Addressing Disparities in Care for Patients with DLBCL

Dr. Armitage: Welcome to PracticalHematologist.com. My name is Jim Armitage and I'm a professor of medicine at the University of Nebraska Medical Center. Today, I am joined by Dr. Loretta Nastoupil who is a lymphoma expert, and an associate professor at MD Anderson Cancer Center.

Addressing Disparities in Care for Patients with DLBCL

Faculty Disclosures

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Honorarium: ADC Therapeutics SA, Bristol-Myers Squibb Company, Caribou Biosciences, Inc., Epizyme, Inc., Genentech Inc., Gilead Sciences, Inc., Janssen Pharmaceuticals, Inc., MorphoSys AG, Novartis AG, Takeda Oncology

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Dr. Armitage: These are our disclosures.

Addressing Disparities in Care for Patients with DLBCL

Learning Objectives

- Discuss key data from recent publications and conferences on disparities in care for patients with DLBCL
- Describe current and potential practice implications

Dr. Armitage: Today's presentation will address disparities in care for patients with diffuse large B-cell lymphoma, the most common lymphoma. In this presentation, Loretta will discuss key data from recent publications and conferences on disparities in care for patients with diffuse large B-cell lymphoma and describe current and potential practice implications and we will then conclude by discussing best practice.

This is not a trivial issue, and it's becoming increasingly clear that there are significant disparities. I will now turn the floor over to Dr. Nastoupil.

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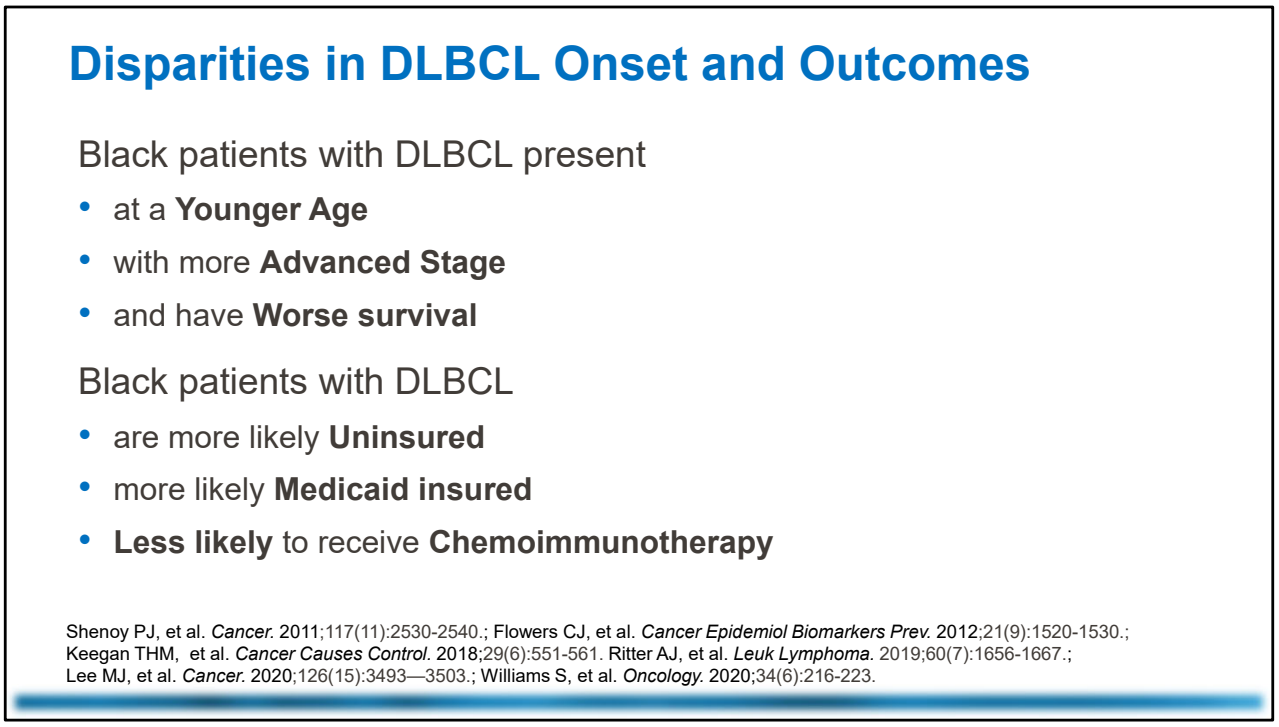

Dr. Nastoupil: Thanks, Dr. Armitage. I think diffuse large B-cell lymphoma is a great area to really dig deep into racial disparities mostly because most patients should anticipate a cure with standard therapy. This does give us the opportunity to really explore, "Is that true for all patients?" What we know about diffuse large B-cell lymphoma and race is that black patients with large cell lymphoma often present at a younger age with more advanced stage and actually have inferior survival. Interestingly, patients with large cell lymphoma, including black patients are more likely uninsured, more likely to have Medicaid insurance, less likely actually to receive chemoimmunotherapy, and I'll show you the data that backs up those statements.

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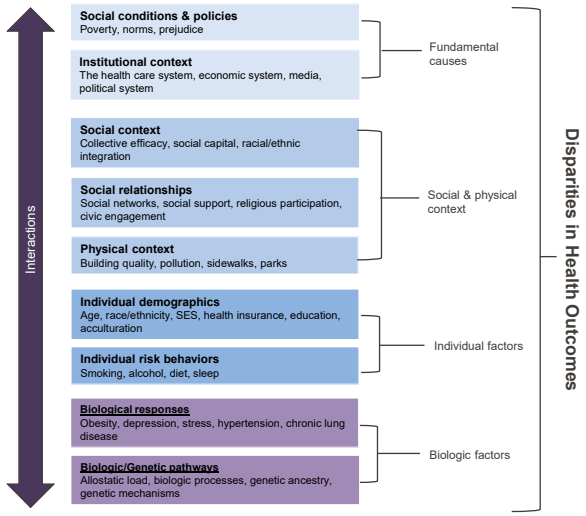
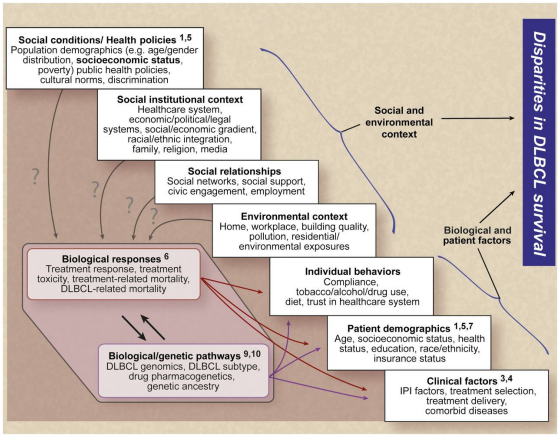
What contributes to survival disparities?





Warnecke RB, et al. *Am J Public Health.* 2008;98(9):1608-1615.; Flowers CR and Nastoupil LJ. *Blood*. 2014;123(23):3530-3531.

