Scale-up of radiotherapy for cervical cancer

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See Articles page 915

Cervical cancer is the fourth most common cancer among women globally, with an estimated 570 000 new cases and 311 000 deaths worldwide in 2018.[1] The incidence is especially high in low-income and middle-income countries, where about 85% of all global cases of locally advanced cervical cancer are detected and where sufficient resources, especially radiotherapy facilities, are scarce or unavailable.[2] The situation is compounded by high burdens in rural areas, where access to health care is especially challenging.[3] With all the international organisations and bodies (ie, WHO, the United Nations, the International Agency for Research on Cancer, the Union for International Cancer Control, and the International Atomic Energy Agency) working towards the elimination (prevention, screening, and treatment) of cervical cancer, the Article by Danielle Rodin and colleagues[4] in *The Lancet Oncology*, which addresses the effects of upscaling radiotherapy facilities, is very important and relevant, especially in the context of the global drive for scale-up of human papillomavirus (HPV) vaccination.

Rodin and colleagues[4] have made a remarkable effort to report on a comprehensive modelling of the health and economic benefits of incremental scale-up of external-beam radiotherapy and brachytherapy facilities for treatment of cervical cancer between 2015 and 2035 in various income settings. The authors report that although the initial investment for this scale-up of radiotherapy facilities is high in low-income and middle-income countries, it could result in substantial health benefits—with 11·4 million life-years gained—and economic advantages, with a net present value of US$59·3 billion (based on a human capital model) or $151·5 billion (based on a full income model). Bivalent HPV vaccination of 12-year-old girls with 75% coverage was predicted to produce a 3·9% reduction in cervical cancer incidence by 2035 and a 22·9% reduction by 2072, leading to 38·4 million women needing external-beam radiotherapy and 28·8 million needing brachytherapy by 2072. Notably, the additional benefits of treating other common cancers (eg, head and neck, breast, and lung cancers) with radiotherapy and its economic effects have not been accounted for or mentioned in their report.

Assuming that national programmes and policy makers adopt the model to scale-up radiotherapy facilities, several challenges exist, especially in low-income and middle-income settings. First, health-care systems in rural regions of low-income and middle-income countries require more attention and investment than urban areas, and an urgent need exists for the development and implementation of management guidelines and the establishment of systematic, effective referral networks and care pathways. Such initiatives are being developed and implemented in different regions, including the efforts of the National Cancer Grid in India.[5] Furthermore, the scale-up of radiotherapy facilities (teletherapy and brachytherapy), as well as capacity building and human resource development for diagnosis, staging (pathology and imaging), and treatment, need to be tailored to the local environments for sustainability and effectiveness.

Second, simple, effective quality assurance programmes and quality indicators for radiotherapy need to be developed and implemented. This issue is an important one in the treatment of cervical cancer, because treatment includes external-beam radiotherapy and brachytherapy. The International Atomic Energy Agency's comprehensive quality audits programme for radiotherapy practices, called Quality Assurance Team for Radiation Oncology, has been successful in analysing the gaps in and barriers to quality care and has recommended and implemented action points.[6] However, such programmes are not well established for brachytherapy. In addition to an urgent need to scale-up brachytherapy facilities, especially in low-income and middle-income countries, commissioning, quality assurance programmes, safe and effective practices, capacity building, training programmes, and trained personnel (eg, nurses, medical physicists, therapists, and engineers) pose major challenges and need urgent attention.[7,8]

Finally, further cooperation, collaboration, and strengthening of ongoing efforts between international, regional, and national organisations, professional bodies, governments, and stakeholders are urgently needed to expedite and augment access to health care and implement cost-effective, pragmatic treatment and research strategies towards the elimination of

cervical cancer. The Article by Rodin and colleagues[4] is a welcome report and should be widely disseminated to policy makers and stakeholders for further consideration and successful implementation to treat patients with cervical cancer, especially in low-income and middle-income countries.

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I declare no competing interests.

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The second wave of checkpoint inhibitors with chemotherapy for advanced non-small-cell lung cancer

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See **Articles** page 924

On the basis of Allison and Honjo's Nobel Prize works, immunotherapy has greatly changed the treatment landscape of advanced non-small-cell lung cancer.[1] Within about 3 years, immune checkpoint blockade went from second-line to first-line therapy, from advanced to locally advanced non-small-cell lung cancer treatment, and from monotherapy to combination therapy. It has made the first-line treatment of advanced non-small-cell lung cancer a competitive battlefield of crucial importance (table).

The PD-1 inhibitor pembrolizumab took the lead on such checkpoint blockade therapy in non-small-cell lung cancer: it has been approved as monotherapy for treatment of non-small-cell lung cancer in patients with more than 50% expression of PD-L1 and as combination therapy with chemotherapy regardless of PD-L1 status.[2–4]

In *The Lancet Oncology*, Howard West and colleagues[5] reported the results of the phase 3, IMpower130 trial. The study compared atezolizumab plus chemotherapy (carboplatin plus nab-paclitaxel) with chemotherapy alone for first-line treatment of stage IV non-squamous non-small-cell lung cancer. There was a significant and clinically meaningful improvement in median overall survival (18·6 months [95% CI 16·0–21·2] in the atezolizumab plus chemotherapy group *vs* 13·9 months [12·0–18·7] in the chemotherapy group; stratified hazard ratio [HR] 0·79 [95% CI 0·64–0·98]; p=0·033) and a significant improvement in progression-free survival (7·0 months [95% CI 6·2–7·3] in the atezolizumab plus chemotherapy group *vs* 5·5 months [4·4–5·9] in the chemotherapy group; stratified HR 0·64 [95% CI 0·54–0·77; p<0·0001]). Overall, atezolizumab in combination with carboplatin plus nab-paclitaxel is an efficacious and a safe regimen and might be an additional treatment option for stage IV non-squamous non-small-cell lung cancer. Notably, these results are almost consistent with those of KEYNOTE-189, another phase 3 trial that published results in 2018. Both trials showed that PD-1 (KEYNOTE-189) or PD-L1 (IMpower130) blockade in combination with pemetrexed (KEYNOTE-189) or nab-paclitaxel (IMpower130) doublet chemotherapy improved overall survival and progression-free survival regardless of PD-L1 status, but patients with high PD-L1 expression (>50%) seemed to benefit more in terms of overall survival from these combinations than did patients with low or no PD-L1 expression.[4,5]

To our knowledge, IMpower 130 is the first study to show that PD-L1 blockade combined with chemotherapy works as first-line treatment of advanced non-small-cell lung cancer. Although the regimen tested in IMpower150 (table) was also approved for non-squamous non-small-cell lung cancer, it added antiangiogenic therapy to the checkpoint inhibitor chemotherapy combination. Second, IMpower130 showed that PD-L1 blockade