Sp04

CML 2023 - State Of The Art And Cutting Edge İssues

Pia Raanani

Division of Hematology at the Rabin Medical Center, Tel-Aviv University

Chronic myeloid leukemia (CML) and its treatment is the prototype of translational research and success of targeted therapy. It was the first disease with a definitive molecular marker where specific targeted small molecular inhibitors, tyrosine kinase inhibitors (TKIs), changed dramatically the course and prognosis from a fatal disease into one with nearly normal survival. TKIs in clinical use are imatinib, nilotinib, dasatinib, bosutinib and ponatinib. Asciminib is a newly developed allosteric BCR-ABL1 inhibitor. Clinicians can personalize treatment based on the toxicity profile of TKIs, taking into account patients' age, comorbidities and lifestyle. Despite the revolution in the treatment and prognosis of CML in the last 3 decades we are still facing some challenges: Vascular adverse events have emerged as a serious side effect of some TKIs and treatment, especially of elderly patients, and this should be taken into consideration. While treatment of chronic phase CML is considered a great success, coping with accelerated and especially blastic phase CML is still a big challenge. The role of allogeneic stem cell transplantation (alloSCT) and donor lymphocyte infusion (DLI) in 2024 is minor but still relevant for some patients. Future treatments combining TKIs with checkpoint inhibitors as well as interferon or asciminib are under investigation. The issue of deep molecular response (DMR) and its implications for treatment discontinuation and treatment free remission (TFR) – who, when and why, has clinical as well as emotional and financial considerations. Matters of quality of life (QOL) and patient reported outcome measures (PROMs) are now in the forefront once the disease changed its course from a fatal to a chronic and even curable one. And finally, can we look into a crystal ball to predict at the outset who will respond to therapy, who will achieve DMR and who will benefit from prolonged TFR and cure.

https://doi.org/10.1016/j.htct.2023.09.005

Sp05

Management Of Early Relapsed Follicular Lymphoma Debate Favoring Non-Transplant Options

Murat Özbalak

Başakşehir Çam ve Sakura City Hospital, Division of Hematology, Istanbul, Turkey

Follicular lymphoma (FL) is the most common non-Hodgkin lymphoma in the United States and Europe[1]. The disease is potentially incurable and, treatment options comprise a wide spectrum from local radiotherapy to chemoimmunotherapy, based on the risk factors. The outcome of follicular lymphoma patient requiring treatment significantly improved with the introduction of rituximab[2,3]. Rituximab or obinituzumab in combination with cyclophosphamide, adriamycin, vincristine, prednisolone (G/R-CHOP) or with bendamustine (BR/OR) are preferred in the frontline setting[4]. RELEVANCE study showed that lenalidomide-rituximab (R2) has similar efficacy to R-chemotherapy approach in the first-line treatment[5].The response rate to first-line chemoimmunotherapy is around 65% and, about 20% of the cases responding to chemoimmunotherapy experience progression of disease within 24 months (POD24) and have poorer overall survival[6,7]. Current prognostic scores are not efficient to predict POD24 cases.

AUGMENT study showed improved efficacy with R2 compared to R in the second line treatment of indolent lymphomas. Eighty-three percent of the cases had FL and 31% of the cohort experienced POD24. The overall response rate (ORR) was 78%, with an improved 2-year progression-free survival rate of 58% compared to 36% with R alone[8]. MAGNIFY study evaluating R2 maintenance following R2 induction reported an ORR of 65% and a median PFS of 27.4 months for POD24 group[9].

Tazemetostat is an oral EZH2 inhibitor. EZH2 is mutated in 20-30% of FL patients. It offered an ORR of 69%, with a median PFS of 13.8 months in early relapsed FL cases with EZH2 mutation. Although the ORR was lower compared to late relapsing cases, the PFS was longer in EZH2 mutant group compared to 5.8 months in wild-type cases[10]. Copanlisib,a pan-class I phosphatidylinositol 3-kinase inhibitor was evaluated in a phase II study in both indolet and aggressive lymphoma patients. The ORR was 58.7% in indolent lymphoma patients[11]. Chronos-3 trial revealed that when copanlisib was combined with rituximab, median PFS was improved to 21.5 months compared to 13.8 months with R monotherapy[12]. Idealisib, duvelisib and umralisib removed their indications for relapsed and refractory FL due to a trend toward lower overall survival (OS) in patients exposed to these agents[13].

CAR-T cell therapy changed the treatment paradigm in B-cell lymphomas. In the ZUMA-5 trial, Axicabtagene ciloleucel reported an ORR of 92% in both POD24 and without POD24 cohort.The 18-months estimated duration of response, PFS and OS rates were 60%, 55% and 85% in POD24 cases, whereas they were 78%, 84% and 94% in patients without POD24[14]. Treatment with Tisagenlecleucel showed lower complete response rates in POD24 patients compared to those without POD24, reported to be 59% vs 87.9%[15].

Treatment with bispecific antibodies, suc as epcoritamab, mosutetuzumab and glofitamab, constitute an alternative to CAR-T. The ORR ranged between 80% and 90% with bispecific antibody monotherapy in early-relapsing FL cases[16-18].

Nonchemotherapeutic approaches have promising outcomes and are currently preferred in second line setting for POD24 patients. The role of stem cell transplantation in controversial in FL. However, there is not any solid data comparing transplantation with nonchemotherapeutic options.

https://doi.org/10.1016/j.htct.2023.09.006