
After choosing your answer, select "Submit" to finalize

Mobile View

Choose Your Answer
Click on the answer (or answers if multiple choice)



Select Submit
After choosing your answer, select "Submit" to finalize

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Question 1

In which country do you currently practice?

1. Argentina
2. Brazil
3. Canada
4. Colombia
5. Chile
6. Mexico
7. Peru
8. Other country in LATAM
9. Other country outside LATAM

Question 2

How would you describe your specialty?

1. General oncologist
2. Lung oncologist
3. General internal medicine
4. Fellow
5. Other

Question 3

Which immunotherapy-associated adverse events have you observed in your patients? *(Select all that apply.)*

1. Fatigue
2. Infusion-related reactions
3. Cytokine release syndrome
4. Dermatologic and mucosal toxicity
5. Diarrhea/colitis
6. Hepatotoxicity
7. Pneumonitis
8. Endocrinopathies
9. Opportunistic infections
10. Other

Question 4

Do you continue immunotherapy after progression in metastatic NSCLC?

1. No, I stop
2. Yes, I continue with the same drug
3. Yes, but I would consider switching to another immunotherapy
4. This completely depends on the situation
5. Other

Question 5

I feel comfortable diagnosing and treating immune-related side effects.

1. Not at all
2. Sometimes
3. In general
4. Most of the time
5. Always

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Interactive Discussion: Regional Challenges in NSCLC Management

Carlos Barrios, MD

Discussion Topics

- Which steps have you taken to optimize multidisciplinary care coordination in your centers? What are your learnings/recommendations from this process?
- How have you organized identification and management of IO and other oncology drug-related AEs with your emergency unit? What are your recommendations to improve this process?
- Is clinical research in lung cancer in LATAM optimally organized, and what are the options to further improve the involvement in important studies?
- Do you have access to CPIs in the 1L setting? Is access restricted to 2L?
- What have been your strategies to get accelerated access to new diagnostics and drugs?
- Do you have access to liquid biopsy?
- How do you approach diagnostic and treatment barriers for patients with limited insurance?
- Should there be more neoadjuvant approaches in your region? If yes, how can this be organized? Do barriers exist? Are your surgeons on board?
- What strategies have you used to optimize management of patients in remote areas?
- Others

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Current Diagnostic Options and Initial Management of Early-Stage NSCLC in Latin America

William William, MD

Management of Early-Stage NSCLCs in Latin America

William N. William Jr, MD

Director of Oncology and Hematology, Hospital BP, a Beneficência Portuguesa de São Paulo

Adjunct Associate Professor, The University of Texas MD Anderson Cancer Center

Let’s Discuss

How often do you participate in multidisciplinary tumor boards?

A. Never
B. Once per week
C. Once every 2 weeks
D. Once per month
E. Less than once per month

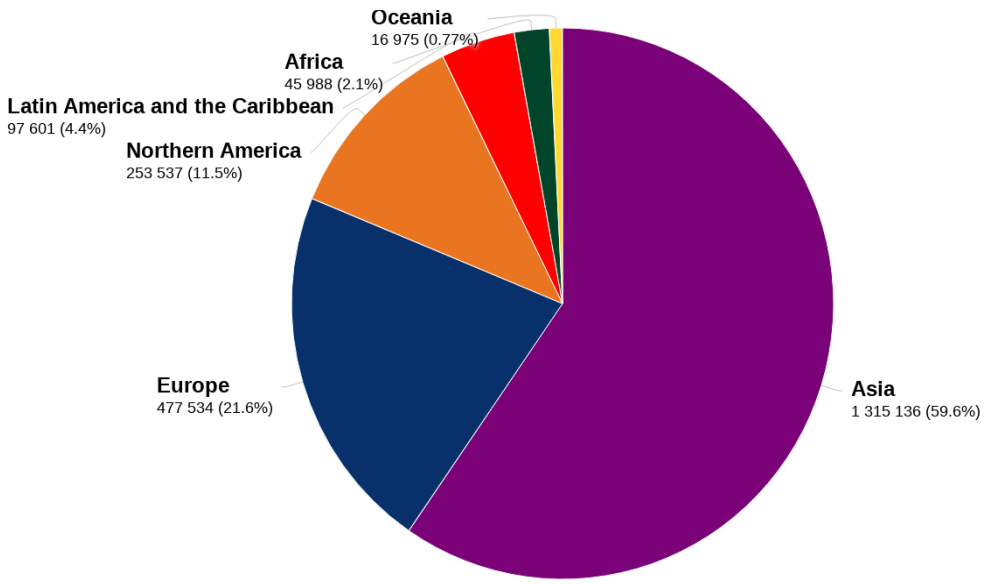
Let's Discuss

How many of your locally advanced NSCLC cases are discussed in tumor boards?

A. 0
B. 0%–25%
C. 26%–50%
D. 51%–75%
E. 76%–100%

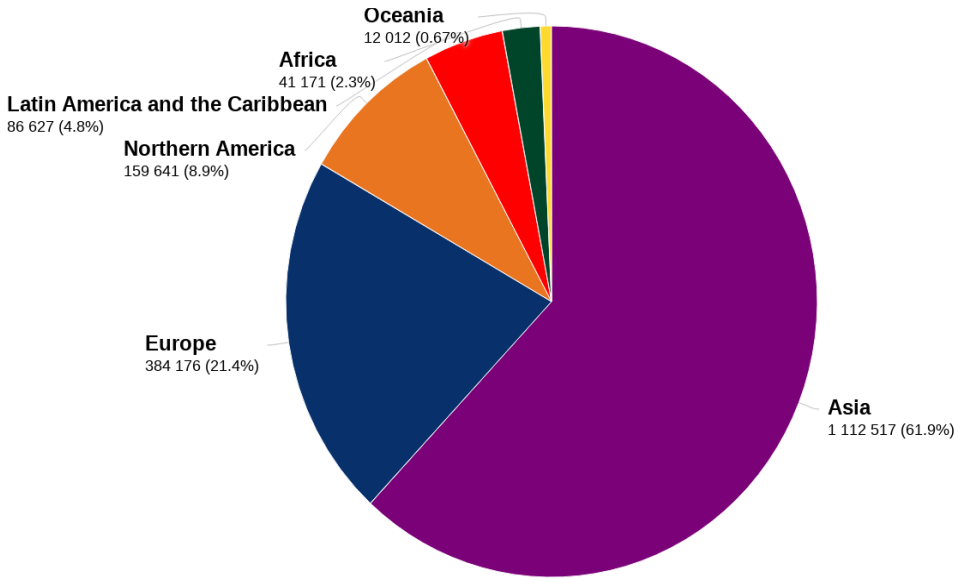
GLOBOCAN Incidence and Mortality

Estimated number of new cases in 2020, lung, both sexes, all ages



Total : 2 206 771

Estimated number of deaths in 2020, lung, both sexes, all ages



Total : 1 796 144

Data source: Globocan 2020
Graph production: Global Cancer Observatory (http://gco.iarc.fr)

International Agency for Research on Cancer
World Health Organization

Leading Cause and Cancer Mortality in Men

Goss PE, et al. *Lancet Oncol*. 2013;14:391-436.

Risk Factor: Tobacco

Smoking rates in selected countries from Latin America, Europe, Asia, and North America.

Country	Population Smoking Rate (%)
Chile	40
Cuba	40
Argentina	27
Brasil	17
Colombia	19
Russia	37
Estonia	36
Latvia	36
Lithuania	34
Kuwait	37
Bangladesh	37
Indonesia	36
China	33
Canada	19.9
Mexico	19.8
United States of America	16.8

Uruguay:

Important decrease seen, based on an effective antitobacco law and an increase in cigarettes cost

Brazil:

Implemented all recommendations by the WHO to reduce tobacco use

***Panel* 3: Anti-tobacco measures in Latin America**

Countries who have ratified the WHO Framework Convention on Tobacco Control:
Antigua and Barbuda, Bahamas, Barbados, Belize, Boliva, Brazil, Chile, Colombia, Costa Rica, Dominica, Ecuador, Grenada, Guatemala, Guyana, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, St Kitts and Nevis, St Lucia, St Vincent and the Grenadines, Suriname, Trinidad and Tobago, Uruguay, Venezuela

Countries with smoking bans:
Argentina, Barbados, Colombia, Ecuador, El Salvador, Guatemala, Honduras, Panama, Peru, Trinidad and Tobago, Uruguay, Venezuela

Countries with regulations on packaging and labelling of tobacco products:
Argentina, Bolivia, Brazil, Colombia, Chile, Cuba, Ecuador, Honduras, Mexico, Panama, Venezuela, Peru

Countries with bans on tobacco advertising, promotion, and sponsorship:
Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, El Salvador, Honduras, Panama, Uruguay

Countries with a tax share of at least 50% of the total price of cigarettes:
Argentina, Brazil, Chile, Colombia, Costa Rica, Dominican Republic, El Salvador, Guatemala, Ecuador, Jamaica, Mexico, Peru, Suriname, Uruguay, Venezuela

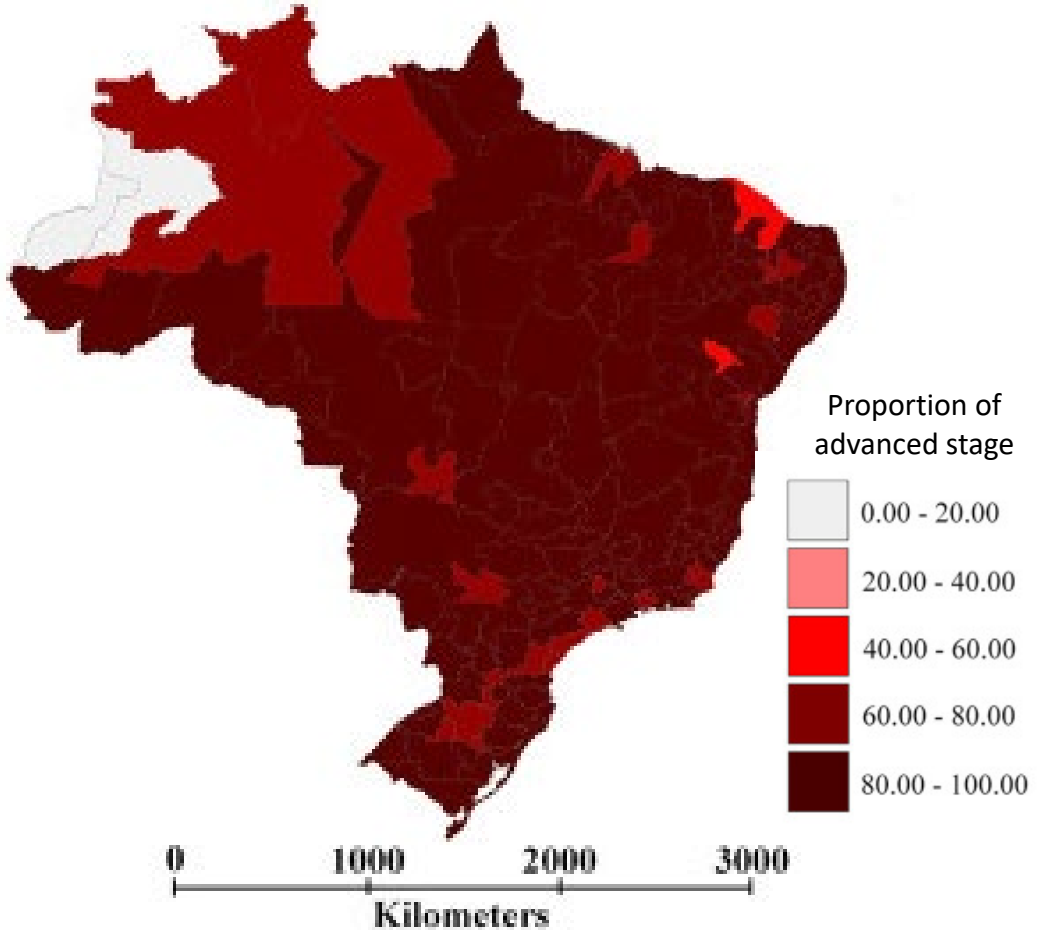
Raez LE, et al. *Lung Cancer*. 2018;119:7-13; Goss PE, et al. *Lancet Oncol*. 2013;14:391-436.

Lung Cancer Stage at Diagnosis

Distribuição proporcional dos dez tipos de câncer mais incidentes estimados para 2020 por sexo, exceto pele não melanoma*

Localização primária	Casos	%	Homens	Mulheres	Localização primária	Casos	%
Próstata	65.840	29,2%			Mama feminina	66.280	29,7%
Cólon e Reto	20.520	9,1%			Cólon e Reto	20.470	9,2%
Traqueia, Brônquio e Pulmão	17.760	7,9%			Colo do útero	16.590	7,4%
Estômago	13.360	5,9%			Traqueia, Brônquio e Pulmão	12.440	5,6%
Cavidade Oral	11.180	5,0%			Glândula Tireoide	11.950	5,4%
Esôfago	8.690	3,9%			Estômago	7.870	3,5%
Bexiga	7.590	3,4%			Ovário	6.650	3,0%
Linfoma não Hodgkin	6.580	2,9%			Corpo do útero	6.540	2,9%
Laringe	6.470	2,9%			Linfoma não Hodgkin	5.450	2,4%
Leucemias	5.920	2,6%			Sistema Nervoso Central	5.220	2,3%

* Números arredondados para múltiplos de 10



INCA 2020; Lima KYN, et al. *PLoS One*. 2022;17:e0265321.

Lung Cancer Screening

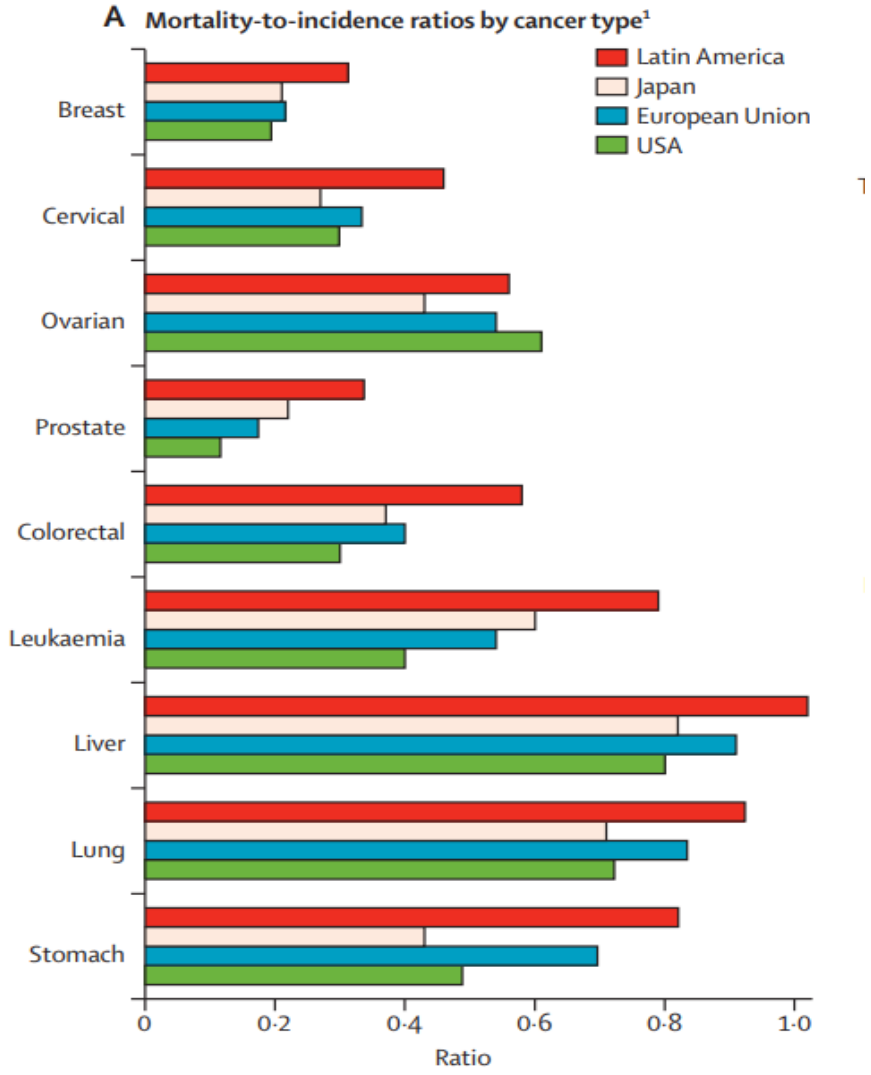
Study	Patients With Cancer, No. (%)	Biopsy Procedures, No. (%)	Lung Cancer Diagnosed, No. (%)
NLST	7,191 (27.0)	758 (2.8)	270 (1.0)
ELCAP	233 (23.0)	28 (2.8)	27 (2.7)
PluSS	1,477 (41.0)	90 (2.5)	36 (1.0)
DLCST	594 (29.0)	25 (1.2)	17 (0.8)
LUSI	540 (27.0)	31 (1.5)	22 (1.1)
DANTE	199 (15.0)	52 (4.1)	28 (2.2)
ITALUNG	426 (30.0)	22 (1.6)	21 (1.5)
LSS	325 (21.0)	57 (3.6)	30 (1.9)
Depiscan	152 (45.2)	NA	8 (2.4)
NELSON	493 (6.5)	NA	200 (2.6)
BRELT1	312 (39.5)	25 (3.1)	10 (1.3)

NOTE. Adapted from dos Santos et al.[2]

Abbreviations: BRELT1, First Brazilian Lung Cancer Screening Trial; DANTE, Randomized Study of Lung Cancer Screening with Spiral Computed Tomography; Depiscan, French randomized pilot trial of lung cancer screening comparing low-dose computed tomography scan and chest radiography; DLCST, Danish Lung Cancer Screening Trial; ELCAP, Early Lung Cancer Action Project; ITALUNG, Italian Lung Cancer Screening Trial; LSS, Lung Screening Study; LUSI, German Lung Cancer Screening Intervention Trial; NA, not available; NELSON, Netherlands-Belgian Lung Cancer Screening trial; NLST, National Lung Screening Trial; PluSS, The Pittsburgh Lung Screening Study.

Raez LE, et al. *J Glob Oncol*. 2018;4:1-10.

All Cancer Mortality to Incidence Ratio



Goss PE, et al. *Lancet Oncol*. 2013;14:391-436.

Unmet Needs

Table 2 Five Major Barriers to Access High-Cost Drugs in the Latin American Region

(1) Lack of adequate investment in research and development in the region. There is a low number of clinical trials or original lung cancer research developing in the area.
(2) Issues in availability of the drugs and the fact that each government has different polices for drug approval.
(3) Limitations in current established health care services with lung cancer services not necessarily being considered a priority yet for most of the countries, owing to the relatively low prevalence compared with other cancers and the current economic constraints in most of the countries in the region.
(4) Limitations in the drug supply system.
(5) Issues of the affordability of the new targeted medications. and the need to have policies to allow better coverage from the government and private payors to the most important drugs.

Raez LE, et al. *Clin Lung Cancer*. 2017;18:e71-e79.

Unmet Needs

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Multidisciplinary care

Raez LE, et al. *Clin Lung Cancer*. 2017;18:e71-e79.

Multidisciplinary Care Models

- United States
  - Integral piece of patient management and outcomes
- United Kingdom
  - Regulated by the NHS
- Brazil (and perhaps Latin America)
  - Standardized approach lacking in most services
  - Fragmented care

Wright FC, et al. *Eur J Cancer*. 2007;43:1002-1010.

Multidisciplinary Care Models

- Format: meetings/conferences, formal referral systems, integrated clinics
- Members

Why Provide Multidisciplinary Care?

- Better patient care (staging and treatment planning)
- Adherence to guidelines
- Development of local algorithms
- Continuing medical education
- Professional satisfaction
- Increased referral to clinical trials
- Rational use of resources
- Increased survival (?)

Multidisciplinary Tumor Boards and Quality Measures

Table 2. Comparison of Patients With and Without Multidisciplinary Conference Care

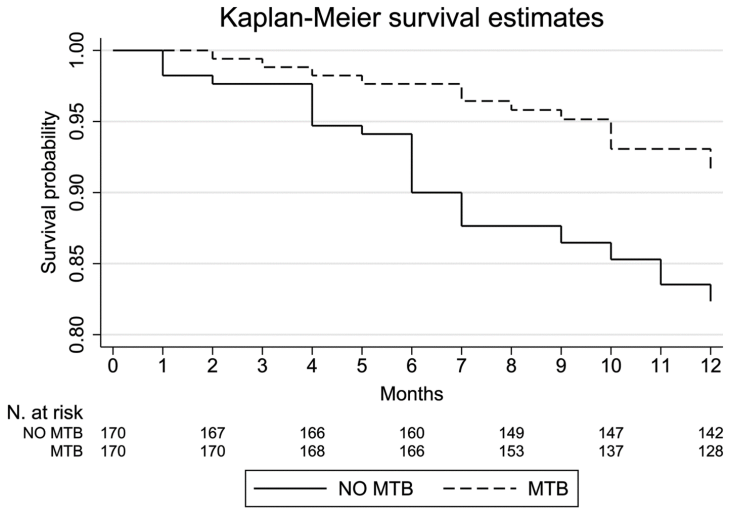
Variable[a]	MDC (n = 6,627)	Non-MDC (n = 6,627)	*p* Value
Complete staging	6,031 (91)	4,572 (67)	< 0.0001
Multispecialty evaluation	5,898 (89)	3,446 (52)	< 0.0001
Diagnosis to treatment, d	19 ± 8	32 ± 11	< 0.0001
NCCN guidelines	5,832 (88)	4,705 (71)	< 0.0001
Research participation	1,127 (17)	398 (6)	< 0.0001
Palliative/hospice care	596 (9)	266 (4)	< 0.0001
Chemotherapy and/or radiotherapy without a tissue diagnosis	199 (3)	331 (5)	< 0.0001
Nontherapeutic surgical intervention	133 (2)	265 (4)	< 0.0001
Mean cost of care, diagnosis and staging, $	7,212.00	10,213.00	< 0.0001

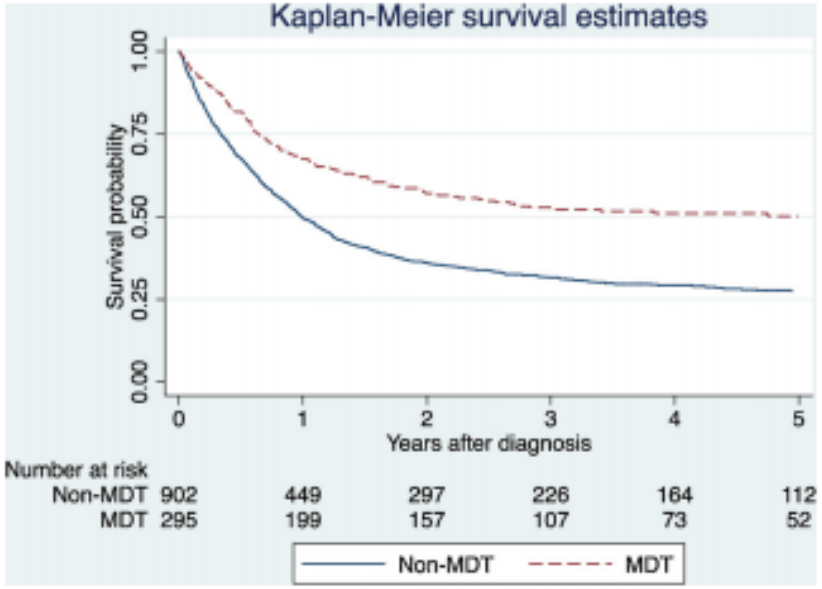
[a] Continuous data are presented as mean ± standard deviation and categoric data as number (%).

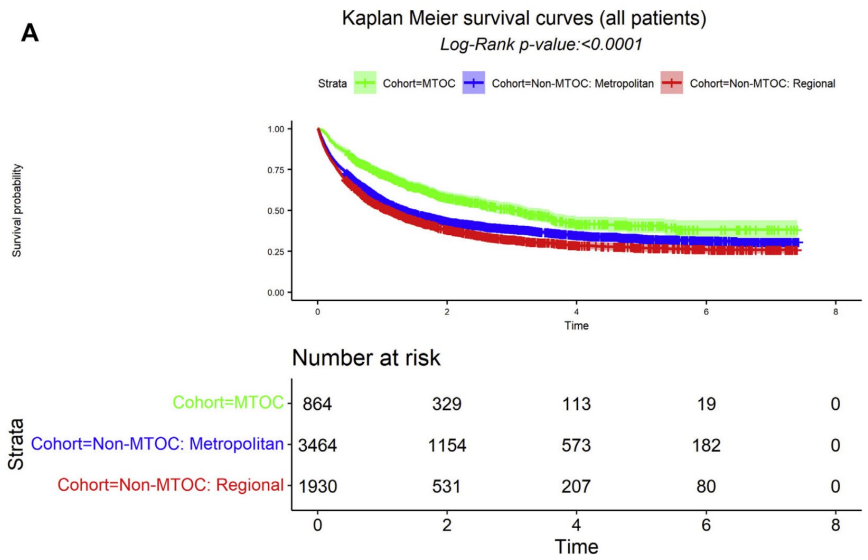
MDC = multidisciplinary conference; NCCN = National Comprehensive Cancer Network.

Freeman RK, et al. *Ann Thorac Surg*. 2015;100:1834-1838.

Multidisciplinary Tumor Boards



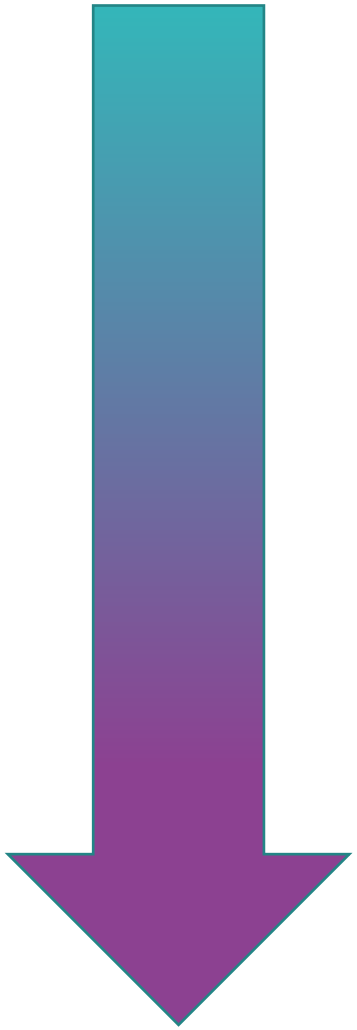




Tamburini N, et al. *Eur J Cardiothorac Surg*. 2018;53:1199-1204; Stone E, et al. *Lung Cancer*. 2018;124:199-204; Ray MA, et al. *JTO Clin Res Rep*. 2021;2:100203.

Stepwise Approach

Decentralized care



Motivated group

Continuing medical education

Multidisciplinary tumor boards

Integrated clinics

Multidisciplinary care

Team Up: 423 Physicians

Educação e Pesquisa

Challenges: Is Latin America Ready?

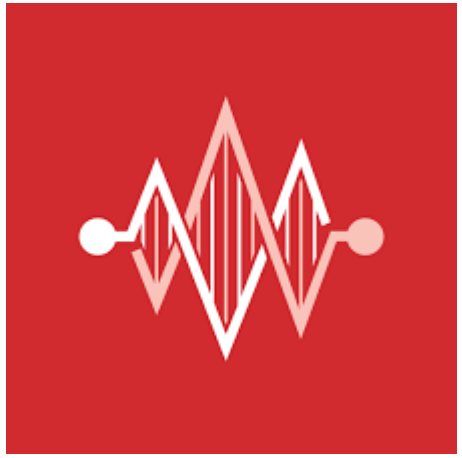
- Lack of time
- Lack of institutional support
- Lack of resources (included, but not limited to, financial resources)
- Lack of motivation
- Lack of coordinated health care system

Challenges: Is Latin America Ready?

- Lack of time
- Lack of institutional support
- Lack of resources (included, but not limited to, financial resources)
- Lack of motivation
- Lack of coordinated health care system

- Can we blame (underserved area) physicians who are not able to provide multidisciplinary care?
- How can we help?

Challenges: Is Latin America Ready?



Conclusions

- Many barriers to improve lung cancer care in Latin America
- Multidisciplinary care is one of the key components of adequate management of early-stage/locally advanced lung cancer
- Implementation of multidisciplinary care is challenging, lengthy, and may not be feasible in all settings
- Opportunity for innovative approaches

Obrigado!!!

Discussion

Global Lung Cancer Academy

Current Treatment Options for Metastatic NSCLC in Latin America

Carlos Barrios, MD

October 2022

Current Treatment Options for Metastatic NSCLC in Latin America

Carlos H. Barrios, MD
Latin American Cooperative Oncology Group (LACOG)
Grupo Oncoclínicas
Porto Alegre, Brazil

Disclosures

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- **Academic Research Projects**: CPO, PUCRS, LACOG, GBECAM
- **Ownership or Stocks:** Tummi, MEDSir
- **Advisory Boards and Consulting**: Boehringer-Ingelheim, GSK, Novartis, Pfizer, Roche/Genentech, Eisai, Bayer, MSD, AstraZeneca, Zodiac, Lilly, Sanofi

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Conflict of Interest Statement

This presentation reflects my personal opinion, and not that of the sponsor of this activity. Its main objective is to stimulate independent scientific discussion and does not intend to promote a specific product or indication.

