KRAS Biomarker Testing & Treatment among Colorectal Cancer Patients

Results from CDC Comparative Effectiveness Research Project

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First presented by Adriana Rico at NAACCR 2015

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Acknowledgements
KRAS Analytic Team

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Outline

- **Background**
  - NPCR Comparative Effectiveness Research (CER) Project
  - *KRAS* test/recommendations
- **Results**
  - *KRAS* testing results
  - Treatment by KRAS testing results
- **Comparison to previous KRAS studies**

2009 Institute of Medicine Report

Initial National Priorities for Comparative Effectiveness

- Set priorities for questions to be addressed by Comparative Effectiveness Research (CER)
- Supported by American Recovery and Reinvestment Act

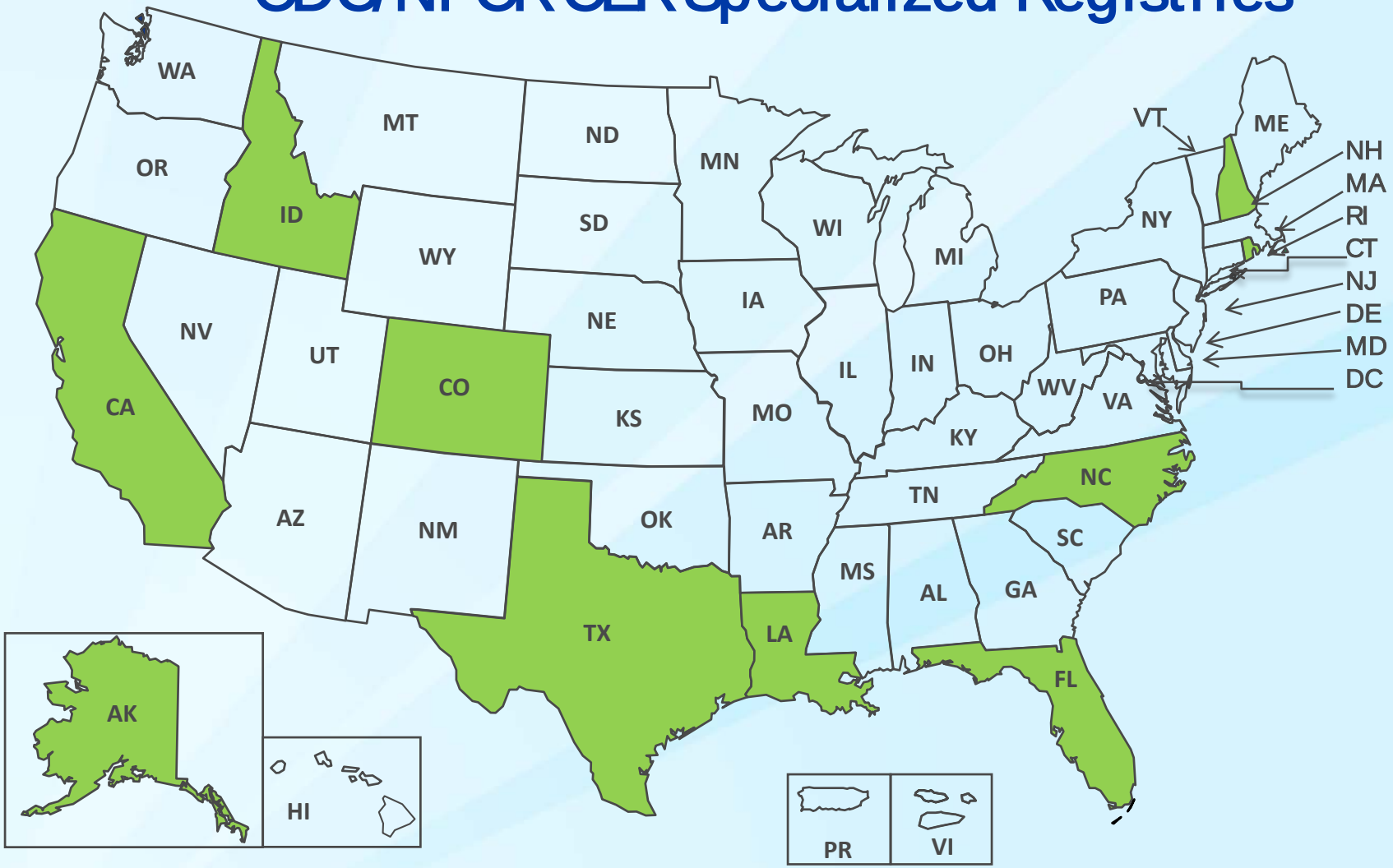
Cancer Registries and CER Priorities

- **Addressing CER questions through central cancer registries**
  - Population-based surveillance already established
  - Enhance cancer registry infrastructure
  - Collect add'l biomarker/treatment data

