G6PD-DEFICIENCY IS ASSOCIATED WITH IMPROVED SURVIVAL IN PATIENTS WITH AML TREATED WITH VENETOCLAX AND AZACITIDINE

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Introduction

G6PD deficiency impairs cellular redox balance through reduced NADPH production and is the most common enzymatic disorder causing anemia. Venetoclax combined with azacitidine targets leukemic stem cells by disrupting oxidative phosphorylation and inducing mitochondrial stress.

Aim

We hypothesized that G6PD deficiency may enhance the efficacy of Ven-Aza in AML by reducing leukemic cell metabolic resilience

Methods

We studied 73 consecutive patients with newly diagnosed (ND) AML treated with Ven-Aza. G6PD activity was systematically assessed at diagnosis in all patients and categorized as normal (n=47), borderline (n=11), or deficient (n=15).

Results

- Composite complete remission rates were 93% in the G6PD deficient group versus 69% in the normal/borderline group (p = 0.03).
- Patients with G6PD deficiency had a significantly longer median OS (23.8 months, 95% CI: 8.9-38.7), as compared to 8.96 months (95% CI: 2.9-15.0) in the normal/borderline group (p=0.034).
- In multivariate analysis, normal G6PD activity was associated with impaired survival as compared to G6PD-deficient patients (HR 3.205, 95% CI: 1.224–8.392, p=0.018). No significant differences were observed across groups in rates of febrile neutropenia, pneumonia, sepsis, or grade 3–4 cytopenia.

Summary

G6PD deficiency is associated with higher response rates and improved survival in patients with ND-AML treated with Ven-Aza.

Discussion

These findings support G6PD deficiency as a potential biomarker of therapeutic sensitivity to Ven-AZA and may uncover metabolic vulnerabilities in AML with potential therapeutic implications.

