Sp05

TREATMENT OF RELAPSED, REFRACTORY DIFFUSE LARGE B CELL LYMPHOMA

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DLBCL represent almost 30% of all non-Hodgkin's lymphoma cases. More than 60% can be cured with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone) chemoimmunotherapy. Patients not responding to R-CHOP often have a poor outcome, particularly those with disease refractory to frontline or subsequent therapies. Approximately 10-15% of patients treated with R-CHOP have primary refractory disease (incomplete response or relapse within 6 months after treatment) and additional 20-25% will relapse after an initial response, typically within the first 2 years. Patients with late relapses (>2 years after treatment) have better prognosis. Patients who are eligible to curative therapy should undergo full restaging to fully assess the status of their disease and to assess prognosis. A repeat biopsy at the time of relapse should strongly be considered to ensure that an alternate histology is not present, as an indolent lymphoma has been reported on repeat biopsy in approximately 17% of cases with late relapses. Gene expression profiling has delineated two distinct molecular subtypes of DLBCL: germinal center B-cell like (GCB) and activated B-cell like (ABC); 10-15% of cases are unclassifiable. Detailed analysis of molecular aberrations have led to proposals of new unique, genetically defined subtypes beyond the cell of origin.

Transplant-eligible patients. Treatment with high-dose chemoimmunotherapy and autologous stem-cell transplantation (ASCT) offers the best chance of cure in patients with chemotherapy sensitive relapsed or refractory DLBCL, but due to advanced age and coexisting medical conditions only half of such patients are considered transplantation candidates. Approximately 50% of patients respond to initial salvage therapy and then undergo ASCT, with an overall cure rate of 25 to 35%.

Management of transplant-ineligible patients. While some elderly fit patients may be eligible to ASCT and exhibit comparable outcomes to younger patients, the majority will have comorbidities that will prevent intensive chemo-immunotherapeutic approach. Few prospective trials have been conducted in elderly patients with relapsed/refractory DLBCL. The combination of R-GEMOX and R-bendamustine have been used for paliative purposes. For these cases, new approaches are warranted and new FDA approved drugs will be discussed on new drugs session.

CAR-T cell therapy represents a major paradigm shift in the management of relapsed or refractory DLBCL. Three products, axicabtagene ciloleucil (axi-cel), tisagenlecleusil (tisa-cel) and lisocabtagene maraleucel (liso-cel) are FDA-approved as third line treatment of DLBCL and are commercially available. In pivotal studies, axi-cel, tisa-cel and liso-cel have been associated with overall and complete response rates in the range of 52-82% and 40-54%, respectively, among patients with R/R aggressive B-cell lymphoma. All three agents had characteristic toxicity profile with severe (grade > 3) CRS in 1-22% of patients, and severe (grade > 3) neurotoxicity in 12-28% of patients. Long-term outcome of ZUMA-1 trial recently published and 4 year OS is 41%, median OS is 25.8 months (17), on the other hand in Juliet trial, 5 year PFS is 31%.

Novel therapies. Despite the advance of CAR-T cell therapy, novel therapies are needed. Several agents are FDA-approved for the treatment of R/R DLBCL. **Polatuzumab-Bendamustin-Rituksimab** has received approval based of randomised phase 2 trial involving transplantation ineligible patients with significant improvement rates of complete metabolic response, PFS and OS as compared with BR alone. **Selinexor** has also received approval for patients with R/R DLBCL who have received at least two lines of therapy, as a phase 2 study has shown modest single-agent acitivity. **Tafasitamab** is a humanised anti-CD19 monoclonal antibody with augmented Fc gama receptor afinity. Results from a phase 2 study of tafasitamab combined with lenalidomide showed efficacy, leading to regulatory approval for patients DLBCL ineligible to transplantation.

Bispesific antibodies (bsAbs) refers to an antibody that has binding specificities for two different antigens. A variety of bsAbs are currently under development as therapy for B-cell lymphoma. These bsAbs target CD20 on B-cell and engage T-cells by CD3 in a 1:1 or 2:1 CD20:CD3 Fab format. In general, CRS and neurotoxicity are significantly less frequent than observed with CD-19 directed or blinatumomab therapies. In R/R DLBCL, ORR range from 37 to 90% with CRR from 19 to 55%. However, follow-up for these new bsAbs is short and the durability of responses remains to be established.

Loncastuximab tesirine is a CD-19 directed antibody-drug conjugate. It has substantial single-agent antitumour activity and produces durable responses with an acceptible safety profile. 145 patients were enrolled with diagnosis of R/R DLBCL including high-risk characteristics for poor prognosis such as double-hit, triple-hit, transformed or primary refractory DLBCL. ORR was 48% with 24% CR rate, potencially offering a new therapeutic option for heavily pre-treated patients with R/R DLBCL.

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Sp06

HAPLOIDENTICAL VERSUS UNRELATED ALLOGENEIC STEM CELL TRANSPLANTATION FOR ADULTS WITH ACUTE LEUKEMIA

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Allogeneic hematopoietic cell transplantation (HSCT) remains an important curative treatment modality for patients with high risk acute leukemia (AL) (1). A matched unrelated donor (MUD) or a haploidentical related donor (Haplo HSCT), are both valid options in the absence of a fully HLA-matched sibling donor (MSD) for HSCT in AL. In my presentation I will present and discuss focusing on the Acute Leukemia Working Party (ALWP) of the European Society for Blood and Marrow Transplantation (EBMT) registry based studies in recent few years (2-6) comparing MUD and Haplo HSCT for both acute