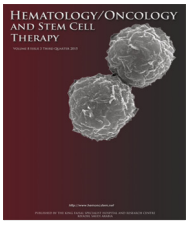
Hematol Oncol Stem Cell Ther (2016) 9, 129–130

Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/hemonc



LETTER TO EDITOR

CD56 and RUNX1 isoforms in AML prognosis and their therapeutic potential

Syed Z.A. Zaidi [a,c,*], Ibraheem H. Motabi [a,c], Ali Al-Shanqeeti [b,d]

[a] Department of Adult Hematology/BMT, King Fahad Medical City, Riyadh, Saudi Arabia
[b] National Blood and Cancer Center, Riyadh, Saudi Arabia
[c] Faculty of Medicine, King Saud Bin Abdulaziz University of Health Sciences, Riyadh, Saudi Arabia
[d] King Abdulaziz City for Science and Technology, Riyadh, Saudi Arabia

Received 20 November 2015; accepted 28 November 2015
Available online 12 December 2015

KEYWORDS
AML;
Anti-CD56 antibody;
CD56;
NCAM;
Prognosis;
RUNX1

Abstract
Neural cell adhesion molecule (NCAM/CD56) expression in acute myeloid leukemia (AML) has been associated with extramedullary leukemia, multidrug resistance, shorter remission and survival. Recently, Bloomfield et al. published a succinct review of issues surrounding the AML prognostication and current therapeutics. However, we want to reiterate the prognostic value and therapeutic potential of CD56 that is frequently expressed in AML as was also reported by their own group earlier. In addition, novel RUNX1 isoforms contribute in controlling CD56 expression in AML cells. Anti-CD56 antibody therapy deserves exploration as an arsenal against AML patients expressing CD56. Relevantly, targeting RNA splicing machinery or RUNX1 isoform-specific siRNA may also become part of future therapeutic strategies for AML with CD56 overexpression.

To the Editor,

Neural cell adhesion molecule (NCAM/CD56) expression in acute myeloid leukemia (AML) has been associated with extramedullary leukemia and multidrug resistance. Recently, Döhner et al. [1] published a succinct review of the issues surrounding AML prognostication and current therapeutics. However, they seem to have missed mentioning the prognostic value and therapeutic potential of CD56 that is frequently expressed in AML, as, among others, it was also reported by Baer et al. [2] earlier (Fig. 1) [2]. Additionally, novel RUNX1 isoforms contribute to controlling CD56 expression in AML cells [3]. A plethora of data,

* Corresponding author at: Department of Adult Hematology and BMT, Comprehensive Cancer Center MBC 30104, King Fahad Medical City, P.O. Box 59046, Riyadh 11525, Saudi Arabia.
E-mail addresses: szazaidi@hotmail.com, szaidi@kfmc.med.sa (S.Z.A. Zaidi).

http://dx.doi.org/10.1016/j.hemonc.2015.11.006
1658-3876/

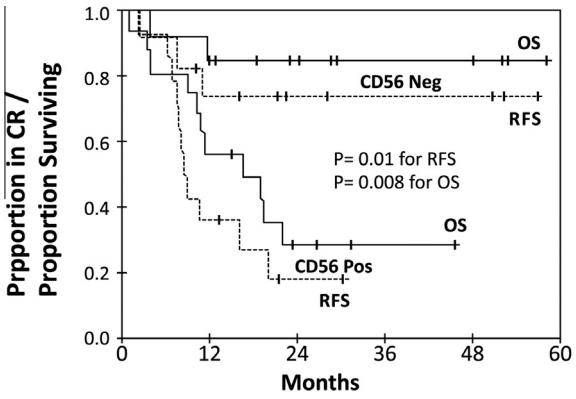


Fig. 1 OS and RFS for patients with AML with t(8;21) with and without CD56 expression. *Note:* Adapted from ''Expression of the neural cell adhesion molecule CD56 is associated with short remission duration and survival in acute myeloid leukemia with t(8;21)(q22;q22)" by Baer et al. [2]. AML = acute myeloid leukemia; OS = overall survival; RFS = relapse-free survival.

