the European CanCer Organisation (ECCO) initiated a European audit; European Registration of Cancer Care (EURECCA). The aim of the present study is to assess treatment variety and short term outcome of rectal cancer patients in a combined population based dataset from Norway, Sweden, Denmark and the Netherlands.
**Methods:** Patients diagnosed with rectal cancer in 2008 and/or 2009 and underwent surgical treatment were selected from the Norwegian Colorectal Cancer Registry, the Swedish Colorectal Cancer Registration, the Danish Colorectal Cancer Database and the Dutch Surgical Colorectal Audit (n = 6597), all population-based registration projects. Differences in age, gender, stage at diagnosis and the use of radio(chemo)therapy were compared between the countries using chi square tests. The use of radio(chemo)therapy was also compared according to stage within the countries. We further compared the 30-day mortality between the countries with a logistic regression model build to assess independent predictive factors.
**Results:** Overall, the Netherlands had a slightly younger population, no differences in gender distribution were found, and in the Norwagian data stage at diagnosis was more often unknown. The use of radio(chemo)therapy was the lowest in Denmark (24.9%), followed by Norway (50.3%), Sweden (60.7%), and the highest in the Netherlands (81.2%). The use of radio(chemo)therapy differed per stage for each country: in Denmark and the Netherlands patients with stage I, II, and III more often received radio(chemo)therapy; while in Norway stage IV and in Sweden for stage II, and III patients received more often radio(chemo)therapy. Results of the 30-day mortality analyses will be presented late breaking at the 2011 European Multidisciplinary Congress in Stockholm.
**Conclusion:** In western Europe, there are substantial differences between the use of radio(chemo)therapy. The first results of international comparisons in the population-based EURECCA-project may be the first step to find the right balance between under and over treatment.

**6001** ORAL

**Surgical Care in Low Rectal Cancer Patients Can Be Improved − an Analysis of 4084 Patients From the Dutch Surgical Colorectal Audit (DSCA)**

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**Background:** Oncological outcome for rectal cancer has improved considerably since the introduction of TME surgery. However, in patients with low rectal cancer requiring an abdominoperineal excision (APE) the number of irradical resections and tumour perforations remain high. A surgical audit was performed In order to evaluate the quality of (peri) operative care and to determine areas for improvement.
**Patients and Methods:** A pooled analysis was performed on 4084 patients that were included in the audit between 2009 and 2010.
**Results:** In 2010, 92 out of 94 hospitals in The Netherlands participated in the DSCA registration (98%) compared to 89% in 2009. When the data of 2009 is compared to that of the NKR (Dutch cancer registry) it is estimated that 85% of the patients have been entered. The average age at diagnosis was 67 yrs and 83% of the patients were ASA I or II. Preoperative staging with MRI as advised in the Dutch Guidelines was made in 89% of all elective patients and 88% was discussed in a multidisciplinary meeting. Of all patients with an indication for neoadjuvant treatment 87% did receive (chemo)radiotherapy. The distance of the tumour to the anal verge was <5 cm in 37% and 5−10 cm in 41% in which an APE was performed in 65% and 14% respectively. A large variation is found when the type of surgery (LAR vs. APE) is compared among hospitals. Even though the importance of circumferential resection margins ($\geqslant$1 mm) is widely accepted, these data were missing in 43% of the patients. Positive CRM were found in 12% and occurred more often in APE than LAR (16% vs. 10%). In T4 tumours receiving APE involved margins were found in 25% and 15% in tumours close to the anal verge (<5 cm). Adjuvant chemotherapy was administered to 15% of the patients which is conform the Dutch guideline recommendations.
**Conclusion:** The high registration rate clearly demonstrates that the Dutch surgical community is dedicated to improve the transparency and the quality of peri-operative care. High standard preoperative care is provided for most patients with low rectal cancer. However, there is a considerable variation among hospitals in the APE rates and pathology reports. The large number of missing CRM is worrying since it serves as a key measure of the quality of rectal surgery. The audit has identified areas for improvement in low rectal cancer patients in The Netherlands. In order to ameliorate surgical care standardized pathology reports and surgical workshops are required to decrease the number of irradical resections during APE.

