834P Role of assessment of IL-6, IL-15 and Soluble PD-L1 levels as prognostic and predictive biomarkers in nivolumab-treated relapsed/refractory Hodgkin lymphoma

A.M. Chekalov[1], D.I. Shmidt[1], K.V. Lepik[1], N.D. Yolshin[2], N.P. Volkov[1], A.R. Muslimov[1], N. B. Mikhailova[1], E. V. Kondakova[1], L. A. Tsvetkova[1], Yu. R. Zalyalov[1], E. S. Borzenkova[1], I. S. Moiseev[1], V. V. Baykov[1], T.I. Ionova[3], A.D. Kulagin[1]

1 Raisa Gorbacheva Memorial Research Institute of Children Oncology, Hematology and Transplantation, Pavlov University; 6–8 L'va Tolstogo St., 197022 Saint Petersburg, Russia
2 Smorodintsev Research Institute of Influenza, Ministry of Healthcare of the Russian Federation, 15/17 Professora Popova str., 197376 St. Petersburg, Russia
3 Multinational Center for Quality of Life Research, 1A Artillerijskaya St., 191014 Saint-Petersburg, Russia

BACKGROUND

The introduction of immune checkpoint inhibitors (ICI) into the clinical practice revolutionized the treatment of relapsed/refractory classical Hodgkin lymphoma (r/r cHL). Despite the high objective response rate, the majority of patients treated with ICI experiences a disease relapse or progression (2-year progression-free survival (PFS) 24.4%, (Momotow et al., 2019). At the same time continuous ICI treatment in responding patients creates a risk of immune-related toxicity and introduces a significant financial burden, raising the question of optimal therapy duration. Thus, there is an unmet need for the introduction of novel biomarkers that would help to stratify the prognosis of patients to optimize the ICI treatment strategy. Therefore, we aim to characterize the concentration of serum biomarkers, namely soluble programmed death-ligand 1 (sPD-L1), interleukin-6 (IL-6) and interleukin-15 (IL-15) during nivolumab therapy and association of their level with clinical factors, safety of the treatment and survival.

MATERIALS AND METHODS

We analyzed blood serum samples from 52 patients with r/r cHL, who received treatment with nivolumab at Pavlov University, Saint Petersburg, Russian Federation. Patients characteristics presented in table 1 and Fig.1.

Dose of nivolumab was 3 mg/kg intravenously every 2 weeks until unacceptable toxicity or treatment change due to disease progression. Four-year overall survival (OS) was 93%, 4-year progression- free survival (PFS) was 26 % (median 20.6 months). At the start of nivolumab therapy patients had no active infectious process.

The levels of IL-6, IL-15, sPD-L1 in the serum of patients were determined by enzyme-linked immunosorbent assay (ELISA) before starting nivolumab therapy and in the period of 3-6 months after the treatment start.

Table 1: Patient characteristics

Patients charecteristics	n (%)
Patients number	52
Median follow-up(range),months	56,2 (19,6-62,57)
Median age(range),years	25 (12-48)
Gender,n(%):male/female	25 (48)/ 27 (52)
Advanced stage(III-IV) at diagnosis,n(%)	36 (69)
Extranodal lesions, n(%)	38 (73)
Early relapse,n(%)	3 (5,8)
Median of previous treatment lines(range)	5 (2-10)
B-symptoms at the time of nivolumab initiation,n(%)	36 (70)

Fig. 1A: 4-year Overall survival.

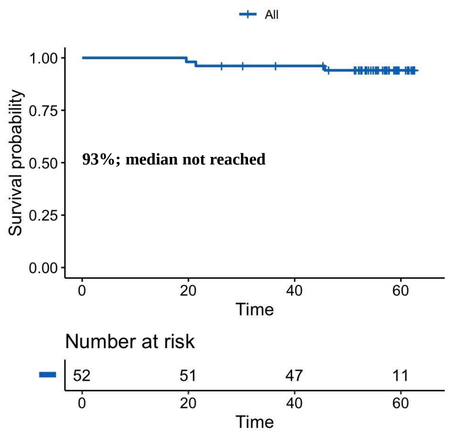


Fig. 1B: 4-year Progression-free survival.

