RWD20

Clinical and Economic Outcomes Following Treatment for Unresectable or Metastatic Esophageal Cancer

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CONCLUSIONS

- This study highlights a substantial unmet need in the management of advanced unresectable/metastatic EC
- Nearly half of patients identified lacked evidence of treatment with 1L systemic therapy, highlighting a critical gap in care, and those who were treated faced high toxicity, significant costs, and limited survival
- Earlier biomarker testing in the 1L setting may broaden access to more effective and better-tolerated options
- The poor outcomes and high economic burden underscore the need for wider, earlier use of PD-1 inhibitors and other innovative therapies

INTRODUCTION

- Esophageal cancer (EC) is the eighth most common cancer and the sixth leading cause of cancer-related mortality worldwide[1,2]
- Often diagnosed at an advanced stage, EC has high morbidity and mortality, with a 5-year overall survival (OS) <20%[3,4]
- In patients with late-stage disease, systemic therapies, targeted therapies, and immunotherapies (IOs) such as PD-1 inhibitors are used in various combinations[5]
- Recently, PD-1 inhibitor therapies have become central to EC management[6]
- Before the US Food and Drug Administration's 2024 Oncologic Drugs Advisory Committee (ODAC) recommendation to restrict first-line (1L) PD-1 inhibitors in metastatic or unresectable EC to patients, IO could be used in all patients irrespective of PD-L1 status

OBJECTIVE

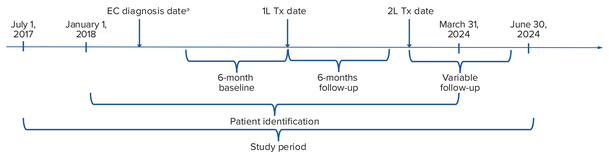
- To examine demographic characteristics, treatment patterns, adverse events (AEs), effectiveness (treatment persistence), and healthcare costs in patients diagnosed with and treated for advanced unresectable/metastatic EC

METHODS

Patient Population and Study Design

- This was a retrospective cohort study using administrative medical and pharmacy claims from the Optum Research Database
- Continuously enrolled adult patients with a diagnosis of EC (*International Statistical Classification of Diseases, 10th Revision* codes C15.3-C15.9) who initiated treatment from January 2018 to March 2024 were identified (**Figure 1**)
- Metastatic cancers were identified by a diagnosis of metastasis on or after the EC diagnosis date. Unresectable cancers were identified by no metastasis and no surgery within 90 days post diagnosis
- Included patients were stratified by line of treatment (LOT), namely 1L or second line (2L), and by mutually exclusive treatment regimens:
  - Chemotherapy: Chemotherapy (platinum or non–platinum based) or chemotherapy and targeted therapy
  - IO combination: Nivolumab and chemotherapy, pembrolizumab and chemotherapy, or pembrolizumab and targeted therapy
  - IO monotherapy: Pembrolizumab or nivolumab
  - Other: Chemotherapy (non–platinum based or no targeted therapy)
- Untreated patients were included in the demographic data only
- Patients were examined for a baseline of 6 months prior to treatment initiation and through follow-up, which ended at disenrollment, death, end of the study period (June 2024), or initiation of next LOT

Figure 1. Study Design



[a]Evaluation of metastases took place in the 90 days following EC diagnosis date.
Abbreviations: 1L, first line; 2L, second line; EC, esophageal cancer; Tx, treatment.

Demographic Characteristics, Treatment Patterns, Clinical Outcomes, and Healthcare Costs

- Patient demographics, clinical characteristics, treatment patterns, and clinical outcomes were examined descriptively
- The most common AEs included anemia, nausea, neutropenia, dehydration, and peripheral neuropathy
- Treatment persistence was measured from treatment initiation to end of treatment (initiation of new treatment regimen, end of continuous enrollment, disenrollment from the plan, end of the study period, or death). It was evaluated using a Cox proportional hazards model adjusted for regimen, EC type, demographics, tumor location, comorbidities, biomarker testing, smoking status, and baseline EC-related healthcare resource utilization
- All-cause and EC-related healthcare costs were calculated on a per-patient per-month (PPPM) basis

RESULTS

Study Population

- A total of 2551 patients met the inclusion criteria; of these, 1158 remained untreated
- Among treated patients, 1393 received 1L therapy and 458 went on to receive 2L therapy

Demographic Characteristics

- Patients who were receiving 1L or 2L treatment or were untreated had a mean (SD) age of 69.8 (9.2) years, 69.0 (8.8) years, and 72.4 (9.4) years, respectively; were primarily male; and identified as non-Hispanic White