**6002** ORAL

**Short Term Outcome After Neoadjuvant High Dose Rate Endorectal Brachytherapy or Short Course External Beam Radiotherapy in Resectable Rectal Cancer**

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**Background:** Total mesorectal excision (TME) together with preoperative radiotherapy has reduced the local recurrence rates after resection for rectal adenocarcinoma. However, preoperative radiotherapy increases the risk of long term and short term postoperative complications. The standard choice is preoperative external beam radiotherapy, but preoperative endorectal brachytherapy has been used as an alternate neoadjuvant treatment. The purpose of this study was to compare immediate postoperative outcome between preoperative external beam radiotherapy and preoperative endorectal brachytherapy.
**Material and Methods:** 318 patients treated with preoperative endorectal brachytherapy (HDEBRT) at the McGill University Hospital, Canada were matched (age, gender and stage) to patients from the Swedish Rectal Cancer Register treated with; short course preoperative radiotherapy, SCRT, (n = 318) and TME-surgery alone, RT− (n = 318). The brachytherapy group was given 6.5 Gray (Gy) daily endoluminal over 4 days followed by TME-surgery after 4−8 weeks. The SCRT-group was given 5 Gy daily over 5 days and TME- surgery the next week. Patients were followed until 30 days post operatively. Complications were divided into surgical, cardiovascular and infectious.
**Results:** A total of 954 patients were included in the analysis. The SCRT group had a lower number of cardiovascular complications than both HDEBRT (10 vs 25, p = 0.0136) and RT− (10 vs 23, p = 0.0273). The HDEBRT patients had fewer minor surgical complications than patients in the SCRT-group (53 vs 91, p = 0.0042). No difference could be seen between the three groups regarding major surgical complications or infectious complications. The HDEBRT group had a lower frequency of R2 resections than both Swedish groups and the proportion R0-resections were higher in the HDEBRT group than in RT− (p = 0.0250).
**Conclusions:** Preoperative irradiation given as brachytherapy yields less surgical complications than SCRT and a higher number of patients with R0-resections. There are differences in registration between Sweden and Canada, especially regarding complications. A longer interval between radiotherapy and surgery is beneficial for tumour regression and this could be reflected in the number of radical resections.

**6003** ORAL

**Role of KRas Status in Patients With Metastatic Colorectal Cancer Receiving First-line Chemotherapy Plus Bevacizumab − a TTD Spanish Group Cooperative Study**

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**Background:** Data suggest that Kirsten-ras (KRAS) mutational status has no predictive role in patients with metastatic colorectal cancer (mCRC) treated with bevacizumab and chemotherapy [Ince et al. 2005]. The prognostic role of KRAS status is less clear. To investigate this further, an exploratory, retrospective analysis of the MACRO randomized phase III study [Tabernero et al. ASCO 2010, abstract 3501] was performed to investigate the relationship between KRAS status and clinical outcome in patients with mCRC who received first-line treatment with chemotherapy plus bevacizumab (Bev) followed maintenance therapy with Bev ± chemotherapy.
**Methods:** Patients with mCRC received capecitabine/oxaliplatin (XELOX) plus Bev for 6 cycles followed by maintenance therapy with XELOX plus Bev or single-agent Bev. Tumour samples from consenting patients were collected at baseline and analyzed for KRAS status. The relationship between KRAS status and overall response rate (ORR), progression-free survival (PFS) and overall survival (OS) was analyzed: (i) in all evaluable patients; and (ii) by maintenance regimen.
**Results:** The intent-to-treat population included 480 patients. KRAS status was analyzed in 331 patients; 180 (54.4%) had KRAS wild-type (WT) and 151 (45.6%) had KRAS mutant (MT) tumours. In the XELOX-Bev

maintenance therapy group (161 patients), 95 (59.0%) patients had KRAS WT and 66 (41.0%) had KRAS MT tumours. In the Bev maintenance therapy group(170 patients), 85 (50.0%) patients had KRAS WT and 85 (50.0%) had KRAS MT tumours. ORR, PFS and OS by mutation status are shown in the table.

