INTERLEUKIN 3 RECEPTOR (CD123) EXPRESSION IN ACUTE MYELOID LEUKAEMIA PATIENTS IN RELATION TO DISEASE CHARACTERISTICS AND TREATMENT OUTCOME

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Introduction

In spite of the remarkable progress in basic and preclinical studies of acute myeloid leukemia (AML), the five-year survival rate of AML patients remains poor, highlighting the urgent need for novel and synergistic therapies.

Over the past decade, increased attention has been focused on identifying suitable immunotherapeutic strategies for AML, and in particular on targeting leukemic cells and their progenitors. However, the clinical outcome of patients with acute myeloid leukemia (AML) remains suboptimal, despite recent approval of new promising targeted therapies.

With the evolution of targeted AML therapies, novel agents continue to be developed with the goal to improve efficacy while minimizing toxicity.

CD123 (alpha subunit of the interleukin 3 receptor) is a cell membrane protein overexpressed in several hematologic malignancies which makes it an attractive therapeutic target.

It is composed of three extracellular domains (287 amino acids), a single-pass trans membrane domain (30 amino acids), and a short intracellular region (53 amino acids).

Upon lig and binding, the IL-3R heterodimer comprised of alpha and beta chains signals through Jak2, leading to a downstream activation of effectors that result in a net increase of cell proliferation and survival.

Aim of the Work

The aim of the present work was to assess inteleukin-3 receptor (CD123) expression in acute myeloid leukaemia patients and its relation to disease characteristics and to detect its impact on response to induction chemotherapy.

Patients and Methods

The study included sixty four newly diagnosed acute myeloid leukaemia patients admitted to the Haematology Unit, Internal Medicine Department, Alexandria Main University Hospital in the period from January 2022 to December 2022.

All patients enrolled in the study received induction chemotherapy which included, cytarabine 100-200 mg/m2 x 7days with daunorubicin 60-90 mg/m2 or idarubicin 12 mg/m2 x3 days.

After recovery from chemotherapy induced bone marrow aplasia, patients were evaluated for response to therapy.

Patients were divided into two groups according to response to induction chemotherapy.

Responders: included patients who achieved complete remission following induction chemotherapy.

Non Responders: included patients who didn,t achieve complete remission following induction chemotherapy.

METHODS:

-The expression of CD123 on bone marrow blast cells was analyzed using flow cytometric analysis. The proportion and MFI of CD123 positive cells were evaluated .Expression of the marker on the surface of more than or equal to 20% of the cells was a prerequisite to consider it positive.

- Conventional Cytogenetics analysis.

-PCR analysis of FLT3 mutation and NPM mutation was done for selected patients.

Results

Table 1: Comparison between non responder and responder group regarding CD123%.

	Non responders (n = 42)		Responders (n = 22)		Test of sig.	p
	No.	%	No.	%		
CD 123 %						
Negative (<20)	9	21.4	12	54.5	c^2= 7.182*	0.007*
Positive (≥20)	33	78.6	10	45.5		
Min. – Max.	0.20 – 100.0		0.50 – 96.0		U =96.0*	0.038*
Mean ± SD.	58.66 ± 33.66		36.85 ± 37.11			
Median (IQR)	73.50 (27.0 – 81.0)		12.75 (4.0 – 70.0)			

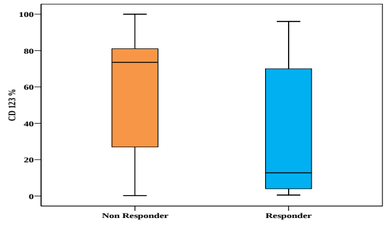

Figure1: Comparison between non responder and responder groups as regards CD123%

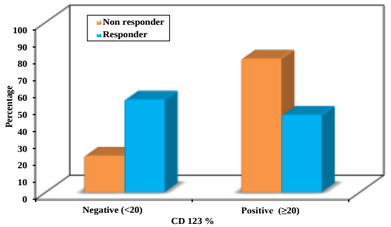

Figure2: Comparison between the two studied groups according to presence or absence of CD 123

Table 2: Relation between CD123 % and combinations of FLT3 and NPM mutations

	N	CD 123 %			Test of sig.	p
		Min. – Max.	Mean ± SD.	Median		
Combination of FLT3 and NPM mutations						
Unmutaed FLT3s and Un mutated NPM	22	0.70 – 96.0	49.28 ± 35.29	66.0	H = 10.026*	0.018*
Un mutated FLT3s and Mutated NPM	4	20.0 – 94.0	59.50 ± 34.08	62.0		
Mutated FLT3s and Un mutated NPM	1		0.20	0.20		
Mutaed FLT3s and mutated NPM	4	84.0 – 95.0	91.0 ± 5.23	92.50		

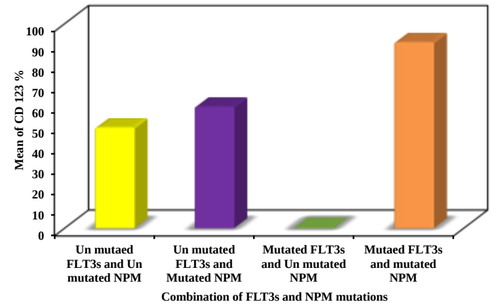

Figure 3: Relation between CD123% and combinations of FLT3 and NPM mutations

Conclusion

-CD123 is a membrane-bound protein that is overexpressed in acute myeloid leukemia and represents a promising therapeutic target.

-CD123 may be considered as a cardinal marker for response evaluation in AML.