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