I think health disparities is a very complicated issue. It's a complex interaction from a number of variables, not only patient demographics but also socioeconomic status, where these patients reside, access to healthcare, not only at the time of diagnosis but potentially preventative strategies, early detection, access to what we would consider good quality standard of care, but there's probably also some underlying underpinnings of the biology of the disease that may describe some of these disparate outcomes. It's important to explore all of these variables if we really do intend to minimize these disparate outcomes and either influence policies or access to care for all patients.

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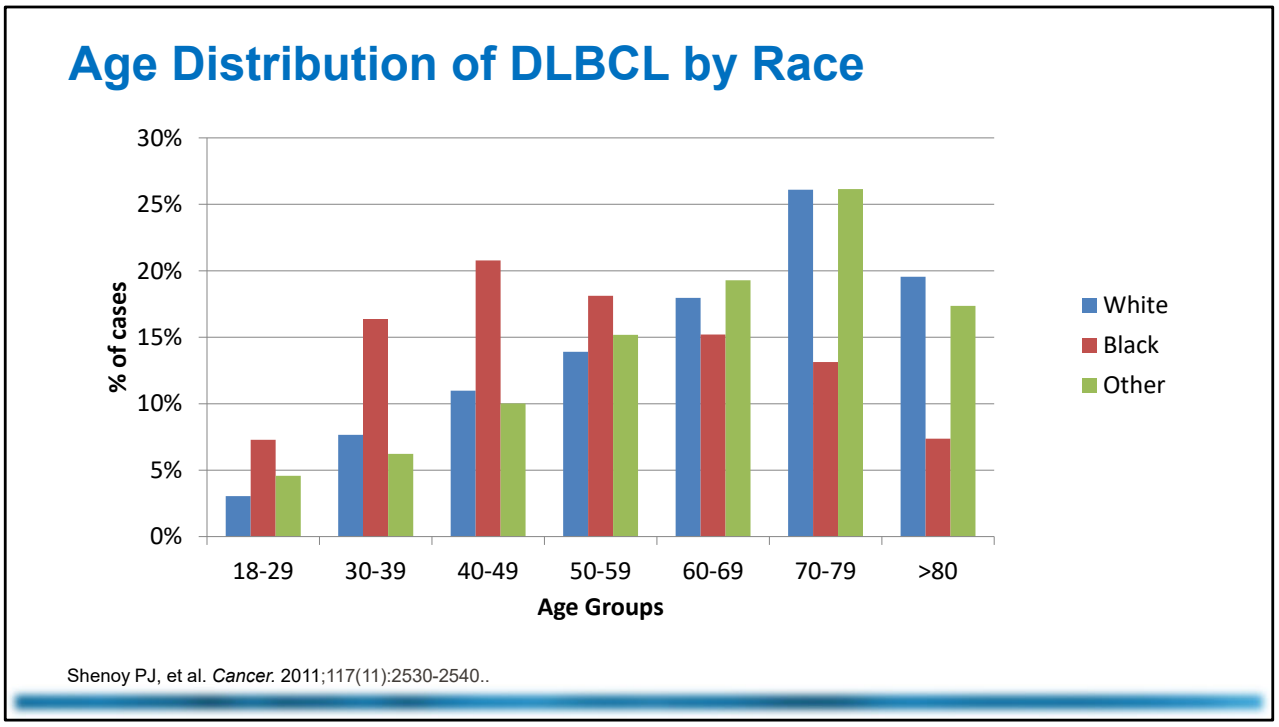

I mentioned that African American or black patients present at a younger age. This is SEER data, looking at the age of diagnosis according to race. You can see here outlined by the blue bars. Those are white patients, the red bars are black patients, and then green is other. You can see this age of distribution. You see younger patients or patients that were black presenting at a younger age. That looks quite starkly different to me than those patients who are white, who present primarily in their 60s to 70s.

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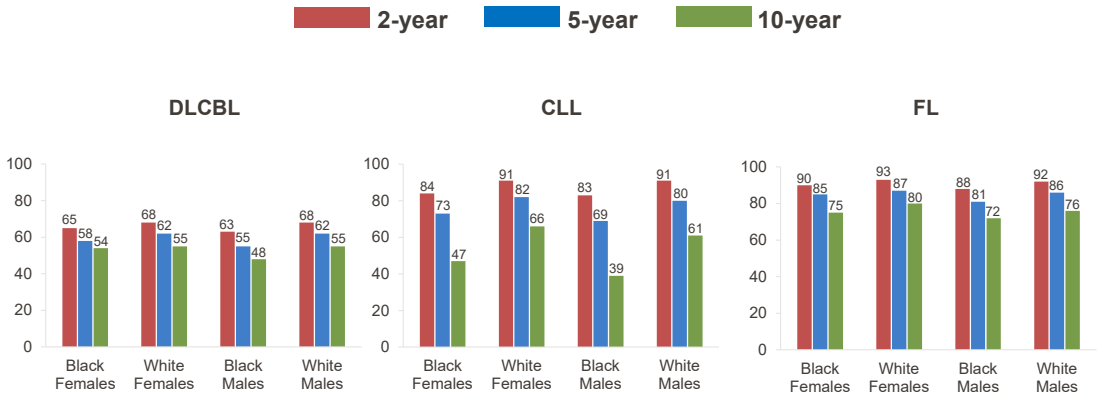
Survival by Gender and Race for Cancer Subtypes



U.S. cancer statistics for lymphoid malignancies by World Health Organization subtypes

Teras LR, et al. *CA Cancer J Clin.* 2016;66(6):443-459.

We also know that survival is different. Again, looking across the National Cancer Database according to race, not only large cell lymphoma, but other heme malignancies such as CLL and follicular lymphoma. We'd look at race and gender, so black males tend to have the worst survival, particularly with diffuse large B-cell lymphoma, even less favorable than black female patients, but both do worse than white male or female patients. Again, highlighting that these patients are facing inferior survival, both at two years, five years, and even 10 years.

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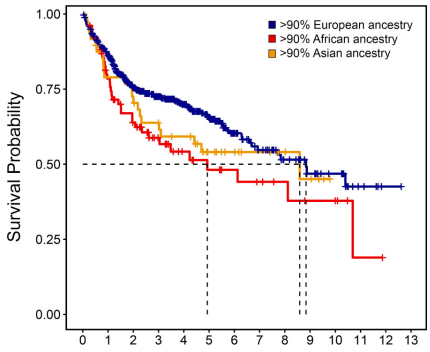
Genome-Defined African Ancestry is Associated with Distinct Mutations and Worse Survival in Patients with DLBCL



Driver mutations	European Ancestry	African Ancestry	P - value
ATM	7.75 %	21 %	< 0.001
MGA	5.33%	19.7 %	< 0.001
SETD2	5.17 %	17.3 %	< 0.001
TET2	5.82 %	12.3 %	0.029
MLL3	4.36 %	11.1 %	0.013
DNMT3A	4.52 %	11.1 %	0.016

Lee MJ, et al. *Cancer.* 2020;126(15):3493-3503.; Shenoy PJ, et al. *Cancer.* 2011;117(11):2530-2540..

