Concurrent TMZ followed by adjuvant TMZ for 6 months.

RCC is the standard adjuvant Rx. Current RT recommendations for RCC are limited access to clinical examination. Surgery is the primary treatment for RCC. Radio therapy along with CT is better option. Brain-as the vital organ every mm needs to be preserved during metastasis. RCC accounts for 11% of all CNS tumors. Incidences are more in males aged 55-65%.

Increasing with age worsen the program. Recent advances in radiation treatment include: IMRT, IGRT: An approach to conformal therapy that not only conforms high dose to tumor tissue but also conforms low dose to surrounding sensitive and normal structures. Stereotactic irradiation: The most accurate form of radiation Advanced technologies available in AIIMS are Brain suite, cyber Knife, tomotherapy – includes serial tomotherapy - delivery of multiple fan beam discrete radiation Advanced technologies available in AIIMS are Brain suite, cyber Knife, tomotherapy – includes serial tomotherapy - delivery of multiple fan beam discrete radiation Advanced technologies available in AIIMS are Brain suite, cyber Knife, tomotherapy – includes serial tomotherapy - delivery of multiple fan beam discrete radiation Advanced technologies available in AIIMS are Brain suite, cyber Knife, tomotherapy – includes serial tomotherapy - delivery of multiple fan beam discrete radiation and IV are called as malignant glioma. Glioblastoma is the Deadliest cancer in the human body. No improvement is seen in last 80 years. Management of Glioblastoma can be done using surgical resection and adjuvant therapy including RT + Temozolomide. Extent of surgery has significant prognostic value. Maximal safe surgical resection- is the aim of surgery.

MG is an aggressive entity and prognosis continues to be dismal. Surgical resection is the main treatment. RT is the standard adjuvant Rx. Current RT recommendations for MG include localized field RT Dose preferred is 60 Gy/30-33F/6-7 wks. Concurrent TMZ followed by adjuvant TMZ for 6 months.

Low grade gliomas (LGG) and High Grade Glioms (HGG) are distinctly separate entities. Grade I and grade II are called LGG. Gliomas are limited access to clinical examination. Surgery is the primary treatment for Gliomas. Radio therapy along with CT is better option. Brain-as the vital organ every mm needs to be preserved during metastasis. LGG accounts for 11% of all CNS tumors. Incidences are more in males aged 55-65%.

Increasing with age worsen the program. Recent advances in radiation treatment include: IMRT, IGRT: An approach to conformal therapy that not only conforms high dose to tumor tissue but also conforms low dose to surrounding sensitive and normal structures. Stereotactic irradiation: The most accurate form of radiation Advanced technologies available in AIIMS are Brain suite, cyber Knife, tomotherapy – includes serial tomotherapy - delivery of multiple fan beam discrete radiation Advanced technologies available in AIIMS are Brain suite, cyber Knife, tomotherapy – includes serial tomotherapy - delivery of multiple fan beam discrete radiation Advanced technologies available in AIIMS are Brain suite, cyber Knife, tomotherapy – includes serial tomotherapy - delivery of multiple fan beam discrete radiation Advanced technologies available in AIIMS are Brain suite, cyber Knife, tomotherapy – includes serial tomotherapy - delivery of multiple fan beam discrete radiation and IV are called as malignant glioma. Glioblastoma is the Deadliest cancer in the human body. No improvement is seen in last 80 years. Management of Glioblastoma can be done using surgical resection and adjuvant therapy including RT + Temozolomide. Extent of surgery has significant prognostic value. Maximal safe surgical resection- is the aim of surgery.

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Personalised medicine for early colon cancer: prognostic biomarkers

