soho2023
ELEVENTH ANNUAL MEETING

THE CLONALITY OF MYELOID-DERIVED SUPRESSOR CELLS IN CHRONIC MYELOID LEUKEMIA PATIENTS

T. CHITANAVA[1], N. SHNALIEVA[1] ,R. VLASIK[1] , O.KULEMINA[1], L.KHORDZHASOV[1], T.NIKULINA[1], O.MERZLIKINA[1], Y.MIROLUBOVA[1], E.TOLSTOPYATOVA[1], V.SOLOVYEV[1], P.BUTYLIN[1], N.LUCHKINA[1], A.ATAMAN[1], A.ARONOV[1], E.LOMAIA[1]

1. Almazov National Medical Research Centre, Saint-Petersburg, Russian Federation

INTRODUCTION

Myeloid-derived suppressor cells (MDSCs) are immature myeloid cells that might suppress immune responses against cancer. Recently, an accumulation of granulocytic (Gr) and monocytoid (Mo) subpopulations of MDSCs has been found in the peripheral blood of chronic phase chronic myeloid leukemia (CP-CML) patients. Are they part of the tumor clone showing BCR/ABL expression?[1,2]

AIM

To determine the clonality of MDSCs in CML patients

METHOD

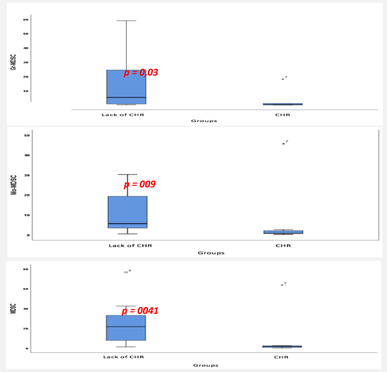
A total of 11 samples of 9 adult CP-CML patients were analyzed. Patients distributed as follow: 5 were treatment-naive for CML, 2 were resistant pts with BCR::ABL>10%, in other 2 pts the responses were MR2 and MMR in whole blood on tyrosine kinase inhibitors.

Fluorescence in-situ hybridization (FISH) and RT-PCR for BCR::ABL were performed in total MDSCs that were defined as HLA-DRlow/- CD11b+ CD33+ [2]. Suppressive activity of MDSCs was confirmed by co-cultivation with T-reg and T-cyt to confirm the MDSCs feature of the cells.

RESULTS

The median number of total MDSCs by flow cytometry was 33x10^9/L (range, 1,36-76,6). The number of MDSCs (total or subpopulation) was much higher in patients without hematological response (Pic. 1). BCR::ABL expression by RT-PCR test was analyzed in total MDSCs samples of 6 patients (3 newly-diagnosed, 2 resistant, 1 with MR2). All samples showed a high level of BCR::ABL expression with median 80% (range, 16–100%) (Tabl. 1). Dual FISH test was performed in 5 samples. All samples from newly-diagnosed patients (n=3) and resistant patient (n=1) detected a high level of BCR::ABL + cells (27–100% Ph+). In one patient with optimal response, no BCR::ABL cells were revealed. In 1 resistant pt no BCR::ABL positive ceels were found, but the number of analyzed cells were only 54 (Tabl. 2).

Pic. 1. Expression of myeloid suppressor cells depending on the presence of a hematological response in CML patients on TKI therapy



Tabl. 1. The level of BCR::ABL transcript according to RT-PCR in total MDSCs samples.

Group	PCR BCR::ABL1, %
Treatment naïve of CML	
patient 1	73%
patient 2	91%
patient 3	100%
Patients resistant to therapy	
patient 1	87%
patient 2	72%
Patient with MMR	16%

Tabl. 2. The rate of BCR::ABL transcript according to FISH test in total MDSCs samples.

Group	FISH (Ph+), %
Treatment naive of CML	
patient 1	100%
patient 2	93%
patient 3	27%
Patient with MMR	0%
Patient without response	0%

CONCLUSIONS

It seems that MDSCs in CML patients arise within CML clones. Experiments to evaluate whether the sensitivity of these cells are comparable to non-MDSCs CML cells are ongoing in our centre.

REFERENCES

1. C.Giallongo et al. Monocytic myeloid-derived suppressor cells as prognostic factor in chronic myeloid leukaemia patients treated with Dasatinib. J. Cell. Mol. Med. Vol 22, No 2, 2018 pp. 1070-1080

2. C. Giallongo et al. (2015) Myeloid derived suppressor cells in chronic myeloid leukemia. Front. Oncol. 5:107.

ACKNOWLEDGEMENTS

The work was financially supported by the Ministry of Science and Higher Education of the Russian Federation (Agreement No. 075-15-2022-301)

CONTACT INFORMATION

T.Chitanava: chitanava.tamara@yandex.ru

N.Shnalieva: shnalieva@yandex.ru

E.Lomaia: lomelza@gmail.com