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Treatment of metastatic poorly differenciated neuroendocrine carcinoma (PDNEC) with irinotacan plus cisplatin

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Background: Metastatic poorly differenciated neuroendocrine carcinoma (PDNEC) has an aggressive clinical course. Although it is often treated with chemotherapy with small cell lung cancer regimen; the response rate and survival time remain suboptimal.
Method: We retrospectively reviewed records of 18 consecutive patients with microscopically confirmed metastatic PDNEC who received irinotecan plus cisplatin. All patients received irinotecan at 70 mg/m^2/dose on day 1 and 15 of a 28-day cycle, plus cisplatin at 80 mg/m^2/dose on day 1 of a 28-day cycle. Toxicity was evaluated using the CTCAE v3.0. The therapeutic responses were evaluated by RECIST v1.0.
Results: Eighteen patients with PDNEC have been enrolled with the following demographics: Median age was 65 years (31−75), male14, female4, ECOG 0:1 = 12:6. Primary site was located in the esophagus (28%), stomach (17%), rectum (11%), unknown (22%) and others (22%). There were 1 and 2 or more organ-sites of metastatic lesions in 7 (29%) and 11 (71%) of patients, respectively. Patients received median of 4 cycles (1−13). Relative dose intensity of irinotacan was 78% and cisplatin was 85.5%. The most frequently encountered grade 3−4 toxicities expressed as % of treatment cycles are: neutrophils (89%), leukocytes (61%), haemoglobin (39%), platelets (17%), hyponatremia (11%), nausea (6%), anorexia (6%), febrile neutropenia (6%) and creatinine (6%). Median progression-free survival was 131 days and median survival was 474 days. Three (17%) patients achieved CR, while 6 (33%) met criteria for PR. The objective response rate was 50%. Eight (44%) patients had SD, whereas the remaining four (29%) had PD.
Conclusion: The combination of irinotecan and cisplatin is feasible and active treatment option for patients with metastatic PDNEC.

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A cross sectional study of Imatinib trough plasma level in patients with advanced gastrointestinal stromal tumour

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Background: It has been reported that Imatinib (IM) trough plasma level (C_{min}) correlates with the treatment outcome in patients with gastrointestinal stromal tumor (GIST) (2008 ASCO abstract #4523). The present study is to evaluate the correlation between IM C_{min} and clinical characteristics of patients with GIST in Korea.
Methods: IM C_{min} at steady state was measured in 108 GIST patients on IM. Blood samples were collected prior to the morning dose (mostly 22−26 hours after previous dose). Two measurements were obtained at two different times. The plasma IM level was measured by liquid chromatography-tandem mass spectrometry. In 92 patients treated with 400 mg/day, IM C_{min} was correlated with age, body weight, body surface area (BSA), duration of imatinib use, previous surgical type, hemoglobin, white blood cell counts (WBC), platelet, and serum albumin at the time of blood sample by using linear regression and Mann-Whitney test.
Results: IM C_{min} (mean±standard deviation) in patients with 400 mg (n = 92), 300 mg (n = 7), 600 mg (n = 2), or 800 mg (n = 11) daily dose was 1305±633 ng/mL, 1452±830 ng/mL, 1698±725 ng/mL, and 3330±1592 ng/mL, respectively. Out of total 92 patients with IM 400 mg/day, 25 (27%) patients received IM as adjuvant therapy and 67 (73%) patients for advanced disease. Fifty nine (63%) were men, median age was 55 yrs (range, 28−76) and median duration of IM use before sampling was 8.8 months (range, 0.5−67.6). The mean inter- and intra-subject variability of patients with IM 400 mg/day was 44.7% and 26.5%, respectively. In univariate analyses, high C_{min} was correlated with old age ($p = 0.02$), low hemoglobin ($p = 0.01$), low albumin ($p < 0.001$), and a low C_{min} with major (total or subtotal) gastrectomy ($p = 0.002$). IM C_{min} was significantly lower in patients who had major gastrectomy (n = 17, 937±339 ng/mL) than in those without major gastrectomy (n = 75, 1388±656 ng/mL). Body weight, BSA, WBC, other types of surgery (minor gastrectomy, small bower resection, or hepatic resection) and duration of imatinib use were not associated with IM C_{min}. In a multivariate analysis, hemoglobin ($p = 0.04$), serum albumin ($p = 0.002$) and major gastrectomy ($p = 0.002$) were significantly correlated with C_{min}.
Conclusion: In patients with GIST, IM C_{min} at steady state appeared to be associated with hemoglobin, serum albumin, and previous major gastrectomy. Monitoring IM plasma level might be important for patients with low C_{min} levels especially in patients with major gastrectomy.

