Author's response to reviews

Title: Phase II study of preoperative radiation plus concurrent daily tegafur-uracil (UFT) with leucovorin for locally advanced rectal cancer

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Dear Editor,

I am writing you on behalf of Dr Boisdron Celle, to send you back the revised manuscript “Phase II study of preoperative radiation plus concurrent daily tegafur–uracil (UFT) with Leucovorin for locally advanced rectal cancer” by Patrice Cellier et al.

Concerning reviewer’s 1 report:
The detailed energy photon has been clarified in the methods ie photon beam energy minimum required by the protocol was at least 6 MeV. At this time considering this multicentre study the photons were mainly > to 10 MeV, and generally equal to 25 MeV. The minimum of 10 MeV Photons has been specified in the methods.

The required time period between DPD detection/ -genotyping and start of UFT + radiotherapy at most10 days. This 10 days period has been specified in the methods.

Concerning reviewer’s 2 report:
Indeed in the other phase III trials CAO/ARO/AIO-94 and FFCD 9203 it seems that chemotherapy dose intensity was higher. In these trials, it is interesting to notice that chemotherapy was administered only during 2 weeks : the first and fifth week of radiotherapy. Tolerance and compliance are better with short length or chemotherapy.

In the Sauer’s paper (NEJM 2004) not much is specified for chemotherapy compliance, once it is notified “received full dose of chemotherapy” then “chemotherapy was given as planned” in 89 % of pts. It is not possible to do the difference between full dose i.e. 100% of the theoretical dose, and between adapted doses according to tolerance.

In the Gérard’s paper (JCO 2006) it is specified that 93% of patients received 2 cycles. Only 78 % of patients received full protocol dose over 2 cycles.

In our study, the length of chemotherapy was longer than the one observed in these previous trials. The way of administration was also different ; oral instead of iv. We relied on patients to take their tablets at home. Compliance and tolerance were strictly studied. We strictly followed the adaptation scheme dose in case of toxicity. This might explain our low (56 %) rate of full dose treated patients. Adding adapted dose patients to full dose patients we observed 74 % of patients treated with neo adjuvant UFT.

I do apologize, again, for the delay answering you, due to Dr Boisdron-Celle absence.

Yours sincerely

For Dr Michèle Boisdron-Celle,

Virginie BERGER, MD, PhD