PRECISION MEDICINE

Uptake of KRAS Testing and Anti-EGFR Antibody Use for Colorectal Cancer in the VA

Daniel J. Becker, MD[1,2]; Kyung M. Lee, PhD[3]; Steve Y. Lee, MD[4]; Kristine E. Lynch, PhD[3,5]; Danil V. Makarov, MD[1,2]; Scott E. Sherman, MD[1,2]; Christy D. Morrissey, MD[1]; Michael J. Kelley, MD[6,7]; and Julie A. Lynch, PhD[8,9]

PURPOSE Advances in precision oncology, including *RAS* testing to predict response to epidermal growth factor receptor monoclonal antibodies (EGFR mAbs) in colorectal cancer (CRC), can extend patients' lives. We evaluated uptake and clinical use of *KRAS* molecular testing, guideline recommended since 2010, in the Veterans Affairs Healthcare System (VA).

MATERIALS AND METHODS We conducted a retrospective cohort study of patients with stage IV CRC diagnosed in the VA 2006-2015. We gathered clinical, demographic, molecular, and treatment data from the VA Corporate Data Warehouse and 29 commercial laboratories. We performed multivariable analyses of associations between patient characteristics, *KRAS* testing, and EGFR mAb treatment.

RESULTS Among 5,943 patients diagnosed with stage IV CRC, only 1,053 (17.7%) had *KRAS* testing. Testing rates increased from 2.3% in 2006 to 28.4% in 2013. In multivariable regression, older patients (odds ratio, 0.17; 95% CI, 0.09 to 0.32 for ≥ age 85 v < 45 years) and those treated in the Northeast and South regions were less likely, and those treated at high-volume CRC centers were more likely to have *KRAS* testing (odds ratio, 2.32; 95% CI, 1.48 to 3.63). Rates of potentially guideline discordant care were high: 64.3% (321/499) of *KRAS* wild-type (WT) went untreated with EGFR mAb and 8.8% (401/4,570) with no *KRAS* testing received EGFR mAb. Among *KRAS*-WT patients, survival was better for patients who received EGFR mAb treatment (29.6 v 18.8 months; P < .001).

CONCLUSION We found underuse of *KRAS* testing in advanced CRC, especially among older patients and those treated at lower-volume CRC centers. We found high rates of potentially guideline discordant underuse of EGFR mAb in patients with *KRAS*-WT tumors. Efforts to understand barriers to precision oncology are needed to maximize patient benefit.

BACKGROUND

Colorectal cancer (CRC) is among the most frequently diagnosed cancers for both men and women, and one of the leading causes of cancer-related deaths.[1] An estimated 145,600 new cases of CRC will be diagnosed in the United States in 2019 and an estimated 51,020 will die from the disease.[2] The 5-year survival rate of metastatic CRC has doubled in the past few decades, thanks in part to advances in targeted and personalized therapies.[3] Cetuximab and panitumumab, both monoclonal antibodies (mAb) targeting the epidermal growth factor receptor (EGFR), extend survival in patients whose tumors lack *RAS* gene mutations but are ineffective in those with *KRAS* and NRAS mutations.[4,5] To assure appropriate selection of therapy, *RAS* mutation testing is the standard of care and has been included in both ASCO and National Comprehensive Cancer Network recommendations since 2009.[6-9] Testing for *RAS* mutations

ensures that patients with mutations will neither waste precious time on EGFR antibody therapy nor be exposed to toxicities from medications unlikely to help them.

Emerging studies suggest that many patients with advanced cancer are not receiving guideline concordant molecular testing. Our previous work found underuse of EGFR testing, also essential for selection of targeted therapy, in patients with advanced lung cancer in both Veteran Health Administration (VA) and Medicare populations.[10,11] A recent analysis of the SEER database demonstrated that only 30% of patients with stage IV CRC had *KRAS* testing between 2010 and 2013.[12] Other studies, conducted on different patient populations, however, report more extensive uptake of molecular testing.[13] The true rates of molecular testing are unknown and may vary by patient population, care setting, and disease-related issues. The limited study of predictors of *KRAS* testing in

CONTEXT

Key Objective

Did Veterans Affairs Medical Centers effectively integrate *KRAS* molecular testing and anti–epidermal growth factor receptor monoclonal antibody (EGFR mAb) therapy into clinical care for patients with stage IV colorectal cancers between 2006 and 2015? Few studies have used large, comprehensive patient databases to evaluate the uptake and application of cancer molecular testing, the cornerstone of precision oncology.