Is there underlying biological differences that may explain these disparate outcomes? One approach to try and address this was a large study where they performed whole exome sequencing to look at underlying again, biological drivers of this disease. They had a comparison with those of European ancestry versus African ancestry versus other. You can see there were actually genes that were statistically more significantly found in patients of African ancestry, and they're outlined on this slide, suggesting that there is indeed some differences in the underlying drivers of diffuse large B-cell lymphoma.

Now again, how we might translate that into clinical practice, we need a larger validation set, and we need more information how to potentially identify these genes and whether or not treatment should be modified as a result, but it does shed some light, at least in my opinion, that again, this is a complex issue. It's not just access to care but also potentially some underlying biological differences.

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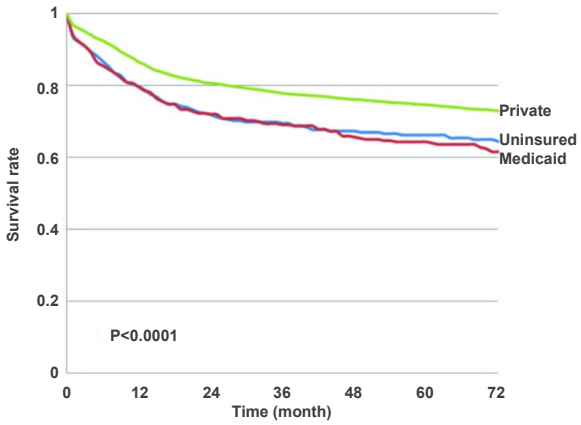
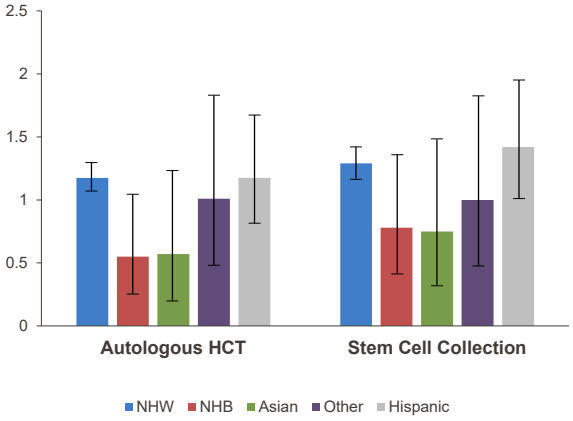
Differences in survival not explained by biology alone

DLBCL Patients with Private insurance had better survival



Han X, et al. *Cancer.* 2014;120(8):1220-1227.

Minorities less likely to receive standard of care Stem Cell transplant



Vaughn JL, et al. *Cancer Med.* 2021;10(20):7330-7338.

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Biology doesn't explain this in isolation. As I also mentioned that the onset, the type of insurance patients have is also associated not only with survival but access to care, including therapies like stem cell transplant. Patients who are privately insured have better survival, and again, black patients or Hispanic patients were less likely to receive standard-of-care stem cell transplant, potentially considered a very resource-rich therapy, again, suggesting that many of these patients may have barriers to access to care.

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Disparities in the Early Adoption of Chemoimmunotherapy for Diffuse Large B-cell Lymphoma in the United States

Objective

To investigate the factors affecting diffusion of chemoimmunotherapy for DLBCL.

Approach

Using National Cancer Database (NCDB) to compare chemoimmunotherapy use with chemotherapy alone, authors collected data on demographics, stage, health insurance, area-level socioeconomic status (SES), facility characteristics, and type of treatment for DLBCL patients diagnosed in 2001–2004.

- Among 38,002 patients with DLBCL, 27% received chemoimmunotherapy and 50% chemotherapy alone.
- Patients who had localized disease, who were black, uninsured/Medicaid insured, or lower SES were less likely to receive any form of chemotherapy
- Patients who were black and >60 years were less likely to receive chemoimmunotherapy.
- Multivariable log binomial models examined associations between race, insurance, and treatment allocation, adjusting for covariates.

Flowers CJ, et al. *Cancer Epidemiol Biomarkers Prev.* 2012;21(9):1520-1530.

One study we set out to look at was when you have a drug like rituximab that has clearly altered the natural history of this disease, improving survival for patients, do black patients have the same access to care? Utilizing the National Cancer Database, we looked in the early years following the introduction of rituximab into the treatment landscape of large cell lymphoma and demonstrated that black patients were less likely to receive chemoimmunotherapy. Again, that's rituximab in combination with anthracycline-based treatment but also less likely to receive chemotherapy altogether.

Now, again, there were additional factors such as insurance status, socioeconomic status, but being black and being over the age of 60 resulted in the observation that they were less likely to receive chemoimmunotherapy. Again, this was in the setting where we knew that these agents potentially could improve survival.

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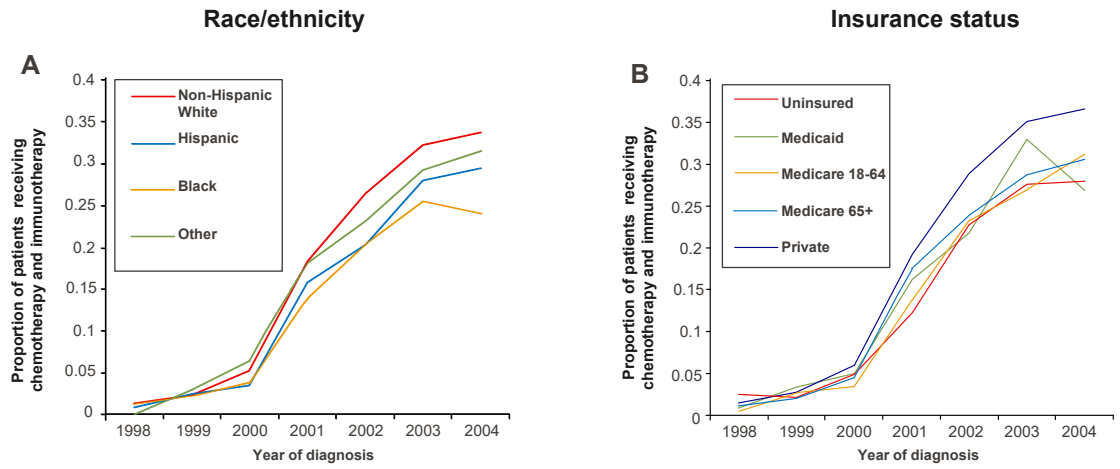
Receipt of chemotherapy and immunotherapy



This figure provides the distribution of therapy received by patients in the NCDB between 1998 and 2004

Flowers CJ, et al. *Cancer Epidemiol Biomarkers Prev.* 2012;21(9):1520-1530.

Again, distinguishing this from insurance status and access to care is quite complex.

Once again, black patients and those that were underinsured either having Medicaid or no insurance at all, all were independent variables that were associated with inferior survival, suggesting that we may need to address policies that provide equal and equitable access to adequate insurance that may then translate into better treatment options.

