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ORIGINAL ARTICLE

Safety and efficacy of preoperative chemotherapy for muscle-invasive bladder cancer in elderly patients

Clément Dumont[1,2] · Amélie Aregui[3] · Mathilde Hauchecorne[3] · Madeleine Lefèvre[3] · Quiterie Aussedat[1] · Pierre-Louis Reignier[4] · Hélène Gauthier[1] · Christophe Hennequin[2,5] · Virginie Fossey-Diaz[3] · Evanguelos Xylinas[2,6] · Atanas Pachev[7] · François Desgrandchamps[2,4] · Alexandra Masson-Lecomte[2,4] · Stéphane Culine[1,2]

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Abstract

Purpose This study aimed at describing the feasibility and oncological outcomes of standard cisplatin-based neoadjuvant chemotherapy (C-NAC) for muscle-invasive bladder cancer (MIBC) in patients aged ≥ 75 and assess the impact of baseline geriatric parameters.

Methods This retrospective study included patients with stage cT2-4NanyM0 MIBC aged 75 and older treated with ≥ 1 cycle of C-NAC from 2011 to 2021 at a high-volume academic center. Primary outcome was overall survival (OS). Secondary outcomes were chemotherapy feasibility (administration of ≥ 4 cycles), safety, and pathological downstaging.

Results Fifty-six patients were included. Median age was 79 (range 75–90). C-NAC regimen was ddMVAC in 41 patients and GC in 15. Seventy-three percent of patients received ≥ 4 cycles of C-NAC. Grade ≥ 3 toxicity was observed in 55% of patients. The febrile neutropenia rate was 7%. Thirty patients underwent cystectomy, and 13 underwent chemoradiotherapy. Three-year OS was 63%. Geriatric parameters polypharmacy, undernutrition, and age-adjusted Charlson comorbidity index ≥ 8 predicted worse OS.

Conclusion Standard-of-care C-NAC and local treatments are feasible in selected elderly MIBC patients, with efficacy and safety findings similar to that observed in pivotal trials with younger patients. The prognostic impact of geriatric parameters underlines the need for specialized evaluation before treatment initiation.

Keywords Urinary bladder cancer · Neoadjuvant treatment · Chemotherapy · Aged · Aged 80 and over

Abbreviations

aaCCI	Age-adjusted Charlson comorbidity index
BMI	Body mass index
CGF CrCl	Creatinine clearance according to the Cockroft and Gault formula
CKD-EPI eGFR	Glomerular filtration rate according to the Chronic Kidney Disease Epidemiology Collaboration equation
C-NAC	Cisplatin-based neoadjuvant chemotherapy
ddMVAC	Dose-dense methotrexate vinblastine doxorubicin cisplatin
GC	Gemcitabine–cisplatin
MIBC	Muscle-invasive bladder cancer
OS	Overall survival

Introduction

Cisplatin-based neoadjuvant chemotherapy (C-NAC) is recommended for eligible patients with muscle-invasive bladder cancer (MIBC) [1, 2] based on randomized trials [3–5] and meta-analyses [6]. In locally advanced disease, chemotherapy optimizes disease control and helps selecting patients for locoregional treatment. Common regimens are ddMVAC (dose-dense methotrexate, vinblastine, doxorubicin, cisplatin) and GC (gemcitabine–cisplatin).

Median age at bladder cancer diagnosis in the USA is 73. However, in pivotal C-NAC trials, median age of participants is 63–64 [3, 5, 7]; less than 20–25% are aged ≥ 70. In routine practice, patients aged ≥ 70 may be offered C-NAC thrice less frequently [8]. Only small retrospective studies

Clément Dumont and Amélie Aregui contributed equally and share first authorship.

Extended author information available on the last page of the article

have reported outcomes in patients aged ≥ 70 treated with GC or gemcitabine–carboplatin [9, 10]; 3 cycles of neoadjuvant ddMVAC was reported feasible in 43 patients aged ≥ 75 [11].

Here, we report on 56 well-characterized MIBC patients aged ≥ 75 treated with C-NAC. We report applicability, safety, and efficacy of standard-of-care C-NAC in this understudied population.

