

# Population-Based Testing and Treatment Characteristics for CML

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North American Association of Central Cancer Registries  
2015 Annual Conference



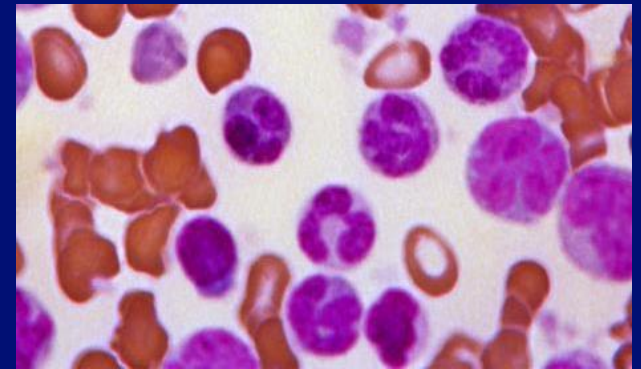
# Disclosures

- **No financial disclosure**
- **The opinions presented here are mine and do not necessarily represent the opinion of the CDC**

# Background

## ■ Chronic Myeloid Leukemia

- Myeloproliferative neoplasm originating in the Bone Marrow
- Increased Myeloid Cells – neutrophils, eosinophils, monocytes, etc.
- Associated with the BCR-ABL1 fusion gene (i.e. Philadelphia (Ph) chromosome, describing translocation of chromosomes 9 and 22)
- Produces uninhibited tyrosine kinase protein that triggers signal transduction pathways resulting in deregulation of cell line and abnormal apoptosis



# Background

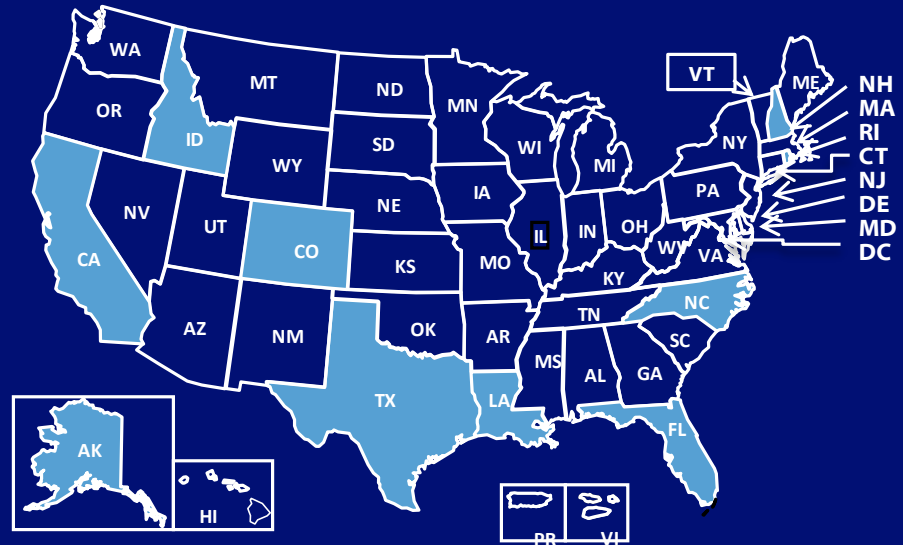
- **Tyrosine Kinase Inhibitors**
  - Imatinib (Gleevec) developed in late 90s and approved 2002 for first line
  - Targets the BCR-ABL tyrosine kinase production
- **National and International Hematology Practice Guideline Recommendations**
  - BCR-ABL gene testing
  - Prompt treatment with tyrosine kinase inhibitors (TKI)
  - Imatinib, Dasatinib, and Nilotinib

## Purpose

- **Describe population-based testing and treatment practice characteristics for patients diagnosed with CML**
- **Assess ability of registries to collect treatment data that may be given primarily in outpatient setting**
- **Provide a real world look at testing and treatment practices outside of randomized clinical trials (RCT)**
- **Evaluate patient characteristics that may affect diagnosis and testing, such as demographic, SES, and clinical features such as comorbidities**

# Methods

- **NPCR's Comparative Effectiveness Research (CER) Project to Enhance Cancer Registry Data**
  - Funding via American Recovery and Reinvestment Act of 2009
  - 10 Specialized Registries (AK, CA\*, CO, FL\*\*, ID, LA, NC, NH, RI, TX)
  - 2011 diagnosis year
  - Detailed Testing & Treatment
    - BCR-ABL test type / result
    - Chemotherapy Agents

