In this issue of The Sarcoma Journal*, a few additional presentations from the Connective Tissue Oncology Society 2018 annual meeting, held in Rome this past November, are highlighted. The studies were featured in a session that examined chemotherapy of soft tissue sarcomas.*

EARLY RESULTS FIND OLARATUMAB COMBO WITH DOXORUBICIN PLUS IFOSFAMIDE SAFE

Initial results of the phase 1b study of olaratumab plus doxorubicin and ifosfamide have shown the combination to be safe, reported Sebastian Bauer, MD, of the West German Cancer Center, University of Duisburg-Essen, Essen, Germany, and his colleagues at CTOS 2018.

The phase 1 trial (NCT03283696) enrolled 16 patients with advanced or metastatic soft tissue sarcomas. Patients had received no prior lines of systemic therapy and had an ECOG performance status of 0-1. Adequate follow-up data were available for 10 patients.

Olaratumab (Lartruvo), which binds platelet-derived growth factor receptor alpha (PDGFRα), was given at 15 mg/kg in combination with doxorubicin (75 mg/m^2 on days 1-3) and ifosfamide (10 g/m^2 on days 1-4). This was followed by mandatory granulocyte-colony-stimulating factor therapy in cycles 1-6 on a 21-day cycle. Doxorubicin could be administered by continuous infusion or bolus administration and with cardiac protection. Mesna dosing was at least 60% of the ifosfamide dose.

Two of the 10 patients had dose-limiting toxicities; one had grade 4 febrile neutropenia and the other had grade 3 febrile neutropenia and grade 3 mucositis. Common related adverse events occurring in over 30% of patients included fatigue, anemia, neutropenia, thrombocytopenia, constipation, and nausea. One patient discontinued study treatment due to progressive disease, and all others were on study treatment as of the data cutoff. Among 7 patients evaluated for tumor response, 3 patients had a partial response according to RECIST and 3 other patients had stabilized disease as best overall response, for a disease control rate of 86%.

Given that 8 of 10 evaluable patients have completed the dose-limiting toxicity period without dose-limiting toxicities at the 15 mg/kg dose level of olaratumab, the study has proceeded to the next cohort. In those patients, an olaratumab loading dose of 20 mg/kg will be evaluated in cycle 1, followed by 15 mg/kg of olaratumab in subsequent cycles with the same doses of doxorubicin plus ifosfamide, the researchers wrote in their abstract.

NOTE: Since CTOS 2018, olaratumab plus doxorubicin did not meet its phase 3 endpoint of overall survival (OS) advantage in the full study population or in the leiomyosarcoma subpopulation compared to doxorubicin alone.

ANTHRACYCLINE-BASED REGIMEN EXCELS IN FIGO-1 UTERINE LEIOMYOSARCOMA

Patients with uterine leiomyosarcomas treated with anthracycline-based regimens experienced longer disease-free survival compared to patients treated with gemcitabine and docetaxel, according to a retrospective analysis reported at CTOS 2018.

Roberta Sanfilippo, MD, of Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, and her colleagues reviewed all patients with FIGO stage I uterine leiomyosarcomas at two Italian centers who underwent hysterectomy with or without oophorectomy and were then treated with adjuvant chemotherapy with anthracycline-based or gemcitabine-based regimens.

INVESTIGATORS BELIEVE FUTURE TRIALS TO ASSESS THE EFFICACY OF ADJUVANT CHEMOTHERAPY IN UTERINE LEIOMYOSARCOMA SHOULD INCORPORATE ANTHRACYCLINES.

Of 145 patients, 97 were treated with an anthracycline-based regimen and 48 with gemcitabine and docetaxel. The median number of cycles of anthracycline-based therapy patients received was 4 (range 2-6) and the median number of cycles with gemcitabine and docetaxel was 5 (range 3-7). Disease-free survival was 31 months in patients treated with anthracycline-based chemotherapy and 19 months in patients treated with gemcitabine and docetaxel.

These results suggest that future trials to assess the efficacy of adjuvant chemotherapy in uterine leiomyosarcoma should incorporate anthracyclines, the investigators maintain.

TRABECTEDIN AND CONCURRENT LOW-DOSE RADIOTHERAPY FEASIBLE

Trabectedin concurrent with low-dose radiotherapy is being examined as an option for patients with pulmonary metastatic soft tissue sarcoma (NCT02275286).

› TRABECTEDIN WITH CONCURRENT RADIOTHERAPY REDUCED 71% OF IRRADIATED LESIONS IN PATIENTS WITH PULMONARY METASTASES REGARDLESS OF HISTOLOGIC SUBTYPE.

In a phase 1 study, long-lasting dimensional responses were seen in 71% of the irradiated lesions. Based on those results, trabectedin (Yondelis) at 1.5 mg/m^2 will be the recommended dose for phase 2, according to Javier Martín-Broto, MD, of the Institute of Biomedicine Research (IBIS)-University Hospital Virgen del Rocio/CSIC/University of Seville, Spain, and his colleagues, reporting at CTOS 2018.

For the study, trabectedin was given along with radiotherapy (30 Gy) in 10 fractions (3 Gy/fraction). Three dose levels of trabectedin were administered: -1 (1.1 mg/m^2), 1 (1.3 mg/m^2), and 2 (1.5 mg/m^2). Dose-limiting toxicity was defined as grade 3 or greater events excluding grade 3/4 neutropenia lasting less than 5 days, grade 3 transaminitis if it did not lead to trabectedin delay, and grade 3/4 nausea/vomiting due to inadequate prophylaxis.

Ten of the 18 patients enrolled had synovial sarcoma; 3 had undifferentiated pleomorphic sarcomas, and the other patients had either myxoid liposarcoma, dedifferentiated liposarcoma, G3 not otherwise specified sarcoma, leiomyosarcoma, or malignant peripheral nerve sheath tumor.

Patients received a median of 1 prior line of chemotherapy (range: 0-3). Twelve patients received trabectedin at dose level 1 and 6 patients at dose level 2. Grade 3/4 adverse events were neutropenia, seen in 8 patients; alanine aminotransferase (ALT) elevation, seen in 2 patients; gamma-glutamyl transferase (GGT) elevation, seen in 2 patients; anemia, seen in 2 patients; febrile neutropenia, seen in 1 patient; and pneumonitis, seen in 1 patient.

There were two dose-limiting toxicities: transient grade 4 ALT elevation at the level 1 dose and grade 4 neutropenia for more than 5 days at the level 2 dose.

Based on central radiological review of 17 evaluable patients, 2 patients achieved complete response, 3 had partial responses, 6 had stable disease, and 6 had progressive disease. The local review reported complete responses in 2 patients, partial responses in 5, stable disease in 4, and progressive disease in 6.

Of the irradiated lesions, 71% had long-lasting dimensional responses: 4 completely responded, 8 responded partially, 4 were stable, and 1 progressed.

With a median follow-up of 18 months, median progression-free survival was 2.83 months (95%CI: 2.3-3.3 months). Thirteen patients have died, with a median overall survival of 8.77 months (95%CI: 3.6-13.9) and a 12-month overall survival rate of 48%.

The investigators concluded trabectedin with concurrent radiotherapy was feasible in patients with pulmonary metastatic soft tissue sarcoma regardless of their histologic subtype. **TSJ**