Assessment of Lenvatinib Toxicity Profile in Patients with Endometrial Cancer

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Introduction

- The Keynote 775 trial compared pembrolizumab and lenvatinib to chemotherapy alone in patients with endometrial cancer who had previously received platinum-based chemotherapy[1]
- This study noted improved overall survival with lenvatinib and pembrolizumab in both the mismatch repair–proficient (pMMR) subgroup and in the overall population[1]
- This regimen is currently recommended by the National Comprehensive Cancer Network (NCCN) as a category 1 recommendation for patients with recurrent pMMR disease[2]
- Currently, there is a lack of treatment options for second line or subsequent therapy for recurrent endometrial cancer. The regimen of pembrolizumab and lenvatinib is the only category 1 recommendation made by the NCCN in this setting[2]
- Although the study started patients on lenvatinib 20 mg daily, the median tolerated dose was 13.8 mg[1]
- This study aims to characterize the use of lenvatinib and toxicities requiring modifications in therapy in clinical practice

Objectives

- **Primary outcome**: Percentage of patients that require dose adjustments at each initiation dose
- **Secondary outcomes:** Assessment of the starting and ending doses and the toxicities associated with each therapy modification (defined as a dose reduction, hold in therapy, or discontinuation of therapy)

Methods

- Single-center, retrospective chart review
- **Data Collection Points:** Number of therapy modifications (defined as a dose reduction, hold in therapy, or discontinuation of therapy), reason associated with therapy modifications, initiation dose, subsequent dosing, and baseline characterizes (listed in Table 1)

Inclusion Criteria

- Diagnosis of endometrial cancer
- Prescribed lenvatinib by a University Hospitals gynecologic oncologist between July 2021 and August 2023

Results

Table 1. Baseline Characteristics (n = 27)*

Age at initiation - years (IQR)	68 (63.5 – 73.5)
Number of previous therapies (Range)	1 (1-2)
Patient with CrCl > 30 ml/min at initiation	27 (100)
Patients with Child-Pugh C status at initiation	0 (0%)
On antihypertensives at baseline	17 (62)
On thyroid supplementation at baseline	3 (11)

*Expressed as n (%) unless otherwise specified

Figure 1. Patients requiring dose reductions based on initiation doses

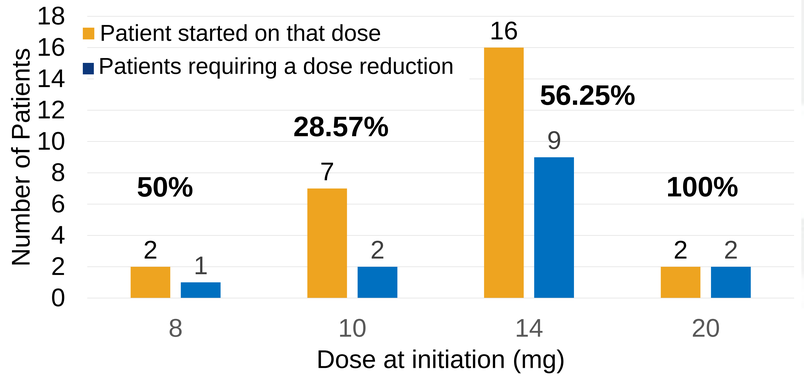
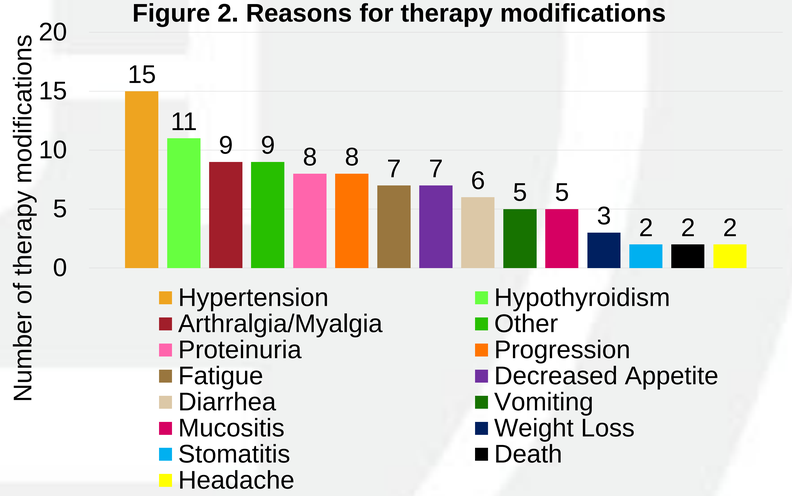


Table 2. Ending Doses Prior to Discontinuation at Each Initiation Dose

Starting Dose (mg)	Median Ending Dose (mg)	Percent Dose Reduction	Median number of therapy modifications
8 (n = 2)	6	25%	3.5
10 (n = 7)	10	0%	0
14 (n = 16)	10	28%	1
20 (n = 2)	9	55%	3

Results (Continued)

Figure 2. Reasons for therapy modifications



Conclusions

- The percentage of patients that required dose reductions increased with larger initiation doses
- The majority of patients were started on 14 mg of lenvatinib
- The most prevalent toxicity requiring a therapy modification was hypertension followed by hypothyroidism

Future Opportunities

- Investigate cost savings to patient/health system opportunities
- Inter-professional collaboration to optimize lenvatinib starting dose prescribing practices

Disclosure/References

1. Makker V, Colombo N, Casado Herráez A, Santin AD, Colomba E, Miller DS, et al; Study 309–KEYNOTE-775 Investigators. Lenvatinib plus Pembrolizumab for Advanced Endometrial Cancer. N Engl J Med. 2022 Feb 3;386(5):437-448.
2. Abu-Rustum N, Yashar C, Arend R, Barber E, Bradley K, Brooks R, et al. Uterine Neoplasms, Version 1.2023, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2023 Feb;21(2):181-209.