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EDITORIAL

"WHERE ARE WE IN ONCOLOGY - 2019"

The past year has been a year of many "firsts" for the oncology community. The field witnessed several revolutionary advances in the research and treatment of cancer. FDA approved immunotherapeutics including first CAR-T- cell immunotherapy. Comprehensive next – gen companion diagnostic test was also approved to identify the right patients for the right molecularly targeted therapeutics.

Immunotherapy While immunotherapies lead to long lasting responses for some patients, a sizable portion of patients don't respond to these agents; some patients who respond ultimately develop resistance and we still don't have precise biomarkers to predict who will respond and who will not. The same is true of targeted therapies where treatment resistance continues to be a major road block. Immunotherapy combinations are being approved. A combination of anti PD-1 and anti CTLA4 antibodies is already approved for melanomas.

Clinical studies on therapeutic vaccines including mRNA vaccines, DNA vaccines and those that involve utilizing patient's tumour to develop personalized vaccines, in combination with other immune agents are being introduced.

There are many challenges, most importantly that 80 % of the patients don't respond to immunotherapies. It has been found that tumours with high mutational load are likely to respond better to immunotherapies than those with low mutational load. The T cells only recognize certain neo antigens among the thousands of them present on the tumour cells. Can we target these good quality neo antigens is a million dollar question?.

Precision Medicine

We have all been infatuated with the idea that there may be a single magic bullet for solving the cancer problem, for instance by using targeted therapy or immunotherapy approaches, but such views are "rather simplistic." Cancer is a complex disease requiring equally complex solutions that can only be achieved by embracing an integrative and quantitative approach.

There has been significant attention on the utilization of genomic approaches to understand how to reactivate immune responses by targeting the cancer cells which evade immune system, In addition, several laboratories are developing better biomarkers to predict immunotherapy response, liquid biopsies are becoming integral to the landscape of precision oncology, artificial intelligence (AI) is being utilized in assisting physicians with identifying the right treatments for patients. The use of biology-driven models, for instance based on the underlying regulatory logic of cancer cells, can dramatically simplify our ability to extrapolate realistic conclusions, compared to unconstrained machine-learning methods.

By using AI you are essentially starting from a 'white board' where everything is possible, thus depriving yourself of the wisdom of biological knowledge. The complexity of biology requires novel paradigms for analyzing and interpreting large data sets, both from a genomic perspective and from a computational analysis perspective.

Advances in Surgery and radiotherapy

Advances in telesurgery, single port robotic surgery and transplant surgery have been made. Advances in radiation technology have focused on precision, Precision and Precision.

Addressing Cancer Prevention and Health Disparities

"We are seeing a time where there are significant gaps between social/behavioral scientists and basic/translational scientists in embracing interdisciplinary approaches to constructively address cancer disparities. There are still significant gaps in cancer screening among un-disprivileged populations. For instance, it is now widely recognized that colonoscopy can significantly reduce mortality rates from colorectal cancer, screening rates for this cancer in medically underserved communities continue to remain inadequate. Similarly, cervical cancer rates are higher within some communities because of gaps in the utilization of and access to cervical cancer vaccine, which could be improved upon, While it is well recognized that factors related to race, socioeconomic status, and environmental factors influence cancer health disparities, there is a significant dearth of information on the biology of cancer for patients from underrepresented communities, Some aspects related to under represented communities and genetic ancestry could confound some of the precision medicine approaches. We have to make sure that everybody is included in the research so that we can be more precise in our precision medicine approaches.

There is a lot of good science coming out right now and we have the right tools to follow up on these advancements to make noticeable progress.

Dr. A. K. Dewan
Director - Surgical Oncology

RELAPSED DIFFUSE LARGE B CELL LYMPHOMA & AUTOLOGOUS STEM CELL TRANSPLANT

Relapsed lymphoma refers to the recurrence of the lymphoma after patient has achieved complete remission (CR) or partial remission (PR) after front line therapy. An average of 70% of patients with B cell lymphomas of aggressive histologic types like diffuse large B cell lymphoma (DLBCL) can be cured using front line therapy with RCHOP. The remaining 30% will either be refractory to front line treatment (around 15%) or relapsed (around 15%). Primary refractory disease is defined as failure to achieve at least a PR with front line therapy. Early relapse is usually defined as relapse in the year after diagnosis or the 6 months after the end of treatment. Late relapsing patients are characterized by a better response to salvage chemotherapy along with longer Progression Free Survival (PFS) and Overall Survival (OS) than those with refractory disease or early relapse.

