associated with better functional capacity, metabolic and inflammation profiles, and recently with better survival. In fact, the results of intervention studies indicate that resistance training enhances MusS and endurance, muscle mass, functional capacity, risk profile for cardiovascular disease, and quality of life, which are well-known predictors of overall mortality.

This study is limited by the small sample size and SCD cases, which may partially contribute to no significant result in the upper third of MusS. However, the reduction in SCD risk for those with moderate MusS or the combination of both high MusS and CRF was even higher (69% or 72%, respectively) than that previously found for CRF alone (44%-48% risk reduction) in a larger sample of the Aerobics Center Longitudinal Study cohort (n=59,611). Further studies are needed to assess the combined effects of MusS and CRF on the prevention of SCD.

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Clinical Activity of Sunitinib and Regorafenib in Endometriosis

To The Editor: Endometriosis is a sex hormone-dependent gynecological disease characterized by the presence and growth of endometrial tissue outside the uterus that affects up to 10% of women of reproductive age. Endometriosis lesions harbor dense vascularization, and angiogenesis has been shown to play a critical role in its establishment and progression. Hence, targeting the vascular endothelial growth factor (VEGF) signaling pathway is considered a promising approach for the treatment of endometriosis.

We herein report the case of a patient with concomitant endometriosis and metastatic gastrointestinal stromal tumor (GIST), in whom the anti-VEGF agents sunitinib and regorafenib led to a complete regression of a biopsy-proven endometriosis lesion.

A 37-year-old woman with a history of pelvic endometriosis (documented by laparoscopy, and treated by promegestone 0.5 mg a day) was diagnosed with an ileal GIST with synchronous liver metastases in November 2015.

The primary tumor was resected, and a biopsy was performed on one
of the liver metastases. The diagnosis of GIST with KIT exon 11 mutation was made, and she was started on imatinib 400 mg a day, which resulted in a partial response.

In May 2017, progressive liver disease was diagnosed. At the same time, while she remained on promegestone, she complained of a painful 20-mm umbilical nodule that had appeared and progressively grew over the past 3 months. A biopsy was performed on the umbilical nodule as well as one of the progressive liver lesions. Pathological examination confirmed that the umbilical nodule was an endometriosis lesion, whereas the liver lesion was a GIST metastasis with KIT exon 11 and 13 mutations. Imatinib was stopped, and she was started on sunitinib at the approved dose of 50 mg a day, 4 weeks on, 2 weeks off.3,4 She was also referred to her gynecologist to discuss an alternative systemic treatment for endometriosis or to consider resection of the umbilical nodule.

At the visit scheduled 1 month later, the umbilical nodule had disappeared. She reported that the nodule had shrunk during the first week of sunitinib intake, and she did not consult her gynecologist.

The best response of GIST lesions to sunitinib was stable disease according to response evaluation criteria in solid tumors (RECIST).5

In August 2017, she discontinued promegestone, without medical advice and without recurrence of the umbilical nodule.

In September 2018, progressive liver disease was diagnosed. Sunitinib was stopped, and she was started on regorafenib at the approved dose of 160 mg a day, 21 days on and 7 days off.3,6 The best response to regorafenib was stable disease.

At progression in January 2019, imatinib 400 mg daily was reintroduced, according to international guidelines.3,7 She died of progressive disease in April 2019. Notably, the umbilical endometriosis nodule had never recurred.

In the current case, the umbilical endometriosis lesion had developed while the patient was under imatinib, a multikinase inhibitor (MKI) targeting KIT but not VEGF receptors. This lesion regressed under sunitinib (a MKI with a broader spectrum than imatinib, encompassing VEGFR1-3) and did not recur under regorafenib (another MKI targeting VEGFR1-3), suggesting a critical activity of VEGFR inhibitors in endometriosis. Moreover, the umbilical lesion did not recur when promegestone was stopped nor when imatinib was re-introduced, suggesting that anti-VEGF agents had prolonged activity against endometriosis.

Sunitinib and other anti-VEGF agents have demonstrated activity against endometriosis but only in preclinical models.8-13

To our knowledge, the current report is the first clinical demonstration of sunitinib and regorafenib activity in endometriosis and provides a rationale for future clinical trials. Whether lower doses or shorter courses of sunitinib or regorafenib could be active in this setting remains to be explored.
Myelodysplastic Syndrome Over Time: A Comparative Analysis of Overall Outcome

To the Editor: We read with interest the paper recently published by Al-Kali et al., who assessed, in a large cohort, the overall survival of patients with myelodysplastic syndrome (MDS) over 3 periods of diagnosis (2004 to 2006, 2007 to 2009, and 2010 to 2013). The authors found that the overall outcome did not improve over time. Therefore, we would like to discuss and compare their results with data from a single Brazilian university institution.

MDS is a heterogeneous group of clonal bone marrow disorders. Apart from intrinsic genetic heterogeneity, regional differences, probably owing to ethnic and racial characteristics and environmental factors, have also been suggested as playing a role. With the advent of new therapies, it is tempting to speculate on the impact on overall outcome of MDS. In our retrospective study, 288 patients with newly diagnosed MDS were evaluated at a University Hospital in northeast Brazil. Only patients with at least 12 months of follow-up were included. The patients were divided into 3 periods of diagnosis (2003 to 2007, 2008 to 2012, and 2013 to 2017). The study was approved by the local ethics committee. Clinical and laboratory parameters were evaluated by medical records review.

The Kaplan-Meier method was used to estimate overall survival (OS). For between-group comparisons, a log-rank test—stratified for a 5-year window of diagnosis—was used. Pearson’s χ² test was performed using SPSS software version 20.0 (SPSS Statistics, IBM, Armonk, New York). P<.05 was considered significant.

Eighty-seven patients were included in the 2003 to 2007 group, 99 in the 2008 to 2012 group, and 102 in the 2013 to 2017 group. The median age at diagnosis was 69.3±15.6 years. Most patients, 68% (n=198) were older (≥65 years), and 50.3% (n=145) were female. Age and gender were similar among the groups.

The most common subtype was refractory cytopenia with multilineage dysplasia (RCMD) (48.6%), followed by refractory anemia with excess blasts (RAEB) (22.9%), refractory anemia with ringed sideroblasts (RARS) (13.2%), refractory anemia (RA) (10.4%), therapy-related MDS (t-MDS) (2.1%), unclassified (2.1%), and 5q— (0.7%). From patients with Revised International Prognostic Scoring System (IPSS-R) available, 29.5% were classified as lower risk, 11.8% as intermediate, and 14.2% as higher-risk MDS.

Patients with RA had the longest median OS (73.9 months), and patients with RAEB had the shortest median survival (18.6 months). Patients with RCMD, RARS, unclassified, and t-MDS subtype had 53.9, 55.9, 73.1, and 35.0 months of survival, respectively. No significant difference in OS by 5-year window of diagnosis was observed (P=.41) (Figure).

Our results, tested in a different population and geographic area, corroborate the results published by Al-Kali et al. No difference in outcome over the three 5-year periods was observed, despite the emergence of new therapies. The impact on survival of different treatments for MDS was analyzed by the Duesseldorf group. With the exception of allotransplant, MDS treatment was generally palliative. Although the number of allografts performed in patients aged 70 years and older markedly increased over the past decade in the United States, increased survival in this...