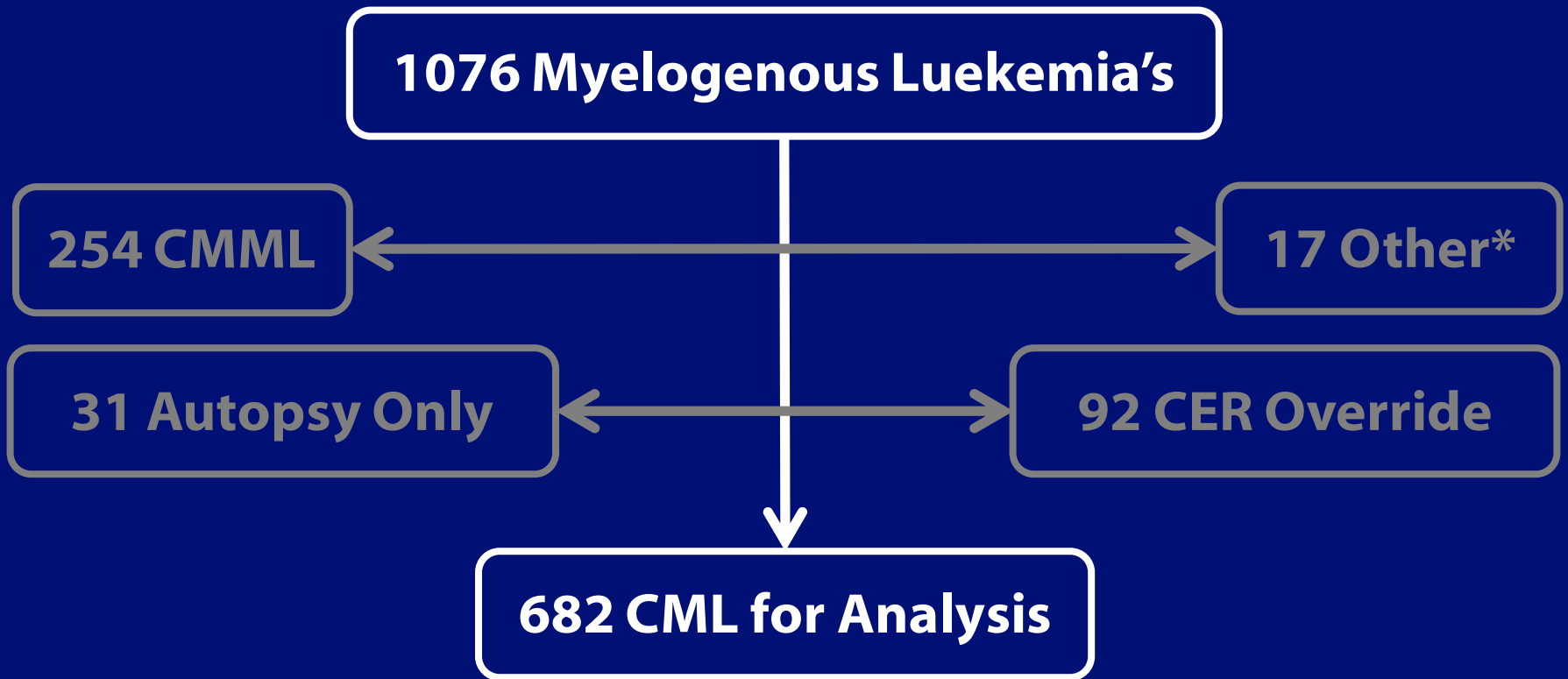


\*Sacramento Area

\*\*Miami-Dade Area

## Methods

- NPCR's Comparative Effectiveness Research (CER) Database



\*Includes aCML and Juvenile Myelomonocytic Leukemia

# Methods

- **Performed Descriptive Analysis using SAS 9.3**
  - Univariate statistics
  - Bivariate Analysis
  - Multivariable Logistic Regression



## Case Demographics (n = 682)

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<b>Male</b>	<b>55%</b>
<b>Median age (range) in years</b>	<b>58 (1–100)</b>

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**Median age (range) in years** **58 (1–100)**

