Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

1514P Anti-tumor effects of the novel KIT mutant inhibitor M4205 in gastrointestinal stromal tumor (GIST) xenograft models

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Background: Majority of GIST are driven by constitutively activated KIT/PDGFRA kinases and susceptible to treatment with tyrosine kinase inhibitors. During treatment most tumors will develop secondary mutations in *KIT* or *PDGFRA* inducing drug resistance, so there is an unmet need for novel therapies. We tested the efficacy of M4205, a novel specific *KIT* inhibitor* with high activity towards the most relevant *KIT* mutations, in GIST xenograft models. * Blum et al. *Proceedings: AACR Annual Meeting 2021.*

Methods: NMRI *nu/nu* mice were transplanted with patient-derived GIST xenograft models UZLX-GIST9 (*KIT*:p.P577del;W557LfsX5;D820G) known to be resistant to both imatinib and sunitinib, with the dose-dependent imatinib-sensitive and sunitinib-sensitive models UZLX-GIST2B (*KIT*:p.A502_Y503dup), UZLX-GIST25 (*KIT*: p.K642E) and the cell-line derived model GIST882 (*KIT*: p.K642E). Mice were treated daily with vehicle (control), imatinib (100mg/kg), avapritinib (5mg/kg), sunitinib (20mg/kg), or M4205 (10mg/kg, 25mg/kg). Efficacy was assessed by tumor volume evolution, histopathology and immunohistochemistry. Histologic response (HR) was graded as previously described°. Mann Whitney U and Wilcoxon Matched Pairs tests were used for statistical analysis, with $p<0.05$ considered as significant. Agaram et al. *Clin Cancer Res.* 2007.

Results: M4205 (25mg/kg) caused tumor volume shrinkage in UZLX-GIST2B, -GIST25 and GIST882 with relative decrease to 45.6%, 35.1% and 57.3% on the last day as compared to baseline. In UZLX-GIST9 tumor growth to 132.4% was observed in M4205 (25mg/kg)-treated tumors as compared to baseline. We observed antitumor activity superior to imatinib in UZLX-GIST9, -GIST2B and GIST882, and to sunitinib in -GIST25. Compared to controls, M4205 (25mg/kg) induced a significant decrease in mitosis in all models. In -GIST25 and GIST882 grade 2-4 HR with myxoid degeneration was observed in all tumors.

Conclusions: M4205 has significant antitumor activity in patient- and cell line-derived GIST xenograft models. The novel kinase inhibitor induces volumetric responses, decreases mitotic activity, has antiproliferative effects and in models with *KIT* exon 13 mutation leads to characteristic myxoid degeneration.

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1515P Nationwide management of soft tissue sarcoma (STS) in France, before (2019) versus during COVID-19 pandemic (2020)

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Background: COVID-19 pandemic has disorganized cancer care management, with a significant decrease in diagnosed common cancer cases such as colon or breast. In France, the management of STS is organized by a network of multidisciplinary tumor boards (MTD) covering the French territory. We describe the number of incident STS cases, delay between diagnosis and 1st surgical procedure, and rate of neoadjuvant treatments in 2019 versus 2020.

Methods: Eligible cases were confirmed cases of STS (diagnosed within or outside the accredited network) in adult patients; arising in limbs, girdles, superficial and internal trunk. Osseous, and visceral (e.g., GIST) were excluded. The data collected in the national database (NETSARC+) describe the activity of the 25 labelled MTD dedicated to sarcoma management. We present the data using percentages, mean and standard deviation (DS).

Results: Incident cases slightly decreased: 1,463 in 2019 versus 1,415 in 2020. Mean age, rate of male patients, tumor size, rate of Grade 1 tumors and M1 at diagnosis were similar: 62.2 (DS: 17.3) versus 63.3 (DS: 16.7); 54.8% versus 52.4%; 104 mm (DS: 79.2) versus 105.3 (DS: 77.5); 14.2% versus 14.1%; and 10.0% versus 10.5%, respectively. In 2019, 68.8% of STS were operated compared to 73.8% in 2020. The mean delay between diagnosis and surgery was 70.4 days (DS: 86.7) versus 72.2 (DS: 76.8). Surgery was performed in accredited centers in 53.5% in 2019 compared to 61.2% in 2020. Outside the network, the rate of R0 resection was 19.9% versus 27.8%. Inside accredited centers, the rate of R0 resection was 60.9 versus 69.8%. In parallel, the use of neoadjuvant treatment was 21.0% in 2019 and 26.4% in 2020.

Conclusions: During COVID-19, we observed a slight decrease in STS incidence, while patients' characteristics did not differ between 2019 and 2020. Both the rate of patients operated in accredited centers and R0 resections increased. There was no neoadjuvant treatment increase nor surgery delay. The accredited network therefore appears particularly robust in the event of major Health crisis.

