

# Recent Advances in Medical Oncology

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In this interview we are discussing about the “recent advances in medical oncology” in terms of diagnostic techniques, management and future options.

**Q. What are the major advances in cancer management over the past 2 decades?**

A. I would describe it in 2 broad categories:

- **Therapeutic:** There has been a greater understanding of the biology of cancer and identification of drugable targets such as Her2Neu receptor in breast cancer. Together with this, major advancements in diagnostic techniques have made it possible to accurately diagnose and stage patients with cancer.
- **Preventive:** Less dramatic but arguably more profound has been the success of preventive strategies. There is a much greater awareness of the harmful effects of tobacco, which has translated at least partly to behavioral changes and has resulted in a decline in smoking related cancers. Wider application of screening tools such as PAP smear, mammography, colonoscopy etc has also made it possible to diagnose some of the common cancers early and thereby improving the overall survival.

**Q. What are some of the examples of curable cancers at the present day?**

A. Based on treatment options;

- Surgically curable diseases include early stage cancers of Cervix, Breast, Uterus, Lung, Colon, H&N region, Kidney, Melanoma etc. Adjuvant treatments with chemotherapy and radiation have improved survival rates further in some of these cancers.
- Cancers curable with chemotherapy include Hodgkins and Non Hodgkins Lymphoma, Testicular cancer with cisplatin based chemotherapy regimens, Acute Leukemias in young adults and children.

- Radiation therapy by itself can achieve cure or long term durable remissions in some early stage non small cell lung cancers, and certain lymphomas
- Bone marrow transplants have been curative in several refractory lymphomas, and Acute Leukemias in appropriately selected patients.
- There are some cancers which are not curable but can have long term survival rates with current treatments such as CML (Chronic Myelogenous Leukemia), CLL (Chronic Lymphocytic Leukemia), indolent lymphomas such as follicular lymphoma, marginal zone lymphoma and also multiple myeloma.

**Q. What are some of the cancers with the poorest prognosis?**

A. Cancers of the Pancreas, Stomach, Esophagus, Ovary, Lung (non small cell and small cell) generally present at late stages because of the difficulties in early diagnosis. Most of these have expected survivals of only about a year. Acute Leukemias (both myelogenous and lymphocytic) have very poor prognosis in older adults and many of them succumb to the toxicities of current chemotherapy regimens.

**Q. Has there been any new insights into the understanding of the cause of cancer?**

A. Though we have made significant progress in terms of diagnosis and treatment of several cancers, there has been disappointingly little progress in the identification of causes. Known heredity and environmental factors together account for only about a 3rd of the cancers, the remaining 2/3rd appears to be from random mutations, the causes of which remain unknown at the present time. Smoking is one of the few factors that we have been able to clearly link to multiple cancers in epidemiological studies. The role of diet and several

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other environmental factors are not very clear at this point.

**Q. What are the some of the newer diagnostic techniques that have helped cancer management?**

A. CT guided biopsies by interventional radiologists have made it much easier to get diagnosis with minimally invasive procedures. PET (Positron Emission Tomography) scans have improved the diagnostic and prognostic accuracy of several cancers including Lung, Breast, Esophageal, Lymphomas, Myeloma etc. Endoscopic ultrasound (EUS) has made it possible to accurately stage esophageal and rectal cancers and procure biopsies. Endoscopic Bronchial Ultrasound (EBUS) has treating improved the diagnostic accuracy of bronchoscopes. Endoscopic Retrograde Cholangiopancreatography (ERCP) has become a very useful technique in procuring biopsies of pancreatobiliary system.

**Q. What are some of the new drugs that have impacted the course of cancer care?**

A. The best known example of this is imatinib (along with its newer generation drugs: nilotinib, dasatinib) targeting bcr-abl fusion protein in CML (Chronic Myelogenous Leukemia). This has revolutionized the management of CML, and turned it from a disease with very little treatment options in the 1990s to one where patients can expect to have a near normal life span after the diagnosis.

