Poster Discussion Presentations (Sun, 25 Sep, 11:15−12:15)

Gastrointestinal Malignancies − Colorectal Cancer

6008 POSTER DISCUSSION

The Cell Saver is Safe to Use in Rectal Cancer Surgery

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Background: Preservation techniques for the patient's own blood during cancer surgery have not been adopted widely for fear of introducing viable tumour cells, which may give rise to metastases. However, the use of fresh autologous blood is related to better post-operative outcome and less morbidity and mortality. In this study we present our results of using the cell saver in surgery for locally advanced and recurrent rectal cancer.
Material and Methods: From 1994 until August 2010, data on 546 patients who have been treated for locally advanced (n = 444) or recurrent (n = 102) rectal cancer was collected prospectively. For more than ten years, the cell saver was used to collect, filter, wash and return the patient's own erythrocytes. Blood was not returned when contaminated by faeces or pus or when no transfusion was deemed indicated. Four quartiles representing the volume of blood loss were created: Q1 less than or equal to 1250 ml (n = 153), Q2 1251 up to 2500 ml (n = 140), Q3 2501 up to 5000 ml (n = 138), Q4 5001 ml or more (n = 115).
Results: For locally advanced and recurrent rectal cancer, surgery is complex and extra-anatomically. Hence mean blood loss was 3697 millilitres, 3110 millilitres for locally advanced rectal cancer patients and 6209 millilitres for recurrent rectal cancer patients. Autologous blood was returned in 315 patients (58 percent). Cancer specific 5-year survival for all patients and per quartile blood loss volume was higher when the cell saver was used: 74, 78, 87, 71 and 63 percent compared to 57 ($p = 0.001$), 69 ($p = 0.363$), 62 ($p = 0.054$), 50 ($p = 0.012$) and 38 ($p = 0.027$) percent for those without cellsaving. Metastases free 5-year survival rates were 70, 59, 81, 70, 66 percent and 61 ($p = 0.036$), 72 ($p = 0.743$), 66 ($p = 0.337$), 57 ($p = 0.085$), 35 ($p = 0.005$) percent, respectively. Local recurrence rates were 12, 9, 5, 13, 22 percent and 22 ($p = 0.007$), 13 ($p = 0.227$), 17 ($p = 0.047$), 30 ($p = 0.014$), 42 ($p = 0.151$) percent, respectively.
Conclusions: Five-year cancer specific survival, metastases free survival and local recurrence rates for the whole group of patients were all statistically significant in favour of the use of the cell saver. Especially in the higher blood loss quartiles. More specifically, patients did not develop more metastases when the cell saver was used. Therefore we conclude, that introduction of the cell saver did not compromise oncological outcome and thus is safe to use in rectal cancer surgery.

6009 POSTER DISCUSSION

Progression Free and Overall Survival After Neoadjuvant Treatment of Colorectal Liver Metastases With Cetuximab Plus FOLFOX or FOLFIRI − Results of the CELIM Study

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Background: Cetuximab plus FOLFIRI or plus FOLFOX induces high response rates in patients with k-ras wild-type, colorectal liver metastases and increases the rate of metastasectomies (Van Cutsem ASCO-GI 2011).
Methods: Patients with initially non-resectable colorectal liver metastases were randomized to treatment with cetuximab/FOLFOX or cetuximab/FOLFIRI and re-evaluated for resectability after eight and then every four cycles. Resectable patients were offered liver resection. KRAS status was retrospectively determined.
The response and resection rates were reported elsewhere (Folprecht et al, Lancet Oncol 2010).
Results: Fifty-six patients were randomized to cetuximab/FOLFOX, fifty-five to cetuximab/FOLFIRI. In all patients, the median progression free survival (PFS) was 10.8 [95% CI 9.3–12.2], the median overall survival 33.7 [26.0–40.2] months.
According to treatment arms, the median progression free survival was 11.2 [7.2–15.3] with cetuximab/FOLFOX and 10.5 [8.9–12.2] months with cetuximab/FOLFIRI. In KRAS wild-type patients, the PFS was 11.9 [8.3–15.6], in KRAS mutant patients 9.9 months [4.5–15.22].
The overall survival was 35.7 [30.0–41.5] and 29.0 [18.7–39.3] for cetuximab/FOLFOX and cetuximab/FOLFIRI, respectively, and 36.1 [25.1–47.1] and 27.4 [15.7–39.1] months for KRAS wild-type and mutant patients (not significant).
Resected patients had a significantly longer progression free survival (15.1 [12.8–17.4] vs 7.07 [6.0−8.1] months,$p < 0.0001$) and a significantly higher overall survival compared to non-resected patients (table 1, $p < 0.0001$).
Conclusions: Liver resection can successfully be performed after neoadjuvant treatment with cetuximab plus chemotherapy in patients with initially non-resectable liver metastases and is associated with favorable survival rates.

Table 1: Progression free and overall survival rates according to Kaplan–Meier est.

