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Real-world treatment drop-off among recurrent or metastatic cervical cancer patients: A US community oncology-based analysis

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HIGHLIGHTS

- > 50% of the patients with r/mCC did not go onto another line of therapy following 1L
- Additional novel therapies are needed in subsequent treatment to address the significant unmet needs of patients with r/mCC
- The key to maximizing treatment outcomes will be generating more clinical data informing optimized sequencing

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ABSTRACT

Objective. Understanding real-world treatment patterns and proportions of eligible patients in each line of treatment is imperative to inform future clinical trial designs and multi-line treatment algorithm development.

Methods. We conducted a retrospective observational cohort study of adult women who received first-line (1 L) therapy for r/mCC between 01 September 2014 and 31 December 2019, using The US Oncology Network electronic health records and chart review data. Patients were followed to 31 December 2020. Patient demographic and clinical characteristics, treatment patterns, and clinical outcomes were assessed descriptively.

Results. A total of 262 patients with r/mCC met study inclusion criteria (mean age = 53 years). The majority of patients in 1 L received platinum-based chemotherapy doublet plus bevacizumab (66%) or chemotherapy doublet alone (24%). Nearly half the patients (48%) completing 1 L received 2 L therapy. Among these patients, there was no consistent 2 L treatment of choice. Overall median time to treatment discontinuation was 3.5 months from 1 L treatment initiation, and median overall treatment-free interval was 2.1 months from 1 L discontinuation. Besides elevated serum creatinine, abnormal BMI indicated a directional trend for lower likelihood of receiving 2 L. Other predictors may include no prior bevacizumab, worse ECOG, and earlier disease prevention.

Conclusions. >50% of the patients who initiated 1 L treatment did not receive 2 L therapy, highlighting the need for novel and effective treatment options. As the treatment landscape continues to evolve, we anticipate that more patients will live longer with more treatment options across multiple lines of therapies in the r/mCC setting.

1. Introduction

In 2022, an estimated 14,100 new cases of invasive cervical cancer will occur in the United States, and an estimated 4280 women will die from the disease [1]. Up to 16% of women with cervical cancer present at the metastatic stage, a setting historically characterized by limited treatment options and poor disease prognosis [2]. Even among women presenting with an earlier stage at diagnosis, up to 61% have

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been reported to develop metastatic cervical cancer within the first 2 years of completion of therapy [3].

Cytotoxic chemotherapy agents have been used to treat patients with recurrent or metastatic cervical cancer (r/mCC) progressing on first-line (1 L) systemic therapy, but these agents are characterized by low response rates and survival outcomes [4–9]. In recent years, however, the r/mCC treatment landscape has been evolving, with novel therapeutic options emerging in both the previously treated and untreated r/mCC settings [10–13].

Pembrolizumab monotherapy was granted accelerated approval in June 2018 for previously treated patients with r/mCC whose tumors express PD-L1 (Combined Positive Score [CPS] ≥1) [14]. The Food and Drug Administration (FDA) subsequently granted pembrolizumab regular approval in October 2021 for use in combination with chemotherapy ± bevacizumab for patients with PD-L1 expression in the 1 L setting [15]. Also, in September 2021, tisotumab vedotin-tftv, an antibody-drug conjugate directed to tissue factor, received FDA accelerated approval for treatment of adult patients with r/mCC who experienced disease progression on or after chemotherapy [16]. In addition to r/mCC, there are ongoing development activities in the locally advanced cervical cancer setting, such as the CALLA trial of durvalumab [17], and the ENGOT-cx11/KEYNOTE-A18 trial of pembrolizumab, both exploring the addition of immunotherapy to chemoradiotherapy [18]. At the time of this manuscript, CALLA has reported not meeting its primary endpoint of superior progression-free survival.

After almost a decade of very limited advancement in treatment options, the therapeutic landscape for advanced cervical cancer has been, and continues to be rapidly evolving. Thus, contemporary data on treatment receipt following progression on systemic therapy is needed to provide a baseline of current real-world practice patterns. These data may also help enable assessment of the impact of new agents becoming available as well as informing development of emerging therapies to address the most urgent unmet needs. While we had previously published findings from analyses from The US Oncology Network to understand treatment patterns and outcomes among r/mCC patients who received at least two lines of therapy [19], the present study estimated the real-world proportion of patients with r/mCC who received 2 L treatment following progression from 1 L using more recent data. We also investigated patient factors associated with receipt of 2 L therapy, prior to the anticipated landscape change.

