

The Role of Proteomic Testing in Improving Prognosis And Care Planning Quality Measures for Lung Cancer

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INTRODUCTION

Non–small-cell lung cancer (NSCLC) provides a critically relevant example of the importance and difficult nature of planning for cancer care as defined within recent value-based payment programs and care delivery models adopted by the Centers for Medicare and Medicaid Services (CMS). The Medicare Access and CHIP Reauthorization Act of 2015 (MACRA), the Oncology Care Model (OCM), and accountable care organizations (ACOs) all reflect the national movement to steer the health care system away from traditional fee-for-service and toward programs that provide incentives for high-quality care, using the leverage of Medicare reimbursement policies (CMMI 2015). With the dual aim of improving quality of care and lowering costs, these systems are designed to incorporate quality performance metrics as a partial determinant of Medicare reimbursement.

NSCLC is a terminal disease. Although recent and continuing therapeutic advancements for NSCLC offer better care and hope for life exten-

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ABSTRACT

Purpose: The Oncology Care Model (OCM) is a payment model from the Centers for Medicare and Medicaid Services designed to reduce costs and improve quality in cancer care. Key components of quality for the OCM originate from the 13-component cancer care plan. We surveyed the literature to understand the value of prognosis in OCM-directed planning for non–small-cell lung cancer (NSCLC) care and to investigate how the results of a prognostic, proteomic biomarker test, the VeriStrat test, can help OCM-participating providers meet the specific quality measures.

Design: A targeted literature review was supplemented by real-world author experience.

Methodology: Available MEDLINE-indexed literature on the topic of lung cancer prognosis and cancer care planning (1997–2017) were reviewed. Authors also included relevant commentary based on their own real-world experience with VeriStrat testing and prognostic conversations.

Results: There was near-universal consensus in guidelines and literature about the critical importance of early, candid, and ongoing physician-patient discussions about prognosis, which informs most components of the OCM care plan. The VeriStrat test has been shown to provide accurate predictions of outcomes in all lines of therapy and in various treatments for patients with NSCLC, including chemotherapies and EGFR-TKI therapies.

Conclusion: Accurate prognostic estimates, such as those provided by the VeriStrat test, are useful for predicting and documenting expected response to treatment, avoiding ineffective and costly overtreatment and for facilitating meaningful conversations with NSCLC patients about the timing of best supportive care and hospice care when appropriate, thereby improving cancer care planning and quality scores.

KEY WORDS

Lung cancer, Oncology Care Model, quality measures, prognosis, care planning, physician patient communication, treatment preferences, end of life, proteomics

sion, none are curative. Furthermore, a high proportion (>79%) of patients are diagnosed with lung and bronchus cancer at an advanced, metastatic, and highly aggressive stage (Howlander 2017), with five-year survival rates of only 15% for men and 21% for women (ACS 2017).

Biomarker tests are now available to help guide treatment decisions, but

few tools are available for accurate prognosis of NSCLC. As a result, oncologists are often forced to make imprecise estimates of prognosis based on patient-performance status or population statistics—indicators that may not always be reliable (Christakis 2000, Glare 2003, Gripp 2007, Llobera 2000, Taniyama 2014, Viganò 1999).

The VeriStrat test, a serum-based

ABBREVIATIONS

- ACO – accountable care organization
- APM – alternative payment model
- BSC – best supportive care
- CMS – Centers for Medicare and Medicaid Services
- NAM – National Academy of Medicine, formerly the Institute of Medicine of the National Academies
- MACRA – Medicare Access and CHIP Reauthorization Act of 2015
- MIPS – Merit-based Incentive Payment System
- NSCLC – non–small-cell lung cancer
- OCM – Oncology Care Model
- OS – overall survival
- PFS – progression-free survival
- QALY – quality-adjusted life-years

BOX 1

Information in a cancer care plan

Utilizing patient-centered communication and shared decision making, the cancer care team collaborates with patients to develop a cancer care plan. Here are some examples of the components in a patient-specific cancer care plan:

- Patient information (e.g., name, date of birth, medication list, allergies)
- Diagnosis, including specific tissue information, relevant biomarkers, and stage
- Prognosis
- Treatment goals (curative, life-prolonging, symptom control, palliative care)
- Initial plan for treatment and proposed duration, including specific chemotherapy drug names, doses, and schedule as well as surgery and radiation therapy (if applicable)
- Expected response to treatment
- Treatment benefits and harms, including common and rare toxicities and how to manage these toxicities, as well as short-term and late effects of treatment
- Information on quality of life and a patient’s likely experience with treatment
- Who will take responsibility for specific aspects of a patient’s care (e.g., the cancer care team, the primary care/geriatrics care team, other care teams)
- Advance care plans, including advanced directives and other legal documents
- Estimated total and out-of-pocket costs of cancer treatment
- A plan for addressing a patient’s psychosocial health needs, including psychological, vocational, disability, legal, or financial concerns and their management
- Survivorship plan, including a summary of treatment and information on recommended follow-up activities and surveillance and risk reduction and health promotion activities

Sources: CMMI 2015, IOM 2013

proteomic test, is a promising tool offering direction in achieving more accurate NSCLC prognoses. VeriStrat is a sole-source test offered by Biodesix, in Boulder, Colo. The test uses a single blood draw that is sent to the Biodesix laboratory for processing, and it renders results for physicians within 72 hours of receipt of the sample. VeriStrat uses matrix-assisted laser desorption ionization time-of-flight (MALDI-ToF) mass spectrometry to measure the presence of circulating immune-related proteins associated with the aggressive disease (Taguchi 2007).

