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From the Desk of Director Research

The field of cancer vaccines has greatly advanced due to a wave of technological innovations as well as a deeper understanding of the immunological response to both cancer cells and potential vaccines. The "Special Feature" in this issue highlights the Cancer Fighting Vaccines, whereas, "Perspective" focuses on Fluorescent in-situ Hybridization, a new tool to diagnose submicroscopic abnormalities with its analysis extending the routine cytogenetic banding methods.

Prashanti, a healing centre for men, women and children with cancer, is the first of its kind in India, operating under the aegis of the Indian Cancer Society; it has been covered under the section "In Focus".

A symposium on Recent Advances in Head and Neck Oncology, a live webcast on Changing Perspectives in First Line Treatment of Non Small Cell Lung Cancer; and a National Training Workshop on Practical Pediatric Oncology, were organized by the Institute. A new wing of the Institute was inaugurated by Sh Tajender Khanna, Hon'ble Lt Governor of Delhi. Brief descriptions of these events have been given under RGCI & RC activities.

We express our special thanks to Siemens Medical Solutions for supporting this issue of the Cancer News.

The Institute gratefully acknowledges the contributions made by Shri D. S. Negi, Dr D. C. Doval, Dr (Col) R. Ranga Rao, Dr Vineet Talwar, Dr J. B. Sharma, Dr Himesh Gupta, Dr Vivek Arora, Dr Abhishek Puri, Dr Kumar Deep and Ms Renuka Prasad.

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This publication aims at disseminating information on pertinent developments in its specific field of coverage. The information published does not, therefore, imply endorsement of any product/process/producer or technology by RGCI&RC.

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SPECIAL FEATURE

CANCER FIGHTING VACCINES

Introduction

For many years, the treatment of cancer was focused primarily on surgery, chemotherapy and radiation. The long-held hope that vaccination strategies might be effective against cancer has motivated numerous attempts over the past century to put the idea to test in the clinic. The development of cancer vaccines aimed to enhance the immune response against a tumor is a promising area of research. The Cancer Research Institute Cancer Vaccine consortium across the United States and Europe, is the leading initiative on cancer vaccines and for immunotherapy discovery and development to improve patient care by making cancer vaccines part of the standard-of-care in oncology. The consortium interacts closely with the existing CRI/LICR (Cancer Research Institute/Ludwig Institute for Cancer Research) Cancer Vaccine Collaborative's international network of academic, clinical and laboratory centers to create a single strong voice in the cancer vaccine arena.

Cancer vaccines are of two types, therapeutic vaccines and prophylactic vaccines. Therapeutic vaccines prevent the growth of existing cancers, recurrence of treated cancers and eliminate the cancer cells not already killed. Prophylactic vaccines target cancer-causing viruses and prevent viral infection. To date, commercial success has come in prophylactic vaccines and therapeutic vaccines are being investigated in the clinical trials.

Immune System and Cancer

Cancer immunotherapy attempts to shift the balance of the immune system towards the rejection of cancer. In the last several years, important advances have been made in the understanding of the regulatory mechanisms that govern the immune system. The key steps in the generation of an immune response to cancer cells include loading of tumor antigens onto Antigen Presenting Cells (APC), presenting antigen in the appropriate immune stimulatory environment, activating cytotoxic lymphocytes and blocking autoregulatory control mechanisms. This knowledge has opened the door to antigen-specific immunization for cancer, using tumor derived proteins or RNA or synthetically generated peptide epitopes, RNA or DNA. The critical step of antigen presentation has been facilitated by the

co-administration of powerful immunological adjuvants, the provision of co-stimulatory molecules and immune stimulatory cytokines and the ability to culture dendritic cells. These advances have led to multiple novel immunotherapy intervention strategies that are being tested in the clinical trials.

Vaccines under Investigation

1. Antigen/ Adjuvant Vaccines

Antigen vaccines were some of the first cancer vaccines investigated. They use specific protein fragments or peptides to stimulate the immune system to fight the tumor cells. One or more cancer cell antigens are combined with a substance that induces an immune response known as an adjuvant. A cancer patient is vaccinated with this mixture. It is expected that the immune system will also respond to tumor cells that express that antigen.

2. Whole Cell Tumor Vaccines

Taken either from the patient's own tumor (autologous) or tumor cells from one or more other patients (allogeneic), these whole cell vaccine preparations contain cancer antigens that are used to stimulate the immune response.

3. Dendritic Cell Vaccines

Specialized white blood cells known as dendritic cells (DCs) are taken from a patient's blood through a process called leukapheresis. In the laboratory, the DCs are stimulated with the patient's own cancer antigens, grown in petri dishes and re-injected into the patient. Once injected, DC vaccines activate the patient's immune system's T cells. Activation by DCs is expected to cause T cells to multiply and attack the tumor cells that express that antigen.

4. Viral Vectors and DNA Vaccines

Viral vectors and DNA vaccines use the nucleic acid sequence of the tumor antigen to produce the cancer antigen proteins. The DNA containing the gene for a specific cancer antigen is manipulated in the laboratory so that it will be taken up and processed by the APCs. The APCs then display part of the antigen together with another molecule on the cell surface. When these antigen-expressing APCs are injected into a person, the immune system will respond by attacking not only the APCs but also the tumor cells containing the same antigen. Vector-based and DNA vaccines are preferred because they are easier to manufacture than some other vaccines.

5. Anti-idiotype Vaccines

The unique part of each type of antibody is called an idiotype. An antibody to a particular idiotype of another antibody (an anti-idiotype) will usually look like the antigen that triggered cells to make the antibody in the first place. Injecting the anti-idiotype antibodies into the body causes the immune system to attack the anti-idiotypes, along with the antigens themselves. They can be used as part of a cancer vaccine because they look like the antigens on the cancer cells in the patient's body, thereby triggering an immune response against that specific cancer. Lymphomas are considered to be the most promising targets for anti-idiotype vaccines. Early studies of B-cell lymphoma vaccines have been promising.

Antigens in Cancer Vaccines under Investigation

A. Treatment Vaccines

1. *Patient-specific vaccines* use a patient's own tumor cells to generate a vaccine to stimulate a strong immune response against an individual patient's malignant cells. Each therapy is tumor-specific, so, in theory, cells other than tumor cells should not be affected. There are several kinds of patient-specific vaccines under investigation that use antigens from a patient's own tumor cells.

2. *Prostate specific antigen (PSA)* is a prostate-specific protein antigen that can be found circulating in the blood, as well as on the prostate cancer cells. PSA generally is present in small amounts in men who do not have cancer, but the quantity of PSA rises markedly when prostate cancer develops. A high value suggests malignancy. Patients have been shown to mount T-cell responses to PSA.

3. *Heat shock proteins (HSPs)* (e.g. gp96) are produced in the cells in response to heat, low sugar levels and other stress signals. In addition to protecting against stress, these molecules are also involved in the proper processing, folding and assembling of proteins within the cells. The human vaccine consists of HSPs and associated peptide

complexes isolated from a patient's tumor. HSPs are under investigation for treatment of liver, skin, colon, lung, lymphoma and prostate cancers.

4. *Ganglioside molecules* (e.g. GM2, GD2, and GD3) are complex molecules containing carbohydrates and fats. When ganglioside molecules are incorporated into the outside membrane of a cell, they make the cell more easily recognizable by the antibodies. GM2 is a molecule expressed on the cell surface of a number of human cancers. GD2 and GD3 contain carbohydrate antigens expressed by the human cancer cells.

5. *Carcinoembryonic antigen (CEA)* is found in high levels on the tumors in patients with colorectal, lung, breast and pancreatic cancer as compared with the normal tissue. CEA is thought to be released into the blood stream by the tumors. Patients have been shown to mount T-cell responses to CEA.

6. *MART-1* (also known as *Melan-A*) is an antigen expressed by melanocyte cells that produce melanin, the molecule responsible for coloring in skin and hair. It is a specific melanoma cancer marker that is recognized by T cells found more abundant on the melanoma cells than the normal cells.

7. *Tyrosinase* is a key enzyme involved in the initial stages of melanin production. Studies have shown that tyrosinase is a specific marker for melanoma and is more abundant on the melanoma cells.

B. Prevention Vaccines

Viral proteins on the outside coat of cancer-causing viruses are commonly used as antigens to stimulate the immune system to prevent infections with the viruses.

