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Penile Cancer

Neoadjuvant Chemotherapy in Advanced Penile Carcinoma

Joost A.P. Leijte^a, J. Martijn Kerst^b, Evert Bais^b, Ninja Antonini^c, Simon Horenblas^{a,*}

^a Department of Urology, The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

^b Department of Medical Oncology, The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

^c Department of Biometrics, The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

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Abstract

Objective: Little data on the role of neoadjuvant chemotherapy for advanced penile carcinoma are available. We describe the experiences at our institute.

Methods: A total of 20 patients received neoadjuvant chemotherapy for downstaging of irresectable disease in the period from 1972 until August 2005. During this 34-yr period, five different chemotherapeutic regimens were used. We evaluated clinical tumour response, chemotherapeutic toxicity, rate and type of subsequent surgery, histopathologic features, and long-term clinical outcome.

Results: An objective tumour response was achieved in 12 of 19 evaluable patients. Overall 5-yr survival was 32%. A significant difference ($p = 0.012$) in survival was found between responders (5-yr survival 56%) and non-responders (all patients died within 9 mo). Nine responders underwent subsequent surgery with curative intent. Eight of them were long-term survivors without evidence of recurrent disease. Three nonresponders were operated on to improve local control. All died within 8 mo after surgery. Toxicity of chemotherapy was high with three toxic deaths and discontinuation of treatment in one patient.

Conclusions: Of 20 patients with advanced penile carcinoma, 12 were responsive to neoadjuvant chemotherapy and 8 were long-term survivors after subsequent surgery. These results suggest that neoadjuvant chemotherapy is a valuable treatment option for patients with irresectable penile carcinoma, which is otherwise considered incurable. Surgery should be performed only in patients showing clinical response to chemotherapy because prognosis for nonresponding patients who underwent surgery was dismal and local control was not improved.

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* Corresponding author. Department of Urology, The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands.
Tel. +31 20 5122553; Fax: +31 20 5122554.
E-mail address: s.horenblas@nki.nl (S. Horenblas).

1. Introduction

While therapy for local and locoregionally metastasised penile carcinoma is straightforward, a significant number of patients present with irresectable disease, that is, fixed inguinal lymph nodes or inoperable locally advanced disease. Even in advanced cases, haematogenic spread is rare. Distant metastases are present in 1–2% of patients at initial presentation [1]. Patient delay is an important factor explaining presentation in such advanced state of disease.

If left untreated, prognosis of irresectable disease is ominous, with a 3-yr mortality rate of >90% in early series of untreated penile carcinoma [1–3]. Treatment options for this advanced stage of disease are often limited to palliative radiation and chemotherapy. However, in a selected group of patients without evidence of distant metastasis, neoadjuvant chemotherapy has successfully been used for downstaging disease to enable surgery with curative intent. Literature on this topic is fragmented, as no large series are available and most neoadjuvant chemotherapy cases are described as part of general series of advanced penile carcinoma [4–8]. The aim of this study was to assess the value of neoadjuvant chemotherapy in 20 patients with irresectable penile carcinoma treated at our institute.

2. Methods

2.1. Patient selection and indication for neoadjuvant chemotherapy

We reviewed in our database all patients treated at our institute for penile carcinoma up to August 2005. Only patients with a minimum follow-up of 1 yr were included. Of the 477 patients who were treated in the period from 1972 until August 2005, 20 received neoadjuvant chemotherapy for downstaging of irresectable penile carcinoma.

The indication for neoadjuvant chemotherapy was downstaging of inoperable regionally or locally advanced disease, that is, fixed inguinal lymph nodes or irresectable locally advanced disease in patients with sufficient performance status and without evidence of distant metastasis (M0).

2.2. Staging

Tumour stage was (re)classified according to the 2002 TNM classification [9] and recorded at the start of chemotherapeutic treatment, on the basis of physical examination, radiologic imaging, and histopathologic examination when available.

