1. Introduction

Testicular germ-cell tumours (TGCTs) represent the most frequent solid tumours in young men, with an incidence peak between the ages of 17 and 35 years. According to regional cancer registries in Europe, about 90% of patients present with low-stage disease (TNM stages I-IIB). Most of the patients with
testis cancer (61–78%) have clinical stage I disease confined to the testis with normalised markers after orchidectomy [1,2]. About half the patients are diagnosed with seminoma and non-seminomatous histology, respectively. Patients with clinical stage I testis cancer are expected to be cured in 100% of cases. Treatment options after orchidectomy have changed over the last two decades and regional differences of adjuvant treatment throughout Europe have been minimised after the implementation of guidelines-based treatment recommendations [3]. This review will focus on (1) the modern treatment of the primary tumour including organ-sparing surgery, (2) the research on prognostic factors predicting those patients who will relapse with clinical stage I, and (3) the current treatment recommendations in seminoma and non-seminoma after publication of several large randomised trials.

2. Treatment of the primary tumour and organ-sparing surgery

Standard treatment of a testicular cancer with a normal contralateral testis is orchidectomy via an inguinal approach. This allows for an exact histopathologic diagnosis and in true stage I patients orchidectomy is the only necessary treatment for the patient.

According to the current European guidelines, the patient should be informed about the possibility of a contralateral biopsy and this should be recommended for patients with risk factors for a testicular intraepithelial neoplasia (TIN) such as cryptorchidism, and history of maldescendent testis [3–5]. The incidence of TIN in the contralateral testis is about 5% [6]. Internationally, however, there is still a debate on whether an immediate biopsy at the time of orchidectomy is necessary given the excellent 10-yr survival figures of patients with metachronous contralateral tumors [7,8].

2.1. Small intratesticular lesions

Intratesticular lesions present a special clinical problem. The exact diagnosis rarely can be made by imaging techniques and histologic verification is necessary. However, in benign lesions orchidectomy is an overtreatment and at least in solitary testes low-volume malignant lesions may be managed by organ-sparing surgery [9].

Non-germ cell tumours (e.g., Leydig cell tumours, Sertoli cell tumours, granulosa cell tumours) represent <5% of all intratesticular lesions. However, suspicion of a non-germ cell tumor might be derived from specific ultrasound features and in rare cases special endocrine profiles (e.g., luteinising hormone depression). Most of the non-germ cell tumors are sharp round in ultrasound and have a hypoechoic feature. They are to be differentiated from other peripheral lesions such as tunica albuginea cysts and epidermoid cysts. It is recommended not to biopsy these lesions but rather to perform open surgery [9]. The typical ultrasound feature should direct the surgical strategy to an organ-sparing approach. In some cases, frozen section analysis is able to safely diagnose the non-germ cell lesions [10]. However, there is no need to strictly use frozen section analysis for diagnosis. After an organ-sparing complete resection of the tumour, paraffin histology is safer and in the unusual case of a malignant tumour in the final histology, secondary surgery (e.g., orchidectomy) can be performed without any harm for the patient apart from the second surgical intervention. After a non-germ cell testicular tumor has been confirmed in final histology, there is no need to locally treat the remaining testicle. However, there is an ongoing debate on whether staging (and in some cases therapeutic) retroperitoneal lymph node dissection (RPLND) should be recommended. About 10% of patients will present with metastatic disease and usually they cannot be cured by surgery, chemotherapy, or radiotherapy. With the complete resection of low-volume disease, however, this small cohort of patients usually is cured. Ninety percent of patients, however, do not need this adjuvant surgery. The reported numbers of patients are yet too small to present prognostic features of metastatic disease one can rely on. Old age, high mitotic activity of the primary tumour, high volume of the primary tumour, and vascular invasion are bad prognostic parameters that have been reported. At least these patients should be advised to undergo RPLND.

