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Conference Review

4th molecular oncology conference (MOSCON): Untangling the genetic code

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With the advent of innumerable molecular markers in different malignancies, the role of precision oncology has gained immense importance in the past 5 years. The role of oncophysiologists is no more confined to administration of chemotherapies. We need to broaden the spectrum of molecular oncology which encompasses newer methodologies to the diagnosis, treatment with targeted agents and also improves the overall survival of the patients. To enlighten ourselves, to this most complex subdivision of modern oncology, this year the 4th MOSCON was conducted at Gurugram (DELHI NCR) on February 16 and 17. The meeting brought forward accomplished oncologists and various molecular diagnostic companies from all over the country on a single platform to have brainstorming sessions, debates, and discussions. As the organizing secretary, the initiative to propel this movement would not have been possible without the guidance, blessings of my great teachers.

The conference started with the first session on basics of next-generation sequencing (NGS). The first lecture was delivered by Dr. Anuradha Choughule from TMH, Mumbai. She brought into light the essence of an ideal NGS report and its implications. Dr. Amit Verma discussed the role of liquid biopsy as a diagnostic, prognostic, and predictive tool. He also discussed the role of circulating tumor DNA in breast, lung, and colon cancer in monitoring signs of the early relapse and to study the emergence of genomic events associated with therapeutic resistance to therapy. The session concluded with an interesting debate where representatives from both Thermo Fisher and Illumina discussed the pros and cons of their technology. The debate was concluded by Dr. Anurag Mehta from Rajiv Gandhi Cancer Institute (RGCI) where he pointed that ION TORRENT platform is known for its speed and consumer flexibility in usage, and on the other hand, Illumina is known for its high penetrance and gene coverage which gives answer to many research-based questions.

The brainstorming session on lung cancer heralded with the upcoming role of adjuvant tyrosine-kinase inhibitor (TKI) in Stage 3 lung cancer. It was opined by the speaker that adjuvant ERLOTINIB improved disease-free survival (DFS), i.e., 2 years DFS of 88% in patients with resected epidermal growth factor receptor (EGFR) mutant non-small cell lung cancer (NSCLC) giving the account of PHASE II SELECT trial. In an enthralling debate between Dr. Ullas Batra (Med Onc) and Dr. Anusheel Munshi (Rad Onc) on whether upfront TKI or SBRT/WBRT to be used in oncogene-addicted adenocarcinoma lung with brain metastasis, house was split into multiple opinions. The debate was concluded by expert Dr. Kumar Prabhaskar that while stereotactic radiosurgery remains an excellent option for solitary metastasis, there remains no need to treat asymptomatic patients with brain metastasis with radiotherapy. Furthermore, radiotherapy

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failed to improve overall survival in TKI naïve EGFR-mutant NSCLC patients with brain metastasis.

For head and neck cancers, the emerging role of human papillomavirus (HPV) in molecular staging was briefed in a crisp manner. It was brought to the knowledge that T staging in HPV-positive oropharyngeal cancer (OPC); now, no more includes T4a/4b and clinical N classification in HPV-positive OPC; now, no more give importance of number of nodes or extranodal extension. Lesser known mutations and targeted therapies in thyroid cancers were also brought in limelight. Various biomarkers were discussed and the take-home message was that BRAFv600E, RAS, NTRK, and PTEN can have a predictive role for some of the target-driven approaches in the future for this uncommon disease.

Post lunch session on breast cancer showered the house with recent advancements in the management of breast cancer. Emerging role of P13K inhibitors in advanced breast cancer was propounded by the speaker opening that ALPELISIB is the first-line P13K inhibitor which significantly prolonged the progression-free survival when added with fulvestrant and is a potential new treatment option for patients with P1K3CA mutant, hormone receptor-positive, and Her2Neu-negative advanced breast cancer who have progressed on prior endocrine therapy (with/without a cyclin-dependent kinase 4/6 inhibitor). Dr. Shona Nag discussed about tumor-infiltrating lymphocytes as a reliable and reproducible biomarker for early breast cancer, especially Her2-positive and triple-negative breast cancer.

In yet another brain throttling session by the esteemed Dr. Rakesh Jalali, the house experienced a journey from the age-old techniques in the diagnosis of brain gliomas to the newer developments in the form of various molecular markers such as 1p19 codeletion, isocitrate dehydrogenase (IDH) mutations, ATRX mutation, and their role in management of gliomas. It was propounded that IDH wild-type (negative) and 1p19q non-deleted low-/lower-grade gliomas showed aggressive behavior. It was a learning for all how molecular tumor markers such as BRAF mutation (V600E), IDH, and histone H3K27 when tested in a systematic manner can help in reaching not only to the diagnosis but also in deciding the line of treatment.

There was a special experience sharing session of molecular diagnostics of hereditary breast and ovarian cancer and related syndromes. Various academic institutes and commercial laboratories such as RGCI Delhi, Tata Memorial Hospital Mumbai, Army Hospital Delhi, Amrita Institute Kochi, Core Diagnostics Delhi and Centogene Labs participated in this session.

