Symposium (Mon, 24 Sep, 14:45−16:45)
Adjuvant treatment of colon cancer

30 INVITED

Open surgery for colorectal cancer – quality assurance

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The quality in the treatment of cancer has become more and more important. Based upon available data on colorectal cancer, the difference in cancer specific outcome between surgeons is larger than the beneficial effects of adjuvant chemotherapy. Therefore, it is important to know individual surgeons' outcome.
The only way to have knowledge about the outcome is of course a well organised quality control system. Once quality in surgical technique and surgical outcome has been registered, indicating that the standard of surgical care can be set, it is possible to continue with quality assurance.
In Sweden a quality control system for both rectal and colon cancer have been run for many years as a national registry for rectal and colon cancer. Data from the rectal cancer registry have been reported and evaluated based upon hospital. The difference between hospitals varies based upon number treated per year, i.e. volume. However, the difference in outcome between hospitals with different volumes is less than the difference between outcomes in high volume hospitals.
In conclusion, it is essential with a quality control system to see what standard of care we can expect in colorectal cancer treatment. Once those standards have been set, it is possible to continue with the quality assurance system.

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Five year results from the COST trial testing laparoscopic versus open colectomy for colon cancer

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Background: To test the hypothesis that disease-free and overall survival are not inferior regardless of whether patients receive laparoscopic-assisted (LAC) or open colectomy.
Methods: Sixty-six credentialed surgeons participated through one of 48 enrolling institutions. 5-year data was complete on 90% of patients. Because LAC was not under consideration as a superior oncologic procedure, a non-inferiority trial design was utilized testing time to recurrence as the primary endpoint. Additional endpoints included overall survival (OS) and disease-free survival (DFS) tested using Kaplan Meier.
Results: Patients with curable (TNM Stages I-III) colon cancer were randomly assigned to undergo LAC or open surgery; 872 patients were enrolled between 1994 and 2001 with a median follow-up of 7.15 years. Of 872 patients enrolled and followed until March of 2007, 252 have died and 170 patients have recurred. 5 year rates of cumulative incidence of recurrence (19% versus 22%), overall survival (77% versus 75%) and disease-free survival (69% versus 69%) are the same between the LAC and open arms, respectively. Sites of first recurrence were distributed similarly between arms. Recurrence rates, disease-free survival and overall survival did not differ by treatment arm based or TNM stage.
Conclusion: Results from a prospective randomized multicenter trial confirm that laparoscopic-assisted colectomy for curable colon cancer is not inferior to open surgery.