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Rural and urban patients with DLBCL have lower OS: a National Cancer Data Base study

- Examined 83,108 patients with DLBCL and 43,393 patients with FL to investigate disparities related to geographic population density

Results

- Rural patients less commonly had private insurance and high socioeconomic status
- Rural DLBCL patients ↑ likelihood treatment ≤14 days of diagnosis (OR 0.81, 95% CI 0.72–0.91)
- Multivariable analyses rural patients had worse OS
  - with DLBCL (1.08; 95% CI 1.04–1.11)

Ritter AJ, et al. *Leuk Lymphoma.* 2019;60(7):1656-1667.

Also, where patients reside impacted their survival, so looking at patients that resided in rural areas that may not have access to specialized centers that have expertise in these rare tumor types also were associated with outcomes.

It's actually quite interesting, patients with large cell lymphoma that resided in a rural area were more likely to receive treatment within 14 days of diagnosis. Now, that may seem as a misconception about being associated with less favorable outcomes, but we know that patients with large cell lymphoma who have a longer time from diagnosis to initiation of treatment, actually do more favorable.

That may suggest that these patients get diagnosed at an earlier time point in their disease course, where they have the luxury of setting up staging and treatment in an outpatient setting. Whereas patients who may not have access to adequate care may present at more advanced stage and need to initiate treatment much more urgently. Again, we know that early initiation of treatment has been associated with less favorable outcomes.

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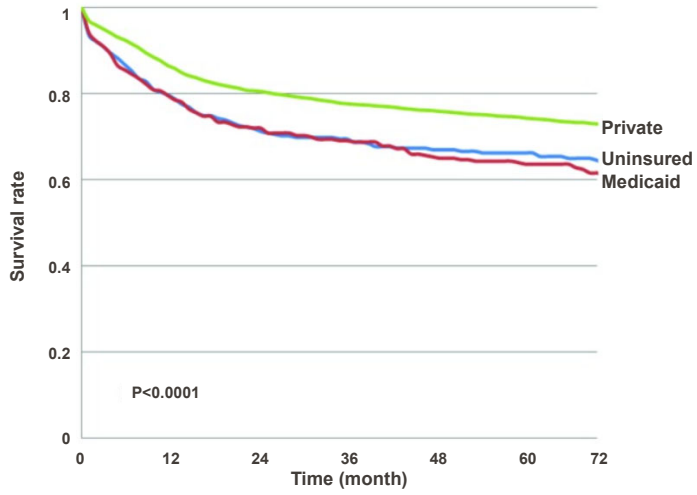
Insurance Status Is Related to DLBCL Survival



Han X, et al. *Cancer.* 2014;120(8):1220-1227.

Again, this probably speaks to whether or not patients have access to care and just more data suggesting that those that are uninsured or even Medicaid insured tend to have less favorable outcomes than those who are privately insured.

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Insurance Status and Outcomes

- Uninsured and Medicaid-insured patients with DLBCL had inferior survival compared with privately insured patients.
- These associations can be explained in part because uninsured/Medicaid-insured patients who have DLBCL present with more advanced-stage disease and comorbid illnesses and less commonly receive standard treatment.
- Access to affordable and adequate health care has the potential to improve survival for patients with DLBCL.

To summarize, these outcomes based off of what we perceive to be access to good quality care, black patients are often uninsured or have Medicaid insurance. That has been associated with less favorable outcomes, more advanced stage at presentation, more likely to receive treatment within 14 days of treatment. This suggests that we may need to do a better job of providing adequate coverage and access to minority patients.

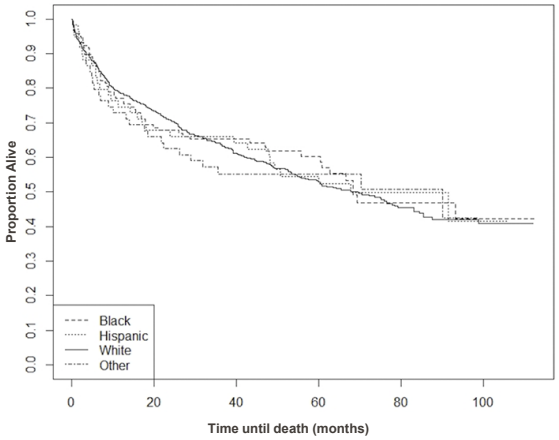
Addressing Disparities in Care for Patients with DLBCL

When similar treatments can be administered, similar outcomes can occur

The Impact of Race and Ethnicity on Diffuse Large B-Cell Lymphoma (DLBCL) Outcomes within the Veterans Health Administration (VHA)

Response rate to first-line chemotherapy and survival					
	All Patients	**Black**	**Hispanic**	**White**	**Other/ Unknown**
Response to Chemo					
CR	641 (66%)	80 (66.7%)	42 (68.9%)	477 (65.3%)	42 (70%)
PR	66 (6.8%)	4 (3.3%)	4 (6.6%)	54 (7.4%)	4 (6.7%)
SD	18 (1.9%)	3 (2.5%)	1 (1.6%)	13 (1.8%)	1 (1.7%)
PD	84 (8.7%)	14 (11.7%)	4 (6.6%)	62 (8.5%)	4 (6.7%)
Response unknown/ no therapy given	162 (16.7%)	19 (15.8%)	10 (16.4%)	124 (17%)	9 (15%)
ORR	87.4%	83.2%	90.2%	87.6%	90.2%
Survival from time of diagnosis					
1-year survival	736 (75.8%)	91 (75.8%)	44 (72.1%)	558 (76.4%)	43 (71.7%)
2-year survival	655 (67.5%)	80 (66.7%)	39 (63.9%)	500 (68.5%)	36 (60%)
Median OS, months	40.5	43	49.2	40.5	33.3

KM Survival Curve by Race



Williams, MH, et al. "The Impact of Race and Ethnicity on Diffuse Large B-Cell Lymphoma Outcomes within the Veterans Health Administration." *Blood*. 2020;136:3-4.

We do know that when patients have access to the same level of care, they tend to have similar outcomes. One way to address this is looking at the VA data set of patients given that these patients should have access to similar care despite where they reside, or again removing the variable of insurance status. You can see, at least in this dataset, race was not associated with outcomes, further emphasizing that, again, if patients have access to the same care, you can actually achieve similar outcomes.

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Less likely to participate in clinical trials

Trial Enrollment for Minorities vs Whites According to Cancer Type, 2000-2002

Racial/Ethnic Group	No. of Trial Participants	Enrollment Fraction, %	Odds Ration (95% CI)	*P* Value
	All Cancers			
Total	37635	1.7		
White	32633	1.8	Referent	
Hispanic	1094	1.3	0.72 (0.68-0.77)	<.001
Black	3062	1.3	0.71 (0.68-0.74)	<.001
Asian/Pacific Islander	745	1.7	0.95 (0.88-1.02)	.16
American Indian/Alaskan Native	101	2.5	1.44 (1.18-1.76)	<.001

Murthy, VH, et al. "Participation in cancer clinical trials: race-, sex-, and age-based disparities." *JAMA*. 2004;291(22):2720-2726.

The other thing that's important to recognize is that minority patients are often underrepresented in clinical trials which may provide additional benefit, particularly in those later lines of treatment, which may also have an impact on overall survival. Again, looking at the NCI data sets, patients who were Hispanic or black were much less likely to enroll on a prospective therapeutic study.

