Presidential Session III
Monday 26 September 2011, 12:15−14:25
2LBA LATE BREAKING ABSTRACT

Laparoscopic Surgery Versus Open Surgery for Rectal Cancer: Short-term Outcomes of a Randomised Trial

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Background: The safety and short term benefits of laparoscopic surgery in patients with rectal cancer remain unclear. The multicentre COLOR II (COlorectal cancer Laparoscopic or Open Resection) trial (NCT00297791) was done to assess safety, oncological radicality and benefit of laparoscopic resection compared with open resection for curative treatment of patients with cancer of the rectum.
Patients and Methods: A non-inferiority phase III trial at 30 centers worldwide was conducted between January 20, 2004 and May 4, 2010. In total, 1103 patients with a solitary rectal carcinoma within 15 cm from the anal verge, staged as T1, T2 or T3 with a margin to the endopelvic fascia greater than 2 mm, were randomly assigned to either laparoscopic or open surgery in a 2:1 ratio. The primary endpoint was locoregional recurrence rate 3 years after surgery. Analysis was by intention to treat. Here, clinical characteristics, operative findings, and short term outcomes are reported.
Results: 1044 (94.7%) of the randomized patients were eligible for inclusion. Patients undergoing laparoscopic surgery had less blood loss than those assigned to open resection (median 320 mL *vs* 552 mL, $p < 0.001$) although laparoscopic surgery lasted longer than open surgery (median 247 min *vs* 200 min, $p < 0.001$). Conversion to open surgery was necessary in 114 (16.4%) patients who had been allocated to laparoscopic surgery. The circumferential resection margin did not differ between groups (laparoscopic surgery 1.3 cm *vs* open surgery 1.4 cm, $p = 0.19$). The distal resection margin was similar in both groups (3.0 cm, $p = 0.54$) while the proximal resection margin was 17.0 cm after laparoscopic surgery and 19.0 cm after open resection ($p < 0.001$). Groups did not differ in the number of removed lymph nodes (laparoscopic surgery 14 lymph nodes *vs* open surgery 16 lymph nodes, $p = 0.085$). Anastomotic leakage occurred in 10% of patients after laparoscopic surgery and in 8.8% of patients after open resection ($p = 0.634$).
Laparoscopic resection was associated with earlier recovery of bowel function ($p < 0.001$) and tolerance of oral fluid intake ($p = 0.006$), decreased need for epidural analgesics ($p < 0.001$) and shorter hospital stay ($p = 0.037$) compared to open resection of rectal cancer. Mortality rates within 28 days after surgery did not differ between groups ($p = 0.141$).
Conclusions: Laparoscopic surgery can be used for safe and radical resection of non-invasive rectal cancer.

Presidential Session I
Saturday 24 September 2011, 13:45−15:35
3LBA LATE BREAKING ABSTRACT

Very Accelerated Radiotherapy (RT) Versus Concomitant Chemo-Radiotherapy (Ct-Rt) In Locally Advanced Head And Neck Cancer: Long Term Results From 2 Phases III GORTEC Randomized Trials

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Background: A very accelerated radiotherapy regimen delivering 64 Gy in 3.5 weeks was previously shown in a randomized trial to be markedly superior to conventional radiotherapy in disease control of locally advanced head and neck carcinomas (Bourhis JCO 2006). This very accelerated RT regimen was further tested in 2 phase III randomized trials against 3 distinct chemo-radiotherapy regimens for which the long term results are reported.
Methods: In these 2 phase III trials (GORTEC 96-01 & GORTEC 99-02), a total of 949 patients with locally advanced head and neck squamous cell carcinomas were randomised to receive either 64 Gy in 3.5 weeks (1.8 Gy BID) or one of the 3 following CT−RT regimens:

1. Conventional CT−RT: 70 Gy in 7 weeks + 3 cycles of 4 days of concomitant carboplatin and 5FU (Calais JNCI 1999)
2. Moderately intensified CT−RT: 70 Gy in 6 weeks + 2 cycles of 5 days of concomitant carboplatin-5FU (CT as from Calais JNCI 1999)
3. Strongly intensified CT−RT: 64 Gy in 5 weeks with concomitant cisplatin 100 mg/m^2 on day 2, 16 and 30 and 5-FU 1000 mg/m^2 on day 1−5 and 29−33 of the RT + 2 cycles of adjuvant cisplatin-5FU.