Adjuvants in Treatment Vaccines

To heighten the immune response to cancer antigens, researchers usually attach a decoy substance or adjuvant, that the body will recognize as foreign.

Table 1: Cancer Vaccines in Advanced Stage Clinical Trials

Category	Defined Antigen	Tumor Type	Company	Trade Name
Whole Cell	No	Prostate	Cell Genesys	GVAX™
HSP-96	No	Melanoma Renal	Antigenics	Oncophage ^R
Dendritic Cell	PAP	Prostate	Dendreon	Sipuleucel-T(Provenge ^R)
Pox Vector (MVA)	5T4	Renal,Colon	Sanofi - Aventis	TroVax ^R
Conjugate	MUC 1	NSCLC	Merck KGaA	Stimuvax ^R
QS-21/CpG	MAGE-3	NSCLC	GlaxoSmithKline	MAGE-A3 ASCI

Adjuvants are weakened proteins or bacteria which “trick” the immune system into mounting an attack on both the decoy and the tumor cells. Some adjuvants are described below:

1. *Keyhole limpet hemocyanin (KLH)* is a protein that initiates an immune response and acts as a carrier for the cancer cell antigens. KLH provides additional recognition sites for immune cells known as T-helper cells and may increase the activation of other immune cells known as cytotoxic T-lymphocytes.

2. *Bacillus Calmette Guerin (BCG)* is an inactivated form of the tuberculosis bacterium and used as a vaccine for tuberculosis. It is added to some cancer vaccines with the hope that it will boost the immune response to the vaccine antigen.

3. *Interleukin-2 (IL-2)* is a protein made by the body's immune system that may boost the cancer-killing abilities of natural killer cells. Several cancer vaccines use IL-2 to boost the immune response to specific cancer antigens.

4. *QS21* is a plant extract that when added to some vaccines, may improve the body's immune response.

Approved Prophylactic Vaccines

Human papilloma viruses (HPV) are the most common sexually transmitted infections worldwide. The quadrivalent HPV (types 6, 11, 16, 18) vaccine called ‘Gardasil’ and the bivalent HPV (types 16, 18) vaccine called ‘Cervarix’, are effective for the prevention of HPV infection. Merck's Gardasil is intended to protect against high grade dysplasia of the cervix or vulva, cancer of the cervix and genital warts that are caused by these HPV infections. It may have a role in preventing some head and neck cancers. It is approved for the immunization of girls and young women (9-26yrs) for use in the US and 80 other countries. GlaxoSmithKline's cervical cancer candidate vaccine ‘Cervarix’ has been approved for use in females (10-45yrs) in Europe and Australia. Hepatitis B virus (HBV) infection is a major global health problem which may cause progressive liver including chronic active hepatitis and liver cancer. Safe and effective HBV vaccines are included in the national immunization schedules for infants and for those children and adolescents who are not vaccinated. In hyperendemic regions, it is a suitable strategy for the adults.

Therapeutic Vaccines in Clinical Trials

US biotech Antigenics has won Russian approval to market Oncophage vaccine to treat kidney cancer but the product is yet to win an approval from the US FDA.

Sipuleucel-T known as Provenge for prostate cancer was expected to be the first vaccine to get approval but the FDA demanded more results and information. GVAX cancer immunotherapy is being developed as a non patient-specific, “off-the-shelf” pharmaceutical product for prostate cancer. Trovax is a novel therapeutic cancer vaccine and a phase III trial in patients with renal cell carcinoma is designed to support product registration in the US in 2009.

Stimuvax (BLP25 Liposome vaccine) is an innovative cancer vaccine and its efficacy and safety is being assessed for the patients with unresectable phase III non-small cell lung cancer. An experimental vaccine MAGE-A3 that works by training the immune system to kill specific tumor cells is showing promise for the treatment of early lung cancer. CDX-110 is in phase II or III testing to treat glioblastoma multiforms. Neuvax (E75) for adjuvant treatment of early stage HER positive breast has been submitted to the FDA for registration.

Challenges

Viral vectors are becoming increasingly attractive as enabling tools in drug discovery research. The obstacle of pre-existing immunity remains an important problem in the transaction of these strategies to the clinic. Therefore, vector standardization is a challenge in the way to success of cancer vaccines. It looks likely that when therapeutic cancer vaccines finally make their way onto the market and into clinical use, it will be alongside the current therapies as part of the combination regimens that keep cancer in check. It is still not clear how best to use cancer vaccines with respect to the disease stage and in combination with the other therapies.

Conclusion

The current vaccines under development do not seem to be the “magic bullet” for cancer, but this field has greatly advanced by a wave of technological innovations as well as a deeper understanding of the immunologic response to both the cancer cells and potential vaccines. Combination therapies, involving vaccination and other treatment modalities may prove beneficial to facilitate the long term survival with a lower risk of generating aggressive tumor escape variants. Compilation of phase III trials would allow oncologists to define the actual role of cancer vaccines in the fight against malignancy.

(The Institute appreciates Dr Dinesh Chandra Doval and Dr Vineet Talwar for their contributions to this Special Feature on Cancer Fighting Vaccines).

PERSPECTIVE

Fluorescent *in situ* Hybridization

Introduction

Fluorescent *in situ* hybridization (FISH) is a relatively new technology, utilizing fluorescent labeled DNA probes to detect or confirm gene or chromosome abnormalities. It provides a simple, fast and reliable means to assess genetic instability in cancer (single base mutation level or chromosomal abnormalities) over a much greater dynamic size than the other techniques. It is particularly useful for the analysis of inter and intracellular genetic heterogeneity within tumors and facilitates the detection of rare events such as disseminated metastatic cells.

Materials

The sample DNA (metaphase chromosomes or interphase nuclei) is first denatured. The fluorescent labeled probe of interest, which has to be long enough to hybridize specifically to the target, is then added to the denatured DNA strands which hybridizes with the sample DNA at the target site as it reanneals back into the helix. The probe signal can then be seen through a fluorescent microscope and the sample DNA scored for the presence/absence of the signal. Specimens that can be used for FISH include peripheral blood cells, cultured cell lines, bone marrow cells, paraffin-embedded tissue section & frozen tissue.

Types

Metaphase FISH in metaphase cells can be used to detect specific microdeletions or identify extra material of unknown origin, deletion in a chromosome or complex rearrangements. In addition, it can also detect some of the specific chromosome rearrangements seen in certain cancers. Interphase FISH can be used in interphase cells to determine the chromosome number of one or more chromosomes as well as to detect some specific chromosome rearrangements that are characteristic for certain cancers. It can be performed very rapidly if necessary, usually within 24 hours, because cell division is not required.

Earlier, FISH utilized DNA probes specific for repetitive DNA sequences, such as those found at centromeres and other heterochromatic regions, because they generated a very intense signal due to the tandem arrangement of complimentary sequences and thus a

very large target size. The probes consisted of cloned genomic repetitive sequences. Unlike the DNA repeat probes, a locus-specific probe (LSP) consists of a repeat-free labeled nucleic acid sequence specific to a single region of the genome. The specific map location and availability of Bacterial Artificial Chromosomes clones have facilitated the acquisition of locus-specific FISH.

Specific Applications

Interphase FISH can be performed on paraffin-embedded, formalin-fixed tissue sections, thereby allowing retrospective analysis of samples for correlating chromosome aberrations with biological and clinical endpoints. Reciprocal translocations can be detected with LSPs that span the breakpoint region. Specific translocations can alter the expression of certain oncogenes and tumor suppressor genes, giving tumor cells a selective growth advantage. For example, tumor cells can be detected using LSPs for the *bcr/abl* translocation involving genes on human chromosomes 9 and 22 in Chronic Myeloid Leukemia or the translocation of the *c-myc* gene to the *IgH* locus in Burkitt's lymphoma.

FISH is also regarded as a potential new tool for the clinical management of bladder cancer by detecting cytogenetic aberrations in noncycling, exfoliated cells from bladder irrigations and also holding promise for early cancer detection, monitoring treatment outcome and predicting recurrence of disease. FISH has been used for the detection of trisomy 8 in myeloid disorders, trisomy 7 in prostate cancer and trisomy 21 in Chronic Lymphoid Leukemia. It can be used in determining the degree of engraftment after sex-mismatched bone marrow and cord blood transplants. It has also been used for clinical-cytogenetic correlation analysis in solid tumors. Chromosome painting is an extension of FISH whereby the whole chromosome can be labeled with fluorescent DNA probe.