Carlos H. Barrios, MD
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Status of Metastatic Lung Cancer Therapy in 2002

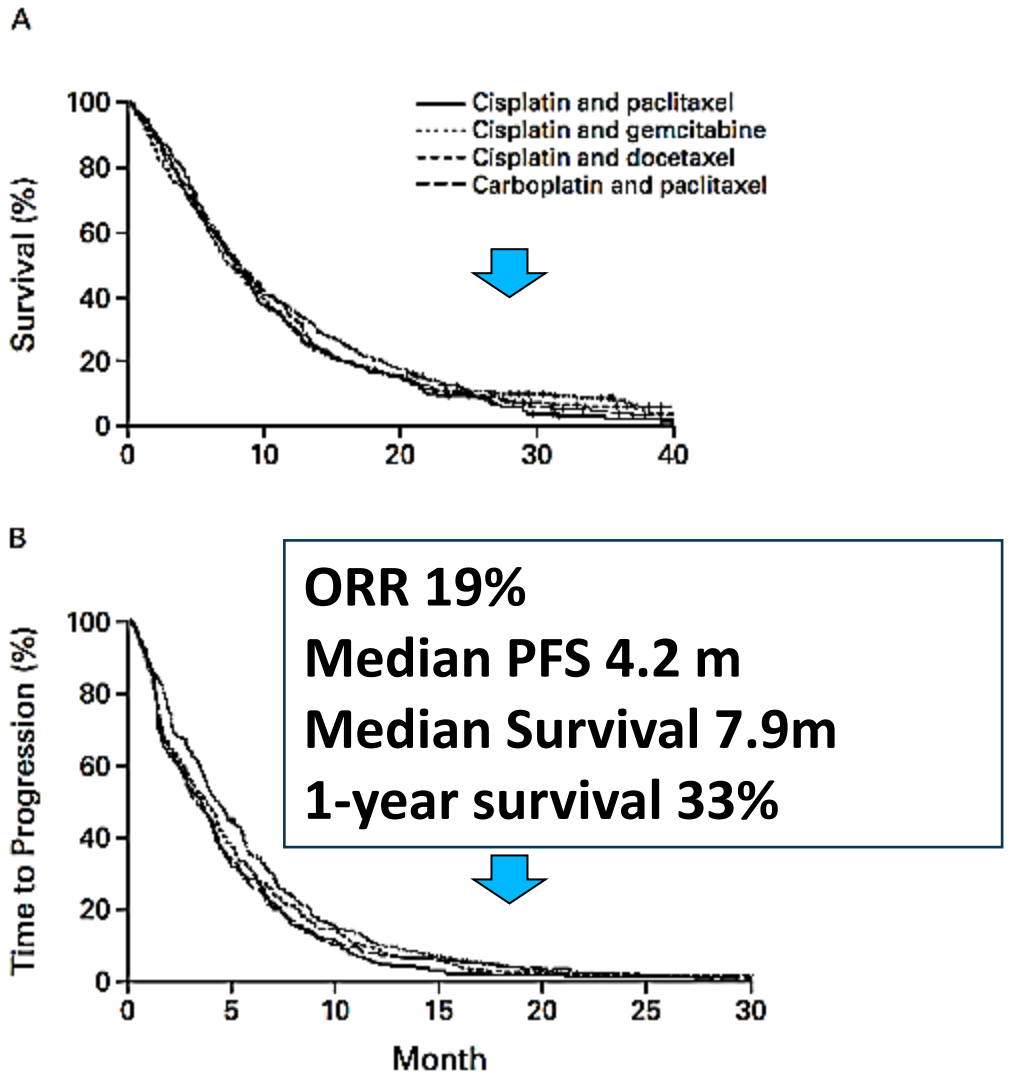
Regimens

Cisplatin plus paclitaxel
- paclitaxel, 135 mg/m² over 24-hr period on day 1
- cisplatin, 75 mg/m² on day 2
- 3-wk cycle

Cisplatin plus gemcitabine
- gemcitabine, 1000 mg/m² on days 1, 8, and 15
- cisplatin, 100 mg/m² on day 1
- 4-wk cycle

Cisplatin plus docetaxel
- docetaxel, 75 mg/m² on day 1
- cisplatin, 75 mg/m² on day 1
- 3-wk cycle

Carboplatin plus paclitaxel
- paclitaxel, 225 mg/m² over 3-hr period on day 1
- carboplatin, AUC 6.0 mg/ml/min on day 1
- 3-wk cycle

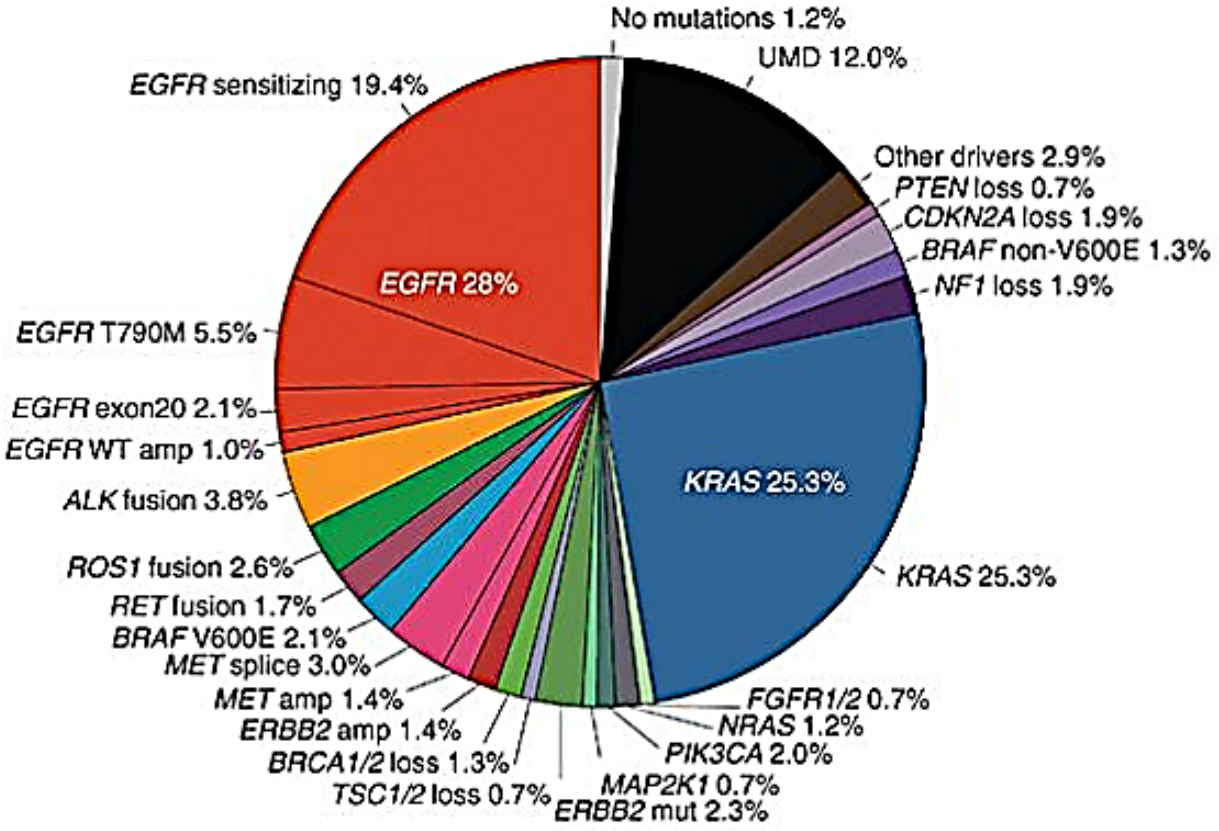


ORR 19%
Median PFS 4.2 m
Median Survival 7.9m
1-year survival 33%

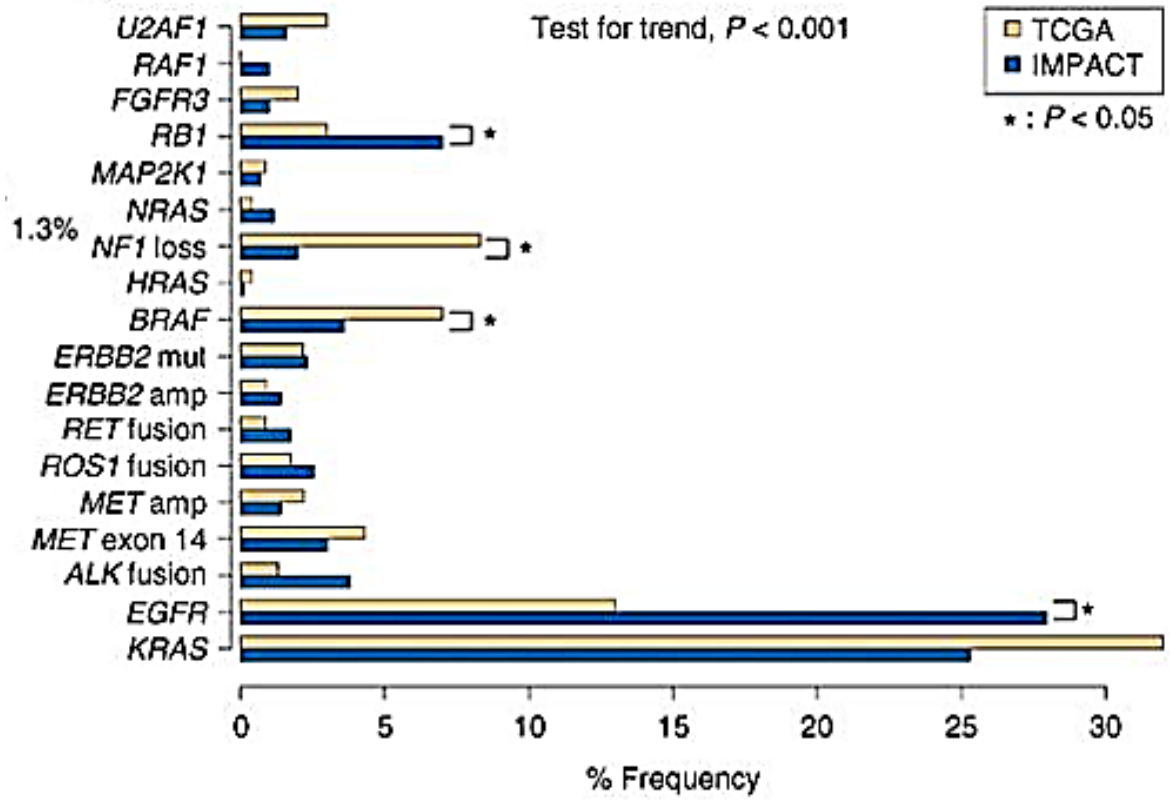
- **Platinum chemotherapy improved survival**
- **All doublets have similar efficacy**
- **No predictive factors identified**
- **All regimens with significant toxicty**

Schiller J, et al. *N Engl J Med.* 2002;346:92-98.

Potentially Actionable Oncogenic Drivers Identified by MSK-IMPACT



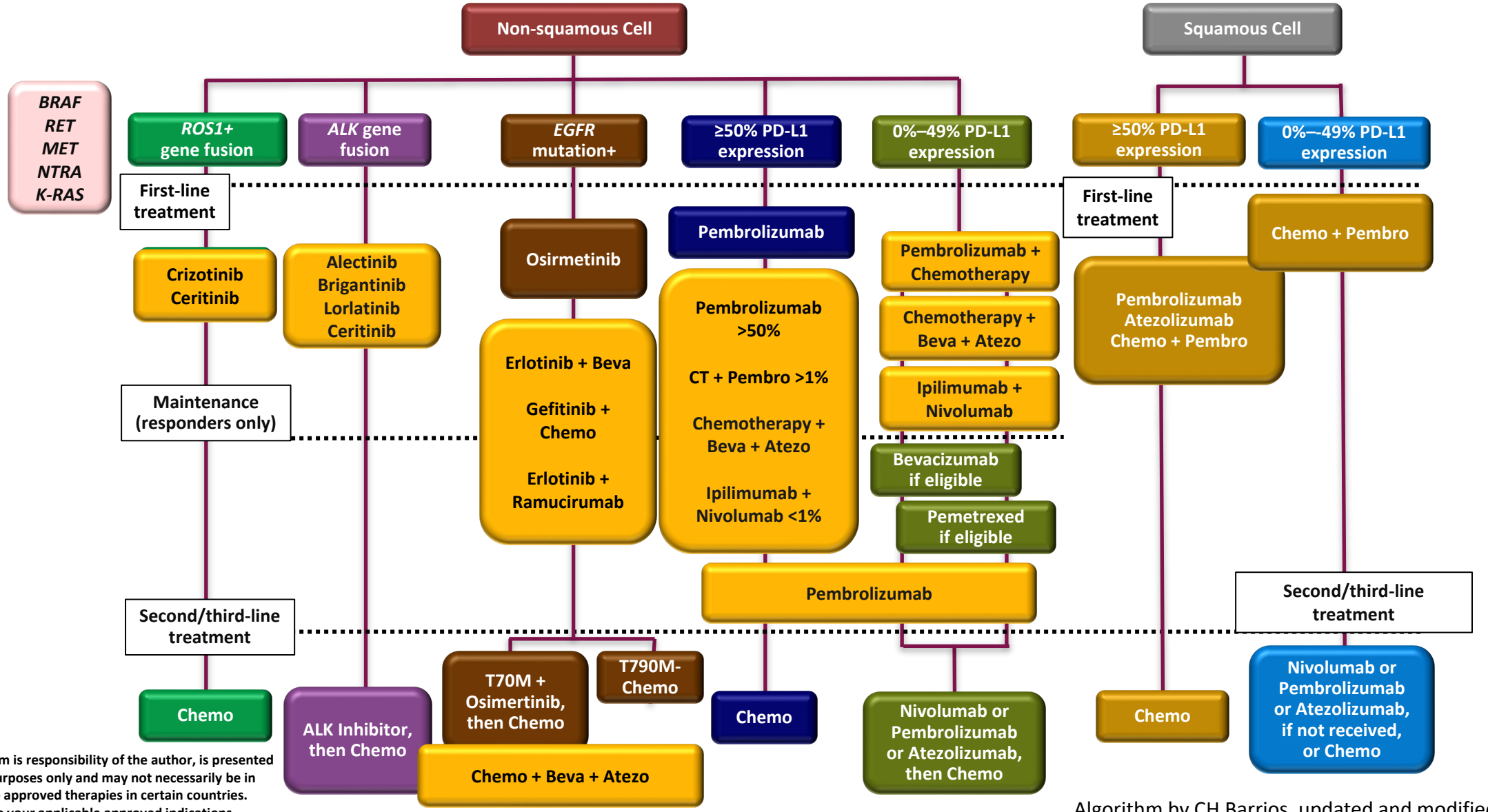
Spectrum of oncogenic drivers assigned to 860 patients with lung adenocarcinoma identified by MSK-IMPACT.



Comparison of selected gene alteration frequencies in the MSK-IMPACT and TCGA.

Jordan EJ, et al. *Cancer Discov.* 2017;7:596-609.

Proposed Standard of Care Treatment Algorithm for Patients With Advanced NSCLC – 2022*

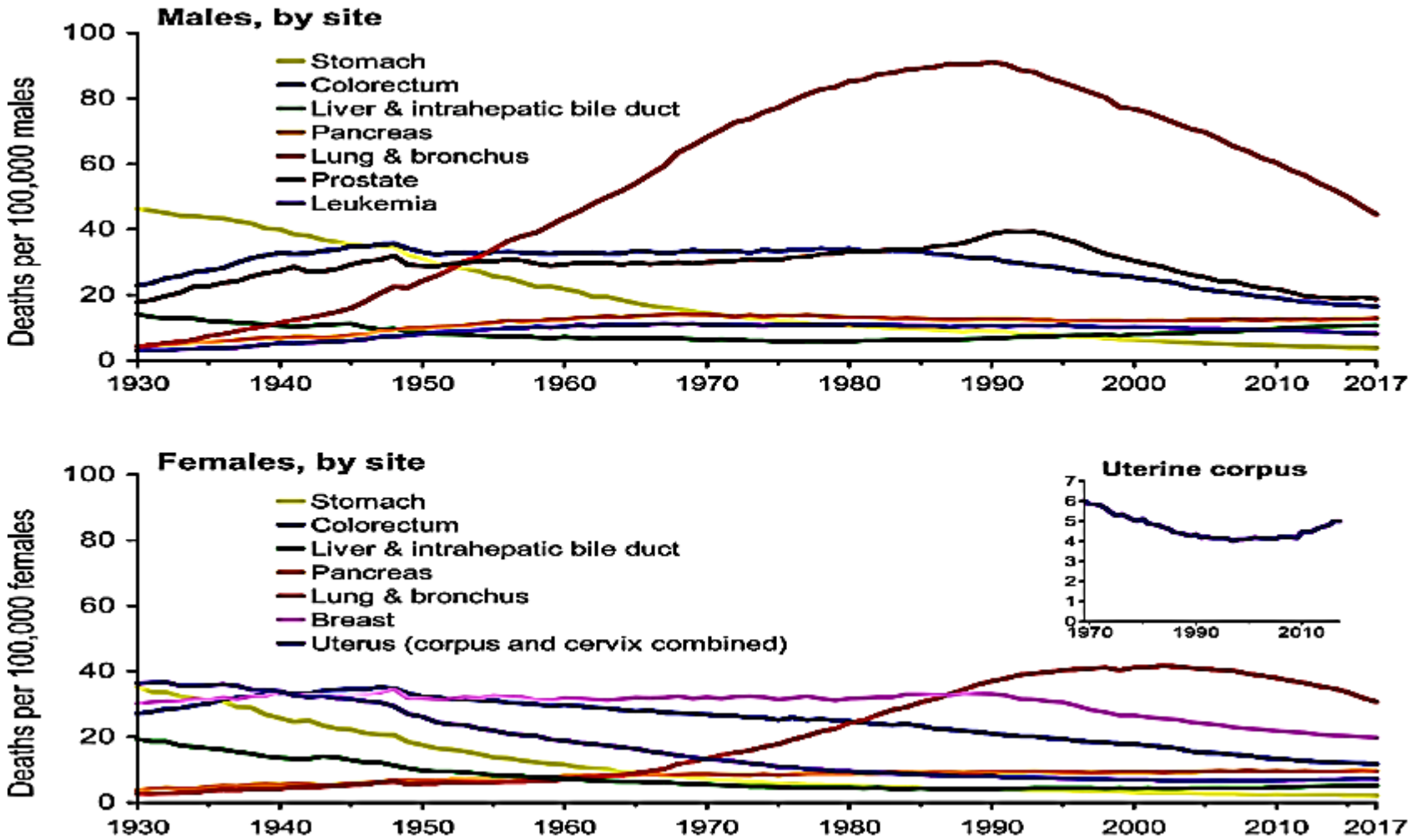


*This algorithm is responsibility of the author, is presented for didactic purposes only and may not necessarily be in accordance to approved therapies in certain countries. Please refer to your applicable approved indications.

Algorithm by CH Barrios, updated and modified from Karen Kelly.

Lung Cancer Mortality Is Improving . . .

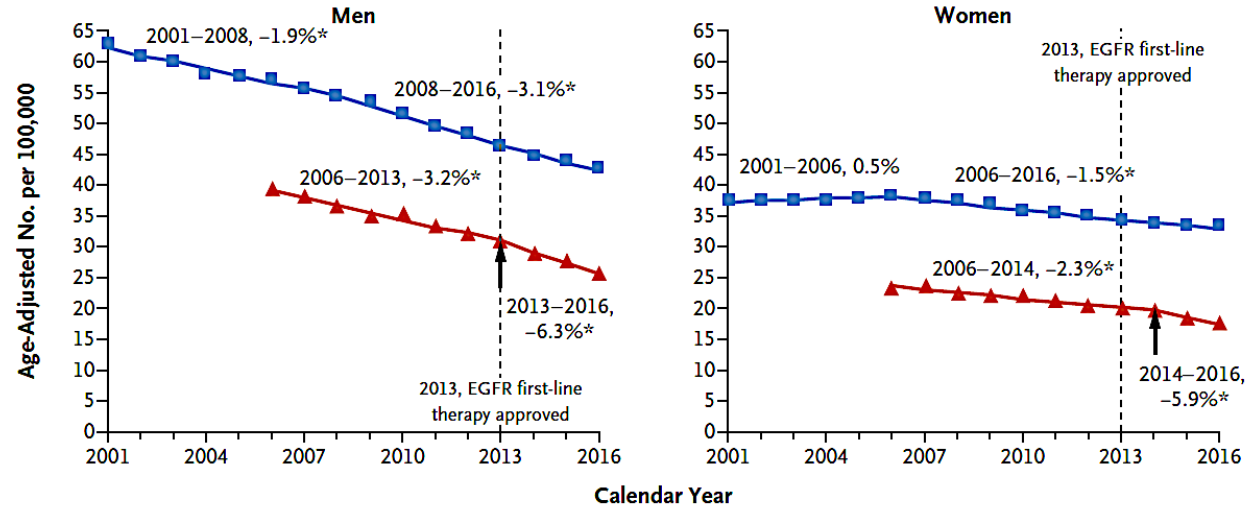
Mortality rates have declined by 51% since 1990 for men (and 26% since 2002 in women) due to reductions in smoking (associated with a decrease in incidence)

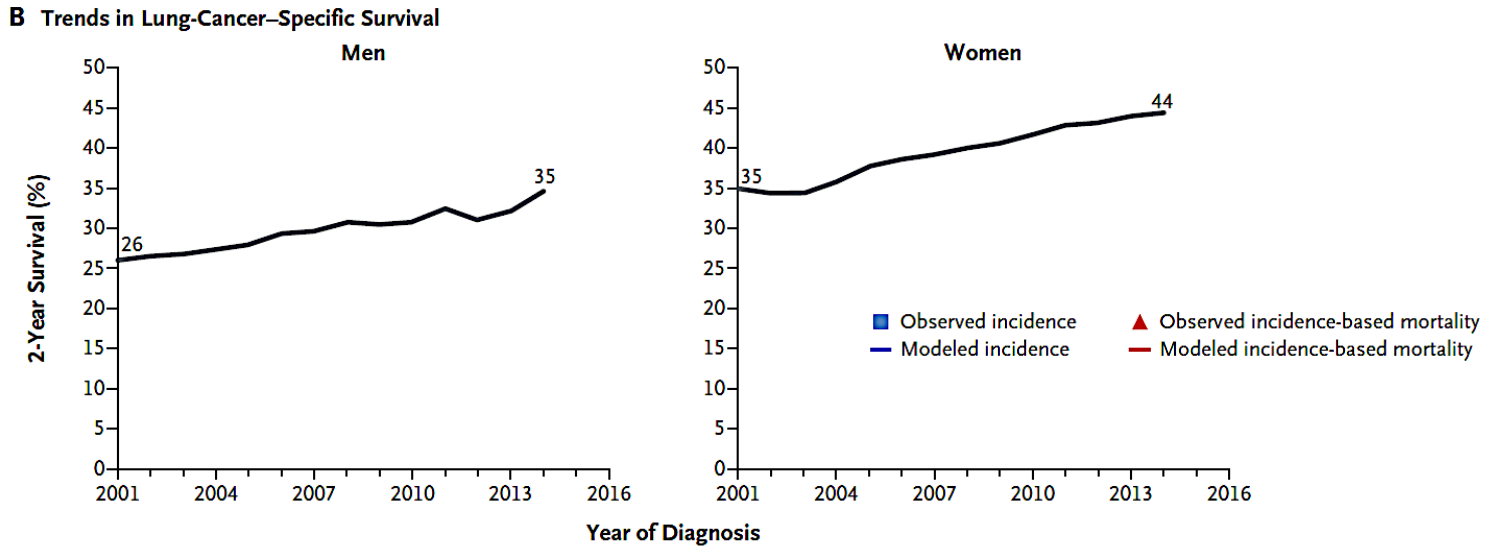


Siegel RL, et al. *CA Cancer J Clin.* 2020;70:7-30; Annual Report to the Nation on the Status of Cancer. *J Natl Cancer.* 2019;111:12; Cancer Facts and Figures, American Cancer Society 2020.

NSCLC Incidence, Incidence-Based Mortality, and Survival Trends among Men and Women

		Average annual percent change
Males	Incidence (2011–15) Mortality (2012–16)	-2.6 -4.3
Females	Incidence (2011–15) Mortality (2012–16)	-1.2 -3.1

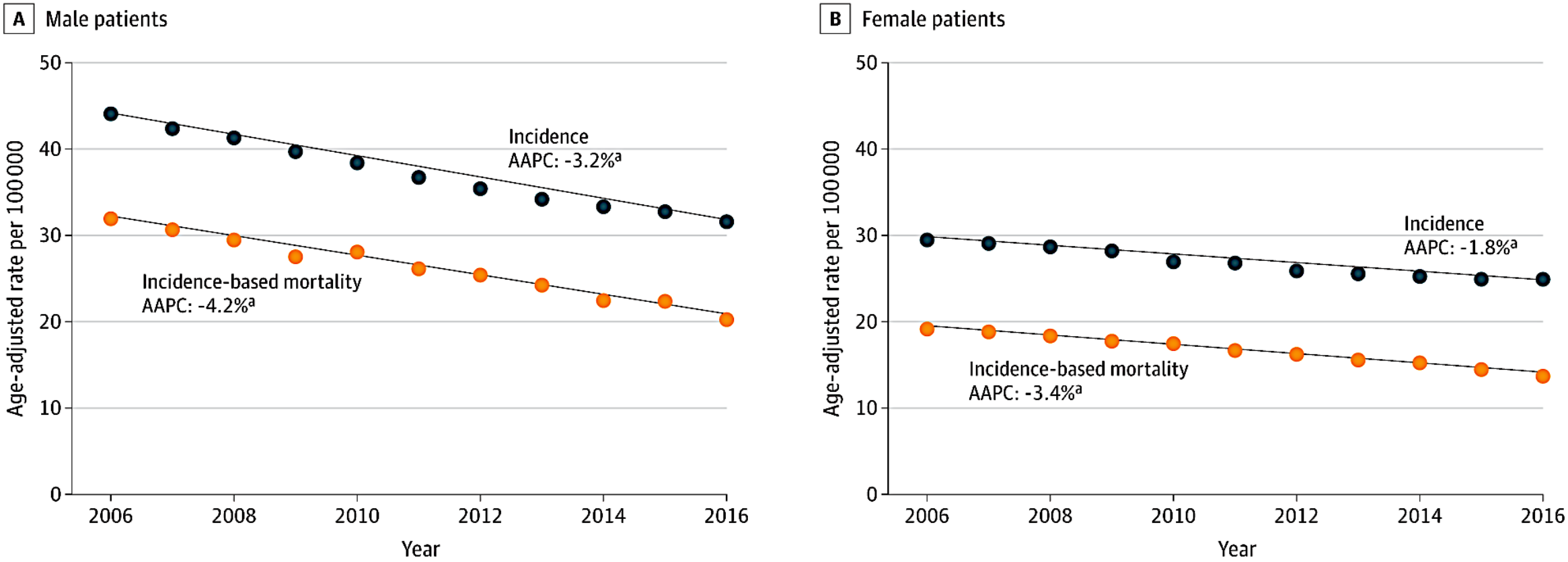




Incidence: age standardized, delay-adjusted rate.
Mortality: age-standardized rate.

Howlader N, et al. *N Engl J Med*. 2020;383:640-649; Siegel RL, et al. *CA Cancer J Clin.* 2020;70:7-30.

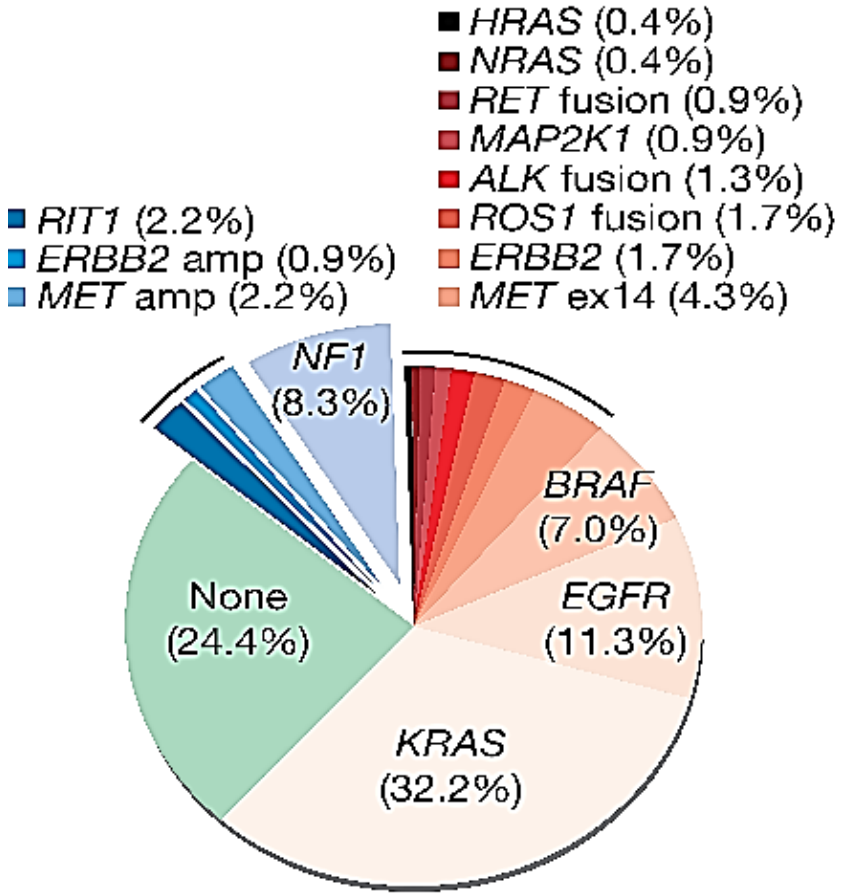
Lung Cancer Mortality Is Improving . . .

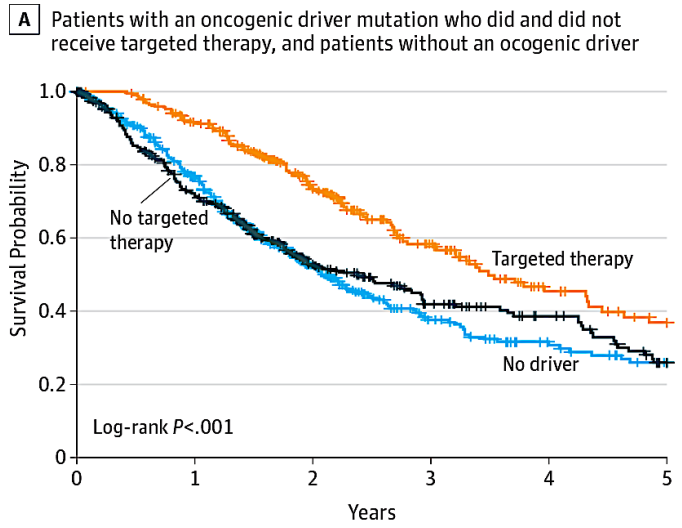


Population-level mortality for NSCLC has decreased from 2006 to 2016. Although advances in treatments, particularly targeted therapeutics, have played a role in affecting mortality, this analysis suggests that decreased mortality is also associated with a diagnostic shift from later to earlier stage lung cancer and a histology shift to adenocarcinoma.

Flores R, et al. *JAMA Netw Open*. 2021;4:e2137508.

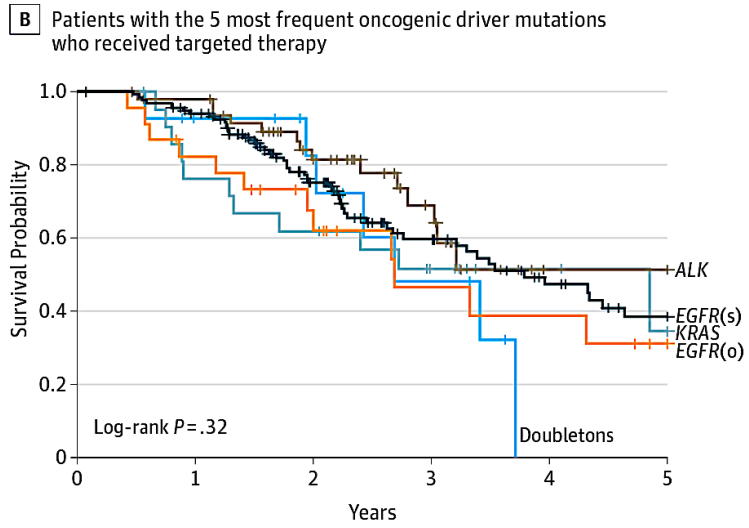
Targeted Therapy Revolution





No. at risk

Patients with oncogenic driver						
No targeted therapy	318	205	110	64	43	20
Targeted therapy	260	225	143	72	36	23
Patients with no driver	360	250	122	59	36	23



No. at risk by oncogenic driver

EGFR(s)	136	122	72	38	24	16
EGFR(o)	23	18	12	6	5	2
ALK	49	46	31	14	2	2
KRAS	22	16	13	8	4	2
Doubletons	14	11	8	4		

Cancer Genome Atlas Research Network. *Nature.* 2014;513:202-209; Kris M, et al. *JAMA.* 2014;21;311:1998-2006.