Table 1. Demographic Characteristics

1L	Total (n=1393)	Chemotherapy (n=1063)	IO combination (n=193)	IO monotherapy (n=72)	Other regimen (n=65)
Age, years					
Mean (SD)	69.8 (9.2)	70.0 (8.9)	67.5 (10.0)	69.8 (10.5)	73.1 (8.0)
Sex, n (%)					
Male	1104 (79.3)	839 (78.9)	164 (85.0)	53 (73.6)	48 (73.9)
Race and ethnicity, n (%)					
White	1075 (77.2)	817 (76.9)	153 (79.3)	56 (77.8)	49 (75.4)
Black	129 (9.3)	102 (9.6)	10 (5.2)	10 (13.9)	7 (10.8)
Hispanic	72 (5.2)	54 (5.1)	12 (6.2)	n<5	n<5
Asian	32 (2.3)	25 (2.4)	n<5	n<5	n<5
Unknown/ uncoded	24 (1.7)	18 (1.7)	n<5	n<5	n<5
No SES data	61 (4.4)	47 (4.4)	11 (5.7)	n<5	n<5

2L	Total (n=458)	Chemotherapy (n=145)	IO combination (n=76)	IO monotherapy (n=126)	Other regimen (n=111)
Age, years					
Mean (SD)	69.0 (8.8)	69.3 (7.9)	67.1 (8.7)	69.6 (8.6)	69.1 (10.1)
Sex, n (%)					
Male	377 (82.3)	123 (84.8)	62 (81.6)	97 (77.0)	95 (85.6)
Race and ethnicity, n (%)					
White	355 (77.5)	110 (75.9)	61 (80.3)	99 (78.6)	85 (76.6)
Black	43 (9.4)	17 (11.7)	7 (9.2)	9 (7.1)	10 (9.0)
Hispanic	26 (5.7)	9 (6.2)	n<5	9 (7.1)	5 (4.5)
Asian	16 (3.5)	5 (3.5)	n<5	n<5	7 (6.3)
Unknown/ uncoded	7 (1.5)	n<5	n<5	n<5	n<5
No SES data	11 (2.4)	n<5	n<5	7 (5.6)	n<5

Abbreviations: 1L, first line; 2L, second line; IO, immunotherapy; SES, socioeconomic status.

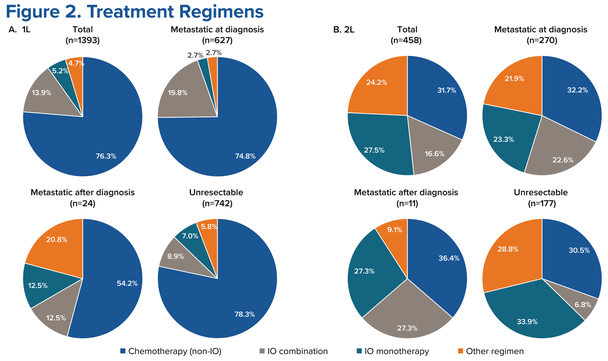
Diagnostic Testing

- For 1L and 2L, 50.0% and 58.5% of patients, respectively, had biomarker testing at baseline or follow-up
- As a result of the low rate of testing, it is unknown what proportion of patients may be likely to benefit from IO

Treatment Patterns

- For 1L, the majority of patients (76.3%) received chemotherapy without IO; IO combination regimens were more common among patients with metastatic disease at diagnosis (19.8%) vs unresectable disease (8.9%) (**Figure 2**)
- 2L treatment patterns were more diverse (**Figure 2**)

Figure 2. Treatment Regimens

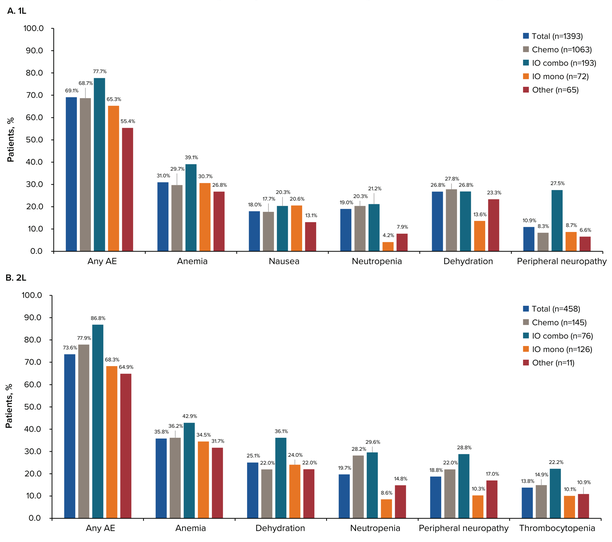


Abbreviations: 1L, first line; 2L, second line; IO, immunotherapy.

