Canada removes ban on physician-assisted suicide

On Feb 6, 2015, the Canadian Supreme Court voted to overturn the prohibition on physician-assisted dying. But the Court stipulated that doctors would only be allowed to help a patient to die if clear consent had been given and the patient faced enduring and intolerable suffering from "a grievous and irremediable medical condition". The judgment was suspended for a year.

Exactly how the changed law will be interpreted remains to be seen. Criminal matters are a federal concern, but health care comes under the aegis of the thirteen individual jurisdictions. Thus, legislators should compose detailed regulations (eg, the province of Quebec already permits end-of-life patients to obtain medical assistance in dying). "Given that assisted dying is a matter that is causing a lot of disquiet in Canada at the moment, it might be prudent for the provinces and territories to draft rules that will govern how physician-assisted dying takes place", stated Juliet Guichon (Community Health Services, University of Calgary, AB, Canada).

Some might do so, some might not, and others might follow regulations adopted by the provincial colleges of surgeons and physicians which act in the same way as the UK's General Medical Council. Guichon and her colleague Ian Mitchell propose a collaboration between the Canadian Medical Association and national bodies representing family doctors, nurses, lawyers, pharmacists, and palliative-care specialists to draft rules, which would then be offered to the provinces and territories to amend and adopt. "Detailed regulations have to be written; if not, it will simply become legal without any enforcement behind it", said Mitchell. "In the meantime, there is tremendous fear on the part of some patient groups that the law will be misused". He thinks that the Canadian model will eventually be more akin to that of Oregon, where assisted suicide is legal, than the western Europe countries of Luxembourg, Netherlands, and Belgium that have legalised euthanasia.

Whether or not the Canadian decision is part of a global trend is unclear. "There are definitively cultural specific factors that influence the practices and the debates on assisted suicide and euthanasia in a particular country", notes Ruth Horn from Oxford University (Oxford, UK). "These differences explain why the debates emerge at different moments, why different arguments are used in each country, and how each country tries to address the problems".

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Pascal Broze/Reporters/SPL

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Lenvatinib improves survival in refractory thyroid cancer

A phase 3 randomised trial has shown that lenvatinib, an oral, multitargeting tyrosine kinase inhibitor, significantly improves progression-free survival in radioiodine-refractory thyroid cancer.

The 10-year survival in patients with this type of cancer is 10% from the time metastasis is detected. The VEGF-signalling network has previously been associated with metastasis of thyroid cancer. Lenvatinib targets VEGF receptors 1, 2, and 3, and other signalling pathways including fibroblast growth-factor receptors.

Researchers in the multicentre study randomly assigned 392 patients with progressive radioiodine-refractory thyroid cancer, 261 patients to lenvatinib (one dose of 24 mg per day in 28 day cycles) and 131 patients to placebo. Patients were treated with lenvatinib for a median of 13·8 months and with placebo for a median of 3·9 months.

Median progression-free survival was 18·3 months in patients treated with lenvatinib compared with 3·6 months in the placebo group (hazard ratio for progression or death 0·21, 99% CI 0·14–0·31, $p<0·001$).

169 (64·8%) of 261 patients responded to lenvatinib, with four complete responses and 165 partial responses. Only two (1·5%) of 131 patients responded to placebo ($p<0·001$).

The most frequent side-effects with lenvatinib were hypertension (67·8%), diarrhoea (59·4%), fatigue or asthaenia (59·0%), and decreased appetite (50·2%). In the lenvatinib group, six of 20 deaths that occurred on treatment were considered to be drug-related but there was no specific pattern in fatal adverse events.

Lead author Martin Schlumberger (Institut Gustave Roussy and University Paris-Sud, Villejuif, France) says, "Lenvatinib will be a standard of care for patients [with radioiodine-refractory thyroid cancer]".

The difference in overall survival between the treatment groups was not significant. But as Schlumberger explains, "this was expected from the design of the study with a crossover".

Keith Bible (Mayo Clinic, Rochester, USA) comments, "The data indicate that VEGFR-targeted kinase inhibitors can delay time to disease progression and induce clinical responses in radioiodine-refractory differentiated thyroid cancer". But he notes, "the data do not, however, yet definitively demonstrate improved overall survival or quality of life from the use of such agents, or clarify what patient population is best suited to these agents".

Susan Mayor

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For the **study by Schlumberger and colleagues see** *New Engl J Med* 2015; **372:** 621–30