02, to 12). For the entire cohort the median number of lymph nodes per specimen was 16+/-11. The mean follow-up time was 60 months. The length of hospital stay was 14 days (range 5 to 100) with an inhospital mortality rate of 1.3%. The overall-five years survival was 80% (74% and 82% in patients submitted to D1 and D2 lymphadenectomy, respectively; p = ns. Fig.2 (a-b).

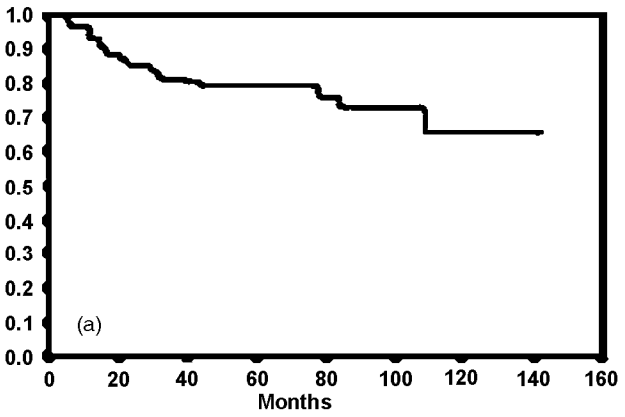


Fig. 2a.

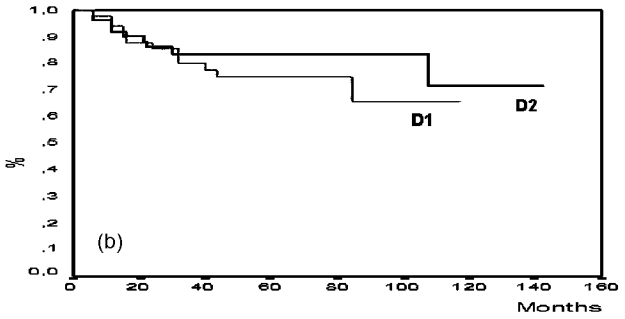


Fig. 2b.

In order to comparing survival, the follow factors were analysed for prognosis: extent of lymphadenectomy (D1 vs D2), patient age, tumor stage, tumor size. In the multivariate analysis only the tumor stage was predictor of outcome (Fig3).

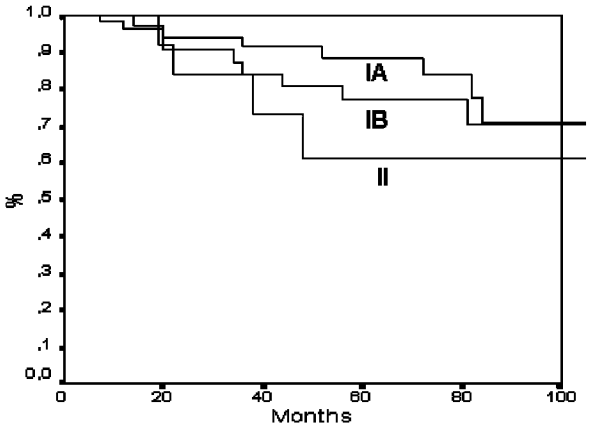


Fig. 3.

**Conclusions:** The high long-term survival rates reported by experienced centers after systematic, standardized extensive D2 and D3 gastrectomies are encouraging. In our center, D2 gastrectomy is become rourine. However, in the multivariate analysis the extent of lymphadenectomy does not influence survival of patients submitted to gastric resection for node negative gastric cancer. In these patients, only T stage is closely related to the clinical outcome.

**737** POSTER

**Chemotherapy in advanced gastric cancer: a systematic review and meta-analysis**

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**Background:** Systemic chemotherapy is the major treatment option for the majority of gastric cancer patients. Uncertainty remains regarding the choice of the regimen.
**Materials and methods:** Our objectives were to assess the effect of
1. Chemotherapy versus best supportive care (BSC)
2. Combination versus single agent chemotherapy
3. The following different combination chemotherapy regimens:
   a. 5-FU/cisplatin combinations with versus without anthracyclines
   b. 5-FU/anthracycline combinations with versus without anthracyclines

