

CyberKnife Therapy Offers Benefits for Recurring GYN Cancers

Robotic Cyberknife radiation therapy will likely expand the treatment options for patients whose gynecologic malignancies recur, researchers reported at the annual meeting of the Society of Gynecologic Oncologists.

A total of 50 patients with recurrent gynecologic (mainly ovarian and endometrial) cancers underwent Cyberknife treatment, which allows targeting of high doses of radiation to the tumor while largely sparing adjacent healthy tissue. In this case, patients received an 8-Gy treatment on each of 3 consecutive days.

Results showed that two-thirds of the patients had a complete response, a partial response, or stable disease 6 months after treatment. Higher-severity acute adverse events were uncommon and consisted of single cases of diarrhea and hyperbilirubinemia.

"This is the first phase II clinical trial of robotic radiosurgery in the gynecologic oncology space. Robotic Cyberknife radiation therapy does definitely provide clinical benefit to your patients," commented lead author Dr. Charles Kunos, a radiation oncologist with the Case Comprehensive Cancer Center in Cleveland and the Summa Cancer Institute in Akron, Ohio.

However, the majority of women ultimately had progression in nontargeted areas of disease, and this progression was the cause of death in 40%. Therefore, the investigators have initiated a phase I trial combining Cyberknife therapy with systemic chemotherapy.

One attendee noted, "As I think we all know, many of these patients who have recurrent side-wall disease from gynecologic cancers have a loop of bowel that's sitting immediately adjacent to the potential target. And we have always felt that you needed to adjust the dose per fraction depending on that in patients with recurrent disease who have been previously irradiated. How do you select your patients for these 8-Gy-fraction treatments?"

"Patient selection is mostly based on target volume and the number of sites that are going to be treated during the course of therapy. ... We find that the 8-Gy dose is extremely well tolerated," he noted. The team is currently performing analyses to determine maximum tissue tolerances and optimally guide patient selection.

Another attendee had a similar question, asking whether any of the lesions treated were located in a previously irradiated field.

"More than 60% of those patients had received prior radiation therapy. Almost all the cervical cancer patients in the trial, as well as the majority of those patients with endometrial cancer, had received prior radiation therapy," Dr. Kunos replied. "The prior radiation therapy is not a barrier for delivering this form of treatment at these doses. Our toxicity rates are extraordinarily low, even in the cases with the prior radiation, so with selection of the patient who has a relatively good performing health status, as well as considering the time of when the previous radiation therapy dose was delivered, I think you can adequately select patients for this type of therapy."

A third attendee posed bigger-picture questions: "Can you tell us a little bit about the cost-effectiveness of the Cyberknife therapy and, given that you have an ongoing phase I trial looking at this in dual-modality [treatment] with chemotherapy, what is the future of this therapeutic approach for gyn malignancies?"

"The NCI [National Cancer Institute] is interested in exploring the radiosurgery platform as a way of testing novel therapeutics as radiation sensitizers, but because the radiation therapy is so exquisitely tuned to the actual cancer target, there is an opportunity to study whether or not there are systemic effects of the novel drugs as well. So I think at some level, the future is relatively bright," Dr. Kunos explained.

"Regarding the cost or the expense of therapy, we are condensing 5, 6, 7 weeks of radiation therapy into 3 days on the trial, so there are considerable savings in that regard to patient

travel and other, social aspects of treatment in trying to get patients back and forth for several weeks of therapy in a palliative situation," he continued. "The radiosurgery itself is expensive; that part of the cost structure will probably continue to come down in the future with the way that patients will be managed."

The cohort enrolled in the [trial](#) included 25 patients with ovarian cancer, 14 with endometrial cancer, 9 with cervical cancer, and 2 with vulvar cancer. All had received at least one chemotherapy or radiation therapy regimen previously.

The patients had up to four targets of disease to be treated. They underwent implantation of gold seeds for target tracking during treatment, and co-registered computed tomography and positron emission tomography scans were used to generate the radiation therapy plan.

The patients received a total of 24 Gy of radiation delivered in three daily doses of 8 Gy each. The median duration of follow-up was 15 months.

Study results, reported at the meeting and recently published ([Front. Oncol. 2012;2:181](#)), showed that 3 months after treatment, 50% of patients had a complete response, 46% had a partial response, and 4% had stable disease, according to Dr. Kunos.

At 6 months, the rate of clinical benefit – capturing patients with a complete response, partial response, or stable disease – was 68%.

Ultimately, 62% of patients had progression in a nontargeted disease site, and 40% died from disease progression.

"Reversible fatigue lasting up to 1 week after treatment was the most noticeable toxicity," Dr. Kunos said. In the first 30 days after treatment, the most common adverse effects were grade 2 fatigue, seen in 16% of patients, and grade 2 nausea, seen in

8%. Only 2% of patients had grade 3 diarrhea, and only 2% had grade 4 hyperbilirubinemia.

Dr. Kunos disclosed that he had no relevant conflicts of interest.