Disparities in Cancer Care and Health Equity Summit

Explaining Lung Cancer Disparities

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Disclosure Information

- **Paid Advisory Board:** Novartis, Celgene, Lilly, Sandoz, AbbVie, Eisai, G1 Therapeutics, Takeda, Seattle Genetics, Bristol-Myers Squibb, MedImmune, BerGenBio, Lilly, Amgen, AstraZeneca, PharmaMar, Boehringer Ingelheim, EMD Serono, XCovery, Bayer, Heron Pharmaceutical, ARMO BioSciences, Merck, Bayer, Jazz

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- IRC/DSMB: EMD Serono, Roche/Genentech

- Co-founder/Stock Ownership: Cambium Oncology; TaoBob LLC

Objectives

- Highlight key determinants of disparate outcomes in lung cancer
- Salient examples of opportunity areas driving disparity
- Strategies to address disparity

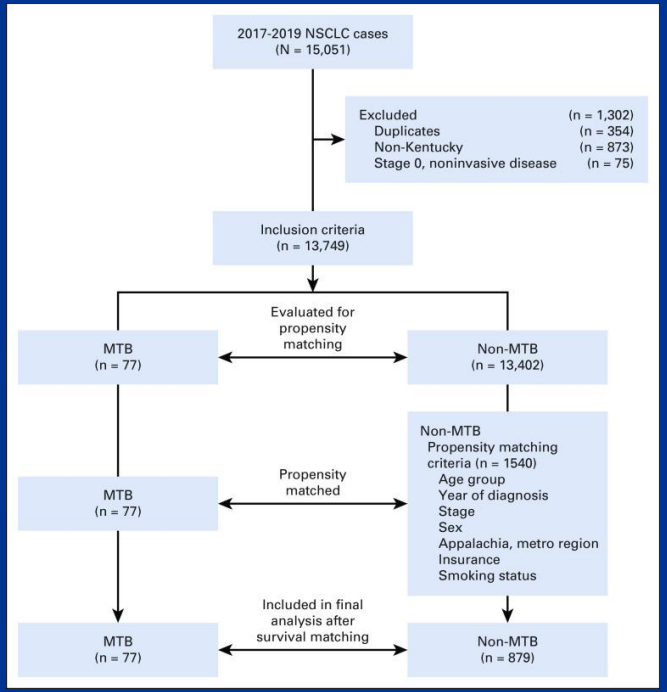
NIH Definition of Disparity

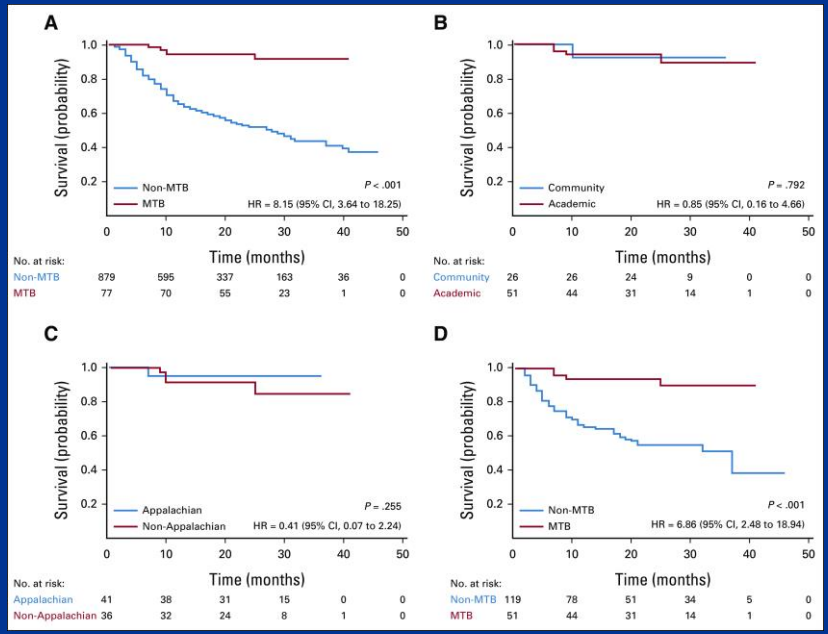
- **Differences** in the **incidence, prevalence, mortality, and burden of diseases** and other adverse health conditions that exist among **specific population** groups in the United States.

Estbalished drivers of disparities in lung cancer outcome

- Age
- Ethnicity/race
- Gender/Sexual orientation
- Rural/urban residence
- SES

Disparity by location of treatment in the Appalachian





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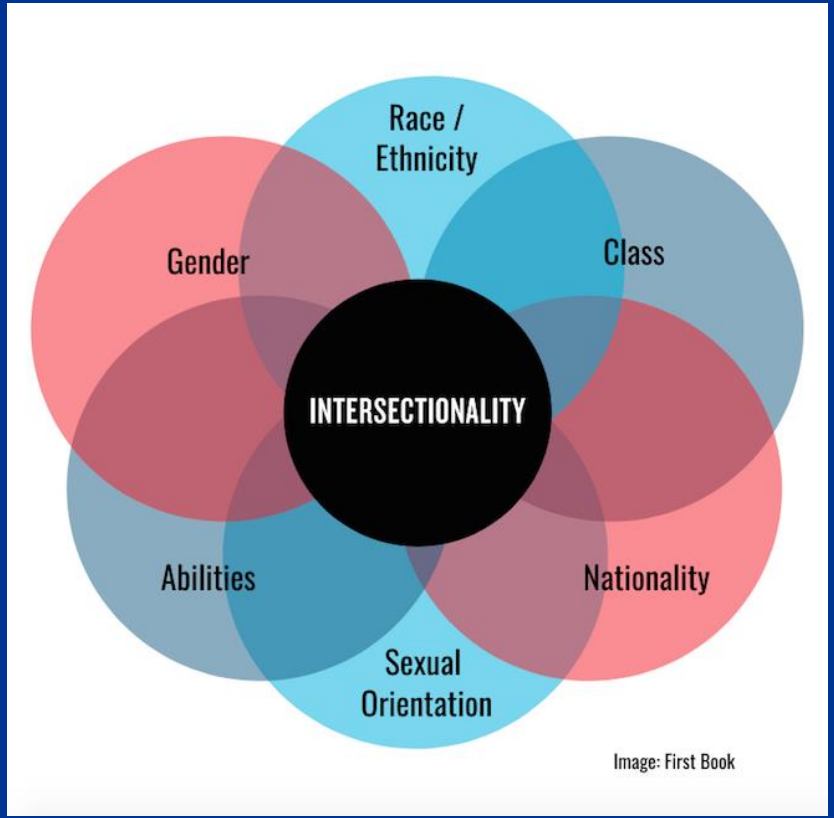
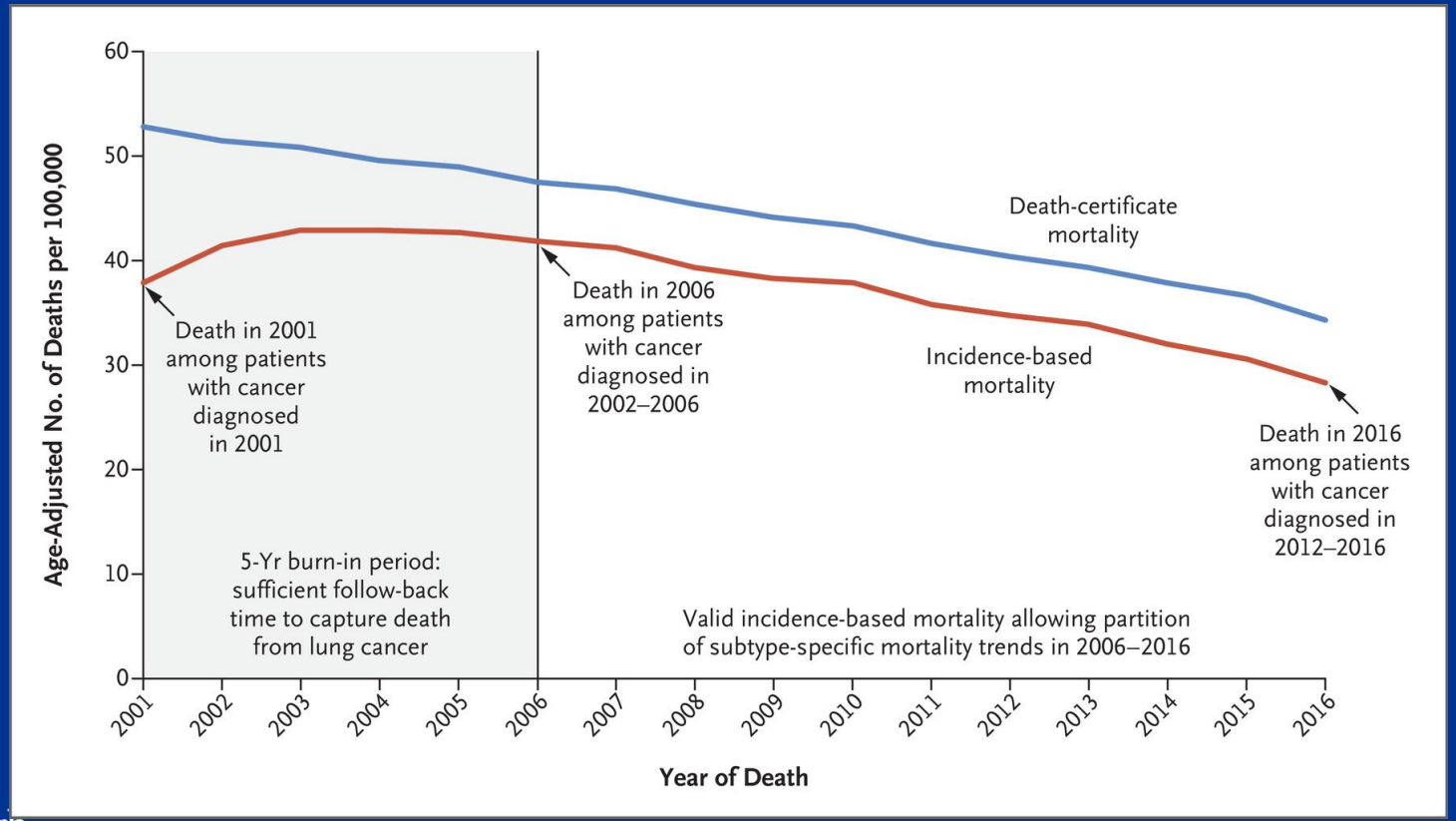
Bin Zhang et al. JCO Precis Oncol. 2021; 5: PO.21.00210.