Since the publication of the PARMA study, which showed in relapsed NHL, at five years, the overall survival was 53% in the transplantation group and 32% in the conventional-treatment group (P = 0.038), second-line salvage therapy followed by high-dose chemotherapy and autologous stem cell transplantation (ASCT) became and continues to be the standard of care for chemo sensitive relapsed diffuse large B-cell lymphoma (DLBCL), even in the rituximab era. Early relapses are associated with the same dismal outcome as refractoriness, and thus patients should be treated as refractory lymphoma. Treatment of the relapsed lymphoma consists of 2-3 cycles of salvage chemotherapy followed by autologous transplant (ASCT) if patient is transplant eligible. Best salvage regimen for relapsed/refractory DLBCL before autologous transplant is not known. Salvage regimen consist of regimens like R-DHAP, R-ICE, R-GDP, R-MIME. In the original analysis of CORAL study, no difference in outcome was found between R-DHAP and R-ICE. However, in the retrospective analysis, which classified the patients according to the cell of origin using GEP, the 3-year PFS was 100% for ABC type DLBCL treated with R-DHAP, and the 3 year PFS for GCB-like DLBCL treated with R-ICE was 27% (p=.01). Those with ABC type DLBCL had a different outcome; the 3 year PFS rate was 60% for R-ICE and 30% for R-DHAP. If patient is not transplant eligible then patient is treated with few more cycles of same salvage regimen followed by lenalidomide maintenance. If available & affordable, BTK inhibitor like ibrutinib, anti PD-1 antibodies nivolumab or pembrolizumb can also be used.

Patient may not be transplant ineligible for various reasons. Old age though in its own is not the contraindication for transplant. If patient is fit and healthy, then autologous transplant may be offered to as old as 70 years. To predict the non relapsed mortality during transplant, HSCT-CI (hematopoietic stem cell transplant co morbidity index) has been developed. The HCT-CI is able to classify patients into three risk groups: low risk (non-relapse mortality 14% at 2-years), intermediate risk (non-relapse mortality 21% at 2-years) and high risk (non-relapse mortality 41% at 2 years).

Patient is not transplant eligible if they are completely refractory to any type of primary chemotherapy and salvage chemotherapy because transplant is likely not to be beneficial at all in this patient group. Other reason for transplant ineligibility is that the inability to harvest adequate stem cell due to poor health of patient or previous use of stem cell toxic chemotherapy. Other known prognostic factors relevant to the salvage setting include the IPI, originally intended for use with front line therapy but also effective in cases of relapsed DLBCL.

Another predictive factor linked to outcome is previous exposure to rituximab as a part of frontline therapy. In the phase III randomized CORAL trial of relapsed or refractory DLBCL, the 3 year event-free survival was significantly lower for patients with previous exposure to Rituximab compared with those who had never received Rituximab. Salvage regimens with acceptable toxicity are necessary because patients with relapse after ASCT have an impaired bone marrow reserve and other patients are elderly and frail. Therefore the search for novel, more effective, and safer salvage combinations is not only opportune but also represents an important unfulfilled need.

The curative potential of ASCT is derived from high-dose chemotherapy or chemo radiotherapy administered as transplant conditioning to enhance tumor cell kill and overcome drug resistance. For patients with relapsed or refractory DLBCL that responds to second line chemotherapy, high dose chemotherapy followed by ASCT results in superior survival rates than chemotherapy alone. Patients with chemotherapy-sensitive relapse, or who have or who have chemotherapy –sensitive disease but have never achieved complete remission have a 30-60% probability of disease free survival at three to five years. In comparisons, patients with DLBCL resistant to second-line chemotherapy have a DFS of < 1 year.

There is not yet ideal conditioning regimen for autologous transplant. Examples of conditioning regimen include - BEAM, LACE, Cy/TBI, Bu/Cy/VP, BEP, CBV, CyVP TBI. Because of the concerns of myelodysplasia and secondary leukemia, most transplant centers and groups have moved away from TBI-containing approaches and have concentrated on chemotherapy-based regimens.

Infections although minimal remain a concern during per transplant period. It is furthermore complicated by co morbidities, mucositis, decreased immunity of the patient. In era of multidrug resistant bugs, a need of calculated approach to infections is the need of hour.

Patients tolerate these regimens quite well and engraftment is prompt and similar among these combinations. Different studies have quoted ASCT resulting in complete remissions in the 60–85% range while at 2–5 years after ASCT have resulted in 34–60% DFS & 26–46% OS rates. These drug regimens differ in the potential toxicity with a treatment-related mortality ranging from 3.8 to 17%.

Patients who undergo autologous SCT should be followed longitudinally for relapse and treatment related toxicities. Most relapses occur during the first two years post-HCT and non-relapse mortality surpasses relapse as the main cause of death beginning approximately eight years post ASCT.

In our institute we have been doing autologous stem cell transplant for relapsed lymphoma with comparable outcomes. Totally, we have done 85 autologous stem cell transplant for relapsed lymphoma patients since 2012. The estimated 3-year EFS for patients who were transplanted in CR1 and >CR1 were 76% and 57% respectively (pvalue=0.736). While the estimated 3-year OS for patients who were transplanted in CR1 (82.6%) was found to be greater than those transplanted in >Cr1.

We highly recommend high dose therapy followed by autologous stem cell transplant for every eligible patient as it may lead to potential cure of the disease.

Dr. Rayaz Ahmed, Head – Myeloma & Lymphoma Unit

BREAST CANCER IN INDIA : IS IT DIFFERENT FROM THE WEST ?