2.2. Malignant lesions

Current European guidelines recommend the organ-sparing approach for malignant tumours in solitary testis with certain precautions. The original technique of organ-sparing surgery was published by Weißbach in 1995 and, based on these technical recommendations, the German Testicular Cancer Study Group (GTCSG) published their experience with the technique in >70 patients in 2001 [11,12]. This experience had been updated with 101 patients for the European Association of Urology meeting in 2006 [13]. The “bottom line” of this experience is that organ-sparing surgery in malignant lesions can be recommended in the following situation:
- Solitary testis
- Volume of the lesion < 2 cm (respectively, ~30% of the testicular volume; Fig. 1)
- Adjuvant radiotherapy of the remaining testicular parenchyma with 20 Gy
- Normal preoperative serum testosterone values
- Patient and urologist fully informed about risks and benefits as well as the follow-up strategy of the organ-sparing approach
- Surgical experience with the approach

In >83% of patients, testosterone production was preserved and local recurrences were rare (4%). Local recurrences are due to the remnant testicular intraepithelial neoplastic cells (no adjuvant radiotherapy) or the teratoma left behind in the remaining parenchyma. Some patients were able to father a child by postponing radiotherapy.

2.3. TIN in the remaining testis

In malignant lesions, the remaining testicular parenchyma always harbours the precursor lesion, TIN, and, thus, these precursor cells of a malignant germ cell tumour need to be treated. In solitary testes, this is usually performed by radiotherapy. However, the time of treatment needs to be discussed. First, the normal testosterone level needs to be confirmed postoperatively (at several occasions at least 3 mo and longer after organ-sparing surgery). Second, the patient has to be aware that radiotherapy will lead to irreversible infertility [14]. Thus, the patient needs to be informed that treatment may be delayed until all fertility issues have been clarified. Third, even with the reduced dose of 18–20 Gy of testicular radiation about 30% of patients will develop Leydig cell insufficiency that demands testosterone substitution (Fig. 2) [15].

3. Clinical stage I non-seminomatous germ cell tumours

3.1. Staging

The clinical staging of the non-seminomatous germ cell tumours (NSGCTs) should be performed at the earliest convenience (if possible before orchidectomy). It includes serum tumor markers (α-fetoprotein [AFP], human chorionic gonadotropin, and lactate dehydrogenase), computed tomography [CT] staging of the chest and abdomen, and ultrasound of the contralateral testis. After orchidectomy, markers should normalise although the AFP normalisation may take some weeks (half-time 6 d). With normalised markers and no metastases found on the CT scans, patients are classified as having clinical stage I disease.

Surveillance only after orchidectomy in patients with clinical stage I NSGCTs reveals a recurrence rate of 28% in a pooled analysis of published series with >100 patients (Table 1). The median time to relapse is 4–13 mo and in most studies 4–5 mo after orchidectomy. Less than 5% of recurrences occur >2 yr after orchidectomy. About 60% of relapses will be found in the retroperitoneum, about 25% in the lung, and about 10% with markers only.

The comparable recurrence rate for patients with seminoma during surveillance is 16% (Table 2).

The clinical staging error cannot be overcome by modern generation imaging techniques. The combination of histopathologic/immunohistochemical evaluation with expert reviewing of CT scans may
diminish the false-negative staging error, but this approach is preserved for specialised centres [31]. Positron emission tomography (PET) is able to improve on the specificity of imaging, but this is more important for clinical stage II disease [32–34]. If CT is unsuspicious in expert review, PET scanning probably will not improve the sensitivity.

Thus, the main issue in the adjuvant treatment of patients with clinical stage I NSGCTs is to tailor treatment to those 28% of patients who have occult metastatic disease. Observation without risk assessment will end up in the treatment of recurrence of about one third of patients with multiple courses of chemotherapy and resection of residual masses. RPLND as well as adjuvant chemotherapy without risk assessment will overtreat about 70% of patients. Therefore, risk factors to identify patients at high risk of occult metastatic disease upfront are necessary.