Intersectionality



https://www.weforum.org/agenda/2021/10/here-s-how-organizations-put-intersectionality-to-work/

Why address sources of disparities



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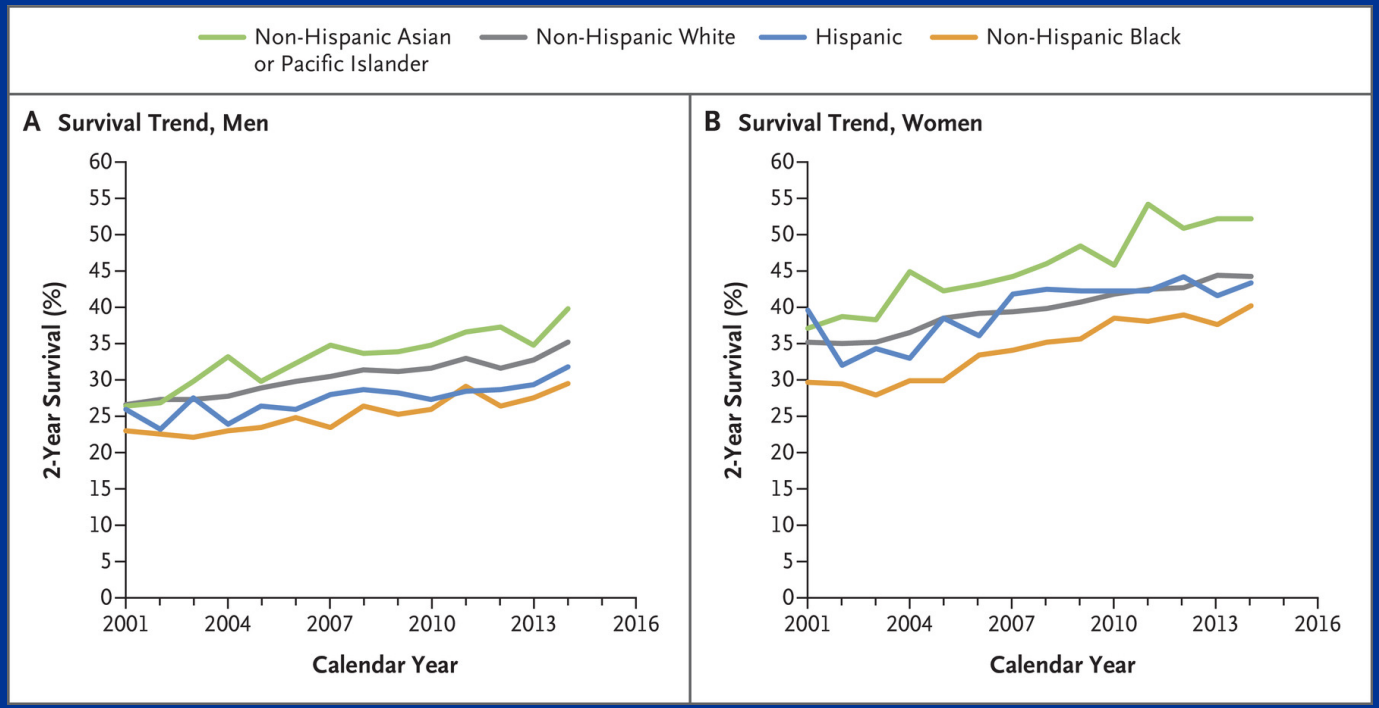
Improved survival for US cancer patients driven mainly by reduced lung cancer mortality



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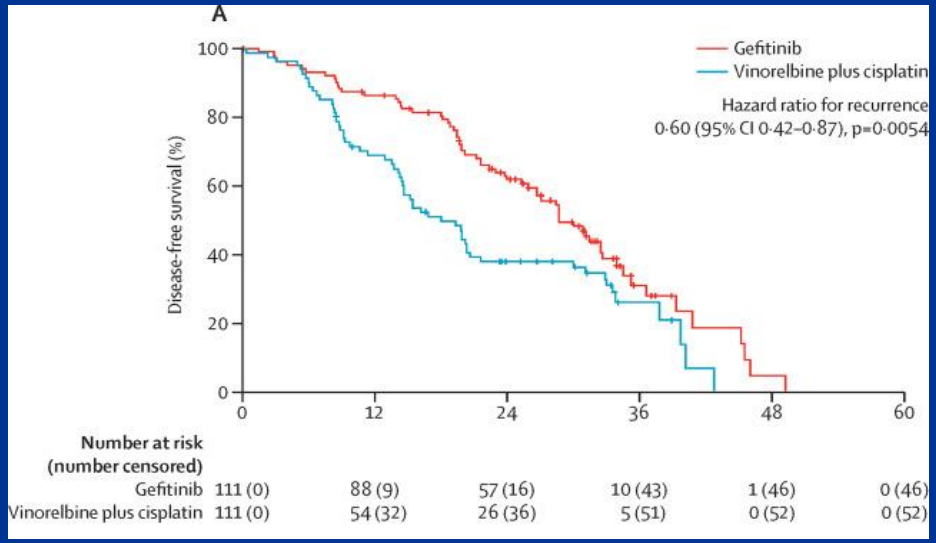
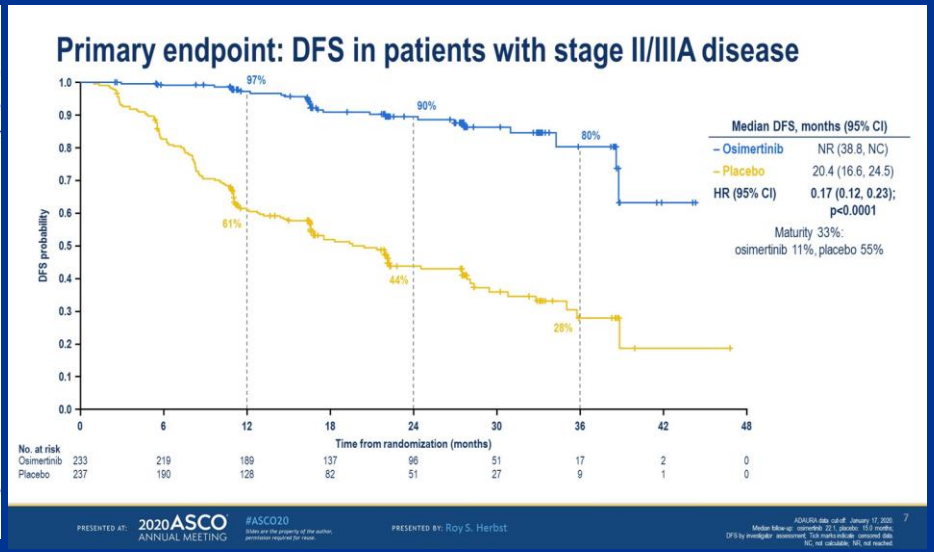
Genomics in early-stage disease: Adjuvant EGFR targeted therapies

CTONG 1104 Adjuvant Gefitinib



Wen-Zhao Zhong et al. Lancet Oncol. 2018 Jan;19(1):139-148.

