Split-dose cisplatin plus gemcitabine use and associated clinical outcomes in the first-line treatment of locally advanced or metastatic urothelial cancer: results of a retrospective, observational study in Germany (CONVINCE)

K. Schlack,[1] T. Kubin,[2] M. Ruhnke,[3] C. Schulte,[4] S. Machtens,[5] A. Eisen,[6] U. Osowski,[7] S. Guenther,[8] M. Kearney,[8] R. Lipp,[9] S. Schmitz[10]

[1]Department of Urology, University Hospital Muenster, Muenster, Germany; [2]Department of Hematology, Oncology and Palliative Care, Klinikum Traunstein, Traunstein, Germany; [3]Clinic for Hematology, Oncology and Palliative Medicine, Helios Clinic Aue, Aue, Germany; [4]Department of Hematology and Oncology, Practice for Hematology and Oncology, Dortmund, Germany; [5]Department of Urology, GFO Hospitals Rhein-Berg, Marien-Hospital, Bergisch Gladbach, Germany; [6]GermanOncology GmbH, Hamburg, Germany; [7]Merck Healthcare Germany GmbH, Weiterstadt, Germany, an affiliate of Merck KGaA; [8]Merck Healthcare KGaA, Darmstadt, Germany; [9]RWE Research, GermanOncology GmbH, Hamburg, Germany; [10]Department of Oncology and Hematology, Medical Care Center for Oncology and Hematology, Cologne, Germany

SCOPE

- **CONVINCE is an retrospective, observational, multicenter study examining treatment patterns and associated outcomes in patients with locally advanced or metastatic urothelial cancer (la/mUC) in Germany**
- **In this analysis, we compare demographics, treatment patterns, and associated clinical outcomes in patients with la/mUC who received first-line (1L) platinum-based chemotherapy (PBC) in the form of split-dose cisplatin and gemcitabine (CG-S), standard-dose cisplatin plus gemcitabine (CG) or carboplatin plus gemcitabine (CbG) regimens**

CONCLUSIONS

- **To our knowledge, this is the first retrospective, multicenter study in the German treatment context evaluating CG-S use and associated real-world (rw) clinical outcomes in patients with la/mUC**
- **Findings from this study provide valuable insights into the use of 1L CG-S in routine clinical practice in Germany, where CG-S is regularly used as 1L treatment for patients with la/mUC as an alternative to CG**
- **The analysis demonstrated comparable outcomes with CG-S and CG or CbG, suggesting that CG-S can be a viable option as 1L PBC for patients with la/mUC for whom CG may be unsuitable, without compromising treatment effectiveness**
- **Future studies evaluating comparative treatment outcomes should control for disease severity and other patient characteristics at baseline. This was not feasible in this study due to the small sample size, especially by subcohorts**
- **Larger prospective studies are needed to further define the extent to which CG-S dosing is used in clinical practice and to identify the appropriate patient groups that would likely derive the greatest benefit from this regimen**

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Correspondence: **Katrin Schlack**, **katrin.schlack@ukmuenster.de**

BACKGROUND

- 1L PBC followed by avelumab 1L maintenance in patients without disease progression is the standard-of-care treatment for patients with la/mUC[1,2]
- In patients who are ineligible to receive a CG schedule (cisplatin: 70 mg/m² on day 1 of each 21-day cycle), alternative treatment options include CbG (carboplatin: area under the curve [AUC] 4 or 5 mg/ml/min) or CG-S (cisplatin: 35 mg/m² on days 1 + 8 or days 1 + 2)[3,4]
- The effectiveness of these regimens compared with CG has not been extensively examined in clinical studies. Also, there are very limited data available from rw studies on the use of CG-S in patients with la/mUC

