

## Clarifications sought for implications of PORTEC-3 in clinics

In their updated analysis,<sup>1</sup> the PORTEC-3 investigators have shown significant improvements in overall survival and 5-year failure-free survival with the use of chemoradiotherapy versus radiotherapy alone in women with high-risk endometrial cancer. The findings of the study imply that chemoradiotherapy should be preferred over radiotherapy for adjuvant treatment in these patients.

Before clinical implementation of chemoradiotherapy, as described in the PORTEC-3 protocol, we request a couple of clarifications regarding the concurrent cisplatin chemotherapy and the adjuvant paclitaxel-carboplatin chemotherapy.

First, the dose of concurrent cisplatin with radiotherapy was 50 mg/m<sup>2</sup>, which was only delivered on the first and fourth weeks of radiotherapy. Although this approach was adopted from the 2006 RTOG 9708 protocol,<sup>2</sup> contemporary thinking would suggest that this dose of cisplatin is too low to be radiosensitising, but that it is able to cause occasional toxicity. If implementing PORTEC-3-based treatment in the clinic, could we omit the concurrent cisplatin during radiotherapy? Since local and pelvic recurrences were not substantially different between the PORTEC-3 trial groups, we believe that the two doses of concurrent cisplatin at 50 mg/m<sup>2</sup> can be safely omitted in routine practice.

Second, the adjuvant chemotherapy after radiotherapy was delivered as four cycles of paclitaxel (175 mg/m<sup>2</sup>) and carboplatin (AUC5). This approach was, again, adopted from the RTOG 9708 protocol. Since the PORTEC-3 trial has concluded that “[d]istant metastases were the first site of recurrence in most patients with a relapse”, could we expect a lower incidence of distant metastases

if six cycles of adjuvant paclitaxel-carboplatin (instead of four) were to be delivered; if the dose of carboplatin were increased to AUC6 (instead of AUC5); or if chemotherapy were to be completed before radiotherapy?

We declare no competing interests.

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- 1 de Boer SM, Powell ME, Mileskin L, et al. Adjuvant chemoradiotherapy versus radiotherapy alone in women with high-risk endometrial cancer (PORTEC-3): patterns of recurrence and post-hoc survival analysis of a randomised phase 3 trial. *Lancet Oncol* 2019; **20**: 1273–85.
- 2 Greven K, Winter K, Underhill K, Fontenesi J, Cooper J, Burke T. Final analysis of RTOG 9708: adjuvant postoperative irradiation combined with cisplatin/paclitaxel chemotherapy following surgery for patients with high-risk endometrial cancer. *Gynecol Oncol* 2006; **103**: 155–59.