(benefit 2%, 31 trials*, 5 269 pts*) whereas the absolute benefit at 5 years was 8% for **concomitant** CT (26 trials*, 3 727 pts*). Exclusion of small trials (<80 pts) or old trials (<1980) did not modified the results. The effect of CT was not significantly different according to the rumor stage and the tumor site (larynx, hypopharynx, oropharynx, oral cavity).

Conclusion: CT led to a small but significant improvement in survival. The observed benefit depended on CT timing and was the highest with CT concomitant to radiotherapy.

**2 trials with 3-arms: 1 neoadjuvant CT, 1 concomitant CT & 1 control*

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Is there still a place for chemotherapy in patients with locally advanced head & neck squamous cell carcinoma?

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Combination chemotherapy such as cisplatin-5fluorouracil is effective in inducing a high rate of tumor responses in patients (pts) with advanced Head & Neck (H&N) cancer. In the recent decades, chemotherapy was included in organ preservation strategies or in combination with radiotherapy to improve the local control in pts with non-resectable diseases. Chemotherapy was also proposed in neoadjuvant and adjuvant settings with the aim of reducing the risk of distant metastases and improving survival. Recent results of an individual-patient based meta-analysis including about 11,000 pts and 63 controlled-trials (from 1965 to 1993) were striking. This study showed a small but significant overall reduction of the risk of death of 10±2% translating in an absolute survival benefit of only 4% at 5 years in pts receiving chemotherapy ($p<0.0001$). The benefit was observed when chemotherapy was concomitantly associated with radiotherapy (reduction of risk of death 19±3%, absolute benefit at 5-year 8%). Conversely, no benefit was observed in pts receiving chemotherapy for larynx preservation or treated in adjuvant settings. Overall, neoadjuvant chemotherapy did not significantly improve survival in pts with H&N cancer. However, a trend toward an increase of survival was observed in patients receiving cisplatin-5fluorouracil regimens. Preliminary results focused mainly on survival. More data generated from this meta-analysis on disease free survival, occurrence of second primary, and non-cancer related deaths (due to concomitant tobacco related diseases) will be required before drawing a definitive conclusion on the impact of chemotherapy in H&N cancer. However, this meta-analysis emphasizes the small benefit of current routine chemotherapies on the outcome of pts and encourage prospective clinical trials with original drugs and strategies. Th7is shows that more effective anticancer agents are urgently warranted to improve the outcome of patients with H&N cancer. From those investigational agents we will discuss recent data obtained with taxanes, antifolate analogues, and recent biological programs targeting selectively p53 in H&N cancer cells.

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Radiotherapy in head and neck cancer

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The management of Head and Neck carcinomas is nowadays based on multi-disciplinary approaches, especially in patients with bulky tumors. Their configuration varies according to host- and tumor-related factors and are aimed at improving both cure rates and quality of life. Radiation therapy constitutes one of the pillars of this therapeutic management, both for early and locally advanced disease.

In patients with *early disease*, radiotherapy is indeed as safe as surgery as regards local control and survival rates and, as a conservative treatment, it also offers a quality of life surgery is is not always able to offer, especially when radical procedures can not be avoided. The role of new techniques of high conformality radiotherapy and brachytherapy is probably determinant to reduce the incidence of severe late toxicity and offer major opportunities of radiotherapy treatments in patients with second malignancies. In stage III disease the choice in favour of radiotherapy is also guided by health economics considerations.

Larynx preservation trials have demonstrated that neo-adjuvant chemotherapy followed, in responders, by radiation therapy is as safe as strategies based on upfront surgery. Functional larynx can be kept in 30–50% of the cases treated with organ preservation programmes and a significant reduction in distant metastases is usually reported for this type of sequential application of radio-chemotherapy.

Altered fractionation has been extensively investigated over the last two decades, using regimes ranging from strong acceleration to true hyperfractionation. Most of these altered dose schedules have yielded significant improvements in loco-regional control, generally of 10 to 15% compared to those observed after conventional fractionation, with interesting trends as regards survival rates. Severe late toxicity can be observed when strong acceleration regimes are used, especially when the inter-fraction time interval is <6 hours.

Concurrent radio-chemotherapy is now considered by many centers, and not by all, as the standard approach for locally advanced disease since it has been shown to affect significantly not only the loco-regional control but also the disease-free survival, as demonstrated by recent recta-analyses. Long-term toxicity still remains to document more extensively, especially as regards dose-schedules combining cytostatic drugs and altered fractionation.

Finally the increasing role of *re-treatments* with radiotherapy for both second primaries and recurrences is currently under investigation: encouraging results are now documented both as regards tumor long-term control and functional outcome.

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Intermittent CO2 or KTP laser surgery in combined treatment of head and neck cancer

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KTP (Potassium (K+)-Titanyl-Phophate)-laser surgery in tumors of the oral cavity, the pharynx and hypopharynx allows an extended resection offering all the advantages of CO2 laser surgery with a more flexible handling during cutting with direct fiber contact to the tissue and coagulation without contact. A combined chemo-radiotherapy is started in our patients after panendoscopy with tatooing of the tumor margins and a complete staging. Mitomycin, 5 Fluoruracil and hyperfractionated radiation is performed up to 30 Gy in a first cycle. Then the CO2 or KTP-laser surgery is done in the old margins with preferation of the CO2 in the hypopharynx and the KTP laser in the oral cavity and oropharynx. Intermittend neck dissection follows this surgical procedure after a time interval of 10 to 14 days. Then the second cycle of chemoradiation completes the treatment. Bioptic controls follow these protocol after six and twelve weeks. In 20% of the patients treated no vital tumor cells could be found in the laser resected specimen any more. All the other resections were performed within healthy tissue borderlines. Tumor control in all cases including T3 stages could be performed by means of this technique with the advantage of no plastic reconstructive covering of the resection site and better functional outcome, especially for swallowing and no necessity for a tracheostomy.

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Helper-free generation of new oncotropic and oncotoxic vectors derived from MVM autonomous parvovirus

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Autonomous parvoviruses have several features that attracted attention to their potential use as vectors for cancer gene therapy. They have a strong oncotropism through targeting viral-gene and transgene expression to tumor cells, and their non-structural NS1 is responsible for their oncotoxicity. In addition, they are non pathogenic in adult animals, do not integrate into the host genome, are resistant to extreme pH and temperature conditions, are not inactivated by human complement, and, finally, seem to be associated with no or low immunogenicity. Their production was however difficult, their spontaneous titer after transfection was low (10.E + 3–10.E + 4 infectious units [iu]/ml) and stocks were contaminated by wild-type MVM that is generated through recombination between cotransfected vector and helper DNA sequences. We set up a method of concentration and purification, that allows to reach titers of 10.E + 9 iu/ml. We also generated a packaging cell line by integrating helper sequences allowing to reach spontaneous recMVM titers of up to 10. E + 7 iu per ml after three to four rounds of infection, with no concentration procedure. Although undetectable in the