### 3.2. Prognostic factors in clinical stage I NSGCTs

The Medical Research Council (MRC) has performed the first major study to identify risk factors for relapse [16]. The multivariate analysis revealed four prognostic factors for recurrence: vascular invasion of the primary tumour, lymphatic invasion, the presence of embryonal carcinoma, and the absence of yolk sac tumour. A prospective MRC trial based on these prognostic variables found the presence of at least three of these four factors to be predictive for relapse in 48% of patients [19]. Vascular invasion was the predominant finding. This was confirmed in several retrospective analyses and prospective trials that used vascular invasion to determine the high-risk group that subsequently had been treated by adjuvant chemotherapy [35–41]. The relapse rate of patients without vascular invasion who had been managed by observation ranged between 14% and 22%. Unfortunately, in all prospective clinical series the high-risk population had been treated by chemotherapy and the predictive value of vascular invasion, therefore, could not be evaluated. The GTCSG performed a randomised trial that was accompanied by risk factor analysis encompassing all available predictors [42]. One goal of this trial was to define risk factors or a score of risk factors that would more accurately predict the high-risk group of patients. A total of 165 patients with RPLND (pathologic stage I, follow-up >12 mo) or surveillance and a mean follow-up of 3 yr were prospectively evaluated by reference pathology. After multivariate analysis, three adverse prognostic parameters were identified: (1) vascular invasion, (2) proliferation rate by MIB-1 immunostaining (>70% positively stained tumour cells), and (3) percentage embryonal carcinoma (>50%) as a component of the primary tumour. A combination of all three factors predicted patients with occult metastatic disease at a 64% level. In contrast, patients without vascular invasion and a low MIB score (<70%) had only a 13% chance of retroperitoneal metastatic disease. In addition, those risk factors of recurrence have been systematically reviewed in a meta-analysis [43]. Based on these new prognostic factor combinations, risk-adapted treatment strategies have been introduced to select patients for adjuvant treatment with a much higher risk of relapse. The reported relapse rates in the high-risk group treated with chemotherapy were 0% [44,45]. Both trials from the M.D. Anderson Cancer Center and from Toulouse combined at least vascular invasion with embryonal carcinoma to define a high-risk group of patients.

In summary, risk factors have been identified to define a low-risk and a high-risk group of patients with a risk for relapse of 13% and 64%, respectively. These factors have led to a risk-adapted approach to treatment that favours surveillance for patients with low risk and chemotherapy for patients with high risk of recurrence (Fig. 3).

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**Table 1 – Surveillance management of patients with clinical stage I non-seminoma in trials with >100 patients**

<table>
<thead>
<tr>
<th>Authors</th>
<th>No. of patients</th>
<th>Recurrences (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedman et al. [16]</td>
<td>259</td>
<td>70 (29)</td>
</tr>
<tr>
<td>Swanson et al. [17]</td>
<td>100</td>
<td>31 (31)</td>
</tr>
<tr>
<td>Sturgeon et al. [18]</td>
<td>105</td>
<td>37 (35)</td>
</tr>
<tr>
<td>Read et al. [19]</td>
<td>373</td>
<td>100 (27)</td>
</tr>
<tr>
<td>Fossa et al. [20]</td>
<td>102</td>
<td>22 (22)</td>
</tr>
<tr>
<td>Gels et al. [21]</td>
<td>154</td>
<td>42 (27)</td>
</tr>
<tr>
<td>Sogani et al. [22]</td>
<td>105</td>
<td>27 (26)</td>
</tr>
<tr>
<td>Sharir et al. [23]</td>
<td>170</td>
<td>48 (28)</td>
</tr>
<tr>
<td>Oliver et al. [24]</td>
<td>234</td>
<td>71 (30)</td>
</tr>
<tr>
<td>Colls et al. [25]</td>
<td>115</td>
<td>34 (30)</td>
</tr>
<tr>
<td>Francis et al. [26]</td>
<td>183</td>
<td>52 (28)</td>
</tr>
<tr>
<td>Atsu et al. [27]</td>
<td>132</td>
<td>32 (24)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>2032</td>
<td><strong>566 (28)</strong></td>
</tr>
</tbody>
</table>

