

significance, but impact of good TRG% on OS would seem to be greater (mOS 14.97 months vs not reached).

**Conclusions:** These data may have implication in clinical practice. They confirmed the predominant prognostic role of pathologic nodes involvement even after FLOT; while good TRG% retrieve a favorable prognostic role in N+ population. We may assume that subgroup N+ "poor responders" may not benefit from complete post-operative FLOT, while N+ "good responders" can benefit from continuing the same regimen. Similarly, FLOT would not seem benefit in OS for "poor responders" diffuse histotype patients, contrary to "good responders". Chemotherapy omission or immune checkpoint inhibitors should be considered in MSI pts based on risk of relapse. Moreover, further randomized trials are needed.

**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.2023.04.345>

**P-290 Treatment sequences and locoregional therapies for patients with carcinoid and refractory carcinoid syndrome. A multicentric cohort analysis**

A. Oviedo<sup>1</sup>, R. Luca<sup>2</sup>, A. Rodriguez<sup>2</sup>, F. Waisberg<sup>2</sup>, C. Ypa<sup>3</sup>, F. Esteso<sup>2</sup>, S. Iseas<sup>4</sup>, M. Carballido<sup>4</sup>, J. Maquieira<sup>4</sup>, E. Roca<sup>5</sup>, M. Chacón<sup>2</sup>, G. Mendez<sup>6</sup>, J. O'Connor<sup>2</sup>

<sup>1</sup>Hospital de Gastroenterología Dr. Carlos B. Udaondo, Buenos Aires, Argentina; <sup>2</sup>Instituto Alexander Fleming, Buenos Aires, Argentina; <sup>3</sup>Hospital Municipal Oncológico Marie Curie, Buenos Aires, Argentina; <sup>4</sup>Hospital de Gastroenterología "Dr. Carlos Bonorino Udaondo", Buenos Aires, Argentina; <sup>5</sup>Intergrupo Argentino para el Tratamiento de los Tumores Gastrointestinales (IATGI), Buenos Aires, Argentina; <sup>6</sup>Fundación Favalaro, Buenos Aires, Argentina

**Background:** Carcinoid syndrome (CS) is a rare and serious condition that occurs in about 20-25% of patients with neuroendocrine tumors (NETs). Refractory carcinoid syndrome (RCS) refers to persistent symptoms associated with hormone release despite treatment with somatostatin analogues (SSA). Nowadays, treatment decisions for patients with RCS are a matter of debate. Liver Locoregional Therapies (LLRT), such as hepatic artery embolization, radiofrequency ablation, cryoablation, and surgical segment resection are increasingly being used to treat RCS, given their effectiveness in tumor debulking and symptom relief.

**Methods:** A retrospective cohort comprising patients with CS of two institutions from Argentina was analyzed. This cohort was a patient subgroup analysis form a registry of patients with NET diagnosis and liver metastases between March 2016 to December 2022. Descriptive statistics was used to summarize main patient characteristics. Survival analysis was performed using the Kaplan-Meier method, and we evaluated the presence of prognostic factors using multivariate Cox regression models.

**Results:** 81 (26.9%) out of 301 patients included in our registry had CS diagnosis. Mean age was 67.4 (IQR 57-75), 47 (58%) were men, 68 (84%) had multicentric tumors, and small bowel was the primary localization for 58(71.6%) of the cases. NETs was G1 in 52 (64.2%) cases, extrahepatic involvement was evidenced in 50 (61.7%) patients, and carcinoid heart disease was documented in 11 (13.6%) patients. 72 (88.8%) patients were treated with SSA. Median follow up was 50 months. After the first-line treatment for CS, the overall survival at 54 months was 78% (CI95: 67.6-90.7%). Progression free survival (PFS) at 50 months was 56.3% (CI95: 43.8-72.3%). Histological grade and tumor localization were significantly associated with PFS in the multivariate model ( $p < 0.005$ ). A total of 18 (22.2%) patients required subsequent treatment after RCS diagnosis, 12 received LLRT and 6 systemic therapies. At a median follow up of 64 months, PFS after the subsequent therapy was initiated was 52.1% (CI95 28.8-94.3) and 30% (CI95 6.3-100%) for LLRT and subsequent therapies respectively ( $p=0.26$ ).

