28 Combined Cisplatin and Concomitant Continuous Infusion 5-Fluorouracil and Accelerated Radiation in Advanced Head and Neck Cancer

JADRANKA DRAGOVIC

CONTENTS

28.1 Introduction .................................. 239
28.2 Background .................................. 239
28.3 Concomitant Chemotherapy and Accelerated Fractionation Radiotherapy in Advanced, Unresectable Head and Neck Cancer ........ 240
28.3.1 Methods and Materials ................. 240
28.3.2 Preliminary Results ....................... 240
28.4 Conclusion ................................ 242

References ........................................ 242

28.1 Introduction

Advanced, unresectable stage III and IV squamous cell carcinoma of the head and neck has a 2-year mortality of over 70% when standard treatment with conventional radiation therapy is employed (MILLION et al. 1984; MARCIAL et al. 1985). The control of locoregional disease remains a major therapeutic challenge since morbidity and mortality relate primarily to local invasion and lymph node metastases. Among the various new approaches that are being explored in an effort to improve the therapeutic ratio, combinations with adjunctive chemotherapy have attracted major interest.

28.2 Background

While sequential combinations employing neoadjuvant chemotherapy have been associated with high rates of response, most randomized controlled clinical trials have shown no survival benefit (TANNOCK and BROWMAN 1986). Administration of chemotherapy concurrently with radiation has in-
ment time have been shown to result in marked depletion of both acute and late responding tissues (PARECCHIA and SALTI 1981, NGUYEN et al. 1988). In an attempt to decrease the acute toxicity and yet preserve the shortening of overall treatment time, accelerated fractionation regimens have been modified by introducing breaks during the treatment course (WANG 1988; VIKRAM 1987). The breaks are not considered to be detrimental (even though some tumor cell repopulation may occur) as long as the overall duration of the treatment course is reduced in comparison to the conventional radiotherapy to the same dose level.

28.3 Concomitant Chemotherapy and Accelerated Fractionation Radiotherapy in Advanced, Unresectable Head and Neck Cancer

The potential advantages of a combination of interrupted accelerated multiple fraction-per-day radiotherapy with simultaneous infusional chemotherapy are threefold: (a) radiosensitizing properties of 5-FU and cisplatin can lead to increased effect on tumor through synergism; (b) acceleration of radiotherapy can lead to increased effect on tumor through decreased tumor cell repopulation; and (c) the rest intervals between treatment cycles can allow for normal tissue to recover, leading to decreased acute mucosal toxicity.

28.3.1 Methods and Materials

With the above-described background we have designed a treatment program consisting of accelerated, interrupted, twice-a-day radiation therapy concomitant with 5-FU and cisplatin (treatment schema shown in Fig. 28.1). It consists of three 5-day treatment cycles repeated every 14 days. Each cycle consists of cisplatin 60 mg/m² given on day 1, and 5-FU 800 mg/m² per day given concurrently with twice-a-day radiation therapy at 2 Gy per fraction, on days 1 through 5. The two daily fractions are given at least 5 h apart. The total radiation dose is 60–70 Gy in 5–5½ weeks (33–38 elapsed days). This is a reduction of 1–2 weeks in comparison to a conventionally fractionated regimen to the same total dose level. When 70 Gy is delivered, the last 10 Gy in five fractions over 2½ days is given to a reduced field, following the third treatment cycle without a break (other than the weekend), and without concomitant chemotherapy. The spinal cord is shielded after 40 Gy and a shrinking field technique is employed. The volumes and techniques are similar to conventional treatment regimens and electrons are used for posterior neck irradiation.

Prior to study entry, patients undergo a thorough pretreatment evaluation and are considered eligible if they have biopsy documented stage III or IV unresectable squamous cell carcinoma of the oral cavity, oropharynx, nasopharynx, paranasal sinuses, larynx, or hypopharynx, with adequate bone marrow, renal, and hepatic function, age of 75 years or less, and ECOG performance status of 0–3. The characteristics of the first fifteen patients treated on this protocol are presented in Table 28.1.

28.3.2 Preliminary Results

The objectives of this ongoing study are to determine tumor response, acute and late treatment related morbidity, and survival and locoregional control at 2 years. The follow-up duration to date is very brief, ranging from 2 months to 27 months, allowing for evaluation of acute treatment morbidity and tumor response, but not of survival or late tissue effects.