**Table 2 – Surveillance management of patients with clinical stage I seminoma in trials with >100 patients**

<table>
<thead>
<tr>
<th>Authors</th>
<th>No. of patients</th>
<th>Recurrences (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duchesne et al. [28]</td>
<td>113</td>
<td>13 (11.5)</td>
</tr>
<tr>
<td>von der Maase et al. [29]</td>
<td>261</td>
<td>49 (18.7)</td>
</tr>
<tr>
<td>Warde et al. [30]</td>
<td>201</td>
<td>31 (15.4)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>575</td>
<td><strong>93 (16.2)</strong></td>
</tr>
</tbody>
</table>
3.3. Adjuvant treatment

To date, the best prognostic model for patients with clinical stage I NSGCTs indicates an approximate 64% of relapse. It is generally accepted to treat these patients as high risk for metastatic disease. Importantly, 36% of this cohort will not harbour disease. In the United States, therefore, these patients are offered RPLND to better determine pathologic stage. In most European countries, these patients are advised to get adjuvant chemotherapy. The GTCSG randomised 382 patients to either RPLND or one course of adjuvant PEB (cisplatin, etoposide, bleomycin) chemotherapy. Adjuvant PEB could significantly reduce the recurrence rate to 1.1% as opposed to 7.5% using RPLND and adjuvant chemotherapy in cases of pathologic stage II. Adjuvant chemotherapy, therefore, is more efficacious in reducing recurrence rates than surgery and represents a less toxic adjuvant treatment [35].

The Austrian group was one of the first who started adjuvant treatment of high-risk patients (based on vascular invasion) with two cycles of PEB in a controlled, prospective trial in 1985. In 1996, they reported on 42 patients with two relapses and one patient who had died of disease [36]. In the same year the MRC published their experience with 114 patients at high risk; 93 had been followed for >2 yr [37]. Two of 114 patients had a relapse (1.8%) and one patient had died of disease. Klepp et al. [38], Ondrus et al. [39], Hendry et al. [46], and Böhlen et al. [40] confirmed these data with 32, 18, 60, and 59 high-risk patients, respectively. However, some of them used three cycles of PEB for the adjuvant treatment of the high-risk group. Remarkably, in most of these series single deaths have occurred in patients with clinical stage I disease. The M.D. Anderson experience was finally published in 2004 with 99 patients at high risk (vascular invasion or >80% embryonal carcinoma or AFP >80 ng/dl). These patients received two cycles of carboplatin, etoposide, and bleomycin on an outpatient basis and none of them experienced relapse [44]. Comparable results have recently been published by Chevreau et al. [45] who treated a total of 40 patients with either vascular invasion or the presence of embryonal carcinoma in the primary tumour. After two cycles of cisplatin, vinblastin, and bleomycin or PEB, no relapse was seen after an extended follow-up of nearly 10 yr. In summary, adjuvant chemotherapy with two cycles of PEB in the group of patients with vascular invasion provides a long-term progression-free survival of at least 97% [37].

3.4. Toxicity of treatment

Because >50% of patients with vascular invasion as the only risk factor for high risk are still overtreated by this risk-adapted approach, long-term toxicity assessment is crucial. There is a considerably high rate of unfavourable changes in blood pressure and body mass index, which consecutively results in a 2-fold increased risk of cardiovascular disease in patients after chemotherapy for testis cancer [47,48]. Unfortunately, only a few studies of two cycles of adjuvant chemotherapy evaluated long-term toxicities. Reports on the rate of nephrotoxicity [49], neurotoxicity [50], vascular toxicity [49,51,52], and high serum triglyceride levels [53] do not differentiate among different dosages of chemotherapy. Thus, valid conclusions on the impact on long-term toxicity of adjuvant chemotherapy cannot be drawn.