**>56% diagnosed in those 55 or older**

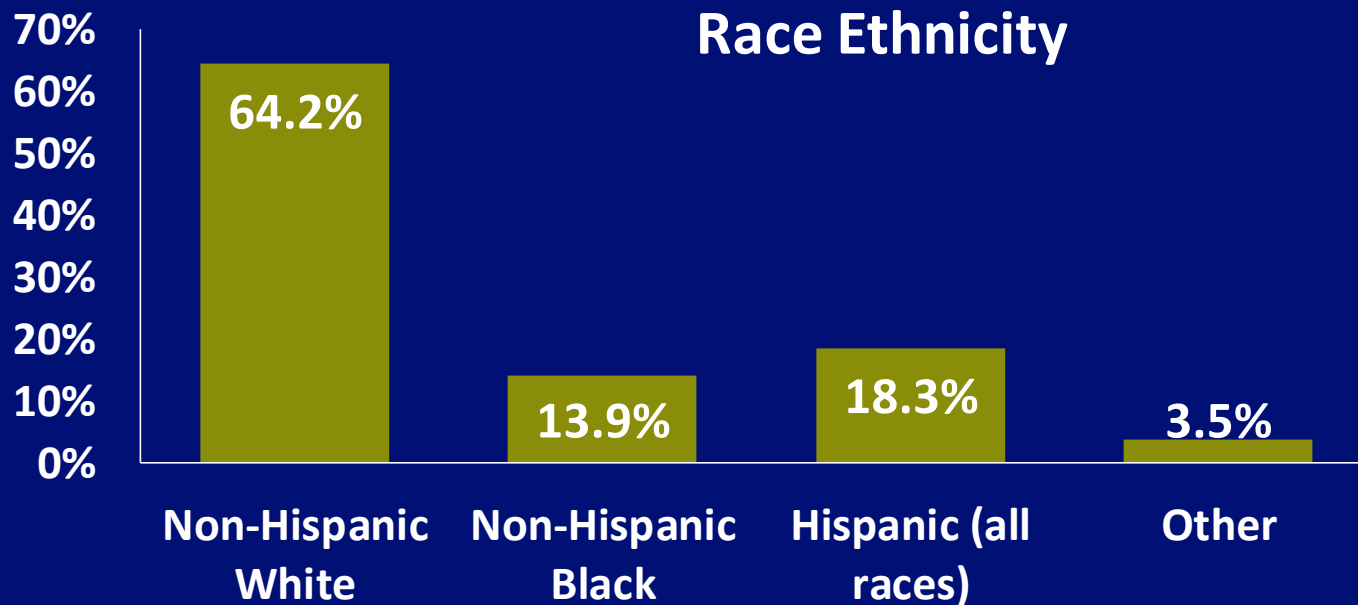
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## Case Demographics (n = 682)

**Male** 55%

**Median age (range) in years** 58 (1–100)

**>56% diagnosed in those 55 or older**



## Results – SES measures

	n	CML (%)
<b>Health Insurance Status at Dx</b>		
Private Insurance	315	(46)
Public: Medicare	153	(22)
Public: Medicaid/Medicare	81	(12)
Other: Military/VA/IHS	7	(1)
No Health Insurance	67	(10)
Unknown	59	(9)
<b>Census Tract Urbanization</b>		
Urban	390	(57)
Rural	54	(8)
Mixed	234	(34)
<b>Census Tract Poverty</b>		
<20% families below poverty	552	(81)
≥20% families below poverty	126	(19)

## Results – Factors affecting treatment or risk

	n	CML (%)
<b>Comorbidity</b>		
Non-Charlson Comorbidity	233	(34)
At least one Charlson	151	(22)
None/Unknown/Missing	298	(44)
<b>Tobacco</b>		
Current Tobacco User	66	(10)
Former Tobacco User	119	(17)
Never Tobacco User	273	(40)
Unknown or Missing	224	(33)

# Results – BCR-ABL Testing

- **Four possible tests**

- Cytogenic
- Fluorescence in Situ Hybridization (FISH)
- Qualitative Reverse Transcriptase Polymerase Chain Reaction (RT-PCR)
- Quantitative RT-PCR

# Results – BCR-ABL Testing

## ■ Possible Qualitative Test Codes

- 000\* - **Negative** result
  - OR **Not applicable** (e.g., information not collected for this case)
  - OR **Test not done** (e.g., test not ordered and not performed)
  - OR **Unknown information** (e.g., not documented in record)
  - OR **Test ordered** (e.g., results not in records)
- 010 - **Positive**