The results of the VeriStrat test can predict patient response to first-line and certain targeted therapies (Akerley 2013a, Carbone 2012, Dingemans 2013, Gadgeel 2017, Gregorc 2014, Grossi 2017, Lara 2016, Stinchcombe 2013, Sun 2014) and have proved to be highly predictive of overall prognosis (Carbone 2012, Gregorc 2014, Grossi 2017, Taguchi 2007). VeriStrat provides independent, accurate prognostic information and enables avoidance of ineffective treatment options, identifying patients for whom inactive treatment options—including best supportive care (BSC) or hospice—may be appropriate.

The availability of high-quality, actionable prognostic information when managing complex diseases like NSCLC under OCM may contribute to attaining performance payments. The OCM quality measures were selected from the National Quality Strategy and align with the quality measures used in other CMS quality payment programs.

While this review focused on the OCM, the analysis applies to other programs with the same quality measures, such as the Merit-based Incentive Payment System (MIPS), Alternative Payment Models (APMs), and other CMS programs. Such programs emphasize quality over quantity of care (CMS 2017).

CMS implemented the OCM to address challenges specific to advanced cancers: namely, the difficult tradeoffs between aggressive treatment, life extension, and quality of life that patients and physicians must grapple with when faced with these often-incurable forms of cancer. The OCM includes financial and accountability for episodes of care surrounding therapy administration to cancer patients. OCM and MIPS quality measures place strong emphasis on patient-centered communication and shared decision making.

The OCM itself is complicated, requiring six enhanced services to be provided to improve patient outcomes, as well as a multitude of quality measures, largely focusing on processes, that each practice must report. However, it is clear from enhanced services requirements that participating practices must prepare for every patient a comprehensive, documented cancer care plan that includes 13 components recommended in a 2013 report prepared by the Institute of Medicine of the National Academies, which is now called the National Academy of Medicine (NAM) (CMMI 2015, IOM 2013). The NAM care plan (Box 1) represents some of the most important clinically focused quality measures in the OCM, and it includes determination of disease prognosis and its effective communication to the patient (IOM 2013). Accurate disease prognosis is essential to developing a high-quality care plan because it informs all the treatment and other decisions that follow.

The following report provides a targeted literature review supplemented with real-world clinical experience from physicians utilizing the VeriStrat test in clinical practice. The goal is to consolidate the current base of knowledge and guidelines regarding the value of prognosis in planning for NSCLC care, within the framework of the OCM and the NAM 13-point

cancer care plan, and to illustrate how VeriStrat is used to help meet the specific requirements in these frameworks.

METHODS

Objective

The objective of this study was to review current evidence and standards of care relating to the establishment and communication of prognosis and care planning for patients with NSCLC, including the use of VeriStrat testing in participating OCM locations. Specific focus was placed on three topics relevant to the OCM and how the VeriStrat test relates to:

1. Current prognostication techniques and the value of the VeriStrat test for improving the accuracy of prognosis and the quality of treatment decision making.
2. The impact of an accurate prognosis on cancer care planning.
3. How VeriStrat prognostic results can be used to meet MIPS and OCM quality metrics and OCM treatment planning requirements from the NAM 13-point care plan.

Identification and screening of the literature

Using the NCBI PubMed database, this study reviewed available MEDLINE-indexed literature (January 1997–January 2017) on the topic of lung cancer prognosis and cancer care planning. The following terms were used either singly or in combination: actionable, biomarker, cancer, communication, cost, end of life, hospice, lung cancer, outcomes, palliative, prognosis, prognostic tools, quality of life, treatment preferences (Table 1).

English-language literature describing U.S. based clinical trials, survey-based studies, clinical practice guidelines, and organizational reports and commentaries were included. Studies that did not discuss prognosis or that focused on diagnostic pro-

cedures or the outcomes of medical procedures, or that were unrelated to lung cancer, were excluded.

Finally, the authors included comments regarding their own experiences with prognosis, the utility of VeriStrat in the clinic, and/or involvement in OCM-participating practices to illustrate how the VeriStrat test has been used in real-world clinical practice to make meaningful treatment decisions about prognosis and to assist in meeting OCM requirements.

RESULTS

The initial search using the terms in Table 1 yielded 356 articles, of which 67 were duplicates and another 175 were determined to be irrelevant. An additional 24 articles identified in the reference lists but not found during the original search were also reviewed. The final number of references reviewed was 138. Because of space limitations, only the most informative and relevant of those were cited in this review.

For OCM applicants and participating organizations, quality measures and requirements related to prognosis and cancer care planning are defined (Table 2). Metrics include establishment of treatment goals and expected response, avoidance of hospital admissions and overtreatment at the end of life, and timely referral to hospice. Meanwhile, requirements for participating OCM organizations—specifically, the NAM’s 13 components of cancer care planning—emphasize the importance of establishing and communicating prognosis, selecting optimal treatment for each patient, and discussing specific treatment goals, expected response to and cost of treatments, and expected quality of life (Box 1). Together, these measures underscore the importance of establishing and communicating prognosis to the patient.

Current prognostication techniques and the value of the VeriStrat test

Even in the face of observable declines in patient health, it can be difficult for physicians to make precise estimates about survival (Detterbeck 2013). Standard cancer prognostication is based on performance status, general survival statistics, and standard laboratory tests, which do not always inform personalized survival prediction (Christakis 2000, Glare 2003, Gripp 2007, Taniyama 2014, Wolf 2013). Predictive models using prognostic factors such as cancer site, metastases, performance score, and patient characteristics have also proven incomplete (Chiu 2015). Therefore, new validated diagnostic tools are needed for precise prognosis.

The VeriStrat test is a noninvasive tool that assists physicians with prognostic discussions. Within 72 hours of blood sample collection, the VeriStrat test provides information regarding expected response to treatment as well as overall prognosis, independent of treatment.

In addition to patient-specific predictions about the efficacy of systemic and EGFR-TKI therapies, the test

provides a binary prognostic answer (“VSGood” or “VSPoor”) that, when combined with clinical information, has been shown to provide the basis of a highly accurate estimate of survival duration (Table 3) (Akerley 2013b, Akerley 2017, Amann 2010, Carbone 2012, Gadgeel 2017, Gregorc 2014, Grossi 2017, Vansteenkiste 2012).