Knowledge Generated

Although molecular testing increased over the years studied, *KRAS* testing peaked at only 28% of patients diagnosed with stage IV colorectal cancer in 2013. Among those molecularly selected for EGFR mAb use by *KRAS* testing, only 35.7% received EGFR mAb therapy.

Relevance

Efforts to understand barriers and to increase rates of molecular testing and targeted therapy are urgently needed.

the Medicare population suggests that patients with Medicaid insurance are less likely to be tested, adding a concerning socioeconomic dimension to the use of molecular testing.[12] Molecular testing can also be costly, which may further complicate attempts to use molecular testing in resource-limited settings.

Following the 2009 ASCO and National Comprehensive Cancer Network recommendations for *KRAS* testing, in 2010, the VA recommended *KRAS* testing in patients with advanced CRC to identify those who may benefit from EGFR-directed therapies.[9,14] We sought to study the uptake of the recommendation for *KRAS* molecular testing in the VA nationwide, the predictors of molecular testing, and the use of molecular testing to direct therapy. The VA is an attractive resource for the study of *KRAS* mutational analysis as the VA maintains comprehensive standardized electronic medical records on more than 9 million enrolled Veterans and eliminates many of the insurance-related challenges to expensive care.

MATERIALS AND METHODS

We conducted a retrospective cohort study of patients with stage IV CRC treated at the VA. We identified patients diagnosed with CRC in the VA between the years 2006 and 2015 using data from the Oncology Raw data set in the VA Corporate Data Warehouse (CDW). Patient demographics, clinical characteristics, and treatment were collected from the CDW data. We aggregated location of diagnosis into one of four census regions: (1) Northeast, (2) Midwest, (3) South, and (4) West. We categorized centers by volume of colon cancer care, based on the number of analytic CRC cases in the cancer registry, and further divided the sites into colon cancer volume quintiles. The five quintiles were defined by the following number of analytic cases/year, averaged over the 10-year period: < 137; 137-208; 209-302; 303-401; and > 402. We calculated the Charlson Comorbidity Index (CCI) for each subject, and divided the CCI into a binary variable with values above and below the mean. We used the percentage of Black patients with CRC

treated at the diagnosis facility as a continuous independent variable.

Patient-level *KRAS* tests from 2006 to 2015 were obtained from 29 commercial sendout laboratories that contract with the VA. We further conducted a search of *KRAS* testing by Current Procedural Terminology codes and keywords in the CDW data fields for laboratory test name and in the laboratory result comment.

We calculated descriptive statistics of our cohort. Chi-square or Fisher's exact test and Student's *t* test were used to calculate univariate associations between clinical or demographic characteristics and *KRAS* testing, *KRAS* mutational status, and treatment with EGFR-directed therapy. Multivariable logistic regression was used to calculate adjusted associations between demographic or clinical characteristics and *KRAS* testing, *KRAS* mutations, and EGFR antibody therapy. Kaplan-Meier survival curves were computed for relevant patient groups and compared by logrank tests. Statistical analyses were performed with SAS V 9.4 (SAS Institute, Cary, NC). All work was reviewed and approved by the VA-NYHHS IRB under protocol number 1586.

RESULTS

Likelihood of Testing

Among the 5,943 patients diagnosed with stage IV CRC from 2006 to 2015, 1,053 (17.7%) had *KRAS* testing. 5,546 had complete data for analyses and constitute our study cohort. Among them, 976 (17.6%) had *KRAS* testing (Table 1). The population had a median age of 66.7 years (not tested) and 63.8 years of age (tested) at diagnosis, and represented all four national census regions, with 42.9% of the patients from the South. The regional distribution of Veterans with CRC is similar to the regional distribution of all Veterans. The Veterans were predominantly male (97.7%), 68.4% White, 20.3% Black, and 11.2% other races, similar to the general VA patient population. The majority of patients were treated in centers in the two highest quintiles of colon cancer volume.