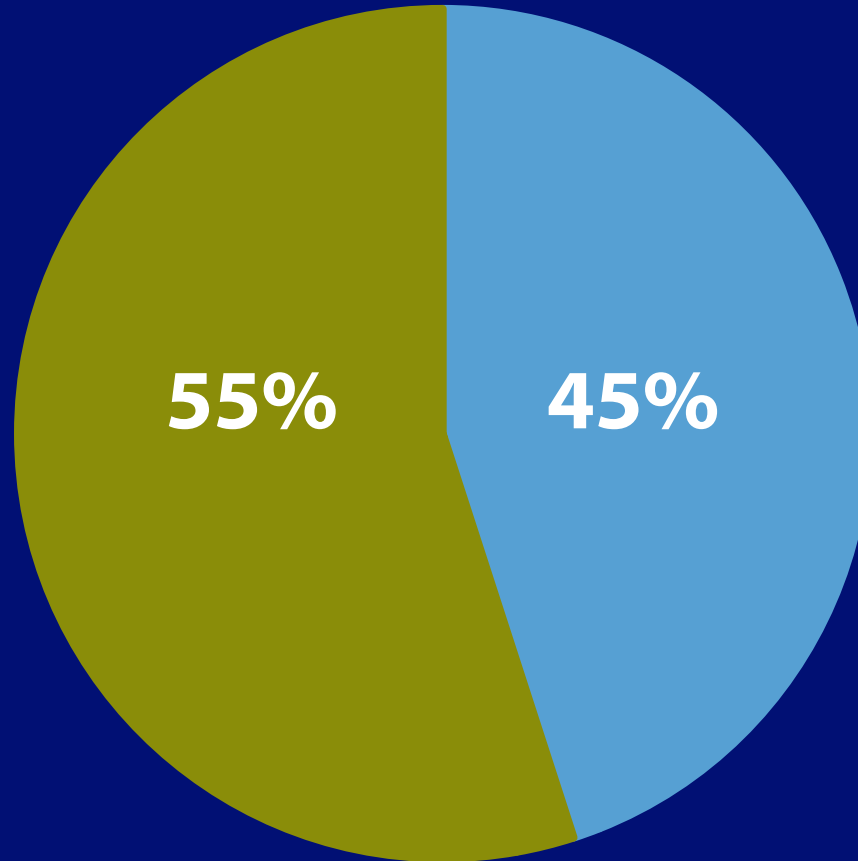
## ■ Possible Quantitative Test Codes

- 000\* - **Same as above**
- 001 - 998 Ratio of 0.001 to 0.998 (enter exact ratio)
- 999 Ratio greater than or equal to 0.999

