comparable to historical mCRC trials, suggesting significant impact of post-progression survival on OS. This exploratory analysis evaluates the association of various pre- and post-treatment variables with OS in BRiTE.
Methods: Pt population and methods have been described previously (Kozloff, ASCO 2006). All pts in BRiTE received BV as part of 1st-line therapy. The use of BBP and choice of CT were at investigator's discretion. Cox's proportional hazard model was used to assess the independent effects of pre- and post-treatment pt-related factors on OS, including age, ECOG PS, albumin, alkaline phosphatase, site of primary tumor, 1st-line CT regimen, exposure to all 3 active CT agents (oxaliplatin, irinotecan, and 5-FU [or capecitabine]), exposure to biologics (e.g., cetuximab), and BBP. Though there was variability observed in patterns of BBP, including continuous and discontinuous use, for the purpose of this analysis, BBP was defined as any exposure to BV after 1st progression (PD).
Results: A total of 1953 pts were treated in BRiTE. At median follow-up of 19.6 months, there were 1445 1st PD and 932 deaths. Among pts with 1st PD, 54% received BBP, 37.8% received cetuximab and 53.8% were exposed to all 3 active CT agents. In a multivariate analysis, BBP and exposure to all 3 active CT agents were independently associated with increased OS (both $p < 0.001$). Age $\geqslant 65$, PS $\geqslant 1$, low albumin, elevated alkaline phosphatase, and colon primary tumor site, were associated with inferior OS.
Conclusions: BBP appears to be associated with longer OS in BRiTE. This finding supports the evaluation of BBP in prospective randomized clinical trials. Other factors that may have impacted this finding, including physician-related variables, will be investigated in future analyses.

3022 POSTER

Long-term outcome of unresectable metastatic colorectal cancer (MCRC) patients (pts) treated with first-line FOLFOXIRI followed by R0 surgical resection of metastases

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Background: Prognosis of pts with initially unresectable MCRC can be improved if chemotherapy induces a significant down-sizing of metastatic disease thus allowing an R0 surgical resection of metastases (mts). In particular it has been demonstrated a clear correlation between the activity of the regimen used and the rate of secondary R0 resections (Folprecht et al, Ann Oncol 2005).
Methods: We studied the triple drug combination FOLFOXIRI (irinotecan 165 mg/sqm d1, oxaliplatin 85 mg/sqm d1, l-LV 200 mg/sqm d1, 5-FU 3200 mg/sqm 48-h flat continuous infusion starting on d1, repeated every 2 weeks) in phase II and III trials. Overall 196 pts with initially unresectable MCRC and not selected for a neo-adjuvant strategy were treated. This regimen was associated with an elevated activity (response rate ranging from 66% to 72%) and 37 patients (19%) could undergo to a secondary R0 surgery on mts.
Results: Characteristics of the 37 radically resected pts were: median age 64 years (45−73), ECOG PS $\geqslant 1$ in 11 pts (30%), median CEA 10 ng/ml (1–288), liver involvement $\geqslant 25\%$ in 16 pts (43%). Sites of disease were: liver only 25 pts (68%), lung only 4 pts (11%), liver + lymphnodes 5 pts (13%), liver + peritoneum 1 pt (3%), liver + lung 2 pts (5%). Mts were synchronous in 25 pts (68%) and metachronous in 12 pts (32%). There was no perioperative mortality. After a median follow up of 55 mos median OS is 39+ mos. The actuarial 5-year survival is 40% from the onset of chemotherapy. In 8 pts progressed after surgery a surgical re-resection and/or radiofrequency ablation was performed.
Conclusions: These data indicate that FOLFOXIRI allows an R0 surgical resection in about one out of five pts with initially unresectable MCRC not selected for a neoadjvant approach. Long term survival of resected pts is significant and comparable with the survival of pts resectable up-front. This FOLFOXIRI regimen should be considered as neo-adjuvant treatment in initially unresectable metastatic colorectal cancer pts. Partially supported by Fondazione ARCO.