2.3. Chemotherapy

During 34 yr, five different regimens were used consecutively (Table 1). Until 1985 single-agent therapy with bleomycin (Bleo) was used; from 1986 until 1999 combination chemotherapy with Bleo, vincristin (Vin), and methotrexate (MTX) was used; and from 1999 until 2001 combination therapy of 5-fluorouracil (5FU) and cisplatin (Cis) was used. Since 2001, a regimen containing Cis, Bleo, and MTX was used. One patient was included in the European Organisation for Research and Treatment of Cancer (EORTC) 30992 study protocol [10] and treated with Cis and CPT-11 (irinotecan). Chemotherapy was discontinued in case of tumour progression or severe toxicity. When necessary, dose adjustments were made on the basis of haematologic and renal toxicity.

2.4. Response

Tumour response was recorded on the basis of physical examination and radiologic imaging at least every two cycles and was divided into the following categories: complete response, partial response, and stable/progressive disease. Complete response was defined as total disappearance of measured lesions on physical examination and imaging; partial response as decrease of the sum of diameters of lesions, without simultaneous increase in size of any of the lesions or the appearance of new lesions; and stable/progressive disease as no measurable response or increase in summed diameter of measured lesions, as well as the appearance of any new lesions.

Table 1 – Overview of chemotherapeutic treatment

Drug/combination/dose	No. of patients	No. of responders (%)
Bleo (Bleo 15 mg iv days 1 and 3, repeated weekly until total maximum dose of 200–300 mg)	3	1 (33)
Bleo/Vin/MTX (Bleo 15 mg iv days 1 and 2, Vin 1 mg iv day 1, MTX 30–50 mg iv day 3, repeated with a 1-wk interval until maximum of 12 cycles)	5	3 (60)
5-FU/Cis (5-FU 1000 mg/m ² iv days 1–5, Cis 100 mg/m ² iv day 1, repeated with a 3-wk interval until maximum of 5 cycles)	1	1 (100)
Bleo/Cis/MTX (Bleo 15 mg iv days 2–5, Cis 20 mg/m ² iv days 2–5, MTX 200 mg/m ² iv day 1, repeated with a 3-wk interval until maximum of 4 cycles)	10	6 (67) [*]
Cis/CPT-11 (irinotecan) [†] (Cis 80 mg/m ² iv day 1, CPT-11 60 mg/m ² iv days 1, 8, and 15, repeated with a 2-wk interval until maximum of 8 cycles)	1	1 (100)

Bleo = bleomycin; Vin = vincristine; MTX = methotrexate; 5FU = 5-fluorouracil; Cis = cisplatin.

^{*} One patient was not evaluable.

[†] Included in the European Organisation for Research and Treatment of Cancer (EORTC) 30992 study [10].

2.5. Toxicity

Information on toxicity was obtained from patient charts and, whenever possible, classified according to the common terminology criteria of adverse effects [11]. In Bleo-containing regimens, chest X-rays and on-indication lung function tests were done to assess possible pulmonary toxicity. Regular blood tests, including renal function, and white blood cell and platelet counts, were done to monitor toxicity.

2.6. Surgery

The procedures performed in patients considered eligible for subsequent surgery after chemotherapy were inguinal lymph node dissection, pelvic lymph node dissection, and partial and total penectomy. Some of the procedures necessitated extended removal of surrounding soft tissue, with or without parts of the pelvic bony structures. Reconstruction was done with the aid of vascularised flaps.

2.7. Statistical analysis

Overall survival was defined as the date of start of neoadjuvant chemotherapy to the last date of follow-up or death. Survival probabilities were estimated with the Kaplan-Meier method. For further analysis all patients receiving neoadjuvant chemotherapy were divided into two groups: nonresponders (stable/progressive disease) and responders (partial and complete response). To analyse possible correlation with survival, univariate analysis with a log-rank test was performed for the following variables: response to chemotherapy, T category, N category, tumour differentiation, and age at start of chemotherapy. One unevaluable patient was excluded from further analyses. All analyses were performed with the software packages Statistical Package for the Social Scientists, version 12.0 (SPSS Inc, Chicago, IL, USA) and SAS (SAS Institute Inc, Cary, NC, USA), version 9.1. A p value <0.05 was considered statistically significant.