\*Some distinction can be made using date and date flag fields

## BCR-ABL Gene Testing? (N=682)

**Tested for  
BCR-ABL  
Gene**

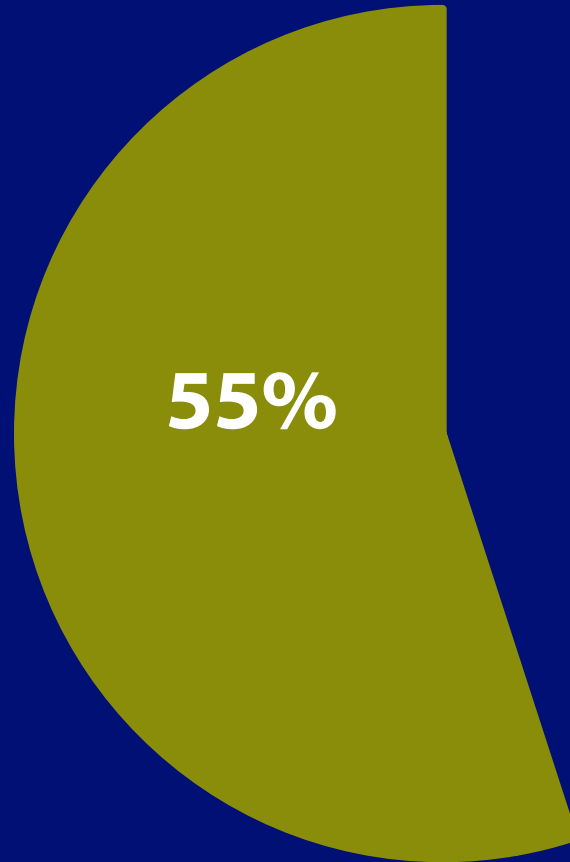


**Not tested /  
Not Applicable /  
Unknown**



## Tested for BCR-ABL Gene (n=375)

Tested for  
BCR-ABL  
Gene



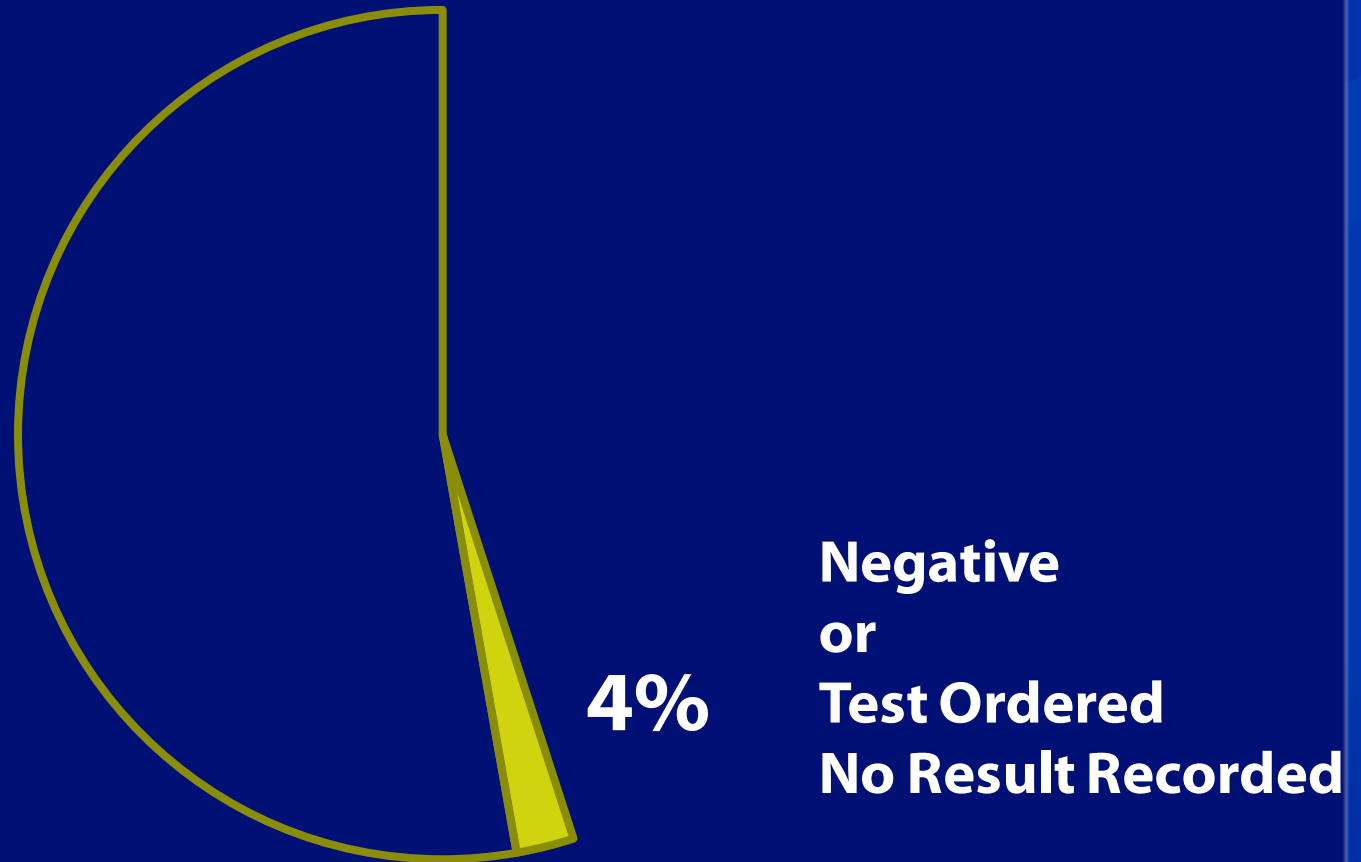
## Positive Test for BCR-ABL Gene (n=360)

Positive  
BCR-ABL  
Gene

96%



**Tested for BCR-ABL Gene  
Negative or No Result (n=15)**



# What factors were associated with BCR-ABL testing?

	CML		Tested		NOT Tested / NA/ Unknown		p value
	n	(%)	n	(col%)	n	(col%)	
<b>Age at Diagnosis</b>							<b>0.0008</b>
<50	239	(35)	152	(41)	87	(28)	
50-59	126	(18)	72	(19)	54	(18)	
60-69	122	(18)	65	(17)	57	(19)	
≥70	195	(29)	86	(23)	109	(36)	
<b>Health Insurance Status at Dx</b>							<b>0.01</b>
Private Insurance	315	(46)	196	(53)	119	(39)	
Public: Medicare	153	(22)	72	(19)	81	(26)	
Public: Medicaid/Medicare	81	(12)	52	(14)	29	(9)	
No Health Insurance	67	(10)	37	(10)	30	(10)	

# What factors were associated with BCR-ABL testing?

	Tested	Not Tested / NA/ Unknown	p value
			<b>&lt;0.0001</b>
State 1	93%	7%	$\chi^2 = 210$
State 2	90%	10%	
State 3	85%	15%	
State 4	83%	17%	
State 5	82%	18%	
State 6	73%	27%	
State 7	66%	34%	
State 8	52%	48%	
State 9	50%	50%	
State 10	<b>24%</b>	<b>76%</b>	