Breast cancer is the most common cancer in women in India and accounts for 14% of all cancers in women. As per GLOBOCON data, this year new breast cancers registered in India are 1, 62,468 and Deaths are 87,090. The incidence rates in India begin to rise in the early thirties and peak at ages 50-64 years. In urban areas, 1 in 22 women is likely to develop breast cancer during her lifetime as compared to rural areas where 1 in 60 women develops breast cancer in her lifetime. For every 2 women newly diagnosed with breast cancer, one woman dies of it in India.

Breast cancer is a global disease. Though the majority of the features are usually uniform around the world, every region has its own uniqueness for that cancer and for India few of these are increasing incidence of BC in younger age groups, late presentation, lack of awareness and screening, aggressive cancers in young.

Breast cancer is the major cause of morbidity and mortality among females ranking number one among females in Indian metropolitan cities whereas in rural areas it still hold a second position. Epidemiology of breast cancer across different registries in India shows increasing trends for incidence and mortality mainly due to rapid urbanization, industrialization, population growth and ageing affecting almost all parts of India. Factors as marital status, location (urban / rural), BMI, breast feeding, waist to hip ratio, low parity, obesity, alcohol consumption, tobacco chewing, smoking, lack of exercise, diet, environmental factors were major risk factors in India leading to increasing incidence of cancer, however, the reason for high incidence of breast cancer in younger women are not well known. Delayed disease presentation due to illiteracy, lack of awareness, financial constrains in some regions of India leads to late diagnosis, which in turn increases mortality rate. Lack of organized breast cancer screening program, paucity of diagnostic aids, and general indifference toward the health of females in the predominantly patriarchal Indian society are also the drawbacks leading to increased breast cancer incidence. Hence majority of patients here are still treated at locally advanced and metastatic stages.

A multidisciplinary approach to breast cancer including awareness programs, preventive measure, screening programs for early detection and availability of treatment facilities are vital for reducing both incidence and mortality of breast cancer in Indian women. The cancer projection data shows that the number of cases will become almost double by 2020. The projections of cancer incidence shows an urgent need for strengthening and augmenting the existing diagnostic and treatment facilities, which is inadequate and unable to handle the current load of cancer in India.

Dr. Kumardeep Dutta Choudhury
Consultant – Medical Oncology

DELHI ISSP CHAPTER CLINICAL MEETING

RGCIRC organized a clinical meeting in association with Indian Society for the Study of Pain (ISSP) Delhi Chapter on Saturday, 24th November 2018 at India habitat Centre, Lodhi Road, New Delhi. Dr. Virender K. Mohan, AIIMS, Delhi delivered a lecture on **Percutaneous Microballoon Compression for Trigeminal Neuralgia: A Rare Vascular Complication** and Dr. Naresh Dua, SGRH, Delhi spoke on **Oral Transmucosal Fentanyl Citrate for breakthrough Cancer Pain in Home Care Setting: Our Experience.** This meeting also had a panel discussion on **Treatment of Lymphoedema in Ca Breast** which was moderated by Dr. Sunny Malik, Consultant - Interventional Pain Management. The panelists of this discussion were Dr. Swarupa Mitra, Sr. Consultant – Radiation Oncology, Dr. Malvinder Singh Sahi, Head – Pain Management, Dr. Leena Dadhwal, Consultant - Surgical Oncology and Dr. Sajjan Rajpurohit, Consultant - Medical Oncology. The meeting was very well appreciated by the gathering.

ACADEMIA 2018

RGCIRC participated in ACADEMIA 2018, organized by IMA East Delhi Branch and West Ghaziabad on Sunday, 25th November 2018 at Hotel Leela Ambience Convention Centre, Shahdara, Delhi. Dr. L. M. Darlong, Sr. Consultant and Chief of Thoracic Surgical Oncology delivered a lecture on **Surgery in Lung Cancer**, Dr. Sajjan Rajpurohit, Consultant – Medical Oncology spoke on **Newer Therapies in Cancer** and Dr. Amitabh Singh, Consultant – Surgical Oncology spoke on **Robot Assisted Partial Nephrectomy in Complex Renal Tumor** in the said conference.

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CME – IMA ALWAR

RGCIRC organized a CME in association with IMA Alwar on Saturday, 1st December 2018 at Govt. Hospital, IMA Bhawan, Alwar, Rajasthan. Dr. Swarupa Mitra, Chief & Sr. Consultant – Gynecological and Genitourinary Radiation Oncology delivered a lecture on **Newer Techniques in Radiotherapy of Breast Cancer** and Dr. Kumardeep Dutta Chaudhary, Consultant – Medical Oncology spoke on **Approaches and Recent Updates in Breast Cancer** in the said CME.

CONGRATULATIONS TO DR. VINEET TALWAR

Times Healthcare Achievers Delhi NCR 2018 made yet another splash in the healthcare ecosystem of Delhi NCR by felicitating medical practitioners and institutes under various categories like; lifetime Achievement of the Year, the Legends of the Year and the Rising Star of the Year. This year TOI felicitated Dr. Vineet Talwar, Director – Medical Oncology from Legends of the Year for his remarkable contribution in the field of oncology.

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