ADURA Adjuvant Osimertinib



Herbst R et al. ASCO 2020 LBA5

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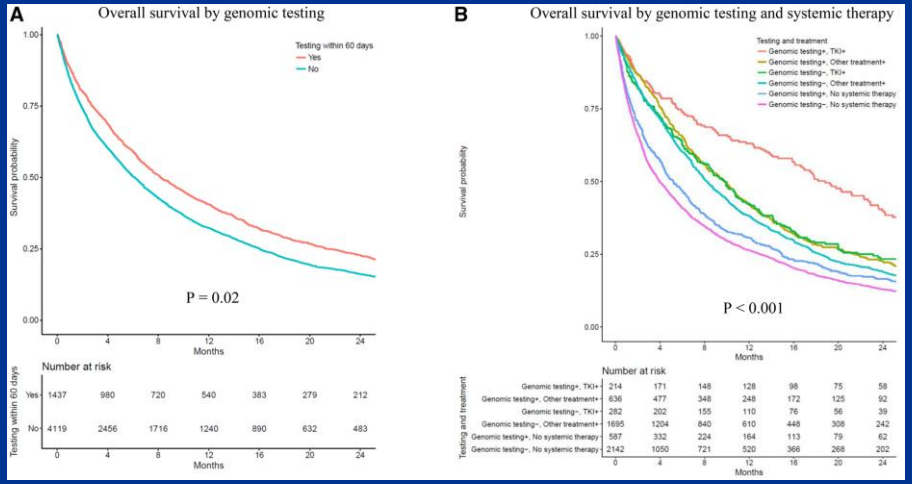
Disparity in genomic testing

- Younger patients < 75 years of age more likely to receive genomic testing (OR, 1.55)
- Race was associated with genomic testing (OR, 0.58, Black vs. White; OR, 2.45, Asian vs. White),
- Female gender had a higher likelihood of getting tested (OR, 1.45);
- Treatment with reference therapy (erlotinib) less likely among low-income patients (OR, 0.32)

Lauren L Palazzo et al. Cancer Epidemiol Biomarkers Prev. 2019 May;28(5):926-934; Julie A Lynch BMC Cancer 2018 Mar 20;18(1):306.

Genomic testing and targeted therapy within 60 days of lung cancer diagnosis associate with survival



- 5556 patients and 1437 (25.9%) had molecular testing
- Testing rates:
  - 14.1% (Blacks)
  - 26.2% (White)
  - 32.8% (Asian) (adjusted $P < .001$);
- Medicaid
  - 20.6% for Medicaid patients
  - 28.4% for non-Medicaid
- 19.9% in the highest poverty rate quintile vs 30.7% in the lowest quintile

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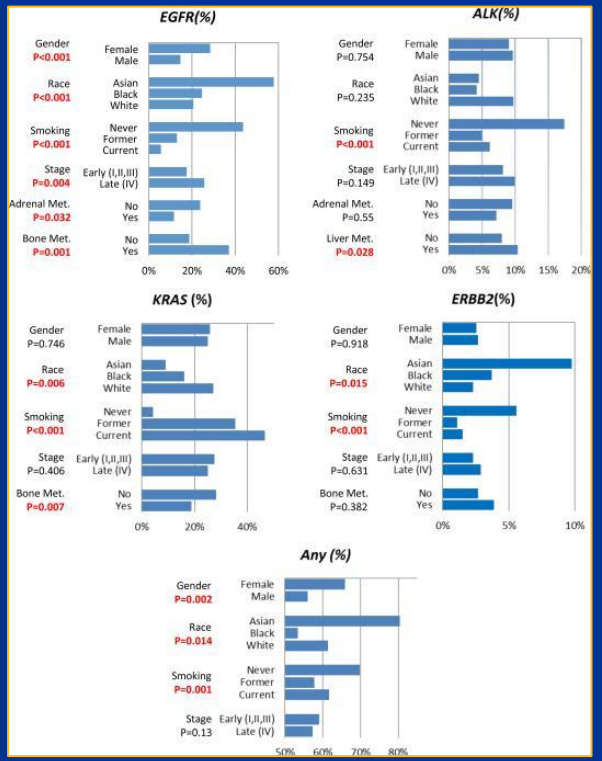
Kehl KL et al. J Natl Cancer Inst, Volume 111, Issue 4, April 2019, Pages 431–434,

Genomic mutational differences in lung cancer by ethnicity/race

	EGFR	KRAS	NTRK2	PTEN
EGFR	1	0	0	0
TP53	1	2	1	1

	BRAF	DDR2	EGFR	EPHA5	KRAS	MET	NRF2	PIK3CA
EGFR	0	0	2	0	1	0	1	0
NOTCH1	0	0	1	0	2	0	0	0
NRAS	0	0	0	0	2	0	0	0
STK11	0	0	0	1	0	0	0	0
TP53	1	1	1	2	4	0	1	2

Bollig-Fischer A et al. J Thorac Oncol. 2015 Feb;10(2):250-5.



Steuer C et al. J Thorac Oncol. 2015 May; 10(5): 768–777.

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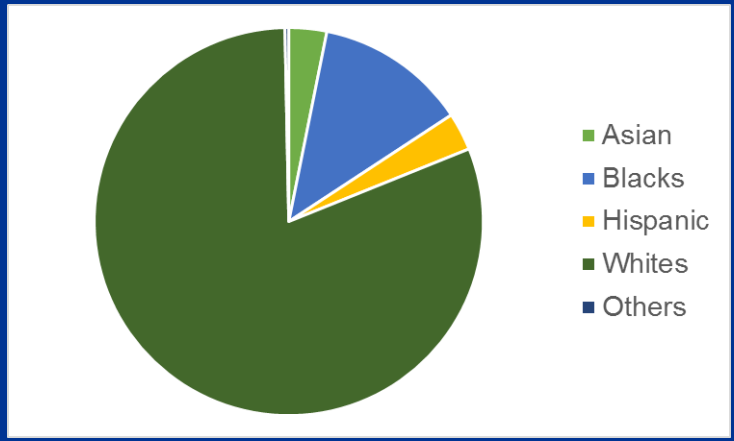
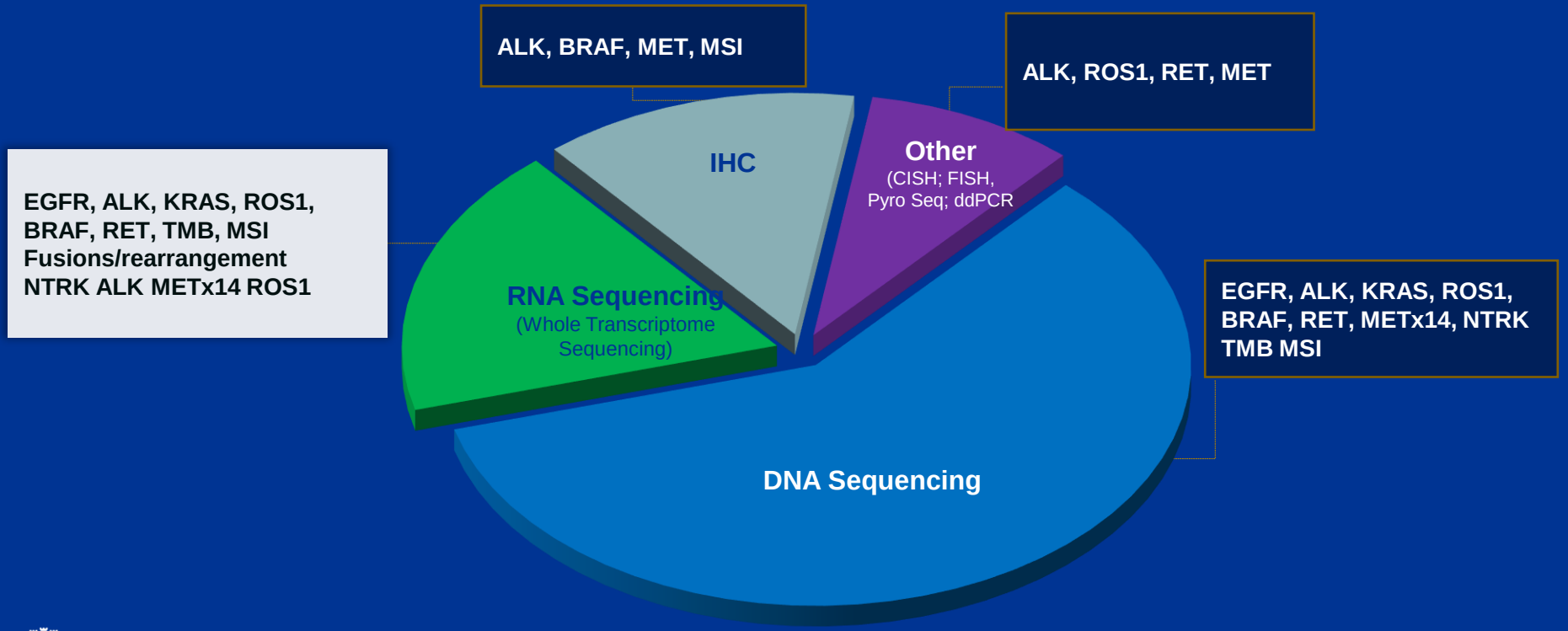
Prevalence of actionable mutations by race and ethnicity in TCGA