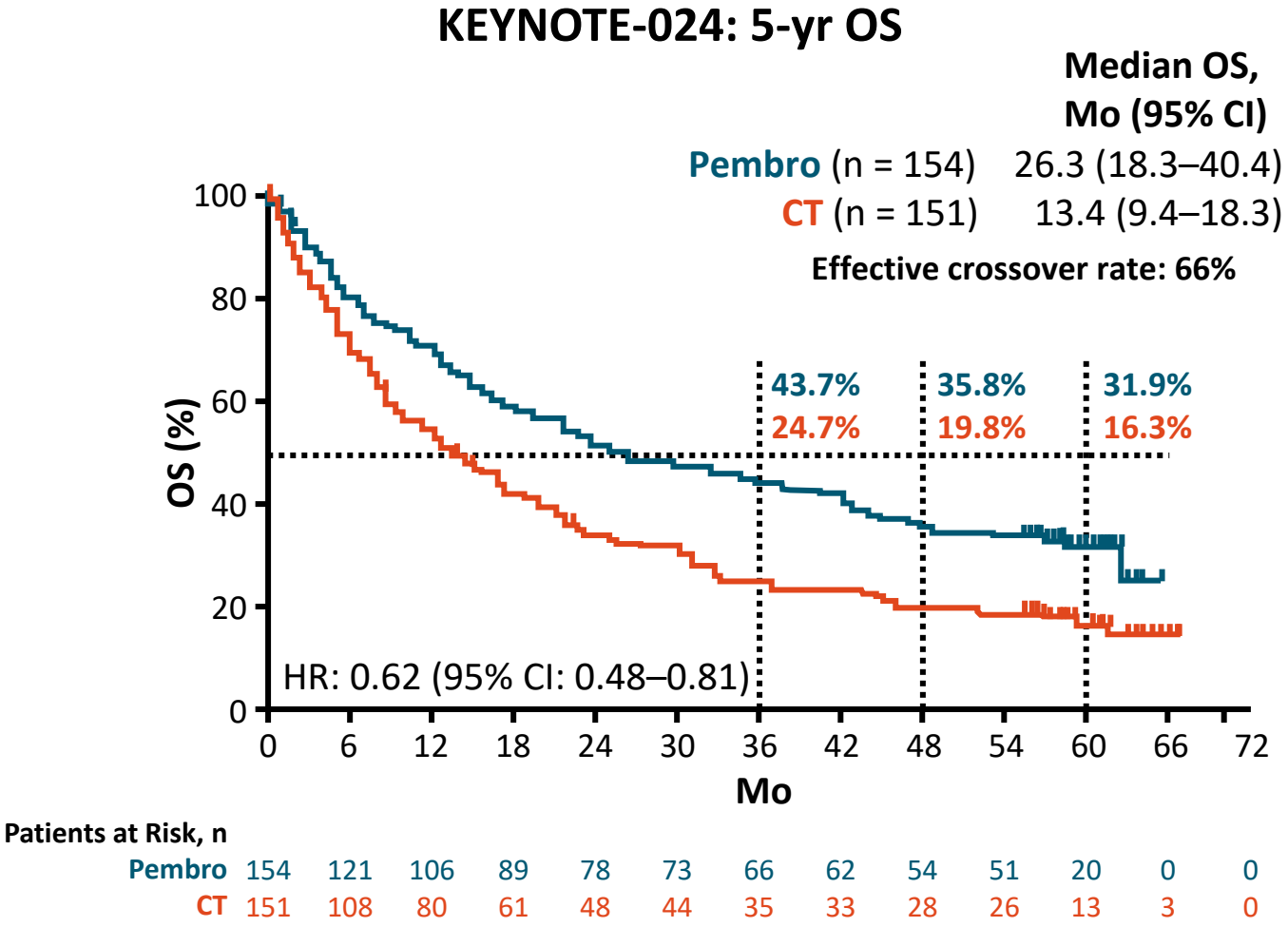
Immunotherapy Options for Advanced NSCLC With High PD-L1 expression Across Histologies

Parameter	KEYNOTE-024: pembrolizumab (n = 154)[1]	IMpower110: atezolizumab (n = 107)[2]	EMpower-Lung 1: cemiplimab (n = 283)[3]	CheckMate 227: Nivo-Ipi (n = 205)[4]	CheckMate 9LA: Nivo-Ipi + CT (n = 76)[5]
PD-L1+ definition	TPS ≥50%*	TC3 or IC3†	TPS ≥50%*	TPS ≥50%‡	TPS ≥50%‡
ORR, %	46.1	40.2	39.0	45.4	38
Median DoR, mo	29.1	38.9	16.7	31.8	26.0
Median PFS, mo	7.7 (HR: 0.50)	8.2 (HR: 0.59)	8.2 (HR: 0.54)	6.7 (HR: 0.60)	7.5 (HR: 0.59)
Median OS, mo	26.3 (HR: 0.62)	20.2 (HR: 0.76)	NR (HR: 0.57)	21.2 (HR: 0.66)	18.9 (0.67)

*By PD-L1 22C3 IHC assay. †Staining of ≥50% tumor cells (TC3) or ≥10% tumor-infiltrating immune cells (IC3) by PD-L1 SP142 IHC assay. ‡PD-L1 28-8 IHC assay. Caution needs to be taken when comparing data across trials.

1. Reck M, et al. *J Clin Oncol.* 2021;39:2339-2349; 2. Jassem J, et al. *J Thorac Oncol.* 2021;16:1872-1882; 3. Sezer A, et al. *Lancet*. 2021;397:592-604. 4. Paz-Arez L, et al. *J Thorac Oncol.* 2022;17:289-308; 5. Reck M, et al. *ESMO Open.* 2021;6:100273.

Immunotherapy in PD-L1+ Advanced NSCLC: Long-term Survival, Cure?



PD-1/PD-L1 Immunotherapy

- Pembrolizumab
- Nivolumab
- Atezolizumab
- Durvalumab
- Cemiplimab

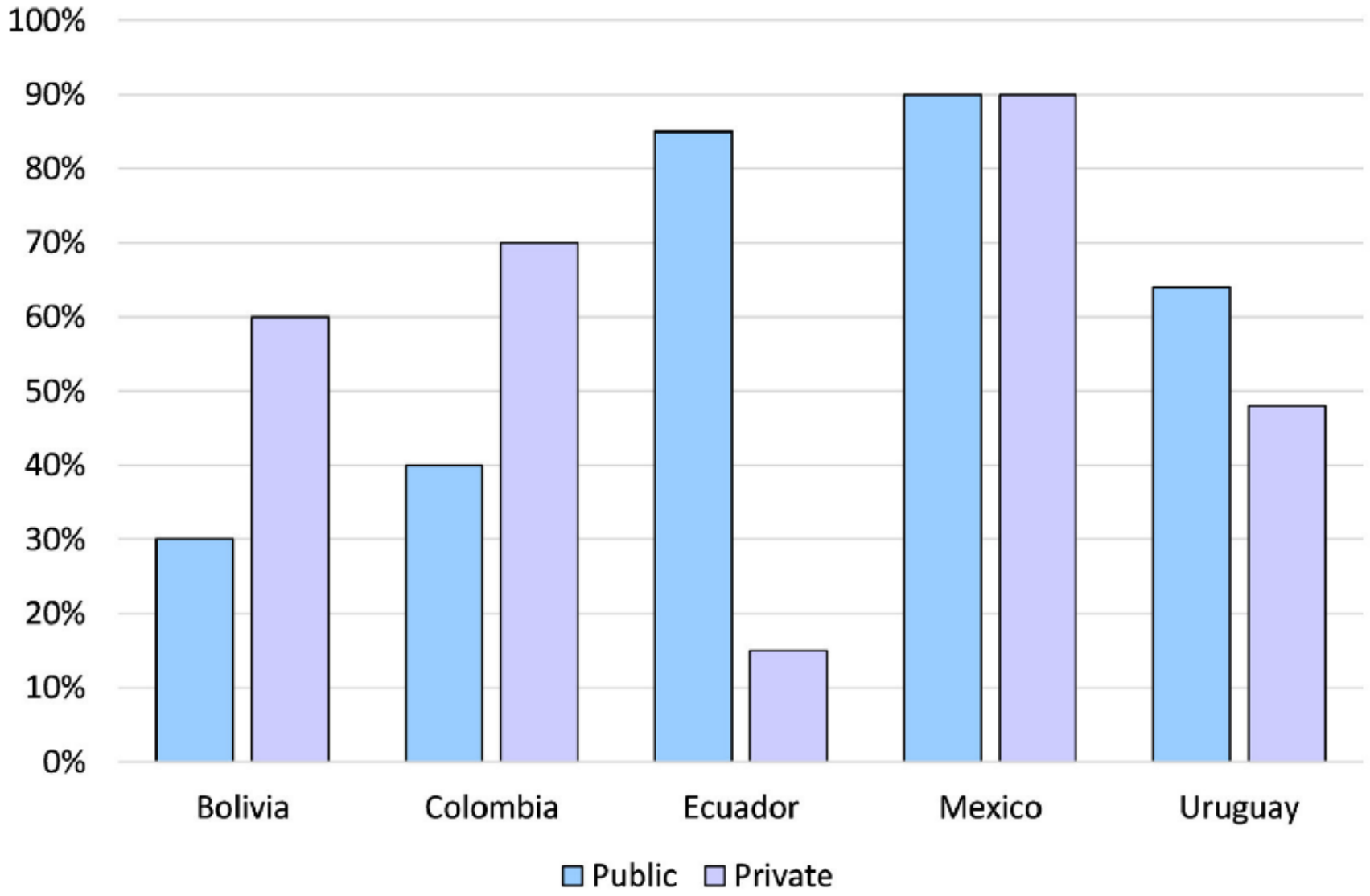
Patient Features

- ✓ Females
- ✓ Smokers
- ✓ No oncogenic driver mutation

Challenging Insights – NSCLC Latin America

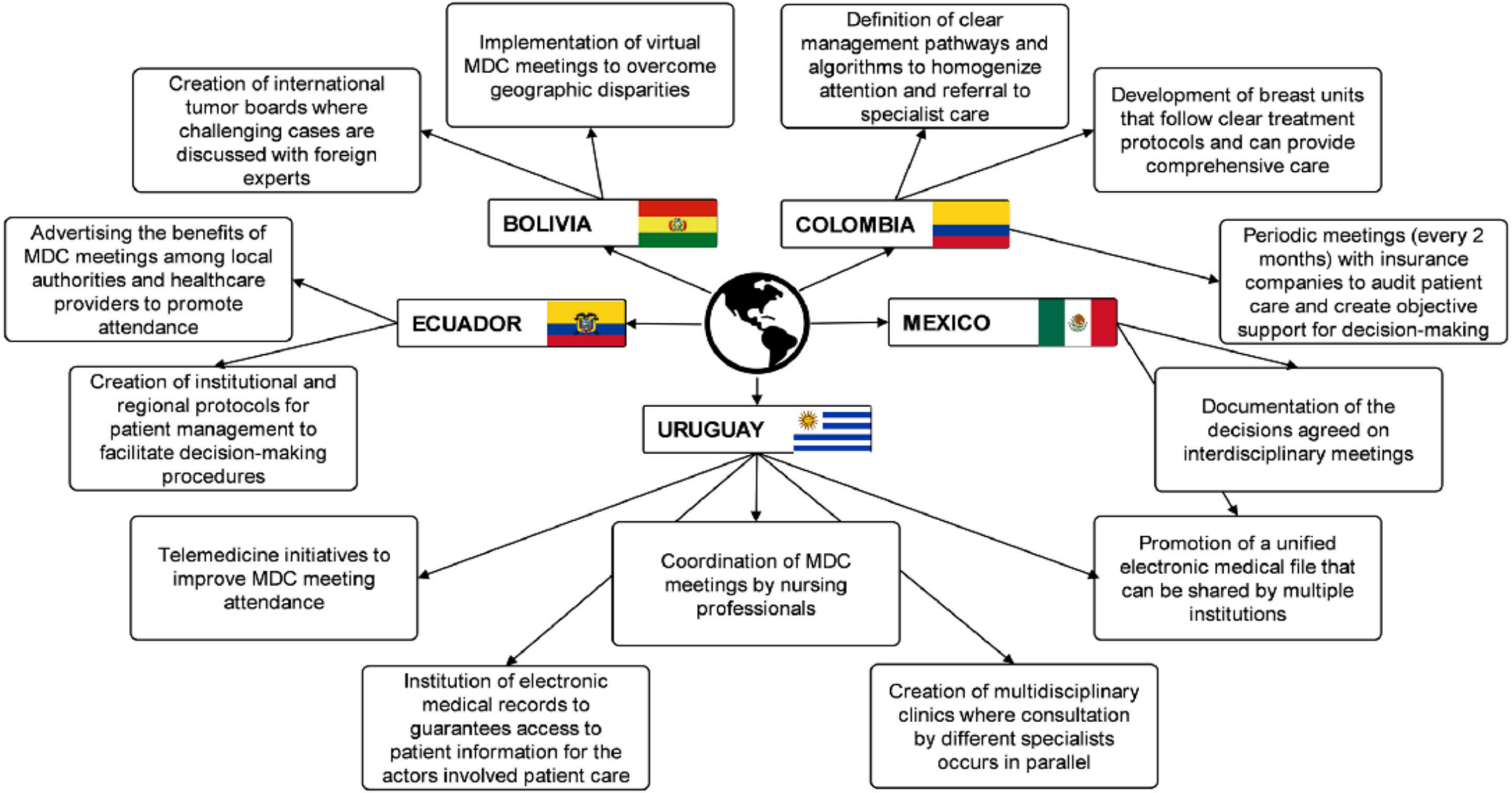
- Multidisciplinary care
- Clinical research
- Access to diagnosis and drugs

Barriers and Strategies for Multidisciplinary Cancer Care in Latin America

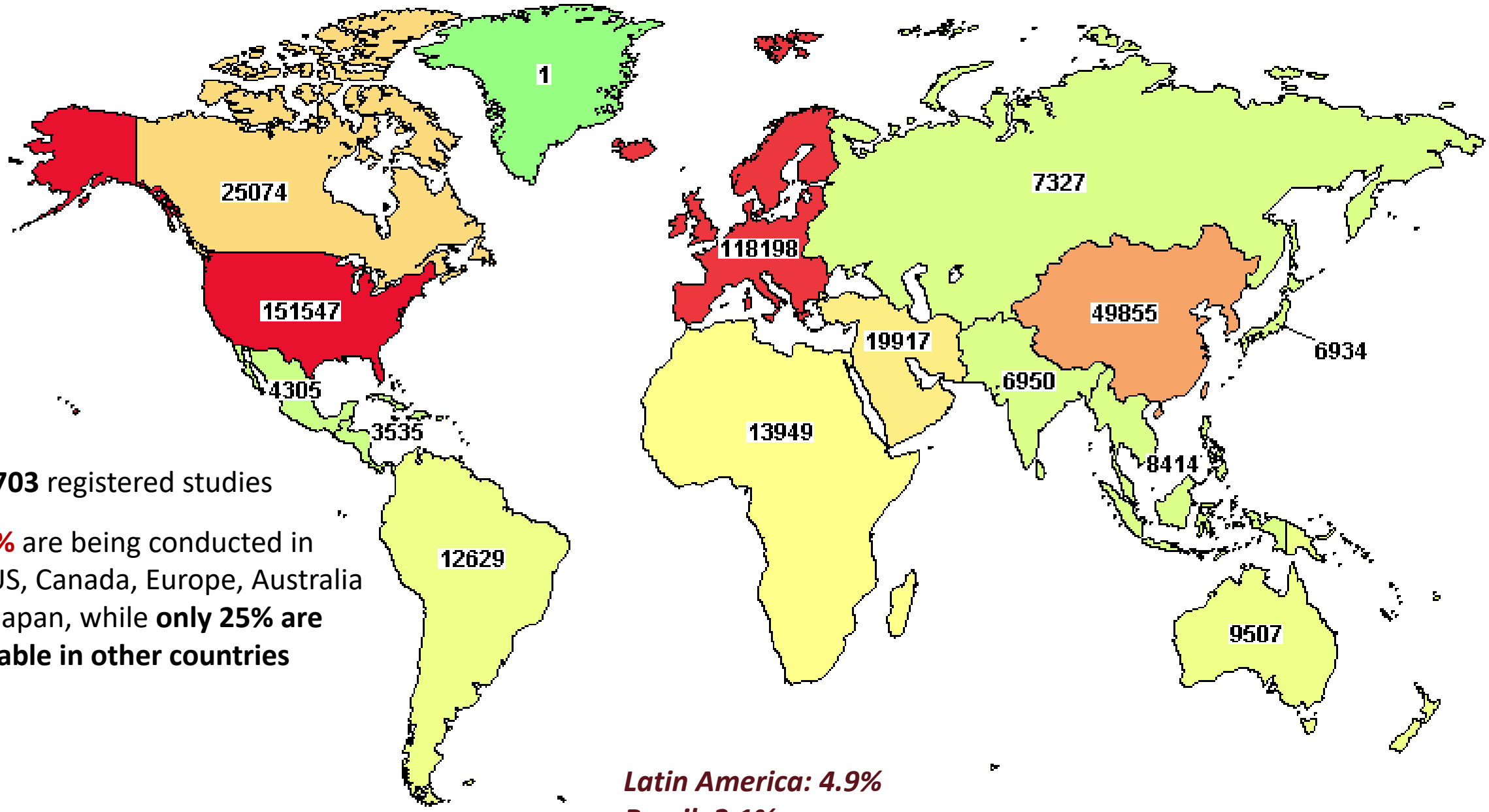


Barrios CH, et al. *The Lancet Regional Health Americas*. July 2022. https://doi.org/10.1016/j.lana.2022.100254

Barriers and Strategies for Multidisciplinary Cancer Care in Latin America



Barrios CH, et al. *The Lancet Regional Health Americas*. July 2022. https://doi.org/10.1016/j.lana.2022.100254



410,703 registered studies

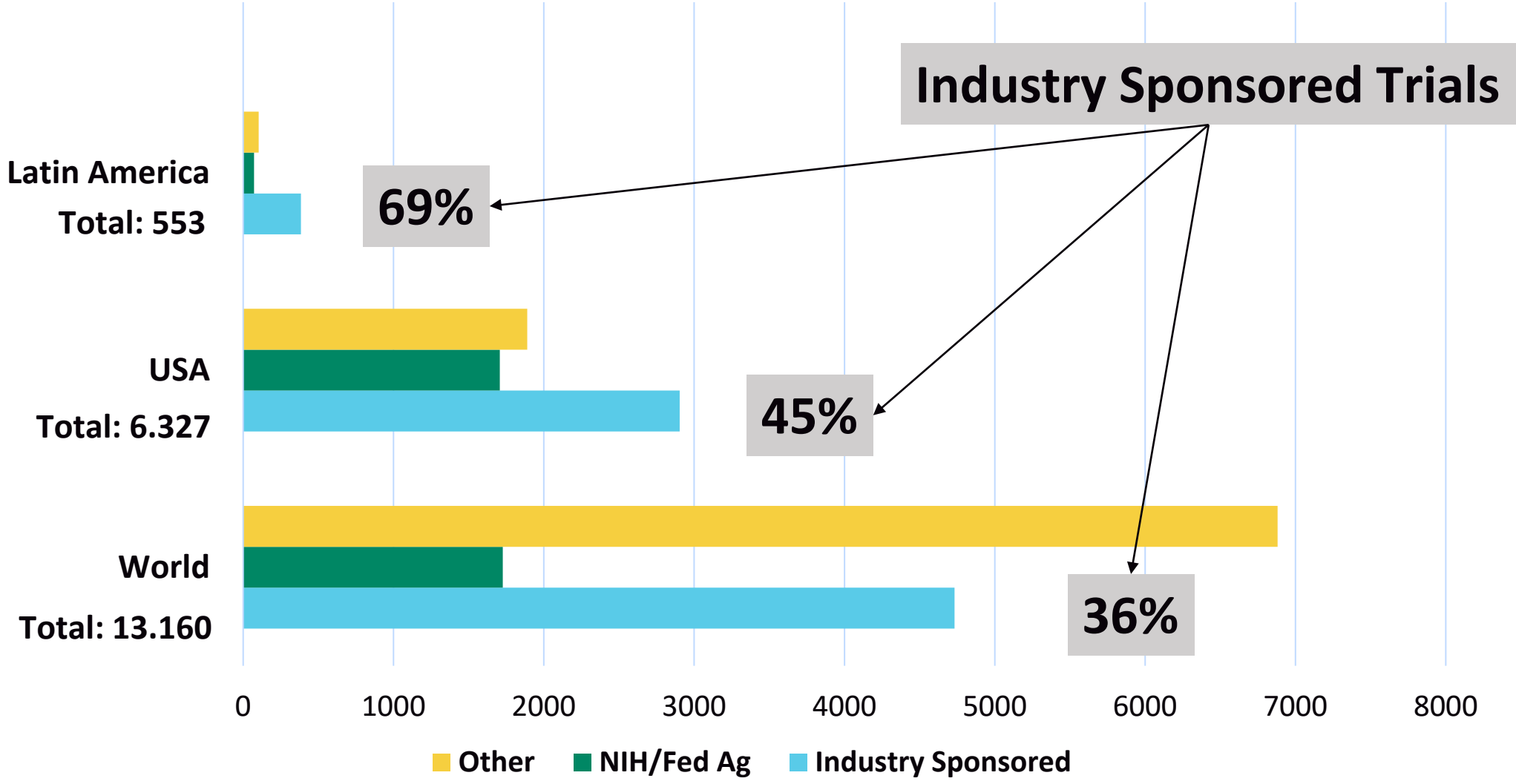
75.7% are being conducted in the US, Canada, Europe, Australia and Japan, while **only 25% are available in other countries**

Latin America: 4.9%

Brazil: 2.1%

ClinicalTrials.gov, accessed April 9, 2021.

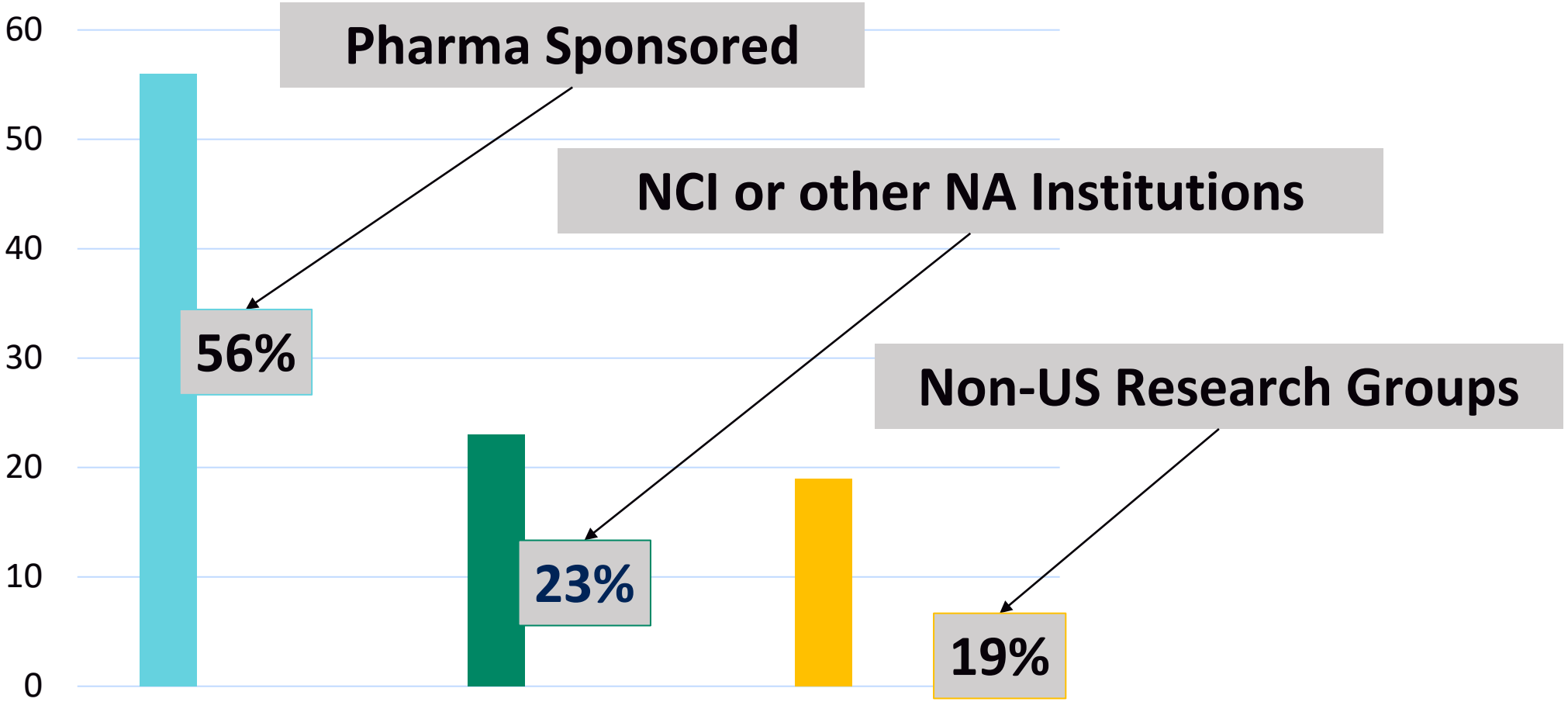
“Sponsor” “Cancer” “Intervention” “Recruiting” Trials



ClinicalTrials.gov, accessed May 1, 2021; Barrios CH, Mano MS. *Am Soc Clin Oncol Educ Book*. 2021;41:1-10.

Research Presented at ASCO's Plenary Session

2000–2020



Meetinglibrary.asco.org, accessed January 2021;
Adapted from: Vandross A, et al. *Semin Oncol.* 2016;43:321–326; Barrios CH, Mano MS. *Am Soc Clin Oncol Educ Book*. 2021;41:1-10.

Registry of Metastatic NSCLC in Latin America LATINO Lung (LACOG 0116)

- To describe the overall survival of advanced NSCLC in Latin America
- Demographic and socioeconomic characteristics
- Diagnostic methods, pathological profile, and disease stage at diagnosis
- Describe treatment practice patterns
- Patient experience of advanced NSCLC and identify unmet needs in their diagnosis and treatment
- 731 patients from Brazil, Mexico, Colombia, Argentina

Clinical Stage of Cancer at Initial Diagnosis (8th Edition)	
IA	2 (0.3%)
IA1	0 (0%)
IA2	2 (0.3%)
IA3	0 (0%)
IB	2 (0.3%)
IIA	0 (0%)
IIB	1 (0.1%)
IIIA	26 (3.7%)
IIIB	23 (3.3%)
IIIC	12 (1.7%)
IV	141 (20.2%)
IVA	188 (26.9%)
IVB	300 (43.0%)

Werutsky G, Barrios CH, et al. LACOG, internal data.

Registry of Metastatic NSCLC in Latin America
LATINO Lung (LACOG 0116)

Primary Tumor Histology	
Adenocarcinoma	419 (57.3%)
Squamous cell carcinoma	116 (16.0%)
Mixed	2 (0.3%)
Large cell carcinoma	4 (0.5%)
Not other specified (NOS)	18 (2.5%)
Other	14 (1.9%)
Missing	154 (21.2%)

Werutsky G, Barrios CH, et al. LACOG, internal data.

Registry of Metastatic NSCLC in Latin America
LATINO Lung (LACOG 0116)

Was an evaluation of mutations performed?	
Yes	486 (66.8%)
No	209 (28.7%)
Unknown	32 (4.4%)
Why was the evaluation of mutations NOT performed?	
Lack of enough tissue	12 (5.7%)
Long turnaround time for testing and results	2 (1.0%)
Poor performance status	4 (1.9%)
Do not have access to the test (eg, refund, logistics)	9 (4.3%)
Patient clinical characteristics (eg, smoking status, gender)	29 (13.9%)
Unknown	153 (73.2%)

Werutsky G, Barrios CH, et al. LACOG, internal data.

Registry of Metastatic NSCLC in Latin America
LATINO Lung (LACOG 0116)

Only for Those Who Have Evaluation of Mutations Performed (N = 333)

Which sample was used for this analysis?

Primary tumor	295 (88.6%)
Metastatic site	19 (5.7%)
Liquid biopsy	13 (3.9%)
Missing	6 (1.8%)

Was *EGFR* status tested?

Yes	295 (88.6%)
No	22 (6.6%)
Unknown	16 (4.8%)

What was the result of *EGFR* test?

Mutated	116 (39.3%)

Werutsky G, Barrios CH, et al. LACOG, internal data.

Registry of Metastatic NSCLC in Latin America
LATINO Lung (LACOG 0116)

Was *ROS1* status tested?	
Yes	142 (42.6%)
No	165 (49.6%)
Unknown	26 (7.8%)

Was *ALK* status tested?	
Yes	231 (69.4%)
No	85 (25.5%)
Unknown	17 (5.1%)

What was the result of *ROS1* test?	
Mutated	0 (0.0%)
Wild type	133 (93.7%)
Unknown	9 (6.3%)

What was the result of *ALK* test?	
Mutated	28 (12.1%)
Wild type	193 (83.6%)
Unknown	10 (4.3%)

Werutsky G, Barrios CH, et al. LACOG, internal data.

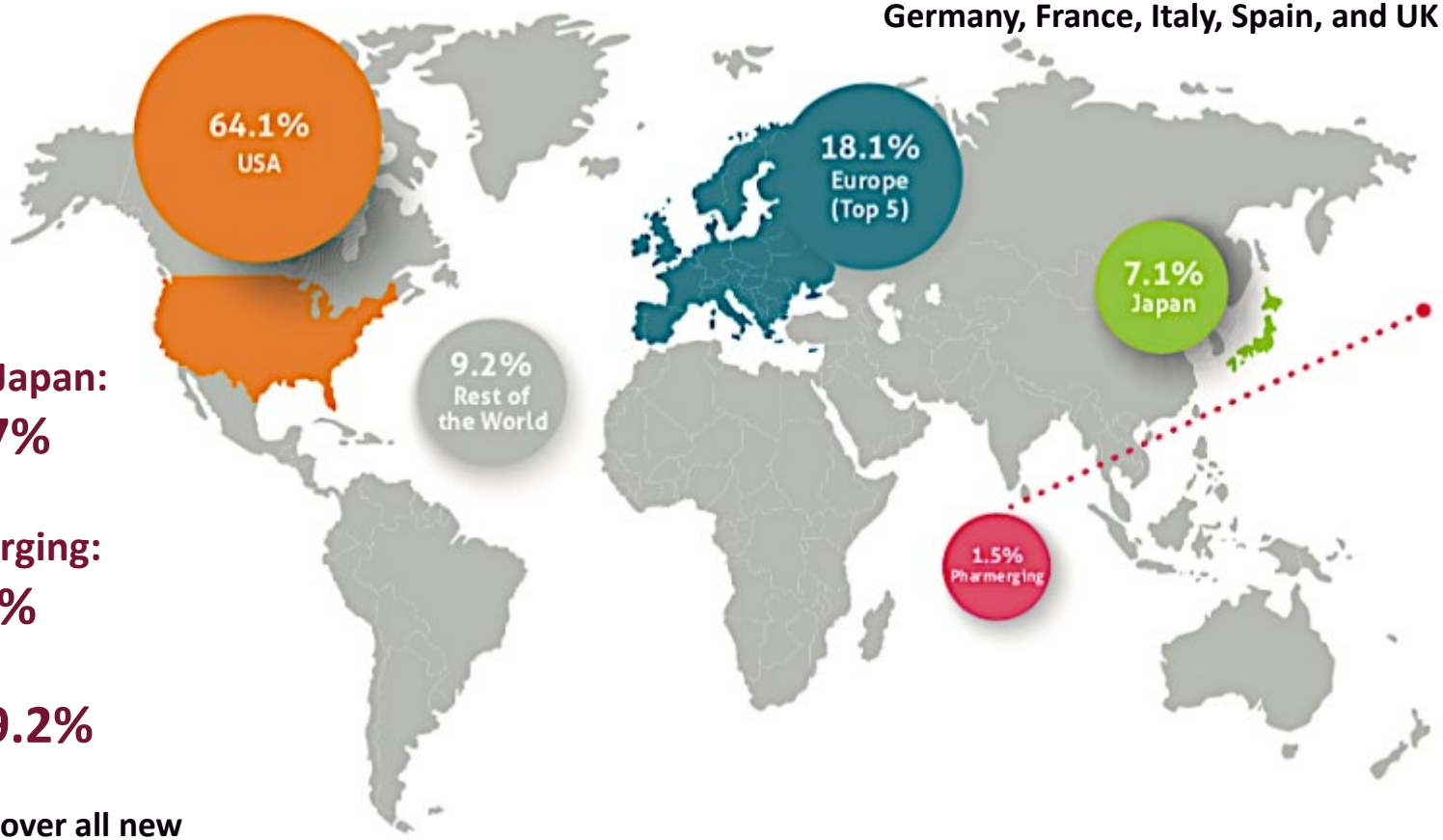
Registry of Metastatic NSCLC in Latin America
LATINO Lung (LACOG 0116)

Was PDL1 status tested?	
Yes	367 (75.5%)
No	97 (20.0%)
Unknown	22 (4.5%)
PD-L1 status	
<1%	152 (41.4%)
1%–49%	116 (31.6%)
≥50%	74 (20.2%)
Inconclusive	1 (0.3%)
Unknown	24 (6.5%)

Werutsky G, Barrios CH, et al. LACOG, internal data.

Distribution of New Medicines Sales in the Last 5 Years

Europe Top 5:
Germany, France, Italy, Spain, and UK



US, EU, Japan:
89.7%

Pharmerging:
1.5%

ROW: 9.2%

Pharmerging:
21 countries with high-growth Pharma Markets
Algeria, Argentina, Bangladesh, Brazil, Colombia, Chile, China, Egypt, India, Indonesia, Kazakhstan, Mexico, Nigeria, Pakistan, Philippines, Poland, Russia, Saudi Arabia, South Africa, Turkey, and Vietnam

New medicines cover all new active ingredients marketed for the first time during the period 2012–2017

Source: IMS Health, MIDAS, May 2018; www.efpia.eu, accessed January 2019.

Real-world evaluation of molecular testing and treatment patterns for EGFR mutations in non-small cell lung cancer in Latin America

	Argentina (n=195)	Colombia (n=96)	Chile (n=64)	Uruguay (n=76)	Total (n=431)
Testing rate, %	**78.8**	**64.6**	**75.0**	**27.6**	**65.7**
PDL-1 testing, %	91.2	87.5	75.0	98.7	89.1
Turnaround time in days, mean	9.9	20.4	10.0	13.5	12.4
Blood (plasma/serum)	4 (2.0)	6 (6.2)	0 (0.0)	0 (0.0)	10 (2.3)
Cytology	0 (0.0)	2 (2.1)	0 (0.0)	0 (0.0)	2 (0.5)
Formalin fixed paraffin embedded tissue	134 (68.7)	44 (45.8)	41 (64.1)	21 (27.6)	240 (55.7)
Fresh frozen tissue	4 (2.0)	0 (0.0)	1 (1.6)	0 (0.0)	5 (1.2)
Unknown/no treatment, n (%)	52 (26.8)	44 (45.8)	22 (34.4)	55 (72.4)	173 (40.1)

Molecular testing frequency for treatment-naïve patients.