TABLE 1. Demographics *KRAS* Tested and Not Tested

Characteristic	Tested (No.)	Row %	Not tested (No.)	Row %	P
No.	976	18	4,570	82	
Age, years					< .01
< 45	24	26	67	74	
45-54	127	26	366	74	
55-64	384	20	1,501	80	
65-74	300	19	1,273	81	
75-84	116	11	955	89	
≥ 85	25	6	408	93	
Census region					< .01
Northeast	99	14	629	86	
Midwest	283	22	988	78	
South	348	15	2,034	85	
West	246	21	919	79	
Race					.04
White	673	18	3,123	83	
Black	214	19	913	81	
Other	89	14	534	86	
Sex					.29
Male	949	18	4,469	82	
Female	27	21	101	79	
Marital status					.81
Married	414	17	1,958	83	
Not married	562	18	2,612	82	
Medicaid eligibility					.55
Noneligible	962	17	4,492	83	
Eligible	14	15	78	85	
CCI					< .01
< 2	485	21	1,868	79	
≥ 2	491	15	2,702	85	
Year of diagnosis					< .01
2006	13	2	557	98	
2007	46	8	562	92	
2008	73	12	545	88	
2009	67	12	500	88	
2010	106	18	499	82	
2011	141	24	442	76	
2012	156	28	408	72	
2013	151	28	380	72	
2014	119	24	378	76	
2015	104	26	299	74	
Colon cancer volume					< .01
Q1	25	12	180	88	

(continued in next column)

TABLE 1. Demographics *KRAS* Tested and Not Tested (continued)

Characteristic	Tested (No.)	Row %	Not tested (No.)	Row %	P
Q2	84	15	480	85	
Q3	182	17	902	83	
Q4	201	14	1,247	86	
Q5	484	22	1,761	78	

Abbreviation: CCI, Charlson Comorbidity Index.

Of the 3,183 patients diagnosed after the 2010 recommendation for testing was instituted, 777 tests were performed (24.4%). Testing rates increased substantially from 2.3% among those diagnosed in 2006 to a peak of 28.4% of patients diagnosed in 2013. In univariate analysis, we found that *KRAS* testing was significantly associated with patient age, census region, race, CCI, year of diagnosis, and institutional colon cancer volume (Table 1).

In multivariable logistic regression, we found that after controlling for all of the demographic or clinical covariates, older patients were less likely to have *KRAS* testing, odds ratio (OR) 0.17 (0.09 to 0.32), for those 85 years of age or older (Table 2). Testing rates varied by census regions, with the lowest rates in the Northeast region and the highest rates in the West region. Marital status, sex, and CCI were not significantly associated with *KRAS* testing. Patient race was not associated with *KRAS* testing, OR 1.10 (0.90 to 1.35), for Black patients relative to White patients, but centers that treated more Black patients with CRC were more likely perform *KRAS* testing, OR 1.01 (1.00 to 1.01). Medicaid eligibility was not associated with *KRAS* testing, OR 1.01 (0.55 to 1.54). We found that the odds of testing increased in more recent years, with ORs ranging from 9.96 in 2010 to 18.93 in 2013. High-volume centers were more likely to perform testing, OR 2.32 (1.48 to 3.63), relative to centers treating the lowest volume of CRC patients.

Timing of *KRAS* Testing

We examined days to testing from diagnosis in two strata: those diagnosed from 2006 to 2010, and those diagnosed from 2011 to 2016. We found that the median time to testing in the 305 tested patients diagnosed during 2006-2010 was 295 days, whereas the median time to testing in the 671 tested patients diagnosed during 2011-2015 was 49 days. We further evaluated percentage of testing complete at 180 days and 360 days to give a rough estimate of testing during first-line and second-line therapy in this real-world population. At 180 days, among those diagnosed during 2006-2010, 41% of all tests were complete, whereas among those diagnosed during 2011-2015, 77% of all tests were complete. At 360 days, among those diagnosed during 2006-2010, 55% of all tests were complete, whereas among those diagnosed during 2011-2015, 86% of all tests were complete.