METHODS

Study design

- CONVINCE, a retrospective, multicenter medical chart review study, was initiated in December 2021 and included patients who received 1L therapy for la/mUC between January 2019 and December 2021
- Data were obtained from 27 oncology or urology institutions (8 hospitals and 19 office-based practices) that were geographically dispersed and of varied size across Germany (**Figure 1**)
- Fully anonymized data were extracted from patient medical charts and entered into electronic case report forms. Parameters included sex, age, UC history, ECOG performance status (PS) at diagnosis, treatments received, and clinical outcomes
- The study population used for this analysis was divided into 3 treatment groups: CG-S, CG, or CbG (**Figure 2**)
- Clinical outcomes, including overall response rate, rw progression-free survival (rwPFS), and rw overall survival (rwOS), were described for the 3 groups and were defined from the start of 1L treatment
- All groups received similar amounts of adjuvant therapies (**Table 1**)
- The choice of regimen administered to each patient (CG-S, GC, or CbG) was determined by the attending physician

Eligibility criteria

- Patients aged ≥18 years with la/mUC diagnosis
- 1L PBC course had to be completed between 01 January 2019 and 30 June 2021 with a follow-up time of >6 months after last administration
- Patients were excluded if they participated in an interventional clinical trial within 30 days before the start of 1L PBC

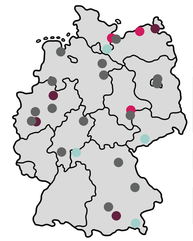
Ethics approval

- This study was performed in accordance with the Declaration of Helsinki
- Because of the retrospective nature of the study and because data collection was anonymized, the need for patient informed consent and advice according to the German doctors' professional code of conduct was waived by the independent ethics board of North Rhine-Westphalia

Statistical analysis

- Descriptive statistics (mean, median, range, SD, and 95% CI) were computed for continuous variables. Categorical variables were described by frequency and percentages
- Response to treatment was determined by physicians per RECIST v1.1[5]
- The data are presented for the CG-S vs CG and CG-S vs CbG groups
- A Cox proportional hazards model was used to evaluate the differences in rwPFS and patient characteristics
- Differences in patient characteristics among the compared groups were assessed using the Student *t*-test or the chi-square test
- Clinical outcomes were analyzed using the Kaplan-Meier method, and the curves were compared using the log-rank test
- All statistical analyses were performed using SAS Analytics Pro version 9.4 (SAS Institute), and p<0.05 indicated a significant difference

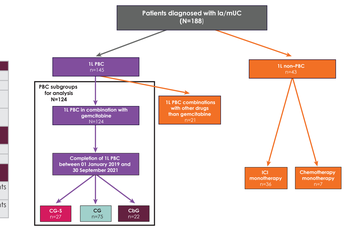
Figure 1. Overview of participating sites and physician disciplines



Participating sites	27 sites
Hospital urology	4
Hospital oncology	4
Office-based urology practice	3
Office-based oncology practice	16
Medical specialty of sites	**27 sites**
Urology	7
Hematology/oncology	20
Distribution of patients by medical specialty	**124 patients**
Urology	54 patients (43.5%)
Hematology/oncology	70 patients (56.5%)

Figure 2. CONVINCE study overview

Inclusion of patients in study and documentation by sites between February 2022 and February 2023



Split-dose cisplatin = 35 mg/m² d1+8 (78% of all administrations) or d1+2 (22% of all administrations).
Standard-dose cisplatin = 70 mg/m² d1.
Standard-dose carboplatin = AUC 4.5 mg/ml/min d1.
Gemcitabine dose = 1,000 mg/m² d1+8 (43% of all administrations) or 1,250 mg/m² d1+8 (43% of all administrations) or 800 mg/m² d1+8 (10% of all administrations).
AUC, area under the curve; **CbG**, carboplatin plus gemcitabine; **CG**, standard-dose cisplatin plus gemcitabine; **CG-S**, split-dose cisplatin and gemcitabine; **d**, day; **ICI**, immune checkpoint inhibitor; **PBC**, platinum-based chemotherapy.

