initiated an individual patient data (IPD) based meta-analysis of all randomized clinical trials in the adjuvant gastric setting with two main objectives: (1) To quantify the potential benefit of chemotherapy after complete resection over surgery alone and to further study the role of various treatments including mono-chemotherapy, combined chemotherapy with FU derivatives, mitomycin-C (MMC), anthracyclines, taxanes, or irinotecan. (2) To validate disease free survival (DFS) as a surrogate endpoint of overall survival (OS) for randomized trials in the adjuvant setting.
Methods: All randomized controlled trials (RCTs) closed to patient accrual at the end of 2005 were eligible. Trials testing radiotherapy, intraperitoneal chemotherapy, or immunotherapy were excluded. The primary endpoint was overall survival (OS), the secondary endpoint disease-free-survival (DFS).
Results: The gastric group set up the largest database of patients treated with adjuvant treatment for gastric cancers. Thirty-two eligible trials (7,517 patients) were identified. As of June 2011, individual patient data were available from 18 trials (4,945 patients, 66% of the targeted data) carried out in 11 different countries (Europe, Asia, USA), with a median follow-up exceeding 7 years. They were the opportunity to gather experts from 12 different cooperative groups in 4 investigators meeting where results were discussed. These data, carefully checked using statistical diagnostic tools, were analysed using meta-analytic techniques to provide robust results: (1) There were overall statistically significant benefits in favour of adjuvant therapy in terms of OS (HR = 0.80, 95% CI 0.77–0.84, $p < 0.0001$) and DFS (HR = 0.79, 95% CI 0.74–0.84, $p < 0.0001$). No statistical heterogeneity in the treatment effect could be detected neither across the included trials nor across the four pre-defined types of regimen. Adjuvant 5FU based regimens appeared to be superior to surgery alone and was recommended as a valid standard for further clinical trials. (2) DFS (rank correlation coefficient, 0.976; 95% CI, 0.965, 0.987) was strongly associated with OS at the individual level. On average, there was also a very high correlation at the trial level between the log hazard ratios log HR_{OS} and log HR_{DFS}. Trial-level R^2 was estimated to 0.989 (95% CI = 0.978, 1.0). Considering the high correlation at both levels, we computed the surrogate threshold effect (STE = 0.90), meaning that a HR_{DFS} of 0.9 predicts a HR_{OS} of 1. Unfortunately, despite implication of the steering committee, it was not possible to collect 33% of the targeted data and some collaborative groups refused to join this international collaboration. Last, but not least the time to constitute the database lead to delay that may slow down the enthousiasm of the participants. Yet, this is a unique ressource to adress numerous questions of interest. We now invite proposals for specific studies using the database from our colleagues in cancer research.

PG 10.04 SPEAKER ABSTRACT
Adjuvant chemotherapy: an option for Asian patients only?

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Recently we presented the results of the CLASSIC trial, an Asian phase III randomized trial testing the effectiveness of adjuvant chemotherapy with capecitabine and oxaliplatin (XELOX) after D2 gastrectomy in patients with stage II or III gastric cancer. This study demonstrated that 8 cycles of XELOX following D2 gastrectomy is superior to surgery alone in terms of disease-free survival, the primary endpoint of the study. Our findings are consistent with the Japanese ACTS-GC trial, in which adjuvant chemotherapy with S-1 for 1 year after D2 gastrectomy was tested. These two studies show that adjuvant chemotherapy following D2 gastrectomy improves outcomes in patients with resectable gastric cancer. A key question would be how generalizable the results of these studies are to other regions of the world. A notable finding from the CLASSIC trial is the good patient outcomes; the 3-year overall survival rate in the surgery-alone group (78%) was considerably higher than those in the US Intergroup-0116 and UK MAGIC populations (30% to 40%). Somebody could argue that the good clinical outcomes in our study are caused by differences in patient populations. However, we believe that the favorable outcomes are a result of the consistent use of D2 resection and the high quality of the surgery. Now that D2 gastrectomy is standard of care in both Europe and the US, we suggest that our study findings are highly relevant for other regions and may be generalisable to Western patients when D2 surgery is performed by surgeons experienced with this type of surgery.

PG 10.05 SPEAKER ABSTRACT
Selecting the best treatment for an individual patient

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Goals: Several factors concur in determining outcome for locally advanced gastric cancer patients. Shockingly, geographical origin of the patient seems to play a major role. In Eastern countries, the high level of surgery that can be expected grants a high percentage of success in a strategy that employs surgery as immediate treatment followed by adjuvant chemotherapy, mainly based on oral fluoropyrimidines (S-1 or Capecitabine), with satisfactory results. In Western countries, the expertise of the surgeon maintains its role as predictor of high likelihood of cure.
Methods: In patients who obtain a good surgical outcome, the benefit of the addition of adjuvant chemotherapy is still debatable: the gain in survival seems to be small (around 8% at 5 years) and with noticeable toxicities. On this basis, neoadjuvant treatment is a promising option even if there is a general lack of conclusive data regarding which is the best regimen to use. Even with the limitation of a small number of studies, neoadjuvant chemotherapy is usually feasible, allows for a greater chance of receiving chemotherapy at all, and opens the possibility of a downstaging and downsizing of the tumour, allowing a easier surgery.
Results: Regarding this strategy preliminary results have also been presented about the addition of monoclonal antibodies. For example, in the TOGA trial, a significant benefit in terms of overall survival, response rate and progression free survival was observed also for patients with locally advanced gastric cancer and not just for the metastatic ones. In the AVAGAST trial also, the addition of Bevacizumab failed to determine a significant improvement in the primary outcome, overall survival, for patients treated with the combination, but in the subgroup analysis, patients with locally advanced gastric cancer had a significantly better overall survival and response rate.
Conclusion: Finally, an increasing interest in the use of hyperthermic intraperitoneal chemotherapy in other types of solid tumours (including those of the gastrointestinal tract) has led to evaluate this treatment modality in gastric cancer patients with peritoneal involvement. It should be noted that it is still to be considered a experimental approach, even though it would be intriguing to evaluate if a particular subset of patients, those who are more likely to develop peritoneal metastasis, may benefit from this technique in the adjuvant setting. It should be considered that other than histologic subtype (diffuse vs intestinal) there seems to be a series of polymorphisms of genes usually involved in cell interaction and migration that can explain a different metastatic pattern in resected patients. Further research on these determinants of metastatic spread could be used to select those patients who may benefit from HIPEC and those who may benefit from standard adjuvant or that gain no benefit at all.