Patients and methods

Patients and treatment

This single-center retrospective study included patients aged ≥ 75 with cT2-4NanyM0 MIBC who underwent ≥ 1 cycle of ddMVAC (methotrexate 30 mg/m^2, vinblastine 3 mg/m^2, doxorubicin 30 mg/m^2, and cisplatin 70 mg/m^2 every 2 weeks for up to 6 cycles) or GC (gemcitabine 1250 mg/m^2 on day 1 and day 8 and cisplatin 70 mg/m^2 on day 1 every 3 weeks for up to 4 cycles) from 2011 to 2021. The treating oncologist determined C-NAC regimen with on-demand decisional help from oncogeriatricians. Locoregional management was determined in multidisciplinary tumor boards.

Before each cycle, renal function was estimated using Cockroft–Gault formula creatinine clearance (CGF CrCl) and body surface area-indexed estimated glomerular filtration rate (CKD-EPI eGFR). Policy for cisplatin administration was as follows: 70 mg/m^2 if CrCl ≥ 60 mL/min; 50 mg/m^2 if 50–59 mL/min; 40 mg/m^2 if 40–49 mL/min; and end of treatment if < 40 mL/min. In the occurrence of grade ≥ 3 toxicities, a 20% dose reduction was done for all drugs.

Outcomes

Primary outcome was overall survival (OS: time from chemotherapy initiation to death from any cause). Secondary outcomes were deliverance of ≥ 4 cycles, pathological downstaging, and safety. Adverse events (AEs) were described using CTCAE v5.0. Subgroup analyses focused on baseline characteristics including age-adjusted Charlson comorbidity index (aaCCI), polypharmacy (≥ 5 medications daily), and nutritional status. Undernutrition was defined as BMI < 21 kg/m^2 and/or significant weight loss (> 5% in 1 month and/or > 10% in 6 months). Skeletal muscle index at third lumbar vertebra level (L3SMI) was assessed on pre-chemotherapy CT scans; previously reported thresholds were used to define sarcopenia (< 41 cm^2/m^2 for women, < 43 cm^2/m^2 for non-overweight men, < 53 cm^2/m^2 for overweight/obese men) [13].

Statistical analysis

Continuous variables were described using median (range) and dichotomous variable using absolute number and/or proportions. Survival was described using Kaplan–Meier estimates and compared using log rank test. Association between clinical factors and OS was explored using univariate and multivariate Cox regression models. Dichotomous variables were compared using Fisher's exact test.

Results

Patients

Fifty-six patients were included Table 1 and Supplementary Table 1. Median age was 79. Most patients had good performance status and low aaCCI. Eight patients had BMI < 21 kg/m^2; 6 had serum albumin level < 35 g/L. In contrast, 42 of 52 evaluable patients had CT-scan sarcopenia.

Treatments

Supplementary Table 2 summarizes C-NAC and locoregional management.

Thirty-one patients received ddMVAC; 15 received GC. GC was more frequently used with increasing age (p value: 0.095 by Student's t test; Supplementary Table 1). Dose reduction was performed in 11% of patients at first cycle (gemcitabine dose reduction: 3; doxorubicin dose reduction: 1; cisplatin dose reduction: 2 ddMVAC patients with impaired CGF CrCl) and in 54% at any time. Median number of cycles was 4; 73% of patients underwent ≥ 4 cycles. Premature C-NAC discontinuation (before 6 ddMVAC cycles or 4 GC cycles) occurred in 66% of patients, due to toxicity (28 patients), locoregional treatment requirements (6), intercurrent infection (1), or patient's death (1). Toxicities prompting discontinuation (possibly concomitant) included renal (11 patients), hematological (10), general/asthenia (10), and digestive (6).

Forty-three patients (77%) underwent curative-intent locoregional treatment (radical cystectomy: 54%; chemoradiotherapy: 23%). Median time from last C-NAC cycle to cystectomy was 49 days (range 32–254).

Five patients (9%) underwent active endoscopic surveillance. Lack of local management in the remaining 8 patients was due to intercurrent affection (lymphoma: 1; SARS-CoV-2 infection: 2), patient's choice (2), disease progression (2), or death (1).