- **CDC's National Program of Cancer Registries**
  - Enhanced data collection for 2011 cases
  - Focus on breast, colon, rectum, and CML
  - CER Project* – May 2010 to September 2013

* Chen VW, Eheman CR, Johnson CJ, Hernandez MN, Rousseau D, Styles TS, et al. Enhancing Cancer Registry Data for Comparative Effectiveness Research (CER) Project: Overview and Methodology. Journal of registry management. 2014;41:103-12.

CDC/NPCR CER Specialized Registries



Specialized Registries (AK, CA*, CO, FL*, ID, LA, NC, NH, RI, TX)

IOM Comparative Effectiveness Research

IOM Priority Question on Biomarkers:

- "Compare the effectiveness of genetic and biomarker testing and usual care in preventing and treating breast, colorectal, prostate, lung, and ovarian cancer, and possibly other clinical conditions for which promising biomarkers exist."

CDC/NPCR Comparative Effectiveness Research question:

- Are colon and rectum (colorectal) cancer patients tested for *KRAS*
  - If tested, are the results used appropriately to determine treatment?
  - If not tested, what patient characteristics influenced no *KRAS* testing?

First time NPCR collecting KRAS testing info/treatment agent

KRASTest

- ***KRAS* test for stage IV colorectal cancer patients***
- ***KRAS* results determine treatment options using anti-Epidermal Growth Factor Receptor (anti-EGFR)**
  - Cetuximab (Erbitux – FDA approved 2004*)
  - Panitumumab (Vectibix – FDA approved 2006*)

* National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology for colon cancer-version 3.2011. 2011 February 25.

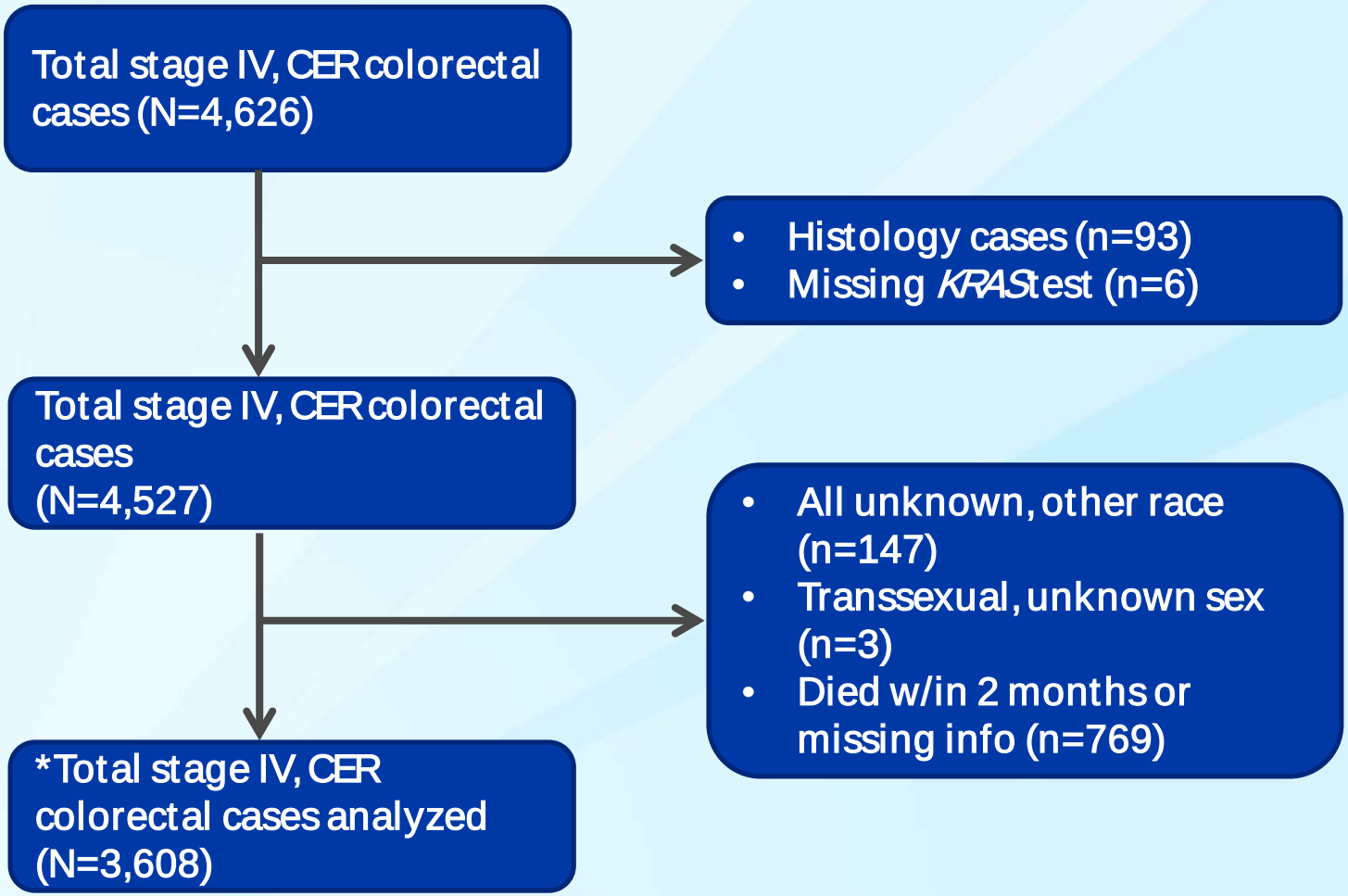
* http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Search_Drug_Name