- 5729 samples
- Somatic mutational frequency:
  - 0.7 (prostate cancer)
  - 9.9 (lung squamous cell cancer)
- All tumor types from white patients contained enough samples to detect a 10% mutational frequency.
- Only Blacks with breast cancer
- Group-specific mutations frequency of 5% not detectable in racial minorities



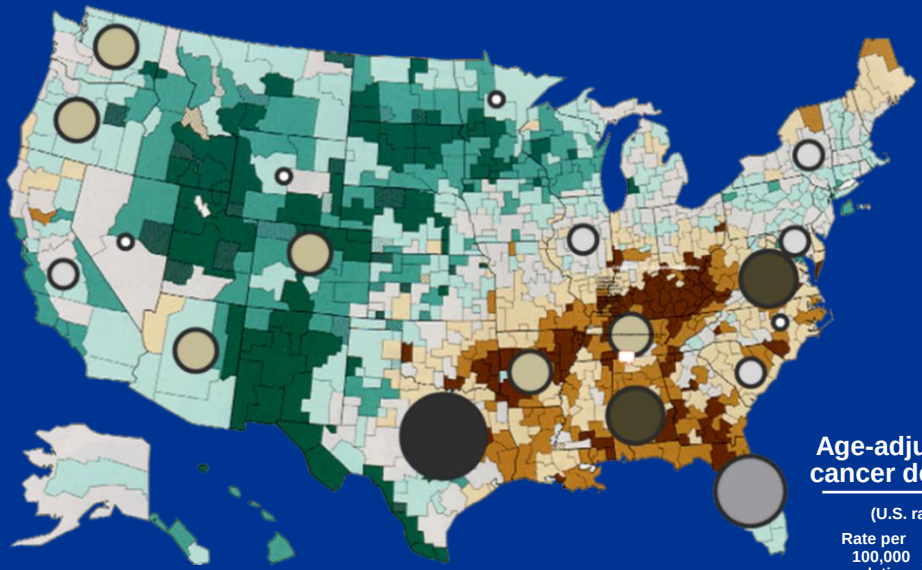
Spratt DE et al. JAMA Oncol. 2016 Aug 1;2(8):1070-4

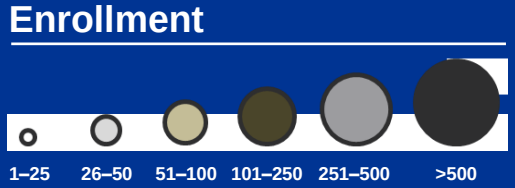
Technology platform for genomic testing for approved targeted therapies



CA209-118: A US Community Study

- The majority of metastatic NSCLC in the US is treated in the community
- CA209-118 is a prospective observational study examining 13 current lung cancer clinical networks/practices (70 investigators) in the community oncology setting
- This sub-study investigates biopsy and biomarker testing practices in stage IV NSCLC patients
- With the first patient recruited in April 2014, this analysis reflects current biopsy practices





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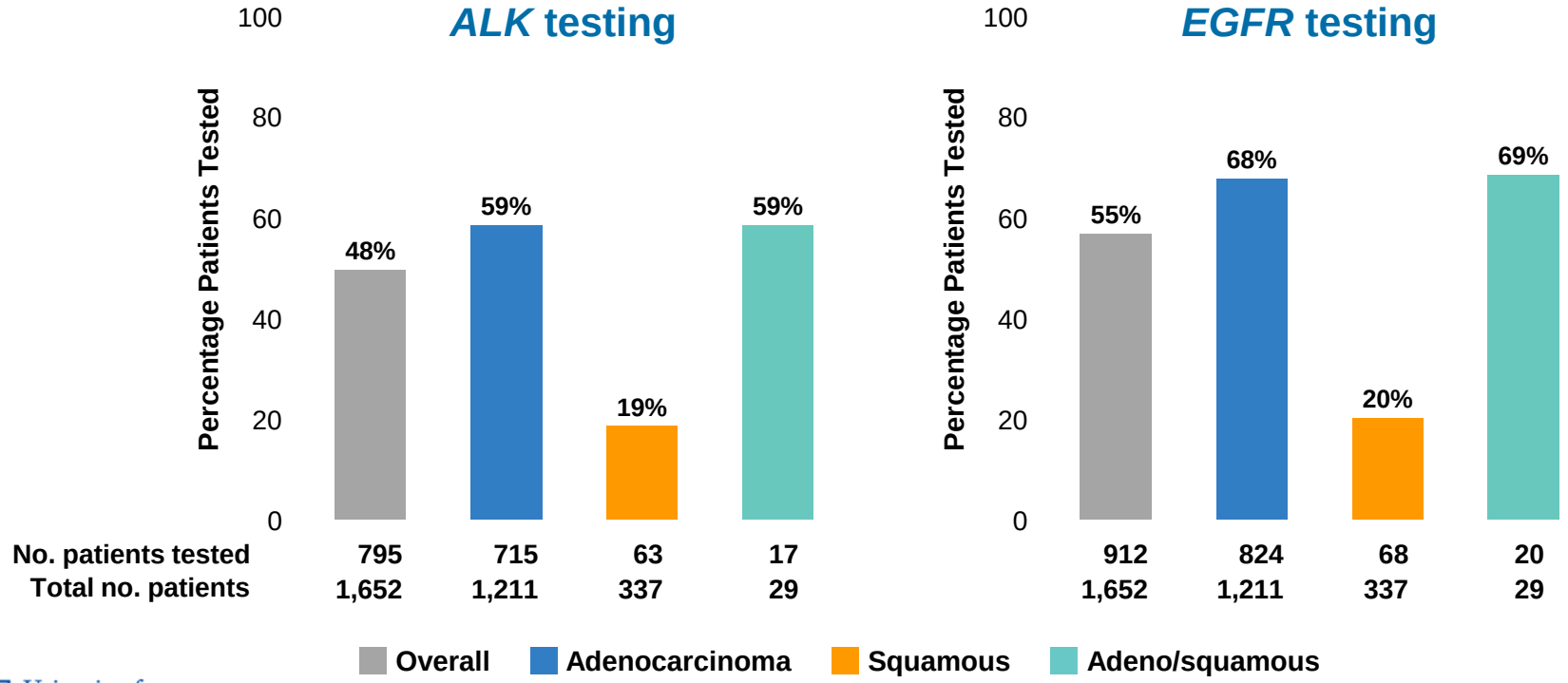
[a]In white males
Source: CDC/NCHS

Adoption of Mutation/Biomarker Testing for NSCLC in the Community



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Other genes widely tested in this population included *KRAS* (13%, 216/1,652), *ROS1* (10%, n=161/1,652), and *BRAF* (5%, n=80/1,652)

