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Original
Explorative model of imatinib resistant wild type GIST and potential immunotherapy strategies / Fiorino, E; Mesiano, G; Cerviere, I; Berrino, E; D'Ambrosio, L; Merlini, A; Venesio, T; Pignochino, Y; Pisacane, A; Gammaitoni, L; Grignani, G; Aglietta, M; Sangiolo, D. - In: ANNALS OF ONCOLOGY. - ISSN 0923-7534. - 31:(2020), pp. S979-S979. [10.1016/j.annonc.2020.08.1859]

Availability:
This version is available at: 11583/2975767 since: 2023-02-08T09:02:18Z

Publisher:
ELSEVIER

Published
DOI:10.1016/j.annonc.2020.08.1859

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29 March 2023

a receiver operating characteristic curve. Patients who underwent surgical intervention were censored at the time of surgery.

Results: The median age of patients was 59 (31−77) years, and 63.4% were male. Compared with C_{min400}, C_{min} at IM 800 mg/day increased after dose escalation (median 2,990 ng/mL vs. 1,235 ng/mL, paired Wilcoxon-test $P<0.001$). The objective response and disease control rates with IM 800 mg/day were 7.2% and 66.4%, respectively, and both rates in the low C_{min400} group were higher than those in the high C_{min400} group (10.3% vs. 0%, $P=0.042$ and 73.6% vs. 51.4%, $P=0.016$). mPFS with IM 800 mg/day ($mPFS_{800}$) was 5.4 months. Despite no significant difference in mPFS with IM 400 mg/day by C_{min400}, $mPFS_{800}$ in low C_{min400} was significantly longer than that in high C_{min400} (7.2 vs. 2.8 months, $P<0.001$). In the multivariate analysis, low C_{min400} and KIT exon 9 mutation were significant favorable factors for $mPFS_{800}$ compared with high C_{min400} and other exon genotypes, respectively (hazard ratio 0.36 and 0.49, $P<0.001$ and $P=0.005$). Patients with KIT exon 9 mutation and low C_{min400} exhibited significantly longer $mPFS_{800}$ than those without (16.7 vs. 4.8 months, $P=0.006$).

Conclusions: Dose escalation of IM after progression on IM 400 mg/day was more effective in patients who had low C_{min400} as well as KIT exon 9 mutation. Along with genotype, C_{min400} should be considered in the treatment decision of dose escalation of IM after failure of the standard dose of IM.

Legal entity responsible for the study: Yoon-Koo Kang.

Funding: Has not received any funding.

Disclosure: Y-K. Kang: Advisory/Consultancy: ALX oncology ; Advisory/Consultancy: Zymeworks; Advisory/Consultancy: Amgen; Advisory/Consultancy: Novartis; Advisory/Consultancy: Macrogenics; Advisory/Consultancy: Daehwa; Advisory/Consultancy: Surface Oncolgy; Advisory/Consultancy: BMS. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1857

1632P Regorafenib is associated with increased skeletal muscle loss in gastrointestinal stromal tumor

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Background: Previous reports suggest sarcopenia affects prognosis and treatment tolerance in patients with various solid cancers. Though it is reported that regorafenib could be associated with increased skeletal muscle loss which relate to poor prognosis in metastatic colorectal cancer patients, it is not well established in gastrointestinal stromal tumors (GISTs). Here we evaluated the impact of regorafenib treatment on skeletal muscle dynamics in GIST patients.

Methods: We retrospectively analyzed the clinical data with GISTs patients who received regorafenib monotherapy in Hokkaido University Hospital. The skeletal muscle index (SMI, cm2/m2) and sarcopenia were evaluated from cross-sectional CT images at the level of the third lumbar vertebra. Sarcopenia was defined BMI-incorporated cutoff values of SMI as <43 cm2/m2 for males with BMI $<$ 25 kg/m2, <53 cm2/m2 for males with BMI $\geq$ 25 kg/m2, and <41 cm2/m2 for females. The SMI assessments were performed just before regorafenib initiation and within 3 months after regorafenib initiation.

Results: We analyzed 15 patients who had received regorafenib between January 2013 and February 2019. At the baseline, 8 (53.3%) of them presented with sarcopenia. A statistically significant skeletal muscle loss was observed after regorafenib initiation (median SMI change: -4.8 cm2/m2 [-6.3%]; P = .0005). We classified the patients into 3 groups—normal muscle mass, new-onset sarcopenia, and stable sarcopenia after regorafenib initiation. One-year overall survival rates of these groups were 100% (2/2 patients), 60% (3/5 patients), and 50% (4/8 patients), respectively (P = 0.762).

