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OUTCOME OF VERY LATE RELAPSE IN HODGKIN LYMPHOMA – A REPORT FROM DEBRECEN, HUNGARY

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Introduction. With modern risk-adapted treatment modalities 80-90% of Hodgkin lymphoma (HL) patients can be cured, however, 30% of the patients may relapse after the first line treatment. Late relapses, that occurred 5 or more years after first diagnosis are rare. Neither clinical characteristics, nor risk factors, nor optimal treatment are well described for very late relapse (VLR) patients. *Aim.* To describe the incidence, clinical presentation, treatment and outcome of VLR in HL patients between 1970 and 2010 at our institute. *Results.* Of 669 consecutive HL patients treated at our institute between 1970 and 2010, 617 (92.2%) patients achieved complete remission after the first line treatment. Relapse occurred in 188 (28.1%) patients, 26 (3.8%) of them 5 or more years after the first diagnosis. VLR were more frequently observed in patients with mixed cellularity histological subtype and stage II/III disease at first diagnosis. In 15 (57.7%) patients, the histologic subtype remained the same at VLR, in 8 (30.8%) cases the region of the relapse was also identical. 24 (92.3%) patients with VLR received polychemotherapies, 5 (20.8%) of them also received involved-field radiotherapy. Primary diagnosis before the age of 20 and treatment with radiotherapy alone at first diagnosis was associated with a higher risk of VLR (p=0.009 and p=0.004 respectively). Compared to early relapse we observed superior OS after VLR. At a median of 244 (91 - 360) months of follow-up, 22 (84.6%) patients with VLR are still alive and disease free. In addition, relapse characteristics, therapeutic approaches, and changes in histologic subtype will be presented. *Conclusions.* VLR occurs in a small number of patients diagnosed with HL. Besides the rarity of these cases, with adequate treatment, late relapse of HL appears to have a favorable prognosis to early relapse HL cases. Subgroup analyses suggest that treatment with radiotherapy alone and first diagnosis before adulthood conveys worse prognosis. Continuous investigations are needed in this setting to determine further risk factors of VLR in HL.

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LIMITED EFFICACY OF BRENTUXIMAB VEDOTIN IN A HEAVILY PRE-TREATED HODGKIN LYMPHOMA POPULATION

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Although HL is highly curable, 10-30% patients (pts) are refractory or relapse after treatment. Salvage second line chemotherapy with autologous stem cell transplant (ASCT) usually achieves 50% responses. Refractory pts and those who relapse after ASCT have a poor prognosis. BV is an anti_CD30 antibody-drug-conjugate with significant activity against refractory/relapsed HL. We report a multicentric retrospective analysis of 34 Portuguese pts receiving BV monotherapy for refractory/relapsed HL between 9/2011 and 2/2016 at 10 centers. BV (1.2 or 1.8 mg/Kg) was administered every 3w. Response was evaluated by PET-CT. Overall (OS) and progression-free-survival (PFS) were estimated using the Kaplan-Meier method; chi-square text was used to evaluate relation between clinical variables and response. Pts (53% female) were diagnosed between 1997 and 2015; 62% had advanced disease. First-line treatment was ABVD in 91% with a 74% overall response rate (ORR). Twenty-eight pts (82%) received salvage chemotherapy with intent to perform ASCT, and 64% underwent transplant. Median age at BV was 34.5 yo (23-69), 76% had advanced disease and 1/3 B symptoms. Median time from initial diagnosis was 44 mo; median number of prior treatments was 4 (2-6), with 79% pts refractory to last one. Median number of BV cycles was 7.5. In 18 pts with early evaluation of response (at cycles 2 to 4), ORR was 67% and CR 33%. At the end of treatment, ORR was 21% (5 CR, 15%), while 76% had either stable or progressive disease. Pts with ≤3 prior lines had ORR 47% as compared to none in pts with >3 (p<0,001). No difference in ORR was noted according to gender, refractory/relapsed state and number of involved nodal areas. Ten pts (29%) were transplanted after BV, only 4 in response; 18 started subsequent treatment after BV. After a median follow-up of 12 mo 11 pts died, mostly of progressive disease. OS and PFS at 12 months were 73.5% and 19% respectively. BV was well tolerated with 18% peripheral neurotoxicity, 33% at least one hematological toxicity and 9% grade 3-4 infections in all pts. In a real-life setting, with a heavily pre-treated and mainly refractory population, responses to BV were lower than previously described. In agreement to others we observed loss of responses with prolonged treatment, suggesting a benefit for early evaluation and treatment consolidation to maximize the benefit of BV. Better ORR was observed after ≤3 prior treatments, suggesting that BV should be offered early.

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THE ROLE OF STEM CELL TRANSPLANTATION IN HODGKIN'S DISEASE; PERSPECTIVES FROM RETROSPECTIVE ANALYSIS

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Purpose. To disclose the prognostic value of status of disease and lines of therapy at transplantation (SCT) either autologous or allogeneic in Hodgkin lymphoma we did a retrospective evaluation. *Patients and Methods.* We accrued all patients who did a stem cell transplant (SCT) procedure following resistance, residual disease, or relapse after previous conventional therapy. The accrual started in October 1998 when we did the first autologous SCT with the use of peripheral stem cells (PSC) and included patients up to December 2015. One hundred eighty one patients with Hodgkin lymphoma did autologous and 40 patients did allogeneic SCT and analyzed for prognosis according to status and number of lines of therapy at transplant. Five categories of patients were identified according the status at transplant: primary resistant, with residual disease, in first relapse, in second relapse and more than second relapse. Autologous SCT was done as II, III, IV line and more than IV line of therapy. High dose therapy followed by autologous PSCT represented a line of therapy for almost all patients who did allogeneic SCT. The analysis included the evaluation of survival according to groups identified and see if there are significant differences. *Results.* Worse chances of survival were for patients primary resistant, 6% at 138 months, and for those with more than two relapses,10% at 120 months; better chance were for patients with residual disease, 88% and those who did transplantation following I relapse, 96% at 194 months (p<0.0001) (Figure 1). In addition better survival was for patients who received autologous SCT as II line of therapy, 93% survival at 194 months, and worse those with more than IV line of therapy, 12% at 146 months (p<0.0001). Allogeneic SCT was done in 38 (95%) patients following autologous SCT; survival was 16% at 175 months and relapse-free survival (RFS) was 18% at 174 months. The stratification of survival in the setting of allogeneic SCT was worse for patients resistant and with previous more lines of therapy. *Conclusions.* Our study demonstrates that Hodgkin lymphoma may be cured by high-dose ther-