

Low-Dose Linperlisib Achieves Rapid Hematological Response in a Patient with Pure Red Cell Aplasia and Moderate-to-Severe Renal Insufficiency: A Case Report

Düşük Doz Linperlisib ile Saf Kırmızı Hücre Aplazisi ve Orta-Ağır Derecede Böbrek Yetmezliği Olan Hastada Hızlı Hematolojik Yanıt Elde Edilmesi: Olgu Sunumu

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To the Editor,

Pure red cell aplasia (PRCA) is a rare hematological disorder characterized by severe anemia, reticulocytopenia, and the absence of erythroid precursors in the bone marrow. First-line therapies, including cyclosporine A (CsA) and corticosteroids, yield variable response rates, with an overall response rate of 74% (95% confidence interval: 66-82) for CsA, yet many patients remain refractory or experience relapse [1]. Recent work by Wang et al. [2] highlighted the efficacy of the phosphoinositide 3-kinase- δ (PI3K δ) inhibitor linperlisib at 80 mg daily in acquired PRCA, achieving transfusion independence within weeks. However, data on linperlisib use in patients with renal impairment are lacking. We report the first case of T-cell large granular lymphocytic leukemia (T-LGLL)-associated PRCA with moderate-to-severe renal insufficiency (creatinine clearance [CrCl]: 30.93 mL/min) successfully treated with low-dose linperlisib at 20 mg daily.

A 70-year-old man with T-LGLL-associated PRCA, diagnosed according to the criteria of the World Health Organization [3] and Chinese expert consensus [4], and chronic hepatitis B developed progressive anemia (hemoglobin [Hb]: 40 g/L) refractory to multiple therapies: CsA (partial response), tacrolimus/prednisone (transient response with nephrotoxicity), sirolimus (no improvement), and cyclophosphamide (hematological decline). Comorbidities included renal insufficiency secondary to tacrolimus treatment (baseline creatinine [Cr]: 166 μ mol/L; CrCl: 30.93 mL/min) and reactivation of the hepatitis B virus (controlled with entecavir). A bone marrow evaluation in February 2025 confirmed persistent erythroid hypoplasia (3.5% erythroid precursors) and clonal CD8⁺ T-cells (TRBC1-restricted, clonal TCR rearrangement, and STAT3 p.D661Y mutation).

Given the limited therapeutic options, linperlisib was initiated at 20 mg daily. Within 1 week, reticulocytes surged from $5.1 \times 10^9/L$ to $134 \times 10^9/L$ (6.32%), followed by a gradual Hb rise from 68 to 92 g/L over 3 weeks without transfusions (Figure 1). The renal function remained stable, with Cr fluctuating within the range of 155 to 163 μ mol/L. Mild bone pain and fatigue resolved spontaneously.

This case underscores two key insights:

1. Dose adjustment in renal impairment: Linperlisib exhibits a pharmacokinetic profile characterized by predominant renal excretion of the unchanged drug via urine, with a minor fraction metabolized hepatically via CYP3A4 and CYP2C8 [5]. In cases of severe renal impairment, reduced drug clearance may necessitate dose reduction to avoid potential accumulation. Notably, clinical trials involving 178 patients reported no renal impairment-related adverse events during treatment [6,7], supporting its safety profile in renal dysfunction. In our case, a reduced dose of 20 mg versus the standard 80 mg achieved therapeutic efficacy without inducing toxicity.
2. Mechanistic relevance: Dysregulated PI3K/AKT/mTOR signaling in PRCA-associated T-cells provides an explanation for targeted inhibition [8,9]. The rapid reticulocyte recovery (1 week) observed with linperlisib in our case mirrors findings from prior studies [2,9] suggesting preserved pharmacodynamic effects even at lower doses.

While previous investigations [2,9] focused on patients with normal renal function, our case demonstrates linperlisib's applicability in severe renal impairment. Further studies are warranted to define optimal dosing and long-term safety in this population.