Breast cancer has also seen major breakthroughs with treatments such as trastuzumab, pertuzumab in Her2 neu receptor positive breast cancer, which is about 15% of all breast cancer patients. In Estrogen receptor positive breast cancer, we now have more options with the advent of Aromatase inhibitors such as Anastrozole, Letrozole etc and lately palbociclib. Even in advanced metastatic breast cancers we are now able to see patients surviving 3-5 years compared to 1-2 years about 20 years ago

In Lung cancer the identification of role of EGFR (Epidermal Growth Factor) mutation had lead to the development of targeted agents such as erlotinib, gefitinib and afatinib which has had a positive impact on survival rates. Overall survivals in metastatic non small cell lung cancer have improved from <10 months to about 2years in those who harbor these mutations over past 15 yrs.

The insights into the role of angiogenesis (new blood vessel formation) in promoting tumor growth and metastasis has led to development of drugs such as bevacizumab, ramcicrumab that have improved survival

rates in cancers of the Colon, Lung, Stomach, Brain (Glioblastoma) though these have been modest, in the order of few months.

In the field of multiple myeloma, where 15+ years back the only major drugs to show any benefit was melphalan and steroids, we now have several potent agents with excellent toxicity profiles such as bortezomib and carfilzomib which are proteasome inhibitors. Lenalidomide, thalidomide, pomalidomide which are immunomodulatory agents. Average OS has improved from about 3yrs in the 1990s to 6-8 yrs now.

CD20 directed antibodies such as rituximab, ofatumumab and obinituzumab have made the treatment of NHL, and CLL more effective and less toxic.

Epigenetic agents: Demethylating agents such as azacytidine, decitabine have been a modest success in myelodysplastic syndrome.

Also of significance are the medicines for supportive care to minimize the toxicities of chemotherapy such as ondansetron, granisetron etc for nausea & vomiting. Newer generations of antimicrobials have made the infectious complications of chemotherapy more manageable. GCSF (granulocyte-colony stimulating factor) has helped to decrease the duration of neutropenia and consequently the risk of infections following chemotherapy. Erythropoetin stimulating agents have helped to decrease transfusion requirements in chemotherapy induced anemia.

One of the latest fields to show great promise is immunooncology where new drugs are being developed that modulate the immune system to fight the cancer, the best examples are nivolumab, pembrolizumab which are PD-1(Programmed cell death) inhibitors with significant activity in melanoma, and non small cell lung cancer.

**Q. What are some of the hurdles in the fight against cancer?**

A. From a preventive standpoint, which should be the major focus, we have to find ways to further cut down the prevalence of tobacco use. India has made major strides in this direction but certainly still have a long way to go.

Screening techniques such as PAP smears, mammograms, colonoscopies, low dose CT chest are not being used to its full potential in large part for financial reasons. The investments which can be expensive in the short run could save the society a lot of money in future.

The cost of cancer care is increasing at an unsustainable level event for the developed countries. In emerging economies such as India, this is a huge challenge. Most of these drugs though are effective and can extend life, are very often not curative, requiring months and years of therapy which can be a huge economic burden on the individual families and society at large. We have to find a way to make these drugs more affordable.

**Q. What do you think is the future of cancer care?**

The future of cancer therapy is certainly very promising. As we understand more about the biology of various cancers we will likely manage patients not on the basis of the sites of cancer but on the underlying

driver mutations. At the present day cure is unfortunately seen only in a small proportion of patients. The major advancements in the past 10-20 yrs, has largely displaced the nihilistic attitude that most treating physicians at least within the oncology community had towards treatment of cancer patients. Today for most cancers, we can provide safe, well tolerated therapies which can extend life with good quality and in a few, even cure. I believe that as we get more and better drugs in this area, it will be possible for cancer patients to live with the disease for several years, such as diabetes or heart disease. The hope of cure unfortunately remains elusive for most late stage cancers. Hence the emphasis should be on the known preventive strategies.