Future Perspectives

FISH on clinical specimens has provided high sensitivity and specificity in neoplastic process, more precisely for the better prognostification of patients, giving strong evidence that it could supplant conventional cytogenetics in this application and effectively monitor treatment.

(The Institute appreciates Dr Vivek Arora for his contribution to this Perspective on Fluorescent In-Situ Hybridization).

RESEARCH AND DEVELOPMENT

Chromosome 8 and Cancer

A recently discovered but not yet understood section of chromosome 8, called 8q24, may contain at least five distinct regions that are associated with different cancers. Recent genome-wide studies suggested that genetic alterations in the 8q24 region are associated with a risk of prostate, colorectal and breast cancer.

The researchers suggest that there may be five distinct sub-regions within 8q24, separated by the sites of frequent recombination, and each associated with different types of cancers. The first sub-region is associated with an increased risk of prostate cancer but not with a risk of breast, colorectal or ovarian cancer. The second is associated only with an increased risk of breast cancer, while the third sub-region is associated with the risk of prostate, colorectal and ovarian cancers, but not breast. Sub-regions four and five are associated with prostate cancer, but not with the other three malignancies.

(J. of National Cancer Institute, June 26, 2008)

Nanotechnology, Biomolecule and Cancer

Researchers from UT Southern Medical Center and UT Dallas, are testing a new way to kill cancer cells selectively by attaching cancer seeking antibodies to tiny carbon tubes that heat up when exposed to near infrared light. They used monoclonal antibodies that targeted specific sites on lymphoma cells to coat tiny structures called carbon nanotubes. Carbon nanotubes are very small cylinders of graphite carbon that heat up when exposed to near infrared light. Near infrared light can penetrate human tissue upto about 1/2 inches.

In cultures of cancerous lymphoma cells, the antibody coated nanotubes attached to the cells' surfaces. When the targeted cells were exposed to near infrared light, the nanotubes heated up, generating enough heat to essentially "cook" the cells and kill them. Nanotube coated with an unrelated antibody neither bound to nor killed the tumor cells.

(PNAS, June 16, 2008)

Next Generation Cancer Therapies

A University of Rochester team has discovered an entire novel class of genes, they believe, will lead to a greater understanding of cancer cell function and the

next generation of effective and less harmful therapies for the patients.

The team found that among 30,000 cellular genes, only about 100 genes responded synergistically to a combination of two of the most prevalent cancer genes, Ras and p53, were expressed differently in the normal and cancer cells. The research group termed these 100 genes as "cooperation response genes" (CRGs). By studying a subset of the CRG's, researchers also found that 14 of 24 CRG's were essential to tumor formation. The significance of Ras and p53 and by association, of the CRG's, is enormous. Ras and p53 are implicated in about half of all the cancers. When p53, a tumor suppressor gene, loses its function and when Ras becomes hyperactive, both genes play major roles in promoting uncontrolled growth of colon, pancreas and lung cancers.

Ras activation and p53 loss of function cooperatively work together through the CRGs which encode proteins that regulate cell signalling, cell metabolism, self-renewal, cell differentiation and cell death. Indeed CRGs may provide us with a surprisingly large and valuable set of targets for interventions that will destroy the cancer cells and leave the normal cells unharmed.

(Biocompare News, May 25, 2008)

PET for Immune System

Researchers at UCLA's Jonsson Comprehensive Cancer Center have modified a common chemotherapy drug to create a new probe for Positron Emission Tomography (PET), which will allow them to model and measure the immune system in action and monitor response to new therapies. The probe is based on a fundamental cell biochemical pathway called the DNA salvage pathway, which acts as a sort of recycling mechanism that helps in DNA replication and repair. In lymphocytes and macrophages, the pathway is activated at very high levels, because of which, the probe accumulates in those cells.

Monitoring immune function using molecular imaging could significantly impact the diagnosis and treatment evaluation of immunological disorders, as well as evaluating whether certain therapies are effective. If the new PET probe can monitor immune response and response to treatment much more quickly (within a week or two), patients would be spared from the therapies that aren't working.

(J Nature Medicine, June 8, 2008)

NEW TECHNOLOGIES

DIAGNOSTICS

Blood Test for Early Cancers

Scientists from University of Pennsylvania in Philadelphia have reported that the pattern of active genes in white blood cells can accurately distinguish people with early stage lung cancer from cancer-free people. They measured the number and different levels of genes expressed in lymphocytes from 44 patients with early stage lung cancer and 52 control subjects matched for age, smoking, gender and race.

The researchers found that differences in just 15 genes could differentiate patients with early lung cancer from controls with reasonable accuracy of about 87%. A diagnostic blood test for lung cancer would have important implications. A peripheral blood smear can fit nicely at that stage if someone has an abnormality on CT scan. Before doing a biopsy, one might want to do a blood test to differentiate which ones actually might have cancer.

(Univ of Pennsylvania, May 19, 2008)

MRI Combination

Two imaging modalities used in combination, Dynamic Contrast Enhanced-Magnetic Resonance Imaging (DCE-MRI) and Diffusion Weighted Imaging-Magnetic Resonance Imaging (DWI-MRI), can accurately spot residual or recurrent prostate cancer in the patients treated with a fairly new treatment called high intensity focused ultrasonic ablation. Researchers feel that these two imaging modalities together are better than either modality alone. High intensity focused ultrasonic ablation is becoming more common as a prostate cancer treatment option, particularly in patients who can't or don't want to undergo radical prostatectomy.

Evaluating these imaging modalities in 27 patients whose prostate-specific antigen levels rose after treatment, DCE-MRI and DWI-MRI had about a 72% accuracy rate in determining which patients needed additional treatment because they had residual or recurrent cancer. DWI-MRI had fewer false positives than DCE-MRI, but DCE-MRI had fewer false negatives. The present findings suggest that the combination of DCE-MRI and DWI-MRI, which takes about 7 minutes to perform, is best for this purpose.

(American J of Roentgenology, May 2008)

EQUIPMENTS

Lasers for Vocal-Cord Cancer

An innovative laser treatment for early vocal-cord cancer, developed at Massachusetts General Hospital, successfully restores patient's voice without radiotherapy or traditional surgery, which can otherwise permanently damage the vocal quality.

The team began applying pulsed lasers to the treatment of early vocal cord cancer more than five years ago. After successfully treating the first eight patients with the pulsed-dye laser, the group switched to the more precise pulsed potassium-titanyl-phosphate (KTP) laser, which is even less likely to damage delicate vocal cord tissue.

The first 22 patients receiving pulsed laser treatment for vocal cord cancer are cancer-free up to 5 years after treatment, without the removal of vocal cord tissue or loss of voice quality. Some have required second or third laser treatments to remove the residual disease, but another benefit of this therapy is that it does not rule out the future therapeutic options. Currently, the optimal angiolytic laser for vocal cord problems, the pulsed KTP laser, is a critical innovation for a laryngeal surgeon.

(MGH News, May 6, 2008)

PEM vs MRI

Naviscan PET Systems®, a company specializing in organ specific high resolution PET scanners, announced the new clinical data using the PEM Flex scanner in breast cancer management. The PEM Flex™ Solo 2 is a commercially available FDA cleared scanner that utilizes PET technology for breast application known as positron emission mammography (PEM).

The PEM technology is more sensitive than Magnetic Resonance Imaging (MRI) in detecting the smallest cancers. PEM demonstrated 91% sensitivity in ductal carcinoma in situ (DCIS) compared to 83% with MRI and better sensitivity in cancers less than 5mm in size. PEM also detected a 2mm DCIS case shown to be negative on MRI.

The ability to image and diagnose these early stage cancers provide the potential for cure and will significantly impact the breast cancer management. PEM Flex scanner is being used as a tool for evaluating additional and unsuspected disease in the breast and compare these findings with that of MRI.

(Medical News Today, June 18, 2008)

TREATMENTS

Drug for Kidney Cancer

New data from an international, multicenter Phase-III clinical trial has found that the experimental targeted therapy 'everolimus' significantly delays cancer progression in patients with metastatic kidney cancer whose disease had worsened on other treatments.

Everolimus, a once-daily oral therapy, targets the mTOR protein and acts as a central regulator of tumor cell division, cell metabolism and blood vessel growth. It is currently being evaluated for the treatment of several cancers like lymphoma and neuroendocrine tumors.