Table 1 Baseline characteristics of patients

Total	56		
Demographics			
Age: median (range)	79 (75–90)		
Age groups			
75–79	34	61%	
80–84	16	29%	
85 and older	6	11%	
Male gender	47	84%	
Risk factors for MIBC			
Current smoker	13	23%	
Former smoker	26	46%	
Radiotherapy to the pelvis	10	18%	
History of NMIBC	11	20%	
Comorbidities			
Diabetes mellitus	9	16%	
Hypertension	20	36%	
Atheromatous disease	7	13%	
Obesity (BMI ≥ 30 kg/m^2)	8	14%	
Age-adjusted Charlson comorbidity score: median (range)	7 (5–11)		
Polypharmacy (≥ 5 medications daily)	16	29%	
ECOG performance status			
PS 0	23	41%	
PS 1	28	50%	
PS 2	3	5%	
Nutritional status			
BMI: median (range)	25.5 (17.3–34.4)		
Patients with BMI < 21 kg/m^2	8	14%	
Patients with BMI < 20 kg/m^2	4	7%	
Serum albumin: median (range)	40 (30–48)		
Renal function			
CrCl by CGF (mL/min): median (range)	63.5 (33.1–96.4)		
Patients with CrCl < 60 mL/min by CGF	22	39%	
Patients with CrCl < 50 mL/min by CGF	10	18%	
BSA-indexed eGFR by CKD-EPI (mL/min): median (range)	78.0 (37.7–96.9)	37.7	96.9
Patients with BSA-indexed CKD-EPI eGFR < 60 mL/min	6	11%	
Patients with BSA-indexed CKD-EPI eGFR < 50 mL/min	2	4%	
Cancer			
Stage cT2N0/x	29	52%	
Stage cT3–4N0/x	15	27%	
Stage cTanyN1–3[a]	12	21%	
Hydronephrosis	16	29%	
Hydronephrosis	15	27%	
Ureteral stent and/or nephrostomy	7	12%	
Incomplete TURBT before chemotherapy	16	29%	
Variant histology (including squamous differentiation)	18	32%	
Squamous differentiation	9	16%	
Lymphovascular invasion	8	14%	

BMI body mass index, *BSA* body surface area, *CGF* Cockroft–Gault formula, *CKD-EPI* Chronic Kidney Disease-EPIdemiology, *CrCl* creatinine clearance, *eGFR* estimated glomerular filtration rate, *MIBC* muscle-invasive bladder cancer, *NMIBC* non-muscle-invasive bladder cancer, *TURBT* transurethral resection of bladder tumor

[a]cN1: $N+8$; cN2: $N=3$; cN3: $N=1$

Safety

Table 2 summarizes AEs from C-NAC. All patients experienced AEs from chemotherapy; 55% experienced grade 3–4 AEs (ddMVAC: 66%; GC: 27%), most often hematological toxicity from ddMVAC. Red blood cell transfusion was performed in 29% of patients and platelet transfusion in 7%. Febrile neutropenia rate was 7%. One patient died shortly after the first C-NAC cycle (cause unknown). Immediate surgical outcomes are described in Supplementary Table 2; 1 patient died from cystectomy complications.

Downstaging

Seventeen of 30 cystectomy patients (57%) had downstaging to ypT < 2N0/x (pT0N0: 14; ypTisN0: 1; ypT1N0: 1; ypT0Nx: 1).

Seven of 15 patients (47%) who underwent post-chemotherapy TURBT and no cystectomy had no residual disease (ycT0) and 2 patients (13%) had non-muscle-invasive residual disease (ycT1).

Survival

Median follow-up from chemotherapy initiation was 36 months (47 months in patients alive at last follow-up).

Twenty-one patients had died; causes were disease progression (14), treatment related (during C-NAC: 1; postoperative: 1), intercurrent disease (3), and unknown (2).

Table 2 Adverse events from chemotherapy

	All grades (%)	Grade 3–4 (%)
Any adverse event	100	55
Anemia	91	21
Fatigue	84	2
Creatinine increase	75	5
Platelet count decrease	70	14
Nausea	61	4
Neutrophil count decrease	54	38
Vomiting	41	2
Weight loss	41	4
Constipation	39	0
Stomatitis	32	7
Diarrhea	27	2
Peripheral neuropathy	25	0
Infection (excluding febrile neutropenia)	11	5
Deep vein thrombosis	7	0
Febrile neutropenia	7	7
Hearing loss	5	0

Three-year OS was 65%; 5-year OS was 60%; median OS was not reached (Fig. 1A). OS was non-significantly better with ddMVAC than with GC; we found no association with locoregional management (data not shown).