Recommendation on *KRAS* Testing

- **National Comprehensive Cancer Network (NCCN)***
  - 2009 – Updated guidelines
  - All stage IV colorectal cancer (CRC) patients should be tested for *KRAS* upon diagnosis and before treatment

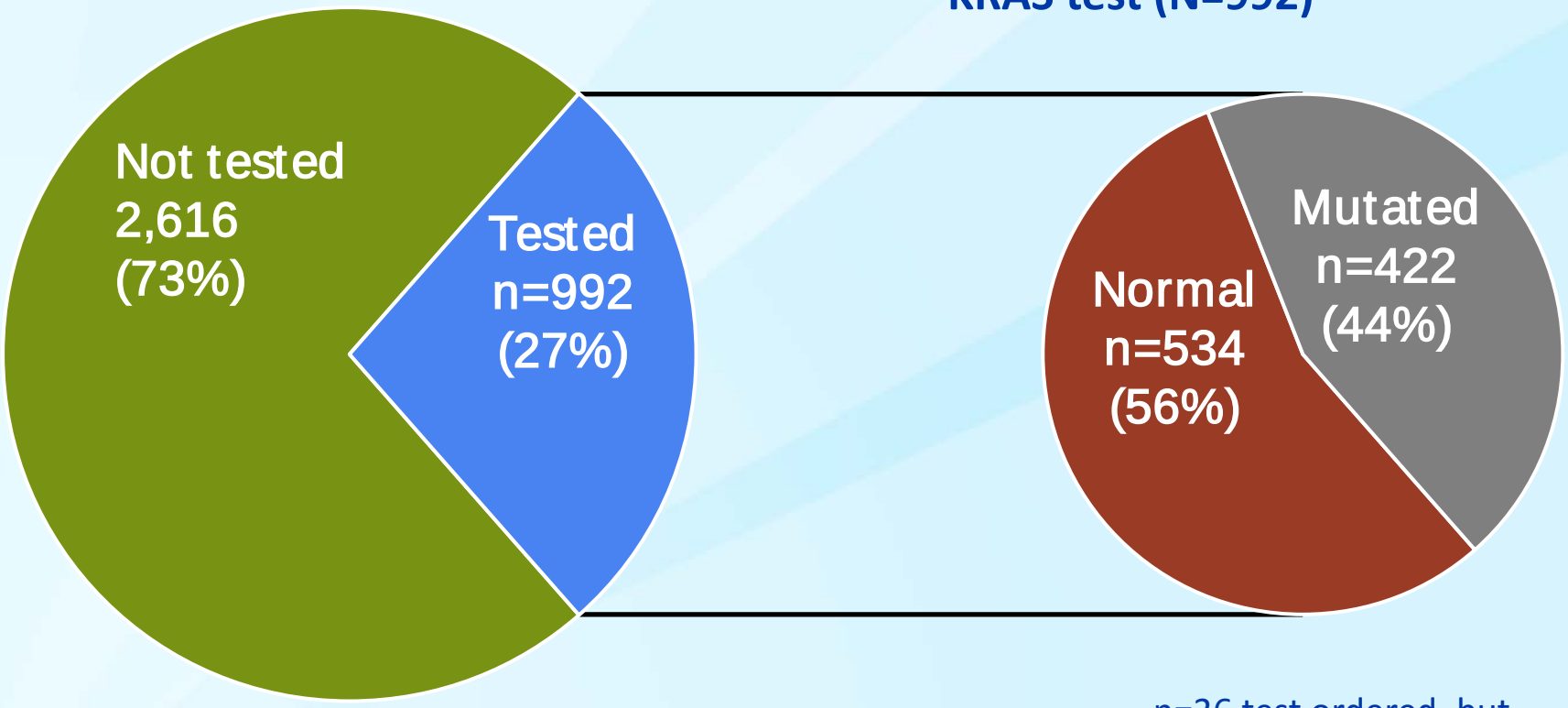
* National Comprehensive Cancer Network. NCCN adds survivorship section to colon and rectal cancer guidelines. February 18, 2009 [cited 2015 April 09]; Available from: http://www.nccn.org/about/news/newsinfo.aspx?NewsID=202