In this study, more than 400 patients, all of whom had disease that had progressed with currently available targeted therapies 'sunitinib' and/or 'sorafenib', were randomized to receive everolimus or placebo. After six months, 26% of the patients in the everolimus group had disease which had not progressed. In February 2008, an independent monitoring committee stopped the Phase III trial after interim results were positive and allowed researchers to offer everolimus to the patients receiving placebo. Kidney cancer is likely to be managed as a chronic disease with these types of treatment advances.

(Cancer Research, UK, May 20, 2008)

Novel Chemo Drug

Men with a certain type of prostate cancer have been shown to respond to a new chemotherapy drug, sagopilone plus prednisone, in an international trial led by Oregon Health and Science University Cancer Institute researchers. Of the 37 study participants with androgen-independent prostate cancer that has metastasized and is no longer responding to hormone therapies, taking the sagopilone and prednisone long enough to be evaluated, the majority showed positive results in the reduction of their prostate specific antigen (PSA).

A 30% reduction in PSA levels in three months is a strong indicator of survival. Sagopilone, a fully synthetic derivation, is a new class drug that inhibits growth and the spread of malignant cell, similar to docetaxel, which has been the gold standard for this type of hormone independent prostate cancer. Docetaxel, however, is not a cure and not all patients benefit from it. The researchers are committed to searching for new drugs that will be effective against advanced prostate cancer.

(Science Daily, June 3, 2008)

Targeted Therapy for GIST

Gastrointestinal stromal tumors (GISTs) comprise a recently defined entity of the most common mesenchymal neoplasms of the gastrointestinal tract. The introduction of imatinib mesylate inhibiting KIT/PDGFR α (platelet derived growth factor receptor alpha) and their downstream signaling cascade, has revolutionized the therapy of advanced (inoperable and/or metastatic) GISTs. Imatinib has now become the standard of care in the treatment of patients with advanced GIST. However, a majority of patients eventually develop clinical resistance to imatinib.

Currently, the sole approved second line drug is sunitinib, a multi-targeted agent, an inhibitor of tyrosine kinase of KIT and PDGFR α/β and of the vascular endothelial growth factor receptors (VEGFRs)-1,-2 and 3, FMS-like tyrosine kinase-3 (FLT3), colony stimulating factor 1 receptor (CSF-1r), and glial cell-line derived neurotrophic factor receptor (rearranged during transfection). However, a number of new generation tyrosine kinase inhibitors, alone or in combination, are being evaluated at present alongside the treatment options, alternative to inhibiting the KIT signaling pathway (as heat shock protein 90 or mammalian target of rapamycin).

(Recent Patents Anticancer Drug Discov, June 2008)

Ultrasound Ablation

Ultrasound ablation induces a progressive necrosis which allows enough time for inflammation and sclerosis to develop and form an inflammatory barrier against sepsis.

Dr David Melodelima of the French National Institute for Health and Medical Research at the University of Lyon, and associates are the first to use intra-luminal high intensity ultrasound for the treatment of esophageal tumors, which were usually not amenable to curative resection. It could induce rapid, complete and well controlled coagulation necrosis. In a small pilot study, a series of four histologically confirmed esophageal cancer patients treated with this method recovered uneventfully and received rapid and significant relief from dysphagia. The duration of the procedure ranged from 20 to 51 minutes. The possibility to exactly tailor the tissue destruction to the tumor extent visualized by endoscopic ultrasound makes this technique particularly appropriate for esophageal cancers.

(J. of Translational Medicine, June 5, 2008)

IN FOCUS

PRASHANTI

Introduction

Prashanti, the first of its kind in India, is a healing centre for men, women and children with cancer. It was set up in July 2006 under the aegis of the Indian Cancer Society (ICS) and is located at Lala Diwan Chand Centre for Complementary Therapies, No. 2 Jain Mandir Marg, Connaught Place, New Delhi.

Aim of Prashanti

The Prashanti programme aims to alleviate the side effects of conventional treatment, help reduce the levels of stress, and improve the quality of life of people suffering from cancer. Family members, who feel stressed out because of taking care of the patients, can also find Prashanti as a haven to help them. It also helps rehabilitate breast cancer patients by providing them with all their requirements, ie, bras, prosthesis, wigs, etc, under a single - window arrangement.

Complementary Therapies

The healing centre uses complementary therapies as supportive approaches along with conventional mainstream treatment (surgery, chemotherapy, radiotherapy and hormone therapy) to heal holistically, both the mind and the body, to make the cancer patients feel better physically, psychologically, socially and emotionally. These therapies are directed to the tumors and the body as a whole. These methods do not cure the disease but help control symptoms and improve the wellbeing and quality of life of the cancer patients. Some hospitals are offering some of these therapies as part of the care pathway for people being treated for cancer.

Activities of Prashanti

At Prashanti, those patients and their families are taken care of who approach the Institute Rotary Cancer Hospital (IRCH) and Rajiv Gandhi Cancer Institute & Research Centre (RGCI&RC) and other hospitals. In these institutions, volunteers from Cancer Sahyog (a Unit of ICS which provides emotional support) and Prashanti visit the patients and their families, many of whom are also provided medical aid. These patients mostly are from economically disadvantaged sections of the society and have come to Delhi for treatment. They

live in various *dharamshalas* and *sarais* run by philanthropists around the hospital areas.

Complementary therapies also provide emotional support for the care givers, who totally neglect their own health and well being while their loved ones are fighting with cancer. While the counselors render guidance and help patients to accept the disease and come to terms with it, the volunteers provide them with a nutritious home-cooked meal after the therapy session.

Complementary Therapies on Offer

- 1) **Individual therapies:** These are Reiki, Reflexology, Theta therapy, Acupressure, Head massage, Magnetic therapy, etc.
- 2) **Group therapies:** These are Yoga, Pranayam, Meditation, Visualization, Vedic mantrachanting, Buddhist chants, Laughter therapy, Smile therapy, Group singing, etc.
- 3) **Self-help therapies:** These are relaxation exercises, imagery, laughter, meditation, prayer, affirmation, self hypnosis, music, aroma, colour therapy, etc.
- 4) **Psychological therapies:** These are counseling and support groups.
- 5) **Hands-on workshops:** These are conducted once a month by a specialist in specific subjects eg, a session on 'Hair Loss after Chemotherapy'.

Charges & Contact

A patient registered at Prashanti is required to pay a one time Registration Fee of Rs 50/-. This entitles him to attend all the group therapies without any further charges. However, if a patient desires to undertake an individual therapy with the therapist, he would be charged Rs 25/- per sitting. At present, Prashanti is open on Tuesdays and Fridays from 10.30 am to 12.30 pm. Prashanti can be contacted on 9350816699, 011-32492199; and Mobile Helpline: 9868216588.

Conclusion

Complementary therapies have been recognized for the positive effects they have on the patients wellbeing. They help people feel better and cope with their illnesses. These therapies are seen as another source of hope. Many people find these therapies helpful in improving their quality of life.

(The Institute appreciates Ms Renuka Prasad, President Prashanti, for her contribution on Prashanti under the feature "In Focus".)

CANCER CONTROL

Altered Gene Expression

Comprehensive diet and lifestyle modifications alter gene expression in prostate tissue in men with low risk prostate cancer. The results of the Gene Expression Modulation by Intervention with Nutrition and Lifestyle study, designed to explore the molecular mechanisms involved, show that expression of genes involved in the tumorigenesis were down-regulated. Two years ago, the same team had published the first randomized controlled trial, showing that intensive lifestyle changes may slow, stop or even reverse the progression of early stage prostate cancer and perhaps breast cancer as well.

The three-month lifestyle intervention involved low fat, whole foods, plant based nutrition, stress management techniques, moderate exercise and participation in a psycho-social support group. Results showed that 48 genes were up-regulated and 453 were down-regulated. Knowing these mechanisms could help motivate people to make beneficial lifestyle changes.

(Proc Natl Acad Sci, June 16, 2008)

Cancer Survivors

Researchers called for the use of a comprehensive geriatric assessment to understand the functional, physical, mental, pharmacotherapeutic and socio-economic factors that affect the course of disease and the outcome of treatment decisions. It was revealed that historically, treatment decisions for elderly cancer patients were often subjectively based on what an individual doctor believed the patient could tolerate. Today, new tools have been developed that provide clinicians with more objective assessment of the health status that could lead to more seniors receiving more aggressive treatments, offering a better chance at long term survival.

