## P-284 Stereotactic body radiotherapy (SBRT) for liver metastasis of colorectal and anal cancer patients: Clinical outcomes of a single centre experience

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**Background:** Hepatic resection of liver metastases (LM) has become the standard therapy in many patients with CCR cancer, increasing the survival rate. Nevertheless, most patients have unresectable LM or are unsuitable for a surgical procedure. Stereotactic body radiotherapy (SBRT) is an emerging treatment option with a control rate of 70-90% and low toxicity profile. The objective of this study is to analyse the outcomes of SBRT in LM from colorectal and anal cancer patients and determine prognostic factors in this setting.

**Methods:** Patients with LM of colorectal or anal cancer treated with SBRT from 2014 to 2022 in Hospital de la Santa Creu i Sant Pau were analysed. Clinical characteristics from LM and molecular status were collected to assess the predictive value after SBRT with univariate and multivariate analysis by Cox regression. Overall survival (OS), progression free survival (PFS) and local control were analysed by Kaplan Meier and log rank test.

**Results:** The study included 30 patients, 70% males and 30% females with a median age of 78 years (31-88 years). The most common primary tumour was left colon cancer (50%) with two patients with anal cancer. Ten patients had a LM resection previous to SBRT and 50% had prior chemotherapy. Median tumour size was 25mm (6.6-77 mm), median SBRT dose was 54 Gy (33-60 Gy) with a median of 3 fractions (3-5 fractions). SBRT was tolerated well with mild toxicity. Twelve patients had a NRAS/KRAS or BRAF mutation, eight patients were wild type and ten patients did not have molecular data. At a median follow-up of 21 months (3 -57 months) the OS was 26.7 months and the median PFS of 6.2 months. Local control of the LM treated with SBRT was of 73.3%. Multivariate analysis showed that mutated molecular status was an independent bad prognostic factor for PFS. Patients with KRAS/NRAS/BRAF mutation had a median PFS of 3 months compared to 9.7 months in wild type patients (HR 0.12; 95% CI 0.02-0.70; p=0.019).

**Conclusions:** The results of this study are comparable to data published regarding good local control rates of SBRT and low toxicity profile. Our study suggests that molecular status can predict a worse control rate in those patients with mutated tumours. These findings suggest that we should include the molecular status in the decision-making discussion for local treatments of LM of colorectal cancer patients.

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## P-285 Basket trials in upper gastrointestinal and hepato-pancreatico-biliary cancers – an emerging entity

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**Background:** Upper gastrointestinal (GI) and hepato-pancreatico-biliary (HPB) cancers have poor prognoses and limited therapeutic options. Basket trials are being increasingly employed in these disease groups and have led to regulatory approvals for tumour agnostic prescribing. This study aimed to explore the success of emerging basket trials including patients with upper GI and HPB cancers, assessing phase of trial, agents used, selection biomarkers and endpoints favoured.

**Methods:** A systematic review was conducted using the combined Ovid and Medline databases, including publications released up to and including April 2022, looking for primary studies reporting the results of basket trials in which patients with upper GI and HPB cancers were eligible for enrolment. A supplementary search on ClinicalTrials.gov was conducted in July 2022. Data on trial duration, treatment used, and endpoints recorded, were collected.