3. Results

3.1. Patient characteristics

All 20 patients had a histopathologically proven squamous cell carcinoma of the penis, of which one was a spindle cell (sarcomatoid) carcinoma. (See Table 2 for further details.)

3.2. Chemotherapy and tumour response

One patient (receiving Bleo/Cis/MTX) died of toxicity within 2 wk after starting chemotherapy, before tumour response could be evaluated. An objective tumour response was measured in 12 of the remaining 19 patients (63%), consisting of 2 complete and 10 partial responses. Stable/progressive disease was found in 7 (37%) patients. (See Table 1 for more details.)

Table 2 – Patient characteristics

Total no. of patients	20
Age at start of chemotherapy, yr (mean [range])	62 (35–79)
Tumour stage	
T1N3	1
T2N3	4
T3N0*	1
T3N3	6
T4N0	1
T4N1	1
T4N3	6
Differentiation	
Good	8
Moderate	5
Poor	6
Unknown	1

* Neoadjuvant chemotherapy for rapidly progressing recurrence of spindle cell carcinoma.

3.3. Survival

Median follow-up was 23 mo (range: 1–134). The overall 5-yr survival was 32% (95% confidence interval [95%CI], 17–62%). A significant difference in survival (log-rank test; $p=0.012$) was found between patients responsive to chemotherapy and nonresponsive patients (Fig. 1). In the group of responders, 5-yr survival was 56% (95%CI, 34–94%), while all nonresponders died within 9 mo after start of treatment. No significant correlation was found between T category ($p=0.75$), N category ($p=0.85$), tumour differentiation ($p=0.65$), age ($p=0.26$), and survival.

3.4. Toxicity

Severe toxicity occurred in 4 of 20 patients: 3 toxic deaths were recorded and treatment had to be discontinued in 1 patient. The first patient died of

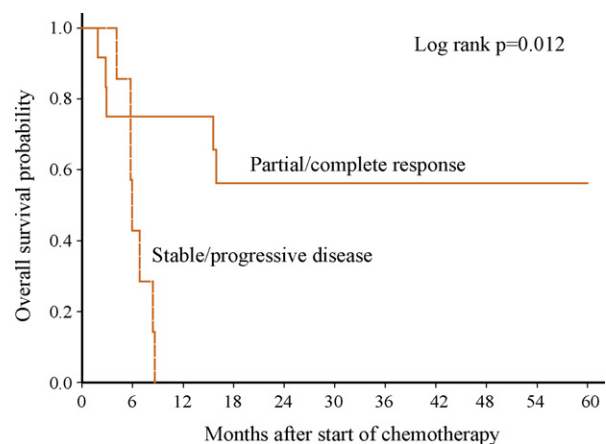


Fig. 1 – Overall survival probability according to clinical response.

an autopsy-confirmed bleomycin pneumonia with lung emboli, 3 mo after start of chemotherapy (Bleo/Vin/MTX). The second patient died of thromboembolic complications involving brain stem infarction, within 2 wk after the start of chemotherapy (Bleo/Cis/MTX). The third patient died of a bacterial pneumonia during a period of prolonged leucopenia, 3 mo after the start of chemotherapy (Bleo/Cis/MTX). The discontinuation of treatment in 1 patient (Bleo/Cis/MTX) was related to severe pulmonary toxicity (grade 3), probably caused by bleomycin. It should be noted that 3 of the 4 patients with severe toxicity received the Bleo/Cis/MTX regimen. Grade 1 and 2 nausea and increased fatigue were almost universally reported side-effects, as was grade 1 or 2 alopecia in a large number of patients.