The panel found that older family members appeared to adjust psychologically and spiritually to the caregiving role, but were at a higher risk for adverse affects on their physical health. Family caregivers with lower education and income suffered from poorer physical health than those with better education and higher income levels. Caregivers who received social support were in better health, suggesting that it is possible to improve the family caregiver's quality of life.

(National Cancer Institute News, June 20, 2008)

Lifestyle Changes and Quality of Life

The American Cancer Society has formulated guidelines aimed at improving the quality of life among cancer survivors. The three main recommendations are physical activity, eating five servings of fruits and vegetables per day and stopping smoking. In a study, the researchers looked for an association between three of these recommendations and health related quality of life scores. Results show that overall, only five percent of survivors met all the three recommendations.

Higher quality of life scores were also observed among survivors who met the lifestyle recommendations, particularly the physical exercise recommendation. Among various types of cancer, significant positive associations were seen between the quality of life scores and lifestyle recommendations among breast, prostate, colorectal, bladder and uterine cancer survivors, as well as melanoma survivors. Researchers concluded that although few cancer survivors are meeting the lifestyle recommendations, many cancer survivors have reported an improvement in the quality of life when they do follow the guidelines.

(Cancer Consultant, May 5, 2008)

Oral Health & Cancer Risk

There may be a link between periodontal disease and the risk of different types of cancers. It is believed that inflammation and immune system responses associated with poor oral health have a role in overall health. Because a significant amount of periodontal disease can be prevented through flossing, brushing and regular cleaning, researchers hope that individuals with good oral health may be able to significantly reduce their risk of cancers.

Researchers from Imperial College, London, recently conducted a clinical trial to explore the potential association between oral health and cancer rates. They found that individuals with periodontal disease had an overall 14% increased risk for developing cancer. Periodontal disease was associated with a 36% increased risk of lung cancer, a 49% increased risk of kidney cancer, a 54% increased risk of pancreatic cancer and a 30% increased risk of hematologic cancers. It appears that oral health, whether it is a sign of an immune system more susceptible to cancer or whether it is a direct cause itself, is associated with cancer risks.

(Lancet Oncology, May 27, 2008)

GENOMICS

Gene Therapy

Researchers at the University of Georgia have created a novel synthetic gene vector that packages DNA into well defined nanostructures that allow it to efficiently deliver genes without triggering immune responses.

So, while the use of viruses as gene delivery vectors has been efficient, it has also led to the unexpected and tragic complications, some of which have been fatal. Synthetic vectors, which use synthetic molecules to package genes, are generally safer than the viral vectors. The team synthesized small peptides that bind to genes and emulate natural proteins to minimize potential immune reactions. The researchers then attached the small peptides onto a biocompatible polymer scaffold to create a clustered effect. The clustered peptides of the combined molecule will automatically assemble with the DNA, while the polymer wraps around the assembly, creating a protective shell.

(Science Daily, June 27, 2008)

MicroRNA and Oncogenes

Scientists have demonstrated that microRNAs (miRNA) can modulate the expression of tumor specific oncogenic translocation proteins and may play a significant role in some human cancers. They used miRNA expression profiling to reveal that one particular miRNA, miR-203, is silenced by both genetic and epigenetic mechanisms in several blood cell malignancies, including chronic myelogenous leukemias and some acute lymphoblastic leukemias.

The study showed that transcriptional silencing of miR-203 led to the upregulation of the oncogene ABL1 and the BCR-ABL1 oncogenic fusion protein in various hematopoietic malignancies. Further, restoration of miR-203 resulted in a subsequent reduction of ABL1 and BCR-ABL1 and decreased proliferation of tumor cells.

Results suggest that miR-203 functions as a tumor suppressor and its re-expression might have therapeutic benefits in specific hematopoietic malignancies. This may be particularly beneficial for the patients who are resistant to small molecule kinase inhibitors like Gleevec, as

resistant isoforms of ABL and BCR-ABL should contain the target site for miR-203 and are likely to respond to restored miR-203 function.

(Cell Press, June 10, 2008)

New Therapy for Cancer Cell

A gene radiotherapy system that detects and treats cancer cells that are resistant to traditional forms of chemotherapy and radiation could eventually prove beneficial for the cancer patients. The new system targets oxygen deficient hypoxic cancer cells that have activated a gene known as HIF-1 which ensures cells survival and makes them unresponsive to most current treatments.

Because cells need oxygen to survive, hypoxic cells instead activate the HIF-1 protein, which changes cell metabolism and enables them to burn sugar for energy without oxygen. Scientists developed a therapeutic system that targets HIF-1 human liver cancer cells in the laboratory. A reporter gene was developed and this gene would simultaneously track the cancer cells and treat them by allowing them to absorb iodine and radioisotope more easily.

(Society of Nuclear Medicine, June 16, 2008)

Risk for Lung Cancer

According to researchers from the University of Texas, people who have never smoked but whose cells cannot efficiently repair environmental insults to DNA, are at higher risk of developing lung cancer than those with effective genomic repair capability.

About 15% of lung cancers occur in non-smokers. This study demonstrates that poor DNA repair capacity is an important predictor of lung cancer risk in non-smokers. Non-smokers with sub-optimal DNA repair capacity (DRC) are twice as likely to develop lung cancer, compared with non-smokers with normal DRC. Second hand smoke exposure is another established risk factor; in participants with inefficient DRC who also reported such exposure, the risk of lung cancer was almost fourfold.

The study comprised patients and matched control participants, all of whom had never smoked. They used the cells to host-cell reactivation assay, a complicated test that introduced a specific carcinogen, benzo[a]pyrene diol epoxide that is highly carcinogenic and mutagenic, capable of changing the composition of DNA. The data also suggests that the trait is heritable to some degree.

(Am Assoc for Cancer Res, June 27, 2008)

CLINICAL TRIALS

Bevacizumab for Breast Cancer

Results of a phase III, double blind, placebo-controlled trial confirm the clinical benefit of combining the first-line bevacizumab with taxane chemotherapy for patients with HER 2-negative metastatic breast cancer.

In the study, a total of 736 women with previously untreated locally recurrent or metastatic breast cancer were randomized for first line therapy with docetaxel plus either placebo or bevacizumab. After a median follow-up of 11 months, progression-free survival, the primary endpoint was significantly superior in both bevacizumab arms compared with docetaxel alone. Tumor shrinkage was seen in 44.4% of women in the placebo plus docetaxel arm, compared with 55.2% and 63.1% of women in the lower dose and higher dose bevacizumab arms, respectively. The rate of grade 3 or higher adverse events was slightly higher in the two bevacizumab arms; 74.8% in the lower dose arm and 74.1% in the higher dose arm, compared with 67.0% in the docetaxel-placebo arm. Also, adverse events leading to death of the patients were comparable in each arm.

(Reuters, June 2, 2008)

Endoscopic Treatment for Barrett's Esophagus

BARRX Medical Inc. has developed treatment solutions for Barrett's esophagus, a precancerous condition of the lining of the esophagus caused by gastroesophageal reflux disease. Its flagship product, the HALO360 System, provides uniform and controlled therapy at a consistent depth, which can remove Barrett's esophagus and allow the regrowth of normal cells. In the largest clinical trial conducted and published to date (the AIM trial), 98.4% of patients were Barrett's free after two and a half years.

Beginning in 2006, the AIM dysplasia trial enrolled 127 patients with a diagnosis of Dysplastic Barrett's esophagus, the most advanced stage of this precancerous condition. The patients were randomly assigned to receive either endoscopic ablation therapy using the HALO ablation system or a placebo. The study endpoints were the disappearance of dysplasia, as well as the more rigorous endpoint of complete eradication of all Barrett's tissue. At one year follow-up, more than three quarters of the treated patients had no detectable Barrett's at the

end of the treatment period, compared to those given placebo (all of whom still had Barrett's).

(BARRX Medical Inc., May 20, 2008)

Gene Therapy for Head and Neck Cancers

A gene therapy invented at MD Anderson Cancer Center is the first to succeed in a US phase III clinical trial for cancer. Researchers have reported results of its phase III trial of Advexin®, a modified adenovirus that expresses the tumor suppressing gene p53 for end stage head and neck cancer. Cells become cancerous when p53 no longer functions. The p53 gene is inactivated in many types of cancers. Its normal role is to halt the division of a defective cell and then force the cell to kill itself.