Impact of baseline parameters

Polypharmacy and aaCCI ≥ 8 were non-significantly associated with decreased chemotherapy feasibility and increased toxicity (Table 3).

In univariate analysis, OS was significantly worse in patients with polypharmacy or aaCCI ≥ 8 (Fig. 1B, C, Table 4). In a multivariate analysis of 56 patients, polypharmacy retained a significant prognostic value (Table 4).

Undernutrition was associated with worse OS in 43 evaluable patients in univariate analysis (Supplementary Fig. 1). Incomplete data and lesser reliability of retrospective assessment precluded integration in the multivariate analysis.

Discussion

In this study, 73% of MIBC patients aged ≥ 75 completed 4 C-NAC cycles and 77% underwent cystectomy or chemoradiotherapy. Nine patients underwent 5 ddMVAC cycles, and 9 other 6 cycles. Grade 3–4 toxicity (including febrile neutropenia), downstaging, and OS compared aptly with those observed in patients aged 15 years younger in median in prospective trials [7, 12]. Interestingly, downstaging in cystectomy patients (ypT < 2N0: 57%; ypT0N0: 47%) was higher than in the recent study with 3 ddMVAC cycles (24%) [11], suggesting a benefit of longer-course ddMVAC.

Clinicians may systematically refrain from offering C-NAC to elderly patients because of perceived frailty. Although age alone is not a criterion, cisplatin eligibility decreases with age solely because of inadequate renal function defined by CGF CrCl < 60 mL/min [13]. Twenty-two patients in our study conformed to this definition: only 5 of them (23%) prematurely discontinued chemotherapy for renal toxicity. Comparatively, this was the case for 6 of 34 patients with initial CGF CrCl ≥ 60 mL/min (18%). CGF CrCl accuracy decreases with age, and guidelines endorse CKD-EPI eGFR to accurately estimate renal function in elderly patients [14]. Only 6 of our patients had CKD-EPI eGFR < 60 mL/min, still with no more frequent discontinuation for renal toxicity. Data from VESPER showed that CGF CrCl ≥ 50 mL/min was sufficient to safely administer C-NAC [15]. To mirror this, we postulate that CKD-EPI eGFR ≥ 50 mL/min may be a reasonable cutoff for cisplatin eligibility in elderly MIBC patients. External validation focusing on long-term renal outcomes is warranted.

Polypharmacy and aaCCI were significantly associated with OS and non-significantly with C-NAC feasibility and

