Background: The standard treatment of Pseudomyxoma Peritonei (PMP) is cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) due to the presence of pseudomyxoma. No consensus was reached on treatment of unresectable or recurrent disease. PMP is considered chemoresistant for its low mitotic index but non-randomized series showed promising results with regimens for gastrointestinal tumors. Metronomic schedules may be preferred for their antiangiogenic and immunomodulatory activity.

Methods: We conducted a single center prospective single arm trial. Inclusion criteria were histologically confirmed PMP, unresectable or relapsed after CRS/HIPEC, in progression to surgery or previous treatments. Patients received continuous metronomic capecitabine (625 mg/sqm b.i.d.) plus cyclophosphamide (50 mg/day) until progression to surgery or previous treatments. The primary endpoint was progression free survival (PFS); secondary endpoints were disease control rate (DCR), overall survival (OS) and safety profile. Ion Torrent® next generation sequencing technology (Hot-spot Cancer Panel) was used to characterize molecular profile.

Results: 23 consecutive patients were enrolled from April 2015 to October 2017. At a median follow up of 13.5 months, median PFS was 9.5 months and 1-year OS rate 73.7% (95% CI 47.3%–88.3%). No partial or complete responses were observed but DCR was 74% and 22% patients achieved a prolonged disease stability (>13 months). A significant tumor markers reduction (>20%) was seen in 43% patients for CA19.9, 22% for CA125 and 39% for CEA. The safety profile was manageable; 78% patients reported G1/2 drug related adverse events, only 17% G3 and none G4/5. As expected, the main toxicities were anemia, neutropenia, nausea, diarrhea, fatigue and hand foot syndrome. Only 17% patients required capecitabine dose reduction. Molecular profile was available in 15/23 patients and showed various mutations. Bevacizumab-based therapy increased survival in metastatic colon cancer in the presence of KRAS mutations but was tolerated and did not increase significant toxicity in our series.

Conclusions: Metronomic capecitabine plus cyclophosphamide is an active and well tolerated regimen in unresectable or recurrent PMP, with a safety profile comparing favorably with historical data. Further studies are needed to identify predictive biomarkers for novel treatment strategies.

Legal entity responsible for the study: Istituto Nazionale dei Tumori di Milano, Fondazione IRCCS.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.