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Evaluation of our gastrointestinal stromal tumour cases and their response to treatment

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Background: In this analysis we evaluated gastrointestinal stromal tumors (GIST) which are one of the most frequent mesenchymal tumors of the gastrointestinal system and their response to Imatinib treatment.
Materials and Methods: Seventy-five patients diagnosed as GIST and applied to our center in between 1998–2008 were taken a part of this study and their demographic and clinicopathological characteristics were examined as well as Imatinib response.
Results: Median age of the cases was 56 (26−78), 57.3% of them were male. Median follow up was 39.9 months. Firstcoming symptoms were abdominal pain (30.7%), gastrointestinal bleeding (14.7%), weight loss (4.0%) and jaundice (1.3%). Diarrhea, constipation, abdominal mass were other symptoms and signs (13.3%). Stomach was the most common primary localization site (41.3%). Others were as follows: small intestine (33.3%), rectum (6.7%), colon (5.3%), retroperitoneum and others (13.3%). Median tumor volume was 9 cm (0.4−35 cm) and largest tumors were located intraabdominally. Total resection with negative surgical margins were achieved in 74.4% of the cases. C-kit positivity was found in fifty-six (74.4%) of the patients. We classified them according to risk groups: majority of them were in high risk group (64.0%). Percentage of the very low, low and intermediate risk groups were 2.7%, 12.0% and 17.3% respectively. Locoregional recurrence was detected in nine cases and six of them were undergone wide local excision before Imatinib therapy. In three of the patients Imatinib therapy was started immediately (400 mg/day). Two patients were metastatic on admission. Eleven of the cases developed metastases during follow up. Imatinib dose was increased to 600–800 mg/day after progression. No dose limiting or dismissing side effects were seen. Median time to progression was 66.7 months. Three patients have been taken Sunitinib 50 mg/day since Imatinib resistance occured. Overall survival was 31.0 months while it was 28.8 months in locally recurrent cases. Two and five years survivals were 91.0% and 61.6% respectively.
Conclusions: Surgery is a gold standart in GIST management. Detailed and accurate histopathological examination is needed to predict outcome and prognosis. Imatinib is an active, effective and well tolerated drug in GIST. In case of resistance other agents like Sunitinib are promising.

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Minimizing recurrence for desmoid tumours of the anterior abdominal wall: a five-years follow-up monocentric series

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Background: desmoid or aggressive fibromatosis is a rare soft tissue tumor. For those cases localized in the anterior abdominal wall radical resection and reconstruction with a mesh is indicated. Although randomized trials are lacking, in the reported retrospective series, local recurrence is not uncommon.
Material and Methods: we analyzed the records of 15 consecutive patients (3 males, 12 females, median age 36 years, range 25−51 years) affected by desmoid tumor of the anterior abdominal wall treated at the European Institute of Oncology. The surgical strategy was the same in all cases, including wide surgical excision and immediate plastic reconstruction with mesh after intraoperative confirmation by frozen sections of free margin more than 1 cm. We considered long-term outcomes and we also evaluated the overall quality of the treatment using the EORTC QLQ-C30.
Results: no immediate postoperative complication was registered and no patient developed recurrence after a median follow-up period of 60 months. Two female patients experienced mesh bulging within 1 year after the surgical approach. The mean long-term global health status registered was 97/100.
Conclusions: intraoperative margins evaluation by frozen sections plays a central role in minimizing recurrence after resection of desmoid tumors of the anterior abdominal wall. Surgical clearance more than 1 cm confirmed by pathologist invariably followed by mesh reconstruction can provide definitive cure for this rare disease.