Dr. David J Kerr

The Individualized therapy is very essential in the treating of stage II colon cancer. The challenge is which stage II colon cancer patients should be treated with adjuvant chemotherapy? Because, 75-80% are cured with surgery alone, but there are not enough data to identify them. And also benefit of chemotherapy is small and no consensus in guidelines on who to treat. To treat with chemotherapy there will be significant toxicity. Today, decision to give chemotherapy subjectively based on: following aspects; clinical/pathologic markers of risk, MSI status and no other proven molecular markers are available to identify the stage II colon cancer. Overall Goal is to develop and validate a multi-genre expression assay which improves treatment decisions for patients with stage II colon cancer providing individualized assessment of recurrence risk following surgery, identification of patients with differential 5-FU/LV benefit, independent clinical value in the context of other measures such as T-stage and MMR/MSI and optimized for fixed, Paraffin-embedded colon tumor tissue. Assessment of 761 candidate genes in 1,851 patients in the development studies to yield final pre-specified assay for validation in QUASAR. In the parent QUASAR study 2,239 patients were enrolled. Among them 68% (n=1,597) of patients are with collected blocks. And confirmed stage II colon cancer is 69% (n=1,490). In the final evaluation of 1,436 patients, a significant relationship between the risk of recurrence and the pre-specified continuous. Although the recurrence score will likely yield its highest value when used as a continuous measure, to obtain individualized estimates of recurrence risk, an analysis of the QUASAR data permit the identification of “guideposts” which may be useful for clinical decision-making. These guideposts have been identified on the basis of internal consistency within the data and are not in any manner, meant to be prescriptive. Ultimately, decision making with an individual patient should be based on clinical judgment after review of the relevant clinical data, including recurrence score. In conclusion recurrence score has been validated as a predictor of recurrence in stage II colon cancer And a separate score, based on a distinct set of 6 genes, was not validated for prediction of differential 5FU/LV benefit. The implications for clinical practice, RS provides has the greatest clinical utility when used in conjunction with T stage and mismatch Repair (MMR/MSI), particularly for the majority of patients for whom these markers are unknown. This is likely to be applicable to diverse ethnic groups but requires further validation.

Dr. Raju Chacko

Personalization of CT in Breast Cancer

Dr. Raju Chacko

The gene expression arrays identify five molecular subtypes that overlap with clinical-pathologic characteristics, which would drive current medical treatments. The major oncogenic events can be either shared across subtypes (i.e., PIK3CA mutations) or are subtype-specific (FGFR1). Molecular classes could be re-divided according to molecular events. Drugs used targeting HER2 are Trastuzumab, T-DM1, Pertuzumab, Lapatinib, Neratinib. Lapatinib (HGe272) is small-molecule irreversible pan-HER3 kinase inhibitor (Erbb-1, Erbb-2 and Erbb-4) which covalently binds to Erbb receptors at ATP binding site and inhibits tyrosine kinase activity resulting in G0/G1 cell cycle arrest given orally. Targeting HER2/neu by overcoming resistance to Trastuzumab/Bevacizumab (BV), a monoclonal antibody, inhibits vascular endothelial growth factor (VEGFR), a key biomarker of angiogenesis. Three randomized trials (E2100, AVADO, RIBBON-1) have demonstrated significantly improved PFS for BV combined with different chemotherapies as first-line MBC treatment. PFS improved when BV combined with chemotherapy regardless of hormone receptor status, sites of metastases, disease-free interval (DFI), or prior adjuvant taxane use.

Bevacizumab and oral chemotherapy for patients with lymphangiitic breast cancer: A phase II randomized study of Bevacizumab with sequential versus concurrent oral Vinorelbine plus Capetitabine in patients with locally advanced breast cancer. Most of the aim of the study was to assess activity of Bevacizumab in combination settings with Capetitabine and oral Vinorelbine (sequential and concurrent administration).

To conclude, oncogenic events can be shared across molecular classes, no first-in-class agent for triple negative, but clear sensitivity to DNA damaging agents in the neoadjuvant, adjuvant Seven-in-class drugs to reverse resistance to be developed according to molecular profiling. Integrated biology approach could help to improve results in patients who develop resistance.

Dr. Arun Kurkure

Mumbai

Breast Surgeon should be familiar with all Imaging modalities, localization approach, Oncoplastic principles, adj. Systemic Treatment, and conservation of Breast tissue.

Management of Non-Palpable Lesion

In Identification of Abnormality, Localization, Single Wire Vs Multiple Wires, Surgical technique, Complication of Localization, Specimen Mammography, Multiple lesions. Non palpable lesions may not be speculated, Failure to approve US as adjunct tool, Cranio-caudal route may not be shortest route to lesion, Use of more than one guide wire is beneficial, Failure to document lesion in specimen.

Image Detected Breast Cancer: Localization and Biopsy.

