

Commentary on 19th annual scientific meeting of the Society for Neuro-Oncology

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A B S T R A C T

The Society for Neuro-Oncology (SNO) is the premier organization dedicated to the cause of central nervous system (CNS) tumors. Although it is primarily located in North America, it attracts considerable memberships from all over the world with truly multi-disciplinary representations from not only neuro-oncology, neurosurgery, radiation oncology, medical oncology and basic scientists, but also in recent years from imaging, psychology, epidemiology, public health and industry, etc. SNO annual meetings are very much looked forward to with presentations of the latest cutting edge data as well as several educational sessions for trainees and updates for senior members too. The meeting is unique in the way that almost the entire scientific agenda is based on submitted abstracts with very few invited lectures.

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The 19th annual meeting held in Miami from November 13, 2014 to November 16, 2014 attracted participation of more than 1500 members from all around the globe. The 1st day of the meeting, traditionally the education day, focused on CNS metastasis with several talks on neurobiology of cognitive dysfunction, targeting the microenvironment and special talks were pertaining to CNS metastasis from breast and lung cancers. Importance of hippocampal

sparing from medical and radiation aspects with a view to preserve neuro cognition was well highlighted. Talks on neurological and neuropsychological complications of metastatic disease and cancer therapies were very comprehensive and reinforced the need to do more work in these areas. A parallel quality of life (QoL) break-out session on the education day raised the need to promote research in brain tumor survivorship, as well as panel discussions on caregiver advocacy. The main conference over 3 days, as per traditional format, comprised of very well attended sunrise sessions covering diverse topics ranging from molecular pathology, 5-aminolevulinic acid (5 ALA) guided surgery, targeted therapy updates, epilepsy management, The Cancer Genome Atlas (TCGA) update, neuro-imaging, stem cell biology and vaccine therapy etc.

The plenary sessions at SNO meetings highlight latest results from key clinical and basic science research. In this conference on 1st day, Martin van Bent presenting the data on the final analysis of randomized phase II BELOB Trial; (130 patients) of bevacizumab plus lomustine versus lomustine alone in recurrent glioblastoma (GBM) trial (joint winner of SNO Adult Clinical Research Award) showed to some surprise no difference in the overall survival between the two arms, indicating single agent lomustine to be as effective as bevacizumab as well.^[1] Most of the discussions including in the later talks, agreed to omit vincristine in the commonly employed procarbazine, lomustine, and vincristine (PCV) regimen (making PC or even CCNU alone) to be the favored modality in recurrent gliomas (including oligodendroglial tumors).^[2] The much awaited RT 9802 trial, which had been presented earlier in American Society of Clinical Oncology

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(ASCO) as well, was presented in much greater detail and was adjudged joint “adult clinical research awardee” of the meeting. This randomized trial has, for the first time shown the benefit of adding chemotherapy (PCV) along with focal radiation (RT) to result in significantly improved overall survival as compared to radiation alone, in ‘high-risk’ low grade gliomas (age more than 40 years and/or incomplete resection). The most interesting feature of the data revealed the survival curves separating only after several (beyond 3-4 years) of follow up in favor of chemotherapy + RT versus RT arm alone, in contrast to earlier reported experience of no difference in overall survival at a shorter follow-up (Shaw *et al.* JCO 2012).^[3] Median survival times (RT versus RT + PCV) overall, oligodendrogliomas, oligoastrocytomas and astrocytomas respectively, were 7.8 versus 13.3 ($P = 0.002$); 10.8 versus not reached ($P = 0.008$); 5.9 versus 11.4 ($P = 0.05$); and 4.4 versus 7.7 ($P = 0.31$) years. Benefit of chemotherapy expectedly was especially more pronounced in patients with favorable molecular group (isocitrate dehydrogenase 1 [IDH 1] mutation, methylguanine-DNA methyltransferase (MGMT) methylation and 1p, 19q co-deletion). The data are potentially practice changing and had put chemotherapy very much an important part of management guidelines in aggressive low grade gliomas. There was a fair bit of debate as to the choice of chemotherapy and while the purists claiming the available evidence is for PCV but practically, a majority of the people do use temozolomide in view of its ease and favorable toxicity profile than PCV. Dr. Verhaak (lead author of TCGA glioma papers) presented a very comprehensive genomic characterization of lower grade gliomas demonstrating the importance of IDH 1 again as the most important marker.^[4] The work won the “adult basic research award” and sensitized the practicing community of incorporating this marker in routine practice. Data on dendritic cell vaccine in recurrent GBM (Wen *et al.*) and lapatinib in ependymomas (Gilbert *et al.*) generated a fair degree of enthusiasm with a promise to launch suitable phase III randomized trials.^[5,6]

