

EDITORIAL

MORE ABOUT GENERIC DRUGS

Generic drug is a pharmaceutical drug that is equivalent to a brand-name product in dosage, strength, route of administration, quality, performance and intended use. It also refers to any drug marketed under its chemical name without advertising. Although they may not be associated with particular company, generic drugs are usually subject to Govt. regulations. A generic drug must contain same active ingredient as the original brand formulation.

Biopharmaceuticals such as monoclonal antibodies differ biologically from small molecule drugs. Generic versions of these drugs known as biosimilars are typically regulated under an extended set of rules. In most cases, generics become available after the patent protection expires. Once generic drugs enter the market, competition often leads to lower prices for both the original brand name product and its generic equivalent. Manufacturers, whole sellers, insurers and drug stores can each increase prices at various stages of production and distribution.

In 2014, according to an analysis by the Generic Pharmaceutical Association, generic drugs accounted for 88% of the 4.3 billion prescriptions filled in the USA. Experts in India say that more than 70% of 1 lakh crore domestic pharmaceutical market is dominated by branded drugs, whereas patent drugs make up to 9%. Large pharma companies often spend millions to protect their patent from generic competition. They may reformulate a drug or license a subsidiary (or another company) to sell generics under the original patent. Generic sold under license from the patent holder is known as authorized generic. Generic companies incur the cost of manufacturing only without the cost of drugs discovery and development-so they are able to maintain profitability at lower price. The lower cost drugs are useful in less prosperous countries. For example Thailand imported plavix (blood thinner) from India (the leading manufacturer of generic) at 3 US cents/dose.

In 2007, the FDA launched the Generic Initiative for Value and Efficiency (GIVE) in an effort to modernize and streamline the generic drug approval process. Before a company can market a generic, it needs to file Abbreviated New Drug Application (ANDA) with FDA seeking to demonstrate therapeutic equivalence of previously approved listed drugs safely and consistently. FDA requires the bio equivalence of a generic drug to be between 80% and 125% of the innovative products. Biosimilars require clinical trials of immunogenicity in addition to tests establishing bio-equivalency. There were many scandals around generic drug approvals in 1980's in USA in which companies obtained bioequivalence data fraudulently and found corruption at FDA where employees accepted bribes to approve generic companies applications and delaying or denying others.

In India 1970 patent's Act removed composition patents for food and drugs and patents were shortened to a period of 5-7 years. The resulting lack of patent protection created a niche in both the Indian and global markets that Indian companies filled by reverse-engineering new processes for manufacturing low cost drugs. The code of ethics issued by MCI in 2002 calls for doctors to prescribe drugs by the generic names only. The Health Ministry has also asked the MCI to make it mandatory for doctors to write generic name of drugs in legible handwriting in prescription.

Govt. wishes to propose legal framework for doctors so that they prescribe generic drugs. Does the Govt control the mobile user or various mobile schemes used by consumers? Govt. only regulates big mobile companies. Why not regulate pharma companies rather than prescribers. Why not regulate the manufacturers? Why DCGI allows 100 brands of one generic to be released in market? Is there any check on quality of generics?

Considering that medicine crime can kill, today's laws are unreasonably weak. The law hardly punishes those who intentionally deal in substandard medicines. We should have law against manufacturing, trafficking or selling substandard medicine and tools for encouraging whistle blowers to cooperate with law enforcement. I believe that for the medicine crime problem to be solved, law reform is an absolutely necessary condition.

You don't need to check the prescriber or end users. Doctors are self regulated and need only moral and ethical policing. Question is not of legible hand writing of prescription but of quality of drugs. If patient gets good quality of generic drug, why will anyone go for branded item? Let us

1. Ensure good quality of generics.
2. Conduct systematic trials for biosimilars for immunogenicity and bio-equivalency before approval.
3. Approve and release only 3 or 4 brands of one generic in market (brand generics).
4. Have more of generic medicine stores with price and quality control.
5. Legal framework is needed for manufacturers, traffickers or retailers of substandard quality. Doctors cannot test the quality of a drug.

Today the question is quality of medicines rather than the quality of prescription!!