# What factors were associated with BCR-ABL testing?

## ■ Insurance

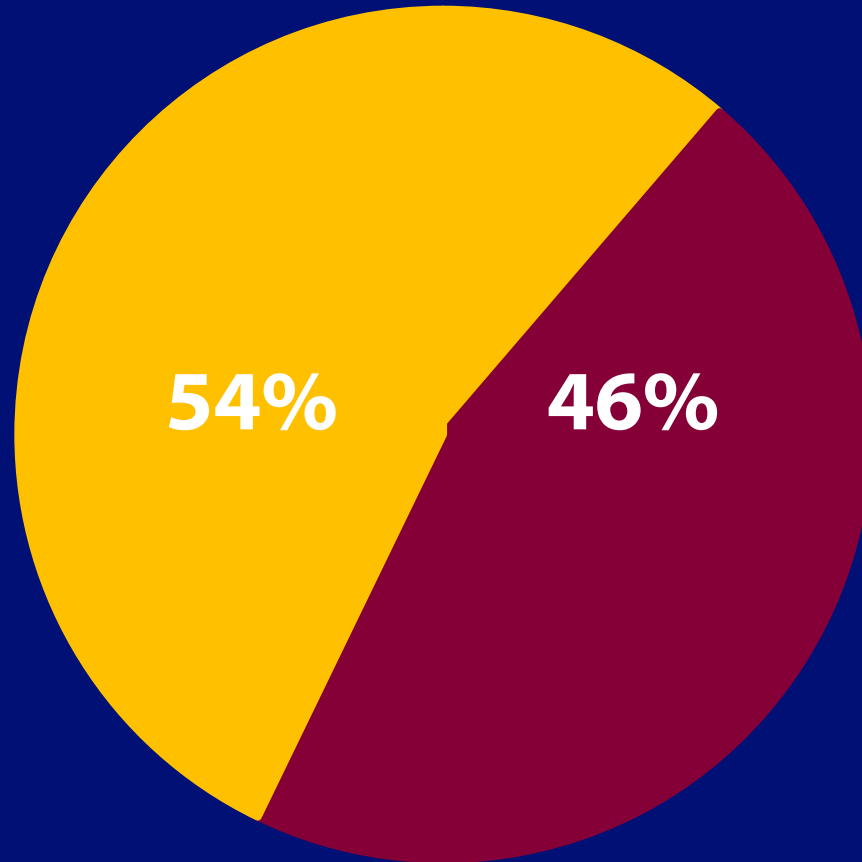
- Drops out after removing State 10
- Drops out after adjusting for age in multivariable analysis with or without State 10

## ■ Age

- Remains significant in multivariable logistic regression
- aOR 0.970, 95% CI (0.953, 0.986)

