Reflections on Lugano

It is now 2 hours into my flight back from Lugano, Switzerland. I have finished a very tedious and unsatisfying book *(The Luminaries)*. I am now settling down to reflect on the presentations that made me think and learn during my 5 days at the 13th International Conference on Malignant Lymphoma, the elite lymphoma conference. My imagination was stimulated not only by the abundance of superb science and the opportunity to meet with old friends and colleagues from around the globe, but by the idyllic setting in which this meeting is held.

The R2 (rituximab/lenalidomide) combination we developed more than a decade ago in the Cancer and Leukemia Group B has resulted in impressive results—in both the relapsed and upfront settings—that are better than those with either agent alone. Not only have these findings led to randomized trials vs standard chemoimmunotherapy that could alter our treatment approach to patients with follicular lymphoma, but also triplets with other drugs have been evaluated. Several abstracts confirmed that bendamustine is a poor choice for such combinations because of the toxicity and unimpressive efficacy. Newer regimens incorporating targeted agents are in development instead.

Despite the high cure rate in Hodgkin lymphoma, controversies remain. Is there still a role for radiation therapy in patients who are no longer ^{18}F-fluorodeoxyglucose-avid after treatment? Should interim scans be performed, and what should we do with the information? The RAPID trial (published by Radford and colleagues in the *New England Journal of Medicine* in 2015) has been deemed a failure by some because it did meet the revised noninferiority boundaries. It did, however, reinforce the concept that statistical significance may be less important than clinical meaningfulness: in this case, protecting almost 96% of patients from unnecessary irradiation. The results of the RATHL trial were presented for the first time, with 2 notable, preliminary observations. First, for patients with a positive interim positron emission tomography (PET) scan, augmenting therapy appeared to improve outcome. Second, bleomycin could be safely deleted thereafter for those with a negative interim PET scan. Other studies suggested that risk-adapted strategies may one day become part of the standard of care.

One of the unfortunate eventualities of follicular and other indolent lymphomas is histologic transformation. We are developing new insights into the molecular pathogenesis of this entity, as well as the role of microenvironmental factors and molecular biomarkers that predict for transformation. Importantly, the selective pressure of certain treatments may create the genetic makeup that leads to the aggressive clone. I hope that science will eventually guide improved treatments for these patients.

One of the highlights of the meeting was a workshop on follicular lymphoma regarding the development of a better understanding of disease biology, and its therapeutic implications. This topic is of particular relevance because more than half of the general population harbors B cells with t(14;18), the hallmark of the disease, although few develop overt lymphoma. Currently, 80% of patients do well with treatment. Planned clinical trials are targeting the other 20% with novel therapeutic interventions. However, it is more critical to identify patients in the latter group before they fail therapy. A validated, biological modification of the Follicular Lymphoma International Prognostic Index (FLIPI), the m7-FLIPI, may do just that and should be performed on patients to identify those at highest risk of failure, requiring novel interventions rather than standard approaches.

I was fascinated by the presentations on functional and structural genomics informing therapy by Dr Louis Staudt, the current genomic and pathologic status of mantle cell lymphoma by Dr Elias Campo, the evolving world of cutaneous B-cell lymphomas by Dr Rein Willemze, and the upcoming revision of the *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissue* by Dr Steven Swerdlow.

I also had the opportunity to present the results of the potentially practice-changing GADOLIN trial, my first podium presentation of a major clinical trial to such an audience in quite a while. Even for an experienced speaker, it was a bit intimidating.

But, the bittersweet takeaway from the meeting was the unambiguous (and oft repeated) announcement of the pending retirement of my good friend and colleague, Dr Randy Gascoyne, from the BC Cancer Agency. Throughout the years, he has made innumerable scientific contributions to the field, has provided countless superb presentations, and has always been good for a scotch and a laugh. His friends and the field will certainly feel the loss. Let's see how long he can take a life of fishing!

Until next month . . .

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