Dr. A. K. Dewan
Director Surgical Oncology



MULTIDISCIPLINARY APPROACH TO TREATMENT OF BRAIN TUMORS AT RGCIRC



Glioblastoma is the most common primary malignant neoplasm of the adult brain. Even after multimodal therapy including surgical resection, radiotherapy, and chemotherapy, treatment outcomes remain poor, with a median survival of approximately 18 months. Glioblastomas are highly invasive cancers, and tumor cells are found at significant distances from the original tumor site. The invasive nature of these tumors, combined with resistance to chemotherapeutic and radiation interventions, necessitates an aggressive investigation of new therapeutic approaches, combined with improved paradigms for monitoring therapeutic efficacy.

Currently, determinations of a patient's clinical prognosis rely upon standard clinical measures such as a tumor's histological grade, patient age, presenting Karnofsky score, and the extent of surgical resection. Genetic and tissue-specific

markers have become increasingly prevalent as potential resources that allow improved stratification of tumor sub typing and determination of prognosis, and may ultimately allow personalization and individualization of tumor treatment.

Multidisciplinary approach to treatment planning of brain tumors is a worldwide increasing practice. This approach is feasible only at dedicated neuro-oncology centres. RGCIRC takes pride in being a major dedicated Neuro-oncology centre in North India. The neurosurgeon along with members of radiation oncology, and neuro- imaging bring their expertise to every case, and together develop a personalized treatment plan for all patients. The team collectively reviews each patient's case to ensure they receive the best care possible. The various components of multidisciplinary approach include neurosurgery, neuroradiology, radiation oncology and neuropathology.

Neurosurgery

We want to ensure maximal safe resection while sparing healthy tissue. To accomplish that, there are state-of-the-art surgical techniques and extensive pre-surgical planning that may include:

- Functional MRIs
- MRI Perfusion
- MRI Tractography
- PETImaging



Figure 1
Preoperative MR head
showing right frontal
extensive lesion



Figure 2
Postoperative MR head
showing complete
excision

Intra-operative navigation is used whenever needed to help guide the neurosurgeon through challenging cases, maximizing tumor removal while minimizing injury to surrounding brain. Microscopy is employed to allow the most aggressive—yet safest—surgery to be conducted on some of the most sensitive areas of the brain.

Stereotaxy is employed whenever needed to biopsy the lesions in deeper eloquent areas of the brain or establish the tissue diagnosis in complicated cases.

After surgery, the clinical care/rehabilitation team works closely with the neurosurgery team to coordinate patient care and follow-up.

Neuroradiology

The Neuro-Oncology team members work closely with the Neuroradiology Section of the Radiology Department at RGCIRC to provide comprehensive neuroimaging evaluations. CT scans, PET imaging, and MRIs are available.

For MRI interpretation, we use a technique called “MRI registration”. It is possible with the help of our IT professionals using the imaging data viewing system “SYNAPSE”. This technology allows us to view digitally matching slices of the MRI across different dates to make more exact comparisons. We can now more accurately detect small but potentially clinically significant changes in a tumor.

In addition to MRI registration, all brain tumor MRIs include the generation of physiological data through various techniques (i.e., MR diffusion, MR spectroscopy, MR blood volumes, and perfusion). These give us a detailed understanding of the potential for tumor growth and response to treatment.

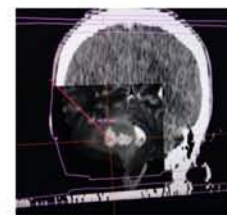


Figure 3
Stereotactic biopsy
planning with CT
and MR fusion technique

PET scans are commonly used to find areas of very active cancer. This often assists in distinguishing a true tumor from areas of post-radiation changes.

Radiation Oncology

Radiation therapy is an important part of treatment for brain tumors. Our radiation oncologists specializing in brain tumor treatment use cutting-edge technologies including:

- Intensity - Modulated Radiation Therapy (IMRT)
- Image-Guided Radiation Therapy (IGRT)
- Stereotactic Radiosurgery (SRS)

These various treatments are used to direct targeted beams at the tumor while minimizing the radiation delivered to normal tissues.

Typically, radiation therapy for brain tumors is a daily treatment (about 1-hour) Monday-Friday for about 6 weeks with or without chemotherapy.

SRS is a specialized delivery system that gives precise high-dose radiation in a single/fractionated treatment and is typically used for benign brain tumors and brain metastases.