## TKIs Given (N=682)

**TKI  
documented  
in record**

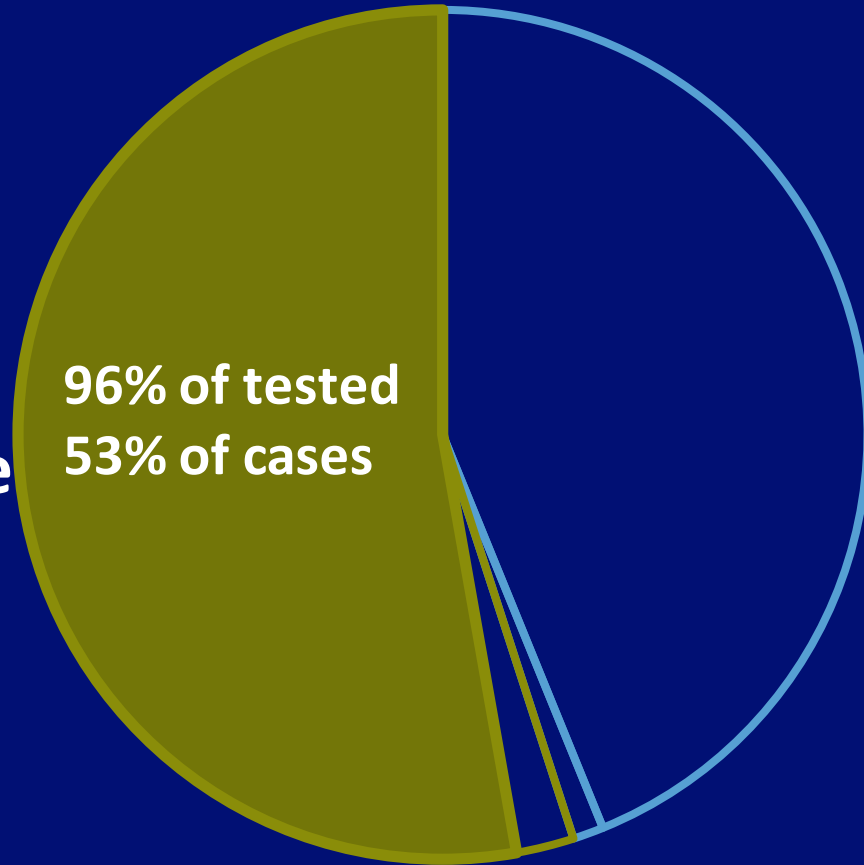


**No TKI  
documented  
in record**

## TKIs Given to BCR-ABL Positive Cases?

**Positive  
BCR-ABL Gene**

**96% of tested  
53% of cases**



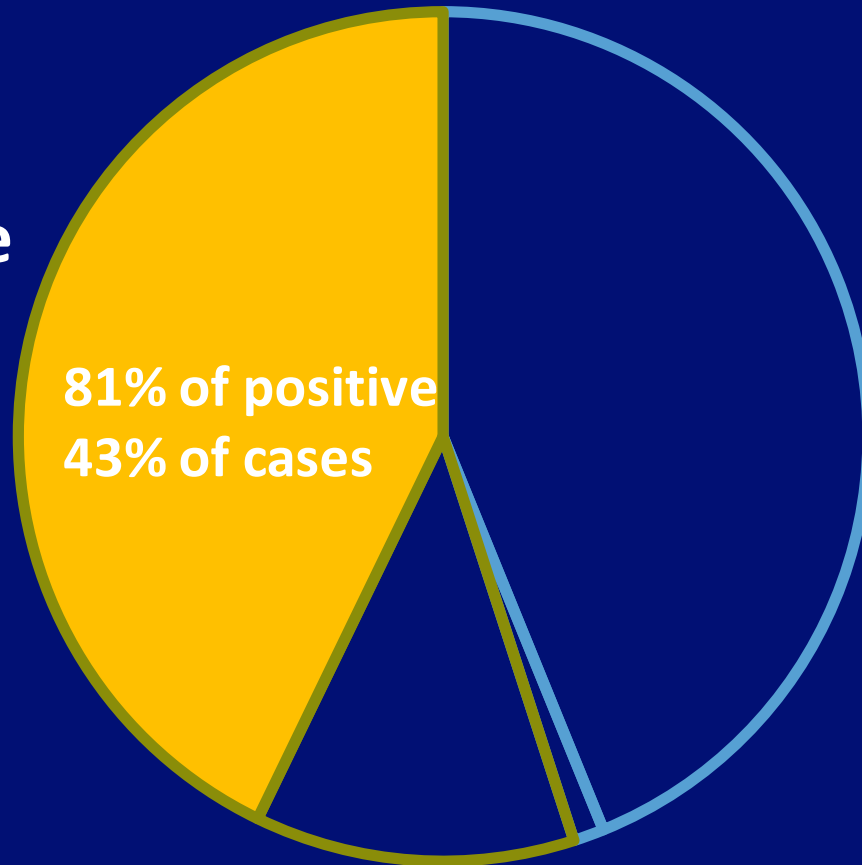


## BCR-ABL Positive given TKIs (n=292)

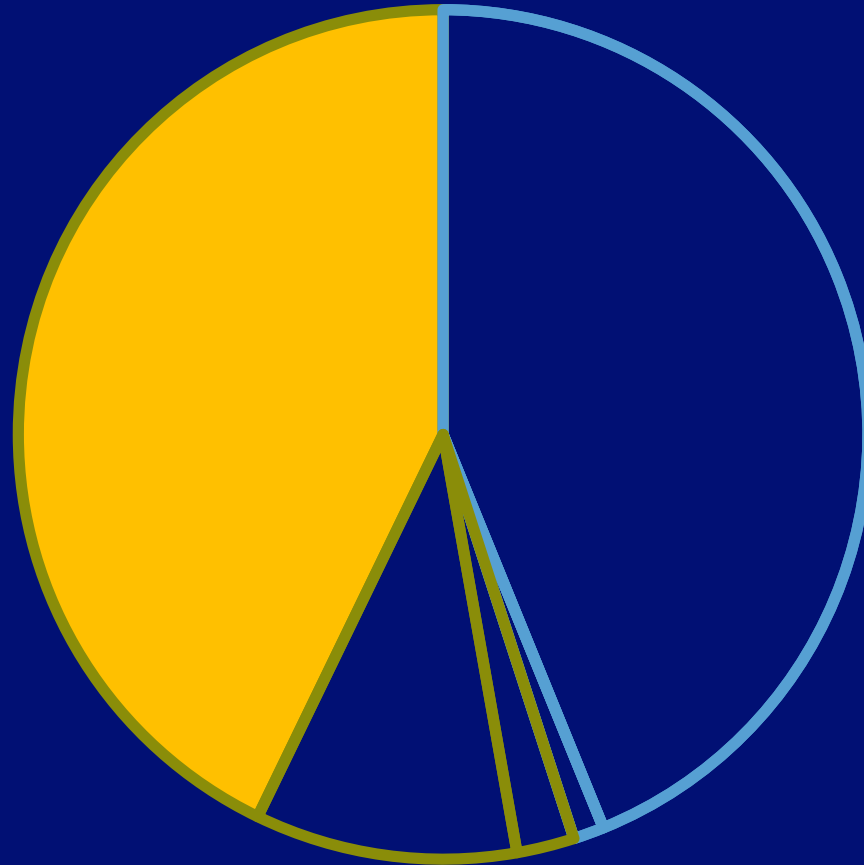
**Positive  
BCR-ABL Gene**

**AND**

**Received TKI**



## TKIs Given – to CML cases with Positive BCR-ABL Gene Test



**TKI documented in record**

## TKIs Given – Tested for BCR-ABL Gene (unknown or negative result)



**TKI documented in record**

# TKIs Given - BCRTA and NKTs Governor Not Applicable



**TKI documented in record**



**No TKI documented in record**

# What factors were associated with TKI therapy?

	CML		TKI Therapy		No TKI Therapy		p value
	n	(%)	n	(col%)	n	(col%)	
<b>Age at Diagnosis</b>							<b>0.011</b>
<50	239	(35)	138	(37)	101	(32)	
50-59	126	(18)	74	(20)	52	(17)	
60-69	122	(18)	71	(19)	51	(16)	
≥70	195	(29)	86	(23)	109	(35)	
<b>Health Insurance Status at Dx</b>							<b>0.026</b>
Private Insurance	315	(46)	189	(54)	126	(47)	
Public: Medicare	153	(22)	76	(22)	77	(29)	
Public: Medicaid/Medicare	81	(12)	52	(15)	29	(11)	
No Health Insurance	67	(10)	31	(9)	36	(13)	
<b>Census Tract Poverty</b>							<b>0.011</b>
<20% below poverty line	552	(81)	310	(85)	242	(77)	
≥20% below poverty line	126	(19)	55	(15)	71	(23)	

# What factors were associated with TKI Therapy?

	TKI Therapy	No TKI Therapy	p value
			<b>&lt;0.0001</b>
State 1	83%	17%	$\chi^2 = 209$
State 2	80%	20%	
State 3	80%	20%	
State 4	80%	20%	
State 5	78%	22%	
State 6	75%	25%	
State 7	75%	25%	
State 8	70%	30%	
State 9	66%	34%	
State 10	<b>21%</b>	<b>79%</b>	

# What factors were associated with TKI Therapy?

## ■ Insurance

- Drops out after removal of State 10
- Drops out after adjusting for age in multivariable analysis with or without State 10

## ■ Poverty

- Drops out after removal of State 10