| Parameter | All patients (n = 331) | XELOX-Bev (n = 161) | Bev (n = 170) | Odds ratio/Hazard ratio (95% CI) |
|---|---|---|---|---|
| ORR, % | | | | |
| KRAS WT | 59 | 62 | 56 | 1.26 (0.70–2.30) |
| KRAS MT | 43 | 39 | 46 | 0.77 (0.40–1.47) |
| Odds ratio (95% CI) | 1.94 (1.25–3.02) p = 0.0031 | | | |
| Median PFS, mo | | | | |
| KRAS WT | 10.9 | 13.1 | 9.9 | 1.19 (0.84–1.67) p = 0.33 |
| KRAS MT | 8.7 | 9.4. | 8.3 | 0.92 (0.63–1.32) p = 0.63 |
| Hazard ratio (95% CI) | 0.67 (0.54–0.89) p = 0.0044 | | | |
| Median OS, mo | | | | |
| KRAS WT | 25.8 | 27.2 | 24.3 | 1.15 (0.81–1.64); p = 0.43 |
| KRAS MT | 17.2 | 17.2 | 17.2 | 0.94 (0.65–1.35) p = 0.73 |
| Hazard ratio (95% CI) | 0.61 (0.47–0.79) p = 0.0001 | | | |

**Conclusions:** Patients with KRAS WT tumours had significantly improved outcomes compared with patients with KRAS MT tumours. Outcomes in patients with WT or MT tumours were not influenced by the type of maintenance therapy received (i.e. chemotherapy plus Bev or single-agent Bev).

**6004** ORAL

**Role of Baseline Circulating Tumour Cells and KRas Status in Patients With Metastatic Colorectal Cancer Treated With First-line Chemotherapy Plus Bevacizumab: a TTD Spanish Group Cooperative Study**

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**Background:** Recent data suggest that baseline circulating tumour cell (CTC) count is a marker for clinical outcomes in patients with metastatic colorectal cancer (mCRC) treated with chemotherapy plus bevacizumab [Tol et al. Ann Oncol 2010; 21: 1006−12; Sastre et al. ESMO 2010, abstract 3476]. An exploratory, retrospective analysis of the MACRO randomized phase III study [Tabernero et al. ASCO 2010, abstract 3501] was performed to investigate the relationship between baseline CTC count and tumour Kirsten-ras (KRAS) mutational status and clinical outcome in patients with mCRC who received first-line treatment with chemotherapy plus bevacizumab followed by maintenance therapy with bevacizumab ± chemotherapy.
**Methods:** Patients with mCRC received capecitabine/oxaliplatin (XELOX) plus bevacizumab for 6 cycles followed by maintenance therapy with bevacizumab ± XELOX. Of the 480 randomized patients, baseline blood samples for determining CTC count by Veridex Cell Search method were collected in 180 patients; a cut-off value of 3 CTCs was selected based on the literature. Baseline tumour samples for determining KRAS status were collected in 331 patients. The relationship between CTC count (<3 or ⩾3 CTC) plus KRAS status (wild-type [WT] or mutant [MT]) and progression-free survival (PFS) and overall survival (OS) was analyzed.
**Results:** Data on both CTC count and KRAS status were available in 130 patients. Efficacy outcomes for each patient subgroup according to CTC count and KRAS status are shown in the Table.
**Conclusions:** Baseline CTC count and tumour KRAS status combined are strong markers for PFS and OS in patients with mCRC treated with chemotherapy and bevacizumab.

