



COLLEGE of AMERICAN
PATHOLOGISTS

Molecular Pathology Tests For Prognosis In Common Cancers

MEDCAC Meeting

March 24, 2015

Jan A. Nowak, MD, PhD, FCAP

Medical Director, Molecular Diagnostics & Cytogenetics

NorthShore University HealthSystem

Evanston, Illinois

Presenter Disclosure Information

Consultant, Roswell Park Cancer Institute

CAP Accreditation Program

- **CAP is deemed by CLIA to accredit and inspect clinical laboratory**
- **The CAP's Laboratory Improvement Programs, initiated 65 years ago, currently has participants in more than 100 countries, accrediting 7,600 laboratories and providing proficiency testing to 20,000 laboratories worldwide.**

MEDCAC Question

Please discuss whether each factor below might change the generalizability of evidence about prognostic molecular pathology tests in Medicare beneficiaries with cancer:

- **Regulatory status of test (e.g., US Food & Drug Administration (FDA) approved/cleared vs. laboratory-developed test)?**
- **Type of performing laboratory (i.e., university medical center laboratories, independent commercial laboratories, or community hospital-based laboratories)?**

MEDCAC Question

For each prognostic test listed, how confident are you that existing evidence is sufficient to confirm the analytical validity of the molecular pathology test to estimate prognosis for Medicare beneficiaries with that cancer type?

CAP Proficiency Test Surveys

CAP Survey	Year Initiated	Current Subscription
KRAS	2009	248
BRAF	2010	204
EGFR	2010	213
MMR (MSI)	2005	128

KRAS Survey Summary

- Year Initiated: 2009
- Current subscribers: 248
- Challenges / year: 3 specimens/twice a year.
- Performance, long term and most recent:
 - Almost all mailings/specimens achieved >90% consensus, reporting the intended response.
- Consequences of PT failure:
 - First failure – lab is instructed to review all aspects of testing to understand source of failure and verify that test is performing adequately.
 - Consecutive failure – lab is instructed to cease testing; failure is reported to CMS

BRAF Survey Summary

- **Year Initiated: 2010**
- **Current subscribers: 204**
- **Challenges / year: 3 specimens/twice a year.**
- **Performance, long term and most recent:**
 - **Almost all mailings/specimens achieved >90% consensus, reporting the intended response.**

EGFR Survey Summary

- **Year Initiated: 2010**
- **Current subscribers: 213**
- **Challenges / year: 3 specimens/twice a year.**
- **Performance, long term and most recent:**
 - **Almost all mailings/specimens achieved >90% consensus, reporting the intended response.**

MMR/MSI Survey Summary

- **Year Initiated: 2005**
- **Current subscribers: 128**
- **Challenges / year: 1 specimen / twice a year.**
- **Performance: 95.4% correct classification for years 2005 through 2012**
 - Boyle, TA, et al. Summary of microsatellite instability test results from laboratories participating in proficiency surveys, Arch Pathol Lab Med 138: 363-370 (2014).

CAP Proficiency Test Surveys

CAP Survey	2014 B Survey Performance
KRAS	>97%
BRAF	>97%
EGFR	98 – 100%
MMR (MSI)	98 – 100%

Methods used for mutation detection

CAP Surveys 2014 : KRAS, BRAF, EGFR and MSI

	KRAS	BRAF	EGFR	MSI
ARMS	8.1	4.3	10.2	
Commercial kit*	30.4	21.8	25.7	
DHPLC			0.3	
LNS/PNA	2.8	2	1.3	
NGS	5	6.3	6.3	
PCR, allele-specific	10.5	13	12.8	
Quant PCR, allele specific	0.9	2.3	2	
PCR, Fragment Analysis	0.6	1.3	7.9	
PCR, Melt Curve Analysis	4.7	2.7	1	
Pyrosuequencing	11.1	9.4	7.2	
Real Time PCR		13.8		
Sanger sequencing	19.3	16.7	15.8	
PCR Capillary Electrophoresis				97
PCR Polyacrylamide Gel Elect				2
Single base extension	3.7	3.7	2.3	
Other PCR	2.8	2.3	4.9	1
	100%	100%	100%	100%

* Category includes, but is not exclusive for, FDA approved assays.

MEDCAC Questions

- Please discuss whether each factor below might change the generalizability of evidence about prognostic molecular pathology tests in Medicare beneficiaries with cancer:

- Regulatory status of test (e.g., US Food & Drug Administration (FDA) approved/cleared vs. laboratory-developed test)?

The CAP PT Survey data shows that regulatory status is not determinant of performance for the analytes in question. Test performance is uniformly good.

- Type of performing laboratory (i.e., university medical center laboratories, independent commercial laboratories, or community hospital-based laboratories)?

The CAP PT Survey data has not discerned any difference in test performance for these analytes based on type of performing laboratory. Test performance is uniformly good and consistent.

MEDCAC Questions

- For each prognostic test listed, how confident are you that existing evidence is sufficient to confirm the analytical validity of the molecular pathology test to estimate prognosis for Medicare beneficiaries with that cancer type?

The CAP Survey data, in conjunction with the other requirements of the CAP Laboratory Accreditation for test validation, taking into account both analytical validity and clinical validity, assure that the analytical validity of testing for these analytes is appropriate for clinical use.



COLLEGE of AMERICAN
PATHOLOGISTS