Study Population



KRAS Testing Results

- Total 2011 colorectal stage IV cases analyzed (N=3,608)
- Total 2011 tested stage IV cases with documented KRAS test (N=992)*



n=36 test ordered, but results not in chart

Characteristics of Stage IV Colorectal Cancer Patients with Documented KRAS Testing - NPCR CER States, 2011 (n=3,608)

Chi-square tests:

- **Age at dx (older age)**
- **Race/ethnicity (Black non-Hispanics/Hispanics)**
- **State of dx (CA, LA, TX, and FL)**
- **Insurance status (public)**
- **Education by census tract (low)**
- **Sex**
- **% of people below poverty level**
- **Rural/urban by census tract**
- **Comorbidities**

} **No significant differences**

Red denotes less likely to receive KRAS test

Characteristics of Stage IV Colorectal Cancer Patients with Documented KRAS Testing - NPCR CER States, 2011 (n=3,608)

Multivariate logistic regression:

- **Age at dx**
- **Race/ethnicity**
- **State of dx**
- **Insurance status**
- **Education by census tract**
- **Sex**
- **% of people below poverty level**
- **Rural/urban by census tract**
- **Comorbidities**

No significant differences

Red denotes less likely to receive KRAS test

Multivariate logistic regression of demographics associated with *KRAS* testing

Characteristic	Value	OR	95% CI	*P*
Age* (per 5-year increase)				<0.0001
	Below 70 years	0.92	(0.88, 0.96)	
	70 years and older	0.76	(0.69, 0.84)	
Race/Ethnicity	White, Non-Hispanic	1.00		0.0837
	Black, Non-Hispanic	0.77	(0.61, 0.97)	
	Hispanic	0.89	(0.70, 1.12)	
State of Dx	TX	1.00		<0.0001
	AK	1.68	(0.71, 3.96)	
	CA	0.70	(0.47, 1.06)	
	CO	1.98	(1.45, 2.70)	
	FL	1.19	(0.93, 1.52)	
	ID	1.97	(1.31, 2.97)	
	LA	0.93	(0.69, 1.25)	
	NH	2.98	(1.84, 4.81)	
	NC	1.79	(1.42, 2.26)	
	RI	2.72	(1.52, 4.85)	