**Conclusions:** In RCS, LLRT is an effective treatment approach, particularly for patients with G1 NETs and limited tumor burden. In this study, RCS patients that received LLRT, and other systemic therapies had comparable PFS. Treatment decisions should be made after a comprehensive patient evaluation, considering factors such as ECOG, liver involvement patterns and primary tumor localization.

**Legal entity responsible for the study:** The authors.

**Funding:** Has not received any funding.

**Disclosure:** G. Mendez Honoraria (self): Merck, MSD, BMS, Roche, Amgen, Servier, Biotoscana Lab, Eli Lilly, Pfizer; Advisory / Consultancy: Merck, BMS, MSD, Pfizer; Speaker Bureau / Expert testimony: Merck, MSD, BMS, Roche, Amgen, Servier, Biotoscana Lab, Eli Lilly, Pfizer; Travel / Accommodation / Expenses: Servier, Pfizer, Amgen, Merck. All other authors have declared no conflicts of interest.

<https://doi.org/10.1016/j.annonc.2023.04.346>

**P-291 Missing colorectal liver metastases after neoadjuvant chemotherapy: Can we improve the prognosis?**

E. Fernandez de Sevilla<sup>1</sup>, M. Collard<sup>1</sup>, I. Sourrouille<sup>1</sup>, L. Benhaim<sup>1</sup>, C. Smolenschi<sup>2</sup>, V. Boige<sup>1</sup>, M. Ducreux<sup>1</sup>, M. Gelli<sup>1</sup>

<sup>1</sup>Gustave Roussy, Villejuif, France; <sup>2</sup>Département de Médecine Oncologique, Gustave Roussy, Villejuif, France

**Background:** Complete disappearance of colorectal liver metastases (CLM) after chemotherapy is considered a good prognostic factor of survival, but the presence of residual tumoral cells arrives to 80% and recurrence rate to 75% of patients. Nowadays, the management of these patients is still controversial. The aim of this study is to evaluate the impact of different onco-surgical strategies in the management of missing metastases after chemotherapy (MM) for patients who undergo a curative surgery.

**Methods:** This retrospective single-center study (1999-2019) includes 69 patients with  $\geq 1$  MM. The patients have been divided into 2 groups: Patients with hepatic arterial infusion (HAI) of chemotherapy (HAI group) and patients without HAI chemotherapy (non-HAI) after surgery. Overall survival (OS), progression free survival (PFS), liver recurrence (LiR) and local recurrence (LoR) have been analyzed in each group.

**Results:** In total, 312 MM of 779 initial CLM have been identified with a median number of 2 (1-5) MM/patient. Ten patients (14%) were resected of original site of MM with a complete pathological response rate (TRG1) of 20% (n=2). 5y-LiR rate was 55% vs 79% (NS) for both groups (HAI and non-HAI groups). The 5y-PFS and 5y-OS were of 51% vs 38% et 59% vs 65% for the HAI and non-HAI groups (NS).

**Conclusions:** Highly chemo sensitive patients who present MM have favorable long-term outcomes in survival. The high rate of residual tumoral cells in resected metastases makes consider that resection of original sites of MM is strongly recommended when it is possible. HAI chemotherapy after surgery does not significantly decrease the risk of local and hepatic recurrence in these patients presenting a great response to chemotherapy.

**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.2023.04.347>

**P-292 The Meta-Lung score: Preoperative clinical score in lung-limited metastatic patients with colorectal cancer**

P. Ziranu<sup>1</sup>, P. Ferrari<sup>2</sup>, F. Guerrero<sup>3</sup>, P. Bertoglio<sup>4</sup>, A. Tamburrini<sup>5</sup>, P. Lyberis<sup>3</sup>, A. Pretta<sup>1</sup>, G. Grimaldi<sup>2</sup>, E. Lai<sup>6</sup>, M. Santoru<sup>2</sup>, M. Dubois<sup>1</sup>, L. Riva<sup>2</sup>, F. Bardanzellu<sup>1</sup>, V. Pusccheddu<sup>1</sup>, F. Mathieu<sup>7</sup>, A. Alzetani<sup>5</sup>, L. Luzzi<sup>7</sup>, P. Solli<sup>4</sup>, P. Paladini<sup>7</sup>, E. Ruffini<sup>3</sup>, R. Cherchi<sup>1</sup>, M. Scartozzi<sup>1</sup>

