Important Principles in Ewing Sarcoma Treatment

In this issue of Pediatric Blood Cancer, Raciborska et al. described their success in implementing complex protocol-based treatment of children under 18 years of age with newly diagnosed Ewing Sarcoma, in Poland, a country with limited health care resources [1]. The authors reviewed the development of a pilot consortium of seven treatment sites; developed regional guidelines based on published EURO-Ewing 99 experience [2] and implemented the centralization of surgical care during the period between 2000 and 2009. They concluded that through national collaborative groups, the coordination and optimization of limited resources are keys to the successful dissemination of complex cancer protocols worldwide.

According to the World Bank, Poland ranks as a high-income country with a population of 38.5 million people and a gross domestic product of $517.5 billion [3]. In a report describing the outcomes for childhood cancer between 2000 and 2007, Poland reported worse outcomes compared to other European countries [4]. However, Poland had only partial representation of its population because of a limited cancer registry and reported the best overall survival within the eastern European category [4]. Furthermore two important attributes were identified: the development of a Polish National Cancer Plan, and the national Polish Society of Pediatric Hematology/Oncology efforts to implement European standards of care for children with cancer. Importantly since the time period overlapped with the current report by Raciborska et al., Ewing sarcoma was recognized as one of several tumors where no improved outcome was noted within the EUROCARE-5 data [4].

In the most recent Children's Oncology Group (COG) non-metastatic Ewing sarcoma study (2001–2005), patients who received the experimental arm of interval compressed chemotherapy experienced a 73% five-year event free survival [5]. This was statistically significantly better than the 65% 5-year EFS for patients who received standard therapy [5]. The results for the non-metastatic Ewing sarcoma patient treated on the EURO-Ewing 99 study have not yet been reported in peer-reviewed literature, so published comparisons are not available, although the 68% estimated five-year overall survival for localized patients, reported by Raciborska et al., is similar to prior international experience [6].

Raciborska et al. emphasized the importance of surgical expertise. Fifty-three percent of patients had local control by surgery alone, and a further 11 patients underwent thoracotomy and metastectomy. While there are abundant data emphasizing the importance of adequate resection in Ewing sarcoma [7], the importance of surgical control of pulmonary metastases is less well defined [8,9] and is not universally implemented. However, centralizing surgery is consistent with recommendations from the ESMO clinical practice guidelines in their emphasis on referral to a specialized bone sarcoma treatment center for such patients [10]. Twenty-six percent of patients achieved local control by a combination of surgery post-operative radiotherapy. The strategy of post-operative radiation for poor tumor necrosis, as recommended by Dunst et al. in their retrospective review [11], has not been incorporated into current COG studies. However, the authors correctly highlight the critical importance of central radiotherapy review, a factor that was highlighted by Cooperative Ewing Sarcoma Study (CESS) experience [12].

Given resource limitations experienced by Raciborska et al. and highlighted by others describing implementation of cancer programs in low/middle income countries (LMIC) [13,14], what can be further learned from this report? The conclusions drawn by Raciborska et al. are consistent with elements outlined by Rodriguez-Galindo et al. who described the global challenge of childhood cancer [14]. Cancer is the leading cause of non-accidental death in children in high-income countries (HIC) and becoming so in less developed countries. Rodriguez-Galindo et al. identified the importance of cancer registries and development of national/regional treatment centers. They emphasized the importance of provider and patient education regarding the presentation and diagnosis of childhood cancer aimed at reducing the likelihood of therapy abandonment and reduction of the lag time between presentation and initiation of treatment. In a more disease focused report, Hunger et al. recommended intensity-adjusted algorithms in planning childhood acute lymphoblastic leukemia treatment and also highlighted the importance of adaptation of therapies [15].

Raciborska et al. have successfully implemented complex treatment strategies for patients with a highly aggressive solid tumor and have identified steps to continue to advance outcomes for children with Ewing sarcoma in their country [1]. In HIC, where the vast majority of worldwide cancer research expenditure is spent and where 94% of global economic cancer related estimated costs exists [14], there are increasing limitations on centralized resources. Experience, such as that documented by Polish colleagues in the current report, reinforces the need to sustain cooperative study.
group funding, to adapt complex cytotoxic regimens for high-risk cancer, such as Ewing Sarcoma by incorporating novel agents and to advocate for more expedient availability of novel agents for evaluation in children.

REFERENCES