Secondary leukemia is a typical risk of high-dose etoposide treatment [54]. The development of other secondary cancers after long-term survival after testis cancer treatment has been studied intensively and suggests an increased probability of various secondary malignancies with radiotherapy and chemotherapy [55–57]. Especially, patients with both treatments have a relative risk of 2.9 to develop solid malignancies such as mesothelioma and cancers of the oesophagus, lung, colon, bladder, and pancreas with no difference between seminoma and non-seminoma patients. The cumulative risk for a 35-yr-old patient treated with radiotherapy and chemotherapy to develop a solid tumor 40 yr later is 36% compared to controls (23%). Again, no long-term data are available for the group of patients with only two cycles of PEB. Fertility was assessed in the

Fig. 3 – Treatment of clinical stage I non-seminoma.
EGCCCG = European Germ Cell Cancer Consensus Group;
BEP = bleomycin, etoposide, Platinol;
RPLND = retroperitoneal lymph node dissection.
studies of Cullen et al. [37], Pont et al. [36], and Böhlen et al. [40]. However, semen analysis was available only in a minority of patients before and after treatment. Only 24 of 114 patients in the study of Cullen et al., 18 of 42 patients in the study of Pont et al., and 27 of 59 patients in the study of Böhlen et al. had semen analysis performed after chemotherapy. Hence, the conclusion of these series that adjuvant chemotherapy has no effect on long-term fertility is based on only a few cases. In a recent report from Norway, Brydoy et al. report on follow-up paternity rates for 1814 men who had different kinds of testicular cancer treatment. Patients with surveillance achieved a paternity rate of up to 92%. Even in patients who had undergone high-dose chemotherapy treatment, 48% achieved paternity [58]. As long as no long-term data on fertility after adjuvant BEP chemotherapy are available, cryopreservation before chemotherapy is recommended [59].

In summary, long-term studies in patients with advanced disease have indicated that there is some long-term toxicity of chemotherapy. Extrapolation of these data suggest no significant long-term toxicities with two cycles of PEB. But there is a lack of long-term data in the group of patients with adjuvant treatment. This demands a long-term follow-up of these patients.

To reduce toxicity, Oliver et al. started to reduce adjuvant treatment to one single cycle of PEB chemotherapy [60]. This approach was published by Corti Ortiz et al. [61] with 18 patients and a median follow-up of 47 mo and by Schefer et al. [62] with 42 patients and a median follow-up of >24 mo for 31 of them. The Swiss group experienced one relapse and the patient unfortunately died due to salvage treatment. In a recently published phase 3 trial of the GTCSG, patients with clinical stage I NSGCT were randomised without risk assessment to either RPLND or to one cycle of PEB. Chemotherapy was superior to surgery in reducing recurrence rates and with the same rate of 1% major toxicities (National Cancer Institute Common Toxicity Criteria [NCI-CTC] IV), one course of PEB had fewer minor toxicities (NCI-CTC I–III) in 6.2% versus 14.9% with RPLND [35]. However, this regimen is still experimental until long-term data have shown that efficacy and treatment of relapsing patients is as successful as compared with standard treatment.

In summary, patients with clinical stage I NSGCTs should be treated according to a risk-adapted treatment policy with surveillance for those with low risk of recurrence (>13%) and adjuvant chemotherapy for those with high risk (64%). Future studies should concentrate on the reduction of treatment for the high-risk group and a better staging, for example, by molecular parameters to avoid toxicity for those who do not need treatment.

4. Clinical stage I seminoma

4.1. Observation studies and prognostic factors

In the group of patients with clinical stage I seminoma, observation studies have shown that about 16% of patients are at risk for recurrent disease (Table 2). The median time to relapse is 12–15 mo with 96% of relapses occurring in the retroperitoneum or inguinal region.