Results: In each trial, there was no imbalance between arms regarding gender, age, tumor stage and tumor site. The most common tumor sites were oropharynx and hypopharynx. With a median follow-up of 5.2 years (99-02) and 10.2 years (96-01), long term results show that all 3 CT−RT arms were significantly superior to the very accelerated RT in terms of loco regional control. As compared to very accelerated RT, the conventional CT−RT regimen also significantly improved progression free survival (PFS) and overall survival (OS). There was also a trend to an improvement of PFS with moderately intensified CT−RT and with strongly intensified CT−RT. No benefit in OS was seen either for moderately intensified CT−RT, or for strongly intensified CT−RT. In addition a high rate of treatment related deaths was observed with strongly intensified CT−RT. No difference was seen in long term normal tissues side effects (grade 3−4), whatever the effect considered. However long-term feeding tube carriers were more frequent with very accelerated RT than with conventional CT−RT. There was also no indication that either the moderate or the strong increase of the dose-intensity of CT−RT could improve the therapeutic index, as compared to conventional CT−RT.
Conclusion: The long term results of these 2 phases III randomized trials show that all the 3 concomitant CT−RT regimens tested were more efficient on loco regional control than very accelerated RT. However these data also show the lack of interest of dose-intensification, with regard to concomitant CT−RT, since among the 3 CT−RT regimens tested, the most favourable therapeutic index was found for the conventional CT−RT.

Presidential Session I
Saturday 24 September 2011, 13:45−15:35
4LBA LATE BREAKING ABSTRACT

Everolimus in Subependymal Giant Cell Astrocytomas (SEGA) Associated with Tuberous Sclerosis Complex (TSC): Results of EXIST-1, a Double-Blind Placebo-controlled Phase III Trial

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Background: TSC is a genetic disorder caused by loss of either *TSC1* or *TSC2* leading to constitutive mammalian target of rapamycin (mTOR) activation and growth of tumors in several organs. In the brain, growth of SEGAs can cause hydrocephalus, usually requiring surgery.
Patients and Methods: Patients of any age with a definitive TSC diagnosis, SEGA $\geqslant$1 cm, and documented serial SEGA growth were eligible for this phase III trial (NCT00789828; trial sponsor: Novartis Pharmaceuticals, Inc). Patients were randomized 2:1 to receive oral everolimus (EVE) 4.5 mg/m^2 qd (titrated to target trough level of 5−15 ng/mL) or matching placebo (PBO) until SEGA progression or unacceptable toxicity. Randomization was stratified by concomitant use of enzyme-inducing antiepileptic drugs. Brain MRI was performed at baseline, months 3, 6, and 12, and annually thereafter. Kidney MRI or CT was done at baseline for all patients and at similar frequency for patients with $\geqslant$1 measurable angiomyolipoma (AML) (longest diameter $\geqslant$1 cm) at baseline. Patients had 24-hour video EEG at baseline and 6 months. Upon SEGA progression, patients were unblinded and offered open-label EVE if on PBO. Primary efficacy endpoint was SEGA response rate ($\geqslant$50% volume reduction by central independent radiologic review confirmed $\geqslant$8 weeks later). Other endpoints: safety, change in frequency of epileptiform events per 24-hour video EEG, time to SEGA progression, skin lesion response rate, and AML response rate.
Results: 117 patients (median age 9 years, range 10 months to 26 years; 17% of patients <3) were enrolled between 08-2009 and 09-2010. Median duration of treatment was 41.93 weeks (range, 24.0–78.9) in the EVE arm and 36.14 weeks (range, 13.9–79.7) in the PBO arm. SEGA response rate was 35% on EVE vs. 0% on PBO ($P < 0.0001$). Reduction of seizures, as per video EEG was similar in both treatment groups. None of the EVE patients progressed compared with 15% on PBO. Higher skin lesion (41.7% vs. 10.5%) and AML (53.3% vs. 0%) response rates were observed