Molecular Pathology Testing To Estimate Prognosis In Cancers

Medical Evidence Development and Coverage Advisory Committee (MEDCAC)

March 24, 2015

Molecular Pathology Testing & Estimated Prognosis in Cancers

Considering the Evidence

CMS and Genomic Testing

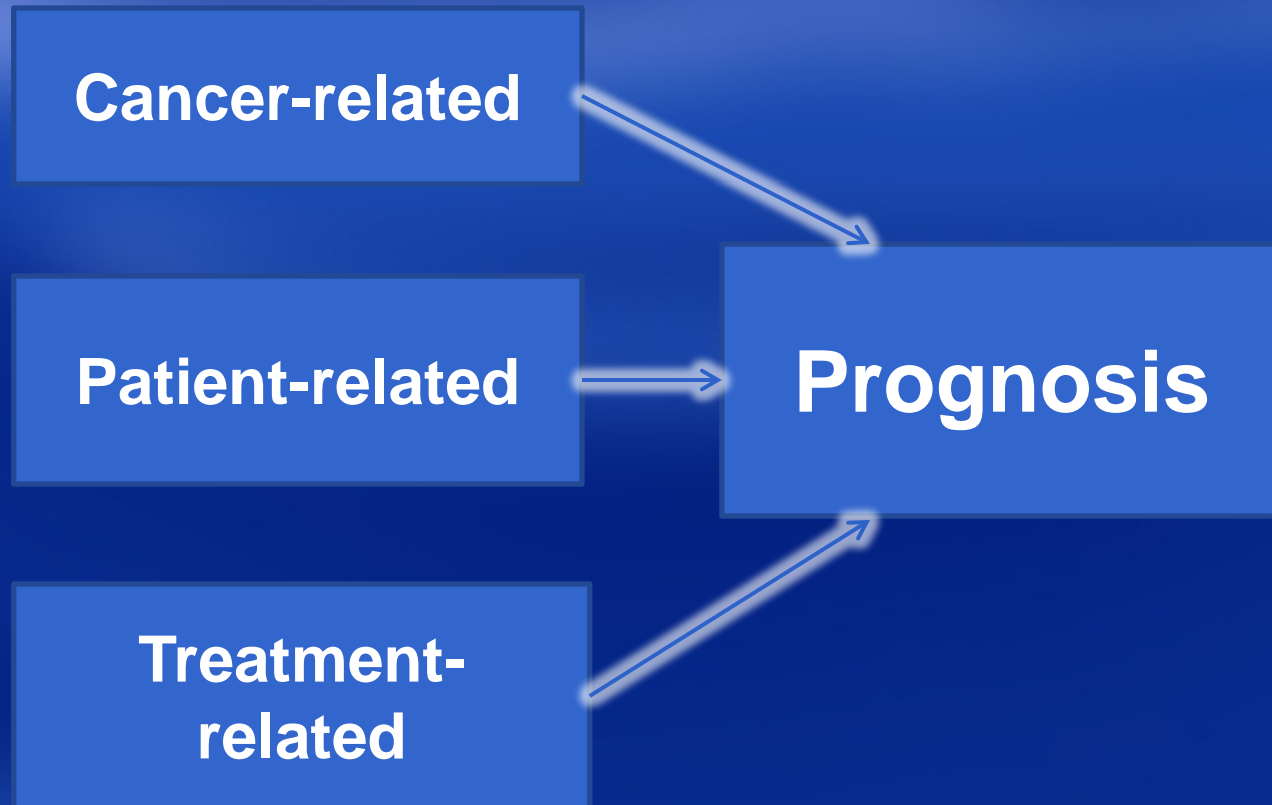| MedCAC Topic	Convened
Genetic (Genomic) Testing	2009 Feb
Screening Genetic Tests	2009 May
Pharmacogenomic Testing in Cancer	2010 Jan
Genetic Tests for Cancer Diagnosis	2013 May
Molecular Diagnostic Tests to Estimate Cancer Prognosis	*2015 Mar*

Prognostic v. Diagnostic

- **Diagnostic test:** a laboratory (or imaging) test performed to aid in the diagnosis or detection of disease in a beneficiary with signs or symptoms of an illness or injury.

- **Prognostic test:** a test performed in a beneficiary with cancer to measure or assess one or more biomarkers thought to be associated with future outcomes.

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What factors affect prognosis?