	KRAS wild-type	KRAS mutant	resected patients	not resected patients
PFS, 1 year	49.3 [6.1]	25.9 [8.4]	66.0 [6.9]	21.1 [5.4]
PFS, 2 years	17.9 [4.7]	7.4 [5.0]	23.4 [6.2]	3.5 [2.4]
PFS, 3 years	6.8 [3.2]	*	10.6 [4.5]	*
OS, 1 year	88.4 [3.9]	96.4 [3.5]	91.3 [4.2]	87.3 [4.5]
OS, 2 years	67.9 [5.6]	53.6 [9.4]	82.6 [5.6]	42.5 [6.7]
OS, 3 years	50.4 [6.2]	39.9 [9.3]	67.0 [6.7]	23.7 [5.9]

all values in % [standard error]. *Not evaluated due to small sample size.

6010 POSTER DISCUSSION

Radiofrequency Ablation Combined With Systemic Treatment Versus Systemic Treatment Alone in Patients With Non- Resectable Colorectal Liver Metastases: a Randomized EORTC Intergroup Phase II Study (EORTC 40004)

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Background: Radiofrequency ablation (RFA) is increasingly used for treatment of non-resectable colorectal liver metastases. However, clear evidence for a clinical effect is lacking. This study investigates the possible benefits of RFA in this setting.
Methods: This phase II study randomly assigned 119 patients with non-resectable colorectal liver metastases and no extra-hepatic disease, between systemic treatment alone (n = 59), or systemic treatment plus RFA (n = 60). Primary objective was a 30-months overall survival (OS) rate >38% for the combined treatment group. Secondary end points were OS, progression free survival (PFS) and HRQoL.
Findings: The primary endpoint was met, 30-months OS rate was 61.7% (95% CI: 48.2–73.9) for the combined treatment group. However, 30-month OS for the systemic treatment group was 57.6% (95% CI: 44.1–70.4), higher than anticipated. Median OS was 45.3 for combined treatment group and 40.5 months in the systemic treatment group ($p = 0.22$). PFS rate at 3 years in the combined treatment group was 27.6% compared to 10.6% in the systemic treatment group (HR = 0.63, 95% CI: 0.42–0.95, $p = 0.025$). Median PFS was 16.8 months (95% CI:11.7–22.1) and 9.9 months (95% CI:9.3–13.7), respectively. The liver, either alone or in combination with extra-hepatic disease, was the first site of progressive disease in 27 patients in the combined treatment group (45%), compared to 45 patients in the systemic treatment alone group (76.3%) ($p < 0.0001$). The percentage of patients treated for first progression was comparable

between both arms, 37 out of 42 patients (88.1%) in the combination treatment group and 46 out of 53 patients (86.8%) in the systemic treatment group. Salvage treatment consisted of systemic treatment in 21 patients (50%) in the combined treatment group, compared to 44 patients (83%) in the systemic treatment group ($p < 0.001$).
Interpretation: This is the first randomized study on the efficacy of RFA. The study met the primary end point on 30-months OS, however the results in the control arm were in the same range. RFA plus systemic treatment resulted in significant benefit on PFS. The ultimate phase II study design does not allow definite conclusions on the benefit or the absence of a benefit of RFA.

6012 POSTER DISCUSSION

Improved Oncological Outcome After Modified Extralevator Abdominoperineal Excision in Low Rectal Cancer Patients

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Background: Introduction of TME surgery has significantly improved the treatment of rectal cancer patients. However, in patients requiring abdominoperineal excision (APE) irradical resections and tumour perforations are still frequent. This study describes an improved oncological outcome when APE was modified to a supine extralevator technique with perineal dissection (sPPD) first.
Material and Methods: From 2000 to 2010, 246 consecutive patients with T3-T4 rectal cancer who underwent an APE were included. All patients were staged with preoperative MRI and received neoadjuvant (chemo) radiotherapy. In 2005 the sPPD approach was implemented as a didactical principle. To avoid false routes and coning in, pelvic dissection must be limited when following the TME planes from the abdomen.
Results: The percentage of irradical resections was 10% for the entire group. After the introduction of perineal dissection first, involved margins were found in 2.2% and 5.7% for cT0−3 and cT4 tumours compared to 6.8% and 30.2% before 2005 ($p = 0.001$). Furthermore, all outcome parameters improved. Local recurrence rate for pre-operativeT4 tumours (cT4) was reduced from 25% to 2.4% and from 34% to 5.6% in pathologic T4 tumours (ypT4). This results in a 3-year local recurrence rate of 1.7% after 2005 versus 11.5% before 2005 ($p = 0.021$). The three year overall survival for the advanced tumours that responded to neoadjuvant treatment (ypT0−3) improved from 83% to 92% as opposed to 52% to 67% in cT4 tumours with no downstaging (ypT4). In a multivariate analysis, perineal dissection first (sPPD) became a significant factor for R1 resection ($p = 0.038$).
Conclusions: The goal in rectal cancer surgery is to obtain negative resection margins. A combination of the appropriate preoperative treatment and improved surgical technique such as sPPD can achieve this goal. From our data it can be concluded that an irradical resection rate below 5% and subsequent local recurrence rate of 2 to 3% should be achievable. In the future it should be unacceptable that suboptimal quality of surgery influences oncological outcome.