The VeriStrat test’s ability to predict which patients will experience longer progression-free survival (PFS) and/or overall survival (OS) in response to treatment has been demonstrated across a multitude of therapies, including first-line standard chemotherapy (Grossi 2017, Vansteenkiste 2012, Amann 2010), second-line erlotinib (Carbone 2012), second-line sorafenib (Dingemans 2013), first-line gemcitabine, erlotinib, and a combination of the two (Stinchcombe 2013), EGFR-TKIs (Sun 2014), erlotinib plus carboplatin/paclitaxel (Lara 2016), and second-line afatinib or erlotinib (Gadgeel 2017). Furthermore, in a multivariate analysis of 76 first-line patients, VeriStrat was found to be the only statistically significant predictor of OS (Grossi 2017). Grossi and colleagues showed that VeriStrat classification (VSGood versus VSPoor)

was the only statistically significant predictor of OS (HR, 0.23; $P < .001$) while ECOG performance score, EGFR, KRAS, ALK mutation status, chemotherapy type, gender, prior radiotherapy, and prior surgery were nonstatistically significant predictors of OS in a multivariate analysis.

Based on the literature review as well as real-world feedback from the authors, the prognostic information provided by the VeriStrat test guides optimal treatment decisions effectively. A 2017 study by Akerley et al analyzed treatment plans of 989 physicians. Treatment considerations were analyzed before and after VeriStrat results for 2,494 patients with NSCLC. The test classified 1,950 patients as VSGood and 544 patients as VSPoor. Prior to receiving test results, active treatments were under consideration for 99% of patients. After testing, physicians changed their recommendations such that BSC was recommended to 25% of patients with a VSPoor result (n=136) and active treatments for 75% (n=408). Overall, 98% of physicians’ treatment recommendations were made in accordance with VeriStrat test results, and these changes in treatment recommenda-

TABLE 1
Search terms and results

Description	Results
S1- NCBI: ((lung cancer) AND prognosis) AND treatment preferences	109
S2- NCBI: (((lung cancer) AND prognosis) AND end of life) AND communication)	33
S3- NCBI: (((lung cancer) AND end of life) AND prognosis) AND palliative) AND quality of life	45
S4- NCBI: (((lung cancer) AND prognosis) AND hospice) AND outcomes	19
S5- NCBI: (((lung cancer) AND end of life) AND prognosis) AND palliative) AND cost	7
S6- NCBI: (((cancer) AND prognosis) AND biomarker) AND actionable)	42
S7- NCBI: (lung cancer) AND prognostic tools	101
Manual additions: referenced in other articles	19
Manual additions: referenced in guidelines	5
Duplicates	(67)
Excluded for nonrelevance	(175)
Total articles reviewed	138

tions resulted in an 89% decrease in ineffective treatments offered to patients with a VSPoor prognosis (Akerley 2017).

Consistent with these findings, a 2017 cost-effectiveness model by Page et al estimated the impact on cost of care and patient outcomes from using VeriStrat to guide treatment decisions. The model derived treatment choices from the Akerley 2017 decision impact data (N=2,494 patients), using the shift between pretest treatment considerations and posttest treatment recommendations to calculate the impact of using VeriStrat. Patient outcomes were derived from clinical

trials, and costs surrounding treatment, surveillance, and adverse event management were estimated from a Medicare perspective. The model concluded that VeriStrat reduced the use of active treatment by 9.1%, changed choice of active treatment in 20% of patients, improved OS by 0.7 months and 0.5 quality-adjusted months, and resulted in a net savings of \$1,050 per patient after factoring in the cost of the VeriStrat test (\$3,480). This represented an overall incremental cost-effectiveness ratio of -\$26,131 per quality-adjusted life-year (QALY). The benefit for patients with a VSPoor result was even more pronounced.

Cost savings was \$10,414 per patient, with a net 24% shift from active treatment to BSC. The shift in therapies, to less expensive and more effective therapies based on test results, creates cost savings that more than offset the cost of testing (Page 2017).

Collectively, the literature shows that the VeriStrat test helps establish prognosis in NSCLC, guide optimal treatment decisions, predict expected response to treatment, avoid costly and ineffective treatment, and identify patients for whom BSC may be most appropriate (Akerley 2013b, Akerley 2017, Amann 2010, Carbone 2012, Gregorc 2014, Grossi 2017, Vansteen-

TABLE 2
Oncology Care Model and Merit-based Incentive Payment System quality measures related to prognosis and cancer care planning for cancer patients

Category	Measure/ number	Requirement or measure description (CMMI 2015)	Impact of prognosis and VeriStrat testing
Cancer care plan	OCM Documented care plan MIPS 47,130,374	The documented cancer care plan must include conversations about prognosis, goals of treatment, and expected response to treatment	Planning and communicating cancer care relies on accurate prognosis. VeriStrat is prognostic and predictive of outcomes across multiple treatments, allowing physicians to have a precise tool to have prognostic conversations with patients with NSCLC when planning care (Gregorc 2014, Stinchcombe 2013, Taguchi 2007).
Hospital/ ICU/ER admissions	OCM-1 OCM-2 MIPS 454,455	Proportion of patients with all-cause hospital admissions, all-cause ED visits or observation stays, all-cause ICU admissions	Prognosis and expected treatment response allows physicians to balance precise treatment benefit with toxicity and to avoid toxic ineffective therapies (Akerley 2017, Grossi 2017). Tissue biopsy for lung cancer patients often results in medical complications, including hemorrhaging of the lungs or infection, at times leading to ED visits (Dale 2012). VeriStrat is a serum-based test that provides prognostic information and does not require tissue biopsy.
Over-treatment	MIPS 453	Proportion of patients who died from cancer while receiving chemotherapy in the last 14 days of life	Precise prognosis using VeriStrat allows physicians to optimize treatment and decrease over-treatment when appropriate (Akerley 2017).
Timing and referral to hospice	OCM-3 MIPS 456	Proportion of patients who died from cancer but were never admitted to hospice	Appropriate timing of referral to hospice requires precise prognosis. VeriStrat acts as a tool to facilitate conversations about timing of palliative or best supportive care when appropriate (Akerley 2017, Page 2017).
	OCM-3 MIPS 457	Proportion of patients who died who were admitted to hospice for <3 days	