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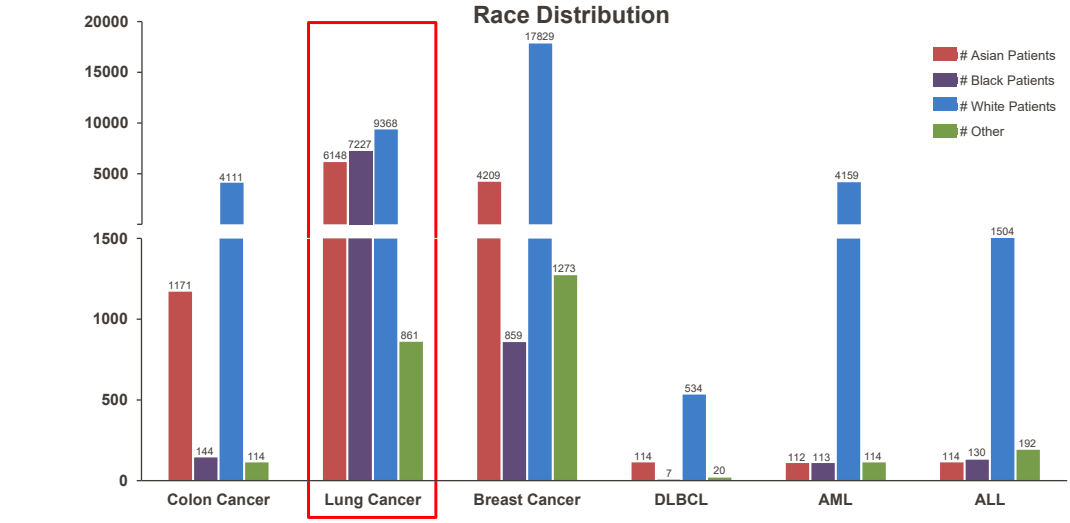
Significant under-representation of minority populations in heme malignancy clinical trials



Gopishetty S, et al. Am J Transl Res. 2020:12, 5977–5983.

When we break that down further and look specifically at trials, treating hematologic malignancies again, very stark difference in black patients participating in large cell lymphoma studies versus even AML and ALL. Again, that looks quite different when you consider that in the context of solid tumors, I'll draw your attention to the lung cancer cohort suggesting that much more comparable participation on studies than what we see in our heme malignancies.

Now, it's important to recognize that the incidence of heme malignancies among black patients might be lower than some of these solid tumors, but I do think draws attention to the fact that we need to do a better job of providing access and enrolling patients on prospective studies.

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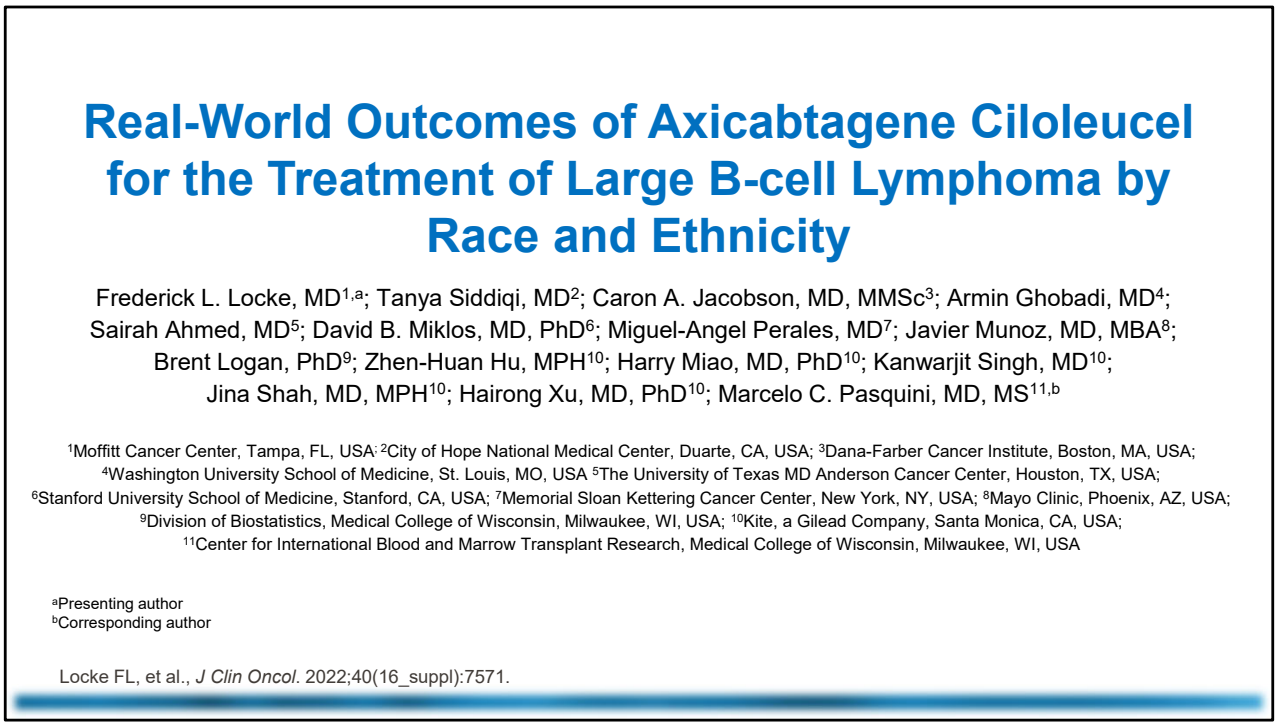

Real-World Outcomes of Axicabtagene Ciloleucel for the Treatment of Large B-cell Lymphoma by Race and Ethnicity

Frederick L. Locke, MD[1,a]; Tanya Siddiqi, MD[2]; Caron A. Jacobson, MD, MMSc[3]; Armin Ghobadi, MD[4]; Sairah Ahmed, MD[5]; David B. Miklos, MD, PhD[6]; Miguel-Angel Perales, MD[7]; Javier Munoz, MD, MBA[8]; Brent Logan, PhD[9]; Zhen-Huan Hu, MPH[10]; Harry Miao, MD, PhD[10]; Kanwarjit Singh, MD[10]; Jina Shah, MD, MPH[10]; Hairong Xu, MD, PhD[10]; Marcelo C. Pasquini, MD, MS[11,b]

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[a]Presenting author
[b]Corresponding author

Locke FL, et al., *J Clin Oncol*. 2022;40(16_suppl):7571.

The last thing I'll cover, CAR T-cell therapy has transformed our approach to relapsed/refractory large cell lymphoma. Similar to the analysis we did, looking at the introduction of rituximab into the treatment landscape, do black patients or minority patients have similar access to these novel therapies that are now entering into the treatment landscape?