Martin C, et al. Mol Clin Oncol. 2022 Jan; 16(1): 6.
Published online 2021 Nov 12. doi: 10.3892/mco.2021.2439

Interactive Question

In your opinion, what is the percentage of first line NSCLC patients with an indication for immunotherapy receive it in Latin America.

1. Less than 5%
2. From 10-20%
3. From 20-30%
4. Approximately 50%
5. More than 80%

Real-world evaluation of molecular testing and treatment patterns for EGFR mutations in non-small cell lung cancer in Latin America

	Argentina (n=195)	Colombia (n=96)	Chile (n=64)	Uruguay (n=76)	Total (n=431)
Chemotherapy					
First line	107 (54.9)	41 (42.7)	41 (64.1)	31 (40.8)	**219 (51.0)**
Second line	14 (7.2)	6 (6.3)	6 (9.4)	3 (3.9)	24 (5.6)
Immunotherapy, n (%)					
First line	12 (6.2)	1 (1.0)	3 (4.7)	0 (0.00)	**16 (3.7)**
Second line	16 (8.2)	3 (3.1)	7 (10.9)	5 (6.6)	29 (6.7)
Targeted therapy, ALK/ROS1 inhibitors					
First line	6 (3.1)	2 (2.1)	2 (3.4)	0 (0.0)	**10 (2.3)**
Second line	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

Martin C, et al. Mol Clin Oncol. 2022 Jan; 16(1): 6
Published online 2021 Nov 12. doi: 10.3892/mco.2021.2439

Take Home

- While still an imperfect exercise, over the last 20 years, clinical research and drug development in lung cancer have impacted patient outcomes in a significant way
- A substantial portion of current clinical research is pharma sponsored; therefore, a number of specific regional problems and important patient outcome questions remain unexplored

Take Home

- Significant discrepancies in access to diagnostic tests, new drugs and clinical trials are identified globally and remain as significant and challenging problems in Latin America

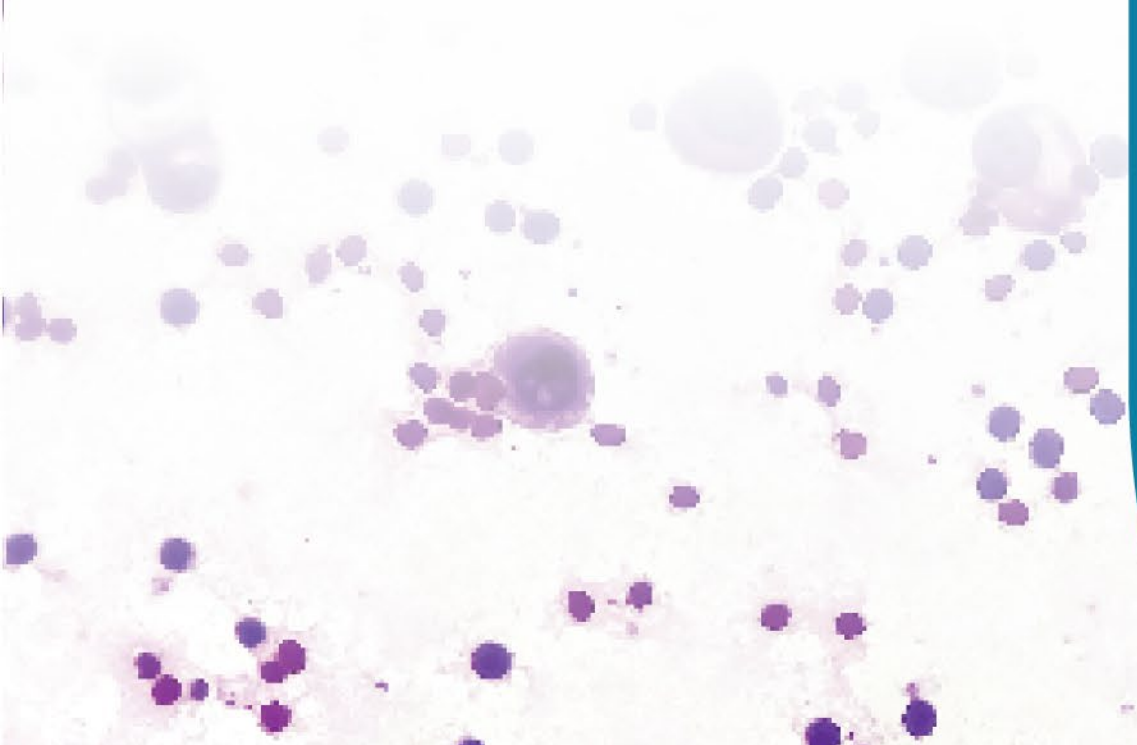
- Collaborative strategies involving government, society, pharma, and academic investigators are mandatory to continue this scientific effort and further improve treatment results

October 2022

Current Treatment Options for Metastatic NSCLC in Latin America

Carlos H. Barrios, M.D.
Latin American Cooperative Oncology Group (LACOG)
Grupo Oncoclínicas
Porto Alegre, Brazil

Global Lung Cancer Academy

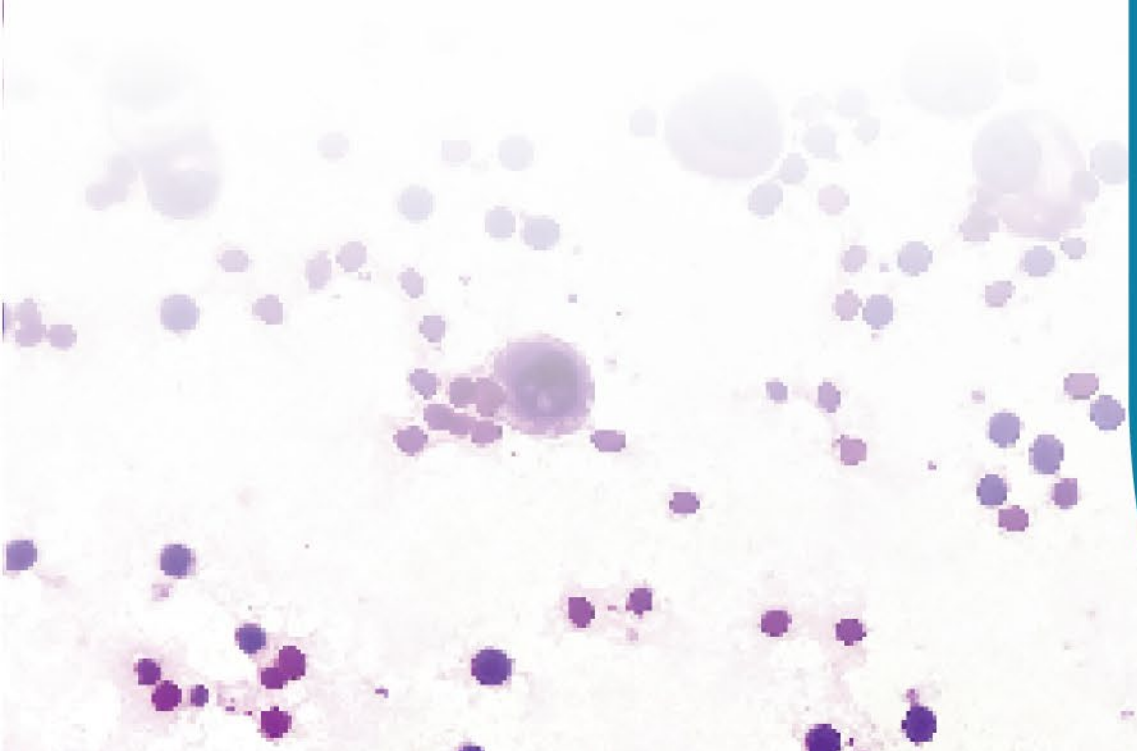


Tumor Board Discussion

Moderator: Carlos Barrios, MD

Case presenter: Caio Abner Leite, MD, and Alvaro Guimaraes Paula, MD

Global Lung Cancer Academy



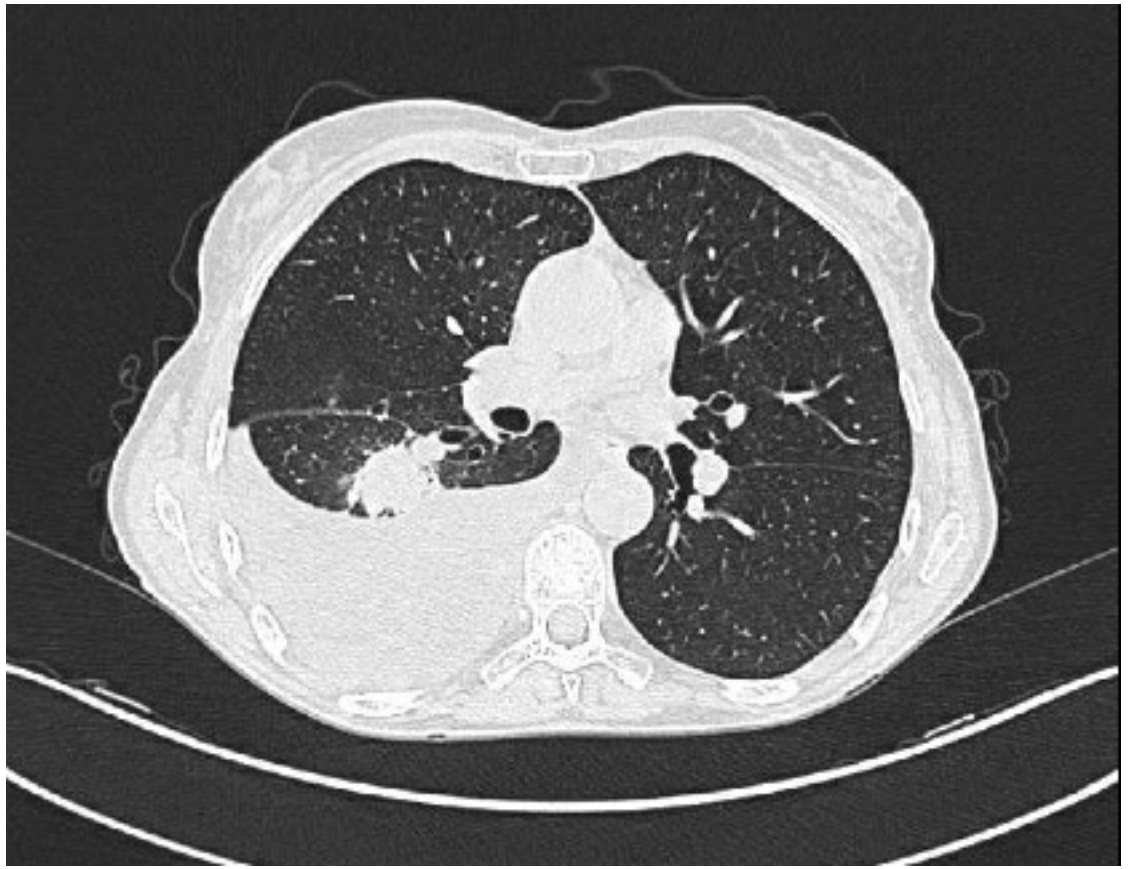
Patient Case 1

Dr Caio Abner Leite

Medical Oncology Fellowship at Beneficência Portuguesa de São Paulo

Case Background

- 72-year-old woman
- No smoking history, no comorbidities
- June 2019: asthenia and dyspnea
- 16 June 2019: computed tomography showing a >3-cm mass in right lower lobe, right pleural effusion, enlargement of thoracic lymph nodes



Case Background

- 19 June 2019: biopsy of 3-cm mass evidencing lung adenocarcinoma
- 21 June 2019: relief pleural drainage with malignant positive cells
- 24 June 2019: PET-CT evidencing 3-cm right lower lobe and right pleural thickening. No brain mets by MR
- 29 July 2019: next-generation sequencing showing *EGFR* exon 19 deletion, *RB1* exon 18 inversion, and *TP53* mutant

Challenge in LATAM

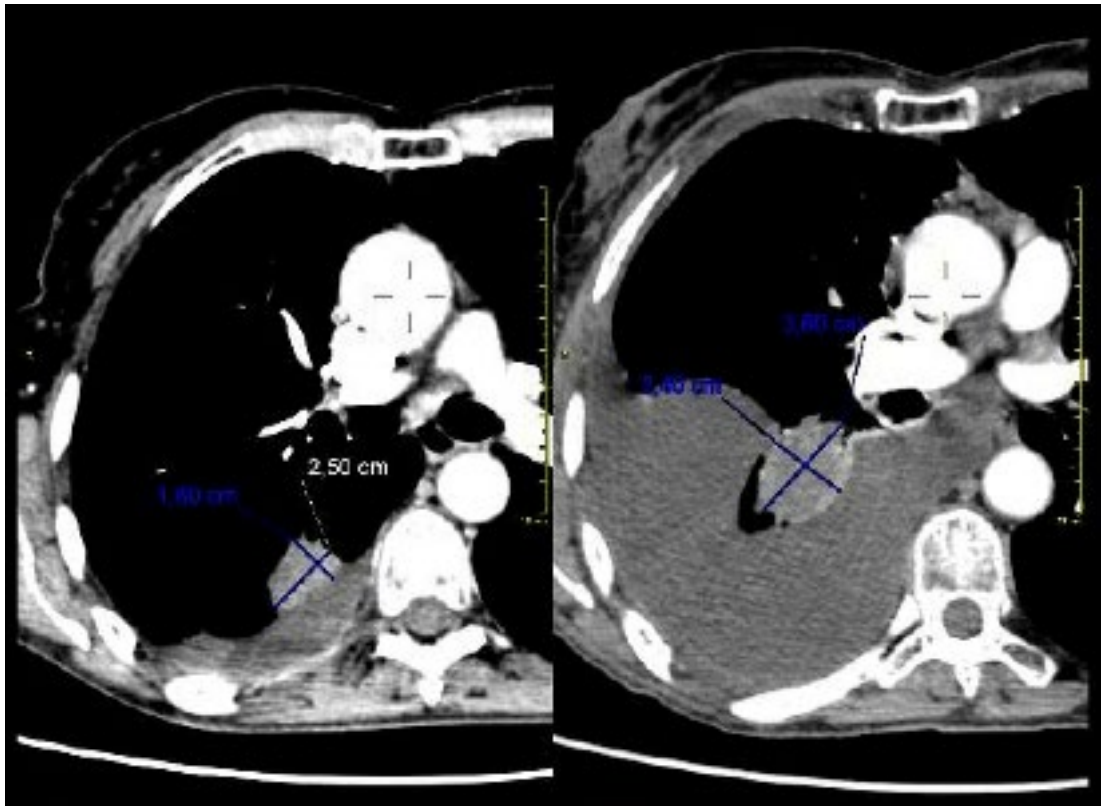
> Access to PET scan for staging NSCLC

> Access to NGS

Treatment

> 27 August 2019: start of osimertinb

Oct 2019 Jun 2019

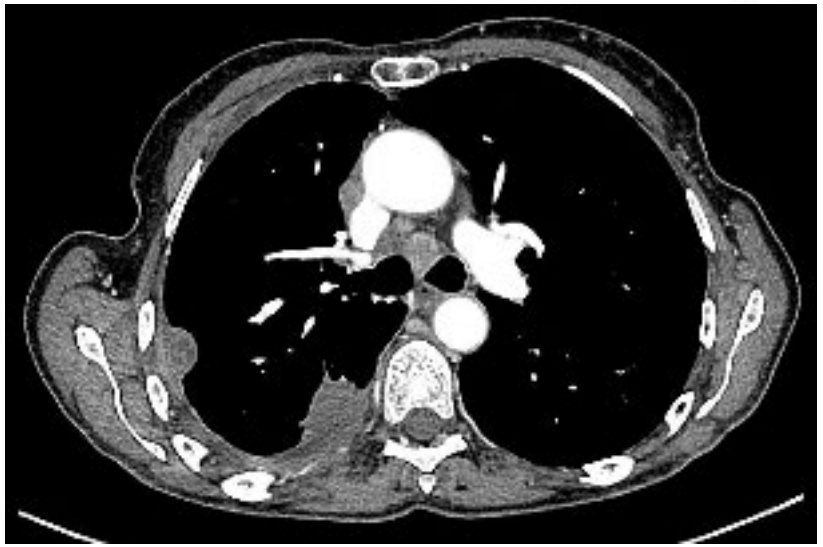


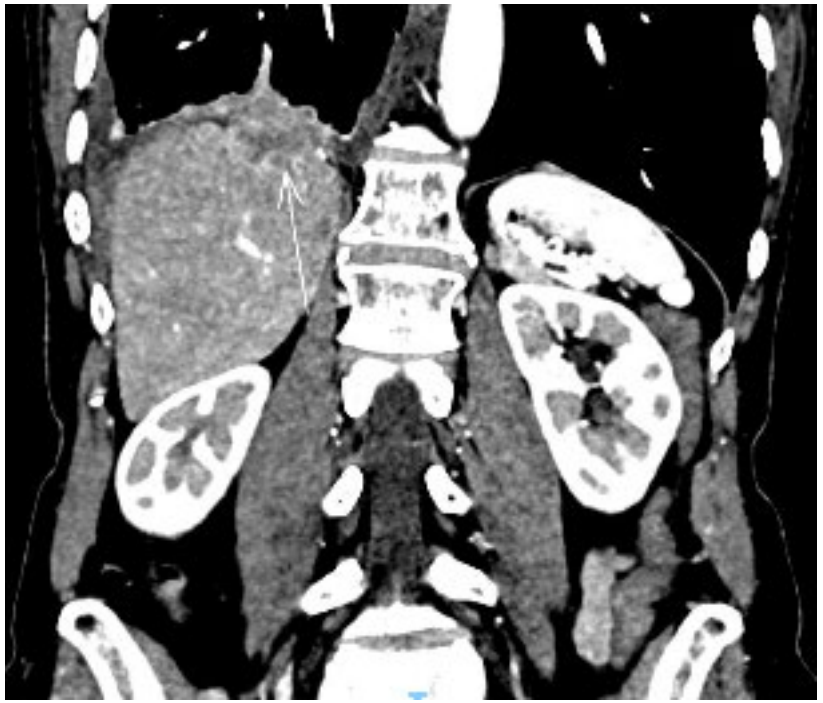
Challenge in LATAM

- Treatment with osimertinib
  - Public services have access only to first-generation TKI
  - Difficulties to evaluate response

Disease Progression

- September 2020: disease progression with right diffuse pleural nodular thickening
- September 2020: right pleural biopsy, small cell lung cancer



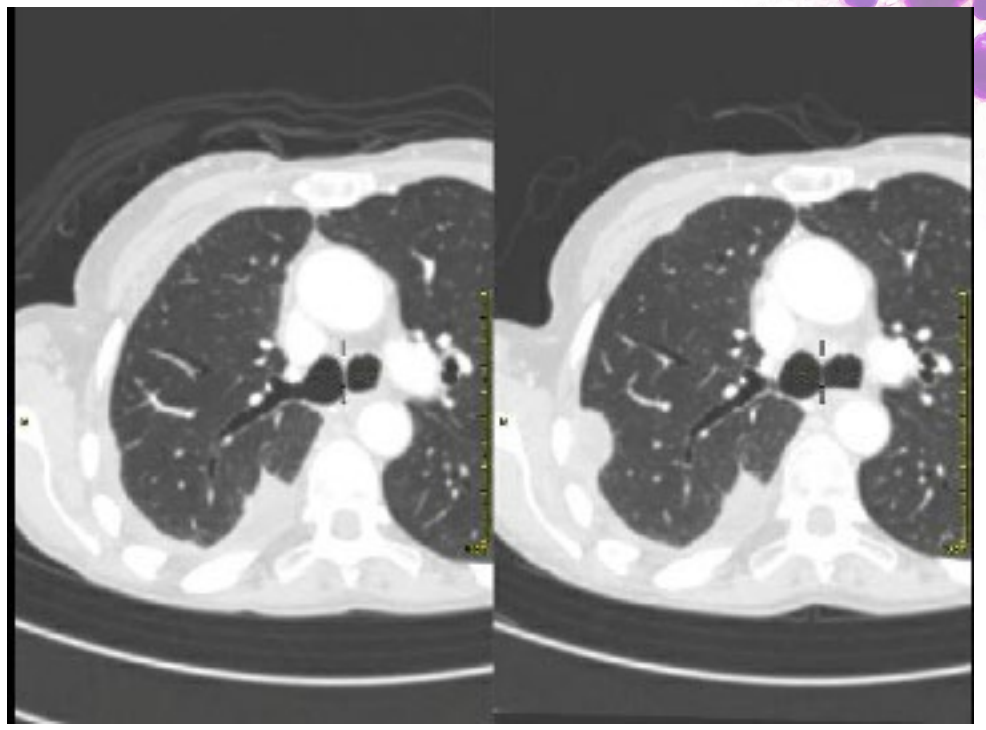


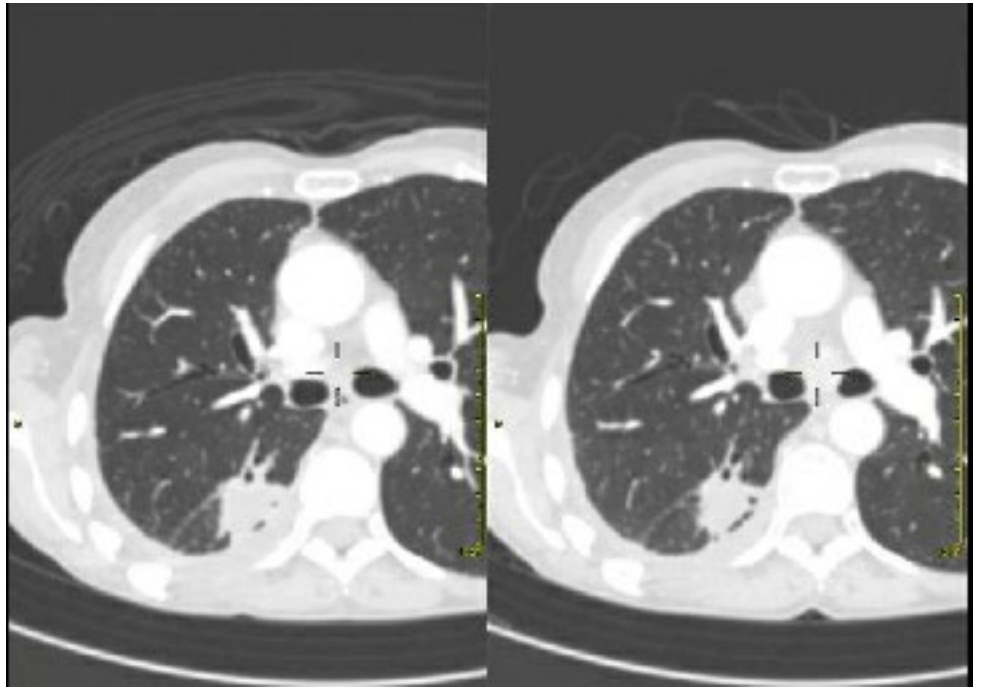
Challenge in LATAM

- Genetic evaluation to study resistance mechanisms
  - NGS
  - Liquid biopsy

SCLC Treatment

- September 2020: carboplatin and etoposide
- November 2020: after 3 cycles, reduction of pleural nodules and stability of primary lesion. This response was maintained after 6 cycles





Challenge in LATAM

- After best response in SCLC, which treatment should be maintained?
  - Osimertinib?

Patient Outcome

- January 2021: rib antalgic, palliative radiotherapy
- January 2021: patient died of femur fracture complications

Global Lung Cancer Academy

Patient Case 2

Dr Álvaro Guimarães Paula

Clinical Oncology Fellow - A Beneficência Portuguesa de São Paulo

Warning 

Trastuzumab deruxtecan does not yet have approval for *HER2*-mutant metastatic lung cancer in Brazil

Woman, 56 Years Old, ECOG 0, Never Smoker

2017: occasional finding in a chest CT: upper lobe nodule in the left lung

---

S/P nodule biopsy: lung adenocarcinoma, TTF1 positive, napsin-A positive

S/P lobectomy + mediastinal lymphadenectomy

S/P adjuvant chemo for 4 cycles (cisplatin + pemetrexed)

S/P mediastinal adjuvant radiotherapy

March 2018: started follow-up

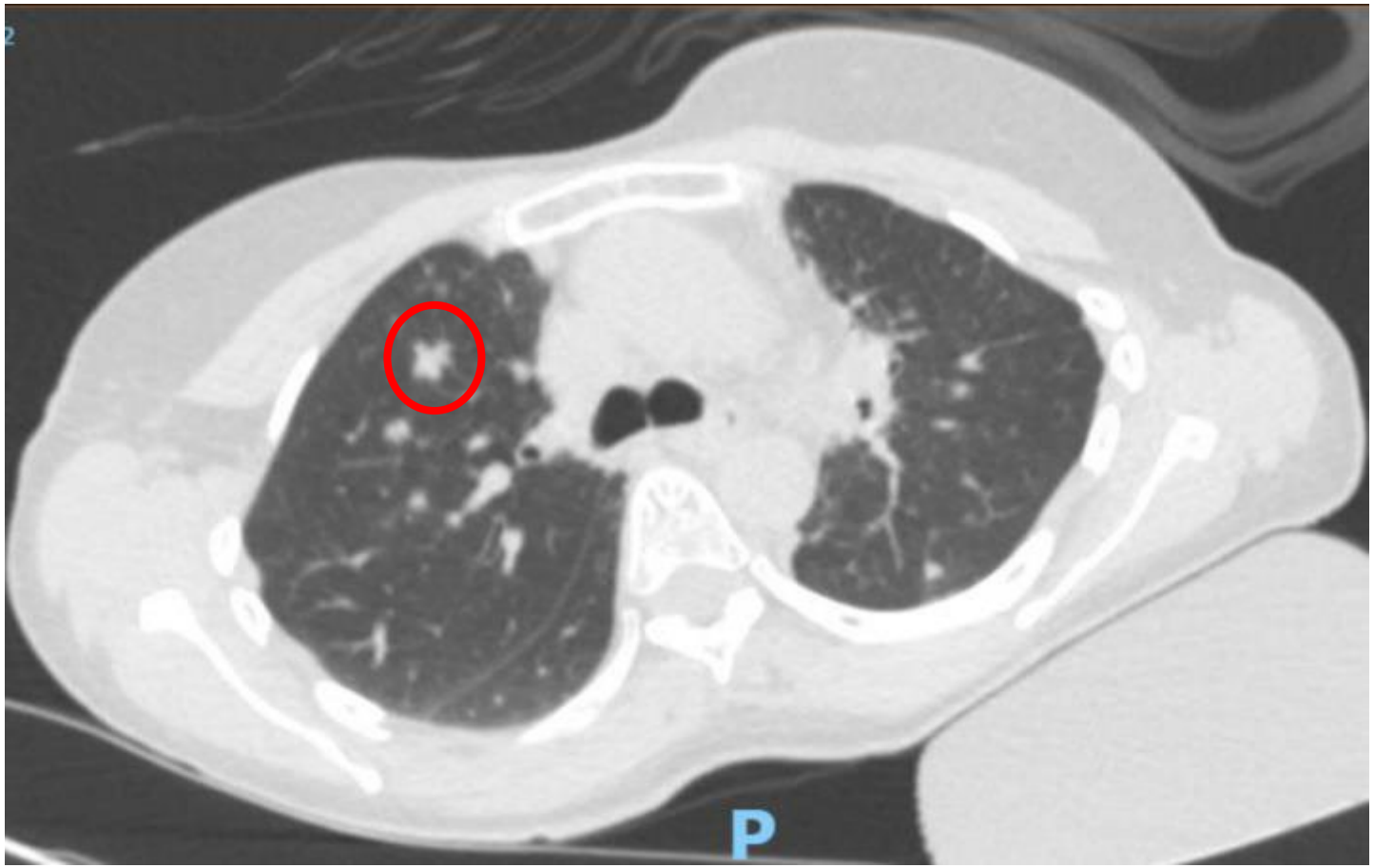
Woman, 56 Years Old, ECOG 0, Never Smoker

2021: multiple new nodules suspicious for malignancy

S/P upper R lobe biopsy: adenocarcinoma

PD-L1 (22c3): 60%

NGS: *ERBB2* A775_G776insYVMA mutation



Woman, 56 Years Old, ECOG 0, Never Smoker

What would be your first-line approach for this patient?

A. **Chemotherapy + immunotherapy**

B. **Immunotherapy**

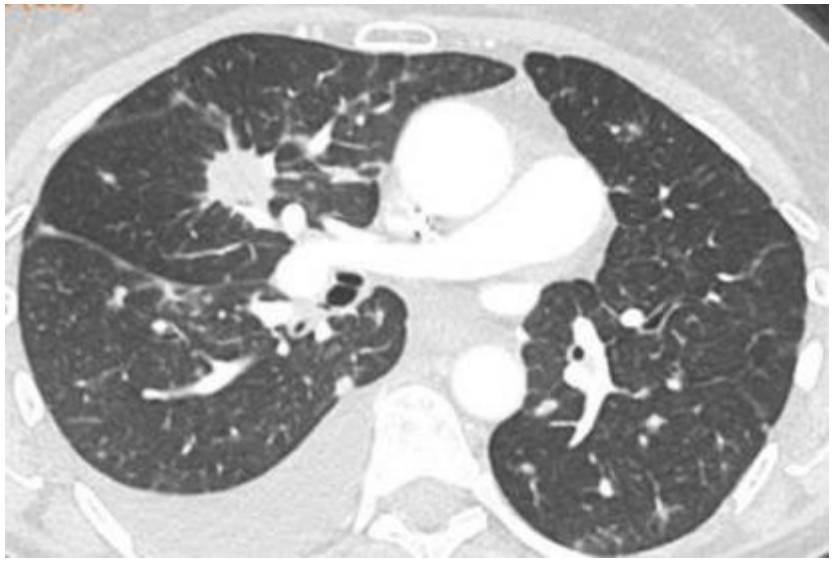
C. **T-DM1**

D. **Trastuzumab deruxtecan**

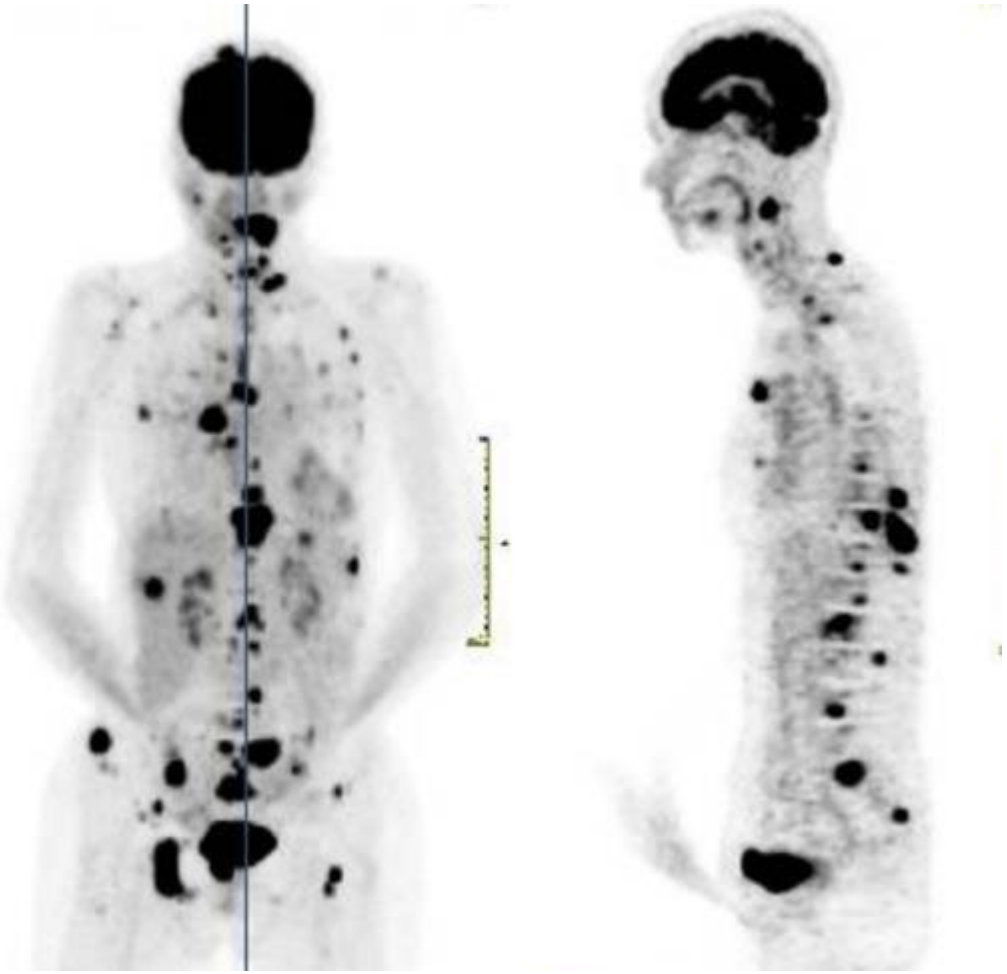
Woman, 56 Years Old, ECOG 0, Never Smoker

June 2021–April 2022: pembrolizumab 200 mg/every 3 weeks, with disease control for 10 months

May 2022: disease progression (lungs, lymph nodes, and bones)



May 2022



May 2022

Woman, 56 Years Old, ECOG 0, Never Smoker

After receiving IO, when is the best time for a patient to receive trastuzumab deruxtecan treatment?