In a multivariate analysis of several retrospective observation studies a tumour size >4 cm and rete testis invasion remained of adverse prognostic value and were suggested as defining a high-risk group for relapse [68]. If both factors are present, patients face a risk of relapse during surveillance of 32%. If both factors are absent, a low-risk group can be defined with a relapse risk of only 12%.

The first prospective study that used risk factors had been performed by the Spanish Testicular Cancer Group [69]. One third of the patients in this Spanish study had neither of the defined risk factors (rete testis invasion and a tumour size of >4 cm) and thus received no treatment (surveillance only) after orchiectomy. Only 6.0% of these patients had a relapse with a median follow-up of about 3 yr. The remaining patients, with one or both risk factors, were treated with adjuvant carboplatin, and showed a relapse rate of just 3.3%. This study is a major step towards targeting postorchiectomy treatment to those patients who harbour occult metastatic disease at the time of orchiectomy. Most interestingly, the relapse rate within the observation group in this currently published trial is much lower than previously reported in observation trials. This may be due to improved staging and histopathologic diagnosis.

4.2. Adjuvant treatment: radiotherapy

Irradiation to the para-aortic and pelvic lymph nodes has been the most favoured adjuvant treatment in Europe. Fossa et al. [70] showed that there are no differences in survival and recurrence rates if the radiation field is limited to the para-aortic lymph nodes only. The acute toxicity was reduced and the sperm count within the first 18 mo was significantly higher after para-aortic irradiation than after irradiation of the traditional dog-leg field. Para-aortic irradiation should be tailored according to the site of
the primary tumour. Adjuvant irradiation of supradiaphragmatic lymph nodes is not indicated in seminoma stage I. After modern radiotherapy nearly all relapses will first occur outside the irradiated field (margin of the radiation field, supradiaphragmatic lymph nodes or in the lungs), most of them in the pelvis [71].

Concerning the dose of irradiation, the MRC recently has finished a large randomised trial of 20 Gy versus 30 Gy para-aortic radiation in stage I seminoma that showed equivalence for both doses regarding recurrence rates [72]. The rate of severe radiation-induced long-term toxicity is <2%. Moderate chronic gastrointestinal side-effects are seen in about 5% of patients and moderate acute gastrointestinal toxicity in about 60%. The main concern surrounding adjuvant radiotherapy is the potentially increased risk of radiation-induced secondary non-germ cell malignancies. A scrotal shield can be of benefit during adjuvant radiotherapy to prevent scattered radiation toxicity in the contralateral testis, but this is not needed for a para-aortic field. At this time it is difficult to evaluate the long-term risks after adjuvant radiotherapy for stage I seminoma because former treatment procedures included larger fields, higher doses of radiotherapy, or the use of alkylating chemotherapy.

4.3. Adjuvant treatment: chemotherapy

Chemotherapy has only recently been added to the adjuvant treatment alternatives. Oliver et al. [73] reported on a series of 53 patients who either had been treated with two cycles of cisplatin (50 mg/m² on day 1 and 2 for 21 d) or two cycles of carboplatin with a dosage calculated according to the formula of Calvert. The relapse rate of the whole group was 4% and with a median follow-up of 51 mo 99% of patients were free of disease. These results could be repeated by several groups (Table 3). Recently, the MRC has published the largest randomised phase 3 trial of carboplatin monotherapy (1 course at area under the curve [AUC] 7) versus radiotherapy as adjuvant treatment in patients with clinical stage I seminoma [74]. There was no statistical difference in recurrence rates after a mean follow-up of >4 yr. However, with a median follow-up of 4 yr the relapse rate with one single course of carboplatin at 3 yr was 5.2% and a considerable number of the relapses occured after >2 yr. This observation reminds us to still be cautious in interpreting the encouraging results of single-agent carboplatin therapy (Fig. 4).