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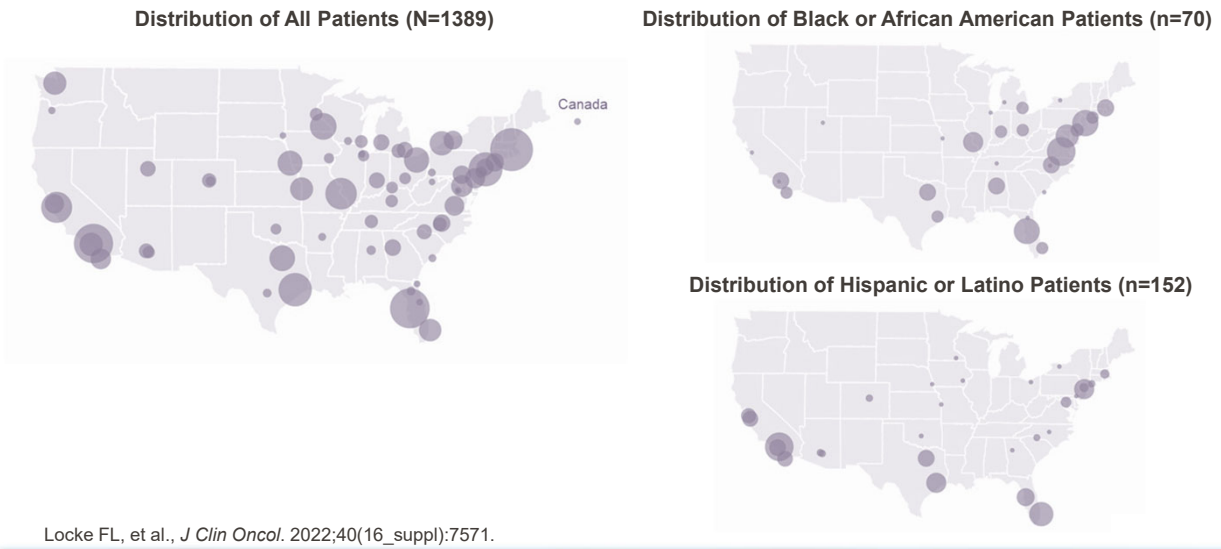
Patient Geographic Distribution



Locke FL, et al., *J Clin Oncol*. 2022;40(16_suppl):7571.

This was data presented by Fred Locke on behalf of his co-authors and analysis of the CIBMTR database.

You can see here the distribution of patients by race across the US. Again, minority patients tend to be more commonly treated at centers along the east and west coast, as opposed to the middle of the country, again, identifying disparate practices.

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Baseline Characteristics by Race and Ethnicity

	Race			Ethnicity	
Key Variable of Interest, n (%)	White N=1127, 81%	Black or African American N=70, 5%	Asian N=81, 6%	Hispanic or Latino N=152, 11%	Not Hispanic or Latino N=1165, 84%
Age ≥65 years	449 (40)	17 (24)	28 (35)	38 (25)	465 (40)
Male sex	749 (66)	42 (60)	43 (53)	99 (65)	757 (65)
ECOG PS ≥2 prior to infusion	48 (4)	1 (1)	9 (11)	4 (3)	56 (5)
Comorbidities					
Pulmonary, moderate to severe	318 (28)	29 (41)	14 (17)	28 (18)	331 (28)
Prior cancer	174 (15)	3 (4)	8 (10)	9 (6)	175 (15)
Obesity (BMI >35 kg/m^2)	103 (9)	9 (13)	1 (1)	15 (10)	103 (9)
Histological transformation	328 (29)	17 (24)	18 (22)	37 (24)	333 (29)
Chemo-sensitive/resistant prior to infusion	253 (22) / 739 (66)	17 (24) / 46 (66)	20 (25) / 54 (67)	44 (29) / 92 (61)	262 (22) / 773 (66)
No. of lines of prior therapies: 1 or 2/ ≥3	310 (28) / 773 (69)	15 (21) / 50 (71)	18 (22) / 56 (69)	43 (28) / 100 (66)	321 (28) / 792 (68)
Prior HCT (any type)/prior ASCT	337 (30) / 321 (28)	18 (26) / 18 (26)	23 (28) / 22 (27)	33 (22) / 32 (21)	348 (30) / 330 (28)
Bridging therapy (any type)	250 (22)	10 (14)	11 (14)	30 (20)	247 (21)
≥12 Months from diagnosis to infusion	663 (59)	50 (71)	50 (62)	89 (59)	682 (59)
≥28 Days from leukapheresis to infusion	549 (49)	42 (60)	37 (46)	73 (48)	577 (50)

Locke FL, et al., *J Clin Oncol*. 2022;40(16_suppl):7571.

When we look at baseline characteristics according to race, again, these were all patients that were considered or treated with CAR T-cell therapy similar to what we've seen in other data sets. There's less representation among black patients in that 65 years or older age cutoff.

They're more likely to have comorbid conditions, including moderate to severe pulmonary comorbidities, interestingly, less likely to have a prior cancer than white or Asian cohorts.

A higher percentage of patients had a longer time from diagnosis to infusion. Now, again, that may suggest more favorable disease biology. It may also suggest barriers to access to care.

If you look at the percentage of patients that were more than 28 days from leukapheresis to infusion slightly higher percentage number among the black versus Asian or white patients.

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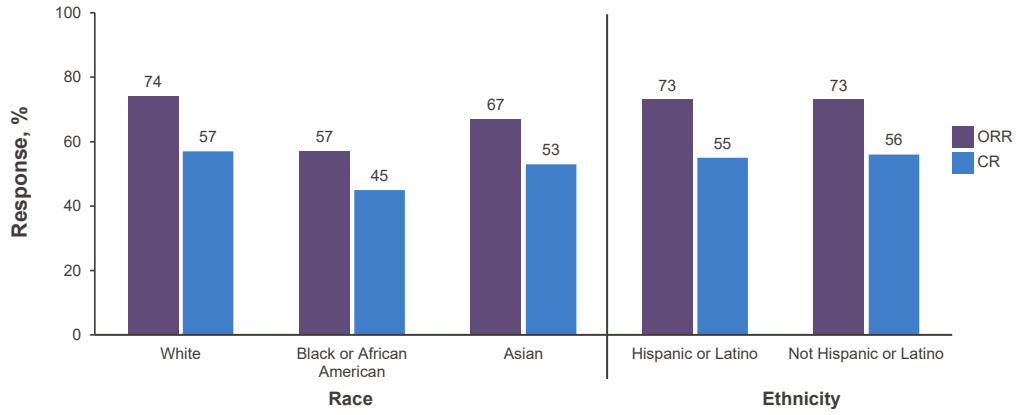
ORR and CR Rate by Race and Ethnicity



Among patients with ≥180 days of follow-up, the ORR was 74% (CR rate, 57%) in White, 57% (CR rate, 45%) in Black or African American, 67% (CR rate, 53%) in Asian, and 73% (CR rate, 55%) in Hispanic or Latino patient groups

Locke FL, et al., *J Clin Oncol*. 2022;40(16_suppl):7571.

How does this impact outcomes in terms of efficacy? Outlined in this slide, you can see the objective and complete response rates broken down according to race. White and Asian patients had higher objective response rates and complete response rates. The black or African American race objective response rate was 57% versus 74% among white patients and a slightly lower percentage achieving a complete response.