A. **3 weeks**

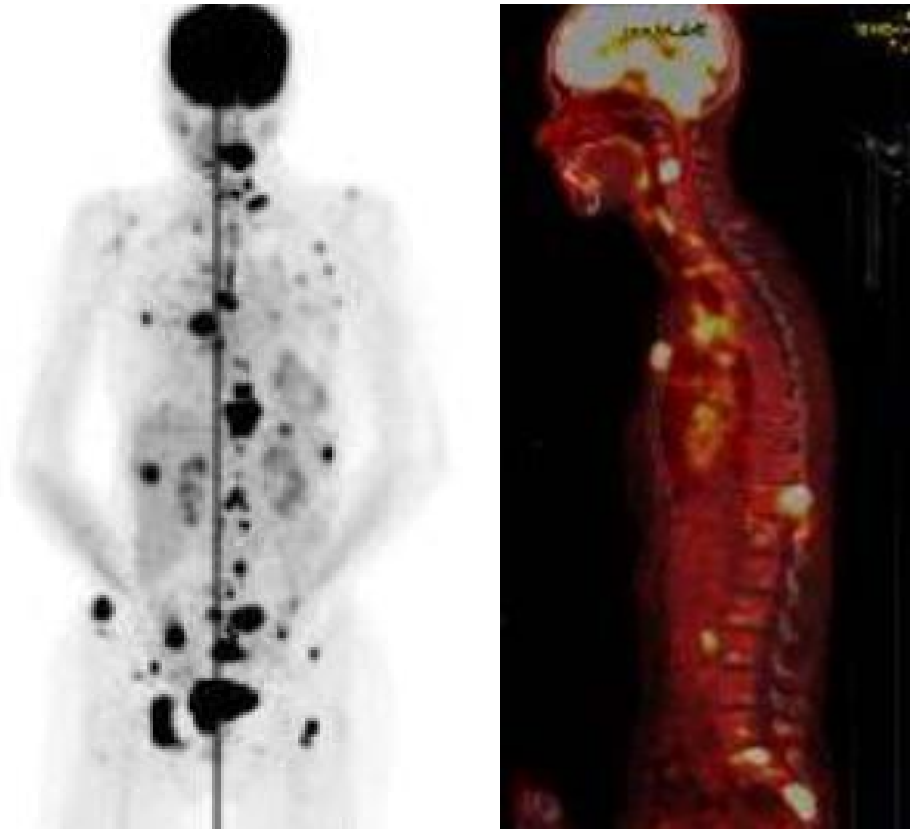
B. **6 weeks**

C. **12 weeks**

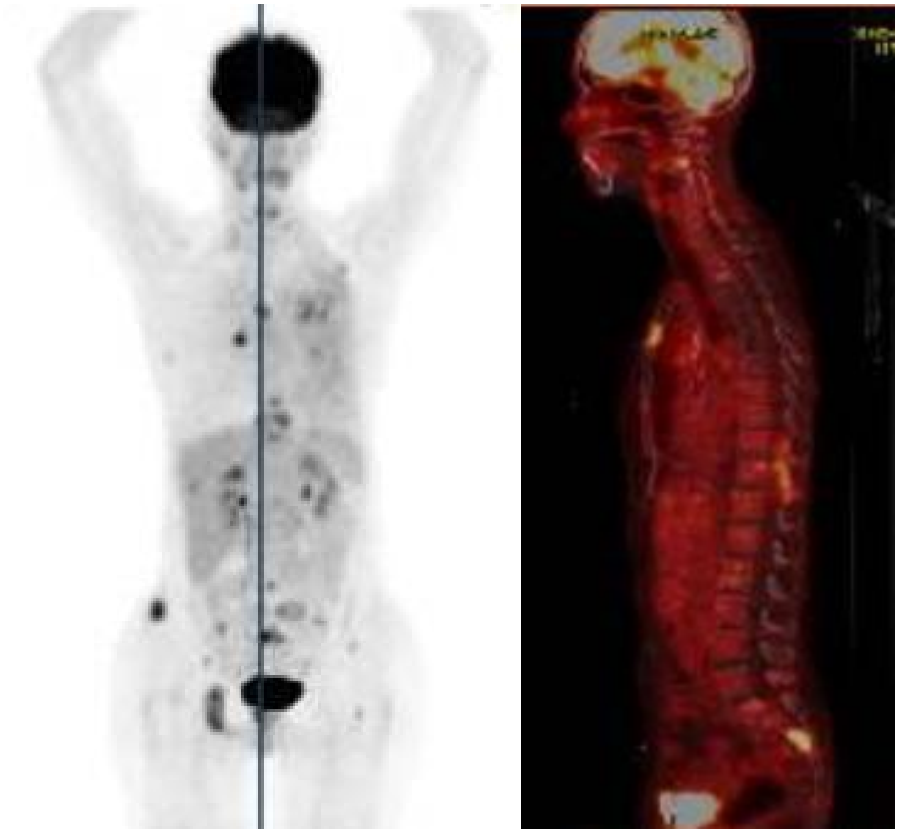
D. **6 months**

Woman, 56 Years Old, ECOG 0, Never Smoker

May 2022: patient was started on trastuzumab deruxtecan, with an excellent response



May 2022

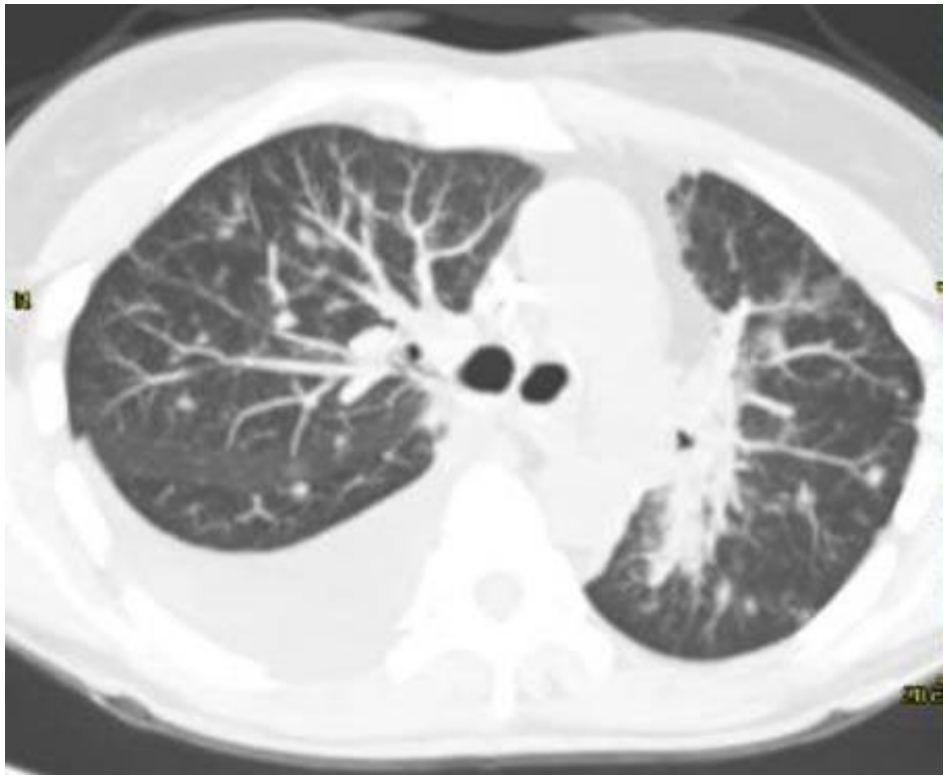


July 2022

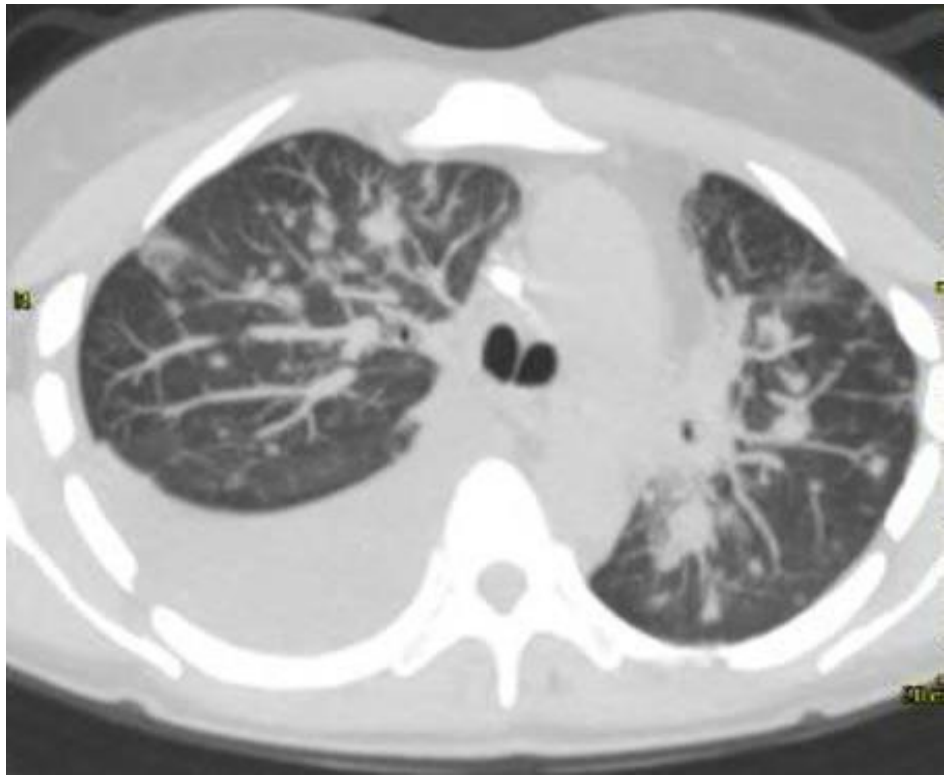
Woman, 56 Years Old, ECOG 0, Never Smoker

August 2022: patient developed cough and dyspnea. The chest CT showed pneumonitis G2

July 2022



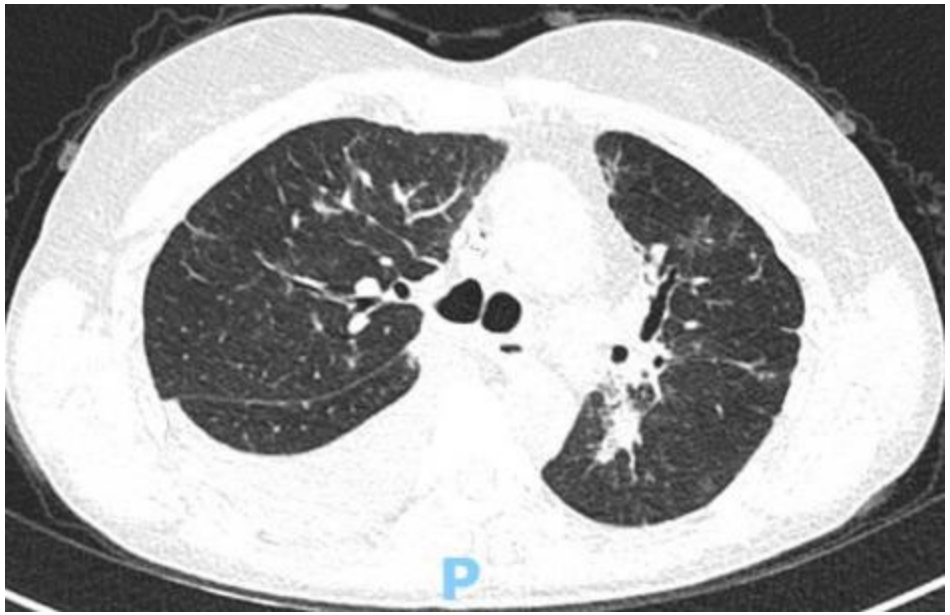
August 2022



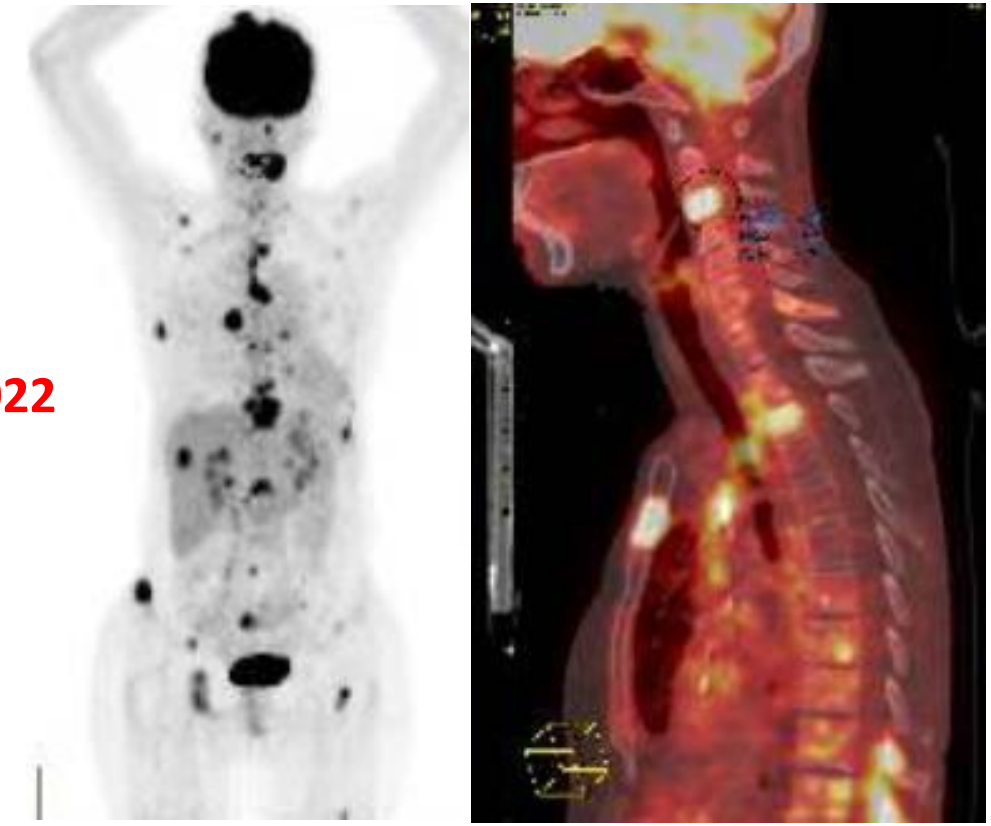
Woman, 56 Years Old, ECOG 0, Never Smoker

September 2022: patient has recovered from pneumonitis after steroids treatment but presented progressive disease

September 2022



September 2022



Woman, 56 Years Old, ECOG 0, Never Smoker

Is there any role for trastuzumab deruxtecan re-exposition?

A. **Yes**

B. **No**

Global Lung Cancer Academy

Tumor Board Discussion

Moderator: Carlos Barrios, MD

All faculty

Global Lung Cancer Academy

BREAK

Coming up

– GLCA Europe (7 and 14 November 2022)

Global Lung Cancer Academy

Monitoring and Managing Immunotherapy-Related AEs

Edgardo S. Santos, MD

Monitoring & Managing Immunotherapy-related Adverse Events (ir-AEs)

Edgardo S. Santos, M.D., FACP
Genesis Care US
Medical Director of Research Services/GC Hematology-Oncology
Thoracic Oncology
Clinical Associate Professor
Charles E. Schmidt School of Medicine/Florida Atlantic University
Treasurer, FLASCO & President, FLASCO Foundation

October 24, 2022

GenesisCare

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Oncology Latin American Association

Global Lung Cancer Academy

SAVE THE DATE

Sharing Best Practices to Optimize Patient Care in Lung Cancer

October 21 and 24, 2022

VIRTUAL MEETING

Friday, October 21, 2022
4.00 PM – 8.00 PM EDT

Monday, October 24, 2022
4.00 PM – 7.00 PM EDT

CHAIR
Corey J. Langer, MD, FACP
University of Pennsylvania Perelman School of Medicine, USA

CO-CHAIR
Carlos H. Barrios, MD
Oncology Research Center Hospital São Lucas, PUCRS, Brazil

Outline

- Diagnosing an ir-AEs
- Timing of ir-AEs
- Monitoring for ir-AEs
- Therapy of ir-AEs
- ir-AE risk in Special Populations
- ICI rechallenge after ir-AE
- Prognostic implications of ir-AE

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Sharing Best Practices to Optimize Patient Care

21 & 24 October – LATAM and Canada

APTITUDE HEALTH

Diagnosing an ir-AES

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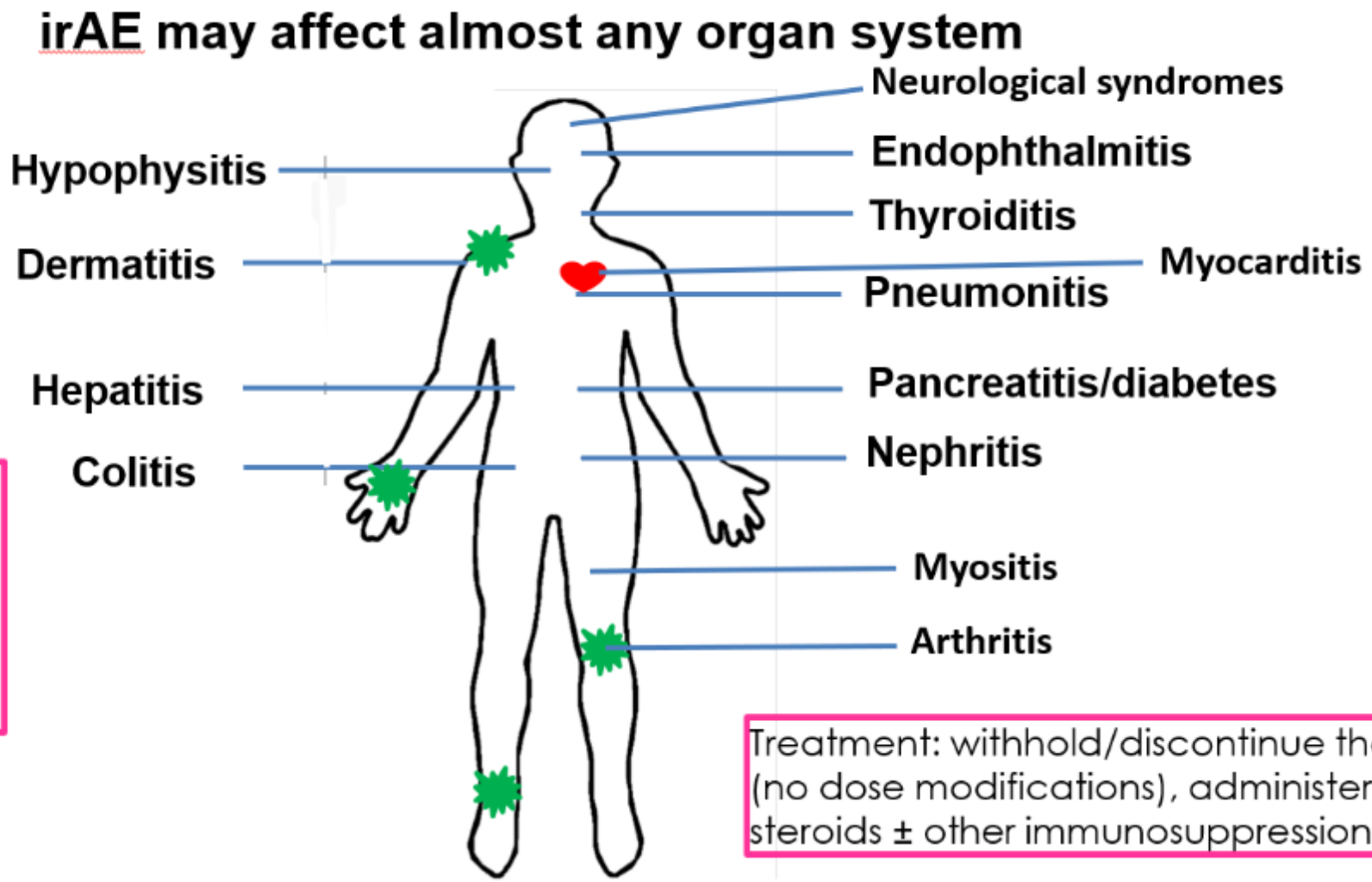
Checkpoint Inhibitors (CPI) may induce *Unpredictable*, *Potentially Severe*, and possibly *Permanent ir-AEs* ....



Pre-existing active auto-immune diseases requiring immune suppression generally considered contraindication to CPI (or at least ineligible for trials)

Treatment: withhold/discontinue therapy (no dose modifications), administer steroids ± other immunosuppression

Courtesy Edgardo S. Santos, MD., FACP

Clinical case.

Question:

72-year-old man with metastatic NSCLC and COPD coming in to restart maintenance atezolizumab and bevacizumab (Impower 150) after completing course of steroids for pneumonitis. He complains of overwhelming fatigue and general malaise. His vitals are: BP-74/56, P-98, RR-18, T-99.2F.

Based on his symptoms, what is your first course of action?

A. Resume prednisone 40 mg
B. Give Rx for medrol dose pack
C. Start IV Solumedrol in clinic

Autoimmune Disease Occurs in a Substantial Minority of Patients With Cancer, and May Be Challenging to Diagnose

Table 1. Characteristics of Lung Cancer Patients With Autoimmune Disease

Patient Characteristics	All Patients, No.	With Autoimmune Disease, No. (%)	*P* Value[a]
Total	210 509	28 453 (13.5)	
Age			
<75	94 804	11 664 (12.3)	<.001
≥75 to <85	92 045	13 529 (14.7)	<.001
≥85	23 660	3260 (13.8)	<.001
Sex			
Female	97 494	16 374 (16.8)	<.001
Male	113 015	12 079 (10.7)	<.001
Stage (AJCC)			
I	36 152	6331 (17.5)	<.001
II	6758	1028 (15.2)	<.001
III	51 542	6692 (13)	<.001
IV	77 833	9302 (12)	<.001
Other	38 224	5100 (13.3)	<.001

Table 2. Prevalence of the 10 Most Common Individual Autoimmune Diseases Among 210 509 Patients With Lung Cancer

Autoimmune Disease	Prevalence, %
Rheumatoid arthritis	5.9
Psoriasis	2.8
Polymyalgia rheumatic	1.8
Addison disease	1.0
Systemic lupus erythematosus	0.9
Ulcerative colitis	0.8
Giant cell arteritis	0.8
Sicca syndrome	0.6
Regional enteritis	0.5
Ménière disease, unspecified	0.5
Total (any autoimmune disease)	13.5

Estimated prevalence:

- **14%** (claims "rule-out" method: ≥2 outpt claims ≥30 days apart or ≥1 inpt claim)
- **25%** (more liberal method: ≥1 claim of any type)

Khan SA et al. JAMA Oncol. 2016;2(11):1507-1508.

If Autoimmune Disease is Difficult to Diagnose, What About ir-AEs?

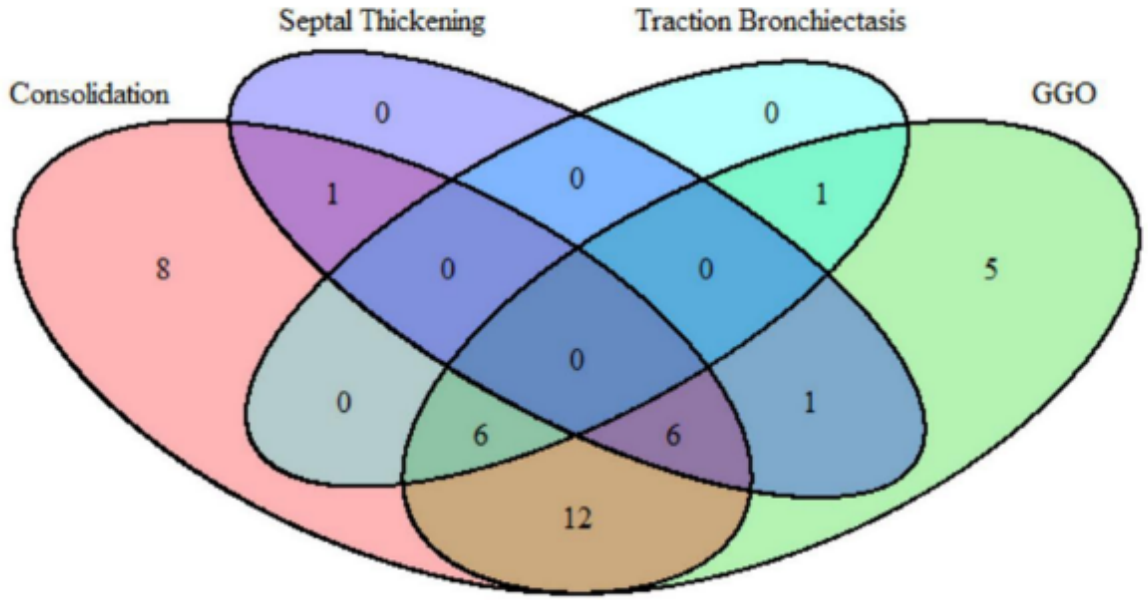
CheckMate 057: 4% pneumonitis

Select adverse event category	Nivolumab n = 287	
	Any Grade n (%)	Grade 3-4 n (%)
Pulmonary		
Pneumonitis	8 (3)	3 (1)
Interstitial lung disease	2 (1)	1 (<1)

Johns Hopkins: 19% pneumonitis

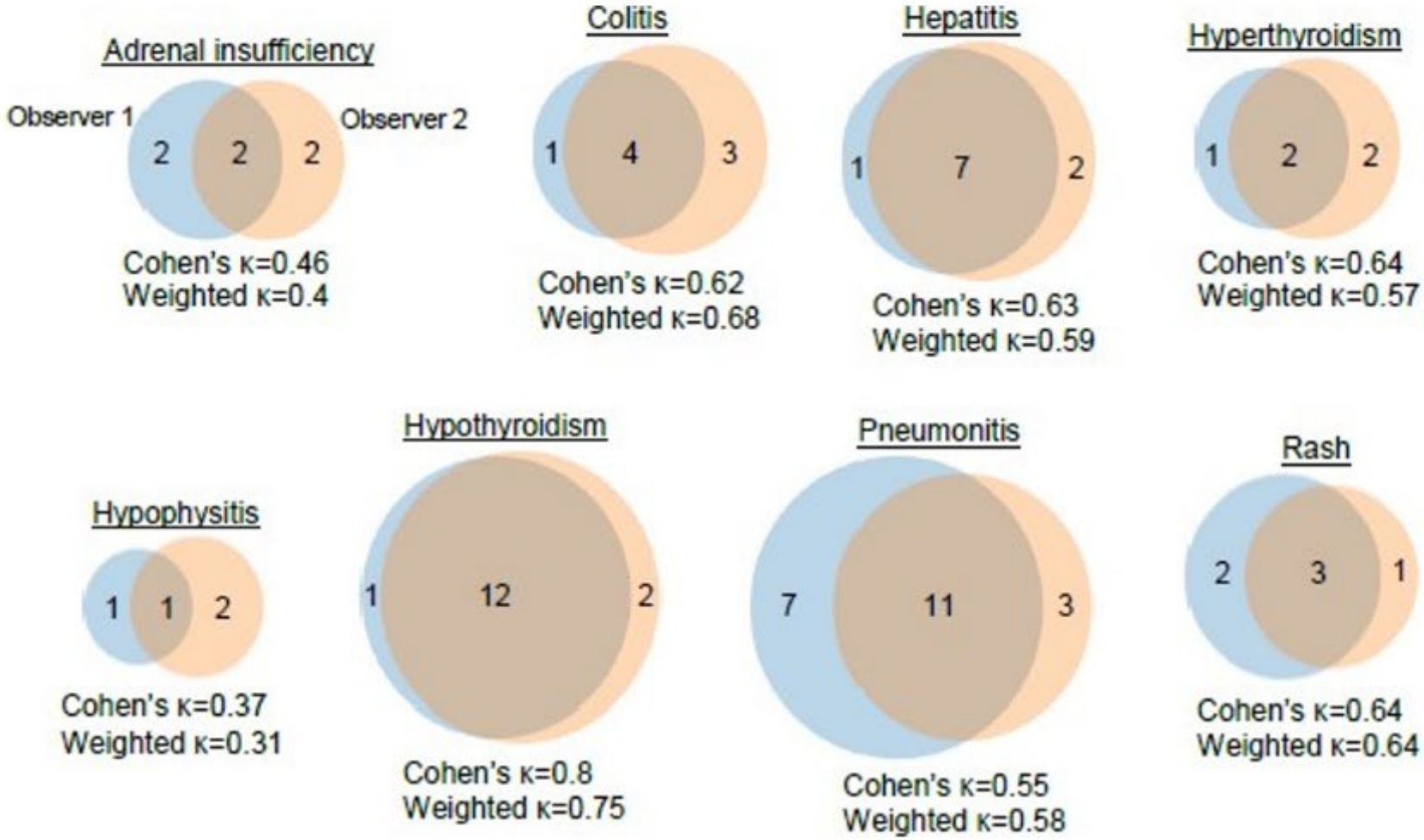
Table 1. Baseline Characteristics

Characteristic	CIP (n = 39)	No CIP (n = 166)	All Patients (N = 205)



Borghaei H et al. N Engl J Med. 2015; 373(17):1627-39; Suresh K et al. J Thorac Oncol. 2018;13(12):1930-9.

Inter-Observer Agreement is Poor (κ<0.7) for All ir-AE Except Hypothyroidism

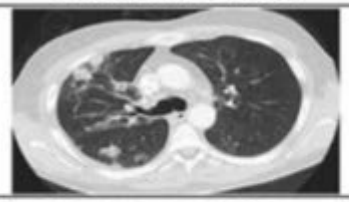
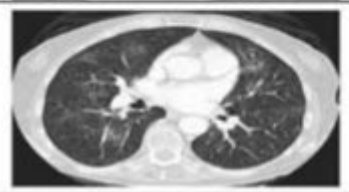
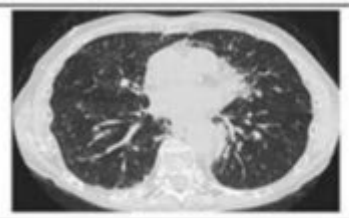
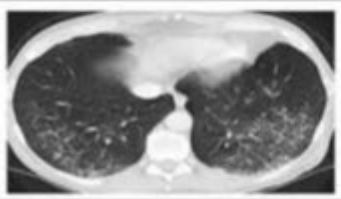
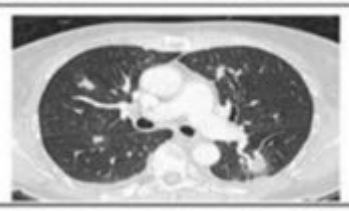


Agreement on immune-related AE grading similarly limited (weighted κ 0.31-0.75)

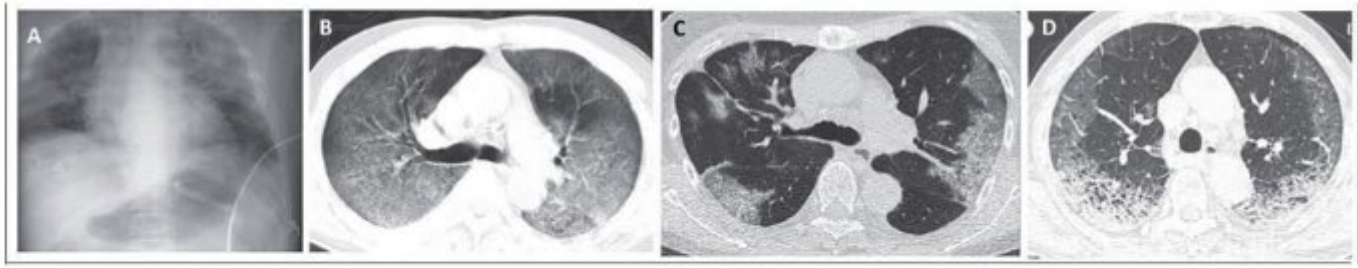
Hsiehchen D et al. JAMA Netw Open. 2019;2(9):e1911519.