TABLE 2. Associations With *KRAS* Testing, Among All Eligible Patients (N = 5,546)

Characteristic	OR	95% CI Lower Limit	95% CI Upper Limit	P
Age, years				
< 45	1			
< 55	1.24	0.73	2.11	.43
< 65	0.87	0.53	1.44	.58
< 75	0.68	0.41	1.13	.14
< 85	0.44	0.26	0.74	< .01
> 85	0.17	0.09	0.32	< .01
Census region				
Northeast	1			
Midwest	1.69	1.31	2.18	< .01
South	0.98	0.77	1.25	.86
West	1.98	1.52	2.57	< .01
Race				
White	1			
Black	1.1	0.9	1.35	.34
Other	0.85	0.66	1.09	.2
Sex				
Male	1			
Female	1.04	0.66	1.65	.86
Marital status				
Married	1			
Not married	0.88	0.76	1.03	.11
Insurance				
Non-Medicaid eligible	1			
Medicaid eligible	1.01	0.55	1.84	.98
CCI				
CCI low	1			
CCI high	0.83	0.71	0.96	.01
Year of diagnosis				
2006	1			
2007	3.53	1.88	6.63	< .01
2008	5.89	3.21	10.8	< .01
2009	5.81	3.15	10.7	< .01
2010	9.96	5.5	18.02	< .01
2011	14.43	8.03	25.95	< .01
2012	16.95	9.44	30.41	< .01
2013	18.93	10.52	34.04	< .01
2014	15.2	8.4	27.5	< .01
2015	16.95	9.29	30.9	< .01
Colon cancer volume				
Q1	1			
Q2	1.36	0.83	2.23	.23

(continued in next column)

TABLE 2. Associations With *KRAS* Testing, Among All Eligible Patients (N = 5,546) (continued)

Characteristic	OR	95% CI Lower Limit	95% CI Upper Limit	P
Q3	1.53	0.96	2.44	.08
Q4	1.25	0.79	1.99	.35
Q5	2.32	1.48	3.63	< .01
PCT race				
Black	1.01	1	1.01	.06

Abbreviations: CCI, Charlson Comorbidity Index; OR, odds ratio.

KRAS Mutational Status and Receipt of EGFR mAb

Of 976 *KRAS*-tested patients, 346 (35.4%) had *KRAS* mutations. Among those 976 patients, 223 (22.8%) received EGFR mAbs. Of those with *KRAS* mutations, 14/346 (4.0%) received EGFR mAbs, guideline-discordant care (Fig 1). Among 499 of patients with *KRAS* wild-type (WT) results, 178 (35.7%) received EGFR mAbs, guideline-concordant care, and 321 (64.3%) did not receive EGFR mAbs, potentially discordant care. Among 4,570 patients who did not have documented *KRAS* testing, 401 (8.8%) received an EGFR mAb, potentially guideline-discordant care.

Of the 976 *KRAS*-tested patients included in the multivariable model, Black patients were no more likely than White patients to have tumors harboring *KRAS* mutations, OR 1.18 (95% CI 0.83 to 1.69). No other demographic or clinical characteristics were significantly associated with *KRAS* mutation status.

Two hundred twenty-three of 976 (22.8%) tested patients in the multivariable model received an EGFR mAb. Three clinical demographic characteristics were associated with receipt of EGFR mAbs: unmarried patients were less likely to receive an EGFR Ab, OR 0.49 (0.34 to 0.69), diagnosis years 2014 and 2015 were less likely to receive EGFR Abs (OR 0.16 and 0.13 respectively), and patients with *KRAS* mutant tumors, OR 0.08 (0.04 to 0.13).

One hundred seventy eight of 499 *KRAS* WT patients received EGFR mAb. In multivariable logistic regression among these 499 patients, we found that nonmarried status, OR 0.45 (0.29 to 0.69), and treatment at a site with higher percentage of Black patients, OR 1.02 (1.00 to 1.04) (a surrogate for urban treatment center), were associated with receipt of EGFR mAb.

Outcomes of Patients Receiving EGFR mAb

In a multivariable Cox proportional hazards model, patients who were tested for *KRAS* mutations had significantly better survival than those who were not tested, hazard ratio 0.63 (0.59 to 0.68; *P* < .001). The model controlled for patient age, location, race, year of diagnosis, insurance, comorbidities,

FIG 1. Guideline concordance of care.

colon cancer site volume, and percentage of Black patients (which serves as a surrogate for urban or rural). Among those who were *KRAS* WT, survival was better for patients who received EGFR mAbs than for those who did not, with median overall survival of 18.8 months (95% CI, 16.4 to 21.7) and 29.6 months (95% CI, 25.9 to 32.0), respectively (logrank *P* = .0016; Fig 2).

