Treatment pattern and overall survival among patients with locally advanced or metastatic urothelial carcinoma – Results from a complete nationwide unselected real-world registry study in Denmark from 2010 to 2017

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SCOPE

- **To characterize treatment patterns, number of first-line (1L) platinum-based chemotherapy (PBC) cycles, and overall survival (OS) in patients with stage IIIb or IV urothelial carcinoma (UC) in Denmark**

CONCLUSIONS

- **A considerable proportion of patients did not receive any relevant systemic anticancer therapy, and few patients survived long term (overall survival >2 years) on 1L cisplatin + gemcitabine (CG) or carboplatin + gemcitabine (CaG) only**
- **Patients receiving more cycles of chemotherapy appeared to have longer OS; however, this finding may be influenced by other factors, eg, performance status, on which data were not available in the registries**
- **The high attrition rate between 1L and second-line (2L) treatments highlights that this is a frail patient population that needs effective and tolerable frontline therapy**
- **This retrospective, observational, and unselected population–based study describes the characteristics of an elderly population with poor outcomes and incorporates prior evidence from data on Danish patients with UC retrospectively obtained from electronic medical records[1]**
- **This study, focusing on the pre–immuno-oncology era, can serve as a benchmark for future observational studies on the effect of novel systemic agents and treatment approaches**

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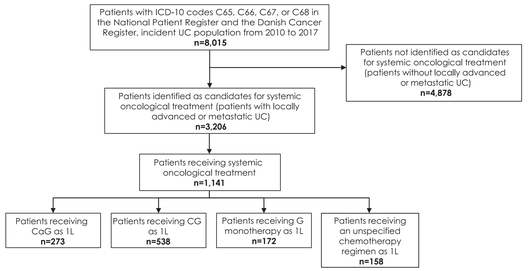
BACKGROUND

- Across all stages, approximately 2,170 Danish patients were diagnosed with UC per year between 2014 and 2018, making it the seventh most common cancer in Denmark[2]
- During the same period, UC was the ninth most common cause of Danish cancer death[3]
- In Denmark, the preferred 1L treatment option for patients diagnosed with locally advanced or metastatic bladder cancer has been CG combination chemotherapy. However, approximately 50% of patients are considered cisplatin ineligible, and for the majority of this group, the recommended treatment has been CaG combination chemotherapy[4-6]
- This study contributes to a growing body of literature on real-world clinical data describing patient characteristics, treatment patterns, and outcomes, including survival

METHODS

- This retrospective, observational, and unselected population–based study is based on data from the Danish national health registries
- From these registries, Danish patients with locally advanced or metastatic UC between 1 January 2010, and 31 December 2017, were identified and followed up until December 31, 2018, excluding patients with concomitant malignancy (except prostate cancer and nonmelanoma skin cancer)
- From this subgroup, patients who received systemic oncological treatment were identified, excluding patients who received neoadjuvant chemotherapy and those with incomplete registration
- Patients were stratified by the number of completed 1L cycles of CG or CaG
- The Kaplan-Meier method was used to estimate OS, number of patients who lived long term (>2 years) on 1L therapy only, and percentage of patients who received 2L treatment

Figure 1. Study population



1L, first line; **UC**, urothelial carcinoma.

RESULTS

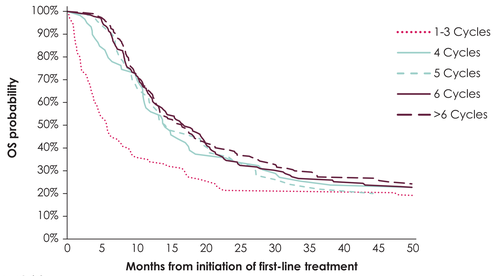
- 36% of patients identified as candidates for systemic oncological treatment received relevant 1L chemotherapy, defined as CG (n=538), CaG (n=273), gemcitabine monotherapy (n=172), or other unspecified chemotherapy regimens (n=158)
- 811 patients (71% of patients receiving systemic therapy) received CG or CaG during the study period (**Table 1**)
- Patients receiving CG were younger (mean, 64.4 vs 70.8 years), had longer median OS (14.2 vs 8.6 months), and longer mean follow-up (28 vs 21.3 months) than patients receiving CaG
- Only 35% of patients receiving 1L platinum-based chemotherapy received 2L treatment within at least 1 year of follow-up
- Of patients receiving 1L CG or CaG only, 14% and 7%, respectively, survived long term (>2 years)
- The median OS in patients treated with CG was 14.2 months, ranging from 5.7 to 17.0 months in patients receiving 1-3 or 6 cycles of CG, respectively (**Figure 2**; **Table 2**)
- The median OS in patients treated with CaG was 8.6 months, ranging from 4.4 to 12.8 months in patients receiving 1-3 or 6 cycles of CaG, respectively (**Figure 3**; **Table 2**)