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1516P Diagnostic delay due to COVID-19 pandemic in sarcoma patients: Single-centre retrospective SarCorD study (COMETA Project)

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Background: COVID-19 pandemic led to reduced access to clinics, interruption of screenings and delay in cancer diagnoses and treatments. Although long-term negative effects emerged in several studies in oncology, fewer data are available in sarcomas. We analysed the impact of COVID-19 pandemic on diagnostic delay in a sarcoma referral centre in Italy.

Methods: We performed a retrospective study including patients (pts) with histological diagnosis of soft tissue sarcoma (STS), bone sarcoma (BS), and aggressive benign connective diseases (ABCD) followed at Regina Elena National Cancer Institute in Rome during the first year of pandemic and the year before. Pts were classified in Control Group (CG) and COVID Group (COVG) according to the date of diagnosis, respectively before or after the start of lockdown in Italy (March 9th 2020).

Results: We enrolled 185 pts affected by STS (129), BS (41), and ABCD (15), male/female 113/72. The median age at diagnosis was 53.9 (range 17-101). 92 pts were classified in the CG and 93 in COVG. We observed a diagnostic delay in the COVG with a median time from the first symptom to the diagnosis of 103 days (d) (95% Confidence Interval (CI) 92,8 - 113,2) *vs* 90 d (95% CI 69,5 - 110,5) in the CG (p 0.024), but not a delay in starting treatment (time from first symptoms to treatment 151 d (95% CI 132,9 - 169,1) *vs* 144 d (95% CI 120,3 - 167,7) in the COVG and CG respectively, p 0.208). Although the diagnostic delay was evident in all the trimesters, this was significant in the trimester Sep-Nov (99 (95% CI 88.4 - 109.5) *vs* 70 (95% CI 59.5 - 80.5) d respectively, p 0.035). We noticed a reduction in the number of diagnoses in the first trimester of the pandemic (14 vs 33), with a subsequent recovery with 33 vs 22, 32 vs 20, and 14 vs 17 new diagnosis in the Jun-Aug, Sep-Nov, Dec-Feb trimesters respectively (p 0.005). No differences in stage at diagnosis was observed (12% *vs* 16.5% in the COVG and CG respectively, p 0.380). Progression free (p 0.897) and overall survival (p 0.725) were comparable in the subgroup of STS pts.

Conclusions: A significant delay in sarcoma diagnosis but not in starting treatment has been highlighted, with greatest impact in the trimester Sep-Nov 2020. No difference in stage at diagnosis, nor in terms of survival have been observed.

Legal entity responsible for the study: Local Ethics Committee.

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1517P Role of geriatric assessment and oncological multidimensional prognostic index (onco-MPI) in older patients (age ≥70 years) with advanced soft tissue sarcoma in a real-world setting

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Background: Incidence of soft tissue sarcomas (STS) increases with age. Older patients (pts) are underrepresented in clinical trials and guidelines are lacking. International oncological societies suggest using geriatric tools to evaluate older pts to optimize treatment. Comprehensive Geriatric Assessment (CGA) is a multidimensional assessment of elderly, based on which pts can be classified as fit, vulnerable or frail. OncoMPI is a CGA-based score which considers tumour characteristics, classifying pts in high-risk, intermediate-risk, low-risk group.

Methods: Consecutive pts with metastatic STS (mSTS) aged ≥70 years treated at Istituto Oncologico Veneto from January 2009 to June 2020 were retrieved from a prospectively maintained database. Pts demographics, CGA and tumor characteristics were analysed. Overall survival (OS) was calculated from diagnosis of metastatic disease to death. Kaplan-Meier curves and a Cox proportional hazards model were used for survival analyses.

Results: Out of 101 pts, 76 received chemotherapy (CHT) (75.3%), which was anthracycline-based for 46 pts (60.5%). Anthracyclines were used in a higher proportion in fit pts (58.9% fit Vs 45.1% vulnerable Vs 12.5% frail). Frail pts and pts in OncoMPI high-risk group experienced higher rate of toxicities. Median OS was 13.8 months (m) (95% CI 11.3-17.7). According to CGA, mOS was 19.53 m (95% CI 15.23-36-8) for fit pts, 12.83 m (95% CI 9.7-17.5) for vulnerable and 7.75 m (95% CI 2.73-30) for frail pts (p=0.005). OncoMPI confirmed a predictive value for 1-year survival, intermediate risk pts not reaching mOS at 1 year, and high-risk pts having median-1 year OS of 11.5 m (95%CI 9.7-NA), p=0.02. In multivariate analysis, oncoMPI and CGA were associated with survival (high risk oncoMPI: HR 5.5, 95%CI 1.25-24.7 p=0.02; fitness at CGA HR 0,552 95% 0,314-0,973; p=0.040) as well as CHT use (HR 0.24, 95% CI 0.11-0.51, p<0.005).