- Drops out after adjusting for age in multivariable analysis with or without State 10

## ■ Age

- Remains significant in multivariable logistic regression
- aOR 0.965, 95% CI (0.942, 0.988)

## Limitations

- **Results valid across population?**
- **Unable to assess source data or evaluate discordant pairs**
  - BCR-ABL gene test Not Applicable but given TKI (or diagnosed CML : BCR-ABL+ histology 9875 )
  - BCR-ABL positive not given TKI
  - BCR-ABL positive but coded CML NOS (histology 9863)
- **Unable to assess if in Blast Crisis**
  - Treatment should still include a TKI
- **Unable to assess comorbidity data with certainty**



## Conclusions

- **Cancer registries are capable of collecting complex genetic testing and cancer treatment regimens**
  - Can include detailed outpatient treatment regimens
  - However, can vary significantly between states
- **In states capable of collecting detailed CML data**
  - Majority of patients had a documented BCR-ABL gene test for definitive diagnosis
  - Majority also received guideline concordant care with a TKI

## Recommendations

- **Continue efforts to collect population based CER/PCOR data**
  - Helps describe testing and treatment outside of clinical trials
  - Take advantage of MU and Electronic Medical Record (EMR) linkages?
- **Collect intermediate and long term outcomes**
  - Allows understand benefits of various therapies on population level
- **Further research to understand coding differences or availability in different states**

# Acknowledgments

## CDC

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Reda Wilson  
David Butterworth

## NPCR CER Cancer Registries

Alaska	California
Colorado	Florida
Idaho	Louisiana
North Carolina	New Hampshire
Rhode Island	Texas

**For more information please contact Centers for Disease Control and Prevention**

1600 Clifton Road NE, Atlanta, GA 30333

Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.