3.5. Surgery

Of 20 patients treated with neoadjuvant chemotherapy, 9 responders to chemotherapy (2 complete and 7 partial) underwent subsequent surgery. Another 3 responders were scheduled for surgery, but 2 of them died of chemotherapeutic toxicity before they could be operated on and 1 patient was declared

unfit for operation. Three nonresponders were operated on in an attempt to improve local control. (See Fig. 2 for more details.)

An overview of performed operations can be found in Table 3. When needed, large skin defects were covered with the use of vascularised flaps and the aid of a plastic surgeon.

There was a significant difference ($p < 0.001$) in survival between the responders and nonresponders after surgery. All three nonresponders had fatal locally recurrent disease: one patient died of bleeding due to invasion in the femoral artery, and two patients with widespread cutaneous metastases died of infectious complications, all within 8 mo after surgery. Only one of nine patients in the group of responders had locally recurrent disease and died of bleeding due to ingrowth in the femoral artery and vein. This patient had extensive invasion in the surrounding tissue, including the pubic and symphysis bones.

3.6. Histopathologic findings

No residual tumour (pT0N0) was found in the two patients with a clinically complete response. All

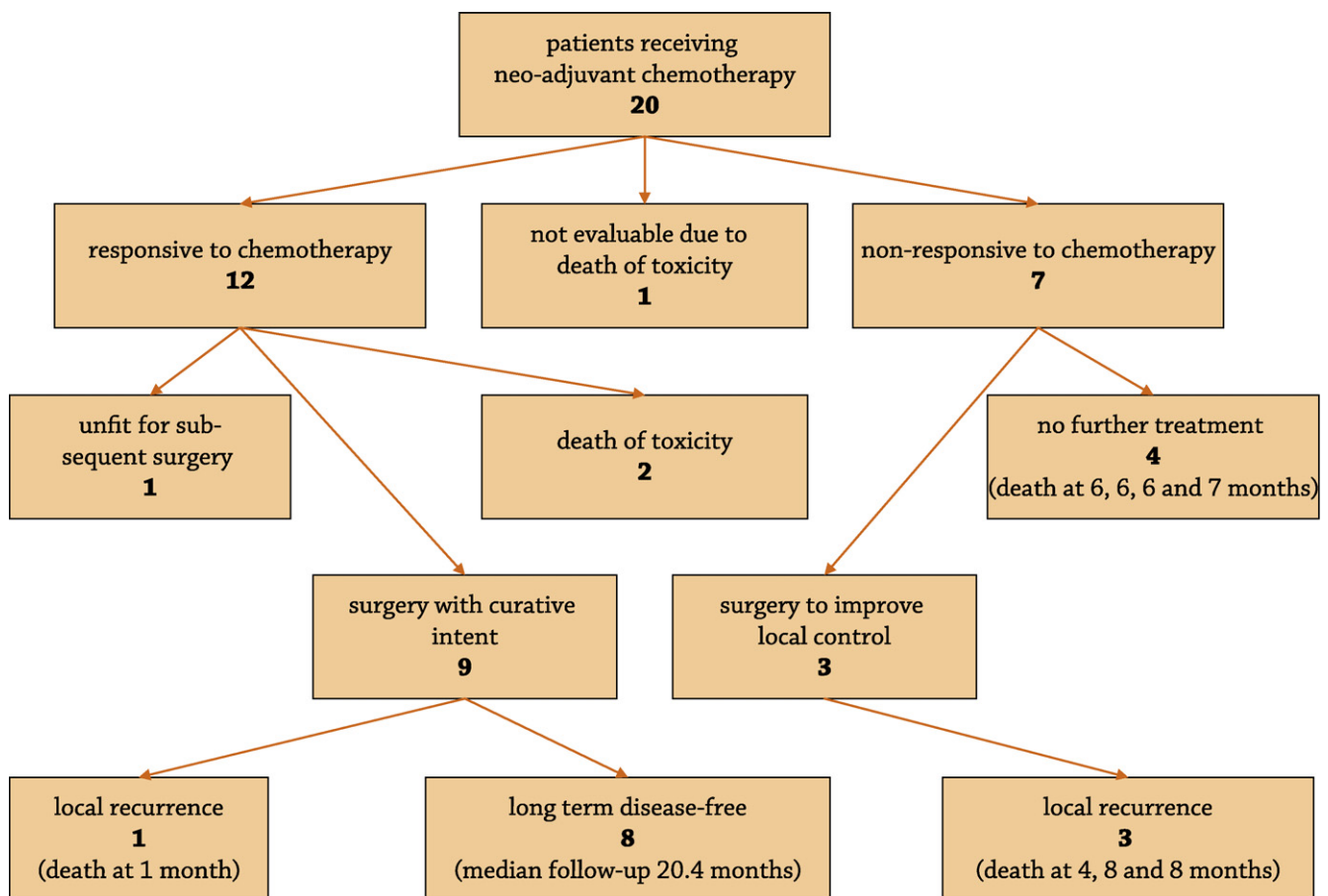


Fig. 2 – Schematic overview of various treatments.

Table 3 – Overview of performed operations

Type of surgery*	Responders (n = 9)	Nonresponders (n = 3)
Inguinal lymph node dissection		
Bilateral	5	0
Unilateral	1	1
Bilateral with en bloc resection of prepubic fat	3	2
Bilateral pelvic lymph node dissection	2	3
Partial penile amputation	3	1
Total penile amputation	2	1
Partial resection of pubic and symphysis bone	1	0

* More than one type of surgery per patient is possible.

partial responders had radically excised residual viable tumour, except for one patient with extensive tumour spread with invasion in the pubic and symphysis bone and prostate (pT4). The three nonresponding patients who underwent surgery to improve local control all had positive inguinal and pelvic nodes (pN3), and local recurrences (as mentioned above) occurred within 3 mo after surgery. Histopathologic findings were related to outcome; pelvic lymph node involvement as well as extensive invasion in surrounding tissue were related to short survival.