Pulmonary Toxicity May Be Particularly Challenging to Diagnose, Even More So During a Viral Pandemic→

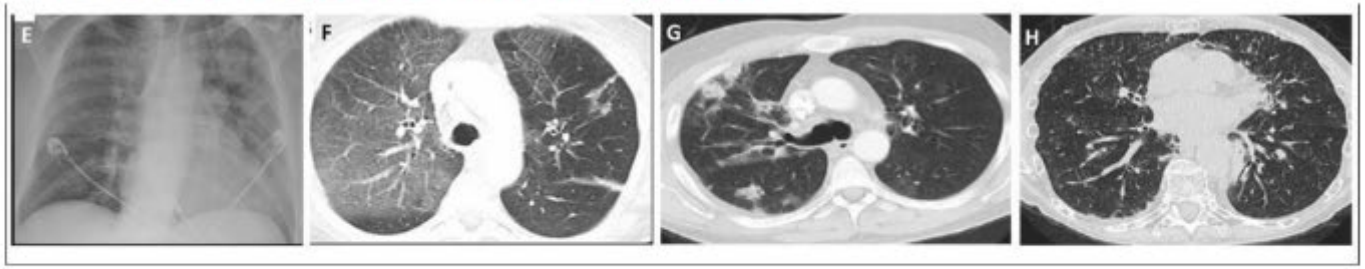
Multiple Radiographic Subtypes

Radiologic Subtypes	Representative Image	Description
Cryptogenic organizing pneumonia-like (n = 5, 19%)		Discrete patchy or confluent consolidation with or without air bronchograms Predominantly peripheral or subpleural distribution
Ground glass opacities (n = 10, 37%)		Discrete focal areas of increased attenuation Preserved bronchovascular markings
Interstitial (n = 6, 22%)		Increased interstitial markings, interlobular septal thickening Peribronchovascular infiltration, subpleural reticulation Honeycomb pattern in severe patient cases
Hypersensitivity (n = 2, 7%)		Centrilobular nodules Bronchiolitis-like appearance Tree-in-bud micronodularity
Pneumonitis not otherwise specified (n = 4, 15%)		Mixture of nodular and other subtypes Not clearly fitting into other subtype classifications

COVID-19



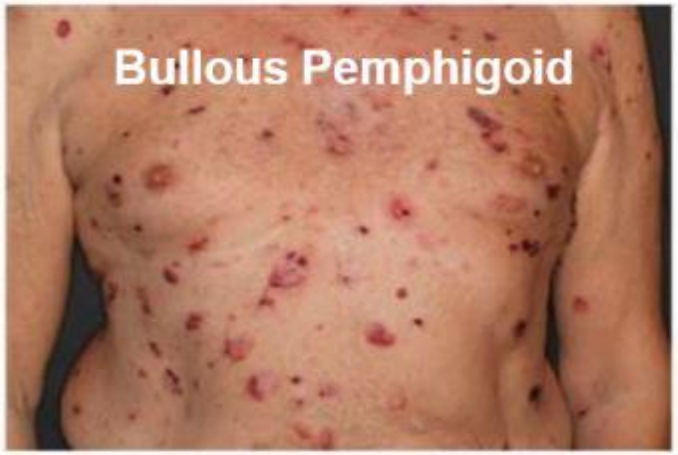
Immune-Related Pneumonitis

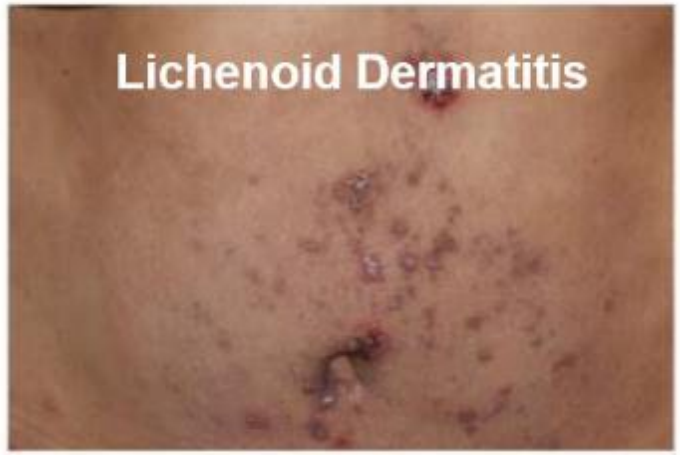


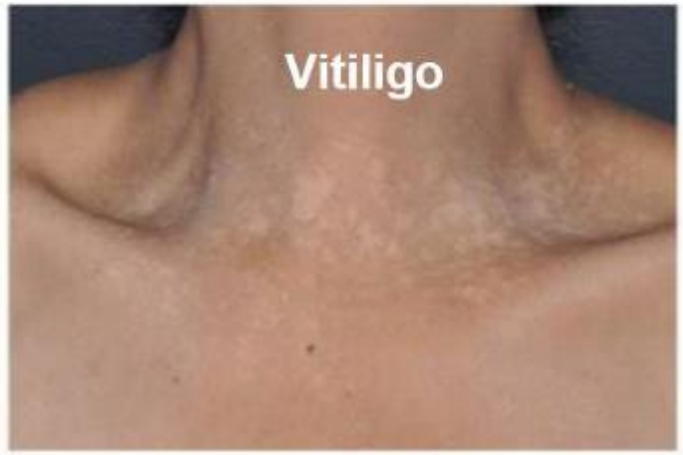
Chen Z et al. Eur J Radiol. 2020;126:108972.

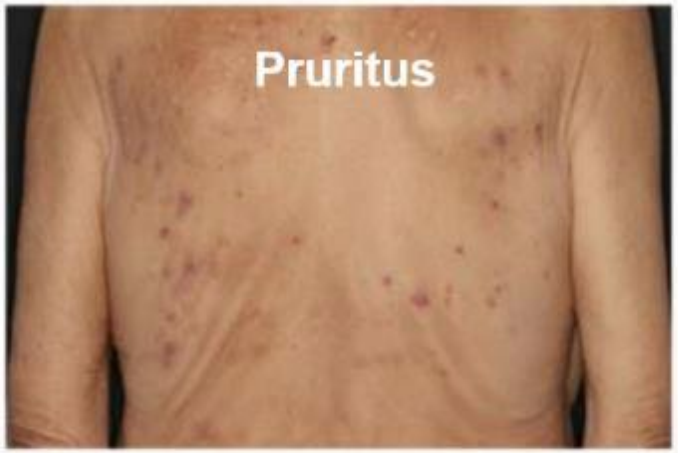
Naidoo J et al. J Immunother Cancer. 2020;8(1):e000984.

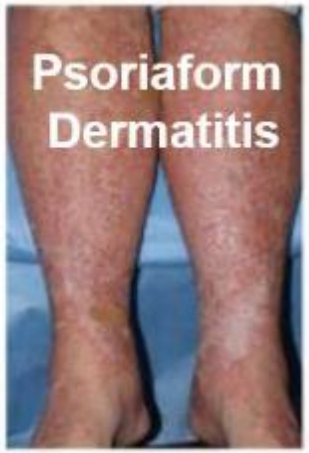
Dermatologic Toxicity is Also Highly Heterogeneous

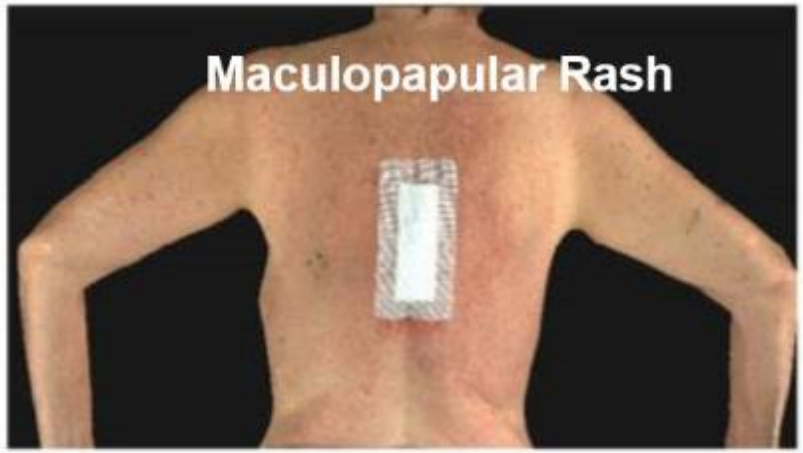




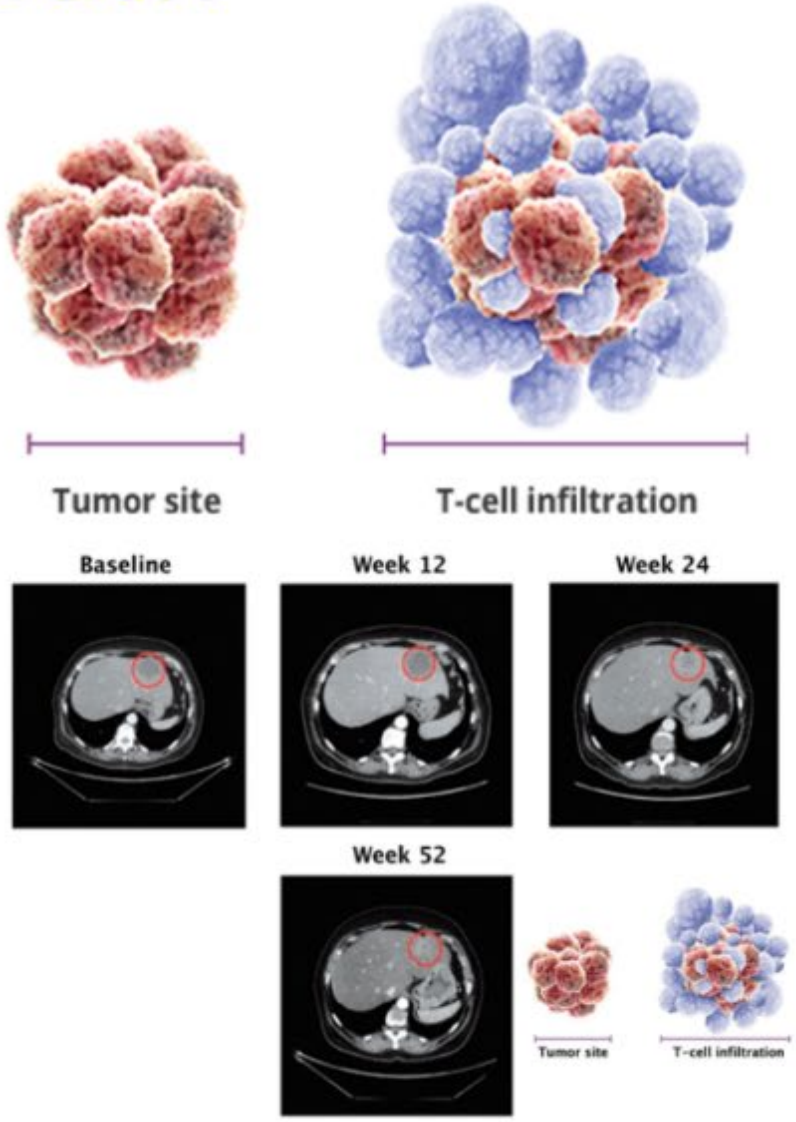


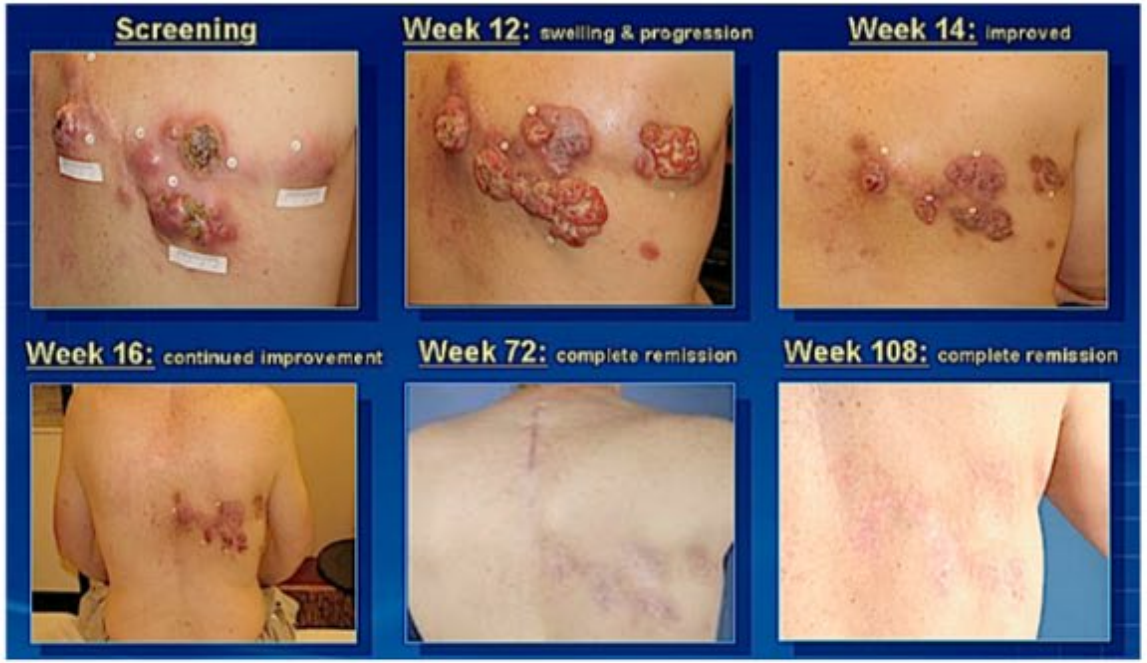






Not all Inflammatory Rxs from CPI are bad…





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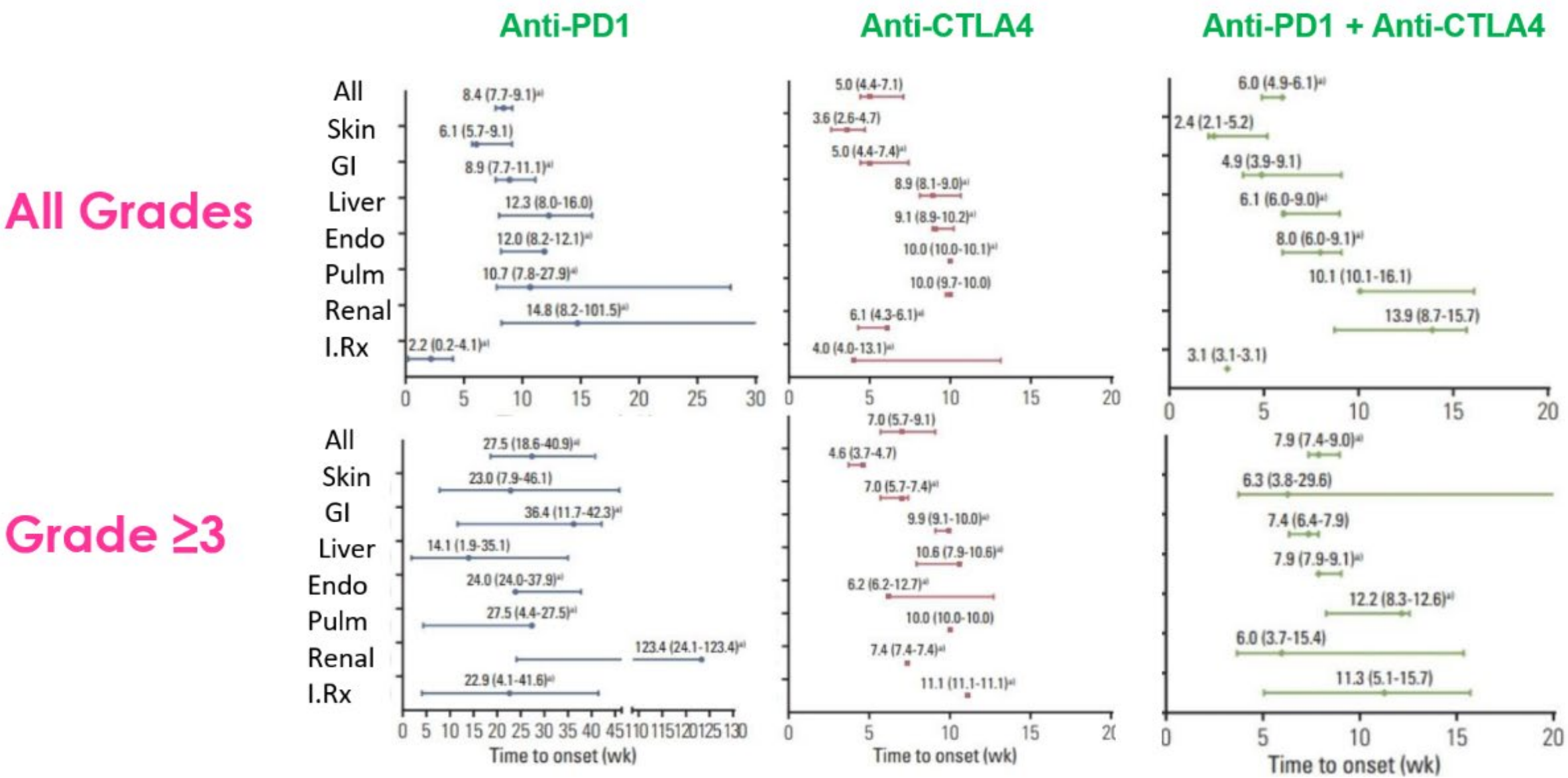
Sharing Best Practices to Optimize Patient Care

21 & 24 October – LATAM and Canada

APTITUDE HEALTH

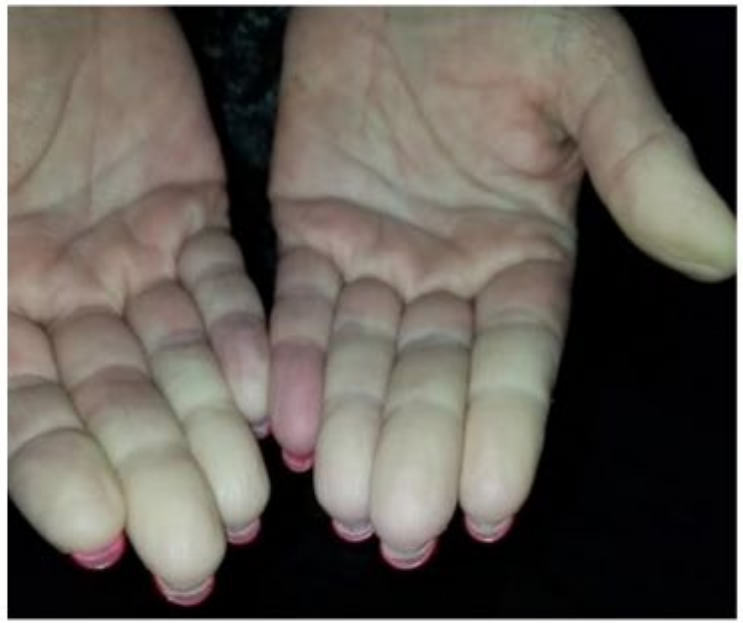
Timing of ir-AES

irAE Timing: Usually Later and Less Predictable Than Toxicities of Chemotherapy or Targeted Therapies →

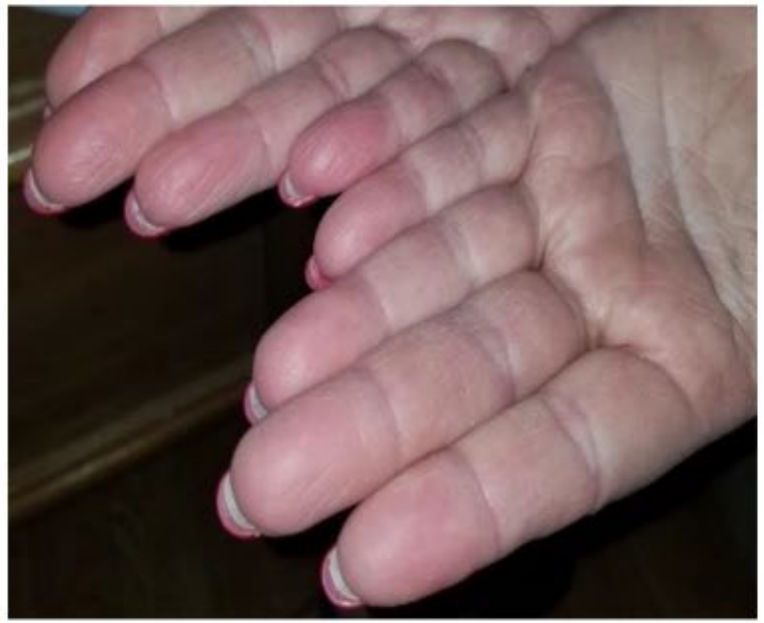


Serial specimen collection may provide insight into the unusual and unpredictable timing of some irAEs →

Raynaud's-like phenomenon 22 months after starting IO



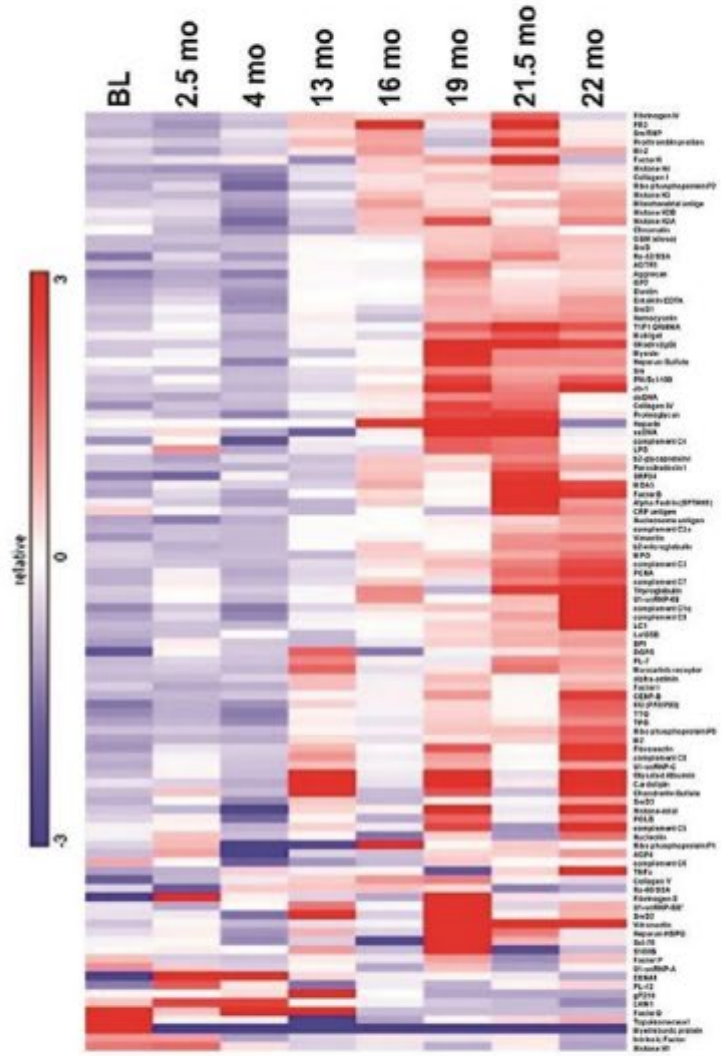
Painful, cold hands due to vasoconstriction

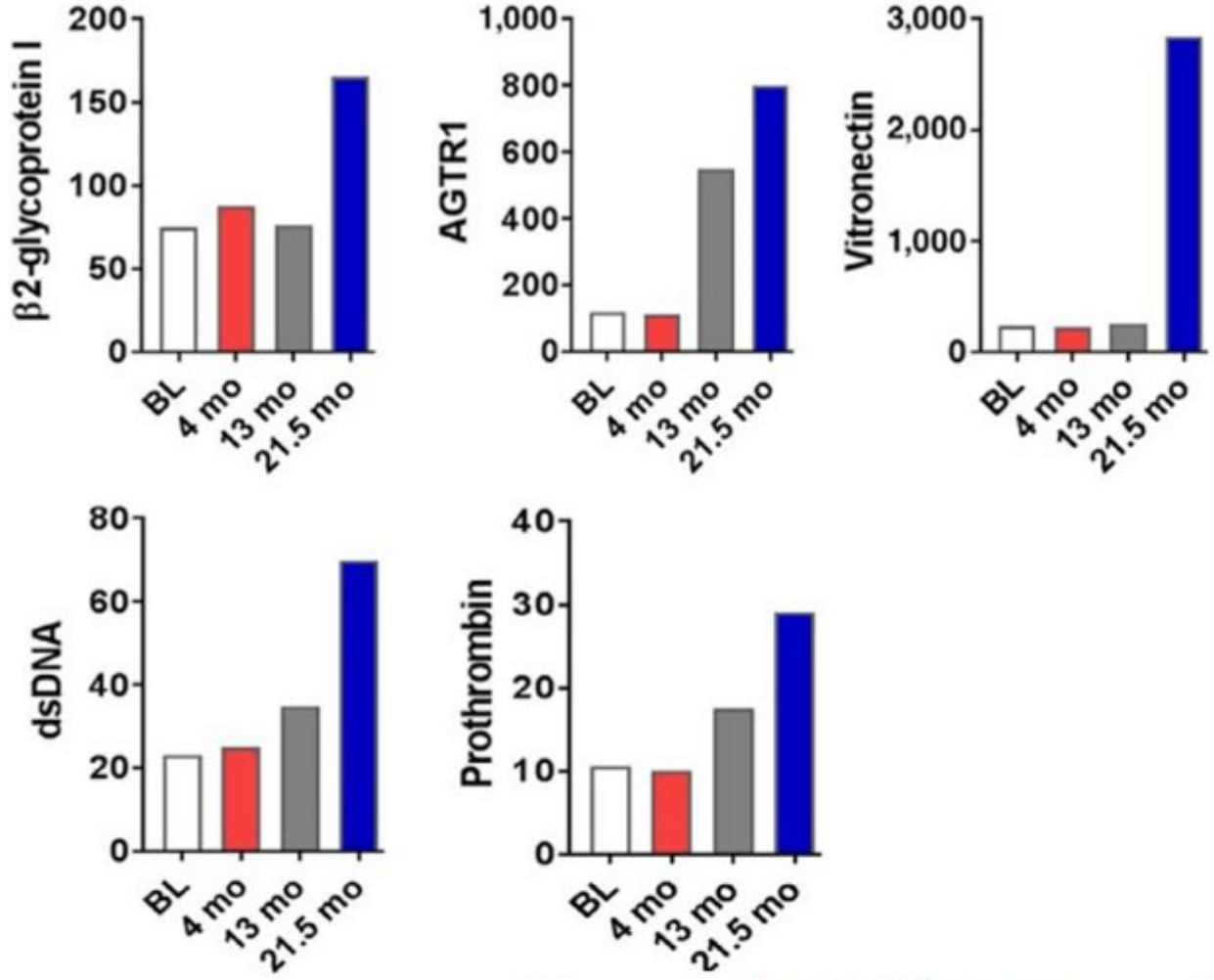


Intense erythema during recovery

Khan S et al. Oncologist. 2020;25(5):e753-e757.

Raynaud's-associated Antibody levels did not increase until more than 1-yr after treatment started !!





Khan S et al. Oncologist. 2020;25(5):e753-e757.

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For me, the most scaring and quick toxicity… unpredictable and either fatal or permanent → Neurological syndromes…

Case Reports of Pembrolizumab-induced Acute Inflammatory Demyelinating Polyneuropathy

Rupesh Manam [1], Jasmine L. Martin [2], Joshua A. Gross [2], Dhishna Chaudhary [2], Sajeel Chowdhary [3], Patricio S. Espinosa [4], Edgardo S. Santos [5]

1. Internal Medicine, Florida Atlantic University Charles E. Schmidt College of Medicine, Boca Raton, USA 2. Department of Internal Medicine, Florida Atlantic University Charles E. Schmidt College of Medicine, Boca Raton, USA 3. Neuro-Oncology, Marcus Neuroscience Institute, Boca Raton, USA 4. Neurology, Marcus Neuroscience Institute, Boca Raton Regional Hospital, Boca Raton, USA 5. Oncology, Lynn Cancer Institute, Boca Raton, USA

Case report 1

A 73-year-old Caucasian male with a biopsy-proven diagnosis of stage IV poorly differentiated adenocarcinoma of the lung, epidermal growth factor receptor mutation negative, anaplastic lymphoma kinase translocation negative, and PD-L1 tumor proportion score of 20% was started on carboplatin, pemetrexed, and pembrolizumab. The patient was receiving the chemotherapy regimen every three weeks and prior to initiating cycle two, he developed generalized weakness. On presentation, he expressed subjective progressive weakness of the lower extremities (LEs) greater than the upper extremities (UEs). The physical exam was significant for 3/5 motor strength and absent deep tendon reflexes in the bilateral upper extremities (UEs) and LEs. Given the clinical presentation, an irAE secondary to an IO agent was suspected, with a differential diagnosis that included Guillain-Barré syndrome (GBS) versus myasthenia gravis-like syndrome. Lumbar puncture revealed albuminocytological dissociation in the cerebrospinal fluid (CSF) of 68 g/L, which further supported AIDP. The paraneoplastic panel was negative. Infectious workup, including CSF cultures, cytogenetic

Case report 2

An 81-year-old Caucasian male with a diagnosis of melanoma on the right anterior chest wall and a wide local excision was found to have a recurrence in the right lung four months after initial diagnosis. Pembrolizumab was initiated, however, treatment was switched to dabrafenib and trametinib once molecular studies confirmed positivity for the BRAF V600R mutation. Nine months after diagnosis, magnetic resonance imaging (MRI) of the brain with and without contrast revealed multiple metastatic lesions in the brain (Figures *1*-*3*), prompting the administration of the second cycle of pembrolizumab in addition to dabrafenib and trametinib. One month following the second cycle of pembrolizumab, the patient was admitted to the hospital with progressive weakness described as originating in the bilateral LEs and then spreading to his bilateral UEs. His neurological exam revealed a strength of 2/5 in the bilateral UEs and 0/5 in the bilateral LEs with areflexia and no bulbar muscle weakness. A lumbar puncture showed an albuminocytologic dissociation with elevated CSF protein (56 g/L), which supported our diagnosis of AIDP. Electromyography was consistent with motor and sensory neuropathy. Infectious workup revealed negative CSF

Manam et al. Cureus 2018; 10(9): e3371. DOI 10.7759/cureus.3371

Any new or worsening neurological symptom in a patient receiving an IO agent (regardless of the diagnosis) should prompt an immediate evaluation by neurology. Clinicians must be keen to recognize AIDP as a complication of IO therapy, as a misdiagnosis or delay in therapy could be fatal. Early intervention can potentially prevent complications such as respiratory failure and death. More research is needed to understand the development of these rare irAEs and attempt to ascertain risk factors, which may predispose cancer patients to these neurological syndromes.

Edgardo S. Santos, MD, FACP
Medical Oncologist-Thoracic
Genesis Care US/Florida Atlantic University

Global Lung Cancer Academy

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APTITUDE HEALTH

Monitoring for ir-AES

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Ir-AEs are *Unpredictable* and *Diverse*…, How can we monitor for them?

Baseline

- CBC + differential
- CMP
- TSH (+/- FT4)
- Consider UA
- Consider baseline EKG and/or Troponin if higher risk for myocarditis (eg, cardiac comorbidities, DM, planned anti-CTLA4 + anti-PD1)
- Consider CPK

Intermittent

- CBC + differential
- CMP
- TSH (+/- FT4)

SITC Guidelines. Brahmer et al. J Immunother Cancer. 2021;9(6):e002435.

