Poster presentations (Tue, 1 Nov)
GI – colorectal cancer

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Predictors of disease-free survival after preoperative radio(chemo)therapy and complete resection of T3–4 rectal cancer with or without adjuvant chemotherapy (EORTC 22921)

G. Calais[1], L. Collette[2], L. Mineur[3], P. Maingon[4], L. Radosevic-Jelic[5], A. Daban[6], E. Bardet[7], A. Beny[8], J.-C. Ollier[9], J.-F. Bosset[10]. [1]*CHU de Tours – Hopital Bretonneau, Radiotherapy Department, Tours, France;* [2]*EORTC Data Center, Biostatistics Unit, Brussels, Belgium;* [3]*Clinique Sainte Catherine, Radiotherapy Department, Avignon, France;* [4]*Centre Georges-François Leclerc, Radiotherapy Department, Dijon, France;* [5]*Institute for Oncology and Radiology, Radiation Oncology Department, Belgrade, Serbia;* [6]*Hopital Jean Bernard, Radiotherapy Department, Poitiers, France;* [7]*Centre René Gauducheau, Radiotherapy Department, Nantes, France;* [8]*Rambam Medical Center, Oncology Department, Haïfa, Israel;* [9]*Centre Paul Strauss, Radiotherapy Department, Strasbourg, France;* [10]*CHR de Besançon – Hopital Jean Minjoz, Radiotherapy Department, Besançon, France*

Background: EORTC trial 22921 is a four arm trial that compared pre-operative radio-chemotherapy to radiotherapy alone and post-operative chemotherapy with LV/5-FU to no adjuvant treatment in patients with resectable T3–4 rectal cancer. The trial results showed no statistically significant difference between the treatment arms as regards the progression-free or overall survival. We investigate the prognostic factors for the long term outcome following surgery in the subset of patients with effective R0 surgery for M0 disease.
Material and methods: 785 patients with R0 tumor resection without distant metastases at time of surgery were considered. The endpoint is the time to relapse or death counted from the time of surgery. Cox proportional hazard models (stratified) by post-operative treatment were used with 5% significance level. Internal model validation by bootstrap re-sampling was performed.
Results: We tested clinical covariates (age > 60 y, sex, CEA >3 ng/ml, overweight, clinical T4, distance from tumor to anal margin >5 cm prior to pre-operative treatment); treatment parameters (time between end of pre-operative treatment and surgery >6 weeks, toxicity of preoperative treatment and pathological factors (number of examined nodes, tumor length, differentiation, histology, down-staging to pT1–2 by pre-operative treatment, pN status and presence of specific invasion). Only absence of down-staging ($P < 0.001$) pN+ status ($P < 0.001$) and a distance <5 cm between the tumor and the anal margin ($P = 0.002$) were independent prognostic factors at the 5% significance level. The presence of venous, perineural or lymphatic invasion was also borderline significant ($P = 0.0522$). A risk score is calculated by counting the risk factors, with pT3–4 and pN+ each counting double. The 5-year post-surgery DFS for patients with a score 0–2, 3–4 or 5–8 risk factors was 74.8%, 54.8% and 35.0%, respectively.
Conclusions: Patients who were deemed pN+ in whom the neo-adjuvant treatment did not result in down-staging and in whom the distance between the tumor and the anal margin was <5 cm or who present with venous, perineural or lymphatic invasion are at increased risk of relapse or death despite R0 resection of their rectal cancer. These findings may be used to shed further light onto the final trial results and to the further treatment decision process post-surgery in these patients.

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Evaluation of the sphincter function and quality of life in French patients with rectal cancer who entered the EORTC 22921 study

M. Mercier[1], P. Pasquet[1], M. Puyraveau[1], J.-F. Bosset[1], G. Calais[2], L. Mineur[3], P. Maingon[4], A. Daban[5], E. Bardet[6], L. Collette[7]. [1]*CHU de Besançon – Hopital Jean Minjoz, Radiotherapy Department, Besançon, France;* [2]*CHU de Tours – Hopital Bretonneau, Radiotherapy Department, Tours, France;* [3]*Clinique Sainte Catherine, Radiotherapy Department, Avignon, France;* [4]*Centre Georges-François Leclerc, Radiotherapy Department, Dijon, France;* [5]*Hopital Jean Bernard, Radiotherapy Department, Poitiers, France;* [6]*Centre René Gauducheau, Radiotherapy Department, Nantes, France;* [7]*EORTC Data Center, Biostatistics Unit, Brussels, Belgium*