Hooks should be placed beyond the lesion. Wires are stable in fibro glandular tissue as compared to fat, position of needle to be confirmed by specimen. And Biopsy.

Dr. Subodh Pande

New Delhi

Up to 43% patients are eligible to receive BCS and similar outcomes are achieved as under further RT. This attitude leaves them at significant risk for local recurrence. The reasons for reluctance are:

Travel and lodging problems
Work and care-giving responsibilities
Remoteness from RT Center
Finance
Counseling and awareness

APBI has an attractive proposition because of the following reasons:

Socio-economic salvage
Higher treatment compliance
Reduced morbidity
Improved QOL
Clinical influences

APBI Techniques includes, Interstitial brachytherapy, intra-cavitary, brachytherapy, intra-operative radiotherapy (IORT), 3-Dimensional Conformal Radiotherapy (3-DCRT)

The pros in the IORT-issues are maximal normal tissue sparing and patient A, pathologic benefit observed. The major two devices are IntraBeam (Carl Zeiss, Germany) which has 50Kv X-rays, 3.2 mm diameter probe, multi-sized applicators for conformal cavity coverage, the dose methodologies are 20 Gy at surface and 5 Gy at 1 cm in 30 minutes. The other IORT device is molybtron (Intraop Med Corporation, CA) it has 4, 6, 9 and 12 MeV electrons, therapeutic ranges up to 4 cm, uniform dose delivery of 10-25 Gy/ SF at 5 Gyminute. The Pilot EUO Trial was conducted by Dr. Veronisi et al., in 1999, this test was conducted in 921 patients, who were thus treated with 2 Gy to the tumor bed. The results were recorded as follows at medical follow up of 42 months, local rec. of 1.6%, hematoma-1.3%, liponecrosis-4.2%, mild fibrosis-2.6% Ongoing Prospective Trial: BCT vs. WBRT vs. BCT + EUOT (21 Gy). In the TARGIT-A trial (2001) Vaidya et al., there were researchers from 31 international centers/ 9 countries. Random selection of 2232 patients of early breast cancer was made in 1,113-Intraop APBI with 20 Gy SF (IntraBeam), vs. 1,119-WBRT to 40-56 Gy/15-25 free margins (+/- 1 boost) PBI is based on the premise of:

Oral recurrences predominantly occur in tumor bed
Reduction of irradiated volume could thus limit toxicity
Treatment time and toxicity
Despite variability of radiation techniques, there should be no compromise in local control or survival of WBRT. No PBI modality could be considered most efficacious and the relative role of the different techniques is yet to be clearly identified PBI currently lags the long-term clinical outcome results. No randomized trial is currently available to unequivocally establish reduction of breast local rec. as effective as WBRT. Till availability of the analysis of NSABP B-39/RTOG 0413, the use of PBI should be done judiciously and within a protocol setting. It is evident that APBI will play a crucial role in the management of a select group of early breast cancer cases in the near future, which would reflect favorably on their long term survival and QOL.
Upper Gastro-Intestinal Cancer

Changing trends in Management of SSC of Oesophagus

Dr. Hemanth Raj

Among the commonest cancers in males stomach cancer has the highest CIR(6.3), in females cervix cancer has the highest CIR(28%). The recent advances have been in epidemiology and biology of ca esophagus, recognition of preinvasive lesion, early diagnosis of invasive cancer, endoscopic interations, multimodality Management burgeoning role of definitive CRT, status of surgery. The recent advances in the diagnostic modules are Trimonial endoscopy- white light endoscopy autofluorescence, NBI, Chromoendoscopy, fluoresence microscope, Elastic scattering spectroscopy. Optical coherence tomography, cytological screening. Gene signatures for scc es, FISH,PCR, and Serum biomarker. High grade Intraepithelial is malignant potential and 30% of lesions are invasive cancer, PET plays an important role in initial staging of disease with no evidence of M1 (NCCN 2010), assessment of response restaging, T staging – limited (43% accurate, 29%-over diagnosis, 29%-underdiagnosed), N status. Recent advances in early esophageal ca are EMR, an endoscopic technique developed for removal of sessile or flat removal of sessile or flat neoplasms confined to the superficial layers of GE tract and ECD is an endoscopic technique for en bloc removal of larger flat tumors involving dissection into the sub mucosa with electrocautery knives. The endoscopic resection plus prophylactic CRT reduce Morbidity of an eso phagectomy and high level failure rates with CRT alone thus it is concluded that in SCC/CRT is early effective and superior to surgery in superficial eso ca. The locally advanced ca esophagus that is Neoadjuvant CT plus surgery showed two survival benefits out of four randomised trials. The survey conducted predicted that Palliative procedure stent or dilatation had a P value of 0.005, 3 month mortality with 0.005 p value and the length of hosp stay had 0.5 p value. The results of planned esophagoctomy after CRT proved in improving only the local area, doubtful effect on OS especially in SS, Respiratory complications, cardiac surgery. Thus, detection of pre invasive and early invasive cancers and their endoscopic management will improve, Surgery or CRT can be regarded as definitive treatment for locally advanced Squamous carcinoosa of oesophagus and Surgery is must for resectable nonresponders residual and recurrence.

