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Original article

Quality of life in patients with cisplatin-resistant urothelial cancer: Typical ailments and effect of paclitaxel-based salvage therapy

Guenter Niegisch, M.D.[a,*], Margitta Retz, M.D.[b], Roswitha Siener, M.D.[c], Peter Albers, M.D.[a]

[a] *Department of Urology, Medical Faculty, Heinrich-Heine-University, Düsseldorf, Germany*
[b] *Department of Urology, Klinikum rechts der Isar der Technischen Universität München, Munich, Germany*
[c] *Department of Urology, Bonn University, Bonn, Germany*

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Abstract

Introduction: Efficacy of palliative second-line treatment in patients suffering from advanced urothelial cancer (aUC) is limited. Accordingly, careful observation of patient-reported and treatment-related changes of quality of life (QoL) is mandatory. Therefore, we evaluated "typical" ailments and treatment related QoL changes in these patients.

Patients and methods: Results of the EORTC QLQ-C30 questionnaire were reviewed in 129 patients included in 2 prospective trials on paclitaxel-based treatment of cisplatin-resistant aUC (gemcitabine/paclitaxel: 102 patients [AB 20/99]; paclitaxel/everolimus: 27 patients [AB 35/09]). Eligible patients had completed EORTC QLQ-C30 questionnaire questionnaire before treatment start and available data on response. Global health status (QL), functional scales (FuSc) and symptom scales (SySc) were compared with published normative data for patients suffering from metastatic/recurrent cancers. Treatment related changes of QoL were evaluated. For statistical evaluation 2-way analysis of variance was used.

Results: A total of 87 patients were eligible (63 men and 24 women, median age = 65 [interquartile range: 60-71] y, AB 20/99: 63 patients [72%], AB 35/09: 24 patients [28%]). Compared with metastatic/recurrent cancers normative data, impaired emotional FuSc (−11.6 [95% CI: −21.0 to −2.1] points, $P < 0.01$) and higher pain SySc (+12.9 [CI: 3.7–22.1] points, $P < 0.001$) were the most relevant differences. QL and further FuSc/SySc were comparable. Pain SySc was significantly lower after 3 (−15.8 [CI: −31.4 to −0.7] points, $P < 0.01$] and 4 cycles (−13.6 [CI: −29.2–2.1] points, $P < 0.05$). Further changes of QL, FuSc or SySc during treatment were not observed. QL, FuSc, and SySc at baseline and during treatment did not differ between responders and nonresponders.

Conclusions: Patients with aUC who received additional treatment demonstrated QoL changes similar to persons with other recurrent/metastatic cancers. Special emphasis should be attributed to pain and emotional problems. Despite treatment related side effects, patients did not report impairment of QoL.

Keywords: Urothelial carcinoma; Chemotherapy; Quality of life; Patient-reported outcomes

1. Introduction

Systemic treatment of metastatic or relapsed urothelial carcinoma (UC) after cisplatin-based upfront chemotherapy is a challenging task. Currently, a standard therapy has not been defined and efficacy of various monotreatment and combinatorial-treatment approaches are at its best modest. For instance, patients treated with vinflunine which is approved in Europe for treatment of relapsed UC after failure of cisplatin-based chemotherapy may expect a median progression-free and overall survival of only 3.0 and 6.9 months, respectively, compared with 1.5 and 4.6 months in patients receiving best supportive care only [1]. Other treatment regimens, e.g., taxane monotherapy or taxane-based combination treatments do not do better [2–4]. Patients undergoing salvage treatment upon cisplatin failure are often prone to treatment-related side effects. Apart from

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* Corresponding author: Tel.: +49-211-81-18110; fax: +49-211-81-16767.
E-mail address: Guenter.Niegisch@med.uni-duesseldorf.de (G. Niegisch).

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myelosuppression, side effects frequently observed are especially fatigue and gastrointestinal complaints [1–4].

