The antitumor activity of T in pts with advanced pre-treated sarcoma is modulated by the pattern of DNA repair functionality. A personalized intervention with T based on the DNA repair signature of tumor seems to be feasible. However, prospective studies are needed to validate these retrospective findings.

7506 ORAL

Up to 6 years follow-up of patients receiving imatinib mesylate (Glivec) to treat unresectable or metastatic gastrointestinal stromal tumors (GISTs)

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Background: Imatinib mesylate (Glivec) is a selective tyrosine kinase inhibitor that targets the deregulated activity of KIT and PDGFRA, the cause of oncogenic activity in GIST. Treatment with imatinib has been well documented to induce high rates of response and disease control which translates into prolonged overall survival relative to historical controls. A phase II, randomized clinical trial of two dose levels (400 vs. 600 mg daily) of imatinib mesylate in patients (pts) with unresectable or metastatic CD117+ (KIT+) GIST was previously published (NEJM 2002;347:472−80). Herein we report the longest follow-up of imatinib therapy in any series of pts with advanced GIST.
Methods: 147 pts with unresectable or metastatic GIST were randomly assigned to treatment with imatinib at either 400 mg/d (n = 73) or 600 mg/d (n = 74) and followed continuously.
Results: At current cut-off (~5−6 years after all pts had been randomized), 28% of pts remain on imatinib study therapy. The overall response (CR+ PR) rate for all 147 pts was 68%, with an additional 15.6% achieving stable disease (SD). Median time to response was 3 months; however, time to maximal response was >12 months in 6% of responding pts. Median time to progression was 24 months for all pts, 20 months for pts who received 400 mg/d, and 26 months for pts who received 600 mg/d (P = 0.3712), and was significantly longer for pts who achieved a response (CR or PR) than for those who achieved stable disease: 33 versus 12 months, respectively (P < 0.0001). Median overall survival (OS) for all pts was 57 months with an estimated 5-year OS of 48%, which is significantly longer than historical controls showing a median OS of <2 years. There was no difference in OS by initial dose, nor by stable or better response status. In pts with CR+PR+SD, the estimated OS was 55% at 5 years (median 64 months). Finally, among pts with GISTs harboring KIT mutations, those who had exon 11 mutations had a higher overall response rate than patients with exon 9 mutations: 86% vs 48%, respectively. Exon 9 patients who received 600 mg initial dose (n = 17) had a higher response rate than those with 400 mg (n = 6): 59% vs 17%, however the number of patients is small.
Conclusion: These long-term follow-up data of up to 6 years confirm that patients with GIST benefit from imatinib therapy, even those that achieve stable disease. Updated information on predictors of OS for patients treated with imatinib will be presented.

7507 ORAL

Optical navigation-assisted surgical planning for sarcoma patients receiving pre-operative radiotherapy

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Background: Contemporary local management of soft tissue sarcoma (STS) requires greater precision in surgical and radiotherapy (RT) integration and delivery. This study examines workflow, accuracy, and precision of a novel optical navigation system for STS patients undergoing pre-operative intensity modulated RT (IMRT) intended to spare tissues from surgical and RT morbidity.
Materials and Methods: An optical tracking process relates predetermined CT data including avoidance tissues required for surgical wound closure and IMRT targets to patient anatomy. 4 fiducial marker locations on a leg phantom were manually acquired with a passive tool and related to their CT position using the least-squares solution to a rigid transformation. 10 fiducial positions were verified and simulated surgical borders outlined. 5 repetitions of the procedure quantified fiducial and target registration error (FRE/TRE). Within an ethics approved protocol, patients returned for pre-surgical consultation where their planning CT was registered to real-time anatomy using treatment positioning tattoos and immobilization. Prospective skin excision borders were reproduced using a passive tool and recorded with a marker, radio-opaque wire, and CT. Bony anatomy was used to register the reference planning and pre-surgical CT to simulate external fiducial set-up. This provided a reference frame allowing the relative position of radio-opaque wires, representing skin excision borders defined pre- and post-RT, to be quantified. In a subset of patients (N = 12), a MATLAB script located the centroid of their contours in the treatment planning system. Absolute mean, standard deviation, maximum, and minimum for 200 adjacent points on these wires were computed and defined as "distance to agreement" measurements (DTA).
Results: Analysis of the system resulted in an FRE of 0.1 mm and a TRE of 3.0 mm. DTA absolute (mean±SD), maximum, and minimum (mm) in the right-left, anterior-posterior, and superior-inferior directions, respectively are: 3.1±1.8, 7.1 and, 0.3; 6.0±2.2, 10.4, and 2.2; 6.4±2.3, 10.7, and 2.7. An efficient method (15.0 min) for multi-disciplinary interaction has been coordinated, workflow/process defined, and hardware/software constructed
Conclusions: Optical navigation facilitates surgical planning/design of sarcoma patients receiving multi-modal treatment by permitting accurate identification of highly irradiated tissues for resection and safe wound reconstruction.

Poster presentations (Tue, 25 Sep, 14:00−17:00)

Sarcoma

7508 POSTER

Clinical follow-up of desmoid tumors and the impact of APC gene mutations

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Background: Desmoid tumors are very rare mesenchymal tumors with a partially aggressive growth pattern and high relapse rates. These tumors may occur intra- or extra-abdominal, sporadically or in association with familial adenomatous polyposis (FAP). Different germline mutations of the APC gene account for desmoid tumors in FAP. The aim of our study was to evaluate the clinical phenotype and genotype-phenotype correlations in a cohort of patients with desmoid tumors.
Material and Methods: We performed a multicentric, retrospective review of 62 primary desmoid tumor cases, treated with surgical resection alone or combination with other treatments (radiation-, chemotherapy, non-steroidal anti-inflammatory drug or hormonal agents) between 1981–2006.
Results: The median follow-up time was 86.4 months. Forty-seven patients were female and 16 were male. The median age was 31.9 years. Family history of desmoid tumor was positive in one case, of colorectal cancer in 6 cases, of Crohn's disease in 3 cases. An antecedent history of trauma to the site of the tumor was elicited in approximately 16% of the cases. In one case desmoid arised from the capsule around a silicone breast implant, in an other case the tumor was multicentric. All surgical resections were macroscopically complete, but the microscopically status of the resection margin was given only in 30 out of the 62 cases. The resection margin was tumor-free in 18 cases (60%) and tumor-positive in 12 cases (40%). Thirty-five patients (56%) experienced local recurrence. Germline mutation testing for the entire coding sequence of APC gene (using multiplex heteroduplex / SSCP analysis and direct sequencing) showed that deleterious mutations in APC gene accounted for the most severe disease outcome.
Conclusions: Deleterious germline mutations in the APC gene were detected in all the FAP families tested, suggesting a strong association of these APC mutations with the development of desmoid tumors in FAP families. Supported by OTKA T046570