CLINICAL UPDATE

Translating Scientific Advances into Clinical Practice

Treatment Approaches to Sarcoma in the Community Setting

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H&O What is the treatment approach to sarcoma in the community setting?

SC Sarcoma is a rare cancer, making up approximately 1% of all cancers. Sarcoma can be classified into 4 subtypes. One type is gastrointestinal stromal tumor (GIST), which is the most common form of sarcoma. The treatment approach in patients with GIST is surgery and/or imatinib (Gleevec, Novartis), which can be given in the community setting. Patients with GIST only need to be referred to an academic center if they do not respond to imatinib and/or for inclusion in a clinical trial.

The second type of sarcoma is bone sarcoma, which comprises osteosarcoma, Ewing sarcoma, and chondrosarcoma. Osteosarcomas and bone sarcomas usually present in patients younger than 30 years of age. For these 2 subtypes, diagnosis and treatment necessitate a multidisciplinary approach that requires an expert pathologist, expert radiologist, and an expert chemotherapist. The treatment for osteosarcoma and bone sarcoma is standard preoperative chemotherapy with drugs such as cisplatin, adriamycin, methotrexate, or ifosfamide, followed by postoperative chemotherapy. Thirty years ago, the majority of patients with osteosarcoma involving the arm or leg received amputation and more than 90% of patients died from this disease. Due to advances in chemotherapy and surgery, we are now able to cure 60–70% of osteosarcoma patients, and can offer them limb-salvage surgery rather than amputation. Similarly to osteosarcomas and bone sarcomas, Ewing sarcoma also presents in younger people. Patients with this type of sarcoma can be treated with chemotherapy including adriamycin, ifosfamide, vincristine, cytoxin, and occasionally etoposide; radiation therapy may also be used. Patients with Ewing sarcoma should also be seen in a medical center that can offer a multidisciplinary treatment approach, particularly because these are very rare tumors that must be treated quickly and aggressively. For patients with chondrosarcoma, the main treatment approach is surgery by an expert surgeon.

Soft tissue sarcoma is the third type of sarcoma, comprising rhabdomyosarcoma, which is the most common type of sarcoma seen in children. Pediatric patients with soft tissue sarcoma should be treated in an academic center by expert pediatric oncologists, radiation therapists, and surgeons.

Finally, there is a broad group of soft tissue sarcomas (approximately 50 different types) that are treated by surgery, radiation therapy, and chemotherapy, and again should be treated in an expert setting.

H&O What are the challenges faced by community oncologists in the treatment of sarcoma?

SC There are not many direct challenges for community oncologists, as they very rarely see sarcoma patients. However, a major challenge in treating patients with these tumors is having to rely on pathology, which may be inaccurate, and relying on the surgeon, who may have never operated on that particular type of tumor. Therefore, the best thing to do is to refer the patient to an academic center that has a multidisciplinary team.

H&O When should a patient be referred to an expert sarcoma center?

SC Ideally, as soon as the community oncologist sees a sarcoma, he or she should refer the patient to an academic

center. Once the academic center has made the diagnosis pathologically and determines that the best course of action is chemotherapy, the patient can then be managed in the community setting. However, periodic consultation needs to be done at an academic center, where the team will discuss the appropriate timing of surgery and radiation therapy.

H&O What role does the community oncologist play in the management of a patient diagnosed with sarcoma?

SC In cases when a patient is referred to a sarcoma center and he or she is advised to begin chemotherapy, the local center can work together with the academic center to continue chemotherapy. Also, in situations when the patient is unable to travel to an academic center, the community oncologist is able to send pathology slides to a center that is experienced in reading such slides—centers with strong sarcoma programs such as Dana Farber, MD Anderson, Memorial Sloan-Kettering, and UCLA.

The multidisciplinary team may include community oncologists, surgeons, orthopedic oncologists (for bone sarcomas) or general oncologists who specialize in sarcoma (for bone sarcomas in the extremities), pediatric oncologists, thoracic oncology surgeons, expert pathologists (to interpret the pathology), and radiation oncologists. In order to provide every patient with the best possible care, we need to work together to make sure the patient is diagnosed early on in the disease course and is treated with the most appropriate therapy.

H&O What progress has been made in sarcoma research?

SC This is a very exciting time for sarcoma research and development. Researchers are investigating new targeted treatments in various areas including neoadjuvant and metastatic settings. Sarcoma is a curable cancer, and chemotherapy has made a major difference in its treatment compared to 30 years ago. We need to do more research in the relapsed and metastatic settings, as these patients are very young. New drugs such as trabectedin (Yondelis, Zeltia/Johnson & Johnson) have been approved in Europe and will hopefully be available in the United States in the near future. Furthermore, there are also very promising ongoing clinical trials in other targeted agents.

At the 2011 American Society of Clinical Oncology meeting, there were many exciting presentations on targeted agents in sarcoma. I presented data on the SUCCEED (Phase III Sarcoma Multi-Center Clinical Evaluation of the Efficacy of Ridaforolimus) trial, an international, double-blind study that randomized 711 patients with metastatic sarcoma to ridaforolimus (Ariad; 40 mg orally for 5 days/week) or placebo as maintenance therapy following stable disease or better response to prior cytotoxic chemotherapy. Progression-free survival, which was the primary endpoint in this study, was improved by 21% in the ridaforolimus group compared to the placebo group.

There were also data presented on a new antiangiogenic drug for soft tissue sarcomas called pazopanib (Votrient, GlaxoSmithKline).

Suggested Readings

Grignani G, Palmerini E, Dileo P, et al. A phase II trial of sorafenib in relapsed and unresectable high-grade osteosarcoma after failure of standard multimodal therapy: an Italian Sarcoma Group study. *Ann Oncol*. 2011 Apr 28. [Epub ahead of print].

Judson I. Targeted therapies in soft tissue sarcomas. *Ann Oncol*. 2010;Suppl 7:vii277-vii280.

Chawla SP, Blay J, Ray-Coquard IL, et al. Results of the phase III, placebo-controlled trial (SUCCEED) evaluating the mTOR inhibitor ridaforolimus (R) as maintenance therapy in advanced sarcoma patients (pts) following clinical benefit from prior standard cytotoxic chemotherapy (CT). *J Clin Oncol* (ASCO Annual Meeting Abstracts). 2011;29:Abstract 10005.