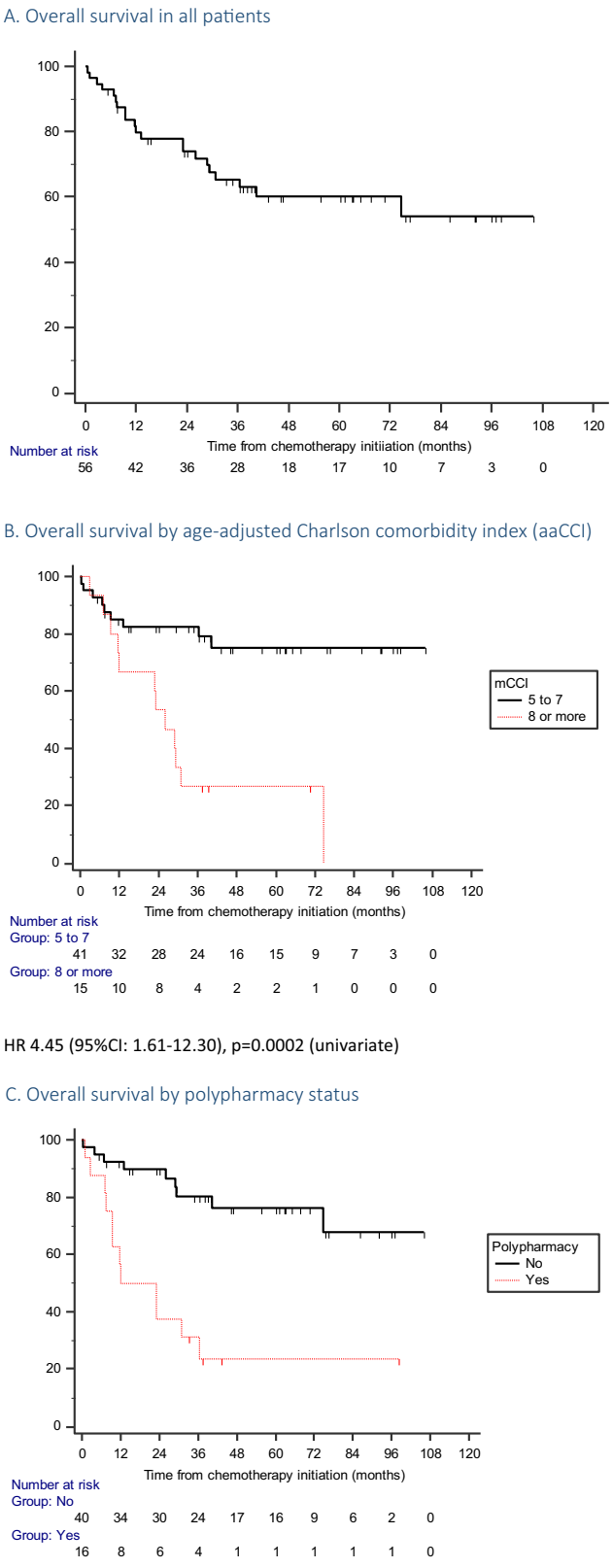

Fig. 1 Overall survival. **A** Overall survival in all patients. **B** Overall survival by age-adjusted Charlson comorbidity index (aaCCI). HR 4.45 (95% CI 1.61–12.30), $p=0.0002$ (univariate). **C** Overall survival by polypharmacy status. HR 4.87 (95% CI 1.72–13.80), $p=0.0001$ (univariate)

toxicity. This emphasizes the need for careful pretreatment evaluation of elderly MIBC patients with comorbidities. Several studies described the prognostic value of aaCCI in cancer: for instance, aaCCI is associated with mortality in non-metastatic patients aged ≥ 70 with diverse primaries [16], or with lower completion of adjuvant chemotherapy for pancreatic cancer [17]. Our observations echo these findings.

Seventeen patients underwent a complete prospective geriatric assessment. Median age was 79 (76–90). Thirteen had ECOG PS 0–1. Twelve had positive polypharmacy status. Median aaCCI was 7 (5–9). Based on a comprehensive assessment [18], 8 patients had undernutrition (moderate: 6; severe: 2). Six of 16 evaluable patients had ≥ 1 functional criterion for impaired muscle function (history of falls, unheld monopodal support, timed get-up-and-go test > 20 s, walking speed < 1 m/s); all 6 had CT-scan sarcopenia. Most had fully preserved autonomy (ADL 6/6: 14; IADL 4/4: 11). This prospectively characterized subset of our study population illustrates its fitness, especially when considering the bias in referring apparently frailer patients for geriatric assessment.

Despite being generally fit, 81% of our elderly patients had CT-scan sarcopenia. Interestingly, in a study of 146 MIBC patients, prevalence of similarly-defined sarcopenia was 45.9% [19] and mean age in sarcopenic patient was 73, as opposed to 66 in non-sarcopenic patients. Thus, conventional thresholds defining CT-scan sarcopenia seem inadequate for elderly patients. Functional assessment is warranted.

Few patients died from intercurrent illnesses, illustrating that the course of cancer defines prognosis in elderly MIBC patients, with negligible competitive mortality. Pathological response to C-NAC retained major prognostic value. Indeed, the life expectancy for a cancer-free 80-year old in France is currently 9–11 years (depending on gender), justifying all feasible curative-intent treatments in eligible elderly MIBC patients, even octogenarians.

Our study has limitations, first its retrospective nature. Outcomes such as number of C-NAC cycles, downstaging and OS are little impacted by memory bias, but safety data should be considered with more caution. Few patients were lost to follow-up. Findings regarding prognostic value of aaCCI and polypharmacy are hypothesis-generating and should be prospectively assessed in a validation cohort. Lack of systematic complete nutritional assessment including muscle strength is a limitation, given the high prevalence and dramatic prognostic value of undernutrition in

Table 3 Univariate analysis of secondary outcomes according to age and comorbidity-related parameters

