pCR after neoadjuvant chemotherapy and survival in localized bladder cancer: A Moroccan experience

Abstract

Background: Neoadjuvant cisplatin-based chemotherapy followed by radical cystectomy is the standard of care for localized muscle-invasive bladder cancer (MIBC). Pathological complete response (pCR) is a strong prognostic marker for survival. However, real-world data from low- and middle-income countries remain limited.

Objective: To evaluate operability and pCR rates after neoadjuvant chemotherapy and their correlation with overall survival (OS) and relapse-free survival (RFS) in Moroccan patients with MIBC.

Methods: We conducted a retrospective, single-center study at the Medical Oncology Department of CHU Hassan II Fez, including 65 patients with MIBC who received at least 3 cycles of cisplatin-based neoadjuvant chemotherapy between January 2018 and December 2023.

Results: The median age was 62 years (range 40–78), with a male predominance (sex ratio 6.2). The operability rate was 55.4% (36/65). The pCR rate was 34.3% (12/35 evaluable patients). pCR was associated with a significant improvement in mean OS (60 vs 34.9 months; gain 25.1 months; $p = 0.026$). Operability also significantly improved OS (49 vs 19 months; gain 30 months; $p < 0.0001$). Mean RFS was longer in the pCR group (59.2 vs 39.8 months), but the difference was not statistically significant ($p = 0.091$). Grade 1 ototoxicity occurred in 20% of patients, with no renal failure.

Conclusion: Neoadjuvant Gemcitabine-Cisplatin achieved a pCR rate of 34.3% in this Moroccan cohort, with a significant survival benefit for pCR patients. However, the emergence of immunotherapy and ADC-based combinations (NIAGARA, EV-304) is changing the treatment paradigm. New real-world studies are needed to evaluate these novel therapies in resource-limited settings.

Keywords: Bladder cancer; neoadjuvant chemotherapy; pathological complete response; overall survival; real-world data; Morocco

Introduction

Muscle-invasive bladder cancer (MIBC) is an aggressive tumor whose standard treatment in cisplatin-eligible patients relies on cisplatin-based neoadjuvant chemotherapy (NAC) followed by radical cystectomy [1,2]. This strategy aims to eradicate micrometastases, reduce tumor volume, and improve overall survival (OS). Pathological complete response (pCR), defined as

the absence of residual tumor on the surgical specimen, is a major prognostic marker associated with significant improvements in OS and relapse-free survival (RFS) [3].

In the literature, pCR rates after NAC range from 30 to 40%, with OS gains of up to 20–30 months in complete responders [4,5]. However, most of these data come from clinical trials conducted in high-income countries with selected populations. Few studies have evaluated the applicability of this approach in resource-limited settings or emerging countries, where constraints such as healthcare access, follow-up losses, and surgical delays may significantly affect outcomes.

The aim of our study was to assess, in a cohort of Moroccan patients followed at CHU Hassan II Fez, the operability and pCR rates after cisplatin-based NAC, as well as their correlation with overall survival and relapse-free survival.

Material and Methods

Study design and setting

We conducted a retrospective, single-center study at the Medical Oncology Department of CHU Hassan II Fez, Morocco, over a six-year period from January 2018 to December 2023.

Patient population

We included all patients with muscle-invasive bladder cancer (MIBC) who received at least 3 cycles of cisplatin-based neoadjuvant chemotherapy followed by planned radical cystectomy. Exclusion criteria were:

- Upfront cystectomy without NAC
- Metastatic disease at diagnosis
- Exclusive chemoradiotherapy
- Incomplete medical records

A total of 65 patients were included in the analysis.

Treatment protocol

The majority of patients received the Gemcitabine-Cisplatin regimen (GemCis). A minority received dose-dense MVAC (dd-MVAC). All patients underwent restaging after NAC, and radical cystectomy was performed when feasible.

Statistical analysis

Data were analyzed using SPSS software. Survival curves were estimated using the Kaplan-Meier method and compared using the log-rank test. A p-value < 0.05 was considered statistically significant.