kiste 2012). Physician feedback agreed with these findings, such that prognosis and evaluating expected response to treatments while considering costs in the OCM are critical components of cancer care planning. Based on this literature review and feedback from the authors using VeriStrat in clinical practice, the information offered by VeriStrat can act as a critical tool to aid in complying with multiple components of the NAM cancer care plan as well as OCM and MIPS quality measures (Table 2).

Impact of an accurate prognosis on planning cancer treatment

With these results as a framework, we reviewed clinical practice guidelines and literature about the importance of communicating a clear prognosis with patients across the continuum of care (Table 4). All nationally recognized clinical practice guidelines supported the importance of early and regular communication regarding prognosis (Detterbeck 2013, Ferrell 2017, Ford 2013, Masters 2015, NCCN 2017a,

NCCN 2017b, Pallis 2014).

The OCM advanced care plan requirements specifically call for establishing goals of treatment (CMMI 2015, IOM 2013), including the associated benefits, risks, costs, and outcomes. Patients can develop realistic personal goals and preferences for care only if they and their care team have accurate prognostic information available at the time when those treatment decisions are being discussed (Ford 2013, Gwilliam 2011). Patients were found to want an accurate prognosis from their physicians as a matter of trust (Kirk 2004), and, indeed, a number of studies reported that as many as 95% of patients wanted to know their prognosis even if it was poor (Hagerty 2004, Hagerty 2005, Kirk 2004, Yun 2004).

The literature review found that prognosis has a definitive impact on treatment preferences (Gwilliam 2011). Patients who believed they were going to live for at least six months were more likely (OR=2.6, 95% CI (1.8–3.7) to favor life-extend-

ing therapy over comfort care compared to patients who thought there was at least a 10% chance they would not live six months (Weeks 1998).

In a study by Mack and colleagues, patients with advanced cancer who understood that their chemotherapy was “not at all” likely to cure their cancer were no less likely to receive chemotherapy, but they were more likely than other patients to enroll in hospice (N= 722, OR=1.97, 95% CI=1.26–2.66) (Mack 2015).

How VeriStrat prognostic results can be used to meet MIPS quality metrics and OCM treatment planning requirements from the NAM 13-point care plan

Lung cancer is the second most commonly diagnosed cancer in the United States and the leading cause of death from cancer (ACS 2016). As such, the OCM, NAM cancer care planning framework, and MIPS quality measures highlight conversations around prognosis, expected response to treatment, palliative care through-

TABLE 3
Patient overall survival by VeriStrat test result

Study	Treatment	6-month survival, %		Median OS, months		P value
		VSGood	VSPoor	VSGood	VSPoor	
Treatment-naïve						
Grossi 2017 (N=76)	platinum doublet (carboplatin/pemetrexed)	70	10	9.4	3.4	<.001
	platinum doublet (cisplatin/pemetrexed)	90	43	17.7	4.2	.001
Vansteenkiste 2012 (N=202)	platinum doublet (cisplatin/gemcitabine)	86	56	14.7	6.3	<.001
Amann 2010 (N=102)	erlotinib	66	37	10.8	3.9	.001
Previously treated						
Carbone 2012 (N=396)	erlotinib (n=252)	67	35	10.5	4.0	<.001
	placebo (n=144)	52	18	6.6	3.1	<.001
Gregorc 2014 (N=287)	erlotinib (n=143)	72	24	11.0	3.0	<.001
	chemotherapy (n=142)	71	51	10.9	6.4	<.001
Gadgeel 2017 (N=675)	afatinib (n=336)	75	43	11.5	4.7	<.001
	erlotinib (n=339)	67	37	8.9	4.8	<.001

out treatment, avoidance of hospital admission, avoidance of ICU admissions, avoidance of excessive ER visits, avoidance of overtreatment at the end of life (CMS 2017), and timely referral to BSC and hospice when appropriate (CMMI 2017). All these measures are directly affected by the decision to undergo active treatment versus inactive treatment options such as patient monitoring, BSC, or hospice—a decision that may be facilitated when the VeriStrat test is included as part of the diagnostic workup prior to initiation of treatment.

Physician-patient communication

Many patients do not currently receive precise prognostic estimates or understand the implications with respect to curative versus palliative therapy. In a large observational trial of patient expectations about chemotherapy, 69% of the 710 stage IV lung cancer patients did not understand that chemotherapy, while life-prolonging, was not at all likely to cure their cancer (Weeks 2012). While some of this gap is likely due to patient-related factors, physicians often find it difficult to have candid conversations with patients and their families or caregivers out of the fear of extinguishing hope (Steinhauser 2001). However, realistic information about prognosis can decrease patient anxiety stemming from fears of the unknown when it is delivered with empathy and honesty (Hagerty 2005).