4. Discussion

The role of chemotherapy in penile carcinoma is not well-defined. Several chemotherapeutic agents have been reported to have an effect on this type of tumour, both as single agents and as combination chemotherapy, but numbers of patients in reported series remain relatively low because of the low incidence of this disease [4–6,8,12–17]. Neoadjuvant chemotherapy seems to be a valid treatment option for downstaging irresectable penile carcinoma. In their review on advanced penile carcinoma Culkin and Beer [1] combined results of available literature on cisplatin-based neoadjuvant chemotherapy. A clinical response was found in 24 of 35 patients (69%), and 15 (43%) underwent additional surgery. Eight (23%) remained alive without evidence of disease for 1–10 yr [1]. These results are similar to ours.

Mitropoulos et al [5] described a series of 13 patients treated with neoadjuvant cisplatin and interferon- α 2B. Response rate was 75% in 12 evaluable patients, and 8 (67%) remained disease-free for 21+ mo. Two patients died of metastatic disease and the remaining two patients had a local recurrence, for which they were successfully treated [5]. The majority of the study population, however, were clinically node-negative T2 and T3 tumours, so the results are difficult to compare.

Subsequent surgery after chemotherapy has an important role in obtaining local control in advanced disease. All but two patients undergoing surgery still had viable residual tumour after chemotherapeutic treatment during histopathologic examination, stressing the need for subsequent surgery. Looking at our results, the marked difference in survival in the group who underwent subsequent surgery between the responder and nonresponder groups suggests that it is wise to refrain from further surgical treatment in the latter group because survival rates were dismal. Moreover surgery in these cases did not add positively to local control in terms of wound management or pain control. Palliation remains difficult in this category of patients, who are unresponsive to chemotherapy and often have coexisting lymph edema, painful ulcers, and foul smelling wounds.