Table 1. Baseline characteristics of the study population

Characteristic	Patients administered CaG (n=273)	Patients administered CG (n=538)
Sex, male	183 (67)	393 (73)
Age, mean (SD), years	70.8 (7.58)	64.4 (7.75)
<60, n (%)	20 (7)	129 (24)
60-75, n (%)	170 (62)	394 (73)
>75, n (%)	83 (30)	15 (3)
Charlson Comorbidity Index score, n (%)*	n=250	n=394
0	149 (60)	282 (72)
1	88 (35)	90 (23)
2	13 (5)	22 (6)
Tumor stage, n (%)	n=135	n=285
Tumor stage T4b	13 (10)	56 (20)
N-stage 2/3	35 (26)	94 (33)
M1-stage (any of the variables indicating metastatic disease)	108 (80)	206 (72)
Prior cystectomy, n (%)	67 (25)	151 (28)
Neoadjuvant chemotherapy prior to cystectomy, n (%)	20 (7)	28 (5)
Location of primary tumor, n (%)		
Renal pelvis (C65)	40 (15)	73 (14)
Ureter (C66)	25 (9)	30 (6)
Bladder (C67)	206 (75)	424 (79)
Other and unspecified urinary organs (C68)	<5 (<2)	11 (2)

CaG, carboplatin + gemcitabine; **CG**, cisplatin + gemcitabine; **SD**, standard deviation.

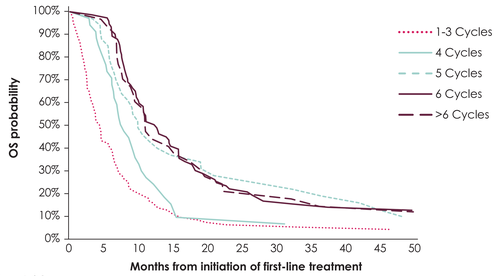
Figure 2. OS from the date of diagnosis of locally advanced or metastatic UC in patients treated with CG (n=538)



No. at risk						
1-3 Cycles	103	37	27	22	22	20
4 Cycles	59	42	22	18	14	14
5 Cycles	50	34	21	14	11	10
6 Cycles	139	100	60	43	35	32
>6 Cycles	187	137	80	62	51	46

CG, cisplatin + gemcitabine; **OS**, overall survival; **UC**, urothelial carcinoma.

Figure 3. OS from the date of diagnosis of locally advanced or metastatic UC in patients treated with CaG (n=273)



No. at risk						
1-3 Cycles	97	22	9	8	7	6
4 Cycles	35	13	<5	<5	<5	<5
5 Cycles	34	17	11	9	7	<5
6 Cycles	76	47	23	14	12	12
>6 Cycles	31	19	9	7	5	5

CaG, carboplatin + gemcitabine; **OS**, overall survival; **UC**, urothelial carcinoma.

Table 2. Effectiveness of treatment in patients who received CaG or CG as 1L treatment

1L treatment	Chemotherapy cycles, n	n (%)	OS, median (SD), months	6, 12-, and 24-month landmark OS rates, %	Long-term survivors on 1L, n (%)
CaG	1-3	97 (36)	4.4 (6.23)	41, 19, 8	5 (5)
	4	35 (13)	7.9 (8.39)	74, 29, 11	<5 (<11)
	5	34 (12)	10.3 (26.03)	79, 44, 29	<5 (<12)
	6	76 (28)	12.8 (14.93)	>95, 53, 24	5 (7)
	>6	31 (11)	11.0 (14.92)	>87, 45, 23	<5 (<13)
	Total	273 (100)	8.6 (10.82)	71, 36, 17	19 (7)
CG	1-3	103 (19)	5.7 (19.44)	47, 34, 21	13 (13)
	4	59 (11)	14.2 (30.33)	80, 58, 36	10 (17)
	5	50 (9)	14.4 (23.08)	>92, 60, 36	9 (18)
	6	139 (26)	17.0 (33.80)	92, 63, 35	22 (16)
	>6	187 (35)	16.7 (39.28)	96, 65, 39	22 (12)
	Total	538 (100)	14.2 (30.49)	83, 57, 34	76 (14)

1L, first-line; **CaG**, carboplatin + gemcitabine; **CG**, cisplatin + gemcitabine; **OS**, overall survival; **SD**, standard deviation; **UC**, urothelial carcinoma.

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