32 INVITED

Adjuvant treatment of stage II colon cancer

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Out of the million of patients (pts) world wide who have a colon cancer in 2007, approximately 20% will have a stage II colon cancer and for most of them the question of administration of an adjuvant treatment will be raised.
In contrast with the stage III for whom there a large consensus in favour of the administration of an adjuvant chemotherapy, using the FOLFOX 4 regimen in absence of counter-indications (Andre T et al. N Engl J Med 2004 and de Gramont A et al. ASCO 2007), there are still no consensus concerning the management of stage II colon cancer
The main reason for such incertitude is due to the fact that there is no large positive trial conducted in this specific population and because a low risk of relapse (15% to 30%) with a low risk of death (10% to 20%) results in a low potential absolute gain in overall survival (OS) estimated, for a HR of 0.80 in favour of chemotherapy, between 2 and 5%.
However 5 meta-analysis and two trials (QUASAR 2 and MOSAIC) give us some indirect arguments in favour of the efficacy of adjuvant chemotherapy using a 5FU based regimen for stage II colon cancer pts.
Two meta-analysis were borderline positive: the IMPACT B2 was a pooled analysis of 5 randomized trials (1016 pts) which reported an advantage of 2% (82% vs 80%) in favour of a 5FU and folinic acid combination but this difference was not significant (HR=0.86, p = 0.057) (IMPACT B2, J Clin Oncol 1999; 17: 1356−63); the Canadian meta-analysis conducted on 8 trials comparing surgery alone to surgery plus a 5FU based chemotherapy (1870 pts) also reported the same HR of 0.86 but also was not significant (p = 0.057) (Figueredo et al. J clin Oncol 2004; 22: 3495–3507).
Two meta-analysis were positive but the NSABP meta-analysis was a compilation of heterogeneous trials (Mamounas E et al. J Clin Oncol 1990; 17: 1349−55), and, the Japanese meta-analysis on 5233 pts was conducted in an heterogeneous group of pts with only 45% of stage II colon cancer for whom a + 4.3% increase in OS in favour of an oral 5FU based chemotherapy was reported (Sakamoto J et al. J Clin Oncol 2004; 22: 484−92). The last was a meta-analysis from the Mayo Clinic which was positive for the DFS (76% vs 72%; p = 0.049) but not for OS (81% vs 80%, NS) (Gill et al. J Clin Oncol 2004; 22: 1797–1806).
The QUASAR 2 study is the largest trial conducted in part in stage II colon cancer and compared, for pts with an uncertain benefit from chemotherapy, a group of pts treated by surgery alone (n=1617) to a group receiving a post-op 5FU and folinic acid combination (n=1622); it reported a significant difference for OS (5-year survival: 83% vs 80% in favour of chemotherapy, p = 0.04) however only two third of the pts had a stage II colon cancer and this trial has not been published (Gray R et al. Proc ASCO 2004; 24: Nº3501). In the MOSAIC trial approximately 40% of the pts had a stage II Colon cancer and these pts benefited from the same reduction in their relative risk of recurrence than the stage III colon cancer, however the DFS was not significantly ameliorated by the administration of the FOLFOX4 regimen compared to LV5FU2 (3-year DFS: 84.3% vs 87%; HR: 0.80 [IC95%: 0.56−1.15]) but the trial was not powered to answer questions on chemotherapy efficacy in stage II colon cancer (Andre T et al. N Engl J Med 2004).
In fact it appears from these studies that stage II colon cancer pts is an heterogeneous group of pts which must be separated into subgroups according to prognostic factors. For instance, in the large SEER cohort reported in 2004 there was an important difference in the OS of pts pT3N0 (stage IIa) (5-year OS: 83%) compared to pts with pT4N0 (stage IIb) (5-year OS: 72%) (O'Connell et al. J Natl Cancer inst 2004; 96: 1420−5).

- Since about 10 years a high risk subgroup of stage II colon cancer has been defined concerning pts with perorated or obstructive or pT4 tumors (Schrag D et al. J Clin Oncol 2002; 20: 3999–4005); other factors may also be considered like the existence of vascular invasion by the tumor, a poor tumor differentiation or a number of analysed lymph nodes <10 which are considered as poor prognostic factors (de Gramont et al. N Engl J Med 2004; 351: 1691−2; Moris M et al. Br J Surg 2006; 93: 866−71; Sarli et al Eur J Cancer 2005).
- Biological markers may also influence the risk of recurrence and for instance the MSS status is recognized as a factor of poor prognosis as well as the presence of a 18q LOH.

For pts having one of these poor prognostic factors and no counter-indication to receive chemotherapy there is an agreement to prescribe an adjuvant chemotherapy for high-risk pts who ask for it after extensive explanations on the benefit/risk ratio of the adjuvant chemotherapy (5FU-folinic acid combination or FOLFOX4 regimen).
In conclusion there is no consensus on the standard adjuvant treatment for stage II colon cancer pts. However in case of high risk of recurrences there is an agreement to propose an adjuvant chemotherapy to selected and informed patients. Ongoing trials will help us to precise the role of adjuvant chemotherapy in stage II colon cancer, in particular the ECOG E5202 trial which compares, in stage II MSS or 18q LOH, a chemotherapy (FOLFOX6) to a combination of this chemotherapy with bevacizumab.

33 INVITED

Adjuvant treatment of stage III colon cancer

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Background: The prognosis of patients with colon cancer depends on the depth of tumor invasion and whether regional lymph nodes are involved.