All patients	Chemotherapy feasibility (≥4 cycles)		Occurrence of grade ≥3 toxicity		Pathological downstaging[a]	
	73%		55%		57%	
Age						
75–79	76%	OR 0.66	59%	OR 0.70	60%	OR 0.68
≥80	68%	$p=0.49$	50%	$p=0.59$	50%	$p=0.71$
Polypharmacy						
No	80%	OR 0.33	50%	OR 2.17	76%	OR 0.045
Yes	56%	$p=0.10$	69%	$p=0.24$	11%	$p=0.0016$
aaCCI						
5–7	78%	OR 0.43	51%	OR 1.88	65%	OR 0.23
≥8	60%	$p=0.19$	67%	$p=0.37$	29%	$p=0.19$

aaCCI age-adjusted Charlson comorbidity index, *OR* odds ratio

[a]Pathological downstaging was analyzed in 30 patients who underwent cystectomy

Table 4 Univariate and multivariate analyses of overall survival

	Univariate analysis			Multivariate analysis		
	HR	95% CI	*p*	HR	95 CI	*p*
Age (continuous)	1.0471	0.9574–1.1452	0.3167	1.0932	0.9775–1.2225	0.1203
aaCCI	**4.4537**	**1.6129–12.2981**	**0.0002**	2.0987	0.7821–5.6319	0.1431
Polypharmacy	**4.8724**	**1.7199–13.8039**	**0.0001**	**4.8404**	**1.5720–14.9041**	**0.0063**
Hydronephrosis	1.6696	0.6047–4.6098	0.2606	2.5144	0.9028–7.0032	0.0792
Lymph node involvement	1.6467	0.5120–5.2959	0.3225	2.5023	0.8364–7.4864	0.1026
Chemotherapy regimen (GC vs ddMVAC)	1.8210	0.6434–5.1539	0.1859	2.5847	0.9976–6.6973	0.0518

ddMVAC dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin, *GC* gemcitabine–cisplatin, *HR* hazard ratio, *aaCCI* age-adjusted Charlson comorbidity index

Bold characters highlight statistically significant results

elderly cancer patients [20, 21]. Treatment selection bias in the decision to administer C-NAC is also a concern; unfortunately we are not able to describe the selection processes that took place at both our institution and referring centers that led to exclusion of patients from C-NAC.

Still, although the number of patients remains small, this is the most-documented series to date of MIBC patients aged ≥75 treated with C-NAC. Our patients were probably more fit than the whole of elderly MIBC patients, so we recommend that clinicians remain attentive to baseline general health status and comorbidities before offering C-NAC, and refer them to oncogeriatricians for pretreatment evaluation.

In conclusion, C-NAC (including ddMVAC) is feasible and effective in selected MIBC patients aged ≥75, who should not be systematically barred from standard-of-care chemotherapy based on age alone. Evaluation of comorbidities and geriatric parameters as well as of tumor characteristic and cisplatin eligibility criteria informs patient selection.

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Author contributions CD was involved in project development, Data collection and analysis, and manuscript writing. AA was involved in project development, data collection, and manuscript writing. MH, ML, QA, P-LR, HG, and AP were involved in data collection. CH, VF-D, EX, and FD were involved in project development. AM-L and SC performed project development and manuscript editing.

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Data availability No publicly available data.

Declarations

Conflict of interest The authors have no competing interests to declare that are relevant to the content of this article.

Research involving human participants Clinical data collection was registered with institutional authorities and approved by the institutional Ethics Committee (No. IRB00006477). This research followed the principles outlined in the Declaration of Helsinki.

Informed consent Patients received written information regarding this study and could oppose research use of their medical data as per national French regulations.