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APTITUDE HEALTH

Therapy for ir-AES

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Steroid Dosing for irAE Management

- Consider evaluating for other causes of toxicities
- In general (exceptions often for endocrine irAE, which may be treated with physiologic replacement only):
  - Grade 2 irAEs: 0.5-1 mg/kg/day oral prednisone or IV methylprednisolone or equivalent.
  - Grade 3-4 irAEs: Hold IO; 1-2 mg/kg/oral prednisone or day IV methylprednisolone equivalent.
- Patients should have significant clinical improvement within the initial 2-3 days. If no improvement is observed either increase dose of steroids up to 2 mg/kg/day or add a second line immunosuppressive agent.
- Whenever second line immunosuppression is planned again re-evaluate for other causes of toxicities (GI, liver or other organs).
- For myocarditis and CNS toxicities, strongly consider higher dosage of methylprednisolone of 1 gm/day for 3-5 days; inter-consult; aggressive immunosuppressive management.

SITC Guidelines. Brahmer et al. J Immunother Cancer. 2021;9(6):e002435.

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Supportive Care and Early Taper Essential When Prescribing High-Dose, Prolonged Steroid Regimens →

- When beginning corticosteroid therapy, patients should be specifically counseled about potential toxicities, including hyperglycemia, mood disturbances, insomnia, gastritis, weight gain, and opportunistic infections.
- Infection prophylaxis may vary by institutional practice, but must be considered early on in steroid therapy.
- Steroids should be tapered as soon as possible after ir-AE symptoms have resolved.
- Consider a 4-6-week taper-off for most toxicities.
- Toxicities may recur upon taper. In these cases, consider adding a second immuno-suppressive agent.

SITC Guidelines. Brahmer et al. J Immunother Cancer. 2021;9(6):e002435.

Management of Steroid-Refractory Colitis Centers on Anti-TNF Therapy

High-grade colitis

Initial: prednisone 1-2 mg/kg/day

Grade 4: IV corticosteroids

→

If no improvement within 3-5 days:

Administer **infliximab.** If necessary can give up to 3 doses of infliximab (5 mg/kg) at 0, 2, and 6 weeks.

→

If symptoms persist after two doses of infliximab:

Hold the third dose of infliximab

Administer up to 3 doses of **vedolizumab** (300 mg) at 0, 2, and 6 weeks

SITC Guidelines. *Brahmer et al. J Immunother Cancer. 2021;9(6):e002435.*

Steroid-Refractory Hepatitis: Avoid the Potential Hepatotoxicity of Anti-TNF Agents

High-grade hepatitis

Grade 2 hepatitis
Initial: IV or po prednisone 0.5-1.0 mg/kg/day

Grade 3-4 hepatitis
Initial prednisone 1.0-2.0 mg/kg/day

If no improvement within 3-5 days:

Administer
Mycophenolate mofetil
Initial at 500mg BID
then 1000mg BID

SITC Guidelines. *Brahmer et al. J Immunother Cancer. 2021;9(6):e002435.*

Steroid-Refractory Pneumonitis: Multiple Potential Therapies:

High-grade pneumonitis

Grade 2: 1-2 mg/kg/day prednisone

Grade 3+: 1-2 mg/kg/day methylprednisolone

If no improvement within 72 hours:

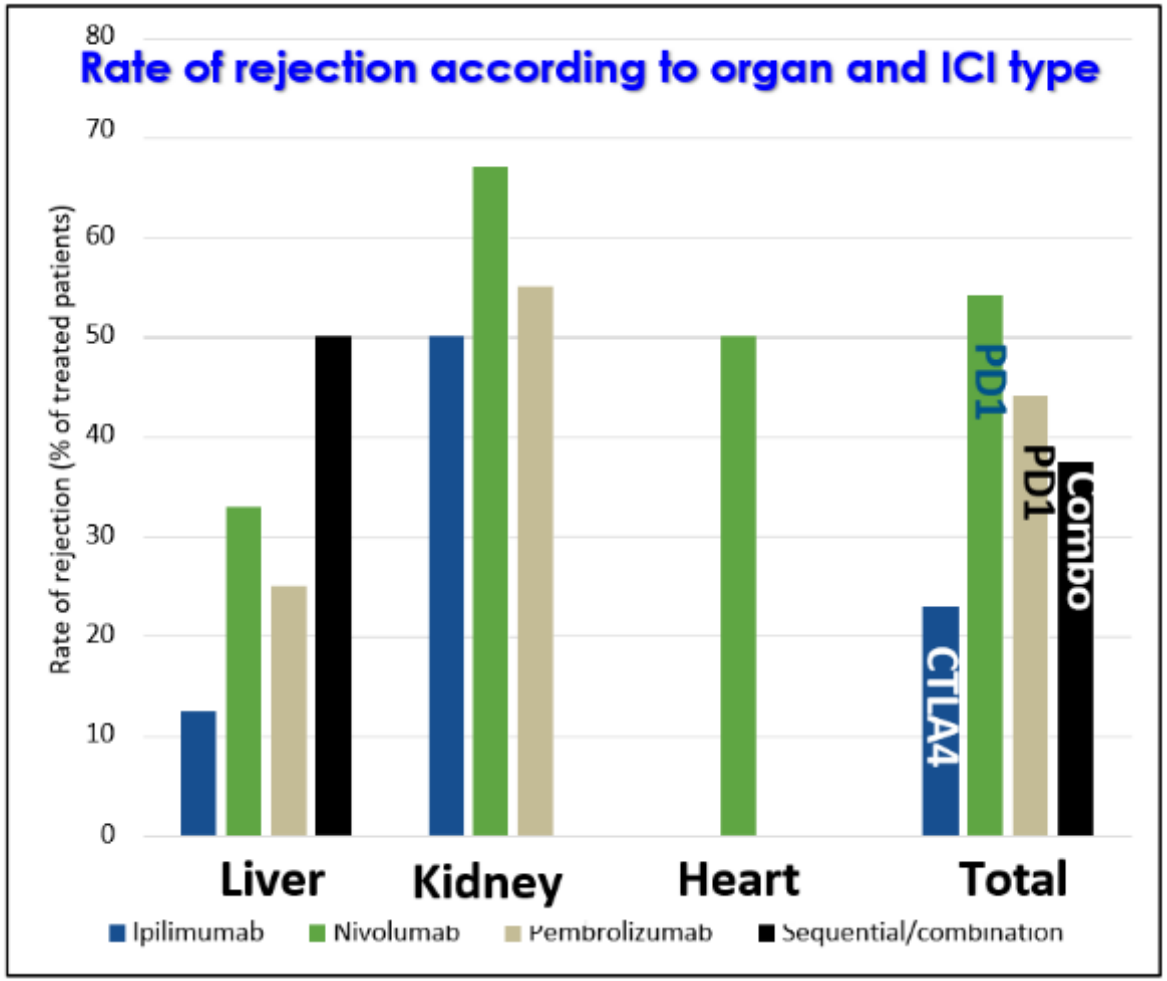
- **Mycophenolate mofetil**: 1-1.5 g twice daily (LE: 3)
- **HD IVIG**: 2 g/kg in divided doses over 2-5 days (LE: 4)
- **Infliximab**: 5 mg/kg, one dose with optional second dose 2 wk later (LE: 4)
- **Cyclophosphamide**: 600 mg/m^2 for 6 infusions (LE: 3)
- **Tocilizumab**: 4 mg/kg (LE: 4)

SITC Guidelines. *Brahmer et al. J Immunother Cancer. 2021;9(6):e002435.*

ir-AE risk in Special Populations

ICI use in stem cell and organ transplant populations complicated by GVHD and organ rejection

- Patients who relapse after allogeneic SCT:
  - Ipilimumab: 32% response (10 mg/kg); 14% GVHD; 21% irAE
  - Anti-PD-1: 77% response; 26% died due to new-onset GVHD
- Solid organ data is limited; most is in renal patients
  - One retrospective study (n=39) reported graft loss in 81% and death in 46%
  - Also reported rapid time to rejection with median onset of 21 days
- PD-1 pathway appears to be more critical in allograft immune tolerance compared to CTLA-4 pathway



Davids MS et al. *N Engl J Med*. 2016;375(2):143-153. Haverkos BM et al. *Blood*. 2017;130(2):221-228. Abdel-Wahab N et al. *J Immunother Cancer*. 2019;7(1):106.

Kumar V et al. Oncologist. 2020;25(6):505–514.

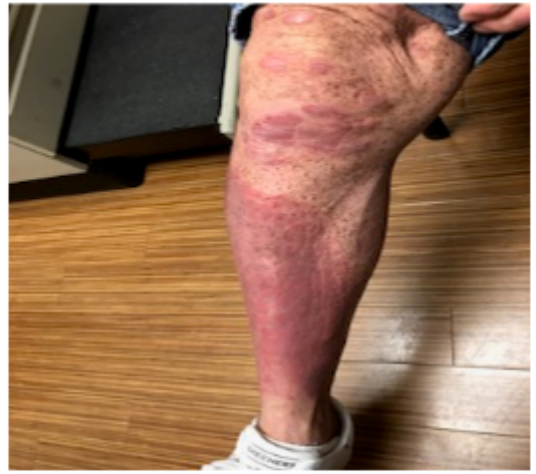
Clinical Case.

A 62-year-old male patient diagnosed with poorly differentiated squamous of the neck (base of the tongue) treated with HD cisplatin and radiation therapy on 4/2017. On 1/2018 PET scan showed lung metastases biopsy proven. Case was presented on tumor board and it was agreed to treat him with CPI single agent. Patient has a history of psoriasis under treatment with Apremilast, well controlled. After given him cycle # 2 of CPI patient developed an exacerbation of his psoriatic lesions.

Question:

What will be your next step on treatment?

- a) Permanently discontinue CPI
- b) Continue CPI + steroids
- c) Hold CPI + reevaluate to decided further treatment



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Sharing Best Practices to Optimize Patient Care

21 & 24 October – LATAM and Canada

APTITUDE HEALTH

ICI rechallenge after ir-AE

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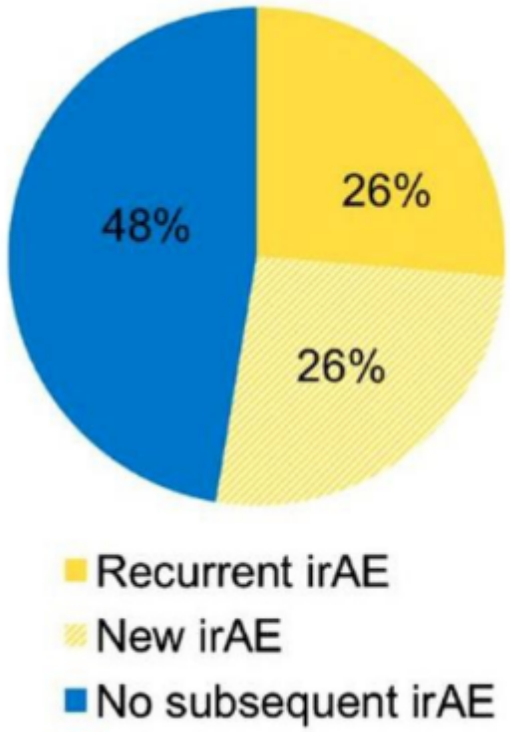
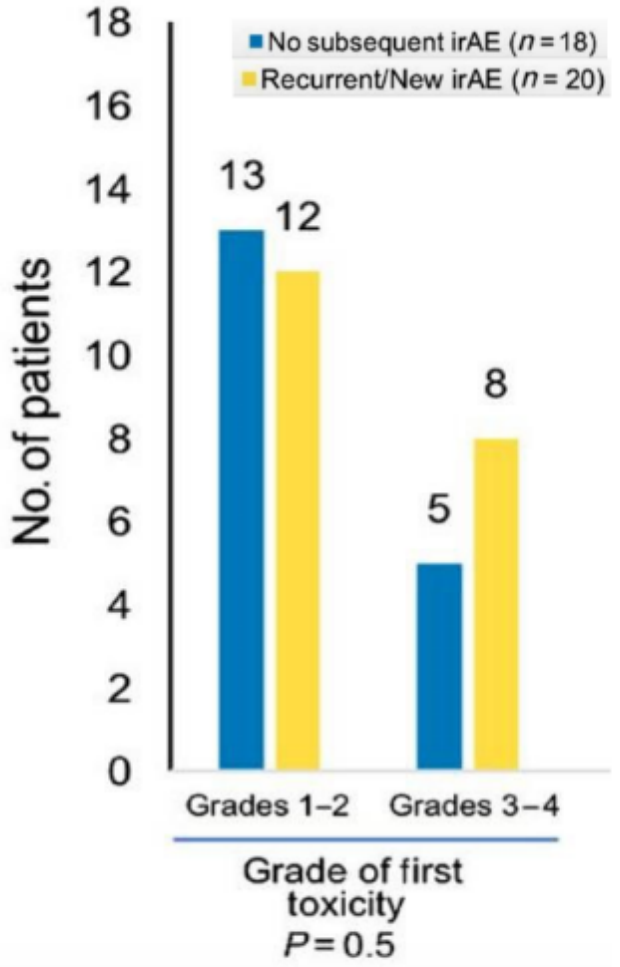
ICI Rechallenge After ir-AE May Be Feasible But Requires Caution

- Patients should not be re-challenged until ir-AE resolved to grade ≤1.
- Re-challenge with anti-PD-1/L1 after anti-CTLA-4 ± anti-PD-1 likely safe.
- Caution in re-challenging with same ICI in patients who previously had grade 3-4 irAEs.





Santini FC et al. Cancer Immunol Res. 2018;6(9):1093-9.

Re-Challenge with PD-(L)-1 After ir-AEs

- ✓ 482 lung cancer patients at MSKCC; 15% (70) patients developed ir-AEs.
- ✓ 38 (54%) were re-challenge.
- ✓ 24% developed same ir-Aes; 26% developed new ir-AEs.
- ✓ 16 were treated successfully; 2 (5%) deaths.
- ✓ Among patients who had response before ir-AEs, no difference whether ICP therapy re-started or not.

Shirish Gadgeel. 2018 ASCO Annual Meeting

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Global Lung Cancer Academy

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Sharing Best Practices to Optimize Patient Care

21 & 24 October – LATAM and Canada

APTITUDE HEALTH

Prognostic implications of ir-AE

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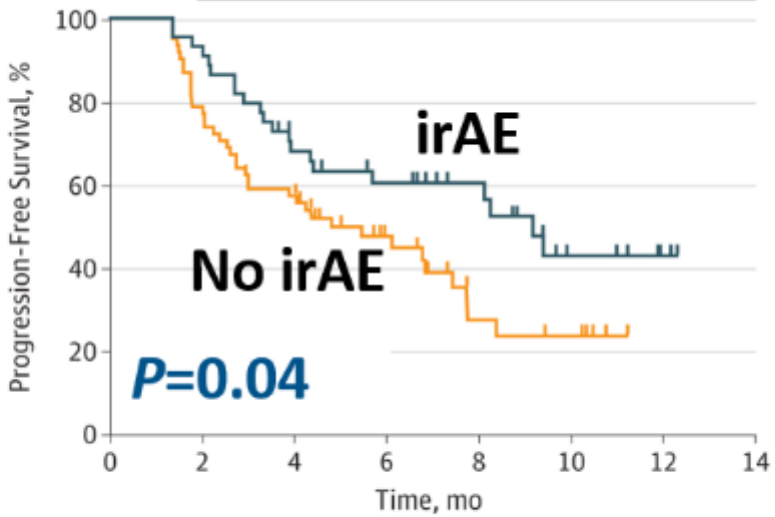
ir-AE Development Has Been Associated With Favorable Outcomes

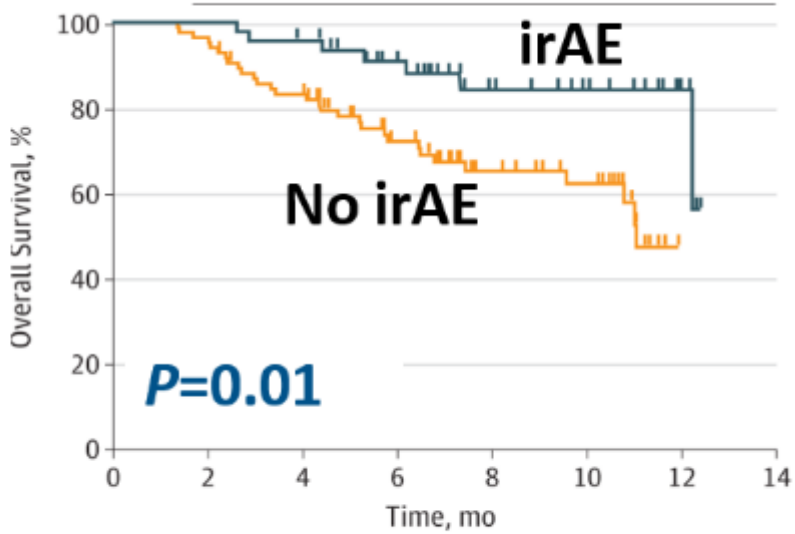
- Some studies associate irAE development with PFS or OS.
- Certain types of irAE may correlate more with outcomes.
- This trend is not consistent across settings, agents or studies.

Haratani K et al. JAMA Oncol. 2018;4(3):374-8.

PFS



OS



Conclusions

- ir-AEs are *unpredictable and potentially severe*.
- Time to onset of ir-AE is more heterogeneous than onset of chemotherapy or targeted therapy toxicities.
- Due to variable presentation, lack of clear diagnostic methods, and overlapping presentation with other conditions, ir-AE may be difficult to diagnose.
- ICI interruption and steroids represent mainstay of ir-AE management.
- *Have a low threshold for specialist consultation* for ir-AE diagnosis and management.
- Occurrence of ir-AE may be associated with improved outcomes from ICI.

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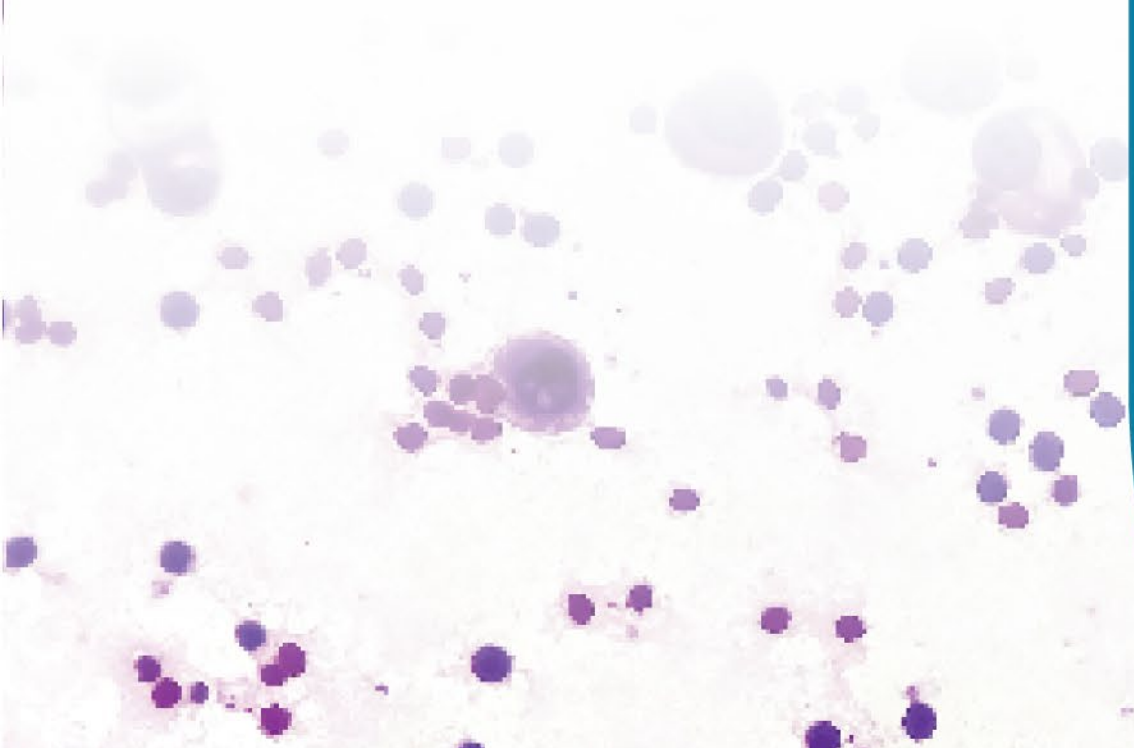


Tumor Board Discussion

Moderator: Corey Langer, MD, FACP

Case Presenter: Barbara Melosky, MD, FRCP

True Case

"Mr DS"

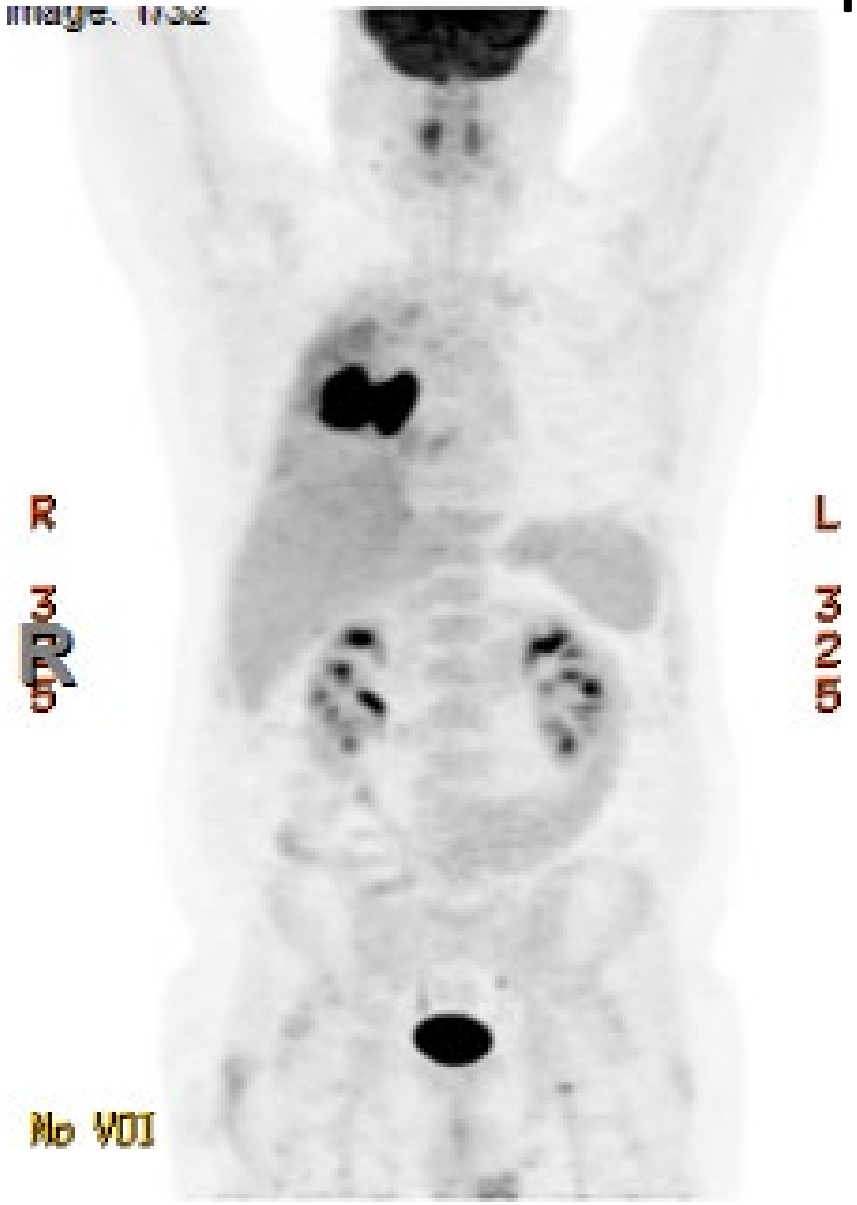
Case

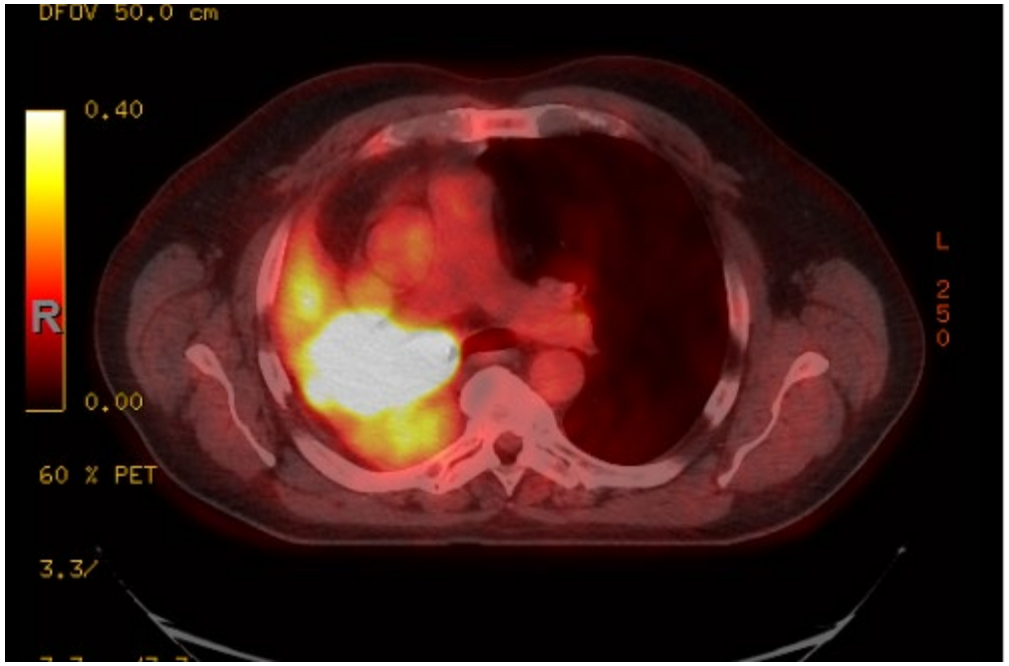
- 54-year-old man, 20 pack/year smoking history
- Increasing SOB, cough, and hemoptysis 2019
- 16-pound weight loss

Diagnosis and Stage

- CT: 6 × 4 × 4.7 cm mass RLL extending to mediastinum
- PET: 7.5-cm mass extending to mediastinum, invading R main stem bronchus, 4R node involved
- T4N2M0 = IIIB
- Squamous histology, PD-L1 1%–49%

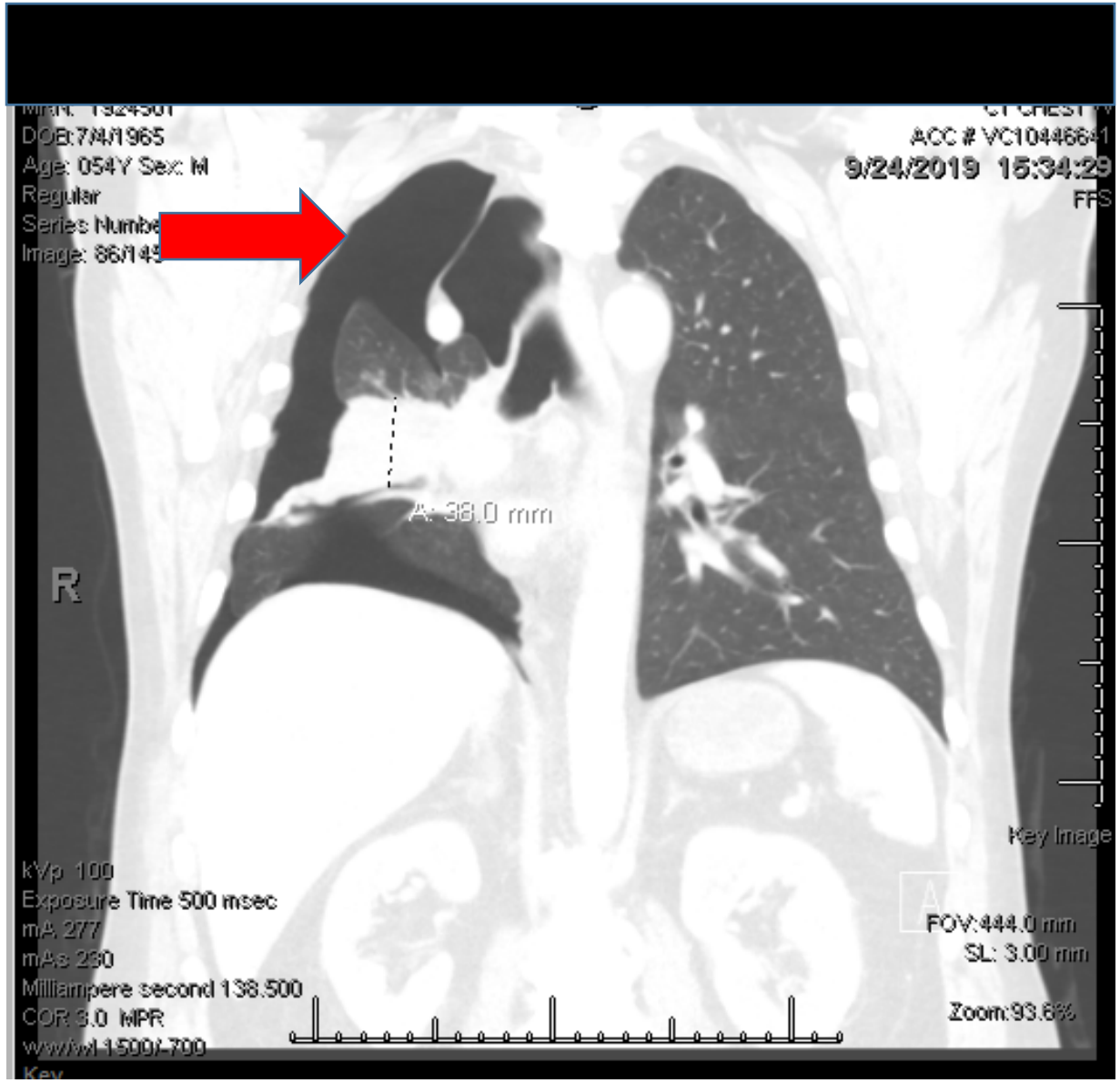
PET SCAN





Course

- Chemo-rads started, 60 Gy with weekly paclitaxel-carboplatin
- Plan on September 9 is to start October 21, 2019
- September 16: spontaneous pneumothorax
- Treatment stopped after 7 fractions



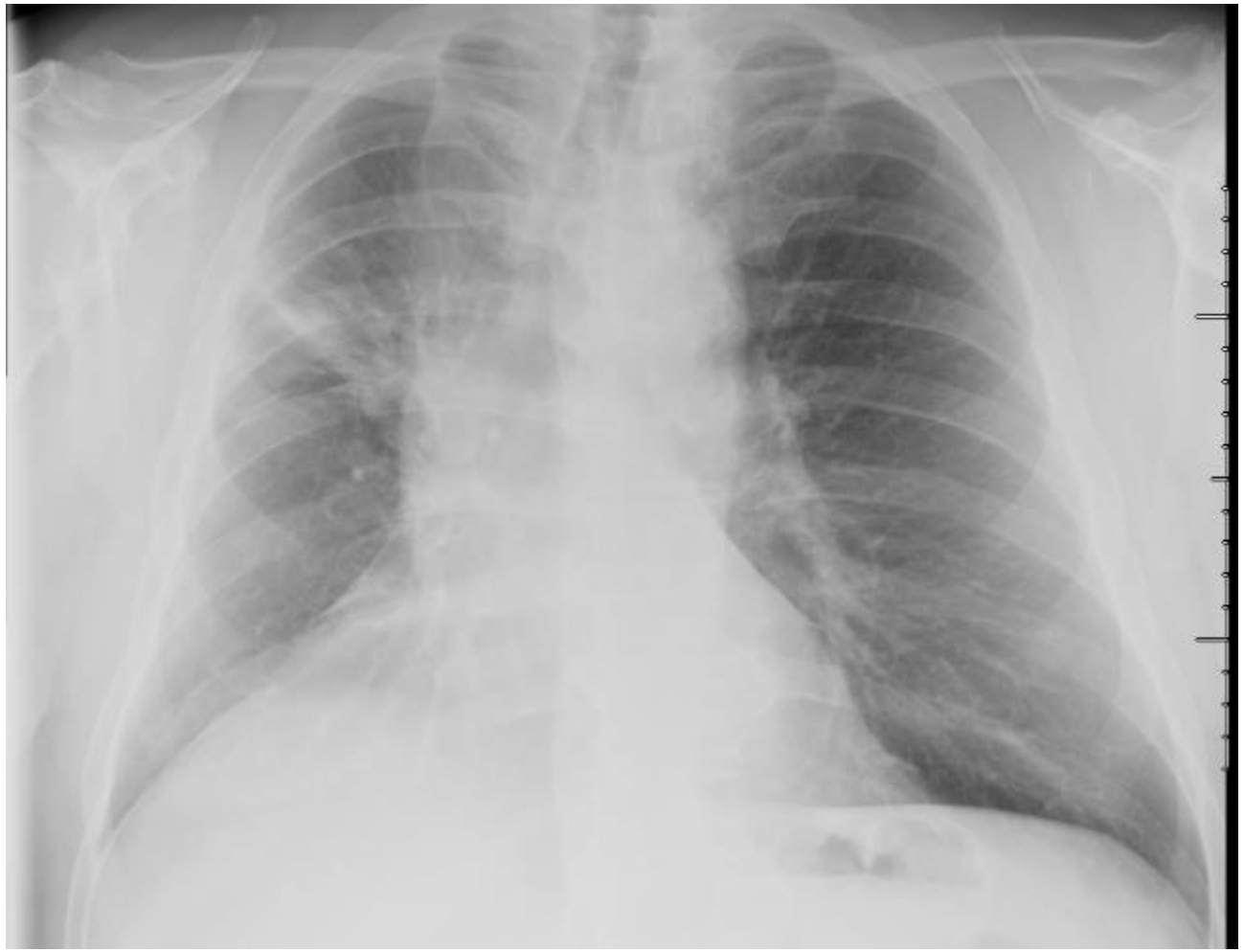
September 24

Question 1

Do you stop all treatment forever?

