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INTRODUCTION

# Contemporary reviews on cancer treatment

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Cancer Chemotherapy and Pharmacology will start a new series of reviews, which will be specifically dealing with novel developments on drugs and approaches that are directed toward "classical drug targets." The FDA has approved more than 120 small molecules and several other compounds such as monoclonal antibodies, for treatment of various cancers (Table 1). Fortunately, several cancers can be treated successfully with this arsenal of drugs, the majority being directly targeted to the molecule DNA (e.g., platinum analogs, nitrogen mustards), while others indirectly target DNA replication, e.g., via affecting synthesis of precursors (e.g., antimetabolites), their cell cycle effect (e.g., taxanes), unwinding and duplication (e.g., topoisomerase inhibitors), or binding to transcription sites. Next to that, there are several classes of drugs that affect cellular proliferation by attacking other targets such as hormones, proteins, and folate homeostasis. A new group of drugs, usually summarized as targeted drugs, consists of small molecules and monoclonal antibodies, which are directed against signaling pathways and angiogenesis. With some exceptions, most of these drugs affect multiple targets within the various signaling cascades. Disruption of these signaling pathways in cancer cells usually leads to inhibition of DNA synthesis.

Research interests often change in time and follow some popular subjects. Currently, immune-checkpoint inhibitors are in the center of research interests along with novel strategies related to cellular therapy such as engineered T cells and vaccination. Other hypes (some larger, some smaller) in the past included development of novel platinum analogs, novel antimetabolites, multidrug resistance (e.g., p-glycoprotein) modulators, topoisomerase inhibitors, taxanes, gene therapy, protein kinase C inhibitors, and currently inhibitors of various signaling pathways, such as the VEGF/VEGFR, PDGF/PDGFR, FGFR, EGFR/RAS/RAF/MEK/Erk, ALK, bcr-ABL, and Pi3K/Akt/mTOR pathways. It is likely that neither one nor another of those weapons will solely provide cure of cancer but more certainly will be incorporated in strategies where combinations and sequences will improve survival of patients with cancer.

This series of reviews will highlight the potential of novel drugs regardless of their mechanism of action, providing comprehensive integrations of preclinical data from experts in the fields using apoptotic stress inducers with novel targeted and immune strategies. Reviews are expected to cover preclinical data focusing on various aspects of pharmacology as well as drug-induced cellular and tumor biology and early phase I/II clinical information. We expect that our readers involved in experimental therapeutics and early drug development will find in these reviews new ideas for developing novel anticancer therapies.

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**Table 1** FDA-approved drugs for treatment of cancer

| Class of drugs | Examples | Number |
|---|---|---|
| DNA synthesis inhibitors | Antimetabolites | 16 |
| DNA damaging drugs | Platinum analogs, nitrogen mustards, anthracyclines | 33 |
| Cell cytoskeleton-modifying agents | Taxanes, vinblastine | 9 |
| Antinutrients | Asparaginase | 1 |
| Gene-transcription modifiers | Bexarotene, all-trans retinoic acid | 2 |
| Radiation-emission drugs | Rad 223 | 1 |
| Hormones/antihormones | Tamoxifen, abiraterone, enzalutamide, letrozole | 16 |
| Immune-system modifiers | Interferon, lenalidomide | 4 |
| Proteasome inhibitors | Bortezomib, carfilzomib | 2 |
| Protein-translation inhibitors | Omacetaxine | 1 |
| Epigenome-modifying agents | e.g., HDAC and DNA methyltransferase inhibitors | 6 |
| DNA-repair inhibitors | Olaparib | 1 |
| Immune-checkpoint inhibitors | Ipilimumab, nivolumab, pembrolizumab | 3 |
| Bone-remodeling agents | Denosumab | 1 |
| Angiogenesis inhibitors | Bevacizumab, sunitinib, sorafenib, regorafenib | 11 |
| Cell-lysis mediators | Rituximab, alemtuzumab, ibritumomab | 8 |
| Therapeutic vaccines | Sipuleucel-T | 1 |
| Cell-signaling inhibitors | Erlotinib, cetuximab, crizotinib, everolimus | 28 |
| | | 144 |

Modified from Supplementary Table 1 in AACR Cancer Progress Report 2015, Clin Cancer Res 2015; 21 (suppl 1); S1–S128. Please note that since the publication of this issue, at least two new drugs have been registered in the DNA synthesis inhibitors class (TAS-102 [Lonsurf] and Onivyde [irinotecan liposomal injection])