Furthermore, the late sequelae of carboplatin treatment (induction of malignancies, treatment response of recurrences, fertility) and the impact on quality of life compared to observation or adjuvant irradiation are unknown. Thus, the long-term results of the published trial have to be awaited before carboplatin can be recommended as treatment intended to provide long-term freedom from recurrence in patients with clinical stage I seminoma.

It is important to reduce immediate adjuvant treatment in as many patients as possible to avoid the acute and, more importantly, late toxicities of chemotherapy and radiotherapy. Therefore, the Spanish approach of a risk-adapted strategy represents a major step in the right direction. In future trials, the group of patients under surveillance with a minimal risk (about 6%) of relapse must be enlarged. If the risk of relapse in patients managed with surveillance is <10%, the number of follow-up investigations can be reduced. Of note is, however, that in the Canadian surveillance series relapses have occured after >5 yr of follow-up. Therefore,

Table 3 – Phase 2 trials of carboplatin monotherapy as adjuvant treatment of clinical stage I seminoma

<table>
<thead>
<tr>
<th>Authors</th>
<th>No. of patients</th>
<th>No. of cycles of carboplatin</th>
<th>Follow-up, mo</th>
<th>Recurrence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Krege et al. [63]</td>
<td>43</td>
<td>2</td>
<td>28</td>
<td>0</td>
</tr>
<tr>
<td>Germa-Lluch et al. [64]</td>
<td>28</td>
<td>2</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Nöst et al. [65]</td>
<td>29</td>
<td>2</td>
<td>52</td>
<td>0</td>
</tr>
<tr>
<td>Dieckmann et al. [66,67]</td>
<td>125</td>
<td>(93)/2 (32)</td>
<td>48</td>
<td>8.6/0</td>
</tr>
</tbody>
</table>

Fig. 4 – Treatment of clinical stage I seminoma. AUC = area under the curve.
surveillance strategies even with a very low risk of recurrence need support by a well-organized health care system.

Another important question is whether adjuvant carboplatin can reduce the number of contralateral tumours in high-risk patients, as demonstrated in the British trial of Oliver et al. This beneficial effect may have occurred in the study of Aparicio et al. as well, because only 3 of 214 patients (1.5%) developed a metachronous contralateral tumour after carboplatin treatment, with a median follow-up of almost 3 yr.

The unsolved problems in patients with clinical stage I seminoma have become more complex. It is difficult to recommend one strategy over another because the differences in health care systems worldwide will guide, for example, the decision for or against surveillance strategies. Nevertheless, major benefits for patients have already been achieved in limiting adjuvant treatment to those who really need it.

References


Some of the points in the article are worth discussing briefly.

Testicle-sparing surgery was first described in 1995 (Refs. [11,12] in the article). It stood the test of time and, after a decade, it is incorporated into the recommendations of the European Association of Urology guidelines (Ref. [4] in the article). Attention should be drawn, however, to all the pertinent conditions listed by the author, including a biopsy at the resection margins. For the treatment of residual carcinoma in situ a dose of radiation therapy at 20 Gy is safe; however, a decrease in testosterone production has been observed in about one half of the cases during follow-up [1]. Notably, after detailed information is provided, most of our eligible patients still choose the organ-sparing option.
The risk-adapted approach points nicely in the direction of limiting the burden of treatment with no compromise for the cure rate, which still represents one challenge for this stage of disease. We should not forget, though, that the prognosticators being used to stratify patients by risk deserve further validation, and the reduction of chemotherapy, either by minimising the number of cycles or by using less toxic agents (e.g., platinum derivatives), does not always equate with minimising the risks of future relapse, as compared to more standard approaches [2].

Finally, surveillance, short-course chemotherapy, and surgery apparently have equivalent outcomes in terms of oncologic results and morbidity. Given that the incidence of TC has more than doubled over the last 30–40 yr [3], costs are likely to be included in the balance [4], even more because this disease is increasingly being diagnosed in countries with fewer resources.

References