**Results:** The literature search identified 164 studies, while ClinicalTrials.gov identified 74: 23 ineligible studies were excluded, based on irrelevance to oncology; the remaining 215 studies were assessed. Fifty-three eligible basket studies were identified; 33 (62%) industry led, 20 (38%) academic. Of the 53 trials (non-randomised), 30 (57%) were phase II, 16 (30%) combined phase I/II and 7 (13%) were phase I; conducted in multiple institutions (not mutually exclusive): USA (N=34), Asia (N=28), Europe (N=17), Australia (N=6), Africa (N=1). The commonest therapeutic agents used were immunotherapy (N=16 (30%)), followed by PARP inhibitors (N=9 (17%)), EGFR inhibitors and HER2-directed agents (N=8 (15%) each). The biomarkers for entry selection were HER2 (N=10 trials), tumour mutation burden, DNA damage repair genes and BRAF/MEK (N=5 trials each), CDKN2A, NTRK, PDL1, NF1 (N=3 each), IDH1/2 (N=2), EGFR, VEGF, FGFR, KRAS (N=1 each), other (N=6). Ten trials did not require biomarker selection for entry. Eighteen trials had either full or interim results reported: N=407 total patients had advanced, previously-treated upper GI/HPB cancers (performance status 0-2) (range 1-43 per trial). The patients had biliary tract cancer (BTC) (N=249 (61.2%)), Oesophago-gastric (OG) (N=82 (20.1%)), pancreatic (N=38 (9.3%)), small bowel (N=36 (8.8%)), and hepatocellular carcinoma (HCC) (N=2 (0.5%)). The primary endpoint for 49 of 53 trials (92%) was response rate (RR). Median RR for all upper GI and HPB cancers across all 18 reported trials was 18.2%. Upper GI cancers had a median RR of 25%, HPB cancers 17.5% and HCC 0%. Five agents (from 18 trials) (28%) have gained tumour agnostic prescribing approval in these disease groups, based on these results: Pembrolizumab, Larotrectinib, Entrectinib, Dostarlimab and Dabrafenib combined with Trametinib.

**Conclusions:** The trials included in this study were early phase, conducted mainly in USA, Asia and Europe, with the most favoured therapeutic agents used being immunotherapy, likely reflecting the era of study. More patients with BTC were included, possibly due to more limited treatment options for rarer malignancies. The majority reported RR as the primary endpoint, allowing earlier read outs, with promising tumour agnostic approval in these disease groups. Evolving basket trial and statistical methodology with dedicated cohorts for these patients with emerging subgroups, will potentially lead to improved patient outcomes.

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## P-286 Clinicopathological profile and outcomes in locally advanced rectal cancer with major pathological response following neoadjuvant therapy

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**Background:** The standard management of locally advanced rectal cancer (LARC) is neoadjuvant chemoradiotherapy (CRT) combined with carcinologic resection. This approach has resulted in down-sizing and down-staging of the tumour. A major pathological response (ypT0-1 N0) is associated with better survival, less local recurrence, and less distant failure. We aimed to describe clinicopathological features and the key determinants of outcome among Tunisian patients with major pathological response.

**Methods:** We conducted a retrospective study including patients diagnosed with rectal cancer in the medical oncology department at Salah Azaiz Institute in Tunisia over a six-year-period (January 2015 to December 2021) who underwent neoadjuvant long course CRT. We categorized them based on the histological response and distinguished those with a major histological response.

**Results:** One hundred and five patients were included. Thirty-two patients had a major pathological response (30.4%). In this category, the mean age at diagnosis was 57.8 years. The sex-ratio was 0.6 with a female predominance. Preoperative carcinoembryonic antigen (CEA) level was elevated in 4 patients (12.5%). According to pelvic magnetic resonance imaging (MRI) assessment, tumor was staged as cT4 in 6 patients (19%) and most patients were diagnosed with stage III RC (75%). Median radiation dose was 50Gy. The median time from neoadjuvant therapy to surgery was 11.7 weeks. Anterior resection and abdominoperineal amputation were performed in 62.5% and 37.5% respectively. Twenty patients had complete pathological response (ypT0N0) and 12 patients showed a nearly pathological complete response (ypT1N0). Adjuvant CT was administered in 40% of cases. After a mean follow-up of 51 months, tumor recurrence was noted in 3 patients. The disease free survival (DFS) rate at 5 years was 93.6%. In univariate analysis, factors associated with better PFS were: age $<$ 70 years (p=0.019), female gender (p=0.042), endoscopic tumor size $<$ 40mm (p=0.007), normal initial CEA level (p=0.005), and non cT4 staging (p=0.026). In multivariate analysis, only non cT4 remains an independent prognostic factor of DFS (p=0.03). Overall survival rate at 5 years was 85.4%. In multivariate analysis, independent prognostic factors for better OS were tumor size $<$ 40 mm (p=0.04), normal initial CEA level (p=0.03), and non cT4 (p=0.030).

**Conclusions:** In our study, major pathological response had a survival rate of over 85% during follow-up. Multivariate analysis identified tumour size, preoperative CEA level and clinical TNM stage as independent factors that affect survival.

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