malignancies. The development of anti-CD19 CAR T-cell therapy represents a major advance in the treatment of patients with chemorefractory B-cell malignancies.

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Sp04

HOW I TREAT DOUBLE-HIT LYMPHMOMA AND HGBL, NOS

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Introduction: The new world health organization (WHO) classification on lymphoid neoplasms, the WHO-HAEM5, renames the former group that double-hit lymphomas were in as "diffuse large B-cell lymphoma/high-grade B-cell lymphoma with MYC and BCL2 rearrangements (DLBCL/HGBL-MYC/BCL2)". This is mainly to highlight that the presence of MYC and BCL2 rearrangements form a unique phenotype, different than the MYC and BCL6 rearrangements (present in the former classification). Those lymphomas are composed of large or intermediate or blastoid cells, with aggressive clinical course and tendency to be resistant to standard chemotherapy. It's a group ideal for new therapies, such as the bispecifics and CAR T-cells, but lack data to support this since are underrepresented in clinical trials. Retrospective studies, with its inherit bias, consistently points to worst prognosis and poor outcomes with standard RCHOP treatment. How to best approach this hard-to-treat lymphoma is still a matter of debate. **Treatment considerations:** Roughly 65% of patients with DLBCL are cure with 6 cycles of RCHOP. When considering this regimen for HGBL, event-free survival (EFS) has been reported as low as 20% in 3 years. More intensive regimens, like R-DA-EPOCH and R-CODOX/M-IVAC, could increase this response, based on retrospective studies, with EFS 3y close to 80%. The role of autologous transplant as consolidation is controversial, and it's not routinely indicated. However, there are data that patients treated with RCHOP could increase progression-free survival (PFS) with this strategy, perhaps eliminating the difference between more intensive regimens. The lack of a direct comparison in a randomize phase 3 study between RCHOP or more intensive protocols precludes a firm conclusion. In the Alliance/CALGB 50303 study, that compared RCHOP with R-DAEPOCH in patients with DLBCL and PMBCL, there were no differences in 2y PFS between arms. But the number of patients with MYC rearrangement was too small to any conclusion regarding HGBL. Dunleavy et al conducted a phase 2 study with R-DA-EPOCH in 53 patients with MYC-rearranged DLBCL (24 were double-hit). EFS 4y was 71% and overall-survival (OS) 4y was 77%. Although this looks pretty good compared to the historic RCHOP, it's not a randomize study. New therapies have emerged as possible rescue in the relapsed/refractory DLBCL population, a group of patients with a dismal prognosis. The chimeric antigen receptor (CAR) T-cells have become a new standard of care for those patients, when available. Albeit with a small number of patients, the three main products (axi-cell, tisa-cell and lisocell), used for rescue of DLBCL patients, had shown activity against HGBL. That holds true in latter lines and as a first salvage treatment, as the recent trials comparing with autologous transplant. The zuma-12 is a phase 2 study with axi-cell as first-line of treatment with high-risk DLBCL patients, a population enriched with HGBL. Early reports are impressive, with nearly 80% of complete remissions. However, long term follow-up will be necessary to see with the responses are durable. Bispecifics are other very important players on that field, with the first reports of high activity in high-risk DLBCL, even after CAR T-cell failure. **Conclusions:** HGBL is an aggressive form of lymphoma, with tendency of a worst prognosis with conventional treatment. Intensive regimens seem to fare better than RCHOP, although with more toxicity and no randomize studies supporting this indication. New treatments, mainly CAR T-cells and bispecifics, are very promising and possibly will became standard of care for such patients but were in the therapy algorithm is still to be decide.

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Sp05

APPROPRIATE MANAGEMENT OF POLYCYTHEMIA VERA WITH CYTOREDUCTIVE DRUG THERAPY

EUROPEAN LEUKEMIANET 2021 RECOMMENDATIONS

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Classical Philadelphia-negative myeloproliferative neoplasms (Ph-neg MPNs) including polycythemia vera (PV), essential thrombocythemia (ET), and myelofibrosis (MF) are characterized by uncontrolled clonal proliferation of multipotent bone marrow progenitors, sustained by acquired mutations in JAK2, CALR and MPL genes. Expansion of the mutated clone triggers an inflammatory response that influences the development of associated vascular complications and disease progression into MF and acute leukemia. This presentation will focus on the recent recommendations by ELN in low-risk PV patients. According to ELN and NCCN patients with PV should be managed by the risk of thrombosis and cytoreductive drugs are recommended in high risk (over 60 y and/or prior thrombosis) while low-risk should be treated with low-dose aspirin and phlebotomy only. These guidelines have been reviewed by international recognized experts in the field of MPN. In January 2021, ELN promoted an international project specifically devoted to updating the clinical indications for using cytoreductive drugs in treating PV. The Expert Panel (EP), the chair and the methodologist were asked to grant the highest quality of the recommendations by adhering to standard methods for developing clinical practice guidelines, namely Grading of Recommendations Assessment,