Proximal Gastric Cancer & CO junction

Dr. Sanjay Sharma

In GE junction cancer pre treatment evaluation CT scan chest and upper abdomen gives out the overall accuracy of about 66-77% and also nodal assessment is poor. Major limitations is failure to detect early gastric tumors and small [<5mm] liver or peritoneal metastases where as Laspanscopy and laparoscopic USG is now recommended by many as essential as it delivers accurate diagnosis of peritoneal and small liver mets. LUS is not easily available, expensive, insufficient data available. In GE junction cancer surgery is the best modality for therapy for resectable tumors. Two important aspects has to be covered in surgery: the extent of resection and extent of lymphadenectomy. RO resection apart from TNM remains important independent prognostic factor. The advantages of peripерoperative treatment are increases rate of curative resection by tumor downstaging, eradication of micro metastatic disease, demonstrates in vivo chemosensitivity, and better tolerated than post-operative therapy. Adjuvant treatment the post op Radiotherapy is recommended for patients with positive regional nodes and in patients with positive resection margins and no significant improvement in overall survival had been demonstrated.

Haematology-Oncology

New drugs in MM

Dr. B. K. Smruti

- Multiple myeloma treatment in 1960's were the alkylating agents ± Prednisolone, in 1980's it was combination CT non resecting interonen, in 1990's it was high dose therapy biphosphates and finally in 2000's novel targeted therapies. The novel drugs include Immunomodulators- Thalidomide and Lenalidomide, Proteasome inhibitors-Bortezomib, Anescic Trioxide, Famesytransfrase inhibitor, 2-methylyctrioxide, VEGF inhibitors, Histone deacetylase inhibitors. Two drug combination: Dexamethasomone +Thalidomide/Lenalidomide/ Bortezomib.Three drug combination: VTD, Dexamethasone +Thalidomide/Lenalidomide/ Pegylated doxorubicin+ Bortezomib+ Dexamethasone, Cyclophosphamide

- Four drug combination: Cyclophosphamide+ Bortezomib + Lenalidomide + Pegylated doxorubicin. Non transplant options for elderly include combinations like MPT, VMP, NMPRT, VMPRT, Rx option continued till stable disease

So, its concluded that novel therapies have significantly improved survival in MM, relapses are substantial dose limiting toxicities reduce compliance, new agents are targeting different targets and differs in toxicities, combination with existing drugs is feasible.

Autologous BMT in MM

Dr. Atul Sharma

- ASCT Procedure has the following objectives: Case selection, Central line insertion, Stem cell mobilization, Stem cell harvest, infusion Conditioning: high dose melphan 200 mg/mi. (Elderly or renal failure: 120-160 mg/m2). Post Tpx proflaxis, Engraftment, Maintenance therapy, Follow up. Remove stem cells from deep freezer, thaw to 37 degree Celcius in liquid nitrogen. Autologous SCT, AILMS diagnosis was conducted in 255 patients. The case of multiple myeloma was observed in total of 188 (65.9%) patients, lymphoma ( Hodgkin's and NHL) was observed in 46 (16%) patients, leukemia was observed in 33 (9%) patients, solid tumors was observed in 18 (7.1%) patients. The median in these patients was 52 (26-68 years). Multiple Myeloma is majorting of constituting of three step models namely, Induction therapy, Consolidation (ASCT), Maintenance therapy. ASCT associated with higher RR. Early transplant, Maintenance therapy. Options of treatments for renal failure were either MPT +, VMP +, NMPRT + or used for Thrombo-embolism. CR is a surrogate marker for overall survival, newer agents have dramatically improved CR rates and survival, Auto SCT remains the standard care in transplant eligible patients. Maintenance is indicated.

