Clinical implications for cediranib in advanced cervical cancer.
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For decades, the management of women with recurrent or persistent cervical cancer not amenable to surgery and women who present with metastatic disease has constituted a high unmet clinical need, with platinum-based chemotherapy being palliative and associated with short-lived responses, rapid deterioration in quality of life, and early death (median overall survival 7–12 months). Some progress has been made following the publication of the phase 3 randomised Gynecologic Oncology Group (GOG) 240 trial; patients who received the anti-angiogenic drug bevacizumab in addition to chemotherapy had a significant overall survival advantage over those who did not (median 17 months vs 13·3 months; HR 0·71 [98% CI 0·54–0·95]; p=0·004). In addition to overall survival, both progression-free survival (median 8·2 months vs 5·9 months) and the proportion of patients who achieved an objective tumour response (48% vs 36%) were significantly improved with the combination of bevacizumab with either of two chemotherapy doublets (cisplatin–paclitaxel or topotecan–paclitaxel). None of these findings were accompanied by a side-effect that occurred in 8·6% of patients treated with chemotherapy being palliative and associated with short-lived responses, rapid deterioration in quality of life, and early death (median overall survival 7–12 months). Some progress has been made following the publication of the phase 3 randomised Gynecologic Oncology Group (GOG) 240 trial; patients who received the anti-angiogenic drug bevacizumab in addition to chemotherapy had a significant overall survival advantage over those who did not (median 17 months vs 13·3 months; HR 0·71 [98% CI 0·54–0·95]; p=0·004). 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Given a new treatment standard of chemotherapy plus bevacizumab, where to position cediranib is not readily discernible. Potential future trial designs might use strategies to study chemotherapy plus bevacizumab with and without cediranib, or randomisation to cediranib maintenance therapy in patients who derive clinical benefit from chemotherapy plus bevacizumab (eg, stable disease). If active as a monotherapy, a maintenance strategy containing cediranib could have major toxicity implications given that the median duration of cediranib treatment in both groups in CIRCCa was 19 weeks and overlapped with chemotherapy. Clearly, the results of CIRCCa provide additional clinical evidence that VEGF-dependent tumour angiogenesis remains a valid target in cervical cancer and that the need to explore novel anti-angiogenesis combinations and sequencing is implicit.

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I have participated on two advisory boards for Genentech/Roche (March, 2014, and July, 2014). I declare no other competing interests.

**Busulfan-based conditioning regimens: not all partners are equal**

Since its introduction in 1987, the combination of busulfan and cyclophosphamide has been the most frequently used non-total body irradiation-containing myeloablative regimen for acute myeloid leukaemia throughout the world.\(^1\) With the introduction of fludarabine-containing reduced conditioning regimens, many investigators replaced the cyclophosphamide with fludarabine in an effort to reduce the toxic effects that were thought to be caused by cyclophosphamide metabolites.\(^2\)–4 The busulfan plus fludarabine regimen has become increasingly popular, and although multiple retrospective comparisons have reported that the combination of busulfan and fludarabine is less toxic and compares favourably with the classic busulfan plus cyclophosphamide regimen, only two randomised trials\(^5\)–6 have been done, with conflicting results. Both trials were hampered by sample size and patient heterogeneity.

In *The Lancet Oncology*, Alessandro Rambaldi and colleagues report the results of a multicentre, randomised trial done through the Gruppo Italiano de Trapianto Midollo Osseo (GITMO) network, which compared busulfan plus cyclophosphamide with busulfan plus fludarabine.\(^7\) The trial was restricted to patients with acute myeloid leukaemia aged older than 40 years. 252 patients were randomly assigned to receive intravenous busulfan (12·8 mg/kg), in combination with cyclophosphamide (120 mg/kg) or fludarabine (160 mg/m\(^2\)). 1-year non-relapse mortality was 17·2% (95% CI 11·6–25·4) in the busulfan plus cyclophosphamide group compared with 7·9% (4·3–14·3) in the busulfan plus fludarabine group (p=0·026), and this difference remained significant even at 2 and 5 years after transplantation. However, no significant difference existed in 5-year leukaemia-free survival between the two groups (42·9% [34·4–53·6] for busulfan plus cyclophosphamide vs 51·8% [43·6–61·7] for busulfan plus fludarabine; p=0·29). 1-year cumulative relapse was similar between groups (22·1%...