2. Materials and methods

2.1. Study design and data sources

This is an observational study of adult women with r/mCC who initiated 1 L systemic therapy within The US Oncology Network between 01 September 2014 (after FDA's August 2014 approval of bevacizumab in advanced cervical cancer) and 31 December 2019, with follow-up through 31 December 2020. The US Oncology Network is affiliated with approximately 1400 physicians in >500 sites of care across 40 states in the United States, representing approximately 12% of US patients newly diagnosed with cancer [20].

Data were obtained via programmatic database abstraction of The US Oncology Network iKnowMed (iKM) electronic health record (EHR) system and supplemented with chart review. Vital status was confirmed with data from the Limited Access Death Master File. iKM captures outpatient practice encounter histories for patients under community-based care, including but not limited to patient demographics, clinical information such as disease diagnosis, diagnosis stages, performance status information, and laboratory testing results, and treatment information, such as line of therapy and treatment administrations within practices within The US Oncology Network practices that utilize iKM.

2.2. Eligibility criteria

Patients eligible for the study were female patients 18 years of age or older at first documented diagnosis of cervical cancer who received systemic treatment indicated for cervical cancer beyond recorded chemoradiation, neoadjuvant, or adjuvant therapy. They also had to have at least two visits within The US Oncology Network during the study period (between 01 September 2014 and 31 December 2020). Eligible patients had to either have received their diagnosis, have evidence of r/mCC, or have initiated the first systemic treatment for cervical cancer from 01 September 2014 through 31 December 2019, as well as have received 1 L systemic treatment for r/mCC following their diagnosis. Patients were excluded from the study if they did not receive any treatment consistent with r/mCC.

Patients were considered to have metastatic disease if they had distant metastases or disseminated disease from the initial/primary site of diagnosis, as documented in the structured data (physician-entered) and confirmed via chart review (as documented in progress notes, scan reports, or pathology reports). Patients were considered to have locally recurrent disease if they had a diagnosis of locally advanced disease and had received prior curative local therapies (surgery, radiation therapy), but their disease had become incurable to these therapies (based on physician assessment/discretion). Locally advanced disease diagnosis was ascertained during chart review (as documented in progress notes, scan reports, or pathology reports). The documented stage of disease was also collected.

2.3. Outcomes of interest

Baseline patient demographic and clinical characteristics, treatment patterns, and prior medical procedures were assessed descriptively. Patient distribution by treatment regimens and line of therapy including 1 L and 2 L were assessed. Outcomes of interest included proportion of patients initiating subsequent therapy following progression on prior systemic therapy, treatment-free interval (TFI) between 1 L and 2 L, and time to discontinuation (TTD) from 1 L treatment initiation, as well as predictors of 2 L receipt.

Categorization of therapy sequences across lines of therapy for r/mCC within The US Oncology Network has previously been described [19]. Briefly, programmatic logic was applied to categorize therapy sequences across lines of therapy based on start and stop dates as well as the predefined line-of-therapy indicator in iKM. Reasons for discontinuation of treatment and initiation of subsequent therapy were documented as recorded in patient charts. Disease progression as the reason for initiation was considered as an advancement in line of therapy.

TFI was defined as the duration between discontinuation of 1 L treatment and start of 2 L treatment. TTD was defined as the interval between the dates of 1 L treatment initiation and discontinuation of all therapies administered within 1 L after removing patients who were lost to follow up ($n = 25$), in ongoing 1 L treatment ($n = 3$), or had neuroendocrine carcinoma ($n = 1$). Patients who discontinued therapy, died, were referred to hospice care, or started the next line of therapy or had a > 60-day gap from last administration date and last follow-up visit date were considered as discontinuation events.

Prognostic factors associated with receiving 2 L therapy were first assessed in a univariate model, including age, race, BMI, region, FIGO stage, Eastern Cooperative Oncology Group (ECOG) performance status (PS), histology, metastatic stage, number of metastatic sites, bevacizumab exposure in 1 L, any prior treatment, numbers and size of metastases, serum creatinine, comorbidities, and adverse events. We included covariates with OR ≤ 0.8 or OR ≥ 1.5 in the univariate model for final analysis in the multivariable model, as well as those considered clinically relevant [21–27].

2.4. Statistical analysis

Descriptive analyses were conducted to assess demographic, clinical, and treatment characteristics for patients initiating systemic treatment Kaplan–Meier curves were constructed to illustrate time-to-event outcome estimates, i.e., TFI and TTD, with medians and 95% CIs for the overall study population and stratified by 2 L treatment. An alpha level of <0.05 was the primary criterion for statistical significance in this study. The analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC), and R 4.0.3 (R Core Team, 2018) with the *survminer* (v0.4.9) package [28].