Conclusions: Regorafenib could be associated with increased skeletal muscle loss in GIST patients. It should be used with caution in the patients with preexisting sarcopenia or a history of recent weight.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1858

1633P Explorative model of imatinib resistant wild type GIST and potential immunotherapy strategies

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Background: While the majority of gastrointestinal stromal tumors (GIST) at diagnosis harbours *KIT*/*PDGFRA* mutations (Mut) and are sensitive to imatinib (IM), a minority of cases may be *KIT*/*PDGFRA* wild type (WT). An imprecise rate of GIST may further convert to WT along their clinical history and medical treatments. Within this setting we aimed at: a) evaluating the rate of Mut to WT conversion, b) generating a preclinical patient-derived model of IM-resistant wtGIST to functionally explore novel therapeutic strategies. We focused on the composite effects of interferons (IFNs) along with an HLA-independent adoptive immunotherapy with cytokine induced killer lymphocytes (CIK).

Methods: We assessed the *KIT*/*PDGFRA* mutational status of surgical GIST samples and set corresponding cell cultures from WT cases. The functional activity by IFNs and CIK immunotherapy was explored *in vitro*.

Results: We found 18 wtGIST in a cohort of 38 GIST, 5 (13%) at baseline while for 13/25 (52%) the original Mut could no longer be detectable after treatment with IM (mean time 26 months).We generated 11 wtGIST-derived cultures (wtGISTc), confirmed consistent with the original surgical sample. All the wtGISTc resulted resistant in vitro to IM (IC50 17 μM) and moderately sensitive to sunitinib (SU) (IC50 6 μM). Treatment with IFNα (72h, 10^4 IU/ml) exerted a direct cytotoxicity *in vitro* (mean mortality 44%) against 4/ 6 wtGISTc, while all of them (6/6) were resistant to IFNγ (72h, 10^3 IU/ml). No synergism was observed by the association of IFNs with IM or SU. Both IFNα and IFNγ determined indirect immunomodulatory effects, with significant membrane upregulation of PD-L1/2 (2.1 fold, $p< 0.05$, 6/6) and the HLA-I/β2M complex (mean 2.1 fold). WTGISTc consistently expressed NKG2D ligands, targets of CIK lymphocytes. Adoptive immunotherapy *in vitro* with patient-derived CIK significantly killed wtGISTc resistant to both IM and IFNs (50% killing at effector:target ratio 10:1 n=4).

Conclusions: We report a relevant GIST conversion rate from Mut to WT, following medical treatment, underscoring the need for longitudinal mutational assessment in the clinic. Preclinical evidence supports the exploration of CIK adoptive immunotherapy as novel approach for wtGIST resistant to medical treatments.

Legal entity responsible for the study: The authors.

Funding: "Associazione Italiana Ricerca sul Cancro" (AIRC), IG-2017 n. 20259 (DS).

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1859

1634P The efficacy of continuous circulatory hyperthermic intraperitoneal chemotherapy (C-HIPEC) following cytoreductive surgery for metastatic gastrointestinal stromal tumors (GISTs)

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Background: Early reports discussed the prognostic factors of patients with metastatic GIST treated with cytoreductive surgery (CRS). However, the role of C-HIPEC, after CRS, for the treatment of peritoneal metastatic GIST remains unknown.

Methods: A retrospective analysis of patients with peritoneal metastatic GIST treated with CRS + C-HIPEC combined with targeted therapy from a single institution was performed. C-HIPEC was introduced 1 or more days after CRS, with mitoxantrone, or doxorubicin with cisplatin. Overall survival (OS), and progression free survival (PFS) from time of surgery was determined. One-to-one propensity score matching (PSM) analyses were conducted to balance selection bias. Univariate and multivariate analysis were performed using a Cox proportional-hazards model.

Results: Between 2007 and 2018, we performed 104 operations on 87 patients with peritoneal metastatic GIST. C-HIPEC was conducted following 35 operations. After a median follow up of 23 months, the median OS and PFS were 40 months and 16 months. After PSM, both C-HIPEC group and non-C-HIPEC group had 28 operations. Either the median OS or PFS was not significantly difference in both groups, with 35 months of C-HIPEC vs 37 months of non-C-HIPEC (HR = 1.22 [95%CI: 0.56-2.67], P = 0.6187) , and 13 months in both groups(HR = 0.99 [95%CI: 0.53-1.85], P = 0.9865). Among all patients, 30 days post-operative grade III-IV morbidity rate was 16.3% (C-HIPEC 14.3% and non-C-HIPEC 17.4%, respectively, [P = 0.901]). Multifocal progression, with liver and/or extra-abdominal metastasis, tumor rupture and diameter of resected tumors $\geq$ 6.5cm were prognostic of worse OS. Multifocal progression, with