840 L.J. Denis

brought proponents from both sides together and resulted in a workshop summary that will form a stable base for future discussions [4]. Some committees on pathology, markers and treatment raised serious questions on, respectively, the overall accuracy and quality control, the standardisation of prostate specific antigen (PSA) and its reproducibility, and the overall morbidity of both radical prostatectomy and conforming radiotherapy. Clinical reality runs ahead of this cautious approach and the National Survey in the U.S.A. revealed that use of the PSA test increased from 5.1 to 66.4% and transrectal ultrasound (TRUS) from 0.9 to 19.7%. The increased early detection of localised tumour led to a resulting increase of radical prostatectomy from 7.3 to 20.3% [5], while the use of radiotherapy remained unchanged. The wealth of data provided by surgery established the principle that PSA has to be used in conjunction with digital rectal examination [6], and that surgery of impalpable and invisible tumours treated insignificant or minimal tumours, moderate tumours and advanced tumours in 26, 37 and 37%, respectively [7]. Results of radiotherapy treatment for localised disease compare well with surgery in the first 5-10 years for localised disease, with a resulting trend to minimise surgery above 70 years of age [8].

The progress made in diagnosis and treatment of localised prostate cancer is not reflected in metastatic disease. There is no doubt that primary hormonal treatment is indicated in symptomatic patients, and a tailored approach to the individual patient is justified [9]. Maximal androgen blockade has emerged as the best treatment to achieve response, and this treatment may increase survival in patients with minimal disease [10]. However, the most important message from the EORTC trial,

from which these data were derived, is that prognostic factor analysis allows the separation of randomised patients in 3 cohorts with respectively 5.2, 2.7 and 1.6 years of survival [1].

The end stage of the disease in its hormone independent state has a poor prognosis. Innovative strategies for early stage are under evaluation, while improved palliative care for advanced disease remains a major challenge.

- Denis LJ. Staging and prognosis of prostate cancer. Eur Urol 1993, 24, 13-19.
- Boyle P. The evolution of an epidemic of unknown origin. In Denis L, ed. Prostate Cancer 2000. Heidelberg, Springer, 1993, 5-11.
- 3. Barry M. Natural history of clinically localized prostate cancer. Semin Surg Oncol 1994, in press.
- Denis L, Murphy GP, Schröder F. Report of the Consensus Workshop on Screening and Global Strategy for Prostate Cancer, Antwerp, 5-7 March, 1994. Cancer 1995, 75, 1187-1207.
- Jones GW, Mettlin C, Murphy GP, et al. Patterns of care for prostate cancer: results of a National Survey of 1984 and 1990. Cancer 1995, in press.
- Catalona WJ, Richie JP, Ahmann FR, et al. Comparison of digital rectal examination and serum prostate specific antigen in the early detection of prostate cancer: results of a multicenter clinical trial of 6630 men. J Urol 1994, 151, 1283–1290.
- Epstein JI, Walsh PC, Carmichael M, Brendler CB. Pathological and clinical findings to predict tumor extent of nonpalpable (stage T1c) prostate cancer. JAMA 1994, 271, 368–374.
- 8. Dearnaley DP. Radiotherapy of prostate cancer: established results and new developments. Semin Surg Oncol 1995, 11, 46-49.
- 9. Denis L. Primary hormonal treatment. Cancer 1993, 71, 1050-1058.
- Denis LJ, Whelan P, Carneiro de Moura JL, et al. Goserelin acetate and flutamide versus bilateral orchidectomy: a phase III EORTC trial (30853). Urology 1993, 42, 119-130.



European Journal of Cancer Vol. 31A, No. 5, pp. 840-841, 1995 Copyright © 1995 Elsevier Science Ltd Printed in Great Britain. All rights reserved 0959-8049/95 \$9.50+0.00

0959-8049(95)00113-1

## Controversies in Testicular Cancer Management

### A. Horwich

TESTICULAR GERM CELL tumours continue to increase in incidence in developed countries, and epidemiological studies have identified testicular maldescent, early puberty and genetic predisposition [1] as important aetiological factors. The tumour is usually associated with carcinoma in situ of the germinal epithelium, and studies of the contralateral testis identify this lesion in a similar proportion of patients to those who develop a second contralateral germ cell tumour [2]. Since this confers a risk of malignant transformation of approximately 50% within 5 years, management options include orchidectomy, close surveillance or localised low dose radiation [3]. Carcinoma in situ cells share, with the majority of germ cell tumours, the unusual cytogenetic abnormality of an isochromosome 12p, and the analysis of 12q deletions may allow the identification of a candidate tumour suppressor gene [4]. However, more detailed analyses allow the detection of genetic differences between teratoma and seminoma, even at the in situ stage, suggesting that these tumour types may evolve separately rather than sequentially [5].

Seminoma is both radiosensitive and chemosensitive and cure rates are extremely high. Nevertheless, there is controversy over management of stage I disease. Traditional radiotherapy may be associated with a small risk of carcinogenesis and this has led to:

(1) Reduction of the radiation field size.

Correspondence to A. Horwich at The Royal Marsden Hospital, Fulham Road, London SW3 6JJ, U.K.