DISCUSSION

In our analysis, we found substantial undertesting of *KRAS* for patients with stage IV CRC in the VA hospital system, with only 17.7% of eligible patients diagnosed between 2006 and 2015 receiving testing. Among those diagnosed in the year 2010 or later, only 24.4% of stage IV CRC patients had *KRAS* testing. *KRAS* testing rates increased substantially from 2.3% among those diagnosed in 2006 to 28.4% for those diagnosed in 2013, but testing rates remained low. We found that high-volume CRC centers were more likely to perform *KRAS* testing. There were no differences in *KRAS* testing rates by race or Medicaid eligibility. Older patients were less likely to be tested for *KRAS* and there was significant regional variability in testing rates. We found that in 2011-2015 *KRAS* testing was performed sooner after diagnosis, than had been done in 2006-2010. We also found underuse of EGFR mAbs, and substantial use among patients with no documentation of *KRAS* testing.

Underuse of *KRAS* testing in the VA population is consistent with previous reports. Charlton et al[12] reported a SEER database analysis, covering approximately 26% of the US population, in which only 30% of more than 22,000 stage IV CRC cases diagnosed between 2010 and 2013 had *KRAS* testing. Some patients are ineligible for antineoplastic therapy because of comorbidities or performance status, and *KRAS* testing would be inappropriate for these patients. The low use of *KRAS* testing reported in both the VA and

SEER, however, suggest that many patients who are eligible for EGFR mAb therapy are not being tested and therefore denied the precision oncology advances dependent upon *RAS* testing results. Carter et al[15] reported higher rate of testing (overall 47.5%) in a cohort of 1,363 patients with stage IV CRC treated in a community-based oncology practice. It is possible that practice patterns vary between the VA, SEER, and community-based practices, and these investigators nonetheless conclude that testing is underused. Uptake of testing may have been better outside of the United States. Ciardiello et al reported a chart review of approximately 3,800 patients being treated for colon cancer in 2010 across 14 countries in Europe, Asia, and Latin America. These authors report that 69% of all patients had *KRAS* testing in 2010. Only limited details of chart selection were provided, so it is unclear if the sampled population is similar to patients studied in the United States. Nonetheless, it may be that more effective systems are in place outside of the United States to increase the uptake of proven molecular testing. Overall, the two largest US analyses, from our VA database and from SEER, conclude that there is substantial underuse of molecular testing in patients with CRC who could benefit from molecular selection of targeted therapy.

Our study found that centers in the highest quintile of CRC volume were 2.32 times more likely than those in the lowest quintile to perform *KRAS* testing on patients with stage IV colon cancer. The relationship between volume of colon cancer surgery and outcomes, including 30-day mortality and 5-year mortality, is well established in both the VA population and the United States at large.[16,17] Few studies, however, have addressed the volume-outcome relationship in regards to medical care for CRCs. And, although multiple studies have sought causes for disparities in medical care for CRC among Veterans,[18-21] none have controlled for the volume of colon cancer treated at each site. It is interesting
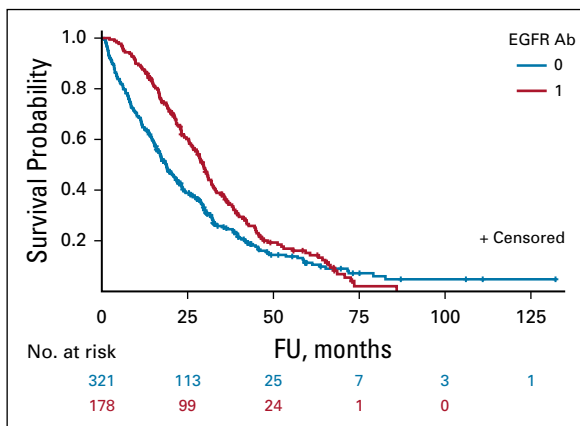
FIG 2. Overall survival among *KRAS* tested and WT by receipt of EGFR mAb. EGFR, epidermal growth factor receptor; FU, follow-up time; mAb, monoclonal antibody; WT, wild-type.

to note that our data do not suggest a clear dose-response relationship between colon cancer volume and molecular testing. Patients diagnosed at the highest-volume colon cancer centers are significantly more likely to have *KRAS* testing than those diagnosed at the lowest volume centers, but it is not clear that each quintile above the lowest does more *KRAS* testing than the previous. The data suggest the possibility that above a certain threshold, *KRAS* testing is performed more regularly. It may be that centers with sufficient colon cancer volume develop more effective systems to perform *KRAS* testing.