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TABLE 4
Guidelines supporting physician-patient communication about prognosis and the planning of cancer treatment

Guideline	Position or statement
ASCO guidelines, palliative care (Ferrell 2017)	Emphasizes early integration of prognostic conversations into goal setting, continual assessment of patient understanding and awareness about prognosis and treatment goals, and early discussion of hospice.
ASCO guidelines, systemic therapy for stage IV non-small-cell lung cancer (Masters 2015)	Recommends initiating conversations about prognosis at time of diagnosis, with new conversations about risks, benefits, and prognosis before each line of therapy.
CHEST guidelines, diagnosis and management of lung cancer (Detterbeck 2013)	Notes the complexity of prognostic classification, which depends not only on stage classification but also on comorbidities, performance status, and treatment given.
CHEST guidelines, palliative and end-of-life care in lung cancer (Ford 2013)	Recommends that clear, consistent conversations about prognosis and goals of care begin at diagnosis and continue throughout the course of the illness to alleviate emotional distress and facilitate informed, timely decision making about end-of-life care.
EORTC Elderly Task Force, Lung Cancer Group and International Society for Geriatric Oncology (Pallis 2014)	Notes that treatment decisions require adequate information and participation of the patient and family and clear information regarding prognosis, treatment options, benefits and risks, and potential negative effects of over- and undertreatment.
NCCN guidelines, NSCLC, v7.2017 (NCCN 2017b)	Notes that good prognostic factors include early-stage disease at diagnosis, good performance status (PS: ECOG 0,1, or 2), no significant weight loss (no more than 5%), and female gender.
NCCN guidelines, palliative care (NCCN 2017a)	Emphasizes clear, consistent, and empathetic communication with the patient and family about the natural history of the patient's cancer, the prognosis, potential response to treatments, and setting therapeutic and palliative care goals that are consistent with estimated life expectancy.

It can also allow patients adequate time to prepare emotionally, spiritually, and practically for their passing (Steinhauser 2001, Temel 2010). Because of its reliable, predictive, and prognostic results, the VeriStrat test has been shown to be an excellent tool for facilitating these difficult but necessary discussions between physicians and patients (Akerley 2017).

Real-world case reports from the authors exemplify the clinical utility of VeriStrat testing to support, facili-

tate, and document physician-patient communication and monitoring in the OCM.

In one case, a 61-year-old female was diagnosed with stage IV adenocarcinoma but was unable to tolerate palliative chemotherapy. The physician ordered first-line testing including VeriStrat to evaluate treatment options. A VSPoor result and presence of metastatic disease were major factors in the author's decision to shorten the follow-up schedule from the standard

6 months to every 3 months. Based on physician-patient discussions and consideration of all clinical factors (metastatic disease, negative for programmed death ligand 1 [PD-L1] expression, positive for KRAS mutation), the patient enrolled in a clinical trial evaluating nivolumab + ipilimumab; however, the patient progressed quickly on therapy. In this case, a VSPoor result assisted the physician in discussing clinical trial options with the patient and determining appropriate monitoring.

Expected response to treatment

As noted above, VeriStrat has been shown to predict which patients are likely to respond to first-line, standard-of-care platinum doublet therapy (Grossi 2017, Vansteenkiste 2012) and to EGFR-TKIs in multiple lines (Carbone 2012, Gregorc 2014). Grossi et al demonstrated that in non-squamous patients treated with standard chemotherapy in the first-line setting, patients classified as VSGood had longer PFS and OS than those classified as VSPoor: 6.5 vs. 1.6 months ($P<.001$) and 10.8 vs. 3.4 months ($P<.001$), respectively. Additionally, VeriStrat testing identifies which patients will not benefit from EGFR-TKI therapies. Carbone et al demonstrated that for patients with tests results of VSPoor, treatment with an EGFR-TKI (erlotinib) was not statistically better than treatment with placebo ($P=.11$). Additionally, Gregorc et al reported that in a prospective randomized phase 3 trial, patients classified as VSPoor had better median survival on chemotherapy compared with treatment with erlotinib (6.4 vs. 3.0 months, $P=.002$). Numerous others studies have confirmed that VeriStrat test results are predictive of response (OS and PFS) to a variety of front- and second-line, as well as targeted, therapies (Table 3) (Akerley 2013a, Dingemans 2013, Gadgeel 2017, Grossi 2017, Lara 2016,

Schwartzberg 2012, Stinchcombe 2013, Sun 2014, Vansteenkiste 2012).

Another case report by the authors describes the use of VeriStrat to understand expected response to therapies and how it was used to discuss treatment options with the patient. The patient, a 71-year-old male, was diagnosed with stage IV metastatic adenocarcinoma of the lung, with poor performance status. Carboplatin with pemetrexed was administered as the first-line treatment with no response. Testing for PD-L1 expression and genetic mutations yielded negative results for driver mutations and positive PD-L1 results at >50%. Targeted therapies were therefore not a viable option, but immunotherapies could be considered. For information regarding prognosis, the physician ordered VeriStrat, and results were VSPoor. Without this information, the physician would typically administer standard chemotherapy. Instead, he had an informed, shared decision making discussion to consider other options based on patient preference. Based on the VSPoor result, the author explained to the patient that he would not do well on chemotherapy and had a median expected survival of about four months. The potential risks and benefits of discontinuing active therapy, considering hospice care, and pursuing immunotherapy were discussed. In the end, the patient chose to receive immunotherapy (pembrolizumab) based on the patient-physician communication around limited expected response to chemotherapy. The patient remains on active treatment and is routinely restaged to assess response.

The results of the literature review showing the prognostic utility of VeriStrat are further confirmed in the experience of the practicing authors (Page, Argento, Schaefer). The VeriStrat test has proven useful during the treatment planning process and to facilitate conversations about

treatment options and expected responses. For patients classified as VSPoor, the test results and supporting studies indicate patients are less likely to respond to treatment. The results can help inform a number of crucial treatment decisions, including the duration of first-line therapy, how long to wait for indications of possible effectiveness, the advisability of enrollment in a clinical trial and, overall, the formulation of realistic expectations about outcomes.