<sup>1</sup>Medical Oncology Unit, University Hospital and University of Cagliari, Monserrato, Italy; <sup>2</sup>Division of Thoracic Surgery at "A. Businco Cancer Center", A.R.N.A.S. Brotzu, Cagliari, Italy; <sup>3</sup>Division of Thoracic Surgery, Cardiovascular and Thoracic Department, Città della Salute e della Scienza, University of Turin, Turin, Italy; <sup>4</sup>Department Thoracic Surgery, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; <sup>5</sup>Department of Thoracic surgery, University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom; <sup>6</sup>Medical Oncology Department, Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milan, Italy; <sup>7</sup>Thoracic Surgery Unit, Cardio-Thoracic and Vascular Department, University Hospital of Siena (Azienda Ospedaliera Universitaria Senese, AOUS), Siena, Italy

**Background:** Radical resection of isolated lung metastases (LM) from colorectal cancer (CRC) is debated. Without specific recommendations, the therapeutic approaches discussed for liver metastases are often applied to treating LM, despite differences in their biological behavior. Our study proposes the identification of a score that correlates with clinical outcomes in CRC patients undergoing lung metastasectomy, aiming better to select the most appropriate surgical and therapeutic intervention.

**Methods:** We retrospectively collected data from 260 pts (aged 18-85) who underwent CRC lung metastasectomy with curative intent from December 2002 to January 2022 at four Italian Centers: the Division of Thoracic Surgery at "A. Businco Cancer Center" in Cagliari, the Division of Thoracic Surgery at "Città della Salute e della Scienza" in Turin, the Department of Thoracic Surgery at "IRCCS Azienda Ospedaliero-Universitaria" in Boulogne, and the Medical Oncology Unit of the University Hospital of Cagliari. We verified the impact of different clinicopathological features on overall survival (OS). Statistical analysis was performed with MedCalc (survival distribution: Kaplan-Meier; survival comparison: log-rank test; association between categorical variables: Fisher's exact test).

**Results:** We analyzed the impact of different clinicopathological features on OS. At the univariate analysis, altered baseline CEA levels ( $p=0.0001$ ), disease-free survival (DFS) less than or equal to 12 months ( $p=0.0043$ ), lung metastasis size larger than 2 cm ( $p=0.0187$ ), multiple resectable nodules ( $p=0.0083$ ), and positive lymph node status of the primary tumor ( $p=0.0011$ ) were associated with poor prognosis. In a COX regression model, these features maintained their independent role for OS ( $p <$

0.0001). BRAF mutation is also associated with a worse prognosis ( $p=0.02$ ). As expected, mutated BRAF was underrepresented in this population (3%), so it was not considered in the score. Other variables evaluated did not show a significant correlation with OS. We assigned one point for each feature, and the resulting score (the Meta-Lung Score) was compared with the patient's clinical outcome after metastasis resection, proving to be highly predictive of long-term outcomes ( $p < 0.0001$ ). The 5-year survival rate in patients with 0 points was 88%, while no patients with a 5-point score survived at 2 years. In order to stratify favorable and poor prognosis patients, we compared the 0-2 versus 3-5 score range, obtaining a significant difference in median OS: 101.7 m (95%CI 64.6 - 101.7) vs. 39.5 m (95%CI 27.3 - 87.5), respectively ( $p < 0.0001$ ).

**Conclusions:** The Meta-Lung Score provides valuable prognostic information to identify patients most benefit from early surgery. Indeed, while upfront surgery should be considered in patients with scores of 0 to 2, it should be cautiously suggested in patients with scores of 3 to 5, for whom early chemotherapy would allow better assessment of tumor biology and appropriate selection for metastasectomy.