Background: EORTC trial 22921 compared preoperative radiochemotherapy (preop CT) to radiotherapy and post-operative chemotherapy (postop CT) with LV/5-FU to no adjuvant treatment in 2×2 factorial trial in patients with potentially resectable T3–4 rectal cancer. The objective of the present side study was to evaluate the sphincter function in patients with conservative surgery and the Quality of Life (QoL) in patients both with and without conservative surgery.
Patients and methods: The QoL cross-sectional study was conducted in French patients surviving without disease. The conservative surgery patients were evaluated with a specific Anal Sphincter-Conservative Treatment questionnaire (ASCT) and with EORTC QoL questionnaires (QLQ-C30 and QLQ-CR38). Non conservative surgery patients were evaluated for QoL only. ANOVA was used for comparing treatment groups ($\alpha = 0.01$, $\Delta \geqslant 5$). QoL and AS-CT scores range 0–100.
Results: 207 of 230 contacted patients (90%) participated to the QoL: mean age 68 years; 146 males and 61 females; 150 pts with conservative surgery; 96 pts preop CT vs 111; 90 pts postop CT vs 117. The mean time from randomization to QoL evaluation was 4.6 years (1–11).
In 150 conservative surgery pts: Preop CT decreases both QLQ-C30 global QoL ($\Delta = -7$; $p = 0.03$) and AS-CT satisfaction with intestinal function ($\Delta = -15$; $p = 0.002$) furthermore it increases QLQ-C30 diarrhoea complaints ($D = -13$; $p = 0.02$) and by AS-CT.
In all 207 pts: Pre-op CT decreases QLQ-CR38 sexual enjoyment ($D = -14$; $p = 0.03$). Postop CT increases QLQ-C30 pain ($D = +6$; $p = 0.01$) and decreases QLQ-C30 physical function ($\Delta = -4$; $p = 0.03$) and role function ($D = -7$; $p = 0.03$). However, for the latter two, the impact of post-op CT was more pronounced for patients with non-conservative surgery.
Socio-demographics factors also play a role: QLQ physical and sexual functions decrease with age ($\Delta = -9$; $p = 0.01$ and $\Delta = 17.2$ $p = 0.001$, re-spectively). QLQ-C30 fatigue ($\Delta = +9$; $p = 0.003$) and CT-related symptoms ($\Delta = +9$; $p < 0.001$) were greater in females. Non conservative surgery negatively affected QLQ-CR38 body image in females ($\Delta = -30$ versus conservative) but not in males.
Time: QLQ-C30 constipation symptoms increase with time since random-ization ($p = 0.01$).
Conclusion: Preop- and Postop-CT seem associated with an increased burden to the patients. This needs to be taken into account when considering the main study results that showed no statistically significant impact of CT onto progression-free survival.

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Serious adverse events in the EORTC randomized phase III trial 22921 comparing preoperative pelvic irradiation to preoperative chemo-irradiation with or without post-operative adjuvant chemotherapy for T3-T4 resectable rectal cancer

E. Musat[1], J. Bosset[2], G. Calais[3], L. Mineur[4], P. Maingon[5], L. Radosevic-Jelic[6], A. Daban[7], E. Bardet[8], A. Beny[9], L. Collette[1]. [1]*EORTC, Brussels, Belgium;* [2]*CHR de Besançon, Besançon, France;* [3]*CHU de Tours, Tours, France;* [4]*Clinique Sainte Catherine, Avignon, France;* [5]*Centre Georges-François Leclerc, Dijon, France;* [6]*Institut for Oncology and Radiology, Belgrade, Serbia;* [7]*Hopital Jean Bernard, Poitiers, France;* [8]*Centre René Gauducheau, Nantes, France;* [9]*Rambam Medical Center, Haifa, Israel;* [10]*EORTC, Brussels, Belgium*

Background: To describe the severe toxicity (grade 3–4 acute toxicity and reported serious adverse events) in the four arms EORTC 22921 randomized phase III study comparing preoperative pelvic irradiation to preoperative chemo-irradiation with or without post-operative adjuvant chemotherapy for T3-T4 resectable rectal cancer.
Material and Methods: Patients were randomised between preoperative pelvic radiotherapy (RT) or radiochemotherapy (RCT) followed or not by postoperative CT (postopCT). Inclusion criteria were: informed consent, age $\leqslant$80 years, no cardiac disease, primary and operable T3-T4 rectal cancer. We report the events of severe toxicity by treatment actually received.
Results: Between 1993 and 2003, 1011 patients were accrued. 99.4% were irradiated and 72% on RCT received 95–105% dose intensity, 24.7% of the patients allocated postopCT could not receive it, resulting in 322 actually receiving RT (32%), 305 RCT (30%), 184 RCT+postopCT (18%) and 200 RCT+ postopCT (20%).
A total of 233 events of severe toxicity were reported in 1011 pts (23.0%): 177 were WHO grade 3 and 39 WHO grade 4 acute toxicity (see table); another 17 events of grade <3 required hospitalization (RT:1, RCT: 2, RT+postopCT: 2, RCT+postopCT: 5). There were 42 (13.0%), 108 (35.4%), 33 (17.9%) and 50 events (25.0%) in patients that received RT, RCT, RT+postopCT and RCT+postopCT, respectively. A total of 41 patients (4%), respectively 6, 19, 4 and 12 were hospitalized for a total number of 73 events: 56 grade 3–4 and 17 grade <3. The majority of toxic events occurred pre-operatively. Pre-operative or perioperative treatment complications prevented delivering post-op CT in 20 patients after RT and 20 after RCT. Another 15 and 10 patients respectively refused the postopCT.
Conclusions: An increase of toxicity has been observed in the concomitant preoperative chemo-RT arms however, this did not seem to markedly affect the post-operative chemotherapy compliance rates.