RESULTS

Patient characteristics

- Of the total patient population enrolled (N=188), 124 (66%) received 1L PBC
- In all treatment groups, the majority of patients were male, and >95% of patients had an ECOG PS of 0 or 1 at first UC diagnosis
- ≥1 comorbidity was reported for 78% of patients in the CG-S group, 84% in the CG group, and 95% in the CbG group; the most common comorbidities were cardiovascular disease, diabetes, and kidney dysfunction (**Table 1**)

Treatment patterns

- Of the 124 patients who received 1L PBC, 27 (21.8%) received CG-S, 75 (60.5%) received CG, and 22 (17.7%) received CbG
- CG-S was administered in 25.9% of patients on days 1 and 2 and in 74.1% on days 1 and 8 of each cycle
- Median follow-up time was 16.5 months. At the time of documentation by sites, 56.5% of patients were still alive (no longitudinal follow-up was possible due to full anonymization)
- The median number of 1L PBC cycles administered was 5, 4, and 6 in the CG-S, CG, and CbG cohorts, respectively (**Table 1**)
- The mean doses of the administered drugs were as follows:
  - **Split-dose cisplatin:** 58.8 mg per infusion (range, 40-89 mg)
  - **Standard-dose cisplatin:** 113 mg per infusion (range, 25-162 mg)
  - **Standard-dose carboplatin:** 367 mg per infusion (range, 170-600 mg)
  - **Gemcitabine:** 1,911 mg per infusion (range, 600-2,748 mg)
- The percentage of patients receiving 2L treatment was highest in the CbG group and lowest in the CG-S group (**Table 1**)

Table 1. Baseline patient and treatment characteristics (N=124)

	CG-S	CG	CbG
Patients, n (%)	27 (21.8)	75 (60.5)	22 (17.7)
Male, %	70.4	73.3	77.2
Female %	29.6	26.7	22.8
Age, median (range), years	66 (50-81)	69 (52-81)	73 (59-84)
ECOG PS, %			
0	59	55	46
1	37	40	50
2	4	5	4
Adjuvant therapies, n (%)	2 (7)	3 (4)	3 (14)
Median number of cycles	5.0	4.0	6.0
Subsequent therapies, n (%)			
2L	16 (59)	49 (65)	16 (72)
≥3L	11 (41)	31 (41)	6 (27)
Comorbidities at start of 1L, n (%)	21 (78)	63 (84)	21 (95)
Cardiac or circulatory diseases	12 (44)	49 (65)	16 (82)
Diabetes	4 (15)	13 (17)	5 (23)
Kidney dysfunction	4 (15)	9 (12)	2 (9)
Other*	Multiple sclerosis: 1 (4)	Polyneuropathy: 3 (4); hearing loss: 2 (3)	Hearing loss: 1 (5)

1L, first line; **2L**, second line; **3L**, third line; **CbG**, carboplatin plus gemcitabine; **CG**, standard-dose cisplatin plus gemcitabine; **CG-S**, split-dose cisplatin and gemcitabine.
*Comorbidities with a possible impact on the general constitution of the patient or treatment decision.

Clinical outcomes

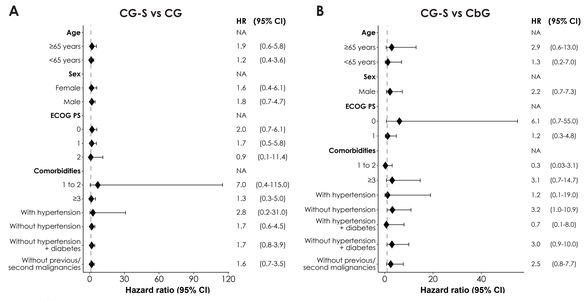
- A Cox regression analysis including several characteristics (age, sex, ECOG PS, and comorbidities) of all evaluable patients (N=124) showed no significant differences for rwPFS between the CG-S group and the CG and CbG groups (**Figure 3A** and **3B**)
- Best overall response to 1L PBC was assessed by physicians. Results for overall response rate (complete response + partial response) are reported for 116 patients (93.5% of all evaluable patients); for the other patients (n=8), response assessments were not performed or documented
- No significant difference was observed for best overall response, rwPFS, and rwOS among the 3 treatment groups, but there was a nonsignificant trend towards a better rwOS for CG compared with CG-S (**Table 2**, **Figure 4A**, and **4B**)