**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.2023.04.348>

### P-293 A single institution experience of SBRT treatment for liver metastases and primary liver tumours

I. Oblak, A. Secerov-Ermenc, D. Grabec, N. Boc, A. Jeromen Peressutti, P. Korosec, G. Praprotnik, V. Zager Marcicus

*Institute of Oncology, Ljubljana, Slovenia*

**Background:** Most malignancies of the liver are metastases and most of them originate from colorectal cancer. The primary treatment for oligometastatic colorectal cancer metastases is surgical resection. Unfortunately, only about 20% of them are suitable for surgical resection due to various reasons, such as unresectability, comorbidity or the patient's preferences. For these and other patients with oligometastatic liver metastases or primary liver tumours, other local treatment methods are available, including stereotactic body radiotherapy (SBRT). SBRT is a novel radiation therapy technique that allows precise delivery of a high dose to a lesion with minimal dose to adjacent healthy tissues. It is a non-invasive painless method where the patient does not need anaesthesia and is performed on an outpatient basis. It provides 70-100% local control and 60-90% overall survival at 2 years and has a favourable toxicity profile.

**Methods:** Between April 2018 and August 2022, 58 (25 female, 33 male) patients with solitary liver metastases or primary liver tumours were treated. With most of the patients only one lesion was treated, with 8 patients 2 lesions and with 2 patients 3 lesions. The majority of the treated lesions were metastases of colorectal cancer, followed by primary liver tumours, breast cancer metastases, and the rest that are rarer. The treatment decision was adopted on the multidisciplinary advisory board. One week before simulation, 3 fiducial markers were inserted in the proximity of the liver lesion with ultrasound guidance by a radiologist. 4-D CT scan was used for simulation and patients were immobilized with vacuum cushion to ensure maximal accuracy and reproducibility of the treatment. An abdominal compression device or active breathing control system was used to reduce the motion of the organs related to respiratory excursion. Multi-modal imaging with MRI or PET CT was performed for better target definition. In general, we used  $3 \times 18$  to 20 Gy for covering the periphery of the target volume, depending on whether the lesion was  $\leq 3$  cm or  $> 3$  cm. In the rare cases, where we have not been able to meet the restrictions, we have made adjustments. Three-dimensional image guided radiation therapy (IGRT) with cone beam CT was performed before each fraction in order to assess the position of the patient and the tumour. Patients were irradiated every other day and closely monitored during and after treatment.

**Results:** The median follow-up time was 24 months (range 6-55 months). At 1 and 2-years local control was 80.8% and 80.8%, disease free survival was 50.8% and 42.6% and overall survival was 94.2% and 82.7%, respectively. One patient had liver hematoma after ultrasound-guided implantation of fiducial markers, but did not require any intervention. One patient experienced G3 nausea and one non-specific abdominal pain, which resolved with symptomatic therapy. In the laboratory results we observed a transient rise of transaminases, but it was clinically silent.

**Conclusions:** We can conclude that SBRT is a non-invasive, well-tolerated and effective treatment for patients with liver metastases and primary liver tumours.

**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.2023.04.349>

### P-294 The outcome of patients with mismatch repair deficient esophagogastric cancer receiving immunotherapy: A systematic review

R. Karia<sup>1</sup>, A. O'Brien<sup>1</sup>, A. Mahipal<sup>1</sup>, S. Chakrabarti<sup>2</sup>

<sup>1</sup>University Hospitals Seidman Cancer Center and Case Western Reserve University, Cleveland, United States; <sup>2</sup>University Hospitals Cleveland Medical Center, Cleveland, United States

**Background:** Remarkable anti-tumor activity of immune checkpoint inhibitors (ICI) in patients with deficient mismatch repair (dMMR) solid tumors prompted studies with ICI-based immunotherapy in patients with early and advanced stage dMMR esophagogastric cancer (EGC) with promising preliminary results. However, these studies have enrolled a modest number of patients limiting their interpretation. Therefore, we systematically reviewed the published studies to provide a comprehensive overview of the outcomes of dMMR EGC patients treated with ICI.