The scientists deleted an important region of the adenovirus genome, preventing it from replicating. They installed a genomic segment that expresses p53. When injected into a tumor, the p53 adenovirus burrows into the cancer cell's nucleus. Instead of replicating in a typical viral manner, it expresses p53, resulting in cell death. Advexin® is also being tested in other cancers in a variety of clinical trials.

(MD Anderson Cancer Centre News, May 29, 2008)

TORISEL for Mantle Cell Lymphoma

Data presented from a phase III trial show that patients with relapsed and/or refractory mantle cell lymphoma (MCL) treated with TORISEL (temsirolimus), a mTOR (mammalian target of rapamycin) inhibitor, experienced a statistically significant improvement in median progression-free survival, compared with single-agent therapy selected by the investigator. TORISEL is currently approved in Canada for the treatment of advanced renal cell carcinoma (RCC).

This three-arm, open-label, randomized, phase III trial compared two different dose regimens of TORISEL with investigator's choice of therapy in patients with relapsed or refractory MCL who had received two to seven prior therapies, which could include hematopoietic stem cell transplantation.

TORISEL was approved by Health Canada in December 2007 and is the only mTOR inhibitor approved to treat RCC. TORISEL is the only renal cancer therapy proven to extend median overall survival compared with interferon-alpha in patients with advanced RCC.

(Medical News Today, June 9, 2008)

WATCH-OUT

Cervical Cancer Diagnosis

Patent No. US2008124702, published on May 29 2008, and entitled “Methods of Diagnosing Cervical Cancer”, provides reagents and methods for detecting pathogen infections in human samples.

Cervical cancer is linked to high risk human papilloma virus (HPV) infection 99.7% of the time. A significant unmet need exists for an early and accurate diagnosis of oncogenic HPV infection. Papanicolaou tests may miss a large proportion of HPV infected persons. Serological assays, sandwich ELISA assays and growth in cell culture are not commercially available and several polymerase chain reaction based tests are fairly expensive.

The present invention provides methods and composition for detection of proteins from pathogens that may result in oncogenic cellular transformation or biological abnormalities in a variety of cell types (eg. cervical, anal, penile, throat). More specifically, methods, compositions and kits are described for the detection of oncogenic HPV, E6 proteins in the clinical samples.

(esp@cenet.com, June 18, 2008)

Imaging Diagnostics

A combined magnetic resonance-ultrasound coil for prostate, cervix and rectum cancer imaging diagnostics has been patented under patent No. US2008132782, published on June 5, 2008. Modern diagnostic imaging techniques currently used for the diagnosis of these cancers include magnetic resonance, computed tomography, ultrasound, positron emission tomography and single photon emission computed tomography.

The present invention relates generally to the field of medical imaging, which can be used for a variety of applications, including but not limited to cancer diagnosis and staging, image guidance and radiation therapy planning. Image guidance may include guiding a biopsy. Histologically confirmed diagnosis, such as the one provided from a biopsy, may prevent unnecessary prostatectomy. Image guidance may also include guiding minimal invasive therapy, such as brachytherapy, a focused ultrasound. The present invention may be used to plan radiotherapy, for example, by detecting and thus sparing healthy tissue from radiation exposure.

(USPTO, June 18, 2008)

Patent for New Procedure

Eugene A. Woltering, Chief of Surgical Oncology at LSU Health Sciences Center, New Orleans, has been awarded a US patent for a one-step method to rapidly identify “sentinel nodes”, the lymph nodes most likely to contain early metastasis from a primary cancer. Research indicates that the procedure which consists of injection of a radiolabeled dye around a cancer, can identify the sentinel nodes that receive lymphatic drainage from the tumor within 10 minutes.

A sentinel lymph node biopsy is used to determine whether all lymph nodes in the drainage area must be removed. The accurate identification and biopsy of the sentinel lymph node (when pathologically negative) means that other nodes will not be removed. The retention of normal lymph nodes benefits the patient by preventing lymphatic fluid accumulation in the arm or other extremity. Dr. Woltering’s new method can be used with solid tumors from a number of cancers including melanoma, breast cancer, head and neck cancer, lung cancer, neuroendocrine cancer, squamous carcinoma and colorectal cancer.

(Science Daily, June 25, 2008)

Targeted Cancer Therapy

US based Light Sciences Oncology Inc has been assigned a patent No. US2008114285, entitled “Energy Activated Targeted Cancer Therapy”, published on May 15, 2008.

The invention is related to energy activated targeted delivery systems for administering a therapy to a target tissue or target composition in a mammalian subject, using an energy source that preferably transmits energy to a treatment site transcutaneously. The systems provide for administration to the subject, a therapeutically effective amount of a targeted substance, which preferably, selectively binds to the target tissue. Energy at a wavelength corresponding to that which is absorbed by the targeted substance is then administered. The energy intensity is relatively low, but a high total fluence is employed to ensure the activation of the targeted energy-activated agent or targeted prodrug product. The claimed energy-activated targeted therapy is useful in the treatment of specifically selected target tissues, such as vascular endothelial tissue, the abnormal vascular walls of tumors, etc.

(www.freepatentsonline.com, June 18, 2008)

GLOBE SCAN

Hair to Reveal Breast Cancer

A world first test to diagnose breast cancer by x-raying a women's hair will be refined in a pilot study in Adelaide, before being released commercially later this year. Results from a trial involving 2000 Australian women found the test effective in treating breast cancer, though the success rate was just 75 %, lower than the 95% the Sydney company Fermiscan had hoped for. The test is based on an Australian University discovery that breast cancer changes the molecular structure of hair. About 1500 of the 2000 women in the trial were correctly diagnosed as negative and 20 were correctly diagnosed as positive. 13 women with cancer were missed by the test, a result likely due to hair damage by perming, dyeing and straightening.

The test would be further refined in a pilot trial involving the Ashford Cancer Centre in Adelaide and hospitals in Italy and Japan. Regulatory approval was being sought to have the \$250 test available without a referral through pathology collection centers.

(Australia: *Cancer Council*, May 12, 2008)

Test for Lung Cancer

An experimental blood test may eventually allow for earlier detection of lung cancer in smokers. In order for the new screening methods to be adopted into the routine clinical care, the measures must identify cancer early enough to improve outcomes, must be economically feasible and must detect cancer with an acceptable degree of accuracy. As well, in order to encourage patient compliance, screening methods must not be too invasive, painful or risky. To-date, no screening methods have been identified that provide a confirmed benefit.

The researchers in Germany have identified an RNA "fingerprint" in blood that was more common in individuals with lung cancer, than in individuals without lung cancer. They then looked for this fingerprint in the blood of smokers who had not yet been diagnosed with lung cancer. Some of these smokers went on to be diagnosed with lung cancer while others did not. The test detected 75% of the lung cancer cases. Among individuals without lung cancer, the test classified 85% as cancer-free.

(Germany: *cancerconsultant.com*, June 6, 2008)

Cancer Pain

OrexoAB, the Swedish pharmaceutical company, announced that the European Medicines Agency (EMA) has issued a positive opinion recommending the approval of Rapinyl for breakthrough cancer pain. Abstral/Rapinyl will be launched in Sweden in 2008.

Abstral is a fast disintegrating tablet for sublingual administration of fentanyl intended for the management of breakthrough cancer pain in patients who are already receiving opioid analgesics.

Breakthrough cancer pain is a brief and often severe flare of pain experienced by patients suffering from cancer that occurs even though a patient may be taking pain relief medicine regularly for their persistent pain. It is known as breakthrough pain because it is pain that "breaks through" a regular pain medicine schedule.

Abstral was referred for review in September 2007 and has now gained a positive opinion recommending approval of the product.

(Sweden: *Medical News Today*, June 30, 2008)

Fake Cancer "Cures"

Warning letters have been sent to 23 US companies and two foreign individuals marketing a wide range of products fraudulently, claiming to prevent and cure cancer, according to the US Food and Drug Administration. The FDA also warned north American consumers against using or purchasing the products, which include tablets, teas, tonics, black salves and creams which are sold under various names on the internet.

These warning letters are an important step to ensure that consumers do not become the victim of false "cures" that may cause greater harm to their health. The FDA urges consumers to consult their healthcare provider about discontinuing the use of these products and to seek appropriate medical attention if they have experienced any adverse effects.