Palliative care, BSC, hospice, and avoidance of overtreatment

Availability of an accurate prognosis has been shown to affect planning for palliative care. Without such care, patients near the end of their lives can suffer from severe uncontrolled pain, functional decline, and confusion (McCarthy 2000). These effects are often related to timing; physicians may refer patients to palliative care too late. In a survey of 2,515 Medicare beneficiaries, patients generally preferred treatment focused on palliation rather than life extension, with 83.9% of patients indicating that they did not want potentially life-prolonging drugs that made them feel worse all the time (Barnato 2007). Consistent with these wishes, adequate palliative care has been shown to have positive impacts on patient quality of life (Akerley 2017, Bakitas 2009, Howie 2013), rates of depression (Hui 2014), hospitalization and associated costs (Hui 2014, Smith 2010, Zhang 2009), in-hospital deaths (Hagerty 2005, Zhang 2009), and aggressive overtreatment at the end of life (Ferrell 2017, Jang 2015, Lambden 2016).

Hospice care is not used enough. While the Medicare program provides hospice care benefits for patients with a prognosis of six months or fewer, the median duration of hospice use is less than a month, with more than a third of patients referred to hospice within the last week of life (NHPCO 2015).

Hospice-associated quality metrics within OCM are meant to ensure that patients receive the benefits of hospice care: dying with dignity, dying at home, reduced pain, and reduced burden on caregivers.

VeriStrat test results were used in another author case to support, facilitate, and document shared decision making discussions related to hospice care. A 67-year-old female diagnosed with stage IIIB metastatic lung cancer with an ECOG performance status of 2–3 was treated with carboplatin plus taxol and radiation in the front line. Within three months, the patient had locoregional progression and metastatic invasion into the esophagus. At this point, the physician changed treatment to immunotherapy with pembrolizumab, but the patient had poor tolerance and response. The patient was restaged (stage IV), and a VeriStrat test resulted in VSPoor. Ultimately, the patient and physician discussed the options available using VeriStrat results, and together determined that enrolling the patient in hospice care was a better option than pursuing more chemotherapy. This discussion was important to the patient, showing her that quality of life at the end of life could be optimized, while physical and financial burden that would come with additional lines of potentially ineffective therapy could be minimized.

These experiences are consistent with the findings from the 2017 study by Akerley and colleagues. Results discussed prior suggest that the VeriStrat test helped patients avoid ineffective overtreatment in favor of the quality-of-life gains afforded by BSC. Additionally, in real-world clinical experience offered by the authors, a prognosis of VSPoor does not always mean an automatic cessation of active care in favor of BSC and hospice. Real-world experiences find that it usually changes the timing of the discussion, but depending on other

patient and disease characteristics, it may be just as likely to prompt a shift toward newer oncology drugs or clinical trials.

Limitations

This report has a number of limitations. We made our best effort to be systematic in our literature search; however, given the short time frame since the implementation of the OCM and 13 steps of cancer planning, we found little to no quantitative data available with which to evaluate the effects of specific approaches, tools, and interventions on providers' ability to comply with OCM and the 13 steps of cancer care planning. Furthermore, while there are a reasonable number of published studies about the utility of the VeriStrat test, none have yet been designed to specifically address this question. The arguments presented here have been extrapolated from multiple, separate pieces of evidence, combined with personal experience and opinion. Rigorous, prospective, studies would be useful to determine the real-world influence of more accurate lung cancer prognoses on cancer care planning, quality scores, and costs.

CONCLUSION

In conclusion, knowledge and communication of prognosis, expected response to treatment, and quality of life are central to quality management of patients with cancer, especially within models like OCM and MIPS. While these payment models are complex, the 13 components of cancer care planning establish steps to better cancer management. Tools to help meet those components are important and at times lacking, but they are important for meeting documented care plan requirements and quality metrics. By combining the predictive and prognostic value of VeriStrat testing with clinical factors, physicians and practices participating

in the OCM are better able to predict and document expected response to treatment, avoid ineffective and costly overtreatment, and have meaningful conversations with patients about the timing of BSC or hospice care when appropriate. By providing independent prognostic information, the VeriStrat test is a validated, commercially available tool that physicians can use to improve cancer care planning and composite performance scores associated with quality payment models.

REFERENCES

Akerley W, Boucher K, Rich N, et al. A phase II study of bevacizumab and erlotinib as initial treatment for metastatic non-squamous, non-small cell lung cancer with serum proteomic evaluation. *Lung Cancer*. 2013a;79(3):307–311.

Akerley WL, Arnaud AM, Reddy B, et al. Impact of a multivariate serum-based proteomic test on physician treatment recommendations for advanced non-small-cell lung cancer. *Curr Med Res Opin*. 2017;33(6):1091–1097.

Akerley WL, Nelson RE, Cowie RH, et al. The impact of a serum based proteomic mass spectrometry test on treatment recommendations in advanced non-small-cell lung cancer. *Curr Med Res Opin*. 2013b;29(5):517–525.

Amann JM, Lee JW, Roder H, et al. Genetic and proteomic features associated with survival after treatment with erlotinib in first-line therapy of non-small cell lung cancer in Eastern Cooperative Oncology Group 3503. *J Thorac Oncol*. 2010;5(2):169–178.

ACS (American Cancer Society). Cancer facts & figures 2017. www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2017/cancer-facts-and-figures-2017.pdf. Accessed Aug. 10, 2017.

ACS. Cancer facts & figures 2016. www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2016/cancer-facts-and-figures-2016.pdf. Accessed Aug. 10, 2017.

Bakitas M, Lyons KD, Hegel MT, et al. Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer: the Project ENABLE II randomized controlled trial. *JAMA*. 2009;302(7):741–749.

Barnato AE, Herndon MB, Anthony DL, et al. Are regional variations in end-of-life care intensity explained by patient preferences? A study of the US Medicare population. *Med Care*. 2007;45(5):386–393.