Gynecological cancers also had their own spotlight and were not untouched by the immune therapeutics. Discussion on endometrial cancer by Dr. Satinder Kaur suggested that

adjuvant treatment for endometrial cancer is still a dilemma; however, integrated molecular classification and testing the tumors for POLE-1, microsatellite instability-high (MSI-H) along with histological factors might help in future. Panel discussion on immunotherapy in ovarian cancer was informative. It was gathered that subtype of ovarian cancer has a role in deciding benefit from immunotherapy stating example of the addition of bevacizumab maintenance in proliferative subtype of ovarian cancer in which there was significant overall survival. Advanced NGS assays have brought a ray of hope in targeted therapies in ovarian cancers. There is an established role of PARPi other than olaparib such as niraparib maintenance in platinum-sensitive ovarian cancer as per Phase III NOVA and rucaparib in relapsed, platinum-sensitive high-grade ovarian carcinoma.

The conference was officially inaugurated in the evening and the occasion was graced by Guest of honor Dr. D.C Doval and Dr. Shyam Aggarwal along with the organizing chairperson Dr. Purvish Parikh. Molecular oncology society also officially relaunched its journal International Journal of Molecular and Immuno oncology which will be published from this year under the banner of Scientific Scholar. The journal aims to provide a platform for highlighting novel and relevant research on molecular and immune-oncology from India.

Day 2 of the conference (Sunday, February 17) started with a session on significance of medicolegal aspects of genetic testing, physician-patient communication of personalized therapy and current status of clinical trials in India by Dr. Purvish Parikh and Dr. Vamshi Krishna. Dr. Govind Babu enlightened the house about CAN script as an upcoming phenotypic platform which has 90% correlation in predicting patient response to cancer therapy. It was received by the house as a tool which helps in evolving care from “PRECISION” to “INDIVIDUALIZED” and a validated platform that will definitely improve the clinical outcome.

Hematolymphoid malignancies were not unappalled by the aura of immune therapeutics. The need of assessment of Minimal Residual Disease in Multiple Myeloma by three different techniques was discussed. Multiparameter flow cytometry, polymerase chain reaction and NGS. Dr. Hemant Malhotra prophesied that chronic lymphocytic leukemia should be tested for FISH (del 17, 11, and 13), DNA sequencing (TP53 and IGVH mutation), flow (CD38, ZAP-70, and CD49d), and cytogenetics for complex karyotype.

The session on variant of uncertain significance detection in hereditary cancer syndromes and its clinical significance was being discussed with utmost precision by Dr. G S Bhattacharyya who gave a refined judgment that variant of unknown significance implies clinical uncertainty, and henceforth, it should not be used in clinical decision-making; rather, efforts should be made to resolve the

classification of the variant as pathogenic or benign. The fragile topic of genetic counseling to provide the family with complete and accurate information about the genetic disorders was also touched on. Panel discussion moderated by Dr. Rajiv Sarin highlighted the need of genetic testing wherever the suspicion of hereditary syndrome arises. He cited examples of MLH-1 mutation in Lynch syndrome, novel mutations, and phenotypic associations in familial adenomatous polyposis such as of APC/MUTYH/NTHL1/POLD1, POLE genes, and STK11 variants and breast cancer in Peutz–Jeghers syndrome.

Gastrointestinal cancers had their own sweet share where management of MSI-H colorectal cancers (CRCs) was presented by Dr. Amit Rauthan. It was propounded that identification of MSI-H or dMMR CRC is important. In yet another enriching discussion on microbiome and immunotherapy, Dr. Vamshi lauded the house with various microbial floras and their active role in anticancer therapy. One such study observed *Bacteroidales* in the immune stimulatory effects of cytotoxic T-lymphocyte antigen -4 blockade and Clostridiales in malignant melanoma with anti-PD 1 therapy. However, it still remains a dilemma whether altering microbioflora will change responses to immunotherapy or not?

To end the meeting, an enthralling discussion was awaited on MSI/tumor mutation burden (TMB) and

immunotherapy headed by Dr. Prashant Mehta. He enlisted approved checkpoint inhibitors such as pembrolizumab for all unresectable or metastatic MSI-H or MMR-deficient solid tumors that have progressed on standard lines of therapy, for MSI-H or MMR-deficient CRC progressed on fluoropyrimidine, oxaliplatin, and irinotecan and for metastatic programmed death-ligand 1 gastric or gastroesophageal junction adenocarcinoma. Role of TMB in immunotherapy was highlighted with an observation where Nivolumab + Ipilimumab was introduced in the first-line NSCLC with TMB > 10 mut/Mb.

The conference ended with prize distribution by Dr. Hemant Malhotra and Dr. GS Bhattacharya to the poster presenters and also announcement was made for the 5th MOSCON. Last but not the least, the 4th MOSCON was an initiative to inculcate, practice, enlighten, and learn about various molecular markers with targeted immunotherapies in different clinical scenarios. There was difference of opinions but to cultivate healthy and correct learning, both sides of the coins have to be seen and with this message, I hope our endeavors have been fruitful to all the participants, faculty, delegates, and students.

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