



# Successful Rechallenge of Low-Dose Lenvatinib in a Metastatic Radioactive Iodine-Refractory Papillary Thyroid Cancer Patient with Grade 3 Proteinuria: A Case Report

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## Background:

- Metastatic radioactive iodine (RAI)-refractory papillary thyroid cancer (PTC) presents significant therapeutic challenges due to limited treatment options.
- Lenvatinib, a multi-targeted tyrosine kinase inhibitor, is the standard first-line treatment. In the SELECT trial<sup>1</sup>, lenvatinib is given at a 24 mg daily in 28-day cycles.
- Proteinuria was a commonly reported adverse effect<sup>1</sup> (any grade, 31%; grade ≥3, 10%); see [Table 1](#) for grading of proteinuria by CTCAE version 5.0<sup>2</sup>.

Grading of Proteinuria in CTCAE Version 5.0 <sup>2</sup> (Note: No grade 4/5 in this version)			
Grade	1	2	3
24hr urine protein	≥ Upper limit to <1g	1 to <3.5g	≥3.5g
Urine dipstick	1+	2+/3+	4+

Table 1. Grading for Proteinuria; CTCAE: Common Terminology Criteria for Adverse Events

**Case:** A 78-year-old Chinese male with history of hypertension, diabetes and hyperlipidemia presented with metastatic PTC. He underwent total thyroidectomy and two neck dissections but progressed with multiple lung and lymph node metastases despite two RAI treatments, rendering him RAI-refractory. Lenvatinib 10mg daily was initiated in March 2021.

One year after treatment, he developed Grade 2 proteinuria necessitating multiple treatment suspensions. Losartan was increased to 50mg twice daily (from 25mg daily) since May 2022. Lenvatinib 10mg was resumed when proteinuria returned to Grade 1. His proteinuria later worsened to Grade 3 in October 2022 (24-hour urine protein up to 6.35g/day), thus treatment was further suspended for one month. 24-hour urine protein then improved to 0.8g/day but thyroglobulin level significantly rebound. Lenvatinib was rechallenged at 4mg daily with vigilant monitoring of 24-hour urine protein monthly, the level was stable at ≤1.5g/day. [Figure 1](#) showed timeline of patient's journey.

Other than Grade 3 proteinuria, patient remained asymptomatic, with stable serum creatinine and no signs of nephrotic syndrome throughout. Patient continues lenvatinib 4mg daily, achieving stable disease on serial CTs ([Figure 2](#)), and enjoys good quality of life as of the date of writing.