including recent meta-analyses, suggests that CD56 expression in AML confers poor prognosis (shorter remission and survival) even in patients with t(8;21) [4,5]. The Cancer Genome Atlas data also support the notion that NCAM overexpression is associated with shorter overall survival; median 424 days for high NCAM expression versus 945 days for low NCAM expression in AML M0/M1 (Alshanqeeti, unpublished data). Hence, we want to reiterate that, among other markers, CD56 overexpression should also be considered as a prognostic marker in any upcoming AML risk stratification model.

Interestingly, targeted therapy with Lorvotuzumab mertansine (LM; or IMGN901), a humanized anti-CD56 antibody attached to the potent cytotoxic agent DM-1, has produced promising results in clinical trials involving CD56+ solid tumors and multiple myeloma, both as a single agent and in combination with chemotherapy [6,7]. Once bound to CD56, LM is internalized into a cancer cell and releases DM-1 to initiate cell death via inhibition of tubulin polymerization. Given that the anti-CD56 antibody was humanized and the cytotoxic compound chosen was maytansine, a clinically proven immunotoxin used earlier in Gemtuzumab Ozogamicin (Myelotarg), LM itself meets important structural criteria that promise good clinical tolerability and efficacy. LM deserves exploration as an arsenal against AML patients expressing CD56, especially for minimal residual disease clearance.

Relevantly, Gattenloehner et al. [3] showed that CD56 expression by AML cells is positively regulated by RUNX1 p48 and negatively regulated by other splice variants, such as p30. At the protein level, p48high p30low versus p48low p30high RUNX1 isoform patterns are the major discriminators between CD56+ and CD56− AML cells, respectively. These results temptingly suggest that tipping the p48/p30 balance toward a p48low phenotype by targeting the RNA splicing machinery or applying RUNX1 isoform-specific siRNAs could become part of future therapeutic strategies for AML with CD56 overexpression [3].

Conflicts of interest

The authors declare no conflicts of interest.

References

[1] Döhner H, Weisdorf D, Bloomfield C. Acute myeloid leukemia. N Engl J Med 2015;373:1136—52.
[2] Baer MR, Stewart CC, Lawrence D, Arthur DC, Byrd JC, Davey FR, et al. Expression of the neural cell adhesion molecule CD56 is associated with short remission duration and survival in acute myeloid leukemia with t (8;21)(q22;q22). Blood 1997;90:1643—8.
[3] Gattenloehner S, Chuvpilo S, Langebrake C, Reinhardt D, Muller-Hermelink HK, Serfling E, et al. Novel RUNX1 isoforms determine the fate of acute myeloid leukemia cells by controlling CD56 expression. Blood 2007;110:2027—33.
[4] Xu S, Li X, Zhang J, Chen J. Prognostic value of CD56 in patients with acute myeloid leukemia: a meta-analysis. J Cancer Res Clin Oncol 2015;41:1859—70.
[5] Zaidi SZ, Motabi IH, Al-Shanqeeti A. Neural cell adhesion molecule (cluster of differentiation 56) in health and disease. J Appl Hematol 2015;6:93—105.
[6] Tassone P, Gozzini A, Goldmacher V, Shammas MA, Whiteman KR, Carrasco DR, et al. *In vitro* and *in vivo* activity of the maytansinoid immunoconjugate huN901-N2'-deacetyl-N2'-(3-mercapto-1-oxopropyl)-maytansine against CD56+ multiple myeloma cells. Cancer Res. 2004;64:4629—36.
[7] Berdeja JG, Ailawadhi S, Weitman SD, Patel M, Kelly KR, Guild R, et al. Phase I study of lorvotuzumab mertansine (LM, IMGN901) in combination with lenalidomide (Len) and dexamethasone (Dex) in patients with CD56-positive relapsed or relapsed/refractory multiple myeloma (MM). J Clin Oncol 2011;29 [Abstr. 8013].