Older patients in both the VA and SEER were less likely to have *KRAS* testing. Multiple previous studies have confirmed that older patients are less likely to receive chemotherapy for colon cancer than younger counterparts.[20] Older patients are more likely than younger patients to have comorbid conditions that may increase the toxicity of chemotherapy, but that relationship may not hold with targeted therapy such as EGFR mAbs.[22,23] Jehn et al reported findings that grade III or IV cetuximab toxicities were limited to approximately 30% of patients, with no difference between patients who were older than or younger than 65 years of age.[24] Although it is difficult to say exactly what percentage of older patients with stage IV CRC are EGFR mAb eligible and therefore should have *KRAS* testing, our data suggest that *KRAS* testing is underused in the elderly for whom targeted therapy may have advantages over conventional chemotherapy.

In an effort to examine racial, socioeconomic, and location-related disparities in the use of *KRAS* testing, we included race, Medicaid eligibility, and percentage of Black patients treated at each site in the multivariable models. As with many previous reports on racial disparities in VA care,[25] we found no racial disparities in *KRAS* testing. Outside of the VA, racial disparities in CRC care are prevalent.[26,27] We did,

however, find that medical centers with more Black patients were more likely to perform *KRAS* testing. We do not suggest that this is a causal association, and suspect that percentage of Black patients is a proxy for other factors that are related to *KRAS* testing, such as urban medical centers, or university affiliation. We also noted that within the VA, Medicaid eligibility is not associated with *KRAS* testing, which is different from findings in the SEER database.[12] This finding is consistent with previous data that the VA single-payer system can decrease disparities in care. It is encouraging to note the VA system minimizes socioeconomic disparities for even the most technologically advanced tests offered.

In our exploration of guideline concordance of care, we found little EGFR mAb overuse in patients with *KRAS* mutations (14/346, 4%; Fig 1). We found potentially large underuse of EGFR mAb in the *KRAS* WT population (321/499, 64.3%). We also found that the majority of patients who received EGFR mAb received them without documented *KRAS* testing (489/957, 51.1%), potentially guideline-discordant care. Few studies have reviewed the clinical impact of *KRAS* testing on treatment choice. Rico et al[28] reviewed data from 10 state population-based cancer registries and found that only 7% of *KRAS* WT patients in 2011 received EGFR mAb. Follow-up in this study was short but the findings are consistent with ours in that EGFR mAb may be underused in practice even among patients with *KRAS* testing.

Our study has several potential limitations. It is possible that not all molecular testing was recorded in the VA CDW. Some VA Medical Centers may have conducted molecular testing through a laboratory for which no VA procedure code was captured. We suspect, however, that these tests likely represent a minority of cases as the national VA contracts with the 29 source laboratories that were supported by the VA central office of laboratory medicine and came with no additional cost to the medical center department of pathology. Second, cetuximab and panitumumab were initially approved in the third-line setting without reference to *KRAS* mutation status. Data suggesting that *KRAS* mutation may affect mAb efficacy were available as early as 2008, but some of the use that we characterized as likely inappropriate may have been before the availability of that information. Third, *KRAS* testing can reasonably be performed after first-line therapy, so rates of testing of those diagnosed in 2014 and 2015 likely underrepresent the testing rate for those patients with continued follow-up.

In conclusion, we found underuse of *KRAS* molecular testing among VA patients with stage IV CRC diagnosed between 2010 and 2015. Older patients and those treated at low-volume colon cancer centers were less likely to have *KRAS* testing, but race and Medicaid eligibility were not associated with *KRAS* testing. *KRAS* testing appears to have been appropriately used to exclude patients from EGFR mAb use, but we found low rates of EGFR mAb use

even among *KRAS* WT patients who were molecularly appropriate for therapy. We also found better survival for *KRAS* WT patients treated with EGFR mAbs, consistent with the benefit previously shown in clinical trials. Additional research is needed to understand barriers to the complete implementation of precision oncology in colorectal and other cancers. The VA has a unified national electronic medical record and a centrally organized Precision Oncology Program, which was instituted after 2015 to help implement molecular tumor testing, but data on its efficacy remain limited.[29] These and other effective systems are urgently needed to help clinicians apply expanding knowledge of molecularly targeted therapy to everyday practice and to improve patient care.