Toxicity was high in our series, with three deaths directly related to toxicity and discontinuation of treatment because of toxicity in one patient. Toxicity was particularly severe in the group of patients who received Bleo/Cis/MTX. Similar results were found in a phase 2 study on the Cis/Bleo/MTX regimen for penile carcinoma, performed by the Southwest Oncology Group [12]. Of the 41 evaluable patients, 5 died of toxicity and another 6 patients had one or more life-threatening toxic episodes.

Because of the low numbers of patients, it is difficult to accurately compare the response and toxicity rates of the different chemotherapeutic regimens. No specific regimen can therefore be recommended; however, in light of the relatively high toxicity in the Bleo/Cis/MTX group, whether the high response rate outweighs the high rate of toxicity in this regimen must be carefully considered.

Future challenges are ahead in optimising treatment of advanced penile carcinoma. With regards to more prevalent squamous cell carcinomas in other areas, such as head and neck and cervix, concomitant chemoradiation therapy has taken a prominent role in the treatment of various stages

of disease. A number of meta-analyses show a significant advantage of chemoradiation therapy over single-modality therapy in disease-free and overall survival, although acute toxicity is potentially higher [18,19]. So far, very little research has been done in this area concerning penile carcinoma.

Another interesting option is the use of newer tumour-active drugs, both as single agents and as part of combination therapy. In the treatment of squamous cell carcinomas of head and neck (SCCHNs), a number of agents have shown promising results, while having more favourable toxicity profiles. New active drugs include taxanes such as paclitaxel and docetaxel, of which docetaxel has also successfully been used as a radio sensitizer [20,21]. A second group of agents target the epidermal growth factor receptor, a receptor that is over-expressed in the majority of squamous cell carcinomas. Examples are cetuximab (a monoclonal antibody) and small molecule tyrosine kinase inhibitors such as erlotinib and gefitinib, which all have been shown to be active in squamous cell carcinomas [22–25]. Concomitant cetuximab and radiation therapy has also been shown to be superior to radiation therapy alone in terms of survival and locoregional control in advanced SCCHN [26].

To obtain sufficient numbers of patients required for investigating these new therapeutic approaches, multi-institutional studies are needed.

5. Conclusions

Neoadjuvant chemotherapy appears to be a valid treatment option for downstaging of irresectable penile carcinoma. An objective tumour response was found in 12 of 19 evaluable patients. Nine patients underwent subsequent surgery with curative intent, 8 of whom were long-term survivors. Toxicity was high in our series with a total of three deaths due to chemotherapeutic toxicity and discontinuation of treatment in one patient. Subsequent surgery seems warranted in only patients responsive to chemotherapy because prognosis of operated nonresponders was dismal and local control was not improved. Because of the different regimens used and the relatively low number of patients, no specific chemotherapeutic regimen can be recommended, although the high toxicity in the Bleo/Cis/MTX regimen should be taken into account when considering this type of chemotherapy.

Conflicts of interest

The authors have nothing to disclose.