3. Results

3.1. Demographic and clinical characteristics

A total of 262 female patients who received systemic treatment in the r/mCC setting met eligibility criteria (Fig. 1). The mean age at 1 L treatment initiation (index) of study participants was 53 years. Most patients had BMI in the normal (32.4%) or overweight/obese (22.5%, 29%) category.

At initiation of systemic therapy, over half (54.6%) of patients had an ECOG PS ≤1. A significant proportion of patients presented with local/

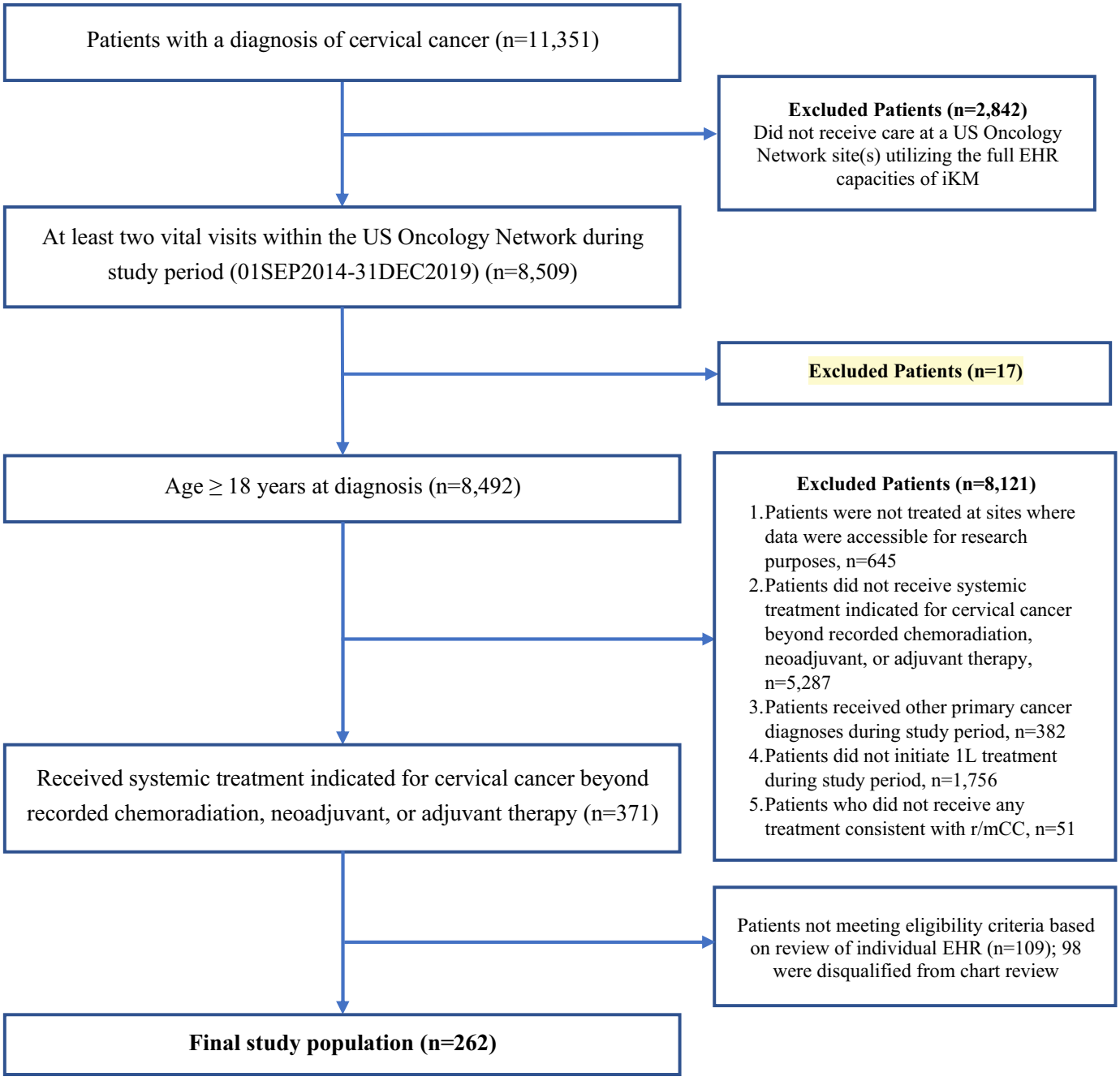


Fig. 1. Patients initiating 1 L r/mCC therapy within The US Oncology Network, 2014–2019.
EHR, electronic health record; iKM, iKnowMed.

regional disease at initial diagnosis including FIGO stages II (B) - IV (A) (43.1%), and most patients ($n = 189$, 72.1%) had undergone prior radiotherapy or surgery (Table 1). Histology subgroup distribution was generally reflective of those reported in the literature for cervical malignancies [4,29]. PD-L1 status was poorly documented (79.0% undocumented), although there is a growing trend towards PD-L1 documentation. In the present study, a higher degree of undocumented PD-L1 was observed before 2018 (89%), when pembrolizumab was approved for r/mCC, than after (65%, p-value<0.05).