Clinical Factors Affecting *ALK*/*EGFR* Testing in Lung Adenocarcinoma

		ALK tested		*EGFR* tested	
		% (tested/total)	*P*	% (tested/total)	*P*
Overall		59 (715/1,211)		68 (824/1,211)	
Sex	Female	57 (353/620)	0.30	70 (431/620)	0.51
	Male	61 (358/584)		66 (388/584)	
	Missing	57 (4/7)		71 (5/7)	
Age at initial diagnosis	<75 years	60 (606/1,009)	0.15	68 (685/1,009)	0.58
	≥75 years	54 (109/202)		69 (139/202)	
Smoking status at initial diagnosis	Current	60 (266/441)	0.64	64 (282/441)	**0.006**[a]
	Former	58 (310/538)		67 (363/538)	
	Never	60 (136/225)		77 (174/225)	
	Missing	43 (3/7)		71 (5/7)	
Race/ethnicity	Caucasian	60 (638/1,057)	0.09	69 (729/1,057)	**0.04**[a]
	African-American	48 (50/105)		59 (62/105)	
	Asian	59 (10/17)		88 (15/17)	
	Other/mixed	63 (10/16)		50 (8/16)	
	Declined/missing	44 (7/16)		63 (10/16)	
Stage at diagnosis	I	51 (38/74)	**0.03**[a]	65 (48/74)	0.38
	II	46 (28/61)		72 (44/61)	
	III	55 (71/130)		62 (81/130)	
	IV	61 (578/946)		69 (651/946)	

- In adenocarcinoma, the frequency of *ALK* testing was influenced by stage at diagnosis
- Ethnicity and smoking status, two characteristics known to affect the prevalence of *EGFR* mutation, influenced the likelihood of performing *EGFR* testing

[a]Statistically significant

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Immunotherapy

Host and Tumor Biomarkers to Predict Better Outcomes with I-O Therapy

Tumor Antigens

- Biomarkers indicative of hypermutation and neo-antigens may predict response to I-O treatment

Examples:

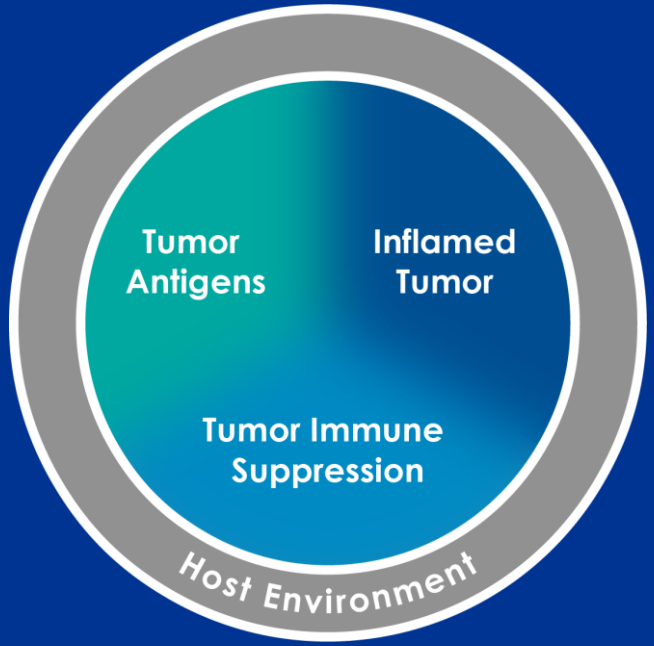
- ***TMB, MSI-high, neo-antigens***

Tumor Immune Suppression

- Biomarkers that identify tumor immune system evasion beyond PD-1/CTLA-4 to inform new I-O targets and rational combinations

Examples:

- ***Tregs, MDSCs, IDO, LAG-3***



Inflamed Tumor Microenvironment

- Biomarkers (intra- or peri-tumoral) indicative of an inflamed phenotype may predict response to I-O treatment

Examples:

- ***PD-L1, inflammatory signatures (IFN-gamma)***

Host Environment

- Biomarkers which characterize the host environment, beyond tumor microenvironment, may predict response to I-O treatment

Examples:

- ***Microbiome, germline genetics***

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CTLA4=cytotoxic T-lymphocyte antigen 4; I-O=immuno-oncology; IDO=indoleamine-2,3 dioxygenase; IFN=interferon; LAG-3=lymphocyte activation gene-3; MDSCs=myeloid-derived suppressor cells; MSI-High=microsatellite instability high; PD-1=programmed death receptor-1; PD-L1=programmed death ligand 1; TMB=tumor mutational burden; Treg=regulatory T cell.

Blank CU et al. *Science*. 2016;352:658-660.

2021 ASCO ANNUAL MEETING

OUTCOMES OF ANTI-PD-(L)1 THERAPY IN COMBINATION WITH CHEMOTHERAPY VS. IMMUNOTHERAPY (IO) ALONE FOR FIRST-LINE (1L) TREATMENT OF ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC) WITH PD-L1 SCORE 1-49%: FDA POOLED ANALYSIS

Oladimeji Akinboro[1], Jonathon Vallejo[1], Pallavi Mishra-Kalyani[1], Erin Larkins[1], Nicole Drezner[1], Shenghui Tang[1], Richard Pazdur[1,2], Julia A. Beaver[1,2], Harpreet Singh[1,2]

[1]Center for Drug Evaluation and Research, U.S. Food and Drug Administration.

[2]Oncology Center of Excellence, U.S. Food and Drug Administration.

