enhance their experience, improve carer involvement and may enhance patient outcomes.

Sarcoma

Tuesday 27 September 2011, 09:00−11:30

30LBA LATE BREAKING ABSTRACT

A Randomized Clinical Trial of Adjuvant Chemotherapy with Doxorubicin, Ifosfamide, and Cisplatin in Localized Uterine Sarcomas. Results On 81 Randomized Patients

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Background: Uterine sarcomas (US) have a high risk of metastatic relapse. No benefit was shown with doxorubicin as adjuvant treatment even though a trend emerged in favor of chemotherapy (CT) (Omura 1985). A multichemotherapy approach in US achieved a good response rate (DECAV therapy: 54% overall response rate), though toxic. Adjuvant API (doxorubicin, ifosfamide and cisplatin) followed by radiotherapy (RT) is a feasible protocol. We conducted a phase III multicenter study of adjuvant CT with API. The objective was to detect an increase $\geqslant$20% of 3 years PFS (a = 5%, power = 80%) in the CT arm. Study was stopped because of lack of recruitment. We present the results of the 81 pts who actually entered the study.

Material and Methods: Pts with FIGO stage $\leqslant$III US after complet surgery, normal thoracic, abdominal and pelvic CT scan, physiological age $\leqslant$65 years, PS $\leqslant$ 2, left ventricular ejection fraction >50%, were randomized (stratification carcinosarcomas [CS] versus others). All patients received pelvic RT (45 grays); vaginal brachytherapy was optional. Chemotherapy consisted in 4 cycles of doxorubicin 50 mg/m^2 d1, ifosfamide 3 g/m^2/d d1d2 + mesna, cisplatin 75 mg/m^2 d3, + lenograstim 150 μg/m^2/d d 7−14; q 3 wks.

Results: 81 patients randomized, 39 in arm A (CT + RT) and 42 in arm B (RT); median age 55 y (39−69), 52 stage I, 16 stage II, 13 stage III; 53 leiomyosarcomas, 9 indifferenciated sarcomas, 19 CS. Gr 3−4 toxicity during API (/37 pts): hematologic gr3 (16%) and 4 (68%); febrile neutropenia (22%) with 2 toxic deaths; renal gr 4 (1 pt); nausea-vomiting gr 3−4 (24%); 28% of pts needed dose reduction. With median follow-up of 4.3 years, 41/81 pts recurred at a median time of 13 mo (5−43 mo), 15 in arm A (38%) and 26 in arm B (62%); median DFS is 33 mo; recurrences sites was: pelvis 11, pelvis + meta 3, meta 27 (25/30 meta: lung). 3 years DFS is 55% in arm A (IC95: 40−70) and 41% in arm B (IC95: 27−57) p = 0.048. 3 years OS is 81% in arm A (IC95: 66−91) and 69% in arm B (IC95: 52−82) NS.

Conclusions: With median follow-up of 4.3 years, API adjuvant chemotherapy increases statistically the 3 year-DFS of patients with uterine sarcoma.. Results have to be confirmed with longer follow-up to see real impact on OS. The 2 toxic deaths may impact the global prognosis. A selection of less toxic chemotherapy is mandatory.

Sarcoma

Tuesday 27 September 2011, 09:00−11:30

31LBA LATE BREAKING ABSTRACT

Response to Imatinib Rechallenge of GIST That Recurs Following Completion of Adjuvant Imatinib Treatment − the First Analysis in the SSGXVIII/AIO Trial Patient Population

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Background: Adjuvant imatinib improves outcome of patients with operable GIST, but many GISTs recur after completion of adjuvant therapy. Efficacy of imatinib in recurrent GIST following adjuvant treatment is unknown, and concern has been expressed that prior exposure to imatinib may reduce efficacy of the drug in the advanced setting. The SSGXVIII/AIO trial recruited patients with KIT-positive GIST, estimated to have a high risk of tumor recurrence based on the modified NIH Consensus Classification from February 2004 to September 2008.

