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PEER-REVIEW REPORT

Name of journal: *World Journal of Experimental Medicine*

Manuscript NO: 99516

Title: Prevalence of RUNX1 gene alterations in de novo adult acute myeloid leukemia

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08168306
Position: Peer Reviewer
Academic degree: PhD
Professional title: Assistant Professor
Reviewer's Country/Territory: China
Author's Country/Territory: Egypt

Manuscript submission date: 2024-07-24

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2024-08-08 06:55

Reviewer performed review: 2024-08-10 11:07

Review time: 2 Days and 4 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Acute myeloid leukemia (AML) is a complicated disease with uncontrolled hematopoietic precursors' proliferation induced by various genetic alterations. Runt-related transcription factor-1(RUNX1) is commonly disrupted by chromosomal translocations in hematological malignancies. This prospective study aimed to characterize RUNX1 gene rearrangements and copy number variations, in newly diagnosed adult AML patients, with emphasis on the impact of clinical, and laboratory features on the outcome. After 44 months of follow-up, RUNX1 abnormalities affected neither patients' response to treatment nor overall survival. The role of RUNX1 mutations in cytogenetically normal AML had been identified, however, the prognostic impact of RUNX1 translocations other than t(8;21)(q22;q22), RUNX1 deletions, and amplifications are still unknown. As a result, addressing such interactions is critical for further risk classification and, eventually, the development of a successful therapeutic plan. In this study, FISH was used to screen for RUNX1 gene alterations in 77 newly diagnosed adult patients with de novo AML, and the results were compared to clinical characteristics and prognosis. Cases positive to RUNX1 abnormalities, translocations

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and amplifications tend to have complex karyotypes. RUNX1 abnormalities were mutually exclusive of NPM1 mutations. RUNX1 deletion was an independent adverse parameter on the DFS. Further trials with larger numbers of RUNX1 abnormal cases are warranted to further highlight the prognostic features and maybe the predictive significance of this abnormality. RUNX1 is an essential transcription factor for normal and malignant hematopoiesis. Germline mutations and somatic alterations (i.e. translocations, mutations and abnormal expression) are frequently associated with acute myeloid leukemia (AML) with RUNX1 mutations conferring unfavorable prognosis. Therefore, RUNX1 constitutes a potential innovative and interesting therapeutic target. Several molecules inhibit the interaction between RUNX1/CBFB and control AML development and progression. BET protein antagonists target RUNX1 (i.e. specific BET inhibitors, BRD4 shRNRA, proteolysis targeting chimeras (PROTAC) or expression-mimickers). All these molecules improve survival in mutant RUNX1 AML preclinical models. A better understanding of RUNX1 function in AML development and progression and its key downstream pathways, may result in more precise and more efficient RUNX1 targeting therapies. At present, many literatures have described that targeted RUNXI therapy can slow down the progression of AML, and the conclusion of this paper is that RUNX1 mutation does not affect prognosis.