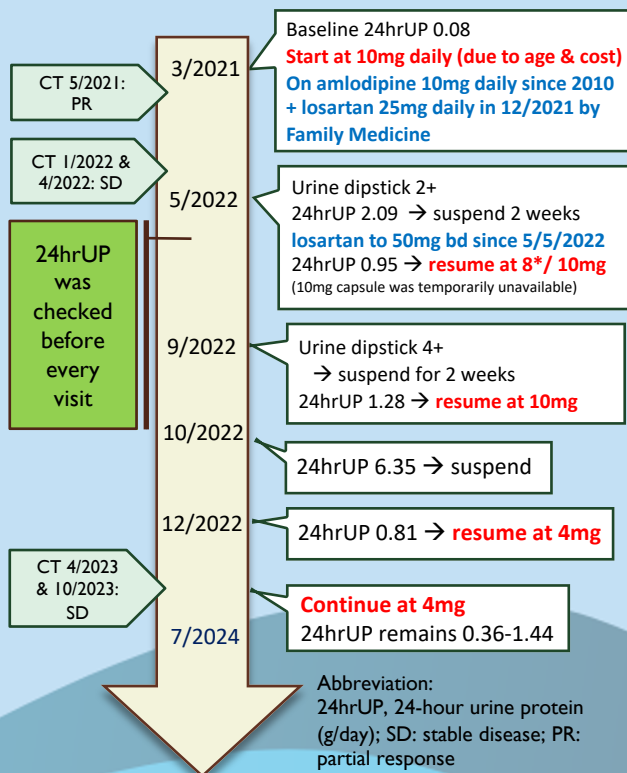


Figure 1. Timeline of patient's journey

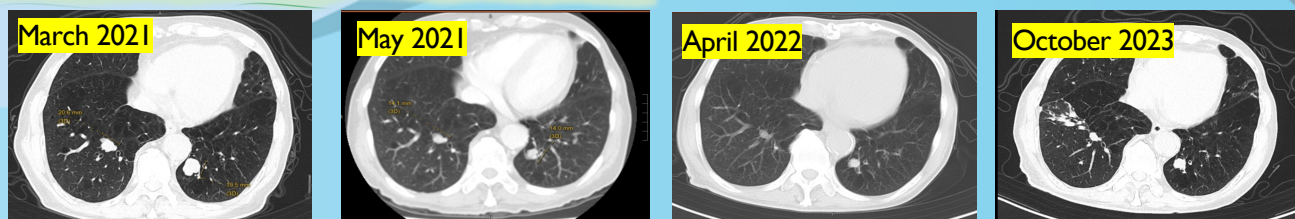


Figure 2. Selected images of index lung metastases on serial reassessment CTs

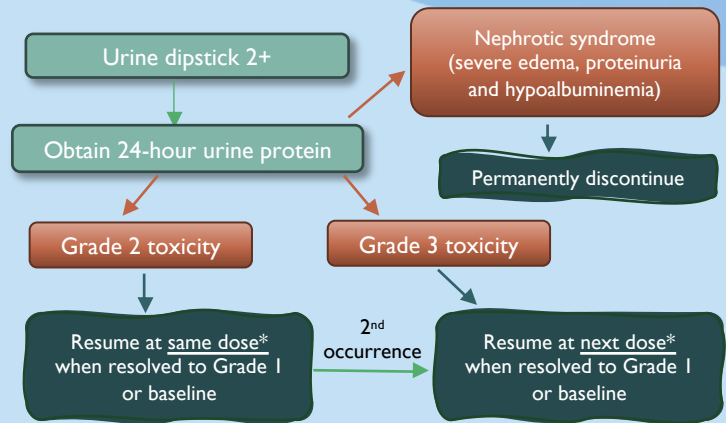


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## Discussion:

In the SELECT trial, proteinuria occurred in 31% of patients, with 10% experiencing Grade 3 or 4 proteinuria. Of those who developed proteinuria, 18.8% required dose interruption or reduction, making it the third most common reason for dose modification after diarrhoea (22.6%) and hypertension (19.9%).

This case demonstrates the management of lenvatinib-induced proteinuria through close clinical monitoring, timely interventions, and dose adjustments. A suggested management strategy is outlined in the accompanying flow chart.



\*Suggested sequential dose reduction: 20mg → 14mg → 10mg daily

Our 78-year-old patient also underscores the importance of managing treatment-related toxicities in elderly patients, and rechallenging at low dose may be a safe alternative in this frail group. In the SELECT trial, 45% of patients were aged 65 or older, and this group showed a trend toward higher rates of severe adverse events and treatment discontinuation (20.8% vs. 13.5%) compared with younger patients<sup>3</sup>. Another retrospective review by Shibutani et al.<sup>4</sup> on thyroid cancer patients with lenvatinib-induced proteinuria also found a higher median age in the high-proteinuria group (Grade 3 or above) compared to the low-proteinuria group (Grade 1-2) ( $p=0.004$ ), with a significantly larger proportion aged 65 years or older ( $p=0.01$ ). Therefore, special care should be taken when managing elderly patients on lenvatinib, balancing the risks and benefits of treatment.

## Conclusion:

Low-dose lenvatinib can be an effective and tolerable therapeutic option for patients with metastatic RAI-refractory PTC who develop significant proteinuria. Rechallenging with dose adjustments and stringent monitoring may facilitate disease control while managing adverse effects, particularly in elderly patients with limited treatment options. This approach allows for continued treatment without compromising safety, which is crucial for maintaining quality of life in this vulnerable population. Further studies are needed to explore optimal dosing strategies for this patient group.

## References

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