(2) Studies of surveillance alone reserving treatment for those who recur [6].

In disseminated seminoma, cisplatin-based combination chemotherapy is highly effective and the standard regimen is the combination of cisplatin and etoposide [7].

The prognosis of patients with testicular non-seminoma is also excellent. There is still wide variation in the management of patients with stage I disease with options including surveillance, retroperitoneal node dissection or adjuvant chemotherapy [8]. Patients with small volume retroperitoneal metastases are treated either by retroperitoneal node dissection or by initial chemotherapy with surgery for residual masses [9]. Patients with advanced metastatic non-seminoma are treated with risk-related chemotherapy regimens, tailoring the aggressiveness of treatment to the prognosis. Major factors defining the prognosis include the tumour marker concentration, the number of lung metastases, involvement of liver, bone or brain, or the presence of a large mediastinal mass [10]. Trials in good prognosis metastatic non-seminoma have analysed the number of treatment cycles required, the role of bleomycin and the use of carboplatin rather than cisplatin. The standard approach is still the combination of bleomycin, etoposide and cisplatin, placing a limit on the total bleomycin dose to reduce the risk of pneumonitis. In advanced non-seminoma with poor prognosis, studies have addressed alternating chemotherapy, intensive cycling and high dose chemotherapy, but as yet, it is unclear that these approaches are superior to standard BEP chemotherapy. The contribution of high dose chemotherapy with blood stem cell support is being investigated, mainly in the context of salvage treatment of those who failed first line chemotherapy [11]. A trial under the coordination of the European Bone Marrow Transplant Group is comparing high dose chemotherapy with standard dose chemotherapy as first salvage treatment. Important issues in this highly curable group of tumours include long term consequences, not only of the tumour diagnosis but also of treatment, and long term follow up of treated patients is important.

- Forman D, Oliver RTD, Brett AR, et al. Familial testicular cancer: a report of the UK family register, estimation of risk and an HLA Class 1 sib-pair analysis. Br J Cancer 1992, 65, 255-262.
- Berthelsen JG, Skakkebaek NE, Von der Maase H, Sorensen BL. Screening for carcinoma in situ of the contralateral testis in patients with germinal testiculr cancer. Br Med J 1982, 285, 1683–1686.
- von der Maase H. Diagnosis and management of carcinoma in situ
  of the testis. In A. Horwich, ed. Testicular Cancer Clinical
  Investigation and Management. London, Chapman and Hall Medical,
  1991, 319-330.
- Murty VV, Houldsworth J, Baldwin S, et al. Allelic deletions in the long arm of chromosome 12 identify sites of candidate tumor suppressor genes in male germ cell tumors. Proc Natl Acad Sci USA 1992, 89, 11006-11010.
- Looijenga LH, Gillis AJ, Van Putter WL, Osterhuis JW. In situ numeric analysis of centromeric regions of chromosomes 1, 12 and 15 of seminomas, nonseminomatous germ cell tumours and carcinoma in situ of human testis. Lab Invest 1993, 68, 211-219.
- Horwich A, Alsanjari N, A'Hern R, et al. Surveillance following orchidectomy for stage I testicular seminoma. Br J Cancer 1992, 65, 775-778.
- Horwich A, Dearnaley DP. Treatment of seminoma. Semin Oncol 1992, 19, 171-180.
- Horwich A. Current issues in the management of clinical stage I testicular teratoma. Eur J Cancer 1993, 29A, 933-934.
- 9. Horwich A. Editorial Comment. Br J Urol 1993, 71, 335
- Mead GM, Stenning SP, Parkinson MC, et al. The Second Medical Research Council Study of prognostic factors in non-seminomatous germ cell tumours. J Clin Oncol 1992, 10, 85-94.
- Broun ER, Nichols CR, Kneebone P, et al. Long-term outcome of patients with relapsed and refractory germ cell tumors treated with high-dose chemotherapy and autologous bone marrow rescue. Ann Intern Med 1992, 117, 124-128.



European Journal of Cancer Vol. 31A, No. 5, pp. 841–844, 1995 Elsevier Science Ltd Printed in Great Britain. 0959–8049/95 \$9.50+0.00

0959-8049(95)00114-X

# Recent Advances in the Management of Lymphoma

### F. Cavalli

#### INTRODUCTION

THE NON-HODGKIN'S lymphomas (NHL) comprise a heterogeneous group of neoplasms that originate in lymphoreticular cells. Their incidence appears to be increasing annually, at least in the western hemisphere [1]. The reasons for this are not entirely clear, although there may be some contribution by

patients infected with HIV. Lymphomas with T-cell immunology markers represent fewer than 15% of the cases in the western hemisphere, while they account for approximately half of the NHLs in Japan [1].

The management of malignant lymphoma is continuously evolving, and this evolution encompasses the biological understanding of the different entities and classifications as well as a better definition of treatment policies. In this summary, we will discuss new aspects which have recently begun to emerge in each of these areas.

Correpondence to F. Cavalli at the Division of Oncology, Ospedale San Giovanni, 6500 Bellinzona, Switzerland.