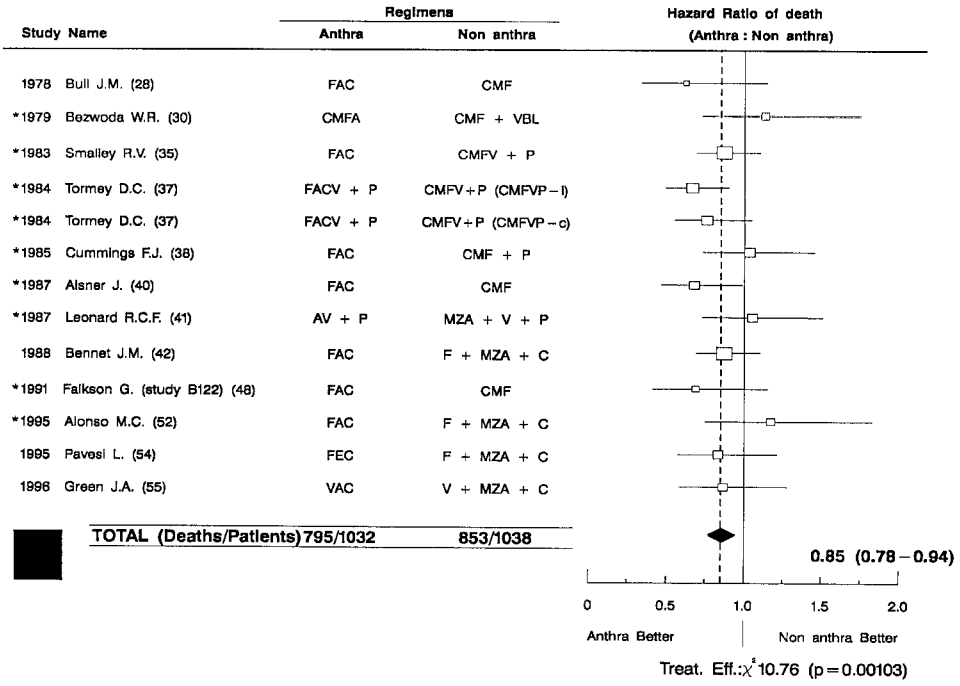

Fig 1. Doxorubicin plus at least two drugs included in the control arm regimen compared with polychemotherapy without doxorubicin. (□) Hazard ratio (HR) for each trial with 99% confidence interval (CI). (◆) Overall HR with their 95% CIs (Tinazzi A, Carinci F, Torri V: Graphical aspect of meta-analysis using SAS/GRAPH and its specific annotate language: A set of specific macro routines to perform and display result of meta-analysis. SEUGI '96, SAS European User Group International, Hamburg, Germany, June 11-14, 1996 [CD-ROM version]) *HR obtained from survival curves. Abbreviations in Figs 1 and 2: A, doxorubicin; C, cyclophosphamide; E, epirubicin; F, fluorouracil; M, methotrexate; P, prednisone/prednisolone; V, vincristine; VBL, vinblastine; c, continuous; i, intermittent; Anthra, anthracycline.

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Docetaxel, Cisplatin, Fluorouracil, and Leucovorin in Locally Advanced Head and Neck Cancer

To the Editor: I read with great interest the recent article by Colevas et al[1] in the November issue of the *Journal of Clinical Oncology*. In this study, as well as in his previously reported study,[2] a combination of docetaxel, cisplatin, fluorouracil (5-FU), and leucovorin (TPFL) was administered and followed by radiotherapy in patients with locally advanced head and neck cancer (HNC). The duration of therapy was compressed into 4 days (TPFL4) rather than 5 days (TPFL5) in an effort to reduce toxicity as well as patient hospitalization. At the time that this information became available, we had already concluded the analysis of data from 20 patients with locally advanced HNC treated at our institution using a similar regimen with docetaxel, cisplatin, and 5-FU (DCF). In our study, the dose of docetaxel was higher (80 mg/m^2 on day 1 *v* 60 mg/m^2 for TPFL4 and TPFL5), the total dose of cisplatin was 80 mg/m^2 (*v* 125 mg/m^2 for TPFL4 and TPFL5), and 5-FU was administered at a dose of 1,000 mg/m^2/d (*v* 700 mg/m^2/d for TPFL4 and TPFL5) for 3 consecutive days but without leucovorin every 28 days. We also had to administer prophylactically granulocyte colony-stimulating factor because of the severe myelotoxicity observed in a previous pilot study. After a total of 60 cycles of DCF and a median follow-up time of 36 months, the overall response rate to DCF chemotherapy was 90%, with 20% complete responses; median disease-free and