Table 1
Selected baseline demographic and clinical characteristics of patients with recurrent or metastatic cervical cancer initiating 1 L therapy.

Variable	Overall
Total patient count	262
Age at index, years	
Mean (SD)	53.0 (12.8)
Age category at index, n (%)	
≤ 40 years	57 (21.8)
41–55 years	101 (38.6)
> 55 years	104 (39.7)
Practice region, n (%)	
West	144 (55.0)
South	74 (28.2)
Midwest	42 (16.0)
Northeast	2 (0.8)
BMI at baseline (categorical), n (%)	
Underweight (BMI < 18.5 kg/m^2)	22 (8.4)
Normal (BMI < 18.5–24.9 kg/m^2)	85 (32.4)
Overweight (BMI 25–29.9 kg/m^2)	59 (22.5)
Obese (BMI ≥ 30 kg/m^2)	76 (29.0)
Not documented	20 (7.6)
ECOG PS at baseline (grouped), n (%)	
0–1	143 (54.6)
2+	34 (13.0)
Not documented	85 (32.4)
FIGO stage (grouped), n (%)	
0 - II (A)	77 (29.4)
II (B) - IV (A)	113 (43.1)
IV (B)	57 (21.8)
IV (NOS)	7 (2.7)
Not documented	8 (3.1)
Histology, n (%)	
Squamous cell carcinoma	179 (68.3)
Adenocarcinoma	61 (23.3)
Adenosquamous	10 (3.8)
Small cell carcinoma	6 (2.3)
Undifferentiated/poorly differentiated carcinoma	3 (1.1)
Glassy cell carcinoma	2 (0.8)
Neuroendocrine carcinoma	1 (0.4)
Patients with any treatment prior to index, n (%)	189 (72.1)
Radiotherapy prior to index, n (%)	166 (63.4)
Surgical resection prior to index, n (%)	97 (37.0)
Metastatic status and sites at 1 L initiation, n (%)	
Any metastasis	
Hematogenous metastases	57 (21.8)
Lymphatic and Hematogenous metastases	102 (38.9)
Lymphatic metastases	79 (30.2)
Local recurrence only	13 (5.0)
Site not specified	11 (4.2)
Number of metastatic sites, n (%)	
0	13 (5.0)
1	87 (33.2)
2+	162 (61.8)
Serum creatinine result [30], n (%)	
Low (< 0.59 mg/dL)	14 (5.3)
Normal (0.59–1.04 mg/dL)	140 (53.4)
Elevated (> 1.04 mg/dL)	57 (21.8)
Not documented	51 (19.5)

BMI, body mass index; ECOG PS, Eastern Cooperative Oncology Group performance status; FIGO, International Federation of Gynecology and Obstetrics; IQR, interquartile ratio; NOS, not otherwise specified; PD-L1, programmed death ligand-1; SD, standard deviation.

3.2. Treatment patterns

In the 1 L setting, the majority of patients ($N = 236$, 90%) received platinum-based chemotherapy doublet ± bevacizumab (66.4% chemotherapy doublet + bevacizumab, 23.7% chemotherapy doublet). Of the patients who completed 1 L treatment, slightly fewer than half received 2 L treatment during the study observation period ($N = 125$, 47.7%) (Fig. 2).

Among the 125 patients who received 2 L treatment, there was no consistent treatment of choice. Common treatments utilized in this setting included other single-agent chemotherapy ($N = 40$, 32.0%), combination therapy ($N = 39$, 31.2%), and pembrolizumab monotherapy ($N = 35$, 28.0%), besides less common choices of bevacizumab monotherapy ($N = 5$, 4.0%) or randomized controlled trial (RCT) agents ($N = 6$, 4.8%). Of the patients who did not initiate 2 L treatment in the study observational period, 55 (23%) patients died after completing 1 L, 31(13%) patients who progressed on 1 L did not receive 2 L treatment at a median follow-up of 12.6 months (95% CI: 6.9–19.7), and 23 (9.7%) patients completed 1 L without documentation of progression.