Cancer-related

Patient-related → Prognosis

Treatment-related

Prognostics Reviewed

Cancer Type	Test to Estimate Prognosis
Adenocarcinoma of the colon and rectum	*BRAF*
	KRAS
	Microsatellite instability
	MLH1 promoter methylation
	Oncotype DX® Colon
Breast cancer (invasive duct and lobular cancers)	MammaPrint®
	Oncotype DX® Breast
Non-small cell lung cancers	*ALK*
	EGFR
	KRAS

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Outcomes of Interest to CMS

- Overall survival;

- Mortality;

- Avoidance of harms of anti-cancer treatment;

- Quality of life; and others.

What's 'reasonable and necessary'

(*CMS' working definition*) A sufficient level of confidence that evidence is adequate to conclude that *the item or device improves clinically meaningful health outcomes* in Medicare beneficiaries

- CMS assesses evidence from peer-reviewed, published articles, which use methods of evidence-based medicine to minimize bias

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MEDCAC Questions

Voting Question Grid

Cancer Type	Test to Estimate Prognosis	Q 1a	Q 1b	Q 2	Q 3
Adenocarcinoma of the colon and rectum	*BRAF*				
	KRAS				
	Microsatellite instability				
	MLH1 promoter methylation				
	Oncotype DX® Colon				
Breast cancer (invasive duct and lobular cancers)	MammaPrint®				
	Oncotype DX® Breast				
Non-small cell lung cancers	*ALK*				
	EGFR				
	KRAS				

Other Acronyms Used

- 'FDA' – The US Food & Drug Administration
  - 'LDT' – Laboratory-Developed Test

- 'CDC' – The Centers for Disease Control and Prevention
  - 'EGAPP' – Evidence for Genomic Applications in Practice and Prevention   (a CDC-sponsored project)

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Test Validity Measures

Analytic Validity (Technical Performance)	Clinical Validity (Strength of Clinical Correlation)
Test's ability to measure genetic trait of interest. • (Analytical) Sensitivity • (Analytical) Specificity • Assay robustness • Quality control	Test's ability to identify or predict the disorder of interest. • (Clinical) Sensitivity • (Clinical) Specificity • Positive Predictive Value • Negative Predictive Value

Source: CDC EGAPP Working Group

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MEDCAC Question 1a

1a) 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?

Scale for voting on Q1a

1 Low Confidence	2	3 Intermediate Confidence	4	5 High Confidence

- *If the answer for Question 1a is at least in the 'Intermediate' range (mean score is 2.5 or more) please vote on Question 1b.*

- *If not, please discuss question 4 (a-d).*

MEDCAC Question 1b

1b) For each prognostic test listed above, how confident are you that existing evidence is sufficient to confirm the *clinical validity* of the molecular pathology test to estimate prognosis in Medicare beneficiaries with that cancer type?

Scale for voting on Q1b

1 Low Confidence	2	3 Intermediate Confidence	4	5 High Confidence

- *If the answer for Question 1b is at least in the 'Intermediate' range (mean score is 2.5 or more) please vote on Question 2.*

- *If not, please discuss question 4 (a-d).*

MEDCAC Question 2

2. How confident are you that there is sufficient evidence to conclude that using the molecular pathology test to estimate prognosis *affects* health outcomes (including benefits and harms) for Medicare beneficiaries with cancer whose anti-cancer treatment strategy is guided by the test's result?

Scale for voting on Q2

1 Low Confidence	2	3 Intermediate Confidence	4	5 High Confidence

- *If the answer for Question 2 is at least in the 'Intermediate' range (i.e., mean score is 2.5 or more) please vote on Question 3.*

- *If not, please discuss question 4 (a-d).*

MEDCAC Question 3

3. How confident are you that there is sufficient evidence to conclude that using the molecular pathology test to estimate prognosis has clinical utility (meaning, that it *improves* health outcomes either due to increased benefits and/or reduced harms) for Medicare beneficiaries with cancer whose anti-cancer treatment strategy is guided by the test's result?

Scale for voting on Q3

1 Low Confidence	2	3 Intermediate Confidence	4	5 High Confidence

- *Please discuss question 4 (a-d).*

MEDCAC Question 4

4. Please discuss whether the following factors change generalizability of evidence about molecular diagnostic tests for estimating cancer prognosis:

a) Regulatory status of test (i.e., FDA) approved/cleared vs. LDT);

b) Performing laboratory type (i.e., academic medical center laboratories, independent commercial laboratories, or other);

c) Demographic subgroups within the Medicare beneficiary population; and

d) Cancer genomic characteristics.