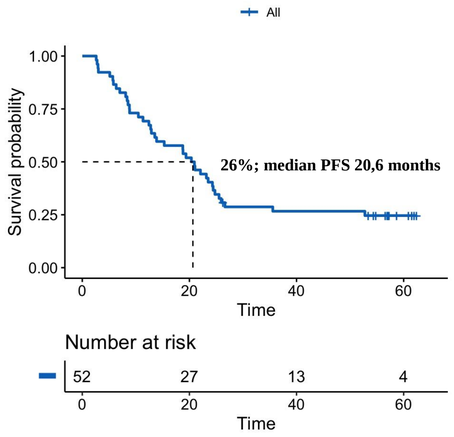
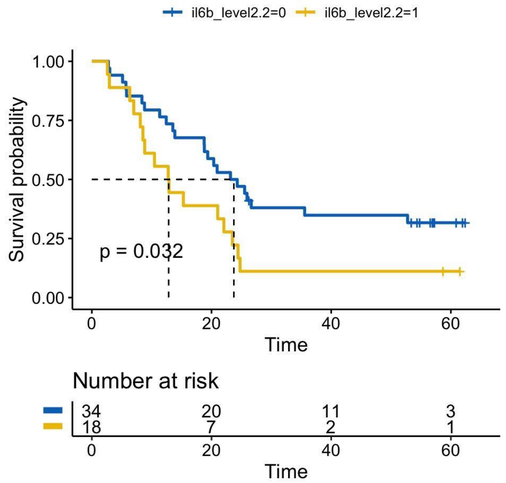


Fig.5:PFS according to serum level of IL-6 before nivolumab treatment



RESULTS

Before treatment initiation the mean level of IL-6 was 7,98 pg/ml (SD=26.3), IL-15 – 12,33 pg/ml (SD=33.6), PD-L1 – 9,9 pg/ml (SD=3.5). We revealed significant association between higher IL-6 level at the start of ICI therapy and presence of B-symptoms (p=0.0086) and extranodal involvements (p = 0.0026). We found a significant decrease of IL-6 and sPD-L1 levels after treatment (p=0.00012, p=0.0066 respectively) (Fig.2,3). Moreover, there was a significant correlation between sPD-L1 and tumor volume before nivolumab initiation (correlation coefficients = 0.4, p=0.0093) (Fig.4). The analysis demonstrated that lower IL-6 level before therapy was associated with advantage in PFS from the start of nivolumab therapy (median PFS – 23.7 months vs 12.6 months, p=0.032; cut-off - 2.2 pg/ml) and decrease in the time to response (median – 2.8 months vs 8.1 months). (Fig.5).

Fig. 2: Dynamics of IL-6 level

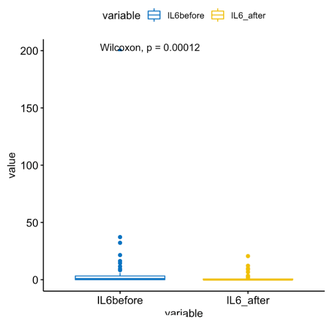


Fig. 3: Dynamics of sPD-L1 level

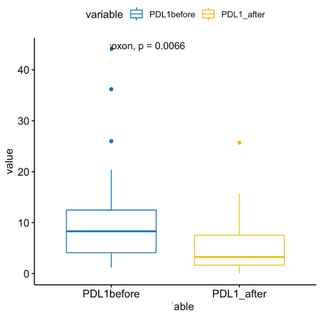
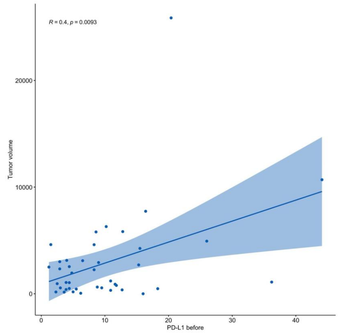


Fig. 4: Correlation between tumor volume and sPD-L1



CONCLUSION

sPD-L1 level has positive correlation with tumor volume before the nivolumab treatment start. IL-6 and sPD-L1 resulted in a significant decrease after nivolumab treatment. In our population, serum IL-6 had predictive significance regarding PFS and time to response from the start of nivolumab. Addional studies are reuiqred to compare the predictive value of IL-6 to clinical predictors of prognosis.

ACKNOWLEDGEMENTS

This study was supported by BMS research grant CA209-8EG