These products claim to cure, treat, mitigate or prevent disease, but have not been shown to be safe and effective for their labeled conditions of use. These are unapproved new drugs, marketed in violation of the Federal Food, Drug and Cosmetics Act. The warning letters are part of the FDA's ongoing efforts to prevent deceptive products from reaching the consumers.

(USA: *Food & Drug Adm*, June 20, 2008)

ACTIVITIES OF RGCI&RC

SYMPOSIUM ON HEAD AND NECK ONCOLOGY

Head & Neck cancer is the 8th most common cause of cancer deaths worldwide, more so in the developing countries than in the developed ones. Head & Neck cancer constitutes 25% of all body cancers, about 12.5% of these belong to the oral cavity itself. India is among the leading countries in terms of age adjusted incidence of oral cancers. About 60-80% of the patients present as locally advanced cancers. Realizing the urgency of the situation, Rajiv Gandhi Cancer Institute & Research Centre, Delhi, organized a 'Symposium on Recent Advances in Head & Neck Oncology' for DNB candidates on 7th May 2008 at City Park Hotel. The speakers had been invited from various departments of the hospital. There was an enthusiastic participation from the various faculty members and the DNB students.

The first speaker, Dr Shweta Aggarwal from the Department of Radiology, compared the current imaging modality, i.e. the Magnetic Resonance Imaging (MRI) with Computed Tomography (CT) scan and said that MRI was better as it provided a better soft tissue contrast resolution. She spoke on the role of Positron Emission Tomography (PET) integrated with CT and tumor detection based on the uptake of FDG (Fluorodeoxy Glucose) based on the principle of Warburg effect. She also mentioned about the diffusion weighted imaging which provides unique insights about tumor biology like cellularity and cell membrane integrity, based on the apparent diffusion coefficient values.

The next presentation was by Dr Kirti Bhushan from the Department of Surgical Oncology. He spoke on the surgical reconstructive procedures and described the recent advances in the development of newer vascularized free flaps for patients undergoing extensive resections and how they have been able to achieve lower incidence of flap necrosis. Mandibular reconstructions by the use of alloplastic implants and corticocancellous bone grafts are recent additions to the armamentarium of a Surgical Oncologist. He rounded up his discussion by saying that the pectoralis major myocutaneous flap remains the workhorse for salvaging or for increasing the primary bulk.

Dr Sandeep Batra of the Department of Medical Oncology presented the data on current standard of care

by concurrent chemoradiotherapy. He mentioned about the addition of epidermal growth factor receptor blocker, like Cetuximab to radiotherapy, and presented supportive data in its favour. He also spoke about the re-emerging role of combination chemotherapy in neo-adjuvant setting pre-operatively with the availability of taxanes, which result in higher response rates and thus better organ preservation. He also mentioned about Gefitinib and Erlotinib which are small molecule Tyrosine Kinase inhibitors and their ability to induce apoptosis in Head & Neck cancers with mild toxicity profiles.

The last presentation was made by Dr Abhishek Puri from the Department of Radiation Oncology. He described the advances made in treatment delivery from older radioactive cobalt to newer techniques like Intensity Modulated and Image Guided Radiotherapy. He briefly mentioned about the altered fractionation schedules and use of radiation protectors, such as amifostine, to lower the toxicity to critical structures like salivary glands. He presented slides on the Conformal Radiation techniques and how they prevent long term tissue toxicity to parotid glands and dysphagia associated structures. He told about the Proton Therapy which is being explored for Head and Neck cancers; its excellent conformality due to inherent physical characteristics like Bragg Peak and the data related to local control.

There was a question and answer session at the end where various faculty members quizzed the participants about their respective presentations. This was followed by a prize distribution session. The first prize went to Dr Abhishek Puri; second prize was awarded to Dr Shweta Aggarwal and the third prize to Dr Sandeep Batra. The exchange of ideas on head and neck cancer was wrapped up on a high note by a lavish dinner at the venue itself.

Lymphoma Awareness Programme 2008

Organiser : Rajiv Gandhi Cancer Institute and
Research Centre, Delhi.
Date : 14 September 2008
Venue : India Habitat Centre (IHC), Jacaranda
Hall, New Delhi
Time : 10 am - 4 pm
Inf : Dr. (Col.) R.Ranga Rao, VSM /
Dr. Kopal
Contact : 011 - 47022440
Email ID : ranga_rr@airtelmail.in
m.oncology@gmail.com

PEDIATRIC ONCOLOGY WORKSHOP

The Department of Pediatric Oncology at Rajiv Gandhi Cancer Institute & Research Centre (RGCI&RC) organized a national level training workshop of North Zone on 'Practical Pediatric Oncology' under the aegis of Pediatric Hematology Oncology' chapter of IAP (Indian Academy of Pediatrics) and SIOP (Society of International Pediatric Oncology) on May 10 and 11, 2008. Pediatric cancers are potentially curable if detected early and managed properly. The aim of the workshop was to educate the pediatricians about the diagnosis and management of pediatric cancers to make them more proficient in its early detection and diagnosis. The other objective was to make them as intermediaries between the patient and oncologist in the management of cancer patients, ie, to make them participate meaningfully in the overall optimal care of a child with cancer (concept of shared care). Professor Archana Kumar of the King George Medical College, Lucknow was the central observer of the workshop.

The workshop was inaugurated by Dr A K Chaturvedi, Medical Director, RGCI & RC and started with a lecture by Dr Gauri Kapoor, Senior Consultant, RGCI & RC. She talked about the approach to diagnosis of cancer in children. This was followed by another lecture by Dr L S Arya (former Professor AIIMS, Delhi), entitled "Principles of Pediatric Oncology". These two lectures introduced the topic and covered the basic considerations in patients of pediatric cancers. The lectures were followed by problem-oriented discussions. Dr Samir Bakshi (Pediatric Oncologist, AIIMS) discussed the approach to mediastinal mass and presented various cases of the same. Dr Himesh Gupta (Pediatric Onco Surgeon, RGCI & RC) then talked about the approach to patients with lump in abdomen. He presented various types of cases and discussed the differential diagnosis and approach to the patients in these cases. The judicious use of biochemical tests and radiology to arrive at the diagnosis was also stressed upon. Dr Arya spoke about white eye reflex and its implications. This was followed by problem-oriented discussion on brain tumor by Dr Sehrawat (Consultant, Radiation Oncology, RGCI&RC) and on cord compression by Dr Jagdish Chandra (Senior Consultant, KSCH, Delhi). All these discussions involved active participation by the delegates and relevant questions were asked which were appropriately answered by the various faculties present.

The workshop also had interactive sessions on practical pediatric oncology issues, like vascular access, chemotherapy complications and case presentations. The risks and benefits of various kinds of vascular access devices were explained by Dr K K Gupta, (Consultant Pediatrician, RGCI&RC). Dr Amita Mahajan (Consultant, Apollo Hospitals, Delhi) talked about the common chemotherapy drugs and their complications. Dr Sunil Gomber (Consultant, GTB Hospital, Delhi) and Dr Himesh Gupta took all the delegates on a visit to a ward where interesting cases were presented by the residents of RGCI&RC and their approach was discussed.

The workshop on the next day started with a lecture by Dr Gauri Kapoor. She talked about the diagnosis and management of childhood leukemia and lymphoma. The delegates discussed the difficulties they generally encountered during the management of leukemia and lymphoma patients. Dr Mahajan delivered a lecture on emergencies and supportive care and highlighted the role of good infrastructure and team approach in the management of children with cancer. The lectures were followed by problem-oriented discussions on extremity masses by Dr Himesh Gupta. He discussed the approach to pediatric extremity masses in various clinical scenarios. Dr Sunil Gomber spoke on the approach to neck lymph node masses. The delegates had many questions on this topic which were answered in a very practical and scientific manner. These were then followed by discussions on febrile neutropenia by Dr VP Chaudhary (former Professor, AIIMS, Delhi) and on long term effects of treatment by Dr Vasantha (Senior Scientist, ICMR).