Results

A total of 65 patients were included in this retrospective study. The median age was 62 years (range: 40–78 years), with a strong male predominance and a sex ratio of 6.2. The median follow-up was 24 months (range: 6–60 months). The majority of patients (95.4%) received the Gemcitabine-Cisplatin regimen as neoadjuvant chemotherapy, while only 3 patients (4.6%) received dose-dense MVAC. Regarding toxicity, grade 1 ototoxicity was observed in 20% of patients, and no case of renal failure was reported. The overall operability rate after neoadjuvant chemotherapy was 55.4% (36 out of 65 patients). The main reasons for non-operability were metastatic progression during chemotherapy (15%), patient refusal of surgery followed by chemoradiotherapy (14%), loss to follow-up (9%), and surgery that was indicated but not yet performed by the time of study closure (6%). Among the 36 operated patients, the pathological complete response (pCR) rate was 34.3% (12 out of 35 evaluable patients). For the entire cohort, the mean overall survival was 38.3 months (95% CI: 28.0 – 46.4 months). Operability was strongly correlated with improved overall survival: operable patients had a mean overall survival of 49 months compared to 19 months for non-operable patients, representing a gain of 30 months ($p < 0.0001$). (Figure 1) Regarding pCR, patients who achieved a complete pathological response had a mean overall survival of 60 months (95% CI: 51.8 – 68.1 months), with the median not reached. In contrast, the non-pCR group had a mean overall survival of 34.9 months (95% CI: 24 – 45 months) and a median of 31.8 months. Thus, pCR was associated with a significant improvement in overall survival, with a mean gain of 25.1 months ($p = 0.026$). (Figure 2) Concerning relapse-free survival, although early tumor relapses were more frequent in the non-pCR group, the difference did not reach statistical significance: the mean relapse-free survival was 59.2 months in the pCR group versus 39.76 months in the non-pCR group ($p = 0.091$). (Figure 3)

