LETTER TO THE EDITOR

Comment on: The UK Experience of a Treatment Strategy for Pediatric Metastatic Medulloblastoma Comprising Intensive Induction Chemotherapy, Hyperfractionated Accelerated Radiotherapy, and Response Directed High-Dose Myeloablative Chemotherapy or Maintenance Chemotherapy (Milan Strategy)

To the Editor: We read with both interest and concern the paper by Vivekanandan published in this journal.[1] While the lower results for metastatic medulloblastoma compared to those originally reported by Gandola [2] were already known,[3] we were quite disappointed by some comments on our experience, and the lack of important, internationally recently shared aspects.

First, it is questionable to gather such data just on the basis of questionnaires (underlying that the report does not concern a clinically controlled protocol), not monitoring clue aspects, such as radiation dosimetry and treatment delivery. This might also explain the authors’ impossibility to discriminate among the reasons of observed toxicities, that is tumor, surgery, or adjuvant treatment effects. They also do not describe if they could administer reduced craniospinal irradiation (CSI) doses (31.2 Gy, originally designed to lower long-term toxicity [2]).

Moreover, the authors allude to selection biases of patients as a potential explanation for better—we add durable results having nowadays 10 years overall survival/event-free survival (OS/EFS) of 64%/67%.[4] Milano center has always been regarded as a national referral, and it is likely that the most complex cases come to our attention. The success of guidelines is not comparable to a Good Clinical Practice protocol focused on the quality of treatment delivery, especially in the context of high-risk diseases when radiotherapy and chemotherapy are applied at the limits of their optimal therapeutic ratio. The authors themselves admit a lack of compliance to treatment schedule as far as times and dosages in many cases. (There are however partially published experiences by some Italian colleagues with a 2-years EFS of 75.6%, therefore very close to the original report [5]).

The paper surprisingly ends by describing unexpected toxicities retrieved by another series of patients with supratentorial primitive neuroectodermal tumors (PNET) receiving the same therapeutic approach inspired by our previous publications.[6,7] One concern lies on the fact that the authors regard as “unexpected” certain toxic effects by using such an intensive treatment, while we and others had already clearly published toxicity data.[8–10] They also omit to discuss the results of an ad hoc meeting held in November 2014 in Milano. On that occasion, the direct review of radiotherapy plans of most children with recorded toxicities in three different series receiving a Hyperfractionated Accelerated Radiotherapy (HART) approach revealed that, while global neurotoxicity occurred in around 5% of children (always younger than 10 years) receiving high-dose thiothepa after HART, without any correlation with radiotherapy technique and dosimetry, myelitis seemed to associate with the erroneous overlapping of upper cervical spine within posterior fossa boost volumes.[11] A careful planning of craniospinal irradiation and posterior fossa boost together, within an accurate quality assurance procedure, is mandatory to avoid such hotspots in the cord with consequent unacceptable toxicity. The conclusions, that would have deserved being mentioned in the paper (most of the authors were present), was that the joint international discussion and face-to-face confrontation of European radiation oncologists and physicists allowed highlighting important clinical and radiotherapy-linked risk factors. Sharing experiences internationally is paramount in assuring quality of radiotherapy in future European studies as we wish for our kids.

Maura Massimino, MD*, Filippo Spreafico, MD
Pediatrics Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy
Emanuele Pignoli, PhD
Physics Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy
Lorenza Gandola, MD
Pediatric Radiotherapy Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy

REFERENCES


© 2016 Wiley Periodicals, Inc.
DOI 10.1002/pbc.25901
Published online 14 January 2016 in Wiley Online Library (wileyonlinelibrary.com).

Conflict of Interest: Nothing to declare.

*Correspondence to: Maura Massimino, Pediatric Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Via Venezian, 1 20133 Milano, Italy. E-mail: maura.massimino@istitutotumori.mi.it
Received 14 December 2015; Accepted 15 December 2015