Given an only modest treatment efficacy on one side and significant side effects on the other side, treatment decision should rely on individual prognostic factors (which may help identify patients likely to profit from salvage treatment) as well as on the effect of salvage treatment on the individual quality of life (QoL) of the patient. Although prognostic factors have been thoroughly investigated, data on QoL in this population is scarce [5–7]. In contrast to other malignancies, no data on typical ailments and virtually no normative data for QoL questionnaires in patients suffering from metastatic urothelial cancer are available. Though several trials have included assessments on QoL parameters, results are published only scarcely and mostly focusing on single items in which improvement or deterioration was observed during the course of the trial. Lack of comprehensive information on the effect of systemic treatment in this population may preclude both patients and physicians from opting to start "second-line" treatment after failure of cisplatin-based upfront chemotherapy, even if effect on both oncological and QoL outcome might be beneficial.

In this context, we re-evaluated QoL assessed in 2 trials on paclitaxel-based treatment of cisplatin refractory urothelial cancer patients to address the question on which ailments we should have a special focus on and whether salvage chemotherapy commonly associated with significant treatment related side effects must necessarily result in an impairment of patients' reported QoL [2,8].

Patients and methods

Data acquisition

Results of the EORTC QLQ-C30 questionnaire (QLQ-C30) were reviewed in 129 patients included in 2 prospective trials on paclitaxel-based treatment of advanced UC after failure of platin-based upfront therapy (gemcitabine/paclitaxel: 102 patients [AB 20/99]; paclitaxel/everolimus: 27 patients [AB 35/09]). In both the trials, paclitaxel (175 mg/m²) was administered following a 3-week schedule. Further details on the treatment schedules are available from the according publications [2,8]. In both the trials, response rate was evaluated according to the "*Response evaluation criteria in solid cancers version (RECIST) 1.1*." In the AB 20/99 trial, Karnofsky performance status was documented instead of the Eastern Cooperative Oncology Group performance status (ECOG PS). Interconversion of Karnofsky performance status to ECOG PS was performed according to the recent suggestion of Ma et al. [9]. For the analysis of baseline global health status (QL), functional scales (FuSc), and symptom scales (SySc), patients with completed QLQ-C30 before the start of treatment and available data on treatment response were eligible. For the analysis of treatment-related changes of QL, FuSc, and SySc patients with available data on treatment response, completed QLQ-C30 before start of treatment and with at least 1 completed QLQ-C30 after the first treatment cycle were eligible. QoL assessment in both trials was performed by QLQ-C30 after randomization either at day 1 of each treatment cycle or immediately before day 1 of each treatment cycle.

Data analysis

QL, FuSc, and SySc were calculated using an R-routine from the raw data according to the EORTC QLQ-C30 Scoring Manual (third edition 2001) [10,11]. Score values used for each scale were continuous measures raging from 0 to 100, where higher scores of QL and FuSc represented a high level of QL and functioning, respectively. High score values of SySc represented a high symptom burden [10,11]. In case of missing items in a completed questionnaire, the according item of the questionnaire was omitted from analysis.

To assess typical ailments of patients with UC after failure of cisplatin-based upfront therapy QL, FuSc, and SySc of this population were compared with published normative data for patients suffering from metastatic/recurrent cancers (MET) [12]. The MET data are based on QoL data of 4,812 patients with either recurrent or metastatic malignant disease (breast cancer—1,147 patients [24%], colorectal cancer—653 patients [14%], esophageal/stomach cancer—642 patients [13%], prostate cancer—640 patients [13%], malignant melanoma—387 patients [8%], testicular cancer—359 [8%], and other malignancies—984 patients [20%]). The MET data do not include patients suffering from UC. QoL assessment in the MET population was performed using the EORTC QLQ-C30 v1.0, v2.0, v3.0 or a newer version in 14%, 43%, 42%, and 1% of patients, respectively.

Score changes were classified into differences with minimal (5–10 score points), moderate (10–20 score points), and strong (>20 score points) clinical significance following the suggestion of Osaba et al. [13].

To follow treatment related changes, individual baseline QL, FuSc, and SySc were compared with QL, FuSc, and SySc as assessed before the according treatment cycles.

In addition changes of QL, FuSc, and SySc in patients with and without treatment response were compared and analyzed depending on sex and performance status.

Statistical methods

A 2-way analysis of variance including Bonferroni's posttest was used to compare trial data to MET normative data. QL, FuSc, and SySc at each time point were compared with the according scale measure at baseline by nonparametric 2-way analysis of variance including Bonferroni's post-test. QoL assessments at each time point were treated as independent measures. Mann-Whitney-*U* and Kruksal-Wallice test were