Advances in Treatment of Low Grade Lymphomas

Dr. Reena Nair

- Follicular NHL has common indolent NHL that is rising in incidence. Variable clinical course are incurable with standard therapy, multiple remissions and relapses, histological transformation and has median survival improvement. With such a long natural history to the disease and competing morbidity in older patients, it is reasonable to ask if delaying Rx as long as possible is a reasonable strategy. 316 patients with low grade histologies (65% follicular) have Stage IE IV disease. Absence of B- symptoms, No organ dysfunction. It is randomized to initial chronic oral chlorambucil or observation. Trials exists utilizing interferon- alpha after chemotherapy- because of statistically significant improvement in OS or TTP was observed. However, some trials still use it as maintenance Rx. Gaiximab induces AIDC in lymphoma cell lines. It delays progression of human NHL by 10-15 years. The geriatric assessment reveals no deficits except for diabetes that is well-controlled. The life expectancy is 10-15 years. From adjuvant on-line (Good health) 31% die because of cancer, 22% die from other causes, 7 of 100 alive because of hormonal therapy, 8 of 100 alive because of chemotherapy and 14 of 100 alive because of combined therapy.

Changing Face of Leukaemia Diagnosis

Dr. Deepak Mishra

- Classification is a language of medicine: should be described, defined and named before they can be diagnosed, treated and studied. A consensus on definitions and terminology is essential for both clinical practice and investigation. A classification should contain diseases that are clearly defined, clinically distinctive, and non-overlapping and that together comprise all known entities. Classification is of two types, biologically rational classification and clinically useful classification. Acute Leukaemia of ambiguous lineage is classified by WHO as follows: Unclassified acute leukaemia. Bilineal acute leukaemia. Biphenotypic acute leukaemia.

Most heterogeneous Gp in AML has normal karyotype by conventional methods.

Gastro esophageal cancer is the 2nd most common cancer. The incidence of GE junction are increasing while that of gastric cancer is decreasing. The incidence of gastric cancer is changing in western populations.

Dr. T. Raja
Shifting Paradigms in use of Taxane in Breast Cancer

Paclitaxel. Nab-Paclitaxel binds to the gp60-albumin receptor on the endothelial cells and shorter infusion time with no requirement of premedications when compared to conventional. Nab-Paclitaxel, albumin bound paclitaxel has a distinctive advantage of being cremophor free, the cornerstone in the management of MBC.

Dr. Bhawna Sirohi: What are the future indications?
Dr. S.H. Advani: NCCN 2011 guideline has stated clearly that Nab-Paclitaxel can be used interchangeably with Paclitaxel. Thus there is a definitive use of Nab-Paclitaxel in adjuvant and neoadjuvant setting. It is absolutely safe and there is no reason for not considering in this setting.

Dr. G.S. Bhattacharyya: Which schedule of Nab-Paclitaxel is preferred?
Dr. Bhawna Sirohi: I would start with 100 mg/m² and reach up to 130 mg/m² weekly.
Dr. Biswas: I would use 100 mg/m² weekly.
Dr. Raja: I prefer to use Nab-Paclitaxel as taxanes are the best drugs for MBC. I would closely monitor for neuropathy.
Dr. Bijwas and Dr. Ganshyam agreed on the same that Nab-Paclitaxel scores over other taxanes.

Dr. G.S. Bhattacharyya: In diabetic patients, would you consider Nab-Paclitaxel?
Dr. Raja: In diabetic patients, I would not consider taxanes, especially if there is prior history of taxane use.
Dr. Bhawna Sirohi: I would prefer to use Nab-Paclitaxel as taxanes are the best drugs for MBC. I would closely monitor for neuropathy.
Dr. Raja: I would consider using Nab-Paclitaxel but with close monitoring.

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