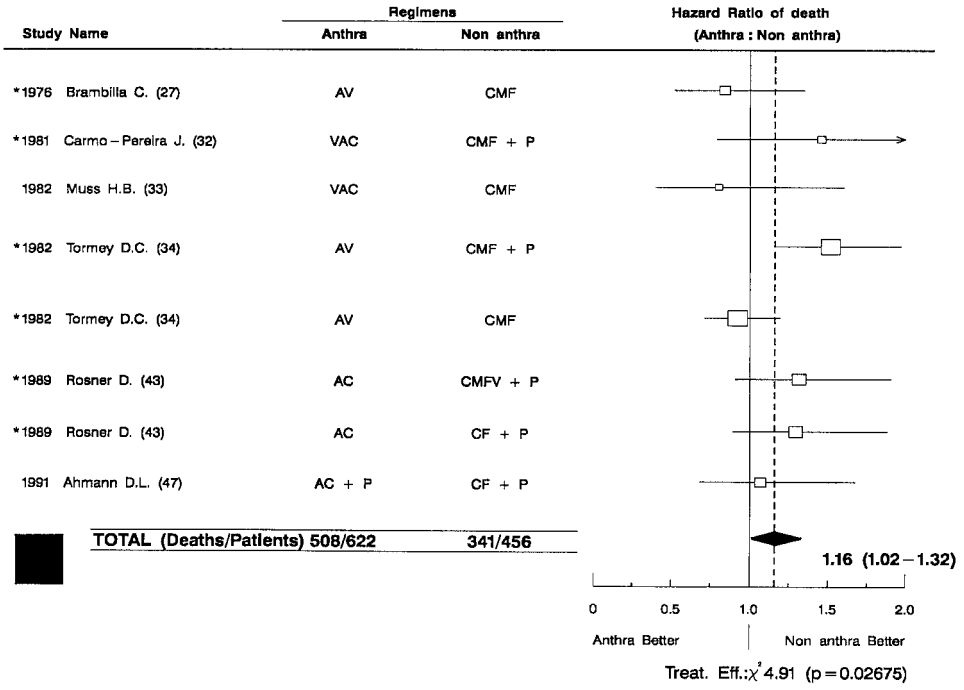

Fig 2. Doxorubicin plus no drug or only one drug included in the control arm regimen compared with polychemotherapy without doxorubicin.

overall survival have not yet been reached. Functional organ preservation was achieved in 53% of the patients. In terms of toxicity, we documented fewer hospitalizations due to toxicity (two patients for febrile neutropenia and one patient for grade 4 diarrhea) and no toxicity-related deaths. Despite the lower complete response rate to DCF compared with TPFL4 (20% *v* 60%), remissions were quite durable. Therefore, it seems that shorter-duration regimens are as efficacious as the more protracted ones with less toxicity. In addition, there is room for further escalation of the docetaxel or cisplatin dose. Finally, if patients would agree to placement of a central venous catheter, the duration of hospitalization could be further reduced, provided that adequate home care nursing was available. With all this data available, I think that once the incorporation of docetaxel into the traditional cisplatin/5-FU regimen has been answered prospectively, other issues to be addressed in future comparative phase III trials should be (a) shorter (3 days or less)- versus extended (5-day)-duration therapies using docetaxel, cisplatin, and 5-FU and (b) docetaxel, cisplatin, and 5-FU chemotherapy in a sequential versus a concurrent modality approach along with radiotherapy.

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In Reply: We agree with Drs Janinis and Panagos that the 4-day docetaxel, cisplatin, fluorouracil, and leucovorin (TPFL4) regimen is only one of a myriad of docetaxel, cisplatin, and fluorouracil–containing regimens of potential benefit to patients with locoregionally advanced squamous cell carcinoma (SCCA) of the head and neck.[1-3] Despite the dramatic reduction in toxicity and hospitalization rates in the TPFL4 trial versus the TPFL5 trial, we agree that further refinement of the regimen in early-phase clinical trials is warranted before embarking on a large comparative trial with standard regimens. We are concerned with the low complete response rates associated with the Saint Anargiri Cancer Center's regimen and look forward to follow-up survival data both from our trials and theirs.[3]

Trials at Dana-Farber/Partners Cancercare, which further dose-escalate docetaxel and reduce hospitalizations associated with chemotherapy delivery, are accruing participants. We are now delivering these regimens on a 21-day cycle rather than a 28-day cycle to reduce overall treatment time and using induction and concurrent chemoradiotherapy in these trials.

We are not wedded to the concept of exclusive sequential chemoradiotherapy and laud the attempts by others to explore concomitant taxane and PF and radiotherapy (AA Abitbol, personal communication). We are concerned, however, about the feasibility of delivering adequate systemic therapy when drugs are given exclusively simultaneously with radiation therapy. Furthermore, it is our impression that the short- and long-term locoregional morbidity of concomitant aggres-