Table 2. Clinical outcomes by treatment group

	CG-S	CG	CbG	p value
Overall response, n (%); n=116 (8 patients were not evaluable for response)				
Evaluable patients	25 (92.5)	69 (92.0)	22 (100)	
Complete response	2 (8.0)	8 (11.6)	4 (18.2)	
Partial response	14 (56.0)	26 (37.7)	9 (40.9)	
Stable disease	6 (24.0)	20 (29.0)	4 (18.2)	
Progressive disease	3 (12.0)	11 (15.9)	5 (22.7)	
Objective response rate	16 (64.0)	34 (49.3)	13 (59.1)	**CG-S vs CG:** p=0.84 **CG-S vs CbG:** p=0.65
rwPFS, n (%); N=124				
Start of 1L	27 (100)	75 (100)	22 (100)	
6 months after start	23 (85)	58 (77)	19 (86)	
9 months after start	17 (63)	43 (57)	12 (55)	
12 months after start	10 (37)	29 (39)	7 (32)	
18 months after start	4 (15)	17 (23)	3 (14)	
rwPFS, median, months	10.5	10.5	9.1	**CG-S vs CG:** p=0.35 **CG-S vs CbG:** p=0.24
rwOS, n (%); N=124				
Start of 1L	27 (100)	75 (100)	22 (100)	
6 months after start	27 (100)	75 (100)	22 (100)	
9 months after start	26 (96)	75 (100)	20 (91)	
12 months after start	23 (85)	64 (85)	19 (86)	
18 months after start	10 (37)	52 (69)	10 (45)	
rwOS, median, months	14.4	18.8	16.7	**CG-S vs CG:** p=0.06 **CG-S vs CbG:** p=0.14

1L, first line; **CbG**, carboplatin plus gemcitabine; **CG**, standard-dose cisplatin plus gemcitabine; **CG-S**, split-dose cisplatin and gemcitabine; **rwOS**, real-world overall survival; **rwPFS**, real-world progression-free survival.

Figure 3. Cox regression analysis for rwPFS by treatment cohort (N=124)

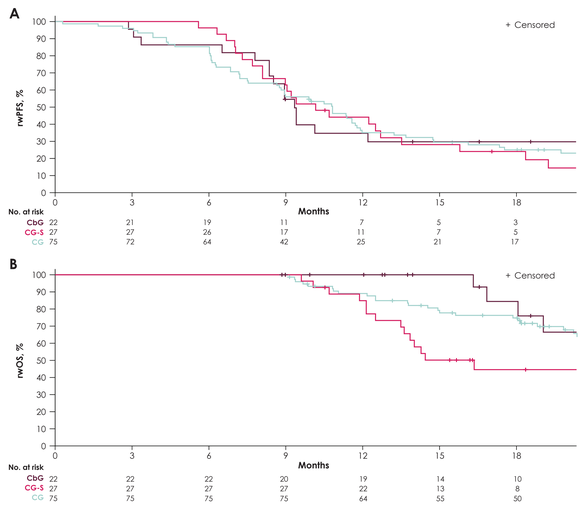


Parameters
- Age: <65 vs ≥65 years at start of 1L
- Sex: female vs male
- ECOG PS: 0 vs 1 vs 2
- Comorbidities: 1 or 2 vs ≥3 diagnoses
- Specific diagnoses: with hypertension, without hypertension, without hypertension and diabetes, or without previous or second malignancies

Interpretation of results
- Split-dose cisplatin = experimental therapy
- Standard-dose cisplatin/carboplatin = standard therapy
- HR ≥1.0, standard therapy is better
- HR ≤1.0, experimental therapy is better

1L, first line; **CbG**, carboplatin plus gemcitabine; **CG**, standard-dose cisplatin plus gemcitabine; **CG-S**, split-dose cisplatin and gemcitabine; **HR**, hazard ratio; **NA**, nonapplicable; **rwPFS**, real-world progression-free survival.