References

1. EAU Guidelines on MIBC—Introduction—Uroweb. Uroweb—Eur Assoc Urol. n.d. https://uroweb.org/guidelines/muscle-invasive-and-metastatic-bladder-cancer. Accessed 19 Apr 2022.
2. Powles T, Bellmunt J, Comperat E, Santis MD, Huddart R, Loriot Y et al (2022) Bladder cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol 33:244–258. https://doi.org/10.1016/j.annonc.2021.11.012
3. Grossman HB, Natale RB, Tangen CM, Speights VO, Vogelzang NJ, Trump DL et al (2003) Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. N Engl J Med 349:859–866. https://doi.org/10.1056/NEJMoa022148
4. Sherif A, Holmberg L, Rintala E, Mestad O, Nilsson J, Nilsson S et al (2004) Neoadjuvant cisplatinum based combination chemotherapy in patients with invasive bladder cancer: a combined analysis of two Nordic studies. Eur Urol 45:297–303. https://doi.org/10.1016/j.eururo.2003.09.019
5. International Collaboration of Trialists, Medical Research Council Advanced Bladder Cancer Working Party (now the National Cancer Research Institute Bladder Cancer Clinical Studies Group), European Organisation for Research and Treatment of Cancer Genito-Urinary Tract Cancer Group, Australian Bladder Cancer Study Group, National Cancer Institute of Canada Clinical Trials Group, Finnbladder et al (2011) International phase III trial assessing neoadjuvant cisplatin, methotrexate, and vinblastine chemotherapy for muscle-invasive bladder cancer: long-term results of the BA06 30894 trial. J Clin Oncol 29:2171–7. https://doi.org/10.1200/JCO.2010.32.3139
6. Yin M, Joshi M, Meijer RP, Glantz M, Holder S, Harvey HA et al (2016) Neoadjuvant chemotherapy for muscle-invasive bladder cancer: a systematic review and two-step meta-analysis. Oncologist 21:708–715. https://doi.org/10.1634/theoncologist.2015-0440
7. Pfister C, Gravis G, Fléchon A, Chevreau C, Mahammedi H, Laguerre B et al (2022) Dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin or gemcitabine and cisplatin as perioperative chemotherapy for patients with nonmetastatic muscle-invasive bladder cancer: results of the GETUG-AFU V05 VESPER trial. J Clin Oncol. https://doi.org/10.1200/JCO.21.02051
8. Posielski N, Koenig H, Ho O, Porter C, Flores JP (2022) Use of neoadjuvant chemotherapy in elderly patients with muscle-invasive bladder cancer: a population-based study, 2006–2017. Oncology (Williston Park N Y) 36:21–33. https://doi.org/10.46883/2022.25920939
9. Chau C, Wheater M, Geldart T, Crabb SJ (2015) Clinical outcomes following neoadjuvant cisplatin-based chemotherapy for bladder cancer in elderly compared with younger patients. Eur J Cancer Care (Engl) 24:155–162. https://doi.org/10.1111/ecc.12282
10. Leone AR, Zargar-Shoshtari K, Diorio GJ, Sharma P, Boulware D, Gilbert SM et al (2017) Neoadjuvant chemotherapy in elderly patients with bladder cancer: oncologic outcomes from a single institution experience. Clin Genitourin Cancer 15:e583–e589. https://doi.org/10.1016/j.clgc.2017.01.014
11. Hemenway G, Lewis B, Ghatalia P, Anari F, Plimack ER, Kokate R et al (2022) Neoadjuvant chemotherapy with accelerated methotrexate, vinblastine, doxorubicin, and cisplatin in patients with muscle-invasive bladder cancer: a retrospective age-stratified analysis on safety and efficacy. Eur Urol Oncol. https://doi.org/10.1016/j.euo.2022.06.005
12. Pfister C, Gravis G, Fléchon A, Soulié M, Guy L, Laguerre B et al (2021) Randomized phase III trial of dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin, or gemcitabine and cisplatin as perioperative chemotherapy for patients with muscle-invasive bladder cancer. Analysis of the GETUG/AFU V05 VESPER trial secondary endpoints: chemotherapy toxicity and pathological responses. Eur Urol 79:214–221. https://doi.org/10.1016/j.eururo.2020.08.024
13. Dash A, Galsky MD, Vickers AJ, Serio AM, Koppie TM, Dalbagni G et al (2006) Impact of renal impairment on eligibility for adjuvant cisplatin-based chemotherapy in patients with urothelial carcinoma of the bladder. Cancer 107:506–513. https://doi.org/10.1002/cncr.22031
14. CKD Evaluation and Management—KDIGO n.d. https://kdigo.org/guidelines/ckd-evaluation-and-management/. Accessed 29 Apr 2022
15. Culine S, Harter V, Gravis G, Fléchon A, Chevreau C, Mahammedi H et al (2021) Chemotherapy for muscle-invasive bladder cancer: impact of cisplatin delivery on renal function and local control rate in the randomized phase III VESPER (GETUG-AFU V05) trial. Clin Genitourin Cancer 19:554–562. https://doi.org/10.1016/j.clgc.2021.08.005
16. Canoui-Poitrine F, Segaux L, Benderra M-A, About F, Tournigand C, Laurent M et al (2022) The prognostic value of eight comorbidity indices in older patients with cancer: the ELCAPA cohort study. Cancers 14:2236. https://doi.org/10.3390/cancers14092236
17. Aoyama T, Yamamoto N, Kamiya M, Murakawa M, Tamagawa H, Sawazaki S et al (2020) The age-adjusted Charlson comorbidity index is an independent prognostic factor in pancreatic cancer patients who receive curative resection followed by adjuvant chemotherapy. J Cancer Res Ther 16:S116–S121. https://doi.org/10.4103/jcrt.JCRT_440_18
18. Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T et al (2019) GLIM criteria for the diagnosis of malnutrition—a consensus report from the global clinical nutrition community. Clin Nutr 38:1–9. https://doi.org/10.1016/j.clnu.2018.08.002
19. Fraisse G, Renard Y, Lebacle C, Masson-Lecomte A, Desgrandchamps F, Hennequin C et al (2020) La sarcopénie est-elle un facteur de morbi-mortalité dans le traitement des tumeurs localisées de la vessie infiltrant le muscle? Prog En Urol 30:41–50. https://doi.org/10.1016/j.purol.2019.11.002
20. Zhang X, Pang L, Sharma SV, Li R, Nyitray AG, Edwards BJ (2019) Prevalence and factors associated with malnutrition in older patients with cancer. J Geriatr Oncol 10:763–769. https://doi.org/10.1016/j.jgo.2019.01.021
21. Poisson J, Martinez-Tapia C, Heitz D, Geiss R, Albrand G, Falandry C et al (2021) Prevalence and prognostic impact of cachexia among older patients with cancer: a nationwide cross-sectional survey (NutriAgeCancer). J Cachexia Sarcopenia Muscle 12:1477–1488. https://doi.org/10.1002/jcsm.12776