6013 POSTER DISCUSSION

Cumulative Exposure to Bevacizumab (BV) After Progression Correlates With Increased Survival in Patients (pts) With Metastatic Colorectal Cancer (mCRC): a Time-dependent Analysis of the ARIES Observational Cohort Study

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Background: BV + chemotherapy (CT) prolongs survival in 1st- or 2nd-line treatment (tx) of mCRC. Prior analyses from ARIES showed that mCRC pts receiving CT/biologics + ⩾1 BV dose within 2 months after 1st progressive disease (PD) had longer post-progression survival (PPS) than pts receiving only CT/biologics. The present analysis evaluated whether cumulative exposure to BV after PD correlates with PPS, with an emphasis on incorporating the dynamic time-varying features of tx patterns seen in the "real world".
Methods: ARIES 1st-line BV-treated mCRC pts who survived 1st PD were included for analysis. PPS was defined as the time from 1st PD to death from any cause. BV exposure, over follow-up, was defined as the cumulative days of BV use from 1st PD. A time-dependent Cox regression model that controls for survival bias towards pts that receive longer exposure to BV was fitted to assess the effect of cumulative BV exposure on PPS, while controlling for potential time-dependent and time-fixed confounders.
Results: As of 2/14/2011, of 1550 enrolled 1st-line pts, 1183 (76.3%) had 1st PD. Characteristics in the 1183 pts were: 56% male, median age of 63 yrs, median ECOG PS of 0, and 76% with colon cancer. The median PPS for all pts with 1st PD was 13.3 months (interquartile range: 5.8, 27.0). Across follow-up, the hazard ratios (HRs) for PPS decreased by an average of 2.1% for each additional 14-day interval of cumulative exposure (range, 1.9–2.3%). Cumulative BV duration was statistically significantly associated with improved PPS ($P < 0.0001$).

Cumulative BV cycles after PD[a]	Follow-up time after PD, days	n(cycles)[b]	n(0)[c]	HR (95% confidence limits)
1	14	191[d]	843[d]	0.977 (0.965–0.988)
2	28	165	766	0.954 (0.932–0.976)
3	42	140	694	0.932 (0.900–0.964)
4	56	120	640	0.910 (0.869–0.953)
5	70	109	607	0.888 (0.839–0.941)
6	84	91	576	0.868 (0.810–0.930)
7	98	84	540	0.847 (0.782–0.919)
8	112	76	514	0.828 (0.755–0.908)
9	126	61	486	0.808 (0.728–0.897)
10	140	49	449	0.789 (0.703–0.886)

[a]A cycle is calculated as 14 days of cumulative exposure after PD.
[b]Pts who received the specified number of post-PD BV cycles by follow-up time.
[c]Pts with no exposure to BV by follow-up time.
[d]Example: At 14 days after PD, 191 pts had a total of 14 days of BV exposure while 843 pts had no exposure to BV.

Conclusions: This analysis suggests that cumulative exposure to BV after PD is associated with corresponding increases in PPS for mCRC pts. Data from a prospective randomized phase III trial testing BV beyond PD are expected soon.

6014 POSTER DISCUSSION

Cetuximab Treatment for Metastatic Colorectal Cancer With KRAS p.G13D Mutation may Improve Progression-free Survival in Japanese Patients

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Background: Anti EGFR inhibitor is recommended for the treatment of metastatic colorectal cancer (mCRC) with KRAS wild type. However, previous study reported that KRAS p.G13D mutation may be associated with a better outcome than the other mutation after treatment with cetuximab. We retrospectively assessed the association between p.G13D mutation and outcome in mCRC.
Material and Methods: We collected records of 98 patients with mCRC genotyped KRAS mutation treated between August 2004 and January 2011 from four hospitals located in Tokyo and Kyushu Island, and reviewed subtypes of KRAS mutation and patient's characteristics. In the patients treated with cetuximab, univariate and multivariate analysis for progression-free survival (PFS) and overall survival (OS) were performed to determine the contribution of KRAS p.G13D mutation.
Results: The frequency of KRAS p.G13D mutated tumour was 23 (23.5%) and the other mutated tumour was 75 (76.5%). Of the 98 patients, 31 were treated with cetuximab; KRAS p.G13D mutation were 9 (29.0%) and the other mutation were 22 (71.0%), respectively. There were no significant differences in age, sex, primary site, pathological type, previous chemotherapy history and irinotecan combination. The univariate analysis for PFS and OS did not show significant difference between the KRAS p.G13D mutation and the other mutations (PFS; median 4.5 months vs. 2.8 months, $p = 0.65$, OS; median 15.3 months vs. 8.9 months, $p = 0.51$). However, the multivariate analysis for PFS showed a trend that