AFFILIATIONS
[1]NYU Grossman School of Medicine, New York, NY
[2]VA-New York Harbor Health Care System, New York, NY
[3]VA Informatics and Computing Infrastructure, Washington, DC
[4]The Permanente Medical Group, Oakland, CA
[5]University of Utah, Salt Lake City, UT
[6]Durham Veteran Affairs Medical Center, Durham, NC
[7]Duke University, Durham, NC
[8]VA Salt Lake City Healthcare System, Salt Lake City, UT
[9]University of Massachusetts, Boston, MA

CORRESPONDING AUTHOR
Daniel J. Becker, MD, Perlmutter Cancer Center, NYU Grossman School of Medicine, and VA-New York Harbor Healthcare System, 160 E 34th St, 10th Floor, New York, NY 10016; e-mail: Daniel.Becker@nyulangone.org.

PRIOR PRESENTATION
Presented at ASCO Annual Meeting, Chicago, IL, June 1-5, 2018 (abstract e18844).

AUTHOR CONTRIBUTIONS
Conception and design: Daniel J. Becker, Steve Y. Lee, Scott E. Sherman, Michael J. Kelley, Danil V. Makarov, Julie A. Lynch
Administrative support: Daniel J. Becker, Scott E. Sherman, Danil V. Makarov, Julie A. Lynch
Financial support: Daniel J. Becker, Julie A. Lynch
Provision of study materials or patients: Daniel J. Becker, Kyung M. Lee, Kristine E. Lynch, Julie A. Lynch
Collection and assembly of data: Daniel J. Becker, Kyung M. Lee, Steve Y. Lee, Kristine E. Lynch, Christy D. Morrissey, Julie A. Lynch
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST
The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/po/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

Steve Y. Lee
Honoraria: Novocure
Travel, Accommodations, Expenses: Galera Therapeutics

Danil V. Makarov
Employment: New Hope Fertility

Michael J. Kelley
Consulting or Advisory Role: IBM
Research Funding: Novartis, AstraZeneca, Bristol-Myers Squibb, Regeneron, Genentech
Other Relationship: IBM
Open Payments Link: https://openpaymentsdata.cms.gov/physician/827136

Julie A. Lynch
Research Funding: Genomic Health, AstraZeneca, Myriad Genetics, Boehringer Ingelheim, Astellas Pharma, CardioDx, Janssen

No other potential conflicts of interest were reported.

REFERENCES
1. Siegel RL, Miller KD, Jemal A: Cancer statistics, 2019. CA Cancer J Clin 69:7-34, 2019
2. National Cancer Institute: Surveillance, Epidemiology, and End Results (SEER) Program. https://seer.cancer.gov/
3. Dekker E, Tanis PJ, Vleugels JLA, et al: Colorectal cancer. Lancet 394:1467-1480, 2019
4. Lievre A, Bachet JB, Le Corre D, et al: *KRAS* mutation status is predictive of response to cetuximab therapy in colorectal cancer. Cancer Res 66:3992-3995, 2006
5. Benvenuti S, Sartore-Bianchi A, Di Nicolantonio F, et al: Oncogenic activation of the RAS/RAF signaling pathway impairs the response of metastatic colorectal cancers to anti-epidermal growth factor receptor antibody therapies. Cancer Res 67:2643-2648, 2007
6. Douillard J-Y, Oliner KS, Siena S, et al: Panitumumab–FOLFOX4 treatment and RAS mutations in colorectal cancer. N Engl J Med 369:1023-1034, 2013
7. Bokemeyer C, Köhne C-H, Ciardiello F, et al: FOLFOX4 plus cetuximab treatment and RAS mutations in colorectal cancer. Eur J Cancer 51:1243-1252, 2015

8. Van Cutsem E, Lenz HJ, Kohne CH, et al: Fluorouracil, leucovorin, and irinotecan plus cetuximab treatment and RAS mutations in colorectal cancer. J Clin Oncol 33:692-700, 2015

9. Engstrom PF, Arnoletti JP, Benson AB III, et al: NCCN clinical practice guidelines in oncology: Colon cancer. J Natl Compr Canc Netw 7:778-831, 2009

