

A New World Order in Lymphoma - Checkpoint Inhibitors, Oral Therapies and Maintenance

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The pendulum has swung again. Fifty years ago, the central paradigm in Oncology World used to be: "All cancer is same". This age saw folate inhibitors, alkylating agents and other non-specific cell cycle toxins being utilized for all cancers regardless of histological subtype in varying combinations. Twenty years ago, the age of "One-Cancer, One-Drug" dawned, with therapies such as Imatinib and Rituximab being based on specific mutations and/or protein receptors exhibited by malignant cell. While this enthusiasm continues into personalized medicine and BASKET trials where patients are randomized based on driver mutations and not histological subtype, the pendulum has indeed swung again. Once the oncolytic potential of somnolent T Cells was recognized, immunotherapies such as CART therapy and Checkpoint inhibitors (PD1, PDL-1, and CTLA4 to name a few) are currently in trials for more than 30 cancers. In other words "All Cancer is same- if you can unleash T Cells on it". This was eloquently demonstrated by Ansell et al. in their landmark phase 2 study of Nivolumab in relapsed and refractory Hodgkin Lymphoma. These outstanding responses were in a heavily pre-treated patient population. Nearly 80% had failed Brentuximab. Another 80% had failed autologous transplant [1-3].

Oral therapies consisting of single pills were unthinkable for aggressive cancers such as Mantle Cell Lymphoma which has traditionally been treated with elaborate regimens such as Hyper CVAD, autologous transplant in first remission or prolonged Rituximab maintenance. FDA approval of Bruton's Tyrosine Kinase Inhibitor, Ibrutinib for relapsed Mantle Cell Lymphoma is thus a giant leap from traditional thinking in the field [4,5]. Ibrutinib is also approved for upfront CLL with 17p deletion and refractory CLL/SLL as well as Waldenstrom's macroglobulinemia. Idelalisib, a PI3 δ kinase inhibitor is approved for relapsed follicular lymphoma and CLL [6-9].

Standard of care for relapsed Hodgkin Lymphoma after auto transplant was observation. Recent approval after AETHERA trail for post-transplant maintenance in high-risk disease (defined as refractory, extra nodal or remission duration <1 year) is a part of big-picture change where maintenance therapies are being pushed across the board in multiple hematological cancers including myeloma and leukemia [10-12].

A new age is upon us. In this new world order, our hard work on cellular pathways, immune responses and microenvironment is finally bearing fruits.

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