on overall survival and toxicity.
Search strategy: We searched: Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, proceedings from DDW, ECCO, ESMO, ASCO until February 2005.
Selection criteria: Randomised controlled trials on systemic intravenous chemotherapy versus BSC, combination versus single agent chemotherapy and different combination chemotherapies as above in advanced gastric cancer.
**Results:** 24 randomised trials with a total number of 3304 patients are included in this meta-analysis. Analysis of 1. Chemotherapy versus BSC consistently demonstrated a significant benefit in terms of overall survival in favour of the group receiving chemotherapy (HR 0.39, 95%CI 0.28–0.52). Analysis of 2. Combination versus single-agent chemotherapy provides evidence for a survival benefit in favour of combination chemotherapy (HR 0.83, 95%CI 0.74–0.93), which is achieved at the price of increased toxicity. When comparing 3a.) 5-FU/cisplatin-containing combination therapy regimens with anthracyclines versus those without anthracyclines (comparison 4 including 501 patients: HR 0.77, 95%CI 0.62–0.95) and 3b.) 5-FU/anthracycline-containing combinations with cisplatin versus those without cisplatin (HR 0.83, 95%CI 0.76–0.91), both demonstrate a significant survival benefit for regimens including 5-FU, anthracyclines and cisplatin. Among these three-drug-regimens, the rate of treatment related deaths was higher when 5-FU was administered as bolus compared to infusional 5-FU (3.3 versus 0.6%).
**Conclusions:** Chemotherapy significantly improves survival in comparison to best supportive care. In addition, combination chemotherapy improves survival compared to single-agent 5-FU, but the effect size is much smaller. Among the combination chemotherapy regimens studied, best survival results are achieved with three-drug regimens containing 5-FU, anthracyclines and cisplatin. Among these, ECF (epirubicin, cisplatin, 5-FU) is tolerated best.

**738** POSTER

**Lymph node ratio as prognostic factor in digestive tumours**

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**Background:** The current TNM classification in digestive cancers uses different rules for the pathologic staging of regional lymph node involvement. For stomach, staging is based on the number of involved nodes, with N1 defined as 1 to 6 regional nodes involved, N2 as 7 to 15, N3 as 16 or more involved. For colon and rectum, N1 means 1 to 3 involved nodes, and N2, four or more. For anal canal, the staging is based on the anatomical location of the involved lymph nodes. For esophagus and other sites, N1 indicates involvement without any subdivision. The different rules can be confusing. It might be asked if a more unified approach can be considered. There is a growing literature suggesting that the lymph node ratio (LNR), defined as the proportion of nodes found involved among excised nodes, might give more accurate prognostic information. The present study investigates whether or not the LNR can be used to consistently define prognostic subgroups.
**Material and methods:** Data was abstracted from the Surveillance, Epidemiology, and End Results public use database 2004. Selection was histology confirmed primary invasive carcinoma diagnosed between 1988 and 1997, surgically resected. Retroperitoneum, peritoneum and unspecified organs were excluded. Three groups were defined based on

the average LNR distributions: low LNR⩽0.25, intermediate LNR more than 0.25 up to 0.75, and high LNR > 0.75. Survival analyses used the Kaplan-Meier method. End-point was death from any cause. Significance testing used the logrank. Chi-square values are reported for stomach and colorectal to allow comparison with the relevant TNM subdivisions.
**Results:** Median follow-up was 91 months. Five-year survival rates by site and by LNR were respectively:

| Site | Nb. patients | Low-LNR | Mid-LNR | High-LNR | Logrank P |
|---|---|---|---|---|---|
| Esophagus | 576 | 16% | 5% | 4% | <0.0001 |
| Stomach | 3381 | 31% | 16% | 7% | <0.0001 |
| Small intestine | 508 | 66% | 52% | 51% | 0.035 |
| Colorectal | 26181 | 49% | 30% | 15% | <0.0001 |
| Anal canal | 102 | 39% | 25% | 22% | 0.187 |
| Hepatobiliary | 346 | 21% | 19% | 7% | <0.0001 |
| Pancreas | 660 | 11% | 9% | 8% | 0.029 |

$Chi^2$ based on relevant TNM subdivisions was 192.3 for stomach, and 1488.7 for colorectal. Respective $Chi^2$ based on LNR were 438.4 and 2723.0, indicating better prognostic separation with the LNR. As in Figure 1, other sites also showed better separation with LNR.
**Conclusions:** The lymph node ratio performed consistently in all digestive sites. Further investigations on its role for staging are warranted.

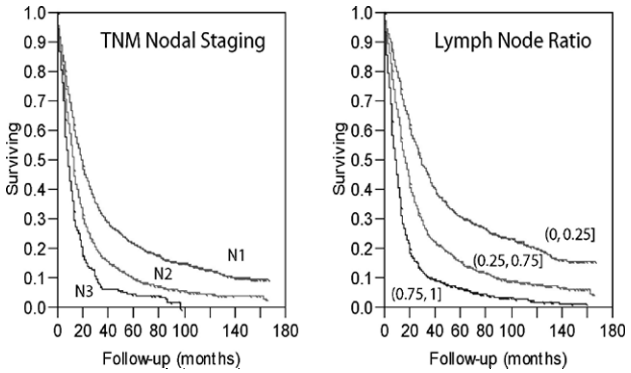


Figure 1. Survival in stomach carcinoma, as classified by the pN nodal staging (left), or by the Lymph node ratio (right). The separation between is notably better with the Lymph node ratio.

