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Treatment Of Classical Hodgkin Lymphoma: The State Of The Art

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WHERE WE ARE?

Patients with advanced-stage classical Hodgkin lymphoma (cHL) have a good prognosis. In most countries, the first-line treatment has been, for at least a couple of decades, the ABVD protocol. Depending on several factors such as age, presence of *bulky* disease, or extranodal involvement, around 75-80% of patients are cured with this regimen[1]. However, there are now new treatment recommendations for advanced-stage cHL. After 6 years of follow-up, the ECHELON-1 study showed overall survival (OS) benefit for brentuximab vedotin with AVD versus the standard ABVD[2]. This has never happened in previous direct comparative trials. Although the BV+AVD was already approved for first-line treatment of advanced-stage cHL patients, based on the gain of progression-free survival (PFS) published a couple of years ago, a benefit in OS makes a much stronger case. Peripheral neuropathy was a special concern, with about 2 out of 3 patients treated with BV+AVD experiencing some form of symptom. Mainly it was grades I 1 and 2, and the symptoms did resolve or improved in almost 90% of cases[2]. But the BV-AVD reign has already been challenged. The SWOG1826 study is a randomized, multicenter, phase 3 trial, that compares the combination of nivolumab with AVD (nivo-AVD) versus BV-AVD[3]. This is a large trial, with almost 1000 patients, that included patients between 12 and 83 years. The 1-year PFS rate was 94% versus 86% (HR 0.48, 99%CI 0.27-0.87; p=0.0005), in favor of Nivo-AVD. OS was similar (99% vs 98%), with a short median follow-up of 12.1 months. Interesting that both arms of this study were for a limited number of 6 cycles, something different that is normally done with checkpoint inhibitors (usually until the progression of the disease, unacceptable toxicity, or up to 2 years). So, a longer follow-up will be paramount to see if this advantage for nivo-AVD will hold in time. The toxicity profile was largely as expected and no new safety signals in both arms. On the other hand, the HD21 study looked at the association between BV and a similar backbone of the escalated BEACOPP (eBEACOPP), known as BrECADD[4]. This new regimen was compared in a multicenter, randomized, phase 3 non-inferiority trial, with the standard eBEACOPP. Using a PET-adapted strategy, where interim PET negative patients completed 4 total cycles versus 6 total cycles in PET positive, BrECADD was non-inferior to eBEACOPP. The 3y-PFS rate was 94.9% versus 92.3%, with a median observation time of 40 months. These impressive results compare favorably with BV-AVD in the ECHELON-1 study (6y PFS of 82.3%) and with Nivo-AVD in the SWOG study (1y PFS of 94%), but with all the restrictions of comparing different trials.

WHAT TO EXPECT FOR THE FUTURE?

Clearly, in one of the lymphomas with the best overall prognosis, the treatment landscape evolved. There are now at least 3 new options for the treatment of advanced-stage cHL in the first line, with better results than ABVD, the standard for a long time. As we continue to improve efficacy, toxicity remains an important issue. Longer follow-ups will be needed to see if we can have great results without impact in our patient's quality of life.

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Sp07

MDS 2023: State of The Art

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The myelodysplastic syndromes (MDS) are clonal bone marrow (BM) stem cell disease(s), characterized by abnormal hematopoiesis, with anemia (95%) and/or other cytopenias. The pathogenesis is based on genetics and inflammation of aging (inflammaging). The median age of onset is 74yr, with increasing incidence with age. Patients are classified as having a lower (LR-MDS) or higher risk disease (HR-MDS), and leukemic transformation occurs in 20%-60%.

We will cover new aspects like quality of life (QoL), novel genetic information, will briefly touch the emerging field of inflammaging, describe new tools for (early) diagnosis, the new classifications, and finally will address MDS treatment. We will skip aspects such as epidemiology, clinical picture and cytogenetics.

Over the last decade QoL has become important in MDS, to study and improve – we will show some data. Genetics is an integral part of evaluation, with at least one mutation in 90% of MDS patients, but as more information is obtained it has become clear that the field is quite complex. The pathogenesis is carefully investigated and inflammation of aging (inflammaging) appears to play an important role.

Diagnosis of MDS has been recognized as a challenge. The introduction of new tools, such as genetic and digital medicine improve the process, make it more accurate, less invasive, and hopefully may identify individuals at risk.

Several new MDS classifications (and guidelines) have been proposed over the last couple of years. We will focus on the new IPSS-Molecular model, and will summarize the 5th WHO and ICC classifications.

RBC transfusions and erythropoietin (EPO) remain the 1st line treatment for anemia in lower-risk MDS. EPO is safe and might delay the need for RBC transfusions. A recent EUMDS study suggests a prolonged survival with EPO. Lenalidomide remains effective for MDS with del(5q) (50% response), but also somewhat effective (27%) in non-del(5q) patients. Luspatercept appears as an effective second-line (maybe 1st ?) agent. Several experimental agents are investigated, including oral azacytidine, imetelstat, a pyruvate-kinase activator and roxadustat. For thrombocytopenia two agents, romiplostim and eltrombopag, were shown to be effective. However, due to safety concerns their development has been stopped.