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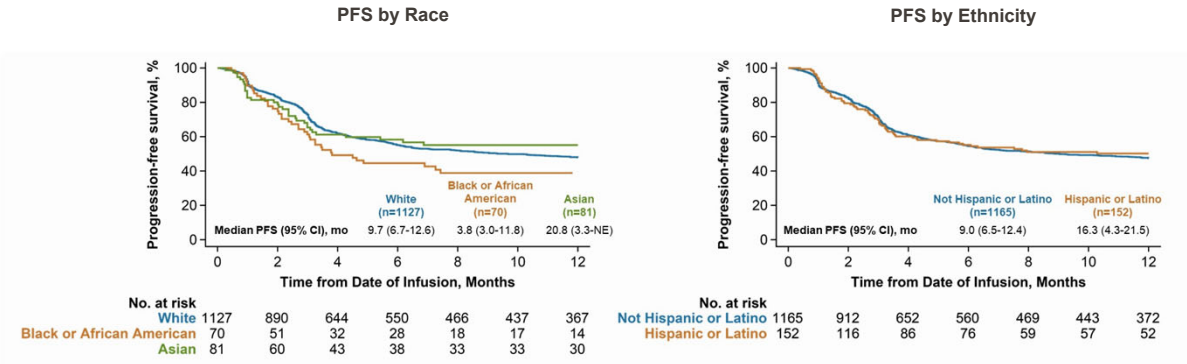
PFS by Race and Ethnicity



The 12-month PFS rate was 48% in White, 36% in Black or African American, 55% in Asian, and 50% in Hispanic or Latino patients

Locke FL, et al., *J Clin Oncol*. 2022;40(16_suppl):7571.

When we look at PFS according to race, African American or black patients had inferior progression-free survival versus those that were white or Asian. We don't see those disparate outcomes when we look at ethnicity, looking at Hispanic versus non-Hispanic.

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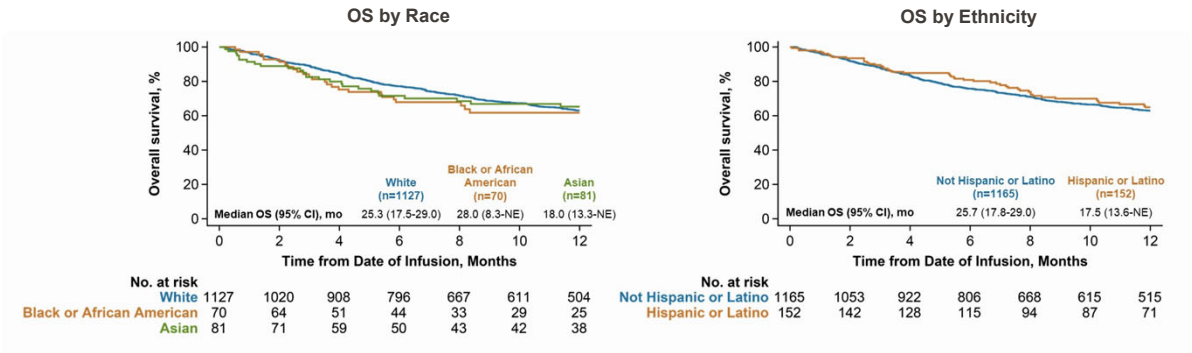
OS by Race and Ethnicity



The 12-month OS rate was 63% in White, 62% in Black or African American, 65% in Asian, and 65% in Hispanic or Latino patients

Locke FL, et al., *J Clin Oncol*. 2022;40(16_suppl):7571.

Fortunately, overall survival is no different in this cohort of patients suggesting despite having inferior~~,~~ PFS, survival is no different suggesting these patients were potentially able to go on to subsequent therapy.

Addressing Disparities in Care for Patients with DLBCL

Conclusions

- Racial disparities in DLBCL have been observed and are likely multifactorial
  - Differences in baseline characteristics, insurance status, access to standard of care therapy
- We need to improve recruitment of minority patients to prospective trials
  - Can outcomes (safety and efficacy) be generalized to the entire population if the study population does not reflect the incidence of the disease?
  - Efforts should be made to recruit minority patients to observational cohorts to explore epidemiology and practice patterns
- Outcomes are comparable when similar treatment is applied
  - Awareness and access to quality care can eliminate disparities in outcomes

I'll conclude by highlighting, there are racial disparities in large cell lymphoma, a disease where many patients should anticipate potential cure, and it's likely multifactorial. In addition to differences in the baseline disease characteristics with less favorable prognosis at the onset, black patients tend to have less access to standard-of-care options that potentially are curative options. They're more likely to be underinsured or uninsured. They're less likely to have access to a clinical trial. What do we need to do to try and reverse or improve these disparate outcomes? We need to do a better job of ensuring these patients have access to good quality of care.

What we're doing right now is getting the message out so that there is knowledge and awareness that may impact local practices. In addition, there are resources that we're exploring to try and recruit or enhance recruitment of minority patients, particularly to novel therapies where we think might provide improvement to the treatment landscape. We need to continue to explore the underlying biologic underpinnings that may then inform differences in treatment approaches. With this, I'm happy to turn it back now to Dr. Armitage and continue the discussion.

Addressing Disparities in Care for Patients with DLBCL

Dr. Armitage: All right, Loretta, thank you. That was a wonderful presentation. This leaves us all sorts of things to talk about, which we can do for the next few minutes. The issue of getting minorities into clinical trials is complex. Some years ago, I led a review group and we produced a white paper for the National Cancer Institute about how to improve participation in clinical research for patients with cancer. One of the interesting things is that all minority groups are not the same in this regard.

If you want to take gay people as a minority group, they were extremely interested in this issue and perhaps more likely to want to be part of it. This was during the time of the HIV epidemic, and they were very interested in learning how to do better with that. Black people were the opposite. We had the head of the National Medical Association, so a senior leader in medicine but for black physicians, speak to us. He said that you have to understand that black people often just don't trust you.

They all know the story of the syphilis studies many years ago. They don't feel that they're likely to get a fair break, and they don't want to be a Guinea pig. It hurt my feelings to know that people felt like that because I don't think we did that, but it doesn't matter what I think, it matters how we make the patients respond. How do you try to address those issues?

Dr. Nastoupil: I think the most important thing is recognizing we have maybe unconscious biases, and you're right. People are going to view clinical trials from the prism that their culture, their history, and what they view might be the outcome for them, personally. One thing that we've tried to incorporate is having staff, we tend to call them patient navigators, that may look like patients and speak like patients that we're trying to communicate effectively with that, may then explain clinical trial risk in language or speech that they feel more comfortable with.

They may even feel more confident asking those uncomfortable questions, just like you mentioned, "Am I really a Guinea pig? Will I tend to benefit? What is the risk to me if I participate in this study?" The other thing that I think we have to acknowledge is oftentimes, minority patients, again, if they're underinsured or they don't have adequate access to care, they may also be providing support not only to their immediate family, their elders, their kids, and they may not be able to miss time from work to participate on a study.

We have to reduce the barriers in terms of number of visits, number of hours that we monitor patients post-infusion to try and minimize the time away from work, or explore resources where we might be able to supplement not directly as an opportunity to profit per se, from participating on a study, but at least reduce that barrier of transportation, parking, missing work, or providing care for an elderly or a child because they're not there to take care of them.

