erative diagnosis of differentiated thyroid cancer.

Methods: We analyzed 119 patients operated for thyroid carcinomas from 1987–1996 and 217 patients operated for benign diseases of the thyroid from 1994–1996. We investigated the value of scintigraphy for operative decision making in both groups. Preoperative standard diagnostics enclosed clinical evaluation, thyroglobulin, ultrasound, scintigraphy, fine-needle aspiration biopsy.

Results: Preoperative diagnosis of thyroid cancer was correct in 47/119 patients. Another 17 malignomas were detected after intraoperative frozen section. Nearly half of the patients had a definite diagnosis only after postoperative histologic investigations (n = 55).

Among cancer patients thyroglobulin measurement had a sensitivity of 77% (44/57 pts.) compared to 80% and 73% sensitivity for ultrasound and scintigraphy, respectively. The specifity of these methods was 50% for thyroglobulin compared to 82% and 62% for ultrasound and scintigraphy. Fine-needle biopsy was performed in 55 cancer patients giving a correct preoperative diagnosis in 40 pts. (cancer in 21 pts., suspected cancer in 19 pts.) (sensitivity 73%, specifity 96%).

Conclusions: Ultrasound and fine-needle biopsy proved to be essentially for definite operative decision making. Scintigraphy was uneffective giving a very low specifity.

1233 ORAL

## Well differentiated thyroid cancer: Analysis of survival for 299 operated patients

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Alm of the Study: 1) Evaluation of the validity of the initial surgery with regard to the initial Prognostic Index (PI) (as defined by the E.O.R.T.C.) — 2) Evaluation of the occurrence of local, regional or distant metastases — 3) Impact on survival.

Material and Method: 299 Patients (PTS) (86 M; 213 F) consecutively operated from 1955 to 1995 in our Institution for well differentiated thyroid cancer with or without adjuvant I₁₃₁ all placed on supressive hormonal treatment. Histology of primary: 220 papillary, 31 follicular, 48 moderately differenciated follicular cancer. Mean age 46.3 years (7 to 81 yrs). 28 PTS had various surgeries before being referred, definitive surgery accomplished = 121 total thyroidectomies (TT), 38 subtotal bilateral lobectomies, 38 total unilateral and subtotal contralateral lobectomies, 96 total unilateral lobectomies, 2 isthmusectomies and 4 biopsies. Tracheotomy mandatory for 13 PTS. Recurrent nerve lymph node dissection: 78 PTS, lateral neck dissection: 90 PTS. I₁₃₁ was given to 138 PTS (122 for thyroid tissue ablation, 11 for residual thyroid tumor, 5 for distant metastases only). 35 PTS: additional external radiation (either for residual thyroid tumor, or for invaded lymph nodes or for "shave-excision").

Results: After a median follow-up of 15 yrs (12 to 488 months), 224 PTS are alive (NED) among 274 PTS for whom neither distant metastases at presentation (n = 11) nor residual tumor was left after the operation (n = 14). The PI inferior or equal to 50 (n = 146 PTS) predicts a 10 yrs Survival of 98.5% versus 75.6% for 128 PTS with PI superior to 50 (p < 0.0001). S 10 yrs of 63 PTS after unilateral lobectomy with PI inferior or equal to 50 is 97% (n = 63; 2 deaths) whereas S 10 yrs of 53 PTS with PI superior to 50 treated with TT is 65% (n = 53; 22 deaths).

1234 ORAL

## Prophylactic thyroidectomy in MEN IIA gene carriers – An intervention with a justifiable morbidity?

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Background: The fate of MEN IIA patients is determined by the medullary thyroid carcinoma. Molecular-genetic diagnostics enable early recognition of the gene carrier and prophylactic thyroidectomy in childhood. Every prophylactic surgical intervention must be critically examined regarding the risks involved for the patient. We have analyzed our prophylactically operated children and adolescents under this aspect.

Methods: In the past 2 years, 8 children and adolescents (4 male/4 female) with MEN IIA underwent prophylactic thyroidectomy and central lymphadenectomy, followed by mandatory exposure of the recurrent laryngeal nerve and parathyroid.