All the delegates were then taken to bloodbank of RGCI & RC where the rationale of component therapy and practical aspects of blood transfusion were discussed by Dr Neeraj Prakash (Consultant, Pathology, RGCI&RC) and Dr VP Choudhry. Dr Dinesh Bhurani (Consultant, BMT, RGCI&RC) described various aspects of BMT and took the delegates around the BMT unit of RGCI&RC. Dr Vivek Arora (Consultant, Microbiology, RGCI&RC) talked about hand hygiene policies and its importance in infection control.

Dr Archana Kumar concluded the workshop with a lecture on the role of pediatricians in the management of oncology patients. The delegates expressed satisfaction at the workshop and described the environment as warm and friendly, which encouraged interactive discussions.

NON SMALL CELL LUNG CANCER

A live webcast (CME) on 'Changing Perspectives in First Line Treatment of Non Small Cell Lung Cancer (NSCLC)' by Dr Nicholas Thatcher, Prof of Medical Oncology, Christie Hospital, Manchester, England was organised on May 23, 2008 in the conference hall of Rajiv Gandhi Cancer Institute & Research Centre (RGCI&RC). The webcast was sponsored by Eli Lilly. It was attended by Dr AK Chaturvedi, Medical Director, RGCI&RC, faculty members, research officers, senior residents and DNB candidates of the Institute.

One of the most common cancers in today's world is lung cancer, in terms of both incidence and mortality. The five-year survival rate measured by Surveillance, Epidemiology and End Results (SEER) programme in the USA is 15%, Europe's average is 10% and 8.9% in the developing countries. Improvement of survival rates are dependent on the early detection and improved systemic therapies applied to surgery and/or irradiation in early stage disease. Unfortunately, most patients have advanced unresectable disease at diagnosis, which has a very poor prognosis. Before 1980, radiotherapy was thought to be the only option for advanced disease. A few years before the turn of the millennium, a meta-analysis of NSCLC trials demonstrated a survival benefit with platinum based chemotherapy. Since that time, meta-analysis has shown that platinum based doublets can improve survival in Stages II–IV NSCLC.

Regarding the role of frontline chemotherapy in advanced Stage III B/ IV lung cancer, Dr Thatcher discussed about the role of first line chemotherapy, special subgroups and newer approaches in advanced lung cancer. Meta-analysis of one vs two and two vs three chemotherapy agents had shown overall response of 13-15% in one vs two arms in favour of doublets, whereas there is an addition of 3-8% benefit when a third agent is added. One-year survival was 5-6% in favour of doublets but there was no advantage after addition of third agent. When third generation agents with cisplatin are compared with cisplatin alone arm, various combination arms of cisplatin have shown statistically significant survival advantages in all the trials.

ECOG Avastin trial (E4599) compared Carboplatin with Paclitaxel on one arm vs Carboplatin, Paclitaxel with Bevacizumab in other arm. One-year survival in Bevacizumab arm is 51% vs 44% in other arm and two-year survival is 23% in Bevacizumab arm vs 15% in

Paclitaxel Carboplatin arm. Treatment related death in Bevacizumab arm is 4% vs 0.5% in chemotherapy only arm. There was an excess of one toxic death for every 24 patients treated in Bevacizumab arm whereas 12 patients required treatment to prevent one death a year.

Blackhall et al compared Gemcitabine and Cisplatin with Gemcitabine and Carboplatin and have shown reduced hospitalization for toxicity without compromising efficacy with 62% reduction in days of hospitalization, 42% reduction in units of blood and 75% reduction in units of platelet transfusion in the Cisplatin arm.

ECOG 1594 trial has shown significantly longer treatment free interval in Gemcitabine/ Cisplatin arm compared with Taxol/ Cisplatin, Taxotere/ Cisplatin and Taxotere/ Carboplatin based regimes.

The Four Arms Cooperative Studies have also shown better median and one year survival in Gemcitabine arm. It was compared with Irinotecan, Paclitaxel and Vinorelbine based combination therapies.

CISCA meta-analysis involving 9 trials and 2968 patients compared Cisplatin vs Carboplatin. Overall responses, median survival and one-year survival are all better in the Cisplatin arm.

The Gemzar meta-analysis have shown absolute benefit of 3.9% in one year in Gemcitabine based regimens.

In a meta-analysis, comparing platinum based therapy with nonplatinum based therapy, increase in 17% of response rate but no survival advantage and more toxicity in nonplatinum based therapy was seen.

Danson et al compared Gemcete/ Carboplatin with Mitomycin, Ifosfamide and Cisplatin. Gemcete arm had less toxicity and less hospital in-patient time.

In symptomatic advanced NSCLC with poor performance status, Gemcitabine was compared with best supportive care, except for dyspnea, all other parameters like emotional pain, pain in chest, pain medication, cough and fatigue, have shown more improvement in Gemcitabine arm.

It can, therefore, be said that chemotherapy can prolong survival, palliative disease symptoms and improve the quality of life compared with the best supportive care in patients with NSCLC. Newer targeted therapies could provide better treatment options, either used alone or with the standard chemotherapy.

NEW WING IN RGCI&RC INAUGURATED

Rajiv Gandhi Cancer Institute & Research Centre (RGCI&RC) is a project of Indraprastha Cancer Society and Research Centre. The Institute provides high quality care and access to the latest advances in cancer diagnosis and treatment, augmented by warm and caring medical and supportive staff. Since its inception in 1996, the Institute would have registered over one lakh patients by the current year.

The new wing of the Institute was inaugurated by Shri Tajender Khanna, Hon'ble Lt Governor of Delhi, on June 6, 2008. The ceremony started with Ganesh Stuti followed by bouquet presentation to the chief guest by Mr K K Mehta, Principal Advisor, RGCI&RC. The lighting of the lamp was graced by Shri Tajender Khanna, Dr K V Swaminathan, Chairman, Mr K K Mehta, Principal Advisor, Mr D S Negi, Chief Executive Officer and Dr A K Chaturvedi, Medical Director.

In his welcome address, Mr Negi welcomed and thanked the Hon'ble Lt Governor for sparing his valuable time for inaugurating the new wing. He conveyed that the Institute is indebted to him for according the mandatory permission to operationalise the new wing. He welcomed the distinguished members of the Governing Council and other guests. He informed that in India, the estimated number of new cancer cases is about 7 lakhs per year and over 3.5 lakh patients die of cancer each year. He stated that the new wing would fulfill the needs of many cancer patients and the management is keen to provide quality patient care and state-of-the-art diagnostic and treatment facilities to the patients.

Dr Swaminathan, Chairman of the Institute and the Research Advisory Committee, welcomed Hon'ble Shri Tajender Khanna. He mentioned that RGCI&RC is the best Institute in Northern India in providing comprehensive cancer treatment and is at par with Tata Memorial Hospital in Mumbai. He told that with the new facility, bed strength has gone up to 225, the credit for which goes to the Governing Council. A new PET-CT and MRI have been installed in the current year and the proposal to acquire Image Guided Radiotherapy is in the pipeline.

During his introductory address, the Chairman emphasized on the quality of cancer care, development of research and technology and income generation. For the quality of care, the Governing Council has a special



committee to look into it. For Research and Technology, strategic alliances are being developed in the form of introducing Dr Jatin Shah from Memorial Sloan Kettering Cancer Center and Dr Paul M Silverman from MD Anderson Cancer Center as Distinguished Members. Moreover, the Institute has a Memorandum of Understanding with the Indian Council of Medical Research to integrate clinical research with basic research. The Institute also needs to develop the basic infrastructure. The Chairman requested Shri Tajendra Khanna for his guidance and support so that RGCI&RC can become a model of excellence in all fields of cancer.

After the introductory address, the Chairman presented a memento to the Chief Guest.

During his inaugural address, the Lt. Governor thanked Dr Swaminathan, Mr Mehta, Mr Negi and Dr Chaturvedi for giving him this opportunity. He appreciated their contributions in the government and private sectors. Looking at the increasing number of the cancer patients, the Lt Governor appreciated the need for further expansion of the Institute, as it is recognized as a Center of Excellence and is facing acute shortage of space. He offered to help to make a plot available in the vicinity of RGCI&RC. Giving importance to the concerns raised by Dr K V Swaminathan, he assured his full support to the Institute.

Dr Chaturvedi informed the gathering that the Governing Council of the Institute has a constant stream of endless dreams and the in-patient facility in the new wing is one of them. He warmly thanked the Lt Governor, Distinguished Members of the Governing Council and the other guests. He appreciated the cooperation and support extended by all the members of the Institute and conveyed immense thanks to everybody.