Carbone DP, Ding K, Roder H, et al. Prognostic and predictive role of the VeriStrat

- plasma test in patients with advanced non-small-cell lung cancer treated with erlotinib or placebo in the NCIC Clinical Trials Group BR.21 trial. *J Thorac Oncol.* 2012;7(11):1653–1660.
- CMMI (Centers for Medicare & Medicaid Innovation). Oncology Care Model (OCM) Request for Applications (RFA) February 2015, Updated June 3, 2015. <https://innovation.cms.gov/Files/x/ocmrf.pdf>. Accessed Aug. 8, 2017.
- CMMI. Oncology Care Model. July 27, 2017. <https://innovation.cms.gov/initiatives/oncology-care>. Accessed June 20, 2017.
- CMS (Centers for Medicare & Medicaid Services). Quality Payment Program: Quality measures. Center for Medicare & Medicaid Services website. <https://qpp.cms.gov/mips/quality-measures>. Published: 2017. Accessed Aug. 8, 2017.
- Chiu N, Chiu L, Lutz S, et al. Incorporation of life expectancy estimates in the treatment of palliative care patients receiving radiotherapy: treatment approaches in light of incomplete prognostic models. *Ann Palliat Med.* 2015;4(3):162–168.
- Christakis NA, Lamont EB. Extent and determinants of error in doctors' prognoses in terminally ill patients: prospective cohort study. *BMJ.* 2000;320(7233):469–472.
- Dale CR, Madtes DK, Fan VS, et al. Navigational bronchoscopy with biopsy versus CT-guided biopsy for the diagnosis of a solitary pulmonary nodule: a cost-consequences analysis. *J Bronchology Interv Pulmonol.* 2012;19(4):294–303.
- Detterbeck FC, Mazzone PJ, Naidich DP, et al. Screening for lung cancer: diagnosis and management of lung cancer, 3rd ed. American College of Chest Physicians evidence-based clinical practice guidelines. *Chest.* 2013;143(5 Suppl):e78S–e92S.
- Dingemans AM, Mellema WW, Groen HJ, et al. A phase II study of sorafenib in patients with platinum-pretreated, advanced (stage IIIB or IV) non-small cell lung cancer with a KRAS mutation. *Clin Cancer Res.* 2013;19(3):743–751.
- Ferrell BR, Temel JS, Temin S, et al. Integration of palliative care into standard oncology care: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol.* 2017;35(1):96–112.
- Ford DW, Koch KA, Ray DE, et al. Palliative and end-of-life care in lung cancer: diagnosis and management of lung cancer, 3rd ed. American College of Chest Physicians evidence-based clinical practice guidelines. *Chest.* 2013;143(5 Suppl):e498S–e512S.
- Gadgeel S, Goss G, Soria JC, et al. Evaluation of the VeriStrat® serum protein test in patients with advanced squamous cell carcinoma of the lung treated with second-line afatinib or erlotinib in the phase III LUX-Lung 8 study. *Lung Cancer.* 2017;109:101–108.
- Glare P, Virik K, Jones M, et al. A systematic review of physicians' survival predictions in terminally ill cancer patients. *BMJ.* 2003;327(7408):195–198.
- Gregorc V, Novello S, Lazzari C, et al. Predictive value of a proteomic signature in patients with non-small-cell lung cancer treated with second-line erlotinib or chemotherapy (PROSE): a biomarker-stratified, randomised phase 3 trial. *Lancet Oncol.* 2014;15(7):713–721.
- Gripp S, Moeller S, Bölke E, et al. Survival prediction in terminally ill cancer patients by clinical estimates, laboratory tests, and self-rated anxiety and depression. *J Clin Oncol.* 2007;25(22):3313–3320.
- Grossi F, Rijavec E, Genova C, et al. Serum proteomic test in advanced non-squamous non-small cell lung cancer treated in first line with standard chemotherapy. *Br J Cancer.* 2017;116(1):36–43.
- Gwilliam B, Keeley V, Todd C, et al. Development of prognosis in palliative care study (PiPS) predictor models to improve prognostication in advanced cancer: prospective cohort study. *BMJ.* 2011;343:d4920.
- Hagerty RG, Butow PN, Ellis PA, et al. Cancer patient preferences for communication of prognosis in the metastatic setting. *J Clin Oncol.* 2004;22(9):1721–1730.
- Hagerty RG, Butow PN, Ellis PM, et al. Communicating with realism and hope: incurable cancer patients' views on the disclosure of prognosis. *J Clin Oncol.* 2005;23(6):1278–1288.
- Howie L, Peppercorn J. Early palliative care in cancer treatment: rationale, evidence and clinical implications. *Ther Adv Med Oncol.* 2013;5(6):318–323.
- Howlader N, Noone AM, Krapcho M, et al (eds). SEER Cancer Statistics Review, 1975–2014. Cancer Stat Facts: Lung and Bronchus Cancer. <https://seer.cancer.gov/statfacts/html/lunggb.html>. Accessed Aug. 10, 2017.
- Hui D, Kim SH, Roquemore J, et al. Impact of timing and setting of palliative care referral on quality of end-of-life care in cancer patients. *Cancer.* 2014;120(11):1743–1749.
- IOM (Institute of Medicine). *Delivering high-quality cancer care: charting a new course for a system in crisis*. Washington, DC: The National Academies Press; 2013.
- Jang RW, Krzyzanowska MK, Zimmermann C, et al. Palliative care and the aggressiveness of end-of-life care in patients with advanced pancreatic cancer. *J Natl Cancer Inst.* 2015;107(3). pii: dju424. doi: 10.1093/jnci/dju424.
- Kirk P, Kirk I, Kristjanson LJ. What do patients receiving palliative care for cancer and their families want to be told? A Canadian and Australian qualitative study. *BMJ.* 2004;328(7452):1343.
- Lambden J, Zhang B, Friedlander R, et al. Accuracy of oncologists' life-expectancy estimates recalled by their advanced cancer patients: correlates and outcomes. *J Palliat Med.* 2016;19(12):1296–1303.
- Lara PN, Moon J, Hesketh PJ, et al. SWOG S0709: randomized phase II trial of erlotinib versus erlotinib plus carboplatin/paclitaxel in patients with advanced non-small cell lung cancer and impaired performance status as selected by a serum proteomics assay. *J Thorac Oncol.* 2016;11(3):420–425.
- Llobera J, Esteve M, Rifà J, et al. Terminal cancer. Duration and prediction of survival time. *Eur J Cancer.* 2000;36(16):2036–2043.
- Mack JW, Walling A, Dy S, et al. Patient beliefs that chemotherapy may be curative and care received at the end of life among patients with metastatic lung and colorectal cancer. *Cancer.* 2015;121(11):1891–1897.
- Masters GA, Temin S, Azzoli CG, et al. Systemic therapy for stage IV non-small-cell lung cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol.* 2015;33(30):3488–3515.
- McCarthy EP, Phillips RS, Zhong Z, et al. Dying with cancer: patients' function, symptoms, and care preferences as death approaches. *J Am Geriatr Soc.* 2000;48(5 Suppl):S110–121.
- NCCN (National Comprehensive Cancer Network). NCCN clinical practice guidelines in oncology (NCCN guidelines): palliative care (v2.2017). 2017a. www.nccn.org/professionals/physician_gls/PDF/palliative.pdf. Accessed Aug. 8, 2017.
- NCCN. NCCN clinical practice guidelines in oncology (NCCN guidelines): non-small cell lung cancer (v7.2017). 2017b. www.nccn.org/professionals/physician_gls/PDF/nscl.pdf. Accessed June. 5, 2017.
- NHPCO (National Hospice and Palliative Care Organization). NHPCO facts and figures: hospice care in America. 2015. www.nhpco.org/sites/default/files/public/Statistics_Research/2015_Facts_Figures.pdf. Accessed Aug. 8, 2017.
- Page R, Arnaud A. Precision medicine: estimated clinical and economic outcomes of using a predictive and prognostic biomarker to avoid ineffective therapies in advanced non-small cell lung cancer. Paper presented at: American College of Medical Quality Annual Meeting; March 29–April 1, 2017; Washington, DC.
- Pallis AG, Gridelli C, Wedding U, et al. Management of elderly patients with NSCLC; updated expert's opinion paper: EORTC Elderly Task Force, Lung Cancer Group and International Society for Geriatric Oncology. *Ann Oncol.* 2014;25(7):1270–1283.
- Schwartzberg LS, Tauer K, Atkins J, et al. eLung: a multicenter, randomized phase IIb trial of "standard" platinum doublets plus cetuximab (CET) as first-line treatment of recurrent or advanced non-small cell lung cancer. Paper presented at: ESMO Congress 2012; Sept. 30, 2012; Vienna, Austria.
- Smith TJ, Dow LA, Virago E, et al. Giving honest information to patients with advanced cancer maintains hope. *Oncology (Williston Park).* 2010;24(6):521–525.
- Steinhausner KE, Christakis NA, Clipp EC, et al. Preparing for the end of life: preferences of patients, families, physicians, and other care providers. *J Pain Symptom Manage.* 2001;22(3):727–737.