Figure 4. Kaplan-Meier analysis of rwPFS (A) and rwOS (B) by treatment cohort from 1L initiation (N=124)



1L, first line; **CbG**, carboplatin plus gemcitabine; **CG**, standard-dose cisplatin plus gemcitabine; **CG-S**, split-dose cisplatin and gemcitabine; **rwOS**, real-world overall survival; **rwPFS**, real-world progression-free survival.

LIMITATIONS

- Because this was a retrospective study, data availability to assess allocation to treatment and clinical effectiveness was limited to what was recorded in the patients' charts as part of routine clinical care
- Although steps were taken to ensure that complete and accurate information was obtained from the medical charts, we cannot fully exclude the potential for information bias if data were missing
- Additionally, owing to the multicenter study design, the dose reduction rate and scheduling of CG-S was not uniform across all sites
- The introduction of bias based on treatment selection is possible as the analyses did not control for variability in patients' baseline characteristics or baseline treatment dose selection or schedules, by matching on select factors known to influence chemotherapy response rates
- Differences in baseline patient characteristics, disease location, and disease behavior may contribute to variability in clinical effectiveness between the 3 cohorts studied
- This study had a small sample size and limited statistical power to definitively compare response rates between treatment and dosing strategies
- The rwOS results must be interpreted with caution due to immortal time bias being introduced during the inclusion period

REFERENCES 1. Powles, T, et al. Ann Oncol. 2022;33:244-58. **2.** Cathomas R, et al. Eur Urol. 2022;81:95-103. **3.** Einstein DJ, Sonpavde G. Curr Treat Options Oncol. 2019;20:12. **4.** Galsky MD, et al. J Clin Oncol. 2011;29:2432-8. **5.** Schwartz LH, et al. Eur J Cancer. 2016;62:132-7.

DISCLOSURES K. Schlack has served in speaker, consulting, or advisory roles for AAA, Amgen, Apogepha, Astellas, AstraZeneca, Bayer, BMS, Eisai, EUSA-Pharma, Fosanis, Ipsen, Janssen-Cilag, Merck, MSD, Novartis (personal and institutional), Pfizer, and Roche; and has received travel expenses from AstraZeneca, Astellas, Bayer, Ipsen, Janssen-Cilag, Merck, and Sanofi-Aventis. **T. Kubin**, **M. Ruhnke**, and **C. Schulte** have nothing to declare. **S. Machtens** has served in consulting or advisory roles for Amgen, AstraZeneca, Bayer, BD, Bebig, Janssen-Cilag, MSD, Pfizer, and Sanofi-Aventis; and has participated in speakers bureaus for Amgen, Apogepha, Astellas, AstraZeneca, Bayer, BD, Bebig, Ipsen, Janssen-Cilag, Merck, MSD, Novartis, Pfizer, Sanofi-Aventis, and Takeda. **A. Eisen** has nothing to declare. **U. Osowski** is an employee of Merck Healthcare Germany GmbH, Weiterstadt, Germany, an affiliate of Merck KGaA. **S. Guenther** and **M. Kearney** are employees of Merck Healthcare KGaA, Darmstadt, Germany. **R. Lipp** has served in consulting or advisory roles for AstraZeneca, Gilead, Janssen-Cilag, Merck, Omnicare, Sanofi, and Takeda; has participated in speakers bureaus for Merck; and has provided project support for AbbVie, AstraZeneca, BMS, Gilead, Janssen-Cilag, Merck, and Pfizer. **S. Schmitz** has nothing to declare. **ACKNOWLEDGMENTS** This study was sponsored by Merck (CrossRef Funder ID: 10.13039/100009945) and was previously conducted under an alliance between Merck and Pfizer. Editorial support was provided by Katherine Quiroz-Figueroa of Clinical Thinking and was funded by Merck.

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