Treatment	Frequency (No.)	Percent (%)
FOLFOX alone	112	13.27
FOLFIRI alone	13	1.54
CapeOx alone	22	2.61
FOLFOXIRI alone	7	0.83
Fluorouacil alone	32	3.79
Capecitabine alone	47	5.57
Oxaliplatin alone	42	4.98
Irinotecan alone	1	0.12
FOLFOX + bevacizumab	201	23.82
FOLFIRI + bevacizumab	30	3.55
CapeOx + bevacizumab	24	2.84
FOLFOXIRI + bevacizumab	18	2.13
Fluorouacil + bevacizumab	4	0.47
Capecitabine + bevacizumab	8	0.95
FOLFOX + cetuximab	**13**	**1.54**
FOLFIRI + cetuximab	**3**	**0.36**
FOLFOX + panitumumab	**4**	**0.47**
Cetuximab alone	**3**	**0.36**
Panitumumab alone	**1**	**0.12**
Other single agent	9	1.07
Any other multiple agents	84	9.95
Unknown chemo agent	166	19.67
Total	**844**	

First Line Treatment among Stage IV CRC patients with a documented KRAS

- **FLOFOX was most common regimen**
- **Bevacizumab used often**
- **24 patients received anti-EGFR (cetuximab or panitumemab)**

First line treatment available (n=844)

Receipt of anti-EGFR* by *KRAS* result among patients with known testing results and known treatment

EGFR inhibitor treatment	Normal (Wild type)	Abnormal (mutated)
YES (received cetuximab or panitumumab)	24	0
NO	330	303
Total	354	303

- Of 354 patients with documented normal KRAS, 24 (6.8%) received anti-EGFR as first line treatment

*First year of diagnosis

Treatment	Number	Percent (%)
FOLFOX alone	191	11.62
FOLFIRI alone	17	1.03
CapeOx alone	45	2.74
FOLFOXIRI alone	5	0.3
Oxaliplatin + Irinotecan	1	0.06
Fluorouacil alone	74	4.5
Capecitabine alone	99	6.02
Oxaliplatin alone	81	4.93
Irinotecan alone	1	0.06
FOLFOX + bevacizumab	325	19.77
FOLFIRI + bevacizumab	41	2.49
CapeOx + bevacizumab	50	3.04
FOLFOXIRI + bevacizumab	14	0.85
Fluorouacil + bevacizumab	27	1.64
Capecitabine + bevacizumab	12	0.73
FOLFOX + cetuximab	**7**	**0.43**
FOLFIRI + cetuximab	**3**	**0.18**
FOLFOX + panitumumab	**1**	**0.06**
Cetuximab alone	**2**	**0.12**
Other single agent	34	2.07
Any other multiple agents	126	7.66
Unknown chemo agent	488	29.68
Total	1,644	

First Line Treatment among Stage IV CRC patients without a documented KRAS

- **KRAS Not Tested (n=2,616)**
  - 1,644 known treatment
  - 755 "no chemo"
  - 204 chemo status unk.
  - 13 discrepancies exc.
- **Similar to patients tested for KRAS in regard to use of FOLFOX and Bevacizumab**
- **13 patients received anti-EGFR without a documented KRAS test!**

Summary of Findings

- **27% received a documented *KRAS* test**
- **73% did not receive a *KRAS* test**
  - Older age was associated with less testing
  - Black, non-Hispanics received less testing than Whites
  - Geographic differences in testing
- **Most cases received FOLFOX + bevacizumab as first-line treatment**
- **Overall, 37 cases received anti-EGFR**
  - 13 cases (35%) received anti-EGFR but no *KRAS* test

Strengths & Limitations

- **Strength:** Population-based registry study capturing 27.3% of U.S.,
  - 25% of African Americans and
  - 44% of Hispanics in U.S.

- **Limitations:**
  - Did we capture all *KRAS* testing? If not documented, not captured.
  - Numbers to determine impact of anti-EGFR treatment are small.
  - Date of test is not captured.
  - Data collection was limited to first year of diagnosis.
  - Testing beyond first year is unknown.
  - Resource intensive.

