Comment on: Consolidation treatment for high risk solid tumors in children with myeloablative chemotherapy and autologous hematopoietic progenitor stem cell transplantation

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This paper reports on a small number of patients with a diverse group of diagnoses that were consolidated with high-dose therapy and rescued with autologous hematopoietic progenitor cells (HPC)[1]. One of the problems with this manuscript and many others is that the studies that have been performed and reported in the literature only reflect those patients who get the rescue and the survival advantage is from that point on. Second the number of patients is small and conclusions about the effectiveness of the procedure are not reliable. The only exception to these two problems has been the report of the only randomized trial for patients with high-risk neuroblastoma that actually includes all patients from diagnosis and shows a slight benefit of autologous hematopoietic stem cell rescue vs. conventional therapy[2]. Does that mean that autologous hematopoietic stem cell rescue is not an effective therapy. My response is that maybe an effective consolidation therapy in a selected group of patients with certain diagnoses. For example, in patients with recurrent Wilms tumors who achieve a second complete remission and are consolidated with high-dose therapy and autologous HPC do very well[3-6] unfortunately the reports about the benefit are with multiple different conditioning regimens some with a single rescue and others with a double rescue where deciding what is the standard to which we can compare results is not available. Other reports have shown that the survival in the same group of patients maybe equally as good without HPC rescue[7].

Maybe we have to start thinking differently about the use of autologous HPC transplants. These transplants are no more than the use of HPC to recover patients from the effects of myeloablative therapy and so the use of multiple cycles of high-dose therapy with an intensification of the therapy to overcome tumor resistance to chemotherapy may be feasible. In fact, there are examples in the literature where this approach has been used in neuroblastoma[8,9], and brain tumors [10,11].

In my view the only way we will be able to determine the true effect of autologous HPC in the treatment of cancer is by performing randomize trials comparing the standard therapy to the use of high-dose therapy with HPC rescue. The reasons that these studies will be difficult to do are: the small number of patients with this type of diagnosis for a randomized trial and how to determine which conditioning regimen is the best. An example could be Wilms tumor which is mostly curable with standard therapy; the number of relapse patients is small and diverse with respect to the site of relapse and the length of the initial response. Then we have to take into consideration what therapy they received for their initial treatment, how much radiation they received and lastly what chemotherapy, surgery or radiation will be given to induce them into a second remission. By the time we accumulate some patients, the results will be difficult to interpret and to make meaningful conclusions. In our own institution in a report by Campbell et al.[3], it took almost 10 years to collect enough patients to report the results.

One last question is whether we should use this approach in the up front therapy as was used in the neuroblastoma study for patients at very high risk of relapse and my response is that it would be an ideal approach to determine whether high dose therapy with HPC rescue has value for each one of the diseases for which this approach was used in this report.

In conclusion, autologous HPC rescue is a safe procedure but we can only conclude that it provides benefits in patients with high-risk neuroblastoma and that further studies with a large group of patients and preferably in a randomized trial with an upfront approach in high-risk patients will be necessary to arrive at the conclusions that Vargas et al. made in this report[1].

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