3.3. Clinical outcomes

From initiation of 1 L treatment, the overall median TTD of the last dose of 1 L regimen was 3.5 months (95% CI: 3.5–3.7), with patients receiving chemotherapy doublet plus bevacizumab having a numerically longer median TTD (3.5 months; 95% CI: 3.5–3.8) compared with chemotherapy doublet alone (3.0 months; 95% CI: 2.2–3.8) (Fig. 3A).

From end of 1 L treatment to 2 L initiation, the median overall TFI was 2.1 months (95% CI 1.6–3.3). Patients who received pembrolizumab (2.7 months; 95% CI: 1.9–5.5) or RCT agents (4.5 months; 95% CI: 2.1-NR) in 2 L had numerically longer median TFI, compared with patients receiving other combo (1.2 months; 95% CI: 0.5–4.9) or mono chemotherapy (2.1 months; 95% CI: 1.4–4.9) as 2 L therapy (Fig. 3B).

3.4. Prognostic factors of receiving 2 L treatment

Table 2 shows the results of logistic regression analyses to assess prognostic factors for patients who did not receive 2 L treatment. Elevated serum creatinine was the only statistically significant prognostic factor, where patients who did not initiate 2 L were more likely to have an elevated serum creatinine (>1.04 mg/dL) [30] (OR = 3.04, 95% CI: 1.13–8.22). Directional trends were observed for abnormal BMI (underweight BMI < 18.5, or overweight BMI > 24.9), no prior bevacizumab exposure as part of 1 L treatment, worse ECOG performance status (score ≥ 2), and earlier disease presentation (FIGO 0-IIA).

4. Discussion

Findings from this retrospective observational cohort study confirmed that the majority of patients with r/mCC received current standard of care in 1 L treatment within the US Oncology Network. However, slightly fewer than half of these patients went on to receive 2 L therapy, and there was no clear single choice of therapy. Real-world patients receiving chemotherapy doublet plus bevacizumab had a longer median TTD vs. chemotherapy doublet alone, consistent with longer duration of treatment for triplet vs doublet therapy in the GOG 240 trial. Patients receiving 2 L chemotherapy had the numerically shortest TFI, which suggests chemotherapy remains the salvage therapy of choice for patients requiring 2 L treatment within a short period of time, such as those who progressed on or shortly after 1 L treatment. Serum creatinine was significantly associated with lower likelihood of receiving 2 L, and we also found a directional trend for other factors: higher or lower than normal BMI, no prior bevacizumab exposure,

