Dr. Shilin N. Shukla Medical Oncology Oration Award - 2024

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The Progress in Oncology Along with My Journey Over Three Decades

There are path breaking collateral developments in all fields of oncology, including medical oncology. The data for adults aged 15 to 99 years indicate that the median survival time of the cancer patients has been constantly improving since 1990 (Figure 1).

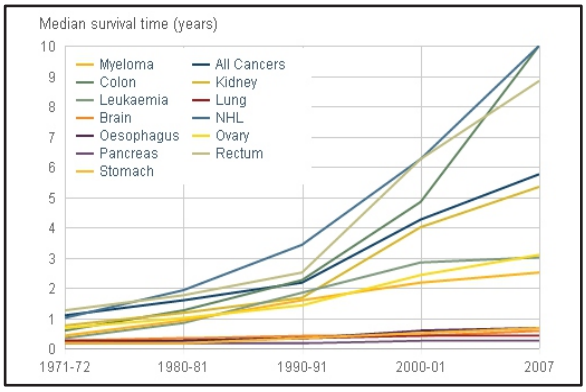

Figure 1: Cancer survival rates in adults aged 15-99 years

The survival rates of the patients with one of the deadliest cancers- Cervical cancer has also been observed to improve based on 11 population based cancer registries (PBCRs) (Figure 2). Such an increase in the overall survival rates of cancer patients since 1990s, was possibly due to development of cancer therapeutic drugs containing new molecular entities (NMEs). Few of the examples include drugs like Cyclophosphamide, Methotrexate, 5 Fluorouracil (5FU), Doxorubicin, Cisplatin, Etoposide, Vincristine/Vinblastine, L-asparaginase, Cytarabine, Procarbazine, Ifosfamide, Mitomycin C, Bleomycin, etc.

The landmark developments in the field of Medical Oncology over last three decades include: fewer cytotoxics, more of TKIs, more of biologicals, immunotherapy, targeted therapies, better imaging and diagnostics, better clinical guidelines, better research methodology, ICH guidelines, better clinical

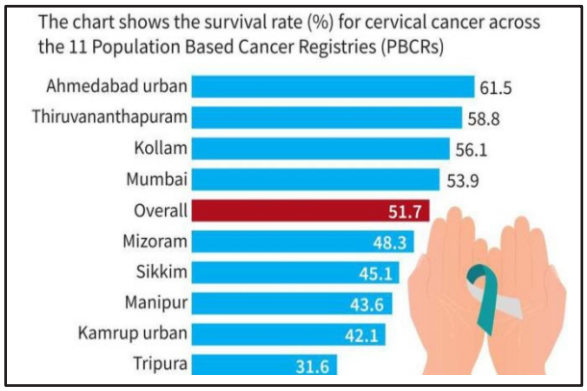

Figure 2: Survival rate (%) for cervical cancer across population based cancer registries

infrastructure, better research infrastructure, better regulatory framework, altogether better science and better translational research leading to better patient outcome.

When I was with GCRI, in early 90s – targeted therapies and MAbs were like fairy tales or SciFi movies. At that time, IACC was renamed to ISMPO during a conference in Ahmedabad, IJKPOC was inaugurated in 1993 and UICC meeting was held in New Delhi. By the end of 90s, Rituximab and Trastuzumab were available and DRL-301 trial was initiated at GCRI. It was my first exposure to clinical trial (sponsored trials) and exposure to Quintiles (now IQVIA). IQVIA is the result of the 2016 merger of Quintiles, a leading global contract research organization, and IMS Health (Intercontinental Marketing Statistics Health), a leading healthcare data and analytics provider. IQVIA is an American multinational company serving the combined industries of health information technology and clinical research. It is a provider of biopharmaceutical development, professional consulting and commercial outsourcing services, focused primarily on Phase I-IV clinical trials and associated laboratory and analytical services, including investment strategy and management consulting services.

With Quintiles, new modalities like monoclonal antibodies (Mabs), Tyrosine kinase inhibitors (TKIs), Photodynamic and many other therapies were established. Temoporfin and Tipifarnib are best examples of this development. Temoporfin is a photosensitizer used in photodynamic therapy for the treatment of squamous cell carcinoma of the head and neck. Tipifarnib is a farnesyltransferase inhibitor. Farnesyltransferase inhibitors block the activity of the farnesyltransferase enzyme which ultimately prevents Ras from binding to the membrane, rendering it inactive. Its efficacy was investigated in patients with HRAS mutant head and neck cancer, peripheral T-cell lymphoma (PTCL), myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML), certain stages of breast cancer and multiple myeloma.

Later on from 1999 to 2006, many more drugs like Imatinib, Erlotinib, Gefitinib and Bevacizumab were approved and the guidelines for many cancers were also streamlined. The development of Imatinib led to the initiation of the magic bullet – GIPAP (Glivec International Patient Assistance Program) which was a unique direct-to-patient program that provided imatinib (Glivec) at no cost to eligible patients in low- and middle-income countries (LMICs) with chronic myelogenous leukemia (CML) or gastrointestinal stromal tumor (GIST). It changed the treatment landscape of these cancers and opened up the avenues for a new area of research in direction of various TKIs like Dasatinib and Nilotinib that followed imatinib. Since 2002 bevacizumab indications expanded from colon to include lung, breast, ovaries, glioblastoma, renal cell cancer. EGFR- Epithelial Growth Factor Receptor was identified and initial EGFR TKIs were Gefitinib and erlotinib, followed by afatinib and dacomitinib and then Osimertinib. PPARγ agonist efatutazone and gefitinib synergistically inhibit the proliferation of EGFR-TKI-resistant lung adenocarcinoma cells. Clincal trials for new TKIs for Dacomitinib, Nintedanib, Vandetinib for NSCLC and afatinib in breast cancer and head and neck cancer were undertaken. The clinical trial for studying the efficacy and safety of Ambraxane (combination of the chemotherapy drug paclitaxel with a protein called albumin) injection formulation for nanodispersion (PICN) in subjects with metastatic breast cancer patients was commenced. Meanwhile, antiemetics, GCSF/PEG-GCSF and bone targeted therapies were familiarized as supportive care to better manage the post chemotherapy effects like pain and oral mucositis.

Unique efficacy/response pattern was identified for immunotherapies like CTLA 4 Blocker-Ipilimumab. Ipilimumab was the first drug to achieve a significant improvement in survival of advanced stage melanoma. This was soon followed by a large number of PD1/PD-L1 blockers Nivo/Pembro/Durva/Avelumab/Atezolizumab. Moreover, first-line maintenance avelumab immunotherapy in patients with metastatic urothelial carcinoma resulted in significantly longer overall survival than best supportive care alone. Further, many multicentric experimental studies for efficacy of targeted therapies like Palbociclib, Enzalutamide and Eribulin in Indian population are still underway and yet to be published.