10. Lynch JA, Berse B, Chun D, et al: Epidermal growth factor receptor mutational testing and erlotinib treatment among veterans diagnosed with lung cancer in the United States Department of Veterans Affairs. Clin Lung Cancer 18:401-409, 2017

11. Lynch JA, Berse B, Rabb M, et al: Underutilization and disparities in access to EGFR testing among Medicare patients with lung cancer from 2010-2013. BMC Cancer 18:306, 2018

12. Charlton ME, Kahl AR, Greenbaum AA, et al: *KRAS* testing, tumor location, and survival in patients with stage IV colorectal cancer: SEER 2010-2013. J Natl Compr Canc Netw 15:1484-1493, 2017

13. Ciardiello F, Tejpar S, Normanno N, et al: Uptake of *KRAS* mutation testing in patients with metastatic colorectal cancer in Europe, Latin America and Asia. Target Oncol 6:133, 2011

14. Allegra CJ, Jessup JM, Somerfield MR, et al: American Society of Clinical Oncology provisional clinical opinion: Testing for *KRAS* gene mutations in patients with metastatic colorectal carcinoma to predict response to anti-epidermal growth factor receptor monoclonal antibody therapy. J Clin Oncol 27:2091-2096, 2009

15. Carter GC, Landsman-Blumberg PB, Johnson BH, et al: *KRAS* testing of patients with metastatic colorectal cancer in a community-based oncology setting: A retrospective database analysis. J Exp Clin Cancer Res 34:29, 2015

16. Schrag D, Cramer LD, Bach PB, et al: Influence of hospital procedure volume on outcomes following surgery for colon cancer. JAMA 284:3028-3035, 2000

17. Rabeneck L, Davila JA, Thompson M, et al: Surgical volume and long-term survival following surgery for colorectal cancer in the Veterans Affairs Health-Care System. Am J Gastroenterol 99:668-675, 2004

18. Zullig LL, Carpenter WR, Provenzale D, et al: Examining potential colorectal cancer care disparities in the Veterans Affairs Health Care System. J Clin Oncol 31:3579-3584, 2013

19. Sabounchi S, Keihanian S, Anand BS: Impact of race on colorectal cancer. Clin Colorectal Cancer 11:66-70, 2012

20. Zeber JE, Copeland LA, Hosek BJ, et al: Cancer rates, medical comorbidities, and treatment modalities in the oldest patients. Crit Rev Oncol Hematol 67:237-242, 2008

21. Zullig LL, Williams CD, Fortune-Britt AG: Lung and colorectal cancer treatment and outcomes in the Veterans Affairs Health Care System. Cancer Manag Res 7:19-35, 2015

22. Repetto L: Greater risks of chemotherapy toxicity in elderly patients with cancer. J Support Oncol 1:18-24, 2003

23. Shahrokni A, Wu AJ, Carter J, et al: Long-term toxicity of cancer treatment in older patients. Clin Geriatr Med 32:63-80, 2016

24. Jehn CF, Böning L, Kröning H, et al: Cetuximab-based therapy in elderly comorbid patients with metastatic colorectal cancer. Br J Cancer 106:274-278, 2012

25. Peterson K, Anderson J, Boundy E, et al: Mortality disparities in racial/ethnic minority groups in the Veterans Health Administration: An evidence review and map. Am J Public Health 108:e1-e11, 2018

26. Tehranifar P, Neugut AI, Phelan JC, et al: Medical advances and racial/ethnic disparities in cancer survival. Cancer Epidemiol Biomarkers Prev 18:2701-2708, 2009

27. Breslin TM, Morris AM, Gu N, et al: Hospital factors and racial disparities in mortality after surgery for breast and colon cancer. J Clin Oncol 27:3945-3950, 2009

28. Rico A, La P, Thompson TD, et al: *KRAS* testing and first-line treatment among patients diagnosed with metastatic colorectal cancer using population data from ten National Program of Cancer Registries in the United States. J Cancer Res Ther 5:7-13, 2017

29. Poonnen PJ, Duffy JE, Hintze B, et al: Genomic analysis of metastatic solid tumors in veterans: Findings from the VHA National Precision Oncology Program. J Clin Oncol 37, 2019 (suppl; abstr 3074)

■■■