Patients and Methods: The intention-to-treat population consisted of 397 patients, of whom 199 were randomly assigned to receive 12 months of imatinib and 198 36 months of imatinib. Imatinib was administered orally at a dose of 400 mg/d in both groups. The patients were monitored with computed tomography at 6-month intervals during follow-up. With a median follow-up time of 54 months, 84 and 50 patients were diagnosed with recurrent GIST or died in the 1-year and 3-years groups, respectively. Patients who did not have GIST at central pathology review (n = 15) and those with metastatic GIST at the time of randomization (n = 24) were excluded from the current analysis.

Results: Eighty-one patients were treated with imatinib for recurred GIST (1-year group, 54; 3-years group, 27). Forty-six (56.8%) out of the 81 patients were evaluable for response (6 were not evaluable, and 29 had missing data or were too early for evaluation). Imatinib was administered at a dose of 400 mg/d for 71 patients (87.7%). The remaining 10 patients received 100 mg (n = 3), 600 mg (n = 1) or 800 mg (n = 6), respectively. Fifteen (32.6%) patients achieved a CR, 14 (30.4%) a PR, 10 (21.7%) had SD and 7 (15.2%) PD as the best response yielding a clinical benefit rate CBR (CR + PR + SD) of 84.8%. There was no difference in the CBR between patients assigned to the 1-year and 3-years groups (87.9% vs. 76.9%, respectively; p = 0.385). The median time to progression after starting imatinib for advanced GIST was 35.7 months (1-year group: 39.6 months; 3-year group: 20.8 months; HR 1.60, 95% CI, 0.67–3.85; p = 0.289).

Conclusions: Most patients diagnosed with recurrent GIST after having received imatinib in the adjuvant setting respond to imatinib. The CR rate observed was high, possibly due to early detection of recurrent disease during follow-up. The observed median time to disease progression appears similar to the times found in patient populations that have not been exposed to imatinib in the adjuvant setting.

Sarcoma

Tuesday 27 September 2011, 09:00−11:30

32LBA LATE BREAKING ABSTRACT

Denosumab Treatment for Giant Cell Tumor of Bone (GCTB) in Adolescent Patients: Interim Results From a Phase II Study

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Background: GCTB is characterized by RANKL-mediated bone destruction. Symptoms include localized tenderness, swelling, fractures, and often severe, intractable pain. In a previous phase 2 GCTB study, 86% of patients had a response to the RANKL inhibitor denosumab, as demonstrated by an elimination of $\geqslant$90% of giant cells or no radiological progression of the target lesion. We report data from a preplanned interim analysis of a 2nd phase 2 study, describing denosumab effects on the adolescent subset of patients with GCTB (Amgen, Inc. ClinicalTrials.gov identifier NCT00680992).

Materials and Methods: Skeletally mature adolescent patients with surgically unsalvageable GCTB (Cohort 1, n = 8) or salvageable GCTB (Cohort 2, n = 2), $\geqslant$12 to <18 years of age, received subcutaneous denosumab 120 mg every 4 weeks with additional doses on days 8 and 15. The primary objective was to evaluate denosumab safety. We also analyzed investigators' assessments of disease progression and the proportion of patients for whom surgery was delayed, reduced in scope, or no longer deemed required. Safety analyses included all patients who received denosumab; efficacy analyses included patients who received $\geqslant$1 dose of denosumab and had the opportunity to be on study for $\geqslant$6 months. Pain was evaluated in patients who had $\geqslant$1 post-baseline pain assessment (Brief Pain Inventory-Short Form [BPI-SF] 0: no pain − 10: pain as bad as can be imagined). The BPI-SF was administered at baseline and before each dose. Analgesic use was quantified using the 8-point Analgesic Quantification Algorithm (AQA 0: no analgesics − 7: strong opioids with >600 mg oral morphine equivalent per day).

Results: Patients included 2 males and 8 females (mean age 15.6 years, range 13−17) who were on denosumab treatment for a median of 9.0 months (range 3.3–17.3). All patients had skeletal lesions. Adverse