I think we need to have people who can have that conversation with patients in a way that they feel comfortable disclosing so that we can approach this from multiple angles and, again, try and minimize that barrier and perceptions about what the risk is to them as an individual.

Dr. Armitage: Those actually are wonderful thoughts and you're putting them into practice, which means you probably have data before you started to do that and after you did that and showing that that actually improves participation would be important, perhaps.

Another thing, I want to talk a little bit about which issues that are unique but need to be thought of in this situation. Are there minority groups where you particularly worry about drug metabolism and being unable to safely use the same agents? How do you address personal beliefs or family beliefs? Sometimes, religious beliefs would alter people's willingness to participate. Would you want to comment on those two issues?

Dr. Nastoupil: I think doing more of those whole exome sequencing or whole genome sequencing projects where we have better representation from minority subgroups is one way to get to the question of “How does the underlying biology impact things like metabolism and toxicity?” Because I think that's what most patients are fearful of. They don't want to have a toxic outcome, and they want to tend to benefit from participating on a study.

That's why it's so critical that we get more heterogeneous patient population so that we can do a better job of informing what is the potential risk. I think it's also critical to be able to communicate to folks in ways that they don't feel either patronized or they don't understand and they don't feel comfortable enough to say, "Wait, stop, repeat that," or, "Can I ask you a question so that I fully understand?" I do think having training in terms of how to communicate things.

Having more staff that looks like the patients, we want to try and do a better job recruiting to studies, meaning, can we do a better job of recruiting minority oncologists, for instance? Can we do a better job of having our ABPs and nurses be more reflective of the population we hope to serve? I think those are some strategies that we have an impact on. I think making sure that patients feel like they are contributing to the general wellbeing of others, and how can we share the information back to them?

I think we do a poor job of communicating back. You participated on this study. As a result of this, this is now a therapy that's available for more people. Can we provide them more feedback of the benefits of participating but also recognize our blind spots or our biases that we think all clinical trial participation is good and we just need more minority patients on those studies?

Dr. Armitage: I appreciate your comments. You made me think of one thing, was if you want to try to help somebody understand this, you probably would be better off if you take the time to not be in a hurry, be their friend. In fact, some of my best friends are patients I've cared for in the past. I think just taking the time to do that is rewarding for you too, but they're more likely to take seriously and listen to what you say, I believe. I think it's useful to keep your hands off the computer while you're doing it, anyway. All right. Next thing.

Language, at least for me can be a nuisance. You probably have more experience than me of having to do H&Ps (history and physical examinations) and have interviews and discussions with patients with whom you cannot talk to them in their native language. How big a barrier do you think using an interpreter is, and how do you get around it?

Dr. Nastoupil: I think it's incredibly important that when we're talking about risk and particularly consent forms, it has to be conveyed in their native tongue and not by a family member. Technology has helped in a lot of ways, but it's also probably hindered the process. Through technology and what I mean by that is in our institution, we have the ability to FaceTime with interpreters, translators across a number of languages, and so you at least get that visual cue where you can see a person speaking.

The problem, as you mentioned, is it inherently adds more time to that visit because there's going to be a delay of the patient communicating to the translator. They communicating to the physician, me communicating back to the translator and then it getting conveyed to the patient. I have to catch myself all the time because I want to interject, or I want to start speaking before all parties have the opportunity to finish that communication. I think it is really key that we do communicate in the native language and explore technologies that are available that can help.

I think, for more common languages like Spanish, for instance, in a center like ours, we are in Texas, we do make an effort to have written information in Spanish that we can provide, but for some of the other particularly Asian-based countries, we're not as good in that regard, so we try really hard to have someone in person walk them through that written consent form. I would say pre-COVID, it was much easier. We had a number of staff on site. Now, in the COVID and post-COVID era, we're relying much more heavily on technology where it can be done virtually. I think we lose a little in that, but I think you highlighted something really important. We just have to be more patient.

Dr. Armitage: All right. Thank you. As usual, you have thoughtful, good advice. How about a more complicated issue, two things I'm going to suggest, you probably have some experience with, people who are incarcerated, and how do you address the issues that come from that? You have to have lots of undocumented patients you see. How do you deal with that?

Dr. Nastoupil: Yes, two really complicated issues. I think the important thing for people, whether they're incarcerated, that's one unique population, but even what about patients who feel desperate that they need something that's going to work for them? I think they both highlight two important groups. We need to make sure that patients are actually providing informed consent, and they're not being pressured into doing something either as the expectation that they need to benefit them, otherwise, they're going to die from their disease, or they don't really have a say because they, again, are in a situation where they don't have autonomy over their day and their routine.

Obviously, we don't have many experiences with enrolling prisoners on studies because generally, it's viewed that they really don't have the autonomy or the freedom to be able to control their time and provide informed consent for participation. I think what I face more often and I think is similarly important is I want patients to go on a study because I think it's important. I do trials. I'm clearly biased towards clinical trials.

I have to step back and make sure is that the right thing for a given patient because we all know there are Phase 1 first in human studies that were super optimistic about the mechanism of action, but there's some patients that start at dose level one, and we know they may not truly benefit from that, so I think that's another situation that is in line with what we're asking here. How do you juggle the need and the want to put patients on trials because you feel strongly about it versus their freedom and autonomy to make the right choice?

Dr. Armitage: I talk to patients about that and about the two reasons to be on the study are you want to benefit and very few people would be on one if they weren't hoping for that but also altruism. I think everybody doesn't always realize how brave these people are trying to make it better for people in the future.

Dr. Nastoupil: I think the last group you touch on is what about patients that are not insured in the US or at least based off of our standard coverage for healthcare. That's a much harder problem. We do have these situations in the US. Patients can present through an emergency situation and we're obligated and we should provide care to them. Where I struggle the most is if I initiate them on treatment because they have a potentially curative lymphoma, but yet I can't follow them in the clinic because their insurance is not covered by our contracts and negotiations, it's quite a bit of effort to try and find practices within the Houston area where I can get them plugged in, where they can continue on that care.

It's a dilemma we face not infrequently. I think most people who are undocumented, they're super nervous about the legal implications of that and oftentimes, they don't want to disclose that information, so I think being mindful of making sure that they feel

comfortable, that we really are trying to help them. We're going to explore every avenue available to us. There are potential resources as long as they can provide some form of documentation. Again, I think it all boils down to how we communicate and really having phenomenal social workers and case managers. They can really explore every single avenue.

Dr. Armitage: A lot of things they didn't teach you in medical school. People that you see with these diseases have every right to believe that their interests are all you care about, and you'll go out of your way, and my line is you'll do anything that's not grossly illegal or immoral to advance their interests. When people believe that that's how you're going to treat them, you're a better doctor and you also get farther in the things we're talking about.

That was wonderful, Loretta. Thank you very much. I tremendously enjoyed listening to it, and I really enjoyed your answers to the controversial issues. I hope you have a great rest of the week. Both Loretta and I want to thank you all for viewing this activity. We hope you enjoyed it and gained from it.

Dr. Nastoupil: Thank you. I really appreciate also spending time with you, Dr. Armitage.