**739** POSTER

**Postoperative adjuvant chemotherapy in Japanese gastric cancer patients using Doxifluridine, an intermediate metabolite of Capecitabine, and 5-Fluorouracil – randomized controlled trial**

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**Objective:** To investigate the usefulness of doxifluridine (5'-DFUR) in comparison with 5-Fluorouracil (5-FU) in postoperative adjuvant chemotherapy for gastric cancer including the association with levels of thymidine phosphorylase (TP) and dihydropyrimidine dehydrogenase (DPD).
**Materials and methods:** Patients with disease stage II, III-a, or III-b and curability of A or B gastric cancer were eligible for the study, and were randomized using minimization method (stratification factors: disease stage, curability, TP level, and gender), patients were allocated either to 5'-DFUR (400 mg/m$^2$) or to 5-FU (100 mg/m$^2$) group. After surgery, patients in each group were administered per orally doxifluridine or 5-fluorouracil daily for 2 years, and they were followed up post-operatively for 5 years. Based on the Kaplan-Meier method, a treatment-specific disease-free survival curves (DFS) and survival curves were estimated for comparison. As the secondary study, levels of DPD were also measured to compare doxifluridine and 5-fluorouracil by the TP/DPD ratio.
**Result:** During the period from September 1995 to August 1998, 212 patients were enrolled at a total of 48 medical institutions. There was no major bias between the two groups in demographic factors. In terms of a DFS curve and a survival curve in all patients at the post-operative 5-year time point, there was no statistical difference between the two groups. In a stratified log-rank test and a TP/DPD ratio-specific investigation as well, similar results to the above were obtained. DFS curves in patients with measurable DPD levels in the high- and low-TP/DPD-ratio groups were estimated. As a result, DFS curves in patients in the high-TP/DPD-ratio group were found to be significantly better (P = 0.043: log-rank test). This tendency was found to be more relevant in patients in the 5'-DFUR group.
**Conclusion:** In comparison of 5'-DFUR and 5-FU treatment in postoperative adjuvant chemotherapy for gastric cancer, no statistical difference was observed in either the DFS curve or survival curve. In the TP/DPD ratio-specific investigation conducted as the secondary study, patients with the high-TP/DPD-ratio group had significantly better DFS and survival curves, regardless of the treatment. Thus, the TP/DPD ratio was considered to be useful in predicting responses in the treatment using fluorinated pyrimidines, especially with 5'-DFUR.

**740** POSTER

**Fluorouracil, leucovorin and oxaliplatin (FLO) versus fluorouracil, leucovorin and cisplatin (FLP) as a first line therapy in patients with advanced gastric cancer –interim analysis of a multicenter, randomized phase II trial**

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**Background:** Cisplatinum-based chemotherapy is widely used as first-line treatment for advanced gastric cancer which is, however, associated with limited efficacy and significant toxicities. The purpose of our study was to evaluate tolerability and efficacy of oxaliplatin combination chemotherapy in patients (pts) with advanced gastric cancer.
**Methods:** Patients were required to demonstrate adequate liver, renal, and haematological function and ECOG performance status 0–2 to participate. Participants were randomised to receive FLO: Fluorouracil (F) 2600 mg/m$^2$ 24 h infusion, leucovorin (L) 200 mg/m$^2$, and oxaliplatin 85 mg/m$^2$ every two weeks or FLP: F 2000 mg/m$^2$ 24 h infusion, L 200 mg/m$^2$, weekly, and cisplatin 50 mg/m$^2$ every two weeks. Primary end point was progression free survival. To evaluate safety and response a planned interim analysis was performed after 80 patients had been randomized and completed at least one treatment cycle.

| | FLO n = 44 | | FLP n = 36 | |
|---|---|---|---|---|
| **Safety (NCI)** | All grades | Grades 3/4 | All grades | Grades 3/4 |
| Vomiting (%) | 29.5 | 4.5 | 44.4 | 2.8 |
| Diarrhea (%) | 25 | 0 | 22.2 | 2.8 |
| Stomatitis (%) | 13.6 | 0 | 11.1 | 2.8 |
| Infection (%) | 4.5 | 0 | 8.3 | 2.8 |
| Neurosensory (%) | 54.5 | 9.1 | 19.4 | 0 |
| Anemia (%) | 45.5 | 0 | 55.6 | 2.8 |
| Leucopenia | 31.8 | 0 | 33.3 | 11.1 |
| Thrombopenia | 31.8 | 9.1 | 19.4 | 0 |
| **Response (WHO)*** | **n/41** | **%** | **n/33** | **%** |
| CR | 2 | 4.9 | 0 | – |
| PR | 14 | 34.1 | 8 | 24.2 |
| SD | 19 | 46.3 | 15 | 45.5 |
| PD | 6 | 14.6 | 10 | 30.3 |

*p = 0.072

**Results:** 140 pts have been randomized so far. Results for toxicity and response on the first 80 pts are shown in the table. Progression free survival was 5.6 months (FLO) vs. 3.6 months (FLP) (p = 0.90).