Review

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Novel Advances in Oncology

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Abstract

Novel technological developments are commonly used in oncology practice. The novel approaches contribute to oncologist for screening, diagnosis, treatment, and follow-up periods. Genetic-based tests and liquid biopsies are well-known novel diagnostic techniques especially in breast and lung cancers. Targeted therapies, immune checkpoint inhibitors, invasive treatment modalities, and radioligand therapies are well-known advances in the treatment of cancer. These novel modalities in treatment are dependent on specific conditions especially mutations and receptor status in different cancer types. In this topic, we summarized the new technological advances in screening, diagnosis, treatment, and follow-up practices.

Keywords: Oncology, new techniques, diagnosis, treatment

Novel Advances in Oncology

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Screening - Diagnosis

Genetic-Based Tests

Stool-based DNA test might be used in patients who had an average risk for colon cancer. The aim of this test is to determine blood and DNA in stool sample. In addition, the sensitivity of this test has been found to be equal to standard colonoscopy. Therefore, the test is recommended to be used every 3 years for screening of colorectal cancer if this test is selected to screen average risk individuals (1).

Next-generation sequencing (NGS) uses sequencing of multiple DNA fragments performed in parallel. It is appropriate to consider exome sequencing or targeted NGS gene panels when a large number of pathogenic genes need to be screened (2). Similarly, exome sequencing or whole genome sequencing should be considered when a condition demonstrates high heritability in a family or is suspected to have a genetic basis, but the number of potential candidate genes is large, or responsible gene(s) are unknown. Some gene examples include *BRCA1* and *BRCA2* if there is a personal or family history of prostate and/or pancreatic cancer, even in the absence of breast or ovarian cancer, screening for inherited causes of gastrointestinal cancers and analyzing tumor tissue to identify genetic abnormalities that may potentially match molecularly targeted therapies.

Other available genetic tests in oncology use gene expression rather than gene sequencing to identify molecular signatures in tumors (e.g., Oncotype Dx panels for breast, colon, and prostate cancers). Gene expression profiling determines the level to which a gene is transcribed, as opposed to variations in gene sequence. The Oncotype Dx 21-gene recurrence score is the best-validated prognostic assay and may identify patients who are most and least likely to derive benefit from adjuvant chemotherapy. In addition, the clinical validity of Amsterdam 70-gene prognostic profile (mammaprint) was demonstrated (3).

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Liquid Biopsies

While molecular diagnostics have traditionally been performed on biopsies of solid tumor tissue, blood-based tests or so-called "liquid" biopsies are gaining popularity as they provide the opportunity to genotype in a less invasive and less expensive manner and may offer a chance to monitor the molecular features of cancer through the course of treatment or predict relapse after adjuvant treatment (4). In 2018, the joint review of the American Society of Clinical Oncology and the College of American Pathologist stated that there is not enough evidence in early stage cancer for the clinical value of circulating tumor DNA (ctDNA) in treatment and follow-up periods or detection of residual tumor (5). There are currently two US Food and Drug Administration-approved ctDNA tests for patients with lung cancer in both the *estimated glomerular filtration rate (EGFR)* mutation-positive setting. It is likely that as more data emerge, the use of liquid biopsies to assess other molecular abnormalities will become more widespread (6).

Treatment

Novel treatment agents that are advancing by technological developments are widely used in oncology practice. Targeted tyrosine kinase, checkpoint inhibitors, invasive treatment modalities, and radioligand therapies are well-known advances in the treatment of cancer.

Tyrosine kinase inhibitors (TKIs) targeting EGFR are erlotinib, gefitinib (first-generation agent), afatinib, dacomitinib (second-generation agent), and osimertinib (third-generation agent) in non-small cell lung cancer (NSCLC). All of these agents improved the outcome in NSCLC. Newer data demonstrate improved progression-free survival (PFS) outcomes with front-line osimertinib compared with gefitinib or erlotinib. In addition, these agents have more tolerable side effect profiles than standard chemotherapy (7-8).

A group of patients with NSCLC have fusion oncogene EML4-ALK. Alectinib, crizotinib, and ceritinib are agents that target ALK. Alectinib had a reduction in risk of progression or death of 53% (HR 0.47, 95% CI 0.34-0.65), with a median PFS not reached versus 11.1 months for those receiving crizotinib at a median follow-up of approximately 18 months. The median PFS rates were 25.7 months with alectinib and 10.4 months with crizotinib (HR 0.50) based on an independent review. The overall survival (OS) results are not yet mature (9).

In HER2 (member of the tyrosine kinase receptor family) positive breast cancer, trastuzumab, pertuzumab, lapatinib, and trastuzumab emtansine are used widely for different points of the disease.

Bevacizumab, aflibercept, ramucirumab (targeting vascular endothelial growth factor (VEGF)), cetuximab, and panitumumab (targeting EGFR) are monoclonal antibodies combined with chemotherapy in metastatic colorectal cancer (10).

Vemurafenib, dabrafenib, and encorafenib (inhibitors of the BRAF serine/threonine protein kinase pathway) combinations with MEK inhibitors (trametinib, cobimetinib, and binimetinib) are used in BRAF mutation-positive metastatic malignant melanoma and improved outcomes in both PFS and OS (11).

VEGFs (TKIs), including cabozantinib, pazopanib, sunitinib, axitinib, lenvatinib, and sorafenib, are commonly used in renal cell carcinoma. Sunitinib and pazopanib are the most preferred agents due to strong evidences (12).

Programmed cell death protein 1 (PD-1) is a transmembrane protein expressed on T cells, B cells, and natural killer cells and can bind to PD-1 and 2 ligands. This binding inhibits the apoptosis of tumor cells and decreases the number of effector T cells. Immune checkpoint inhibitors block this interaction by inhibiting PD-1 or programmed death-ligand 1 (PD-L1). There are two PD-1 inhibitors (pembrolizumab and nivolumab) and three PD-L1 inhibitors (atezolizumab, avelumab, and durvalumab) for approval for cancer treatment.

Non-surgical invasive treatment options include radiofrequency ablation, microwave ablation, laser ablation, high-intensity focused ultrasound ablation, and cryoablation. These options are most commonly used in liver metastasis and primary liver tumors (13).

Peptide receptor radioligand therapies, especially those with radiolabelled somatostatin, are increasingly used in neuroendocrine tumors (14).

Sipuleucel-T is an autologous dendritic cell therapeutic vaccine produced to increase the T cell response against prostatic acid phosphatase in patients with metastatic prostate cancer. This vaccine is prepared from the mononuclear cells of the patient. Then, as ex vivo, these cells stimulated with an immunogen fusion protein consist of recombinant prostatic acid phosphatase and granulocyte-macrophage colony-stimulating factor. Thereafter, these stimulated cells are infused back into the patients (15).

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