Comparison to other KRAS studies
Charlton et al., Am J Clinical Onc, 2015

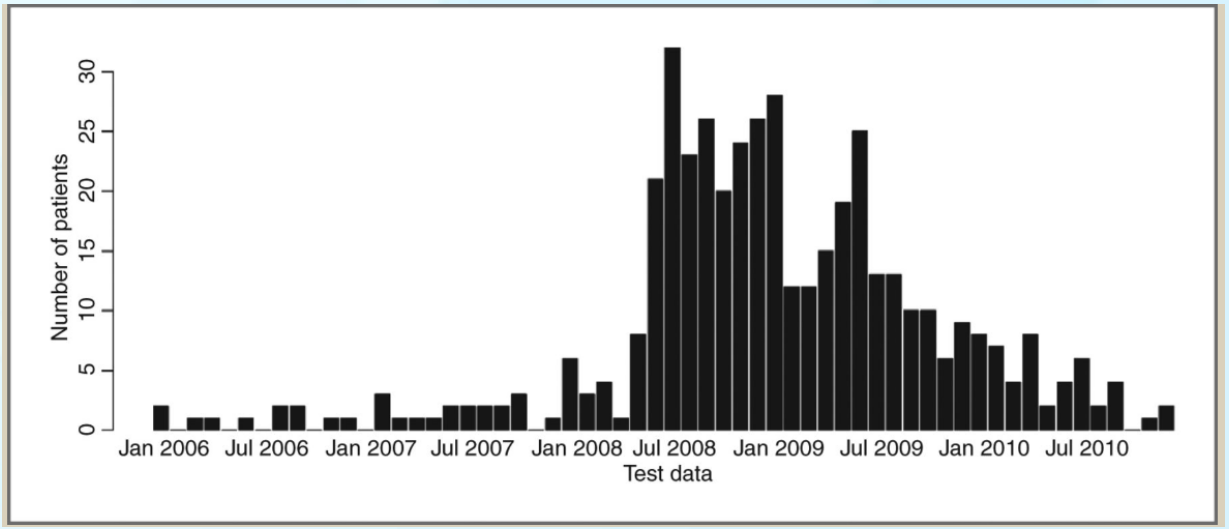
- **SEER (Population-based)**
- **Percentages of documented KRAS among Stage IV colorectal cancer patients are similar**
  - SEER registries (2010) 23%
  - NPCR CER registries (2011) 27%
- **Differences in KRAS testing by age and geographic sites found in both population-based studies**
  - Findings on rural/urban varied

Am J Clin Oncol. 2015 Apr 1.

Comparison to other KRAS studies
Webster et al., CEBP 2013.

- **Seven integrated health care systems**
- **Review of EMR with multiple years of data**
- **1,188 patients with Stage IV colorectal cancer**
  - Diagnosis years 2004-2009
  - 36% received KRAS, 22% received EGFR inhibitors

Overview of KRAS testing for study participants



Cancer Epidemiol Biomarkers Prev. 2013 Jan;22(1):91-101

Conclusions

- **Despite recommendations for KRAS testing in metastatic colorectal cancer, only one in four patients had KRAS testing documented in first year since diagnosis.**
- **Among those with KRAS performed and a normal (wild type) result (i.e., eligible for treatment with anti-EGFR), 15% with known treatment received cetuximab or panitumumab as first-line therapy.**
- **Our findings may support that KRAS testing and targeted therapy are:**
  - Being reserved for progression or recurrence, or
  - Being underutilized
- **Outcome studies will be very important to compare survival among those who received early anti-EGFR to those who did not.**

With additional funding, we demonstrated ability of NPCR to collect biomarkers and treatment to address CER priorities

CDC NPCR Comparison Effectiveness Research

Data is available for analysis!

- This cancer specific CER dataset is available through National Center for Health Statistics Research Data Centers (RDC) which allow researchers access to restricted data.
- Detailed treatment and biomarker data for 2011 cases collected from ten geographically diverse registries
  - Breast,
  - Colon and rectal
  - Chronic myeloid leukemia cases
- For more information
  - http://www.cdc.gov/rdc/index.htm
  - Contact: Dr. Loria Pollack for more information (lop5@cdc.gov)

Enhancing cancer registry data for comparative effectiveness research (CER) project: overview and methodology. Journal of Registry Management 2014;41(3):103–12.

Thank you.

Comments? Questions?

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