Real-world Transition Probability Analyses Of Unresectable Locally Advanced (LA) Esophageal/Gastroesophageal Junction Cancer (EC/GEJC) Patients Treated With Definitive Chemoradiotherapy (dCRT) At Community Oncology Centers

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Background

- dCRT is a guideline-recommended treatment for patients with unresectable EC/GEJC who are ineligible for surgery.[1]
- Despite treatment advancements, survival outcomes for patients with dCRT are poor and disease recurrence is common.[2] Data indicates a 5-year recurrence rate of up to 45%. Among patients with locoregional recurrence, 5-year overall survival (OS) from detection of recurrence was 29%.[3]
- Health state transition probability estimates the likelihood of patients moving between clinical states over time and is often applied in cost-effectiveness analyses to evaluate treatment interventions.[4] There is limited data on transition probabilities based on real-world treatment patterns of patients treated with dCRT.
- Using real world electronic health record data (EHR), this study aimed to evaluate health state transition probabilities between different states and recurrence and mortality outcomes among EC/GECJ patients treated with dCRT.

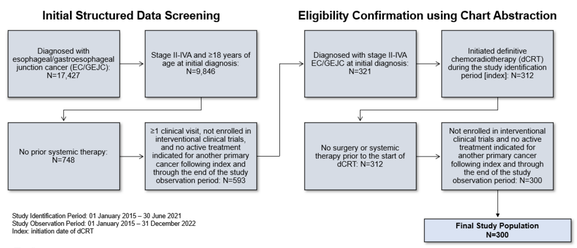
Objective

To evaluate transition probabilities from various pre-defined health states for patients with locally advanced unresectable EC/GEJC treated with dCRT in the United States (US) community oncology setting.

Methods

- **Study Design:** Retrospective observational cohort study
- **Data Source:** Structured and chart abstraction data sourced from iKnowMed, an oncology-specific EHR system which captures outpatient practice encounter histories for patients seen in The US Oncology Network.
- **Study Population:** Adult patients diagnosed with locally advanced, unresectable EC/GEJC who initiated dCRT between January 1, 2015 – June 30, 2021 (see **Figure 1**)
  - The initiation date of dCRT was considered the index date
  - Patients were followed through last patient record or death on/before December 31, 2022
- **Health State Definitions and Transition Probability Estimation:**
  - Event-Free (EF): All patients were considered EF at the start of dCRT prior to the occurrence of any subsequent health state event.
  - Locoregional progression (LRP): A LRP event was defined by documented locoregional disease recurrence or progression after the initiation of dCRT.
  - Distant metastasis (DM): A DM event was defined by documentation of metastatic disease beyond the primary site or regional nodes.
  - Death: Documentation of a death after the initiation of dCRT.
  - Transition probabilities were estimated for each of the following states: EF to LRP, EF to DM, EF to Death, LRP to DM, LRP to Death, and DM to Death
- **Statistical Analyses:**
  - Descriptive analyses were performed to summarize baseline demographics and clinical characteristics.
  - For each transition survival model, a binary variable indicated whether a patient experienced the transition, and a continuous variable recorded the time to event (weeks). The time-to-event data were analyzed by using the Kaplan-Meier method. An exponential model was fit to the time-to-event data, which informed the transition probabilities between states to produce model parameters (i.e., exponential rate and standard errors).
  - Patients without events were censored at the last contact date; those who experienced multiple health state events were counted once in the model starting at the most severe event state and otherwise censored for competing risks.

Figure 1. Study Attrition Diagram



References

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4.Cao X, Zhang M, Li N, Zheng B, Liu M, Song X, Cai H. First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma: a cost-effectiveness analysis. Ther Adv Med Oncol. 2023 May 16;15:17588359231171038. doi: 10.1177/17588359231171038.

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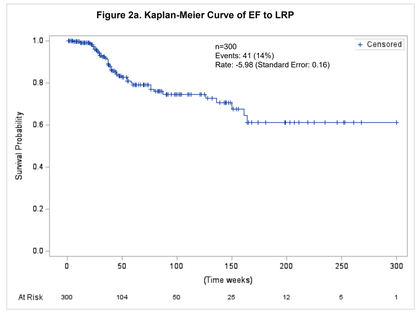
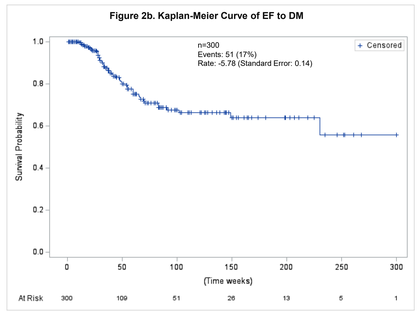
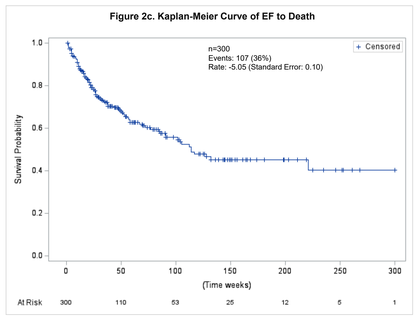
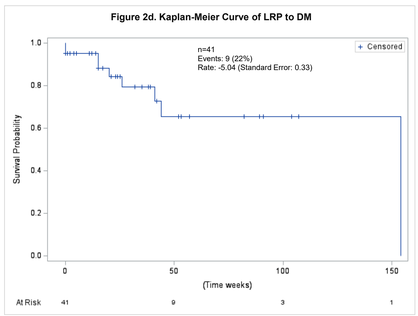
Results