**Methods:** MEDLINE, Scopus, Embase, Web of Science, and Cochrane Central Register of Controlled Trials were searched for publications, including case reports, case series, retrospective studies, and clinical trials reporting the outcome of patients with early-stage (stage I-III) or metastatic dMMR EGC treated with ICI. The primary outcome measures were the overall response rate (ORR) and the incidence of grade 3 or higher toxicities. The review was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

**Results:** The search identified 24 publications that included 208 patients treated with ICI- 51 with early-stage dMMR EGC and 157 with metastatic dMMR EGC. The median age of the cohort was 67 years (range 34 to 92), and 43% (n=90) of patients were female. The treatment consisted of single-agent anti-programmed receptor death 1(PD-1) agents in 174 (77%) patients and dual checkpoint inhibitors (anti-PD1 agent + anti-cytotoxic T-lymphocyte associated protein 4[CTLA4] agent) in 34 (23%) patients. The median duration of treatment was 3 months (range, 1 to 24). Only 2 patients had disease progression on ICI. Among the patients undergoing surgery (n=67) after treatment with ICI, all patients achieved R0 resection, and 27 (40%) patients achieved pathologic complete response (pCR). There was no report of delayed surgery as a result of ICI toxicity. Among the patients in whom radiologic response information was available, the overall response rate (ORR) was 58% (86/148)- 11 ( 8% ) complete responses, and the rest were partial responses. The median progression-free survival ranged from 2 to 24 months among various reported publications. Grade 3 or higher toxicity related to ICI treatment was reported in only 2 publications- 6/32 (19%) in one and 2/6 (33%) in the other. No death was reported related to ICI toxicity.

**Conclusions:** ICIs have substantial anti-tumor efficacy in patients with dMMR EGC, evidenced by a high response rate, both in early-stage and advanced disease settings. In patients undergoing surgery, ICI administration was associated with a high rate of R0 resection and did not delay planned surgery. Disease progression on ICI was rare. ICIs have an excellent safety profile in patients with dMMR EGC. The findings of this systematic review support further investigation of ICI in patients with dMMR EGC, both in early-stage and advanced settings.

**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.2023.04.350>

### P-295 Retrospective cohort study of trifluridine/tipiracil plus bevacizumab versus trifluridine/tipiracil monotherapy for metastatic colorectal cancer: A real-world data from 4 hospitals in Portugal

M. Menezes<sup>1</sup>, J. Araújo<sup>2</sup>, F. Fonseca<sup>3</sup>, D. Neto da Silva<sup>4</sup>, C. Trabulo<sup>5</sup>, I. Dunoës<sup>1</sup>, G. Baió<sup>3</sup>, I. Bastos<sup>3</sup>, A. Oliveira<sup>1</sup>, M. Inácio<sup>1</sup>, R. Dinis<sup>1</sup>

<sup>1</sup>Hospital Espírito Santo, Evora, Portugal; <sup>2</sup>Hospital de Santa Maria - Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal; <sup>3</sup>Hospital Espírito Santo, Evora, Portugal; <sup>4</sup>Hospital Beatriz Angelo, Lisbon, Portugal; <sup>5</sup>Centro Hospitalar Barreiro Montijo, EPE, Barreiro Montijo, Portugal

**Background:** Colorectal cancer (CRC) is the second leading cause of cancer-related mortality worldwide and in Portugal. Trifluridine-tipiracil (TAS-102) has shown significant overall survival benefit compared with placebo in patients with chemorefractory metastatic CRC (mCRC) in C-TASK FORCE and SUNLIGHT. This retrospective study aimed to investigate the safety and efficacy of TAS-102 plus bevacizumab (TAS-Bevacizumab) with TAS-102 monotherapy in patients with pretreated mCRC in 4 hospitals in Portugal.

**Methods:** Records of patients with mCRC refractory to chemotherapy who initiated TAS-102 in 1 hospital and TAS-Bevacizumab in 4 different hospitals in Portugal since 2018 to March 2023 were retrospectively reviewed. Statistical analyses were done using SPSS (v26). Progression-free survival curves were estimated by the Kaplan Meier method, with comparisons done by the logrank test. Hazard ratios and corresponding 95% CIs were estimated by Cox proportional hazard regression. In all analyses, a two tailed p-value of less than 0.05 was deemed to be significant.