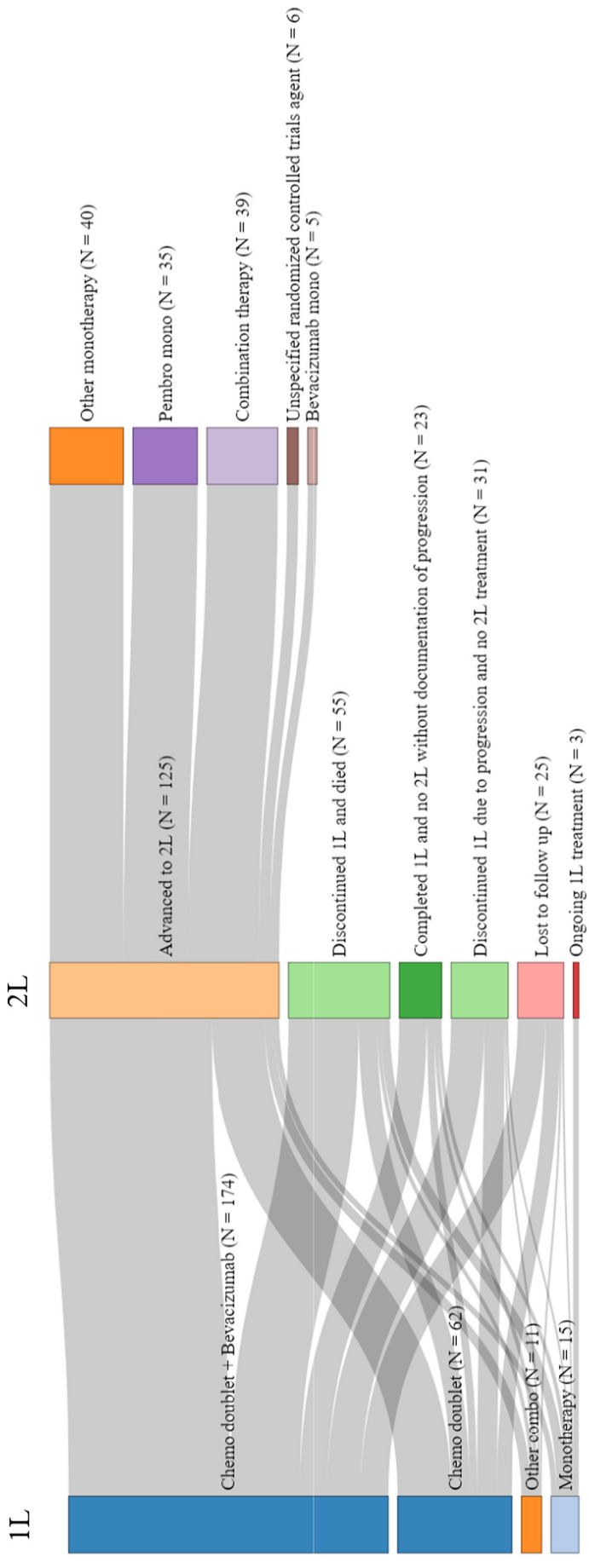
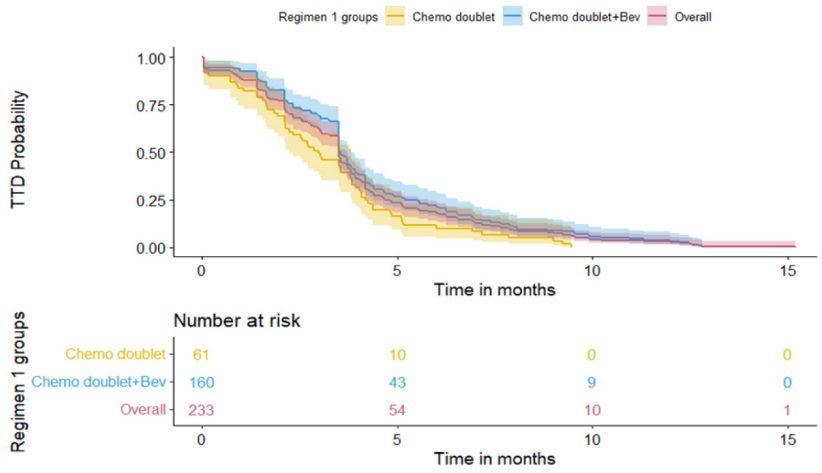


Fig. 2. Treatment pattern Sankey Diagram from 1 L to 2 L treatment.
1 L, first-line; 2 L, second-line; chemo, chemotherapy.

A: Kaplan-Meier Analysis for TTD (by 1L Treatment Groups)



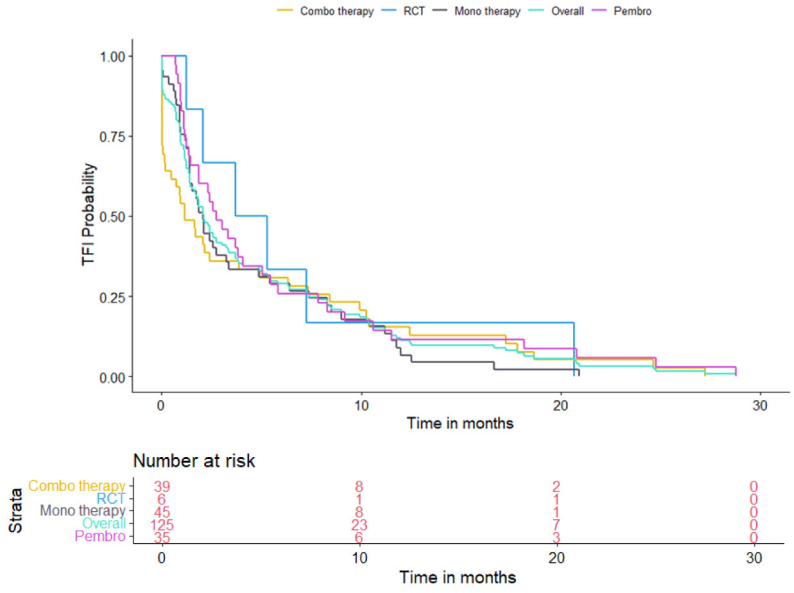
1L Treatment Groups

Variable	Overall[a]	Chemo doublet	Chemo doublet + bevacizumab
Number of Patients	**233**	**61**	**160**
Mean (SE[b]), months	3.92 (.18)	3.22 (0.29)	4.26 (0.23)
Median (95% CI), months	3.48 (3.48-3.71)	2.99 (2.23-3.84)	3.53 (3.48-3.84)
Q1, Q3	2.10, 4.70	1.64, 4.17	2.33, 5.36

