Results of the ACCORD 12/0405 PRODIGE2 randomized trial are in favor of benefit of radiation dose intensification in the neoadjuvant treatment of T3-4 M0 rectal cancer.

**Background**
Following the results of randomized trials (FFCD 9203, RTOG 0012) showing in T3-4 M0 rectal a better local control with neoadjuvant chemoradiation (CT-RT), the ACCORD 12/0405 Prodig2 was launched to define an optimum regimen.

**Methods**
Inclusion was: rectal adenocarcinoma accessible to digital rectal examination T3 or resectable T4 Nx M0 below 80 years. Treatment A: concurrent RT 45Gy/25f/5weeks (w) + capecitabine (800mg/m²/bid). B: concurrent RT 50Gy/25f/5w + capecitabine (800mg/m²/bid/5/7days) + oxaliplatin 50mg/m²/w. Resection with Total Mesorectum Excision was scheduled 6 weeks after the end of CT-RT. Adjuvant chemotherapy was optional. 590 patients (pts) were needed to show an increase in the pathological complete response (Dworak) rate from 11% (arm A) to 20% (arm B). Circumferential positive rectal margin (CRM R1) was defined as the presence of residual cancer cells within 0 to 1 mm from the perirectal surface. Evaluation of sexual and bowel function was made with a specific questionnaire.

**Results**
This trial closed in 07/2008 after randomization of 598 pts since 11/2005. Patients characteristics of 586 eligible pts were well balanced: male 66%, median age 61 years, 66% low rectum, 87% T3 stage. Data base was locked in March 2009. The grade 3/4 all toxicity was respectively 11% (32pts) vs 25% (73 pts) in arm A (Cape 45) and arm B (Capox 50) (p 0.01). Surgery was performed in arm A in 98% of patients (289) and 98.6% in arm B (287 pts). There was no difference in sphincter saving surgery 75% in A and 78% in B. Postoperative death at 60 days was identical in both groups (0.3%). A CRM R1 (0-1 mm) was found in 11% in arm A versus 6% in arm B (18 vs 9 pts, p=0.12), and when the distance for CRM was 0 to 2 mm the difference between A and B was respectively 18% (30 pts) vs 8% (12 pts) p < 0.05. The ypCR (Dworak) was 13.8 (40 pts) in arm A and 18.8% (54 pts) in arm B, p=0.11. Results of sexual and bowel functions at one year will be reported at time of meeting.

**Conclusion**
These results, when compared with other recent phase III trials, show that radiation dose intensification in the Capox 50 regimen does not increase surgical complication and seems to provide a trend toward an increase in negative CRM and yp CR. 50 Gy/25 F/5 weeks (with shrinking field after 44 Gy) could be proposed in locally advanced rectal cancer as an efficient schedule.