| Parameter | KRAS WT | | KRAS MT | |
|---|---|---|---|---|
| | CTC < 3 (n = 35) | CTC ⩾ 3 (n = 37) | CTC < 3 (n = 33) | CTC ⩾ 3 (n = 25) |
| Median PFS, mo | 12.2 | 8.4 | 11.5 | 6.2 |
| Log-rank | p = 0.0021 | | | |
| Median OS, mo | 30.7 | 15.4 | 19.8 | 12.9 |
| Log-rank | 0.0034 | | | |

**6005** ORAL

**A Multicenter, Randomized, Double-blind, Phase II Study of TAS-102 (A) Plus Best Supportive Care (BSC) Versus Placebo (P) Plus BSC in Patients (pts) With Chemotherapy-refractory Metastatic Colorectal Cancer (mCRC)**

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**Background:** TAS-102 is a novel oral nucleoside antitumour agent, consisting of trifluorothymidine and thymidine phosphorylase inhibitor. This agent showed promising results with a disease control rate of 50.0% in 18 mCRC pts in the previous phase I study. This phase II study evaluated the efficacy and safety of TAS-102 compared with placebo after failure of standard therapy for mCRC.
**Material and Methods:** Patients with mCRC who had received standard therapy including fluoropyrimidine, irinotecan and oxaliplatin, adequate organ functions, and ECOG PS 0 to 2 were randomly assigned 2:1 to receive TAS-102 versus placebo. They were administered orally twice daily for day 1 to 5 and day 8 to 12 per every 4 weeks at 70 mg/m$^2$/day. Primary endpoint was overall survival (OS). *KRAS* test (codons 12 and 13) was evaluated by Scorpion-ARMS. In addition, the association among OS and *KRAS* status was analyzed.
**Results:** From August 2009 to April 2010, 172 pts were enrolled, 170 pts were received and 169 pts were assessable (A, 112; P, 57). There was no significant imbalance in baseline pts background between the two arms: males (A, 57.1%; P, 49.1%); median age (A, 63 yrs; P, 62 yrs); ECOG PS 0 (A, 64.3%; P, 61.4%); 2/>=3 prior regimen (A, 15.2/84.8%; P, 22.8/77.2%); prior treatment with bevacizumab (A, 76.8%; P, 82.5%); with cetuximab (A, 63.4%; P, 63.2%). TAS-102 significantly improved OS compared with placebo (median OS, 9.0 vs.6.6 months, HR, 0.56; p = 0.001). Among 170 pts, the observed toxicities of grade 3/4 more than 5% were neutropenia (17.6%) and leucopenia (9.4%), without treatment-related deaths. *KRAS* status was ascertained in 149 of 169 pts (A, 99, P, 50). *KRAS* status was wild-type (wt)/mutant-type (mt) (A, 54/45; P, 24/26). In the *KRAS* wt subset, HR was 0.70, with no significant trend for favoring TAS-102. In the mt subset, HR was 0.44, with a statistically significance for favoring TAS-102. No interaction was observed between wt and mt.

| Patients | Group | N | Median OS (months) | HR | 95% CI | P value |
|---|---|---|---|---|---|---|
| All | A | 112 | 9.0 | 0.56 | [0.39, 0.81] | 0.001 |
| | P | 57 | 6.6 | | | |
| wt | A | 54 | 7.2 | 0.70 | [0.41, 1.20] | 0.191 |
| | P | 24 | 7.0 | | | |
| mt | A | 45 | 13.0 | 0.44 | [0.25, 0.80] | 0.006 |
| | P | 26 | 6.9 | | | |

**Conclusions:** TAS-102 significantly improved OS with a good safety profile in pts with mCRC who failed to conventional cytotoxic agents and targeting agent. TAS-102 is the first cytotoxic agent that showed significant survival prolongation for mCRC in this setting, though this should be confirmed in a phase III study including *KRAS* status analysis.