1L, first-line; bev, bevacizumab; chemo, chemotherapy; SE, standard error; TTD, time to discontinuation

[a]After removing 29 patients: lost to follow up (N=25), in ongoing 1L treatment (N=3), or had neuroendocrine carcinoma (N=1)

B: Kaplan-Meier Analysis for TFI (by 2L Treatment Groups)



2L Treatment Groups

Variable	Overall	RCT agents	Pembro mono	Other mono	Combo
Number of Patients	125	6	35	45	39
Mean (SE), months	5.20 (0.57)	6.71 (2.68)	5.74 (1.19)	4.45 (0.73)	5.02 (1.16)
Median (95% CI), months	2.10 (1.64-3.25)	4.50 (2.07-NA)	2.73 (1.87-5.45)	2.07 (1.41-4.86)	1.15 (0.49-4.93)
Q1, Q3	0.95, 7.40	2.07, 7.26	1.15,7.85	1.18, 7.39	0.03, 8.44

2L, second-line; bev, bevacizumab; combo, combination; pembro, pembrolizumab; RCT, randomized controlled trials agents; SE, standard errors; TFI, treatment-free interval

Table 2
ORs (95% CI) for Prognostic Factors of Drop-off following 1 L Treatment[a].

Variables		Univariate		Multivariable	
Covariate	Level	OR (95% CI)	P-value[b]	OR (95% CI)	P-value[b]
Age	<50 years	1		1	
	≥50 years	1.18 (0.7, 1.99)	0.53	1.84 (0.84, 4.04)	0.13
BMI	Normal (BMI 18.5–24.9)	1		1	
	Underweight (BMI <18.5)	1.52 (0.59, 4.09)	0.39	2.25 (0.59, 8.52)	0.23
	Overweight (BMI >24.9)	0.79 (0.45, 1.40)	0.42	2.17 (0.92, 5.12)	0.08
ECOG PS	0–1	1		1	
	≥2	1.65 (0.75, 3.71)	0.22	1.49 (0.59, 3.74)	0.40
FIGO stage at presentation of cervical cancer	0–II (A)	1		1	
	II (B)–IV (A)	0.86 (0.46, 1.61)	0.64	0.55 (0.23, 1.33)	0.19
	IV (B)	1.46 (0.70, 3.06)	0.31	0.71 (0.23, 2.18)	0.55
	IV (NOS)	1.20 (0.23, 6.39)	0.83	NA	0.98
Numbers of metastatic sites at 1 L	0–1	1		1	
	≥2	0.79 (0.46, 1.34)	0.38	0.85 (0.38, 1.92)	0.70
Bevacizumab exposure in 1 L	No	1		1	
	Yes	0.78 (0.44, 1.39)	0.40	0.64 (0.27, 1.51)	0.29
Serum creatinine [30]	Normal or Low (≤1.04 mg/dL)	1		1	
	Elevated (>1.04 mg/dL)	2.03 (1.06, 3.96)	0.03	3.04 (1.13, 8.22)	0.03

1 L, first-line; BMI, body mass index; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; FIGO, International Federation of Gynecology and Obstetrics; NOS, not otherwise specified; OR, odds ratio.
[a] Removed 29 patients who lost to follow up ($N = 25$), in ongoing 1 L treatment ($N = 3$), or had neuroendocrine carcinoma ($N = 1$). A total of 233 patients were considered.
[b] All reported *p*-values were 2-sided, with a significance level of 0.05.

higher ECOG PS score, and earlier disease presentation; these factors have been associated with poor survival outcomes in other studies.

Overall, patient demographic and clinical profiles in this study generally reflected those reported in the literature for cervical malignancy (e.g., age, squamous as the most common histology subtype) [5,20,31,32]. The GOG 240 trial is the only other study that reported subsequent therapy use upon progression on 1 L r/mCC systemic therapy, which found that at least 37% ($N = 112$) of eligible patients would receive 2 L [21]. However, the trial was conducted prior to the approval of pembrolizumab or tisotumab vedotin in the 2 L setting. Findings from our study, which reflected more recent treatment landscape, suggest that the proportion of eligible patients receiving 2 L treatment could increase with the availability of additional options and effective therapies. Recognizing that our findings were from a single network, we encourage more studies to be conducted estimating receipt of subsequent therapy in different settings. Knowledge of contemporary estimates of treatment receipt following 1 L provides a baseline from which we can evaluate the potential value of future therapeutic options in an actively evolving 2 L landscape.

