Cancer Concepts and Principles: Primer for the Interventional Oncologist—Part II

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ABSTRACT

This is the second of a two-part overview of the fundamentals of oncology for interventional radiologists. The first part focused on clinical trials, basic statistics, assessment of response, and overall concepts in oncology. This second part aims to review the methods of tumor characterization; principles of the oncology specialties, including medical, surgical, radiation, and interventional oncology; and current treatment paradigms for the most common cancers encountered in interventional oncology, along with the levels of evidence that guide these treatments.

ABBREVIATIONS

AFP = α-fetoprotein, AJCC = American Joint Committee on Cancer, BCLC = Barcelona Clinic Liver Cancer, CapeOx = capecitabine/oxaliplatin, CRC = colorectal cancer, DEB = drug-eluting bead, DEBIRI = drug-eluting beads with irinotecan, EASL = European Association for Study of the Liver, EGFR = epidermal growth factor receptor, 5-FU = 5-fluorouracil, FOLFIRI = irinotecan/5-fluorouracil/leucovorin, FOLFOX = oxaliplatin/5-fluorouracil/leucovorin, HCC = hepatocellular carcinoma, IRE = irreversible electroporation, NCCN = National Comprehensive Cancer Network, NCI = National Cancer Institute, NET = neuroendocrine tumor, NSCLC = non–small-cell lung cancer, PV = portal vein, RF = radiofrequency, RT = radiation therapy, VEGFR = vascular endothelial growth factor receptor

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This is the second of two parts of a review of the principles of oncology for interventional radiologists. It intends to build upon the fundamentals of clinical trial design, statistics, and response assessment discussed in the first part in order to provide a framework for understanding the methods of the different oncology specialties, the current treatment paradigms of cancers most frequently treated in interventional oncology, and an overview of the current levels of evidence that guide these interventional oncologic treatments.

TUMOR CHARACTERIZATION AND MANAGEMENT

Staging

Tumor staging reflects the extent of disease, determines treatment and therapeutic options, and has specific prognostic implications. Clinical staging refers to non-invasive staging, including physical examination and

imaging evaluation, whereas pathologic staging refers to findings from tissue specimens and allows for the identification of the microscopic extent of disease that may be subclinical, or not apparent, on physical examination or imaging. For this reason, patient populations with clinically and pathologically staged disease are not necessarily identical and comparable in terms of outcomes.

Staging systems vary with tumor types. The International Union Against Cancer (Union Internationale Contre le Cancer) and the American Joint Committee on Cancer (AJCC) systems were unified into a single system, which is one of the most common staging systems used, and characterizes cancers according to the TNM (tumor, node, metastasis) classification. Cancers are then divided into stages 0 through IV to guide treatment and prognosis (1). Additional staging systems exist, such as for hepatocellular carcinoma (HCC), that will be addressed further in this review.

Systemic and Tissue-specific Tumor Markers

Tumor markers generally refer to a variety of substances, including gene mutations, proteins, and metabolites, which can be measured in tumor tissues, blood, or other body fluids. Tumor markers can be produced by cancerous and normal cells. Certain tumor markers are specific to a type or histology of cancer, whereas others may be increased in several different cancers. The markers may play a role in cancer detection, diagnosis, staging, prognosis, and response assessment. The National Cancer Institute (NCI) provides a concise summary of the most common tumor markers used in oncology, from which **Table 1** is derived (2). Interventional oncologists should be well versed with these tumor markers, as they play an integral role in cancer management.

METHODS OF TREATMENT: MEDICAL, SURGICAL, RADIATION, AND INTERVENTIONAL ONCOLOGY

The anticancer armamentarium includes chemotherapeutic agents, biologic therapies that target specific molecules in the cell-signaling pathways, radiation, and surgical and interventional oncology. Although most cancer treatments use a combination of many, if not all, of these modalities, the timing of administration of these treatments can result in synergistic, detrimental, or toxic clinical outcomes.

The Physician Data Query of the NCI and the National Comprehensive Cancer Network (NCCN) guidelines provide up-to-date information on standard treatment regimens for various cancers of various stages, in addition to references to experimental protocols and clinical trials as alternatives to standard regimens (3,4).

Toxicity is the critical, potentially fatal, limiting factor of any cancer treatment, including chemotherapy and radiation. Therapeutic regimens are designed with toxicity in mind to avoid overlapping or synergistic toxicities. Consistently evaluating and addressing treatment toxicities is inherent to the practice of oncology, and toxicities should be recognizable to all practitioners involved in the care of patients with cancer. The NCI's Common Terminology Criteria for Adverse Events provide a standardized classification of toxicities and side effects related to chemotherapy (5). Toxicities are graded according to severity, whereby grade 1 is mild, grade 2 is moderate, grade 3 is severe, grade 4 is life-threatening, and grade 5 is fatal. In general, only toxicities of grade 3 or greater are reported, as grades 1 and 2 toxicities related to treatment are considered clinically acceptable. This lexicon should be used when describing toxicities related to any oncologic treatment or intervention. In addition, there is often a 30-day cutoff point after treatment, after which many adverse events are not deemed to be treatment-related.

Medical Oncology: Chemotherapy

Chemotherapy is most frequently delivered as a regimen of multiple chemotherapeutic agents delivered to maximize tumor cell kill while minimizing toxicity. The synergistic effects of multiple agents increase the interaction between chemotherapy and tumor cells, and reduce the likelihood of tumor cells developing drug resistance. Because bone marrow cells are often the most sensitive to chemotherapy, standard treatment regimens have traditionally been designed with regard to bone marrow recovery to prevent myelosuppression (6).

Although chemotherapeutic agents are often administered with the intent to cause tumor cell death or cytotoxicity, a number of chemotherapy regimens, particularly those incorporating the molecular-targeted therapies discussed subsequently in more detail, provide clinical value in terms of cytostasis rather than cytotoxicity. Effective cytostasis manifests itself as the inhibition of tumor cell growth or prevention of metastases—namely stable disease—as opposed to tumor shrinkage (7).

Classes of chemotherapeutic agents include alkylating agents, platinum analogues, antimetabolites, topoisomerase-interacting agents, and antimicrotubule agents. **Table 2** lists the most commonly encountered chemotherapeutic agents in interventional oncology.

Chemotherapy use generally occurs in one of four clinical settings. In primary induction, chemotherapy is administered as the initial treatment for advanced cancers for which no alternative treatment, such as surgical resection, exists. Neoadjuvant chemotherapy refers to chemotherapy administered before surgical resection to reduce the size of the primary tumor or minimize the extent of disease to increase the likelihood of an R0 resection, which indicates surgical margins free of tumor. Neoadjuvant chemotherapy can also reduce the