1. Yes
2. No

Resolution of Pneumothorax

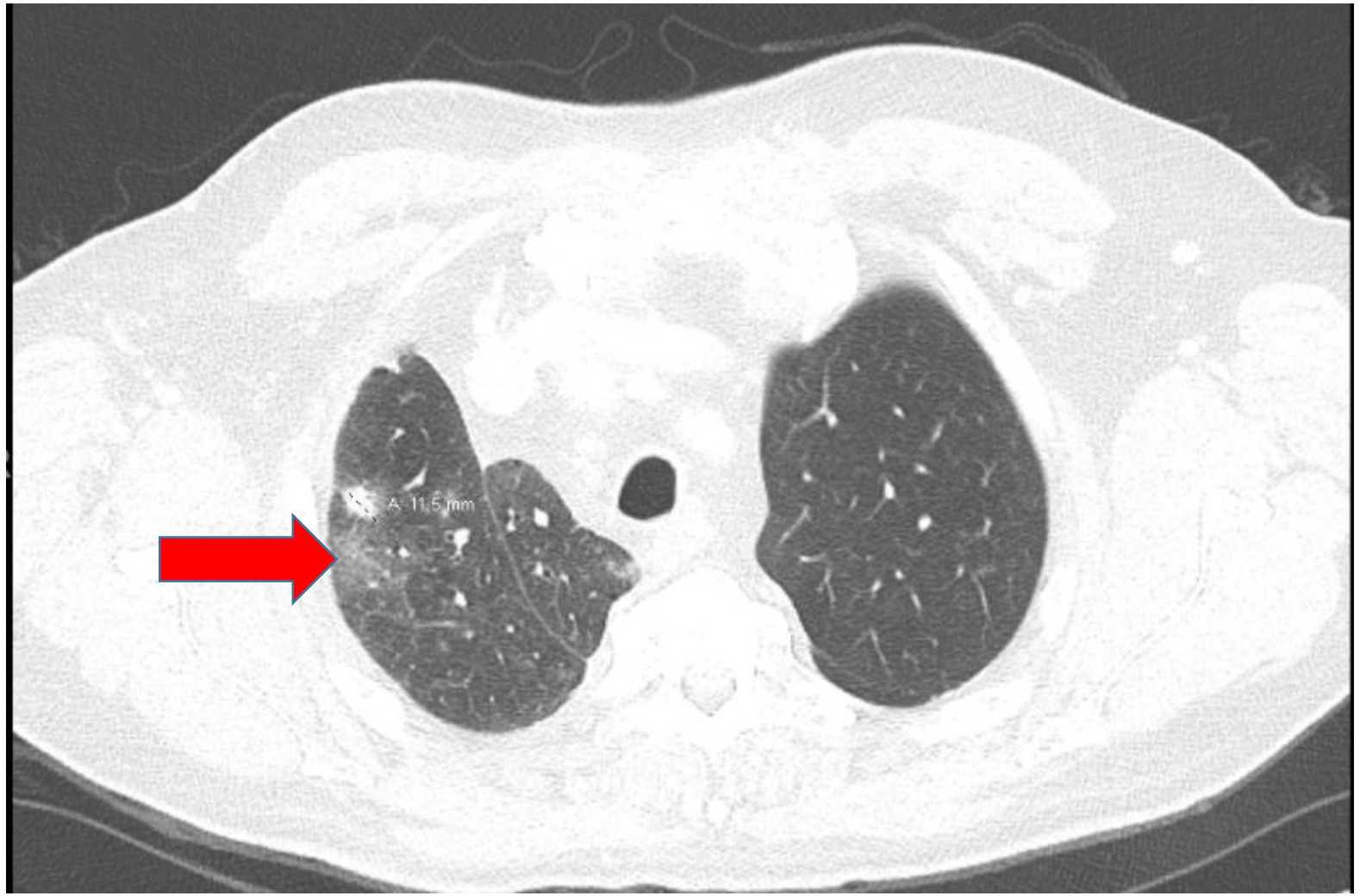


October 8, 2019

Course

- Treatment resumed October 10
- Finished chemo-rads November 13
- Undesignated CAP request for durvalumab
- Denied, “CT showed metastatic disease”

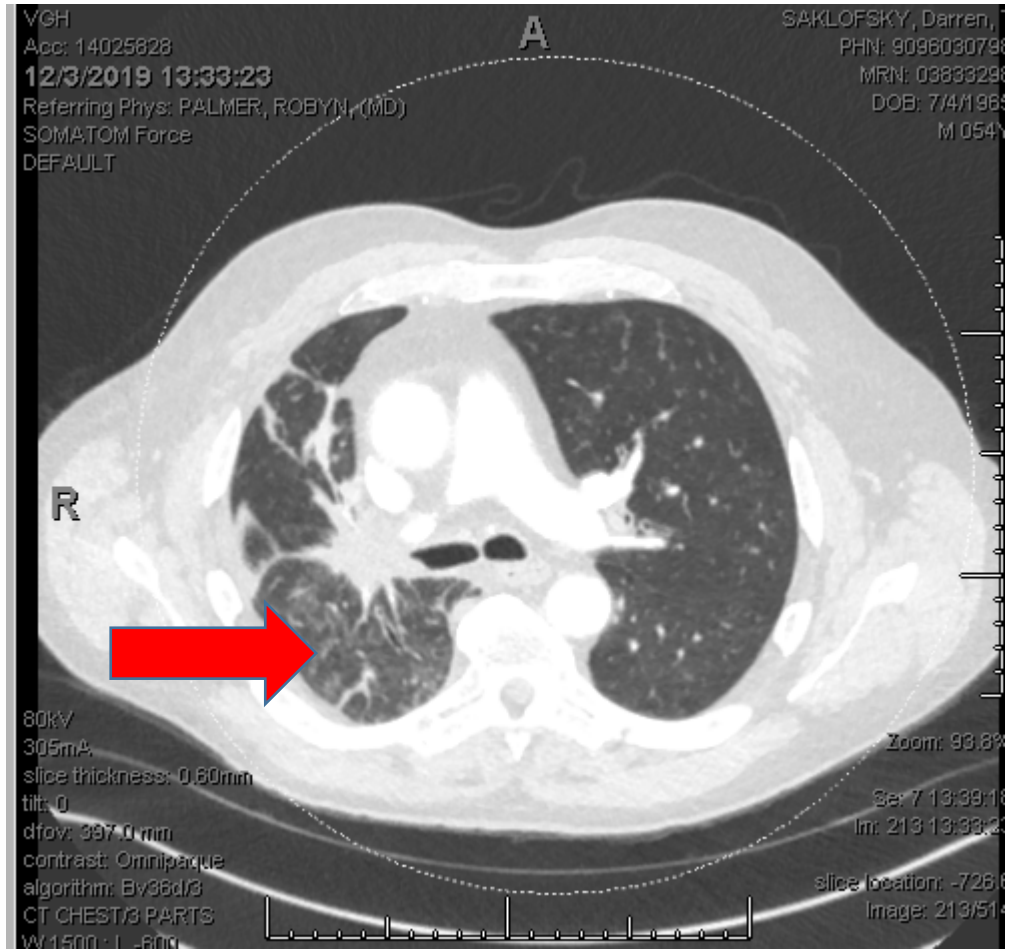
Re-expansion Lung: ? Metastatic Disease

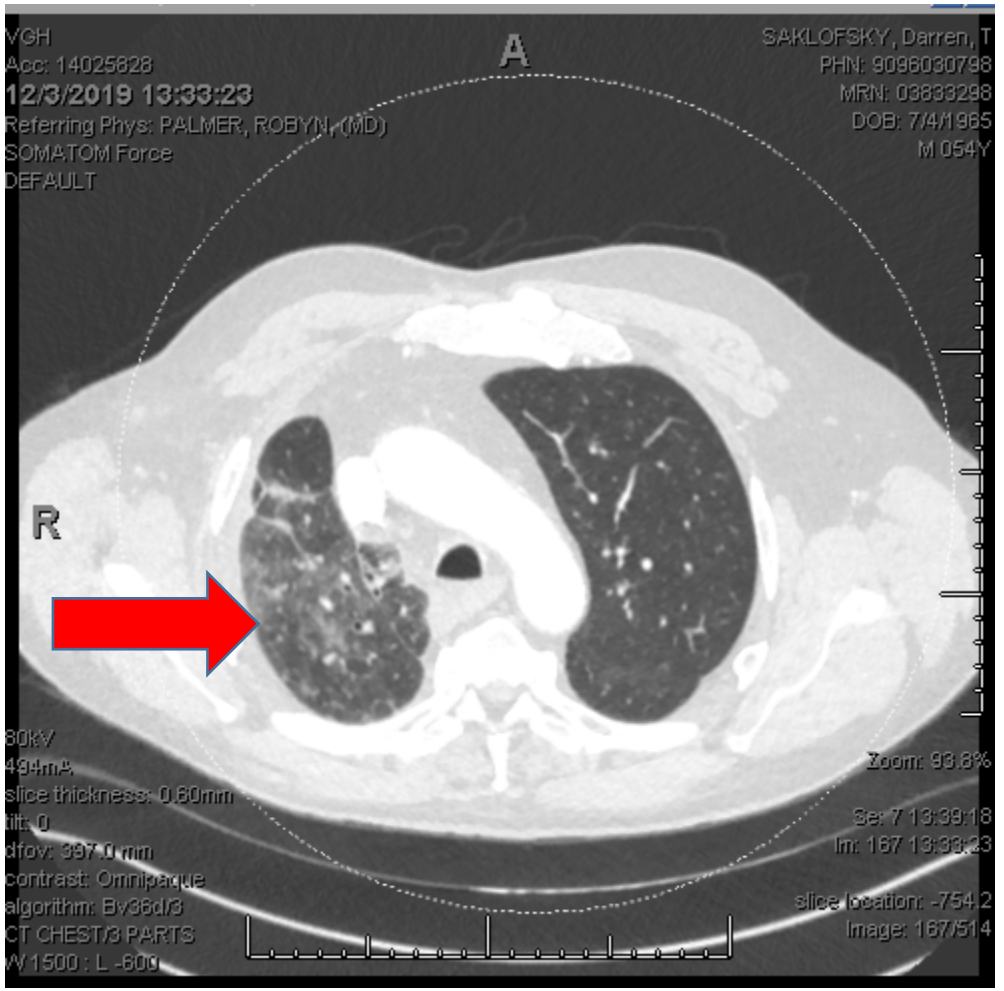


November 24, 2019

Course

- CT December 8, to prove CAP was wrong
- CT significant pneumonitis
- Patient symptomatic
  - Tachycardic 139, hemoglobin 80





December 8, 2019

Question 2

What do you do?

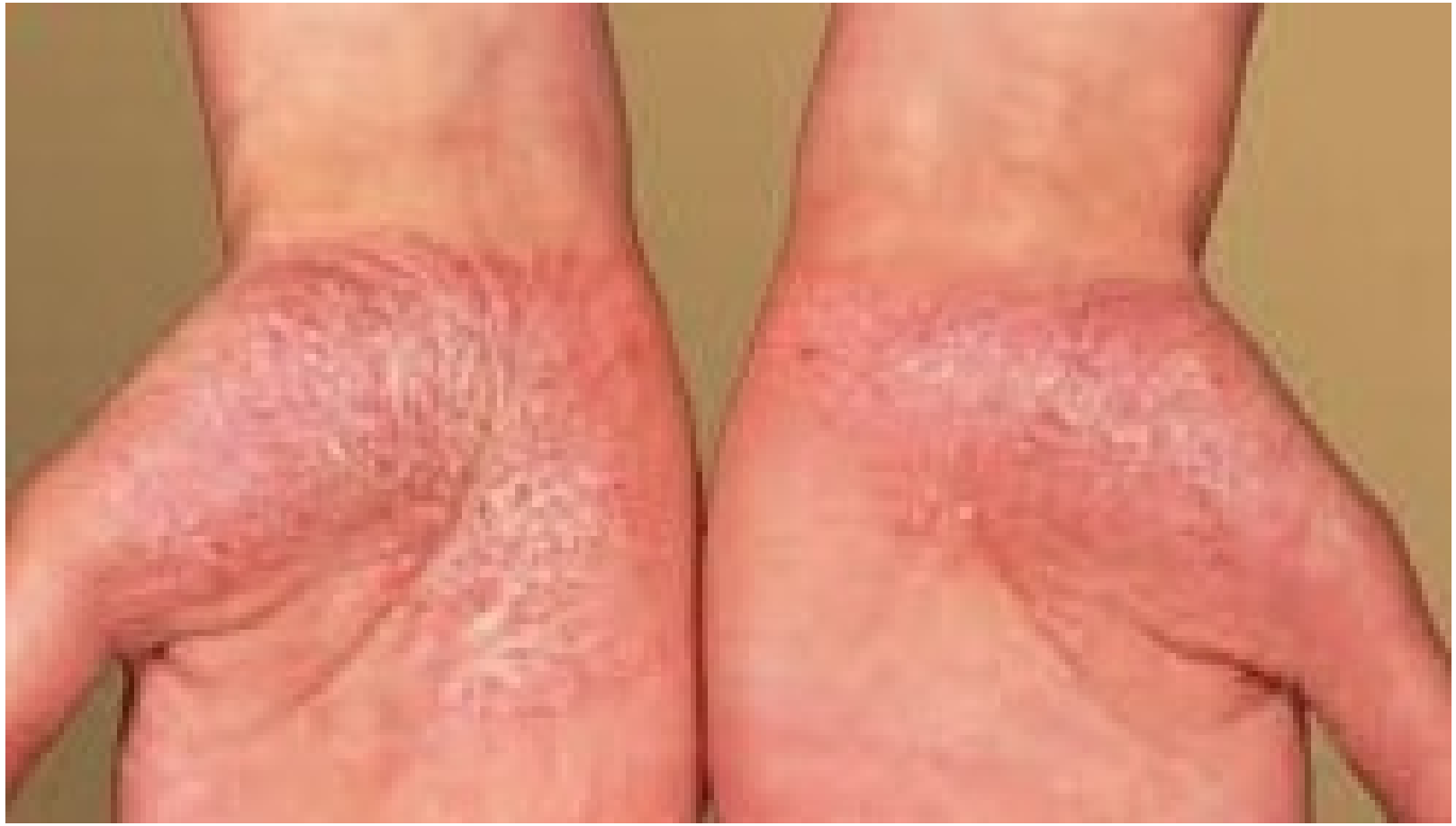
1. Steroids
2. Antibiotics
3. Both

Treatment

- Radiation pneumonitis
- Given 4 weeks tapering steroids

Course

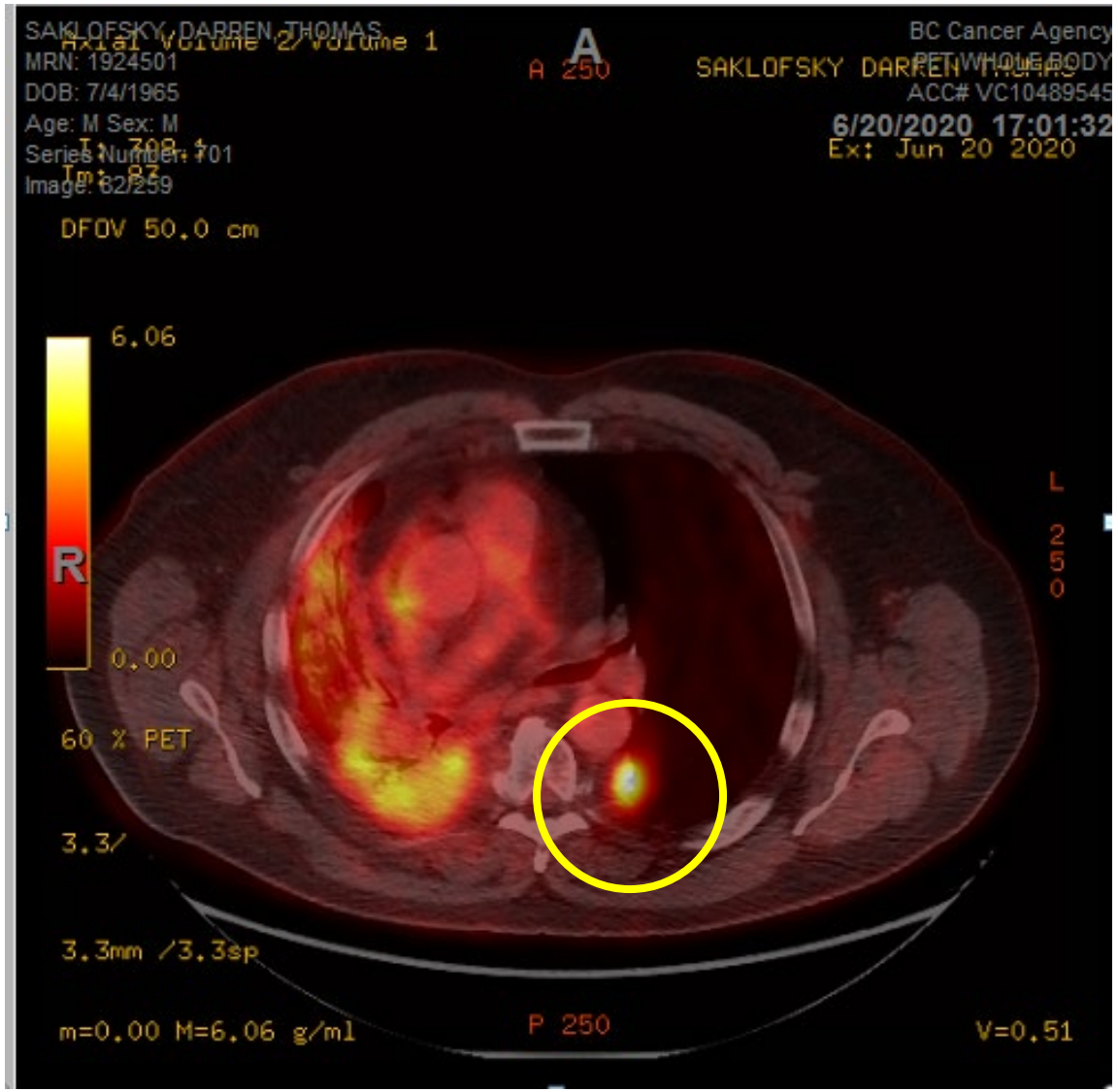
- Durvalumab started Jan 30, 2020 (radiation finished November 13)
- Seen prior to second dose: tomato-red hands
- Psoriasis age 13–18
  - Sent to dermatology
  - Recommended phototherapy and betamethasone .1%



February 21, 2020

Course

- February 20, TSH 78
  - Started on Synthroid .50–200 ug
- June 3, came to clinic extreme SOB
  - Urgent CT and PET
  - Collapse of RUL (okay so what?)
  - **New infiltrate LLL 2.2 cm**


SAKLOFSKY, DARREN THOMAS
MRN: 1924501
DOB: 7/4/1965
Age: M Sex: M
Series Number: 701
Image: 62/259
Axial Volume 2/Volume 1
A
A 250
BC Cancer Agency
SAKLOFSKY DARREN THOMAS
PET WHOLE BODY
ACC# VC10489545
6/20/2020 17:01:32
Ex: Jun 20 2020
DFOV 50.0 cm
6.06
R
0.00
60 % PET
3.3/
3.3mm /3.3sp
m=0.00 M=6.06 g/ml
P 250
V=0.51
L
250

June 10, 2020

Course

- CT-guided biopsy July 3

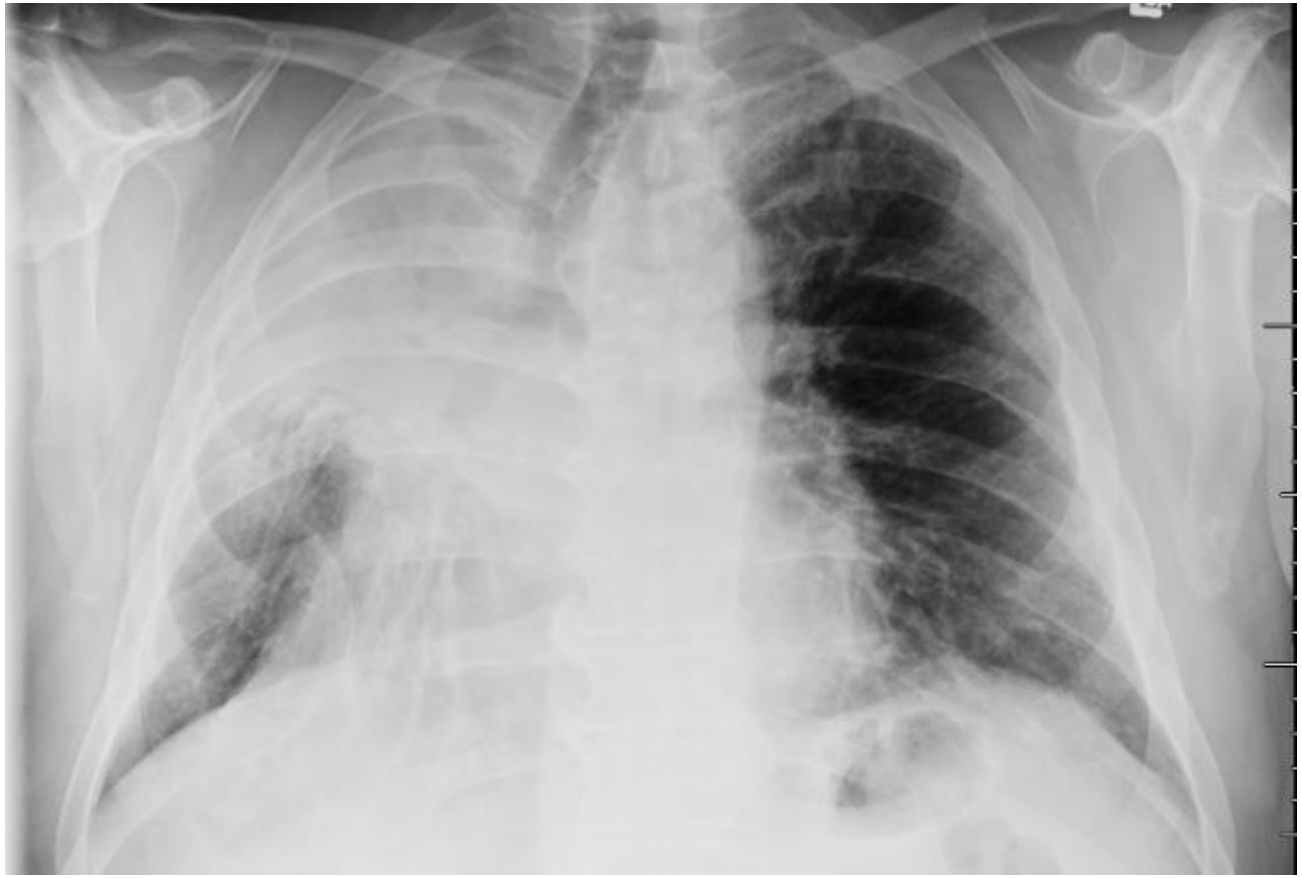
CLINICAL HISTORY>>::
Lung CA. FDG-avid consolidation. 3 x 20 G cores (sample also sent to microbiology).

FINAL DIAGNOSIS>>::
LUNG (LEFT, NODULE), NEEDLE CORE BIOPSY (20-GAUGE, CT-GUIDED, 3 CORES):
- ORGANIZING PNEUMONIA. NEGATIVE FOR MALIGNANCY.

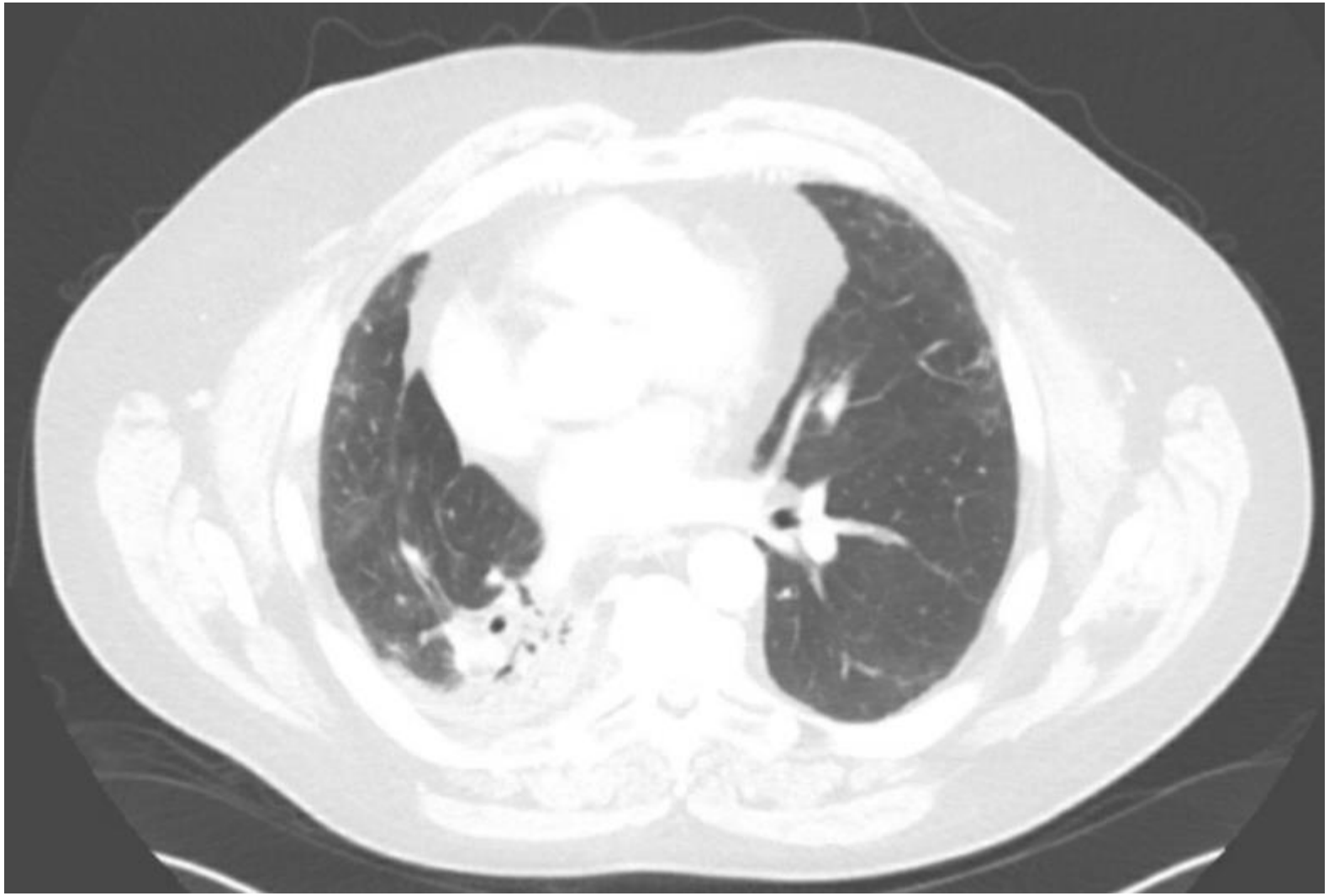
Treatment: amoxicillin clavulanate 2 weeks

Course

- 1 week later: increasing SOB
- Admitted to ICU, intubated
- “Organizing pneumonia” could be a side effect of checkpoint inhibitors
- Antibiotics and high-dose steroid 4 weeks, then taper next 4 weeks
- Extubated September 1



October 26, 2020



April 26, 2022

Summary

- 54-year-old male, squamous carcinoma lung, T4N2 or lllB
- Chemo-rads September 9–November 13
- Durvalumab January–June, 6 cycles
- Pneumothorax, psoriasis, hypothyroid, organizing pneumonia
- Alive today at age 57, crossing my fingers

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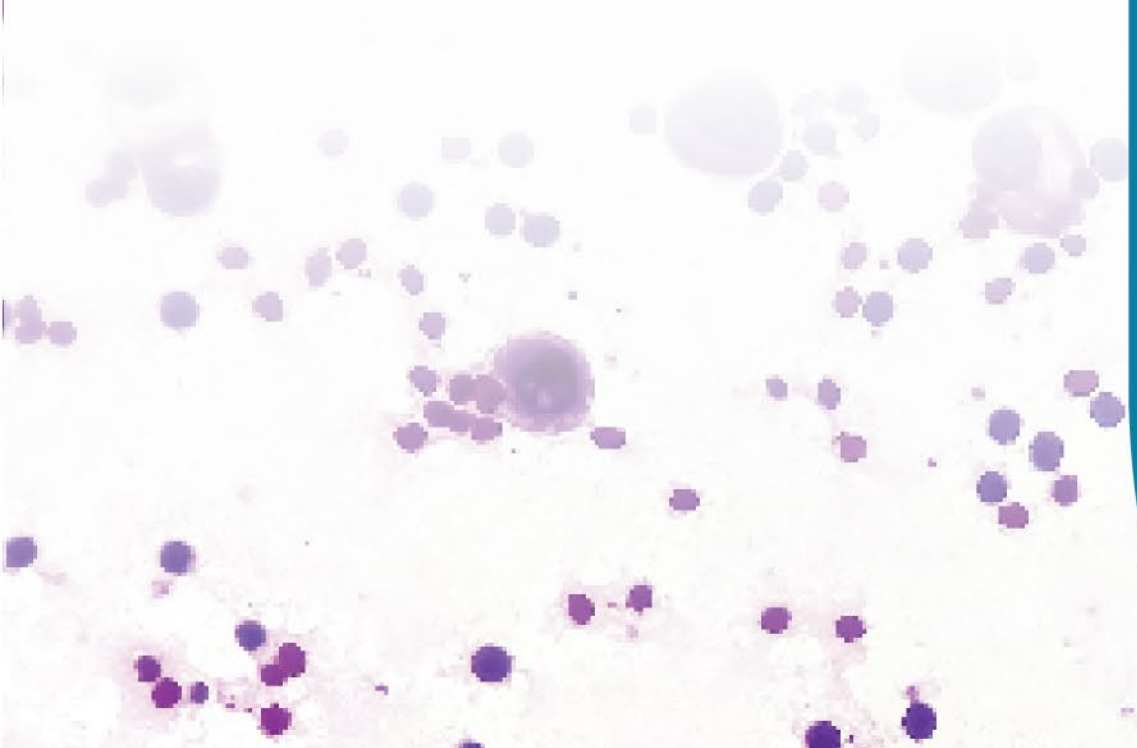

Tumor Board Discussion

Moderator: Corey Langer, MD, FACP

All faculty

Global Lung Cancer Academy

Session Close

Carlos Barrios, MD

Meeting evaluation

> Please complete the **evaluation link** that will be sent to you via chat

Question 1

I feel comfortable diagnosing and treating immune-related side effects.

1. Not at all
2. Sometimes
3. In general
4. Most of the time
5. Always

Thank you!

- Thank you to our sponsor, expert presenters, and to you for your participation
- Please complete the **evaluation link** that will be sent to you via chat
- The meeting recording and slides presented today will be shared on the globallungcanceracademy.com website within a few weeks
- If you have a question for any of our experts that was not answered today, you can submit it through the GLCA website in our Ask the Experts section

THANK YOU!

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