AEs

- During 1L, 69.1% of patients reported at least one AE; the rate of AEs was highest in patients receiving IO combination regimens (77.7%) (**Figure 3**)
- The rate of AEs increased in 2L, with 73.6% of patients reporting at least one AE during 2L therapy;the rate of AEs was highest in patients who received IO combination regimens during 2L (86.8%) (**Figure 3**)
- The rates of hematologic AEs were highest with IO combination regimens, underscoring the need for supportive care and proactive management

Figure 3. Most Commonly Reported AEs by Treatment Regimen

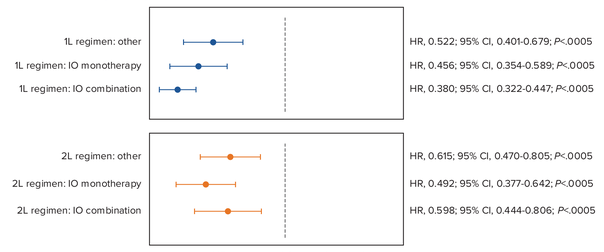


Abbreviations: 1L, first line; 2L, second line; AE, adverse event; IO, immunotherapy.

Length of Treatment

- Among the patients that met the inclusion criteria, 1158 (45.5%) were untreated
- In 1L, compared with chemotherapy, all other regimens were associated with a significantly lower hazard for end of treatment, suggesting longer time on treatment (**Figure 4**)
- In 2L, compared with chemotherapy, all other regimens were associated with a significantly lower hazard for end of treatment, suggesting longer time on treatment (**Figure 4**)

Figure 4. Cox Proportional Hazards Model for Length of Treatment in 1L and 2L by Regimen[a]

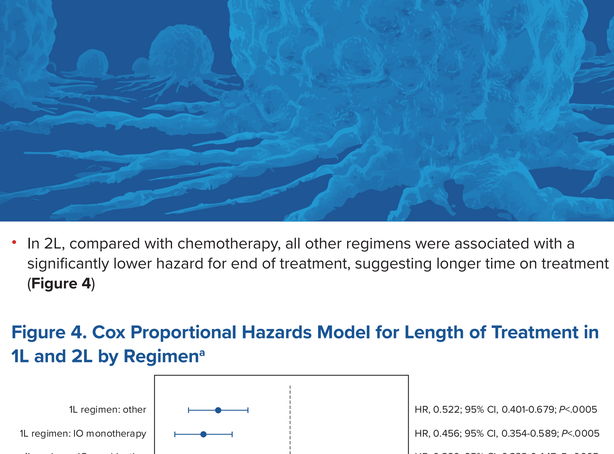


[a]Differences in hazard for end of treatment across regimens should be interpreted with caution. These differences may reflect regimen-specific recommended treatment durations rather than patient persistence alone. For example, guidelines indicate that chemotherapy regimens are typically limited to approximately 18 weeks, whereas IO-based regimens may continue for up to 2 years. Therefore, lower HRs for IO regimens likely correspond to longer expected treatment durations inherent to these protocols.
Abbreviations: 1L, first line; 2L, second line; HR, hazard ratio; IO, immunotherapy.

Healthcare Costs

- Mean all-cause total PPPM costs increased with active therapy, rising from $3654 at baseline to $13,182 during 1L and $12,663 during 2L (**Figure 5**)
- Ambulatory costs were the principal drivers of medical costs. Pharmacy costs were generally modest compared with medical costs
- IO-based regimens were associated with high ambulatory and total costs, potentially reflecting longer treatment durations and more intensive monitoring

Figure 5. Healthcare Costs by Treatment Regimen During Follow-up



[a]All medical costs not already classified into the main healthcare resource utilization categories.
Abbreviations: 1L, first line; 2L, second line; ER, emergency room; IO, immunotherapy.

LIMITATIONS

- The study findings may not be generalizable to uninsured patients or individuals outside of the US insurance system
- Diagnostic and procedural information was derived from secondary-use administrative claims data, which were recorded for the purposes of reimbursement; therefore, identification of patients and AEs may have been subject to incomplete and/or miscoded claims

REFERENCES

1. Schizas D, et al. *J Transl Int Med.* 2018;6(2):70-73.
2. Torre LA, et al. *CA Cancer J Clin.* 2015;65(2):87-108.
3. Deng J, et al. *Medicine.* 2020;99:99.
4. Fan J, et al. *Cancer Med.* 2020;9(18):e03338.
5. Hirano H, et al. *Jpn J Clin Oncol.* 2019;49(5):412-420.
6. Sano M, et al. *Expert Rev Gastroenterol Hepatol.* 2026;20(4):325-334.

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DISCLOSURES

LD: Employment and stock: BeOne Medicines, Ltd.

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