Figure 1 :OS according to operability status

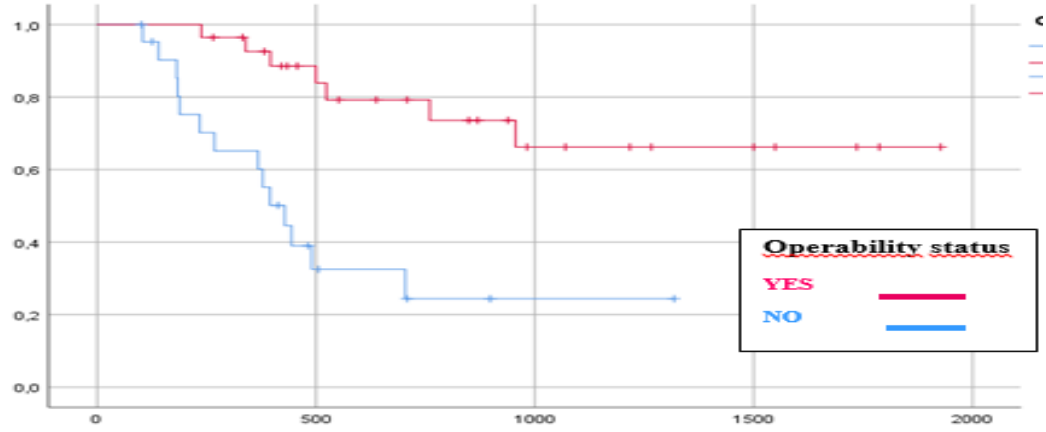

Figure 2 :OS according to pCR

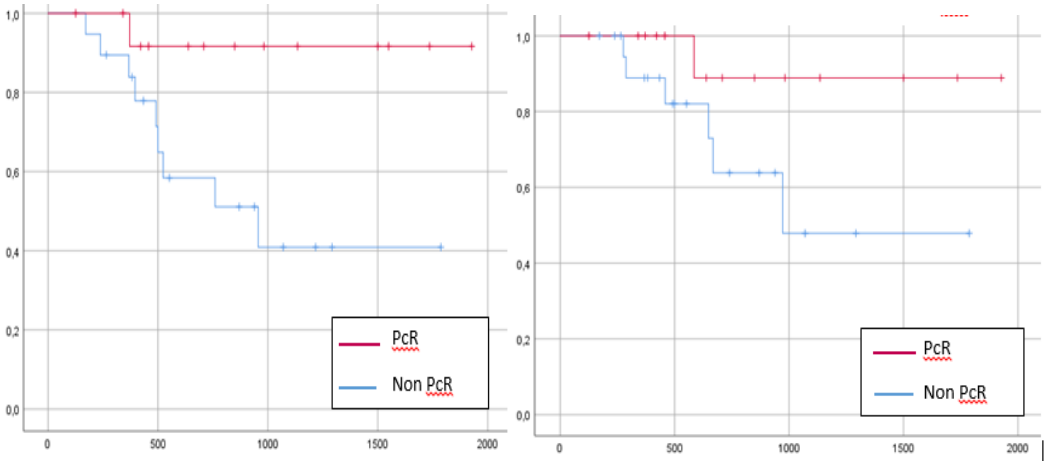

Figure 3 :RFS according to pCR

Discussion

Our study reports one of the first real-world Moroccan series evaluating the correlation between pathological complete response after neoadjuvant cisplatin-based chemotherapy and survival in patients with localized muscle-invasive bladder cancer, with a pCR rate of 34.3% and a mean overall survival gain of 25.1 months in pCR patients (p = 0.026). These results are consistent with historical landmark trials such as SWOG-8710 (pCR 38%, median survival benefit 25 months) [1] and with a large meta-analysis confirming a 5% absolute survival benefit with neoadjuvant platinum-based chemotherapy [2]. Importantly, our pCR rate is also comparable to recent real-world data: a Finnish nationwide analysis of 1,157 patients reported a pCR rate of 34% among those receiving neoadjuvant chemotherapy, with 5-year overall survival of 89% for pT0N0 patients and 82% for those with organ-confined residual disease [3]. Similarly, the Italian RealBLADDER study (173 patients) reported a pCR rate of 33.6% and a non-invasive downstaging rate of 36.8% in routine clinical practice, with 12-month disease-free survival of 73.7% [4]. In a Norwegian real-world cohort of 124 patients, the 5-year actuarial overall survival was 67% among those receiving neoadjuvant ddMVAC, with downstaging to ≤pT1 achieved in 49% of patients [5]. A large US real-world analysis using the National Cancer Database (47,983 patients) confirmed that neoadjuvant systemic therapy was associated with improved overall survival compared to adjuvant therapy, and that pathological downstaging to pT0N0 after NAC was associated with a 5-year overall survival rate of approximately 85% [6]. A recent stage-matched analysis of 513 patients further demonstrated that patients achieving pCR after NAC had excellent outcomes, with a median overall survival of 60.5 months [7]. These real-world findings across different healthcare systems reinforce our conclusion that pCR is a robust prognostic marker even outside clinical trial settings. Beyond clinical outcomes, identifying which patients are most likely to achieve pCR is a critical research priority. A comprehensive review by Miyagi et al. summarizes several predictors of complete response to neoadjuvant chemotherapy in muscle-invasive bladder cancer [11]. These include clinical factors such as baseline tumor stage (cT2 vs cT3-T4) and the absence of hydronephrosis, as well as molecular biomarkers including DNA damage repair (DDR) gene alterations (notably ERCC2, ATM, RB1, and FANCC) and the luminal molecular subtype. In our cohort, we did not systematically collect these predictive factors due to the retrospective design and limited access to molecular profiling. However, our observed pCR rate of 34.3% falls within the range reported in studies that included patients with favorable clinical predictors. Future prospective studies in our setting should incorporate standardized collection of clinical and, when feasible, molecular variables to better identify patients most likely to achieve pCR and thus derive the greatest survival benefit from neoadjuvant chemotherapy. Our operability rate of 55.4% is lower than in clinical trials (typically >80%), but this aligns with real-world challenges including metastatic progression (15%), patient refusal of surgery (14%), and loss to follow-up (9%) – figures that are rarely reported in controlled trials but reflect everyday practice in many countries. Regarding relapse-free survival, although the pCR group had a numerically longer mean RFS (59.2 vs 39.8 months), the difference was not statistically significant (p = 0.091), likely due to our limited sample size and follow-up duration. Concerning the chemotherapy regimen, the vast majority of our patients received Gemcitabine-Cisplatin, which showed a favorable safety profile with only grade 1 ototoxicity in 20% and no renal failure, consistent with real-world tolerability data [5]. Our study has several limitations: it is retrospective and single-center with a relatively small sample size (65 patients); the median follow-up of 24 months is relatively short; we did not collect detailed data on pathological staging beyond pCR status; and loss to follow-up (9%) and refusal of surgery (14%) may have introduced selection bias. It is important to emphasize

that our study was conducted before the advent of immunotherapy in the neoadjuvant setting for bladder cancer. Since then, the treatment landscape has dramatically changed. The ABACUS trial demonstrated a pCR rate of 31% with neoadjuvant atezolizumab alone in cisplatin-ineligible patients [8]. Looking forward, recent groundbreaking trials such as NIAGARA (durvalumab plus chemotherapy) and KEYNOTE-B15/EV-304 (Enfortumab Vedotin plus Pembrolizumab) have reported pCR rates of 37% and 55.8% respectively [9,10], fundamentally changing the standard of care. Given this paradigm shift, new real-world studies are urgently needed, particularly in low- and middle-income countries like Morocco, to evaluate the feasibility, tolerability, and cost-effectiveness of these novel combinations in less selected, real-world populations.

Conclusion

In our Moroccan cohort of patients with localized muscle-invasive bladder cancer, neoadjuvant cisplatin-based chemotherapy achieved a pCR rate of 34.3%, which was associated with a significant 25.1-month improvement in overall survival. Operability was 55.4%, reflecting real-world challenges. While these results confirm the efficacy of Gemcitabine-Cisplatin, the emergence of immunotherapy and ADC-based combinations is fundamentally changing the standard of care. New real-life studies are essential to evaluate the applicability of these advances in resource-limited settings.

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