References

- [1] Culkun DJ, Beer TM. Advanced penile carcinoma. *J Urol* 2003;170:359–65.
- [2] Beggs JH, Spratt Jr JS. Epidermoid carcinoma of the penis. *J Urol* 1964;91:166–72.
- [3] Hardner GJ, Bhanalaph T, Murphy GP, et al. Carcinoma of the penis: analysis of therapy in 100 consecutive cases. *J Urol* 1972;108:428–30.
- [4] Fisher HA. Neoadjuvant therapy with cisplatin and 5-fluorouracil for stage III squamous cell carcinoma of the penis. *J Urol* 1990;143(Suppl):352A (abstract 653).
- [5] Mitropoulos D, Dimopoulos MA, Kiroudi-Voulgari A, et al. Neoadjuvant cisplatin and interferon-alpha 2B in the treatment and organ preservation of penile carcinoma. *J Urol* 1994;152:1124–6.
- [6] Pizzocaro G, Piva L. Adjuvant and neoadjuvant vincristine, bleomycin, and methotrexate for inguinal metastases from squamous cell carcinoma of the penis. *Acta Oncol* 1988;27:823–4.
- [7] Roth AD, Berney CR, Rohner S, et al. Intra-arterial chemotherapy in locally advanced or recurrent carcinomas of the penis and anal canal: an active treatment modality with curative potential. *Br J Cancer* 2000;83:1637–42.
- [8] Shamma FV, Ous S, Fossa SD. Cisplatin and 5-fluorouracil in advanced cancer of the penis. *J Urol* 1992;147:630–2.
- [9] Sobin LH, Wittekind CH. TNM classification of malignant tumours. 6th ed. New York: Wiley-Liss; 2002.
- [10] European Organisation for Research and Treatment of Cancer. EORTC study protocol 30992: phase II study of irinotecan (CPT 11) and cisplatin (CDDP) in metastatic or locally advanced penile carcinoma. 2006. <http://www.eortc.be/protoc/details.asp?protocol=30992>. Date accessed: 1 October 2006.
- [11] National Cancer Institute CTEP. Common terminology criteria for adverse events, v3.0. 2003. Available at URL: <http://ctep.cancer.gov/forms/CTCAEv3.pdf>. Date accessed: 1 October 2006.
- [12] Haas GP, Blumenstein BA, Gagliano RG, et al. Cisplatin, methotrexate and bleomycin for the treatment of carcinoma of the penis: a Southwest Oncology Group study. *J Urol* 1999;161:1823–5.
- [13] Hussein AM, Benedetto P, Sridhar KS. Chemotherapy with cisplatin and 5-fluorouracil for penile and urethral squamous cell carcinomas. *Cancer* 1990;65:433–8.
- [14] Joerger M, Warzinek T, Klaeser B, et al. Major tumor regression after paclitaxel and carboplatin polychemotherapy in a patient with advanced penile cancer. *Urology* 2004;63:778–80.
- [15] Sheen MC, Sheu HM, Huang CH, et al. Penile verrucous carcinoma successfully treated by intra-aortic infusion with methotrexate. *Urology* 2003;61:1216–20.
- [16] Sklaroff RB, Yagoda A. Cis-diamminedichloride platinum II (DDP) in the treatment of penile carcinoma. *Cancer* 1979;44:1563–5.
- [17] Sklaroff RB, Yagoda A. Methotrexate in the treatment of penile carcinoma. *Cancer* 1980;45:214–6.
- [18] Green JA, Kirwan JM, Tierney JF, et al. Survival and recurrence after concomitant chemotherapy and radiotherapy

- for cancer of the uterine cervix: a systematic review and meta-analysis. *Lancet* 2001;358:781–6.
- [19] Pignon JP, Bourhis J, Domenge C, et al. Chemotherapy added to locoregional treatment for head and neck squamous-cell carcinoma: three meta-analyses of updated individual data. MACH-NC Collaborative Group. Meta-Analysis of Chemotherapy on Head and Neck Cancer. *Lancet* 2000;355:949–55.
- [20] Colevas AD, Posner MR. Docetaxel in head and neck cancer: a review. *Am J Clin Oncol* 1998;21:482–6.
- [21] Schrijvers D, Vermorken JB. Taxanes in the treatment of head and neck cancer. *Curr Opin Oncol* 2005;17:218–24.
- [22] Herbst RS, Hong WK. IMC-C225, an anti-epidermal growth factor receptor monoclonal antibody for treatment of head and neck cancer. *Semin Oncol* 2002;29:18–30.
- [23] Bourhis J. New approaches to enhance chemotherapy in SCCN. *Ann Oncol* 2005;16(Suppl 6):vi20–4.
- [24] Cohen EE, Rosen F, Stadler WM, et al. Phase II trial of ZD1839 in recurrent or metastatic squamous cell carcinoma of the head and neck. *J Clin Oncol* 2003;21:1980–7.
- [25] Soulieres D, Senzer NN, Vokes EE, et al. Multicenter phase II study of erlotinib, an oral epidermal growth factor receptor tyrosine kinase inhibitor, in patients with recurrent or metastatic squamous cell cancer of the head and neck. *J Clin Oncol* 2004;22:77–85.
- [26] Bonner JA, Harari PM, Giralt J, et al. Radiotherapy plus cetuximab for squamous-cell carcinoma of the head and neck. *N Engl J Med* 2006;354:567–78.