Results: In 4 patients (age: 4–9 years), C-cell hyperplasia was histologically detected as a precursor of the carcinoma. Three patients (age: 9–24 years) had a T1 carcinoma without lymph node metastases. A 9-year-old boy had a T1 carcinoma with an ipsilateral lymph node metastasis. There were no wound healing disturbances or bleedings. Postoperative recurrence weakness (1 case) or hypocalcemia (3 cases) regressed completely.

Conclusion: Early prophylactic thyroidectomy in MEN IIA patients is oncologically justifiable and should be performed in special centers with an acceptably low morbidity for the children and adolescents concerned.

1235 PUBLICATION

A phase II study of interferon alpha-2a (IFN $\alpha$ ) and modulated 5-fluorouracil (5-FU) in patients (pts) with advanced neuroendocrine tumours (NET)

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Background: Both 5FU and IFNa have shown modest single agent activity in pts with NET, with biochemical responses much more common than objective responses. The combination of 5FU and IFNa has shown synergy in tumour models, and activity in gastrointestinal malignancies.

Methods: 15 pts with advanced NET (12 carcinoid, 2 islet cell, 1 phaeo.) of whom 3 were non-secretors, were treated with leucovorin 200 mg/m2 i.v. infusion over 2 hours, then 5FU 400 mg/m2 i.v. bolus followed by 400 mg/m2 i.v. infusion over 22 hours all repeated on day 2; IFNa was given at 6  $\times$  106 IU s.c. every 48 hours throughout. Treatment was given every 2 weeks for up to 12 cycles. In case of stable disease (SD) or partial response (PR), IFNa was continued until disease progression (PD). All pts were chemotherapy naive; one pt had prior treatment with 1311-metaiodobenzylguanidine.

Results: Patients received a median of 5 courses (range 1–12). Two pts achieved a PR (13%; 95% confidence interval 2–40%), of 3 and 4 months duration. Five pts achieved SD (33%), for a median of 8 months (range, 4–22 months). Both pts who achieved PR and 3/5 with SD had a >50% marker reduction (5-HIAA, VMA, VIP, Gastrin) correlating with symptomatic response. Four pts had PD. Another 4 were not assessable for response due to early toxicity requiring cessation of treatment. Two had grade III—IV diarrhoea and 2 grade IV neutropenia requiring i.v. antibiotics.

Conclusions: These results suggest no clear advantage for the combination of 5FU and IFNa over the individual agents; the combination *may* also result in increased toxicity

1236 PUBLICATION

## Combined therapy for advanced thymoma

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Thymoma (THY) is a locally invasive mediastinal tumor frequently associated to several paraneoplastic syndromes, most notably miastenia gravis. Late local relapses are frequent. Treatment of advanced THY (Masaoka stages III-IV) with local therapy alone has a high incidence of relapse. There are few studies on multimodal therapy in this setting. From 1986 to 1995, 9 cases of THY have been diagnosed at our institution. Median age was 53 years (28-69). Sex (male/female): 5/4. In addition to local symptoms. 2 patients (pts) had miasthenia gravis and 2 had red cell aplasia (pure in 1, associated to thrombocytopenia in 1). Stage (Masaoka): III in 7 pts, IVA (pleural metastases) in 1 and IVB in 1 (single lung metastasis). Two pts were initially treated with surgical resection. The other 5 were treated with cisplatin-containing chemotherapy: CAP (2), PBV (2), PIA (1). All 5 had a partial response (PR), but I died of neutropenic sepsis at 2 months. The remaining 6 pts plus 1 pt with mediastinal relapse after surgery and 1 previously untreated pt received external radiotherapy (45-60 Gy). Response after radiotherapy was complete in 4 pts and PR in 4. With median follow-up of 71 months, 4 pts had a local progression at 30 months (24-36). One is alive with disease at 25 months and 3 died with progressive disease at 24, 26 and 96 months from initial therapy. This last pt achieved successive PRs to 3 regimens of chemotherapy and survived for 60 months after progression. Four pts remain alive and progression-free at 12, 61, 81 and 86 months. Survival for all pts is 60% at 5 years. Pts with advanced THY can have long progression-free survival if adequate local control is achieved. Since advanced THY is very chemosensitive, combined locorregional and systemic front-line therapy is a reasonable approach, in the absence of conclusive evidence from randomized trials, given the rarity of this tumor.