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IN BRIEF

Two Drugs for Soft-Tissue Sarcoma

The anthracycline doxorubicin with or without the alkylating agent ifosfamide is the standard first-line treatment for advanced soft-tissue sarcomas. The FDA recently approved the minor groove DNA intercalator trabectedin (*Yondelis* – Janssen) for treatment of unresectable or metastatic liposarcoma or leiomyosarcoma in patients previously treated with an anthracycline. Trabectedin has been available for years in Europe for treatment of advanced soft-tissue sarcoma. The FDA has also approved the microtubule inhibitor eribulin mesylate (*Halaven* – Eisai), which was approved earlier for treatment of metastatic breast cancer,[1] for treatment of unresectable or metastatic liposarcoma, but not for leiomyosarcoma, in patients previously treated with an anthracycline.

Trabectedin binds guanine residues in the minor groove of DNA, which inhibits active transcription and blocks DNA repair proteins to achieve an antiproliferative effect.[2] It has not been shown to be superior to doxorubicin for first-line treatment of advanced soft-tissue sarcomas,[3] but has shown activity in anthracycline- and alkylating agent-resistant soft tissue sarcomas.[4] FDA approval of trabectedin was based on a randomized, open-label trial comparing it to dacarbazine in 518 heavily pretreated patients with metastatic or recurrent leiomyosarcoma or liposarcoma. Median progression-free survival was significantly longer with trabectedin (4.2 months vs 1.5 months with dacarbazine). Median overall survival, however, was not significantly different (12.4 months with trabectedin vs 12.9 months with dacarbazine).[5] Adverse effects of trabectedin include nausea, fatigue, neutropenia, and transient hepatic enzyme elevations.[6] Trabectedin is administered over 24 hours through a central venous line every 3 weeks until disease progression or unacceptable toxicity occurs.

Eribulin mesylate is a microtubule-polymerizing drug that sequesters tubulin into nonfunctional aggregates.[7] FDA approval of eribulin for treatment of advanced liposarcoma was based on a randomized, open-label trial comparing it to dacarbazine in 452 patients with unresectable or metastatic liposarcoma or leiomyosarcoma previously treated with an anthracycline. Median progression-free survival was 2.6 months in both groups, but overall survival was significantly longer with eribulin (13.5 months vs 11.5 months with dacarbazine). A pre-planned subgroup analysis found that the benefit was limited to patients with liposarcoma.[8] Eribulin is the first drug shown to prolong overall survival in patients with advanced liposarcoma. The incidence of grade 3 or 4 adverse effects, particularly leukopenia and neutropenia, was higher with eribulin (67%) than with dacarbazine (56%). Fatigue, alopecia, peripheral neuropathy, nausea, and constipation also occurred. Eribulin is administered IV over 2 to 5 minutes on days 1 and 8 of a 3-week cycle.

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