Editorial Comment on: Neoadjuvant Chemotherapy in Advanced Penile Carcinoma

Giorgio Pizzocaro

Università degli Studi di Milano-Ospedale S. Giuseppe, Clinica Urologica, via S. Vittore 12, 20100 Milan, Italy
pizzocaro@iol.it

Squamous cell carcinoma (SCC) of the penis is an uncommon disease in Western countries. Organ-sparing surgery may be successful in early-stage disease, but survival depends on nodal metastases [1]. The occurrence of one single intranodal metastasis does not compromise prognosis, but multiple metastases do, and fixed inguinal or pelvic node involvement is extremely ominous. In these cases chemotherapy may be helpful, without the severe side effects of desperation surgery or aggressive radiotherapy [1,2].

Leijte et al [3] report results in 20 patients (of 477 patients!) who received neoadjuvant chemotherapy for down-staging of unresectable penile cancer from 1972 to 2005. Of course, different regimens were used over this long time period. Interestingly, objective responses were observed in all regimens. Overall, 12 patients were responsive and one died of acute toxicity. All 7 non-responders died between 4 and 8 mo, despite 3 having undergone desperation surgery.

Of the 12 responders, 2 died of toxicity and one was unfit for surgery. Eight of the 9 responders who underwent postchemotherapy surgery are long-term survivors. Only one patient died of recurrence. Toxic death occurred in 3 of 10 patients treated with the Southwestern Oncology Group (SWOG) regimen (cis-diamminedichloroplatinum, cisplatin [CDDP], methotrexate [MTX], bleomycin [BLM]). This regimen has been recognised as very active but also as very toxic and the majority of

authors are using the CDDP–5-fluorouracil (PF) combination, which is the same combination that has been used for a long time in SCC of the head and neck with moderately positive results [2]. Recently, taxanes (docetaxel and paclitaxel) have been introduced in the PF combination for locally advanced head and neck SCC. A recent large phase 3 randomised study [4] reported 14% complete response rate in 193 patients treated with PF versus 33% in 189 treated with Taxol–PF (TPF), with good tolerability. Assuming that penile SCC has a similar responsiveness to chemotherapy as SCC of the head and neck, patients with fixed or recurrent inguinal metastases or large pelvic involvement could be treated with TPF in prospective cooperative studies. Preliminary personal results are encouraging.

References

- [1] Solsona E, Algaba F, Horenblas S, Pizzocaro G, Windahl T. EAU guidelines on penile cancer. *Eur Urol* 2004;46:1–8.
- [2] Pizzocaro G, Tan WW, Dreicer R. Chemotherapy for penile cancer. In: Vogelzang NJ, Scardino PT, Shipley WU, Debruyne FMJ, Linehan WM, editors. *Comprehensive textbook of genitourinary oncology*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2006. p. 827–31.
- [3] Leijte JAP, Kerst JM, Bais E, et al. Neoadjuvant chemotherapy in advanced penile carcinoma. *Eur Urol* 2007; 52:488–94.
- [4] Hitt R, Lopez-Pousa A, Martinez-Trufero J, et al. Phase III study comparing cisplatin plus fluorouracil to paclitaxel, cisplatin and fluorouracil induction chemotherapy followed by chemoradiotherapy in locally advanced head and neck cancer. *J Clin Oncol* 2005;23:8636–45.

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