cancer was detected in 6/17440 (0.0344%) cases, suspicion of hereditary CRC was detected in 11/17440 (0.063%) cases.
**Conclusions:** The role of the classical Amsterdam criteria in diagnosing HNPCC in CRC patients of Latvia is quite limited and diagnostic criteria for suspected HNPCC are the most effective to detected MMR gene mutation carriers. The frequency of constitutional mutations within the MMR genes is 1% of all newly diagnosed CRC cases. CHEK2(I157T) variant is associated with slightly increased risk of CRC, but difference is not statistically significant. Increased hereditary CRC risk group was observed in 1.3% of all adult population.

**3025** POSTER

**Impact of pre-medication on the frequency of infusion-related reactions (IRRs) and efficacy in patients (pts) treated with cetuximab plus irinotecan for metastatic colorectal cancer (mCRC): the MABEL study**

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**Background:** Cetuximab (Erbitux®), an IgG1 monoclonal antibody targeting the epidermal growth factor receptor (EGFR), is active alone and in combination with irinotecan in patients (pts) with mCRC failing prior irinotecan therapy. IRRs have been observed in a small number of pts especially at the first cetuximab infusion.
**Methods:** The primary objective of the MABEL study was to investigate the impact of cetuximab plus irinotecan on the progression free survival (PFS) rate at week (wk) 12 in pts with EGFR-detectable mCRC who had recently progressed on irinotecan-containing treatment. Secondary objectives included PFS time, overall survival (OS) time and rates, and cetuximab-related adverse events. Pts received cetuximab (initial dose 400 mg/m$^2$, then 250 mg/m$^2$ wkly) plus irinotecan as pre-study (125 mg/m$^2$ wkly for 4/6 wks; 180 mg/m$^2$ every 2 wks; 350 mg/m$^2$ every 3 wks). Data were retrospectively analyzed regarding the impact of prophylactic pre-medication (classified as antihistamine alone and antihistamine plus corticosteroid) on the frequency of IRRs and efficacy in terms of PFS and OS.
**Results:** Overall, 1147 pts were treated: median age 62 yrs [25–84]; KPS $\geqslant$ 70%; 64% pts male. 1122 pts were pre-treated with antihistamines. IRRs were less frequent in pts receiving antihistamine + corticosteroid as compared to antihistamine alone (9.6% vs 25.6% any grade, 1% vs 4.7% grade 3/4 IRRs). Efficacy results for PFS and OS (see table) by antihistamine alone vs antihistamine + corticosteroid groups suggest no apparent differences related to prophylactic pre-medication.

Efficacy results for PFS and OS

| | Antihistamine alone (n = 422) | Antihistamine + corticosteroid (n = 700) | Total antihistamine pre-treated (n = 1122) |
|---|---|---|---|
| Median PFS, wks [95% CI] | 13.1 [12.6, 16.0] | 16.1 [13.0, 19.3] | 14.3 [13.0, 17.1] |
| PFS rate, % [95% CI] | | | |
| 12-wk | 60 [56, 65] | 61 [57, 65] | 61 [58, 64] |
| 24-wk | 32 [27, 36] | 35 [31, 39] | 34 [31, 37] |
| 36-wk | 16 [12, 19] | 18 [15, 21] | 17 [14, 19] |
| 48-wk | 6 [3, 8] | 6 [4, 8] | 6 [4, 8] |
| Median OS, months [95% CI] | 9.0 [8.3, 10.5] | 9.2 [8.5, 10.0] | 9.2 [8.5, 9.8] |
| Survival rate, % [95% CI] | | | |
| 6-months | 67 [63, 72] | 68 [64, 71] | 67 [65, 70] |
| 12-months | 39 [34, 44] | 37 [33, 41] | 38 [35, 41] |
| 18-months | 21 [16, 25] | 19 [16, 22] | 20 [17, 22] |
| 24-months | 7 [0, 15] | 8 [3, 12] | 8 [4, 21] |

**Conclusions:** The data suggest a reduced incidence of IRRs when both antihistamine and corticosteroid pre-medication is given (grade 3/4 IRRs: 1% vs 4.7% for antihistamines alone). In addition, there is no apparent difference in PFS and OS between the analyzed pre-medication groups.