Authors and Affiliations

Clément Dumont[1,2] · Amélie Aregui[3] · Mathilde Hauchecorne[3] · Madeleine Lefèvre[3] · Quiterie Aussedat[1] · Pierre-Louis Reignier[4] · Hélène Gauthier[1] · Christophe Hennequin[2,5] · Virginie Fossey-Diaz[3] · Evanguelos Xylinas[2,6] · Atanas Pachev[7] · François Desgrandchamps[2,4] · Alexandra Masson-Lecomte[2,4] · Stéphane Culine[1,2]

✉ Clément Dumont
clement.dumont@aphp.fr

Amélie Aregui
amelie.aregui@aphp.fr

Mathilde Hauchecorne
mathilde.hauchecorne@aphp.fr

Madeleine Lefèvre
madeleine.lefevre@aphp.fr

Quiterie Aussedat
Quiterie-Caroline-Marie.AUSSEDAT@aphp.fr

Pierre-Louis Reignier
pierre.reignier@aphp.fr

Hélène Gauthier
helene.gauthier@aphp.fr

Christophe Hennequin
christophe.hennequin2@aphp.fr

Virginie Fossey-Diaz
virginie.fossey@aphp.fr

Evanguelos Xylinas
evanguelos.xylinas@aphp.fr

Atanas Pachev
atanas.pachev@aphp.fr

François Desgrandchamps
francois.desgrandchamps@aphp.fr

Alexandra Masson-Lecomte
alexandra.massonlecomte@aphp.fr

Stéphane Culine
stephane.culine@aphp.fr

[1] Medical Oncology Department, Saint-Louis Hospital, AP-HP.Nord Université Paris Cité, 1 Avenue Claude Vellefaux, 75475 Paris Cedex 10, France

[2] Université Paris Cité, Paris, France

[3] Oncogeriatrics Coordination Unit, AP-HP.Nord Université Paris Cité, Paris, France

[4] Urology Department, Saint-Louis Hospital, AP-HP.Nord Université Paris Cité, Paris, France

[5] Radiotherapy Department, Saint-Louis Hospital, AP-HP.Nord Université Paris Cité, Paris, France

[6] Urology Department, Bichat-Claude Bernard Hospital, AP-HP.Nord Université Paris Cité, Paris, France

[7] Radiology Department, Saint-Louis Hospital, AP-HP.Nord Université Paris Cité, Paris, France