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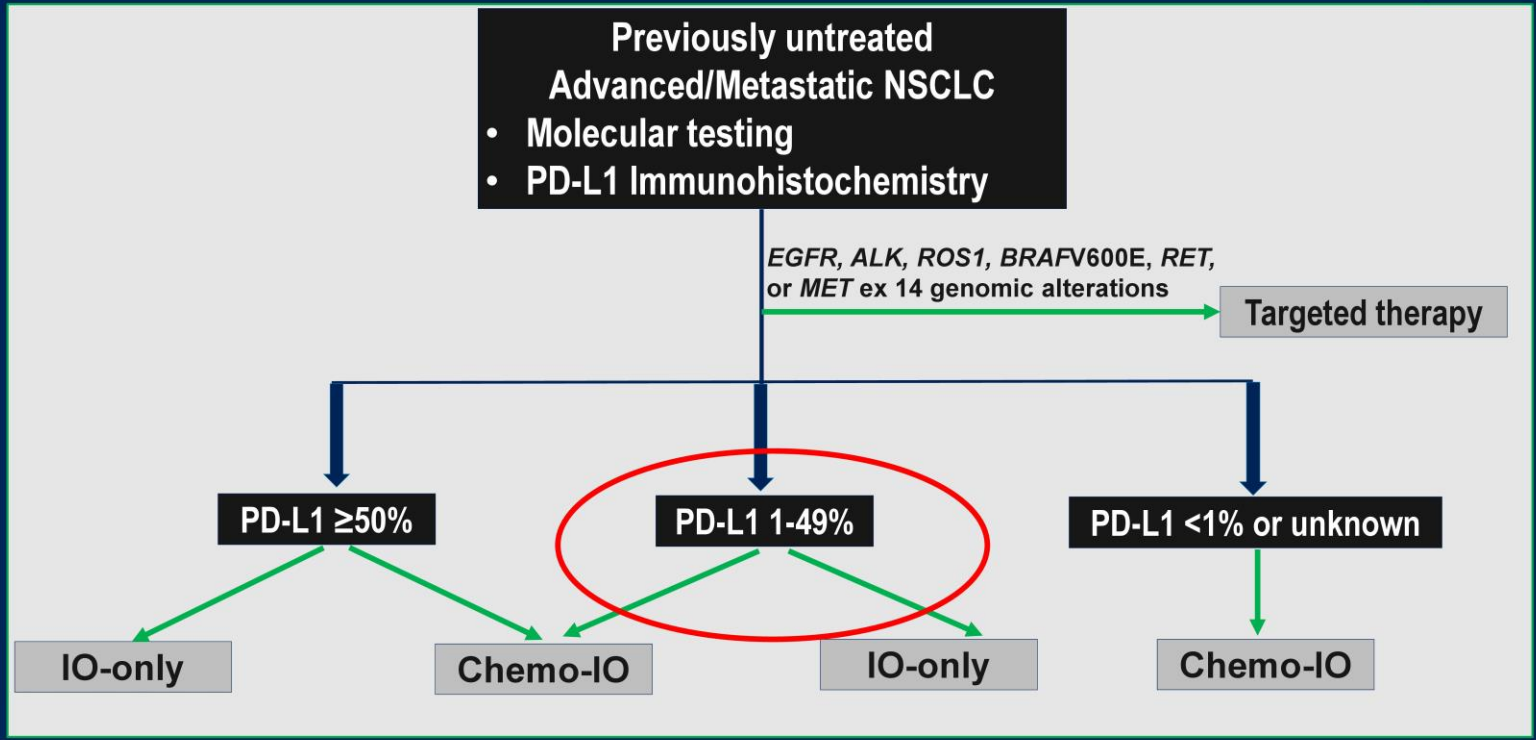
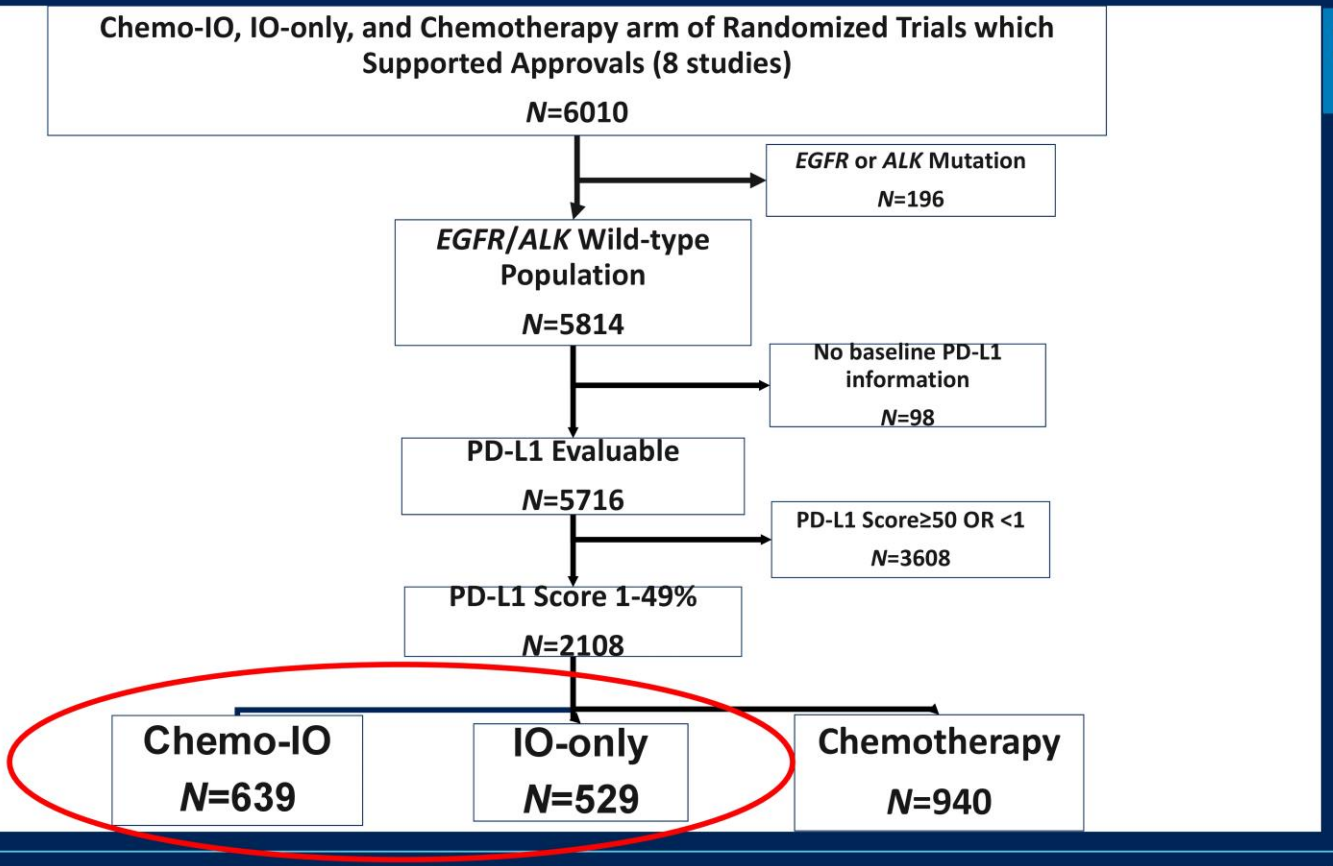
Background