**3026** POSTER

**Loco-regional tumor control and normal tissue reactions after three different fractionation schedules of preoperative radiotherapy for rectal cancer**

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**Purpose:** To evaluate the effectiveness and normal tissue reactions in three different fractionation schedules of preoperative radiotherapy for locally advanced rectal cancer.
**Material and Methods:** Between 1996 and 2002 168 patients with locally advanced rectal cancer were treated as follows: 53 patients received 25 Gy in 5 Gy per fraction (group A), 45 received 30 Gy in 3.0 Gy per fraction (group B), and 70 were treated with accelerated hyperfractionation 42 Gy, 1.5 Gy per fraction, given twice a day with an inter-fraction interval of 6 hours (group C). The clinical characteristics of the groups was comparable, the patients did not receive concurrent chemotherapy. A Cox regression method was used to analyze the factors which may influence loco-regional tumor control (LRC) and overall survival (OS). The evaluation of normal tissue reactions included the analysis of the incidence of surgical complications, as well as of acute and late radiation effects.
**Results:** The following variables significantly influenced LRC: fractionation scheme (5-year actuarial LRC 82%, 71%, and 93% in groups A, B, C respectively, p = 0.02), and hemoglobin concentration before radiotherapy (p = 0.026). The stage of disease, age and sex did not appear significant for LRC. The overall 5-year OS was 64%, 60% and 74% in groups A, B, C respectively (p = 0.08). The OS was significantly influenced by postoperative pathological nodal stage (p = 0.001). The most relevant acute radiation reaction was a mild/severe diarrhea which appeared in 7%, 4% and 12% of the patients (no significant differences between the groups A-C). The spastic ileus appeared in perioperative period in 4%, 2% and 1% of the patients. The median wound healing time in those who underwent abdomino-perineal resections was 6, 6 and 4 weeks, and the persistent fistulas appeared in 4%, 7% and 2% of the patients (groups A, B, C, respectively). Other reactions appeared less relevant.
**Conclusions:** While due to non-randomized character of the study the conclusions should be regarded as hypothesis-generating only, the analysis has shown an acceptable local effectiveness and tolerance of schedules A and C, and disappointing effectiveness of schedule B. The present study supports thus the data which suggest that the clinical effect of preoperative radiotherapy for rectal cancer is influenced not only by total radiation dose but also by overall radiation treatment time and dose per fraction.

**3027** POSTER

**High rate of TRG1–2, and prolonged RFS with OXA/TOM and FU/LFA during preoperative pelvic RT in patients with poor prognosis locally-advanced rectal cancer (LARC)**

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**Introduction:** We have previously reported that 3 cycles of Oxaliplatin (OXA), Raltitrexed (TOMUDEX [TOM]) and 5-Fluorouracile (FU) + levofolinic acid (LFA) during pelvic RT had an acceptable toxicity and produced a complete (TRG1, 42%) or subtotal (TRG2, 29%) pathologic tumor regression in 71% of 31 pts with poor prognosis LARC (Avallone et al, Br J Cancer 2006). Here we report an expanded experience on such treatment.
**Methods:** We enrolled 62 eligible pts (M, 33; F, 29), with median age of 58 (27–79) yrs, and adenocarcinoma of the extraperitoneal rectum, with at least one of the following characteristics: cT4 (N pts), cN+ (N), cT3N0 with tumor location $\leqslant$5 cm from the anal verge and/or CRM +ve (assessed by MRI) (N). Pts received 3 biweekly courses of OXA 100 mg/sqm + TOM 2.5 mg/sqm on day 1, and LFA 250 mg/sqm + FU 900 mg/sqm (31 pts) or 800 mg/sqm (31 pts) on day 2, and concomitant pelvic RT (1.8 Gy/day in 25 fractions, total dose 45 Gy). Surgery with TME was planned 8 weeks after the end of treatment. Pathologic response was evaluated by tumor regression grading (TRG) according to Mandard's modified classification. Pts with cT4, pN+ and pCRM +ve received also 4 months of weekly FU/FA.
**Results:** All pts received full dose of RT, and 98% of the planned CT cycles. Neutropenia was the most common grade $\geqslant$3 toxicity (40%), while grade 3 diarrhea was seen in 19% of pts with FU 900 mg/sqm, and in only 6% of pts with FU 800 mg/sqm. All but 2 pts had a TME with R0 resection, and no treatment-related or perioperative death occurred. Median number of sampled lymph nodes was 36 (range, 10–80). 28 (45%) pts obtained a TRG1, and 17 (27%) pts a TRG2. Activity of the combined treatment was similar in all risk groups (N), regardless of FU dosage. On the whole series of 62 operated pts, 1 pt suffered a local recurrence (after 9 months), and 3 pts had distant metastases (after 22, 33, and 47 months). After a median follow-up of 34 (range 6–54) months, all pts are alive, and the estimated