Conclusions: Both CGA and oncoMPI retain prognostic value for survival in mSTS. Our data show survival for fit pts comparable to younger adults. Pts not fit at CGA and pts within the oncoMPI high risk category should be offered an oncogeriatric management approach in order to optimize treatment.

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1518P An individualized model-based risk score is the best prognostic tool for localized soft tissue sarcoma (STS) cases, but clinical status cannot be neglected

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Background: Patients (pts) with high-grade STS>5cm are at high risk of disease recurrence and death. Adjuvant chemotherapy (CHT) aims to decrease the risk. This study investigated factors impacting the outcome of pts receiving multimodal treatment.

Methods: Among 864 pts treated in 2013-2020, who underwent treatment for extremity/trunk wall STS with radical intent, pts qualified for neoadjuvant chemotherapy with 3 cycles of doxorubicin and ifosfamide were selected (n = 133). We've collected detailed data on tumor and pts characteristics. All pts were additionally evaluated using a SARCULATOR nomogram. The results were analyzed using Cox's proportional hazard model.

Results: Mean age was 52 years. The median follow-up was 30 months (95%CI: 27-34). The most common subtypes were pleomorphic sarcoma, liposarcoma, and myxofibrosarcoma. 81% of the pts had primary tumors; Mean tumor size was 12cm. All but two had high-grade tumors. The most common tumor localization was lower limbs (67%). The median OS (overall survival) was not reached. Among all factors, ECOG status and the ones included in the SARCULATOR were connected with OS in the univariate analysis. The SARCULATOR 10-year score was the best predictor for the OS, with HR 1.04 per percentage point change (95%CI: 1.01-1.06, p=0.004, c-index=0.66). In multivariate analysis, after adjusting for SARCULATOR score, ECOG performance status (0 vs. >0) was predictive for OS, HR = 2.53 (95%CI: 1.02-6.27, p = 0.04) with c-index=0.71. The DFS (disease free-survival) univariate analysis showed significance of SARCULATOR-related variables, initial albumin and hemoglobin concentration below lower limit normal, and ECOG score. The multivariate model for DFS is presented in the table.

Table: 1518P Multivariate model for DFS

	HR	lower .95	upper .95	p
Albumin level at start < 35	2.163	1.119	4.181	0.022
ECOG > 0	1.729	1.007	2.966	0.047
Sarculator per 1%	1.017	1.001	1.034	0.041

Conclusions: SARCULATOR nomogram provides a practical guide in planning adjuvant treatment in STS. Also, additional clinical data on pts general conditions should be taken into account.

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1520P Preferences on treatment decision making in sarcoma patients. Prevalence and associated factors: Results from the PROSa study

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Background: The impact of being diagnosed with a life-threatening illness may influence preferences to participate in treatment decisions. The objective of this study was to identify factors that are associated with sarcoma patients wanting to take a more active or passive role.

Methods: Data was obtained as part of a nationwide multicenter trial (PROSa) aiming to investigate the structure and quality of medical care of sarcoma patients in Germany. The study was conducted between 2017 and 2020 in 39 study centers. For the present analysis, cross-sectional data of adult patients with sarcoma of any entity were analyzed. Control preference was measured with the control preference scale (CPS). Preferences were divided in patient-led, shared, or physician-led-decision-making. Associated factors were analyzed exploratively using multivariable nominal logistic regression models. We included socio-economical and medical variables with stepwise backward variable selection.

Results: We included 1059 patients (51.5 % male). 394 patients wanted to make their own treatment decision while 275 patients preferred the physician to make treatment decisions on their behalf. 390 patients wanted to share responsibility. Comparing patients' preferences to participate, we found the following significant differences: Patient without metastases were more likely to make their own treatment decisions than patients with a metastatic tumor disease who preferred to share responsibility (OR 1.50, 95% CI 1.04; 2.16). With patients between 18 and >40 years as reference category, older patients were less likely to make the decision by themselves: age group: 55-<65 (Odds Ratio (OR) 0.50, 95% confidence interval (95% CI) 0.29; 0.88), age group: 65-<75 (OR 0.39, 95% CI 0.22; 0.69), age group: ≥75 years (OR 0.29, 95% CI 0.15; 0.56). Patients with an education level of high school or higher were more likely to make decisions by themself than those with 8 or 9 years of school education (OR 1.94, 95% CI 1.24; 3.05).