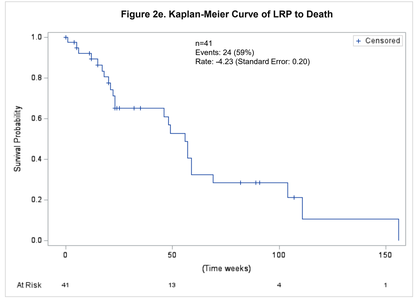
Figure 2a-2f. Kaplan-Meier Curve of Time-To-Event Health State Transitions (EF to LRP, EF to DM, EF to Death, LRP to DM, LRP to Death, DM to Death)











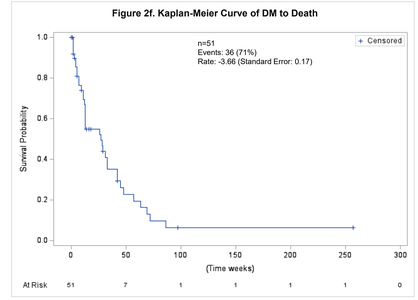


Table 1. Summary of Transition Probability Models Parameters

Health States	Events	Exponential Rate (log)	Standard Error
Transition from EF State (n = 300)			
EF to LRP	LRP = 41 (14%)	-5.98	0.16
EF to DM	DM = 51 (17%)	-5.78	0.14
EF to Death	Death = 107 (36%)	-5.05	0.10
Transition from LRP State (n = 41)			
LRP to DM	DM = 9 (22%)	-5.04	0.33
LRP to Death	Death = 24 (59%)	-4.23	0.20
Transition from DM State (n = 51)			
DM to Death	Death = 36 (71%)	-3.66	0.17

Table 2. Baseline Characteristics

	Overall (n=300)
Median follow-up time, months (IQR)	10.5 (4.0,21.0)
Median age at index, years (IQR)	73 (64,80)
Sex (Male) – n (%)	223 (74.3%)
Race – n (%)	
Black/African American	19 (6.3%)
White/Caucasian	221 (73.7%)
Other	8 (2.7%)
Not documented	52 (17.3%)
Stage at initial diagnosis – n (%)[a]	
Stage II	104 (34.7%)
Stage III	167 (55.7%)
Stage IVA	16 (5.3%)
Not documented	13 (4.3%)
Baseline ECOG performance status – n (%)	
0/1	190 (75.7%)
≥ 2	61 (24.3%)
Histology at diagnosis – n (%)	
Adenocarcinoma	159 (53.0%)
Squamous Cell	116 (38.7%)
Other	25 (8.3%)
Esophageal (vs. GEJ) Tumor – n (%)	212 (70.7%)

ECOG = Eastern Cooperative Oncology Group, IQR = interquartile range.
[a]Those without a documented stage had a documented TNM that met the inclusion criteria.

Summary of Results

- By definition, all 300 patients in this analysis started at the EF state (**Table 1; Figures 2a-2c**).
- A majority of patients were male (74.3%) , diagnosed at Stage III (55.7%), and had esophageal tumors (70.7%); median age in the study population was 73 years at diagnosis and median follow-up time was 10.5 months overall (**Table 2**).
- Starting from the EF state, 41(14%) experienced LRP, 51 patients experienced DM (17%), and there were 107 (36%) death events (**Table 1; Figures 2a-2c**).
  - From the LRP state, there were 9 (22%) DM and 24 (59%) death events, respectively (**Table 1; Figures 2d-2e**).
  - From the DM state, there were 36 (71%) death events (**Table 1; Figure 2f**).
- Kaplan-Meier curves illustrated progressive declines in survival, with the highest rate from DM to Death.

Limitations

- This study utilized an oncology-specific EHR system that captures outpatient encounters for patients receiving treatment within The US Oncology Network practices. It is not used to collect data for research purposes but for clinical practice reasons.
- Treatment administered in academic hospitals or oncology centers outside of this data source is not reflected in this analysis. There may also be differences in how tumor progression is documented at a practice-level.
- Additionally, with a small patient sample, results from this study may not be generalizable to all patients.
- Event counts were smaller in some models so the transition probabilities presented here should be utilized with caution. Transition probabilities were based on an exponential survival model, and alternative models were not examined for potentially better fits for the data.

Conclusion

- This real-world study demonstrated that the hazard of death increases as patients progress through health states, emphasizing the importance of delaying recurrence.
- Health state transition probabilities from this analysis were intended to fill an important research gap as they were derived from real-world treatment patterns instead of tightly controlled clinical trials.
- These findings emphasize an unmet need for more early-stage therapies, given high recurrence rates and improved survival with delayed disease progression.

Disclosures

LW, AD, and SB are employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA (MSD). HL, JS, JM, and GP are employees of Ontada. SN is an employee of the Rocky Mountain Cancer Centers, an affiliate practice within The US Oncology Network.

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