Several platform presentations tried to put together molecular subtype data in a variety of brain tumors including pro-neural GBM molecular subtype responding best in the bevacizumab trials (AVAGlio), RELA gene fusion in ependymomas etc. Pediatric tumor biology and preclinical modeling session show-cased the excellent evolving data of robust molecular sub typing of medulloblastomas, including several potential targets in Sonic-hedgehog subtype, but also in other tumors such as mTOR/Akt signaling inhibitors in DIPG and high-grade gliomas. The pediatric clinical trials plenary session included a wonderful update by Amar Gajjar of major clinical trials and future directions incorporating molecular information in designing trials in medulloblastomas and ependymomas with perhaps among the few tumor types having such a significant

impact in management in any solid cancers. An interesting study from Canada showed the importance of exercise in hippocampal regeneration with a view to preserve cognition. Jalali *et al.*^[7] from TMH, Mumbai presented their randomized trial of focal conformal radiotherapy resulting in significantly better neuro-cognition and QoL when compared to conventional radiotherapy in 200 young patients followed up meticulously for several years. This trial running over a decade demonstrates perhaps for the first time the superiority of high-precision modern radiotherapy generating class 1 evidence and was felicitated with SNO ‘Award for Excellence in Pediatric Clinical Research’.

The outstanding show-stealer of the entire conference was, however, the outstanding data presented by Roger Stupp on behalf of his collaborators of the innovative EF-14 trial.^[8] This was a late breaking abstract and based on an interim analysis, which had been just approved by an independent data safety and monitoring committee. The trial aimed to evaluate the efficacy of a novel treatment modality of alternating electric current (treatment treating fields [TTF], novocure) device worn by the patients 24 h a day till the progression. In a prospective study of newly diagnosed patients with GBM, patients were randomized to receive either TTF device after initial surgical debulking and standard adjuvant therapy (RT plus concurrent and adjuvant temozolomide) versus radiation plus temozolomide alone, randomization being in 2:1 manner in favor of TTF arm. The 2 years survival rate in the experimental arm (RT + Temozolomide (TMZ) + TTF) was shown to be 43%, TCGA, which was significantly better than 29% in patients treated with standard RT + TMZ arm (identical to the landmark Stupp’s original EORTC/NCIC 2005 Trial). Patients treated with TTF together with temozolomide demonstrated a significant increase in overall survival compared to temozolomide alone (median overall survival of 19.6 months compared to 16.6 months, respectively, hazard ratio = 0.75, $P = 0.034$). The data caused an incredible amount of excitement within the audience and even after a fair bit of discussions about the various aspects of the trial, the data appeared genuine and indeed potentially path breaking. The study even at an interim results based on 315 patients, was hailed as the next major step in GBM treatment (after introduction of TMZ a decade ago) and may well represent as the new standard of care. The concept of TTF itself was termed “revolutionary” and Dr. Stupp’s final slide was that “A new cancer therapy has been born.” As soon as the this talk got over, there was a buzz in the media (including NYT) and a clamor to know more about this technique, since not only it is an antithesis to currently in vogue very personalized form of research pursuits, it has a very exciting potential in other nonmetastatic challenging cancers including other brain

tumors, pancreatic cancers, sarcomas and lung cancer etc. Efforts to get the technique to our country (although exorbitantly expensive at the moment) are ongoing.

The meeting also spent a considerable time on novel emerging therapies, most notably the encouraging interest in immunotherapy and vaccines in a range of gliomas as also detailed discussions on evolving role of biological imaging (2HG during MR spectroscopy as a imaging biomarker for IDH), amino acid PET scan etc. Some interesting nuggets including palliative care survey in neuro-oncology (with Indian data as well), latest WHO neuropathology updates and epidemiological data, etc., made the conference even more worthwhile to attend. The 2015 annual SNO meeting is going to be held in November in San Antonio with a distinct likelihood of a dedicated 90 min session on neuro-oncology research and status under the leadership of the Indian Society of Neuro Oncology in India.

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| Important Meeting dates in 2014-2015 | | |
|---|------------|----------------------------|
| Meeting | Venue | Contact |
| 32nd ICON Conference 13th-15th Mar 2015 | Patna | 32ndicon@gmail.com |
| Best of ASCO India 26th-28th Jun 2015 | Panjim | indiabestofasco@gmail.com |
| 33rd ICON Conference 5th-7th Sep 2015 | Coimbatore | bharath37@gmail.com |
| Joint ISMPO – ISO Congress 5th-8th Nov 2015 | Mumbai | dr_jyotibajpai@yahoo.co.in |
| Brinker awardee meeting on breast cancer 14th Nov 2015 | Bengaluru | bhawna.sirohi13@gmail.com |