3023 POSTER

Liposome-based drug delivery using secretory phospholipase A2 as a tumor-specific release mechanism: Evaluation of sPLA2 IIA expression profile in colorectal carcinomas

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Background: Targeting current and future chemotherapeutic agents specifically to tumours is expected to reduce the unwanted side effects associated with current cancer treatments. One of the suggested methods for this is to enclose the therapeutic agent within a liposome. The relative permeability of tumour blood vessels allows liposomes to accumulate in the tumour tissue resulting in persistently high concentrations of liposomes in the extracellular space. So far this strategy has resulted in only limited therapeutic improvements due to the low rate of release of the drugs from liposomes.
We have developed a new generation of liposomes called LiPlasomes which are specifically targeted for degradation by sPLA2. Overexpression of secretory phospholipase A2 type IIA (sPLA2 IIA) has been reported in several tumour types and these tumours are expected to be suitable for treatment with therapeutics enclosed in the LiPlasomes. Previous in vitro experiments comparing LiPlasomes containing cisplatin (named LiPlaCis) and free cisplatin have demonstrated sPLA2-dependent, efficient and synergistic inhibition of growth of tumour cells and cell death using MTT cell viability and clonogenic assays on various tumor cell lines.
Materials and Methods: In this study we examined the expression of sPLA2 IIA in 192 colorectal carcinomas and 8 normal colon samples using immunohistochemistry (IHC) on a commercially available tissue array. The IHC was performed with a standard method using a polyclonal sPLA2 IIA specific antibody and enzyme based colorimetric detection. sPLA2 IIA expression was scored using a weighted histoscore method based on percentage and intensity of staining with 300 representing a very high intensity stain in all tumour cells and 0 representing no tumour cells stained.
Results: Of the 196 tumours, 180 (91.2%) exhibited expression of sPLA2 IIA, 134 (68.4%) of these had moderate to strong staining in more than 1% of the cells. sPLA2 IIA expression occurred in the cytoplasm of the tumour cells and was not correlated with tumour grade in this dataset.
Conclusion: The observation that sPLA2 IIA was frequently expressed in colorectal carcinomas regardless of grade suggests that the LiPlasome based treatment of a large number of patients with colorectal carcinomas is possible. Studies of sPLA2 IIA expression in other tumour types are ongoing.

3024 POSTER

Update on hereditary colorectal cancer screening in Latvia

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Background: This study was undertaken to investigate the clinical and molecular features of hereditary colorectal cancer (CRC) in population and hospital screening in Latvia.
Materials and Methods: From 01/2004 to 1/2007 family cancer histories/blood samples were collected from 763 consecutive hospital based colorectal cancer cases and from 17440 consecutive adult population individuals in particular region of Latvia. Blood samples from 763 CRC cases and 978 population control group cases were collected. All samples were tested for CHEK2(I157T) and NOD2(3020insC) gene constitutional mutations. In families suspected of having a history consistent with Hereditary Nonpolyposis Colorectal Cancer, DNA testing for MLH1, MSH2 and MSH6 genes was performed.
IHC analysis was performed in high risk group patients(HNPCC, HNPCC-susp, HEC, HECsusp).
Results: Among 763 CRC patients only 9 (1. 3%) fulfilled the Amsterdam criteria. 21 (2.7%) cases matched the criteria for suspected HNPCC and 5 (0.7%) cases matched the late onset HNPCC criteria. Only in 2 cases MMR gene test were performed and 2 mutations detected: 1 in MLH1 and 1 in MSH2 (ex6 Cys333Arg). 7 cases in detecting process at the moment. 21 planning in nearest future.
NOD2(3020insC) mutation was positive in 6.91%(31/435) of CRC cancers and in 7.7% (75/978) of control group cases. CHEK2(I157T) gene mutation was positive in 8.52% (38/435) of colon cancer cases and in 6.4% (63/978) of control group cases. CHEK2(I157T) variant is associated with increased odds ratio of CRC 1.33. In population screening group hereditary colorectal