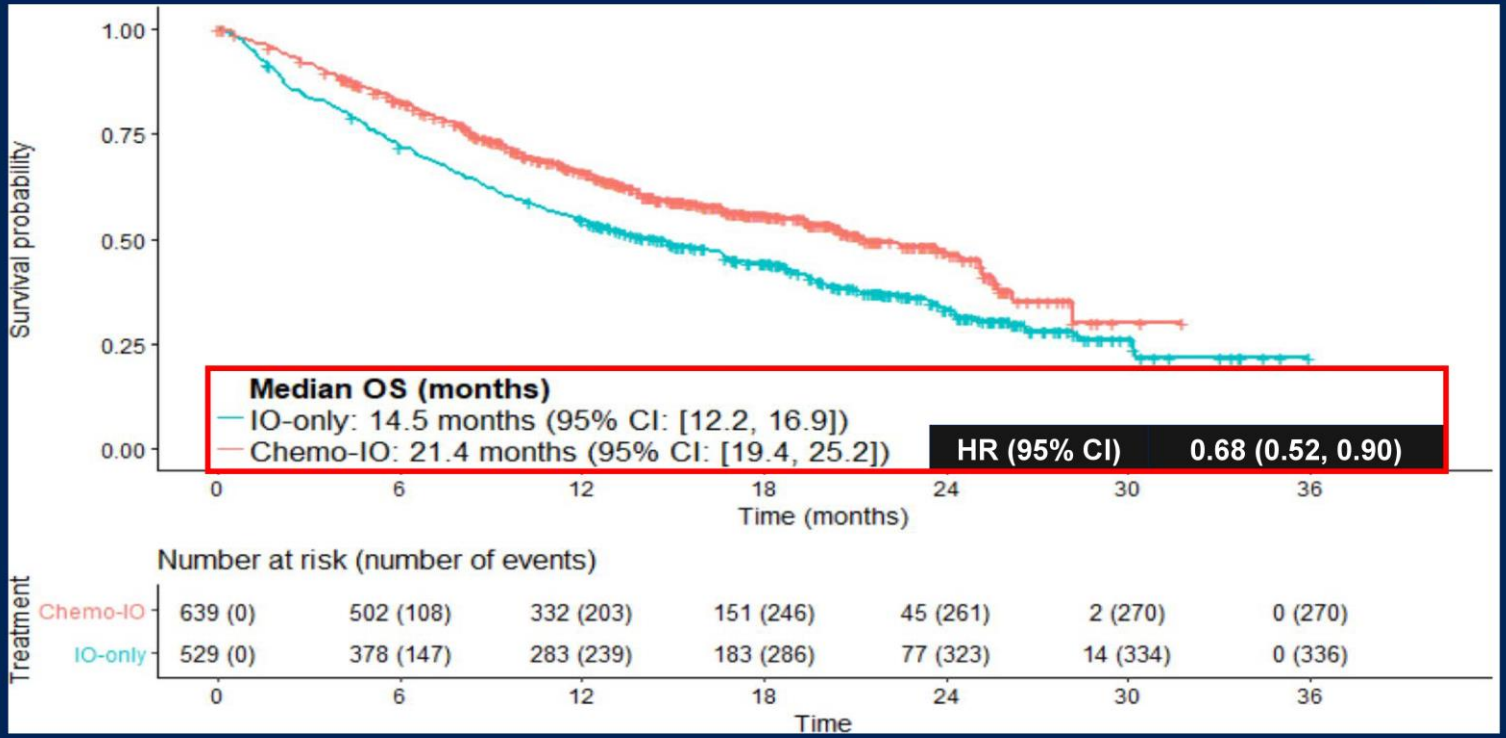
FDA

Demographic and baseline characteristics

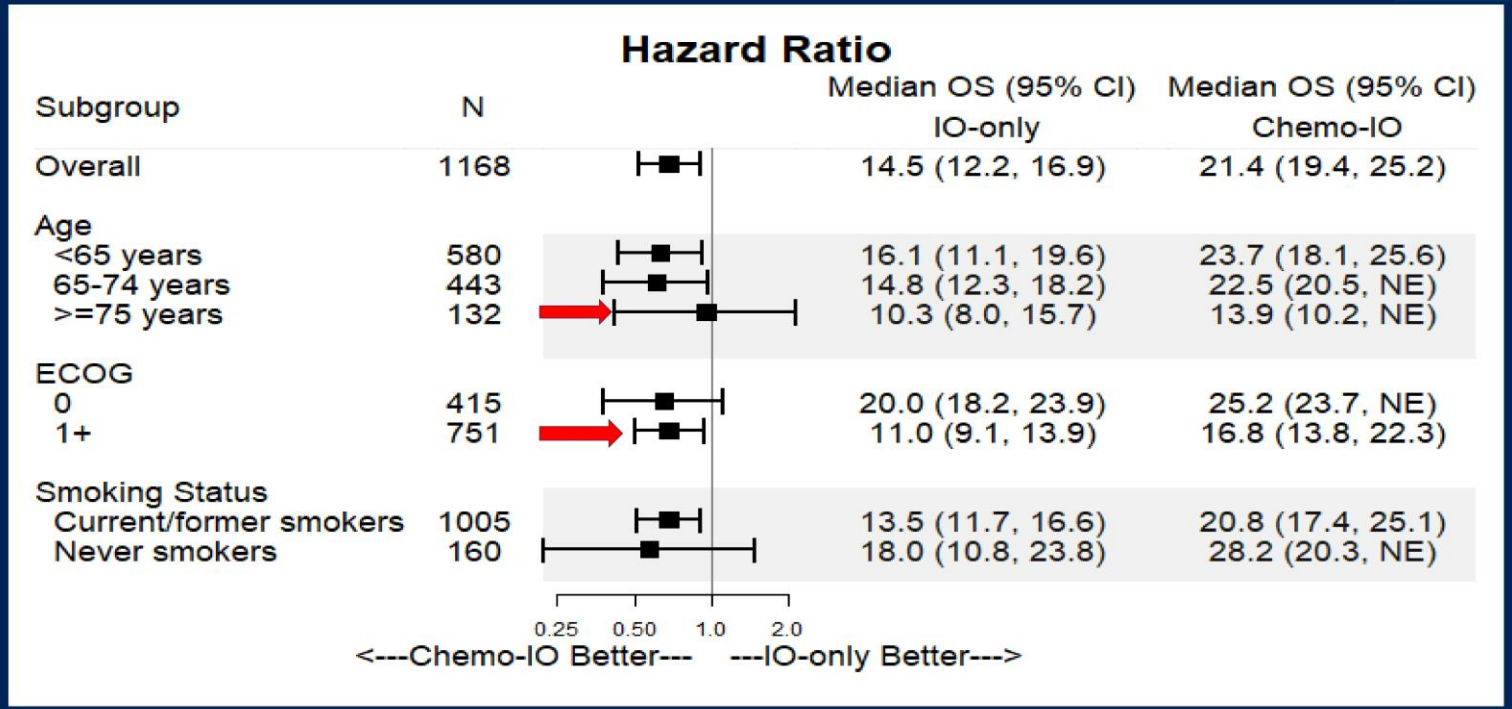
	Chemo-IO (*N*=639) %	IO alone (*N*=529) %	Chemo (*N*=940) %	Overall (*N*=2108) %
Age <65 years	48	53	53	51
65–74 years	40	36	36	37
≥75 years	11	11	12	12
Female	35	31	32	33
White	88	69	78	79
Asian	9	23	19	17
Black/African-American	2	2	2	2
Current/Prior Smokers	91	81	84	85
ECOG-PS ≥1	62	67	67	65
Non-squamous	77	63	64	68
Stage IV	89	91	92	91

Exploratory OS: NSCLC PDL1 1-49%

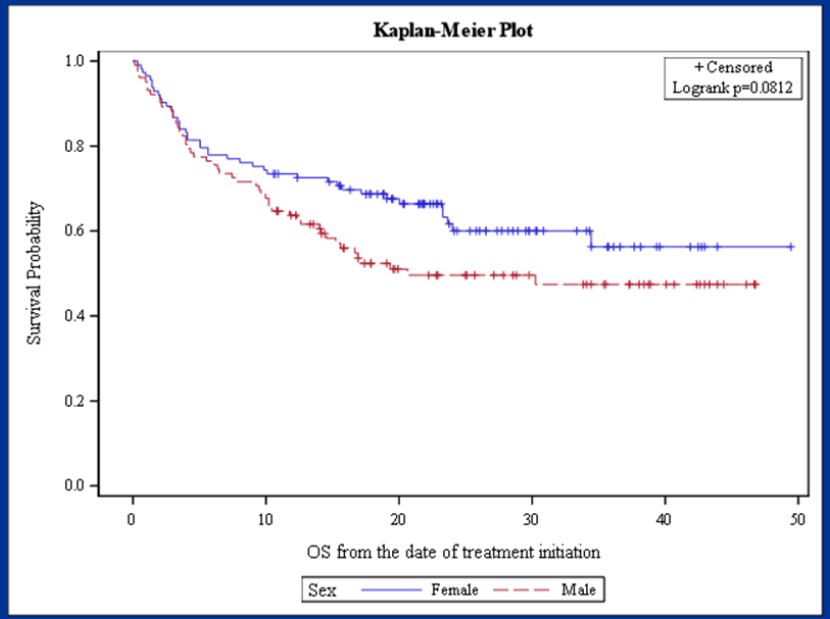
FDA

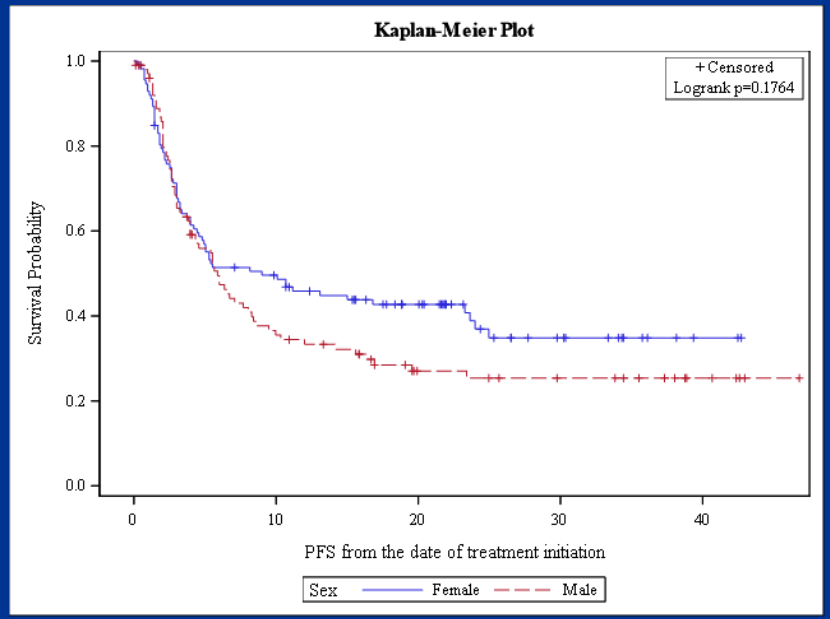


OS in PDL1 1-49%: Subgroup analyses



Efficacy of ICB by gender – Emory Winship Experience





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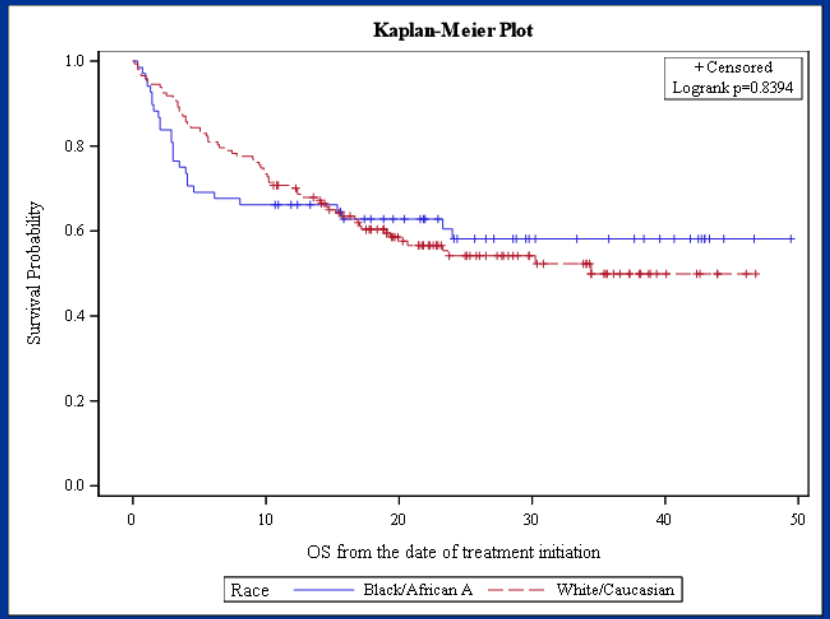
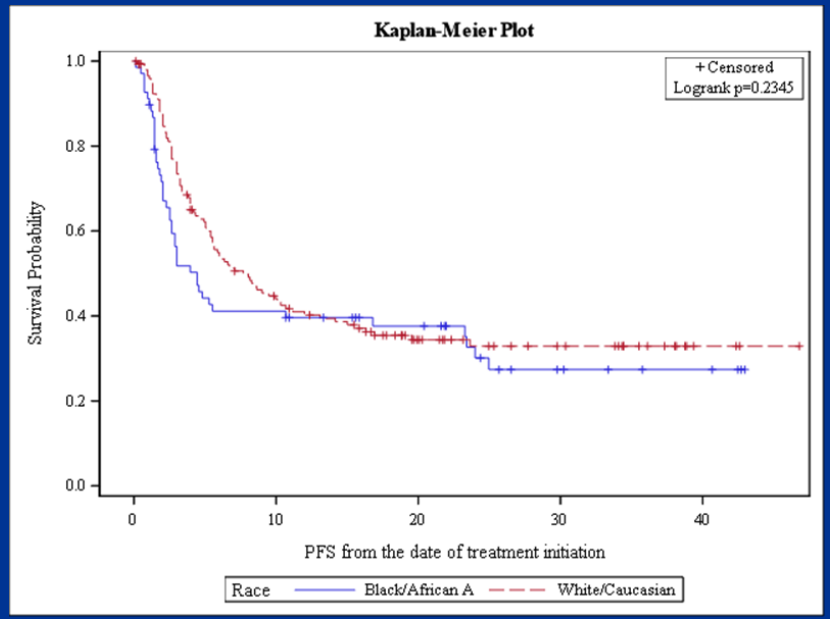
B Nazha et al. ASCO 2020