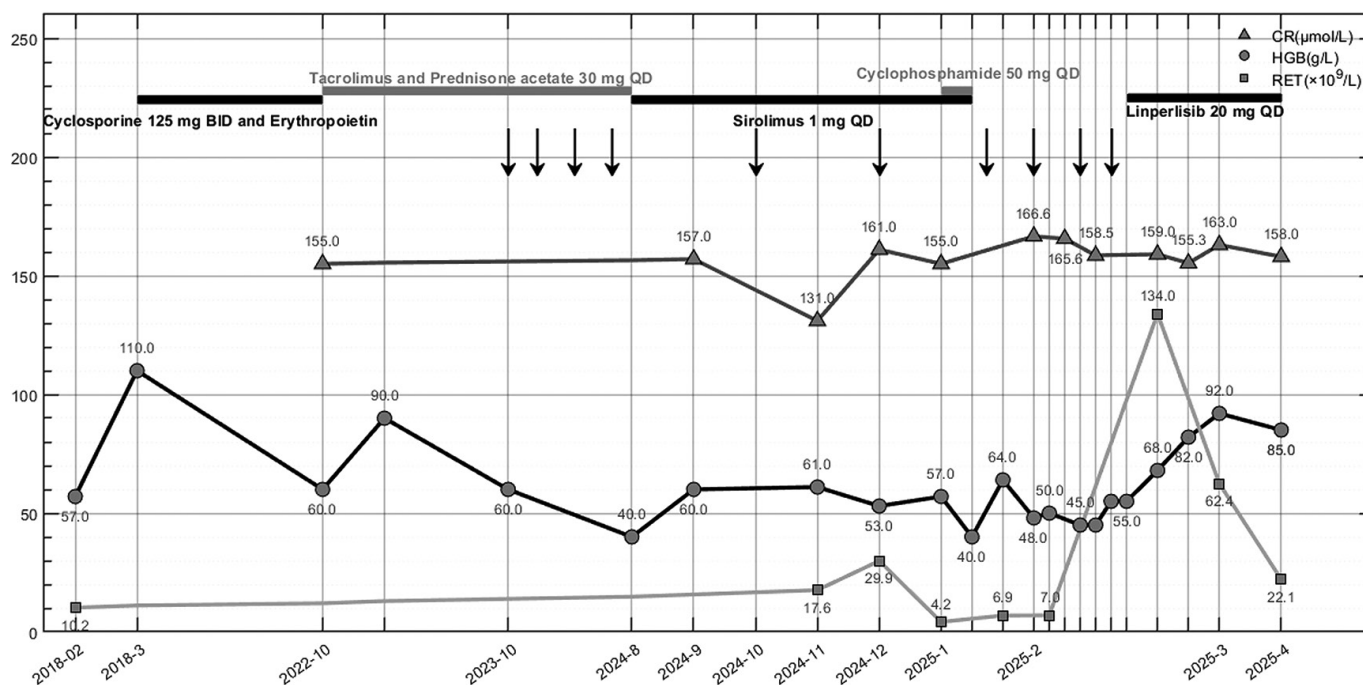


Figure 1. Hemoglobin, reticulocyte, and creatinine trends during linperlisib therapy. The flowchart above the graph shows treatments and downward arrows indicate transfusions.

CR: Creatinine; HGB: hemoglobin; RET: reticulocytes; BID: twice daily; QD: daily.

Keywords: Linperlisib, Pure red cell aplasia, Renal insufficiency

Anahtar Sözcükler: Linperlisib, Pür kırmızı hücre aplazisi, Böbrek yetmezliği

Ethics

Informed Consent: Written informed consent was obtained from the patient for publication.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.C.; Concept: C.L., M.C.; Design: C.L., M.C.; Data Collection and Processing: C.L., M.C.; Analysis or Interpretation: C.L., M.C.; Literature Search: C.L., M.C.; Writing: C.L., M.C.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Received/Geliş tarihi: October 13, 2025
Accepted/Kabul tarihi: December 2, 2025
Epub: December 3, 2025
DOI: 10.4274/tjh.galenos.2025.73745



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