Stinchcombe TE, Roder J, Peterman AH, et al. A retrospective analysis of VeriStrat status on outcome of a randomized phase II trial of first-line therapy with gemcitabine, erlotinib, or the combination in elderly patients (age 70 years or older) with stage IIIB/IV non-small-cell lung cancer. *J Thorac Oncol.* 2013;8(4):443-451.

Sun W, Hu G, Long G, et al. Predictive value of a serum-based proteomic test in non-small-cell lung cancer patients treated with epidermal growth factor receptor tyrosine kinase inhibitors: a meta-analysis. *Curr Med Res Opin.* 2014;30(10):2033-2039.

Taguchi F, Solomon B, Gregorc V, et al. Mass spectrometry to classify non-small-cell lung cancer patients for clinical outcome after treatment with epidermal growth factor receptor tyrosine kinase inhibitors: a multicohort cross-institutional study. *J Natl Cancer Inst.* 2007;99(11):838-846.

Taniyama TK, Hashimoto K, Katsumata N, et al. Can oncologists predict survival for patients with progressive disease after standard chemotherapies? *Curr Oncol.* 2014;21(2):84-90.

Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with meta-

static non-small-cell lung cancer. *N Engl J Med.* 2010;363(8):733-742.

Vansteenkiste JF, Paz-Ares L, Eisen TQG, et al. A plasma proteomic signature predicts outcomes in a phase 3 study of gemcitabine (G) + cisplatin (C) ± sorafenib in first line stage IIIB or IV non-small cell lung cancer (NSCLC). Paper presented at: ASCO Annual Meeting; June 1-5, 2012; Chicago, IL.

Viganò A, Dorgan M, Bruera E, et al. The relative accuracy of the clinical estimation of the duration of life for patients with end-of-life cancer. *Cancer.* 1999;86(1):170-176.

Weeks JC, Catalano PJ, Cronin A, et al. Patients' expectations about effects of chemotherapy for advanced cancer. *N Engl J Med.* 2012;367(17):1616-1625.

Weeks JC, Cook EF, O'Day SJ, et al. Relationship between cancer patients' predictions of prognosis and their treatment preferences. *JAMA.* 1998;279(21):1709-1714.

Wolf JH, Wolf KS. The Lake Wobegon effect: are all cancer patients above average. *Milbank Q.* 2013;91(4):690-728.

Yun YH, Lee CG, Kim SY, et al. The attitudes of cancer patients and their families toward the disclosure of terminal illness. *J Clin Oncol.* 2004;22(2):307-314.

Zhang B, Wright AA, Huskamp HA, et al. Health care costs in the last week of life: associations with end-of-life conversations. *Arch Intern Med.* 2009;169(5):480-488.

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