Efficacy of ICB in Blacks compared to Caucasian – Winship Experience





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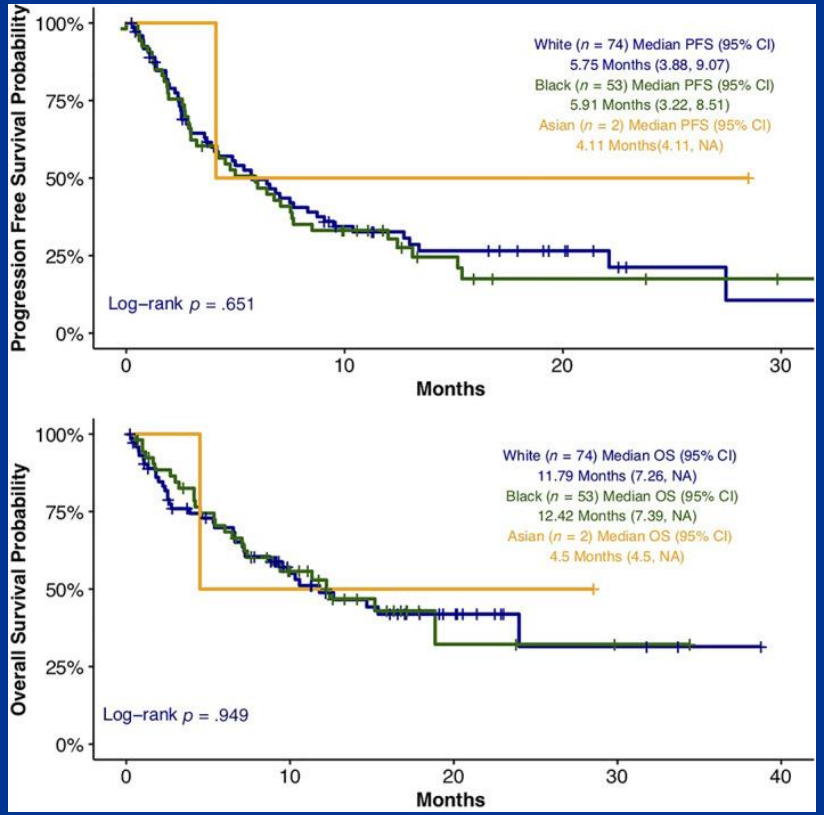
B Nazha et al. ASCO 2020

Independent validation of comparative ICB efficacy by race in the community setting



Peravali et al. Oncologist. 2021 Aug; 26(8): 694–700.

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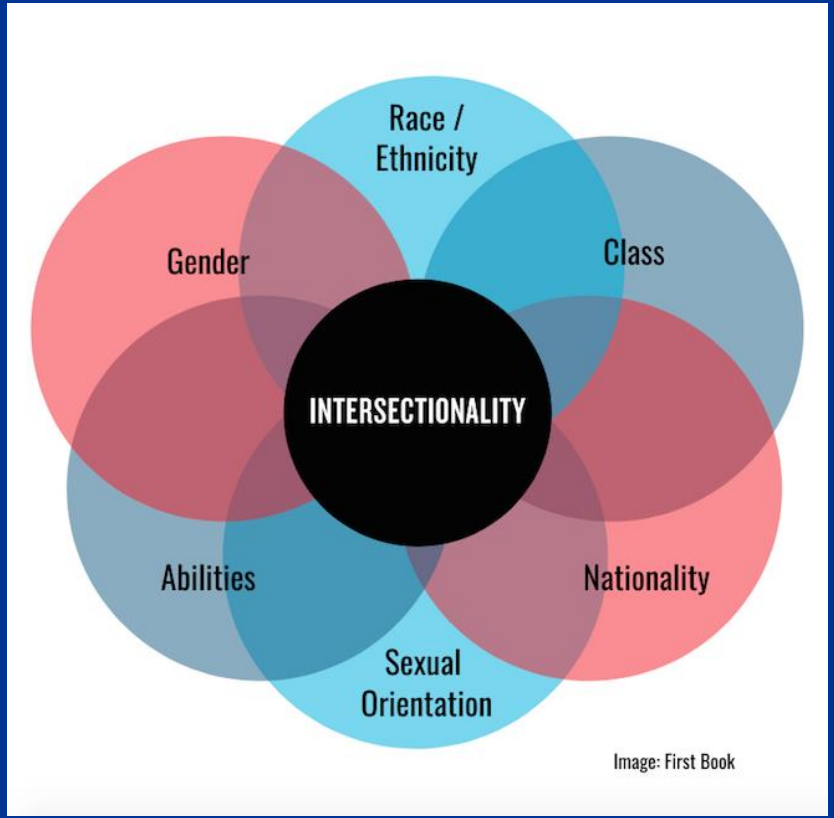
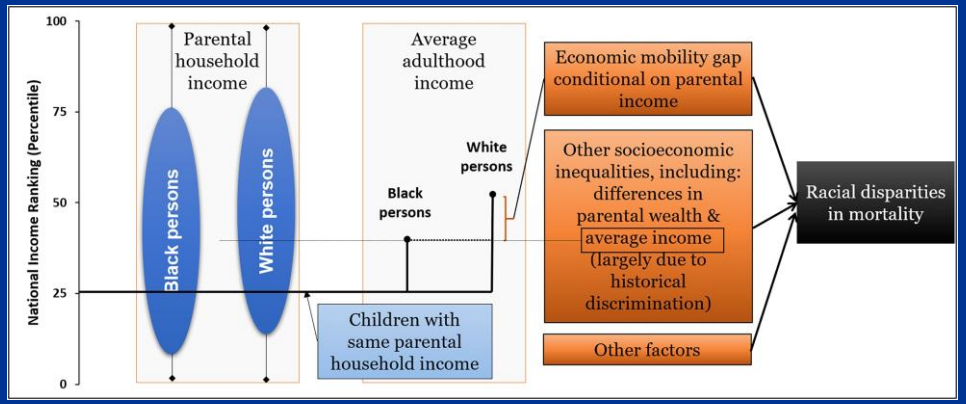
Intersectionality



https://www.weforum.org/agenda/2021/10/here-s-how-organizations-put-intersectionality-to-work/

Racial economic mobility gap and disparities in mortality



	Male	Females
Lung and bronchus	**19.7 (13.5–25.9)**	**−39.4 (−31.0 to −47.7)**
Colorectum	7.0 (3.8–10.3)	7.8 (5.3–10.3)
Pancreas	8.7 (2.6–14.8)	NR
Liver and IHBD	7.1 (2.9–11.3)	12.7 (6.5–18.9)

Islami F et al. Cancer Epidemiology Volume 74, October 2021, 101998

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Conclusions

- Gender, race, rurality and access to care are known drivers of disparities in lung cancer
- Proper recognition of diversity in cancer-associated genetic alterations is critical to the overall success of personalized cancer care
- Low enrolment of US ethnic minorities in local and national tissue acquisition protocols limits ability to detect unique alterations in this population
- Ethnicity, age and other demographic enrichment strategies should be incorporated into tissue science
- Demographic or histologic factor should not play a determinant role in testing decision