



Onco News

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From the Desk of Editor

Dear Colleagues,

Happy Deepawali & Festive Season !

Cancer treatment agents can be conventional cytotoxic drugs, hormonal therapy or newer molecules like targeted agents and immune therapies. Targeted agents are designed to inhibit a specific cell signaling pathway, cell surface receptor, or intracellular process, making them fundamentally different from traditionally cytotoxic chemotherapy, which often interferes with cell division and may not be specific to malignant cells.

Oncology has seen a sea change in management with targeted therapies. Present list of these agents is about to touch benchmark of hundred molecules. A negative aspect of these agents is, barring a few like Imatinib, they don't have curative potentiality being cytostatic in nature. Rising cost of treatment is another negative aspect of these molecules. However they have revolutionised treatment of many malignancies where there was no hope !

Dear Reader

please send your suggestions and feedback to make Onco News a better and more useful onco resource bulletin.

With warm regards

Dr Naresh Somani
M.D.,D.M.

INTRODUCTION :

The number of these targeted agents has increased rapidly and may more such agents are currently under development. Many of these targeted agents are more effective when combined with cytotoxic chemotherapy.

CATEGORIES OF TARGETED AGENTS :

- Small molecule inhibitors
- Antibodies
- Conjugated agents
- Proteasome inhibitors
- Demethylation agents
- Histone deacetylase inhibitors
- Cyclin dependent Kinase inhibitors

Small-Molecule inhibitors :

BCR-ABL kinase inhibitors :

A specific translocation between chromosomes 9 and 22 [Philadelphia chromosome, t(9;22)] fuses the BCR and ABL genes, producing a constitutively active tyrosine kinase that drives the uncontrolled proliferation of mature cells in chronic myeloid leukemia. Effective BCR-ABL kinase inhibitors include the following-

P.T.O.

Imatinib

Uses : Chronic myeloid leukemia, Philadelphia chromosome-positive acute lymphocyte leukemia, gastrointestinal stromal tumor, dermatofibrosarcomaprotuberans.

Dasatinib

Uses : Chronic myeloid leukemia (especially imatinib-resistant disease), Philadelphia chromosome-positive acute lymphocytic leukemia

Nilotinib

Use : Chronic myeloid leukemia

Epidermal growth factor receptor inhibitors:

The epidermal growth factor receptors (EGFRs) are a family of receptor tyrosine kinase that include EGFR/ErbB1, HER-2/ErbB2, HER-3/ErbB3, and HER-4/ErbB4, and these EGFRs are commonly over expressed or overactive in solid tumors. EGFRs initiate intracellular signaling cascades that can control various cell functions, such as promoting cell division and inhibiting apoptosis. Available EGFR inhibitors include the following-

Erlotinib/Afatinib

Use : Non small-cell lung cancer (NSCLC), pancreatic cancer

Lapatinib

Use : HER-2 positive breast cancer

Vascular endothelial growth factor receptor inhibitors:

The vascular endothelial growth factor receptors (VEGFR-1, VEGFR-2, VEGFR-3) are receptor tyrosine kinase. When stimulated by soluble VEGF, these receptors initiate a signal transduction pathway critical for angiogenesis. Since tumors are dependent on the formation of new blood vessels for growth and survival, the VEGF pathway is an important therapeutic target.

Sarafenib

Uses : Renal cell carcinoma, hepatocellular carcinoma

Sunitinib

Uses : Renal cell carcinoma, gastrointestinal stromal tumor

Mammalian target of rapamycin inhibitors:

Mammalian target of rapamycin (Mtor) is an intracellular protein kinase that serves as nutrient sensor and can stimulate cell proliferation, and it may be overactive in malignant cells.

Temsirolimus

Use : Renal Cell carcinoma

Everolimus

Uses : Renal Cell carcinoma, Neuro Endocrine Tumours

Antibodies:

Monoclonal antibody therapies are engineered proteins that binds specifically to soluble factors in the blood or cell surface molecules. These antibodies may block normal function of target molecules and lead to clearance of targets by immune mechanism.

Since antibody therapies are developed using humanized or chimeric versions of mouse antibodies, they carry a risk of infusion reactions including hives, hypertension or rarely anaphylaxis. Clinically useful monoclonal antibodies include the following.

Bevacizumab

Uses : Metastatic colon cancer, metastatic non-small cell lung cancer, renal cell carcinoma. Emerging uses include metastatic breast cancer, ovarian cancer, and pancreatic cancer.

Cetuximab

Uses : Metastatic colon cancer, squamous-cell head and neck cancer

Panitumumab

Use : Metastatic colon cancer

Rituximab

Uses : B-cell malignancies, often in combination with cytotoxic chemotherapy

Trastuzumab

Use : HER-2-positive breast cancer, both in the adjuvant and metastatic settings

Proteasome inhibitors:

When intracellular proteins are labeled by the addition of the ubiquitin protein, they are marked for degradation into smaller peptides by the intracellular complex.

Bortezomib

Uses : Multiple myeloma, mantle cell lymphoma, other non- Hodgkin's lymphomas

Demethylation agents:

Methylation of DNA by DNA methyltransferase can suppress the transcription of tumor suppressor genes. By inhibiting DNA methyltransferase in a malignant cell, innate tumor suppressor activity can be restored. Active hypomethylating agents include the following-

Azacitidine

Uses : Myelodysplastic syndromes, acute myelogenous leukemia

Decitabine

Uses : Myelodysplastic syndromes, acute myelogenous leukemia

Histone deacetylase inhibitors:

Histone deacetylase (HDAC) is a cellular enzyme that modifies histone proteins and regulates DNA transcription, and may lead to a survival advantage in cancer cells. HDAC inhibitors block this enzyme's activity and thus slow cancer cell growth.

Vorinostat

Use : Cutaneous T-cell lymphoma

Cyclin dependent kinase inhibitors:

CDK4/6 kinase has a key role to play in cancer genesis and regulation.

Their inhibitors has shown potentiality in management of many cancers notably in breast cancer .

Palbociclib

Use : it's approved for management of post menopausal metastatic breast cancer patients in first line in combination with hormone therapy Letrozole and as second line with Fulvestrant .

ONCO FACTS :

1. Newer options for second line treatment of Non squamous non small cell lung cancer is Docetaxel in combination with Nintedanib and Immunooncologic drugs like Nivolumab and pembrolizumab.
2. Sunitinib, Pazopanib and Srafinib are currently three approved drugs for treatment of metastatic Renal cell cancer.
3. All patients of stage 2 Colon cancers should be evaluated and risk stratification should be done based on certain molecular tests to judge for adjuvant chemotherapy .
4. Nimotuzumab along with concurrent chemo radiotherapy may improve results in locally advanced head and neck cancers.



BEVATAS

Bevacizumab 100 mg



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SoMex Research & Health Ethics Committee

❖ This committee is registered with DCGI as independent Ethics Committee and works accordingly and so far monitored 18 trials. For details of Ethics committee and its SOP, please login www.somexresearch.com OR contact - e-mail : ec@somexresearch.com

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