Precision Medicine in Oncology Standard of Care

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Objectives: *To review the histologic subtypes and staging of non–small cell lung cancer and metastatic melanoma, as well as the molecular markers used to direct standard therapy.*

Data Sources: *Book chapters and journal articles from medical and nursing literature, as well as published clinical guidelines.*

Conclusion: *Patients with metastatic non–small cell lung cancer and metastatic melanoma have had a paucity of treatment options, most fraught with toxicity with limited benefit. Increased understanding of tumor genetics and molecular markers has expanded the treatment options for these patients, often providing them with durable responses and improved quality of life.*

Implications for Nursing Practice: *To provide education and support to their patients, nurses caring for these patients need to understand the role that genetics and molecular markers play in directing these therapies.*

Key Words: *Precision medicine, molecular targets, oncology standard of care*

Developments in our understanding of cancer at the molecular level have changed the focus of cancer treatment planning from the overall disease to the individual patient's disease. The earliest uses of this personalized approach were the use of estrogen and progesterone markers to guide the treatment of women with breast cancer followed in the late 1990s by the standard use of trastuzumab for patients with breast cancer that overexpresses HER2 *neu*. Another excellent example is the use of the drug cetuximab, which was initially approved by the US Food and Drug Administration (FDA) in 2004 for the treatment of metastatic colorectal cancer.[1] However, further analysis of the patients whose tumors responded to cetuximab revealed the need for a more personalized approach in the use of this drug.[2] Patients who had tumors with *KRAS* mutations were shown to have a poor response to cetuximab[2]; this evolving data led to the FDA changing the labeling of the drug. In 2012, cetuximab became FDA approved only for treatment of KRAS wild-type colorectal cancer, a subset of patients who do not have a KRAS mutation.[3]

Two of the more recent examples of diseases with treatment driven by the results of molecular analysis are non–small cell lung cancer (NSCLC) and melanoma (Tables 1 and 2). In both of these malignancies, standard chemotherapy has reached a plateau or has proven ineffective. We

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TABLE 1.
Cancers in Which Treatment is Directed by Genetic Alterations

Cancer site	Genetic Alteration
Colon	*KRAS*
Breast	HER2
	Estrogen/Progesterone Receptor
Lung	EGFR
	ALK
Melanoma	BRAF

Abbreviations: *KRAS*, K rat sarcoma; EGFR, epidermal growth factor receptor; ALK, anaplastic lymphoma kinase.

are now able to analyze tumors at the molecular level to gain a better understanding of the disease and to design more effective therapies. This has led to a more personalized approach in treatment planning.

The purpose of this article is to discuss the biomarkers that are currently in use in clinical practice, with a focus on NSCLC and melanoma where molecular testing has become the standard of care in recent years. Each marker will be described in terms of its function, testing, characteristics of patients who are likely to be positive for the marker, and whether the marker is prognostic, predictive, or both. The role of the biomarker in guiding therapy will be discussed. In addition, in lung cancer, an increased understanding of the histologic subtypes can help guide the personalization of cancer treatment.

Lung Cancer

Lung cancer is the leading cause of cancer death in the United States, with an estimated 224,210 new cases and 159,260 deaths anticipated in 2014.[4] Only 15.9% of all lung cancer patients are alive 5 years or more after diagnosis.[5] Traditionally, treatment decisions were empiric and based on tumor histology, with platinum-based chemotherapy regimens at the cornerstone.

Histology

Lung cancer is divided into two histological subtypes: NSCLC and small cell lung cancer (SCLC). Of the subtypes, NSCLC is the most prevalent, accounting for 85% of all lung cancers. It includes two major types: 1) non-squamous carcinoma (including adenocarcinoma, large cell carcinoma, and other cell types; and 2) squamous cell carcinoma. Historically, all types of NSCLC were

TABLE 2.
Mutation Analysis in Non-Small Cell Lung Cancer and Metastatic Melanoma

Mutation	Incidence	Clinical Relevance	Agents
KRAS	20% to 30% of patients with adenocarcinoma of the lung	Presence of *KRAS* mutation is prognostic of poor survival Associated with resistance to therapy	None
EGFR	13% of patients with NSCLC Almost exclusive to adenocarcinoma	Predictive of response to EGFR-TKIs Not prognostic of survival independent of treatment	Erlotinib Gefitinib Afatanib
ERCC1	Data inconclusive	Prognostic of better survival independent of treatment Predictive of poor response to platinum based chemotherapy	None
ALK	2% to 7% of patients with NSCLC	Predictive of response to ALK-MET Predictive of lack of response to EGFR-TKIs	Crizitonib
BRAF	45% of patients with metastatic melanoma	Predictive of response to BRAF inhibitors	Vemurafenib Dabrafenib Trametinib

Abbreviations: *KRAS*, K rat sarcoma; EGFR, epidermal growth factor receptor; ERCC1, excision repair cross-complementation group I; ALK, anaplastic lymphoma kinase; TKI, tyrosine kinase inhibitor; MET, mesenchymal-epithelial transition.