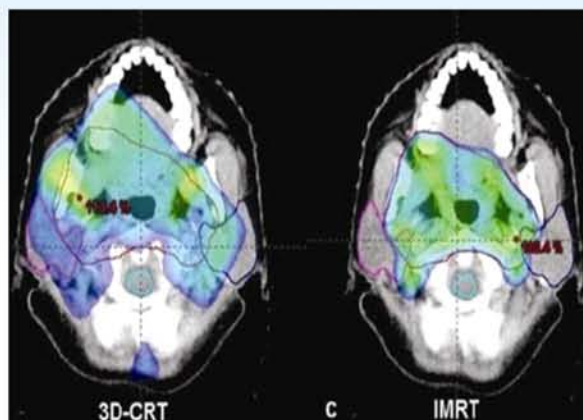


Figure 4 :
Contemporary radiotherapy techniques and planning

Neuropathology

Dedicated Neuropathology team is indispensable for meticulous treatment, specially in complicated cases. The neuropathological diagnosis and the grading of each histotype are based on identification of histopathological criteria and immunohistochemical data. Molecular and genetic profiles may identify different tumor subtypes varying in biological and clinical behavior, indicating prognostic and predictive factors. In order to investigate new therapeutic approaches, it is important to study the molecular pathways responsible for proliferation, invasion, angiogenesis, and anaplastic transformation. Different prognostic and predictive factors for glioma patients were identified by genetic studies, such as the loss of heterozygosity on chromosome 1p and 19q for oligodendrogliomas, proangiogenic factors such as Vascular Endothelial Growth Factor for glioblastomas and the methylation status of gene promoter of Methyl Guanine – Methyl Transferase (MGMT).

Multidisciplinary approach thus provides comprehensive treatment under one roof which is essential for complex and intricate disease like brain tumors where aggression as well as precision is needed.

Dr. R. S. Jaggi
Consultant – Neuro Surgery

THE HUMAN SIDE' OF CANCER CARE

Today cancer has assumed epidemic proportions and patients and care givers obtain substantial benefit from open discussions and knowledge sharing. Subjective symptoms of cancer patients such as pain, anxiety, depression and delirium are now quantifiable and eminently treatable assuming that treating physicians are sensitive to the patient's changing persona with disease progression and intensifying symptomatology.

NCCN guidelines addresses the attitudinal barriers of stigma related to psychosocial care by suggesting use of the word 'distress' as an encompassing word that avoided labeling as "psychiatric or psychological" which was perceived a barrier to both oncology staff and patients.

Advances in cancer screening and treatment have thrown up new psychological issues- "the worried well" population- people who are physically healthy but who bear the knowledge of a positive tumor marker without clinical signs of disease, or those who have a strong family history of a particular cancer and who must deal with whether to pursue gene testing or not. Such people manifest a variable spectrum of response- from denial leading to refusal to follow surveillance guidelines to high anxiety causing a tendency for constant self-monitoring and almost immobilizing anxiety.

Counseling of patients and their families has become an important part of the agenda of dealing with the psychological, social and ethical consequences of this disease and it helps in bearing the treatment, minimizing both, disaffection arising from undue expectations of cure and potential for legal dispute.

In addition to psycho social interventions, the management of psychiatric disorders complicating cancer is greatly enhanced by the array of psychopharmacological agents available to relieve distressing psychological symptoms including relief from pain, nausea, fatigue and emesis which accompany cancer and its therapy.

Other therapies such as meditation, yoga, art and group therapy are also assuming greater significance as complementary and alternative to 'traditional' medicine. There is greater appreciation for the role of spiritual care and affirmation of religious belief especially in end of life care leading to increasing involvement of the spiritual guides and teachers.

While it cannot be confidently concluded that life events, personality features or depression play a role in the onset of cancer, numerous findings suggest that personality is linked to the incidence and experience of negative health outcomes – such as anger suppression in young women “alexithymia” is being linked to breast cancer.

Pain management in cancer requires multimodal approach with pharmacology, psychotherapy, interventional and rehabilitative touch. The adequacy of cancer pain management is influenced very greatly by the lack of concordance between the patient's assessment of their pain experience, observed report of the caregivers and the clinician's assessment especially in high pain scores.

Lastly 'truth telling' is an important part of care ethics in cancer management. Information should be tailored to individual, family and community-cultural values especially whether to withhold or downplay the truth. Studies indicate that in the course of a chronic illness such as cancer, which entails frequent visit to specialists and periods of hospitalization, almost all patients will inevitable be told or will overhear the truth at some point. As a result they may lose trust in the treating physicians and team members who have withheld information from them.

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