The lack of a clear standard of care in 2 L in our study has been well documented in other real-world studies [19,33]. However, where the previous US Oncology Network study reported only 15% utilization of pembrolizumab in 2 L, the present study, which used more recent data from the same network, showed an uptick in the use of pembrolizumab in 2 L (28%), and a reduced use of cytotoxic monotherapy (36% vs 46%). A similar trend was observed in an analysis of commercial administrative claims data [33]. On the other hand, the TFI analysis from our study suggests that patients receiving chemotherapy in 2 L tend to be those needing treatment shortly after completion of 1 L. We infer from these trends and findings that patients will continue to benefit from innovative therapies, which lead to additional differentiated treatment options in the 2 L setting. At the same time, we found that chemotherapies are still widely used, even though they offer limited clinical benefit.

Although there was no statistical difference in TFI across choice of 2 L therapies, there was a trend towards numerically longer TFI among patients receiving 2 L pembrolizumab or RCT agents. Interestingly, the chemotherapy combination treatment group had the numerically shortest TFI compared with pembrolizumab monotherapy or any of the other monotherapies. This result suggests that chemotherapy remains the salvage therapy of choice until innovative and more effective 2 L therapy options for r/mCC become available, and that chemotherapy would remain an important option for patients who require subsequent therapy as soon as possible after discontinuing 1 L treatment.

While there have been no previous studies characterizing predictors of receiving 2 L therapy [19], there have been reports suggesting that factors determining whether a patient receives 2 L therapy are similar to those predicting survival (prior bevacizumab exposure, histology, stage of disease, race, tumor size, metastases, tumor burden [i.e., size and number of tumors], and FIGO staging) [21–27]. Although we were not able to assess directly the correlation between receiving 2 L therapy and survival, the implied association is not surprising. This result further points to the importance of offering additional effective treatment options for patients after progression on 1 L therapy [27,34]. Our finding that elevated serum creatinine levels were predictive of not receiving 2 L therapy is also not surprising, as certain chemotherapy regimens could cause additional kidney damage and would therefore be contraindicated [35].

Advantages and limitations of the iKM EHR have been described in a previous study [19]. Specific to the present analysis, we were only able to assess 2 L receipt and prognostic factors during the study period. However, because the majority of the study patient population discontinued 1 L during the study period, a longer follow-up time may be needed to fully capture a patient's complete medical journey. A patient's chart may also be incomplete if she switched to seeking care at a practice outside of The US Oncology Network. Although we are not able to verify this occurrence in the dataset, it is also possible in some patients that the diagnosis and treatment of r/mCC were associated with job loss and resultant commercial insurance loss, potentially leading to loss-to-follow-up. Lastly, the small sample size and limited outcomes data have also limited our ability to explore a more comprehensive set of positive versus negative predictor variables.

Fig. 3. Patients with recurrent or metastatic cervical cancer initiating systematic therapy within a large community-based oncology network, 2014–2020 demonstrating (A) time to 1 L treatment discontinuation; and (B) treatment-free interval from 1 L treatment discontinuation.
A: Kaplan-Meier Analysis for TTD (by 1 L Treatment Groups).
B: Kaplan-Meier Analysis for TFI (by 2 L Treatment Groups).

5. Conclusion

Findings from the present study demonstrate that there remains a significant unmet need for r/mCC patients who have progressed on prior systemic therapy. In particular, insights from the proportion of patients receiving subsequent therapy, as well as chemotherapy-free interval after progression on 1 L therapy indicate that contemporary r/mCC patients will benefit from having additional effective treatment options with differentiated mechanism of action. The study also suggests that continued efforts to generate clinical data informing therapy sequencing will be key to maximizing treatment outcomes. Finally, given recent approvals of pembrolizumab in 1 L and tisotumab vedotin in 2 L, updated analyses of treatment pattern and drop-off should be performed in the future to assess the impact of new and emerging therapy on r/mCC unmet needs.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2022.07.026.

Ethics approval

Institutional Review Board and Compliance/Privacy approval was gained prior to initiation of the retrospective research. Since this project involved the analysis of existing data and records, study information was analyzed in such a manner that research participants could not be directly identified. Patient-informed consent was not required due to the nature of the study design. Thus, exemption status and a waiver of informed consent were approved by The US Oncology, Inc. Institutional Review Board. Data were handled in compliance with HIPAA and the Health Information Technology for Economic and Clinical Health (HITECH) Act.

Availability of data and material

The raw data used for this analysis are not publicly available due to privacy or ethical restrictions.

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Declaration of Competing Interest

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