manually delineated. Three families of hand-crafted features were extracted from the VOIs of each patient's images, from both CT and PET acquisitions, thus quantifying grey intensity and tissue texture. Statistical features consisted of the moments up to the fourth-order of the first-order image histogram, i.e., the mean, the standard deviation, the skewness and the kurtosis. Texture features were derived from the 3D gray-level co-occurrence matrix (GLCM) and from the Local Binary Patterns-TOP (LBP-TOP). The final dataset was then created by adding clinical data from each patient. The predictive pipeline consisted of a feature selection phase followed by a sequence of two cascading decision trees in which the second used the predictions of the first as additional features for sample prediction. In the training phase, this model optimised the binarization threshold for classification to be applied later in the testing phase. The whole system follows a ten fold cross-validation approach. The quality of the proposed model was appraised by means of receiver operating characteristics (ROC) and areas under the ROC curve (AUC).

Results: Given each 3D VOI in the images, we computed the radiomics features, taking into consideration 12 statistical features, 230 textural features (182 GLCM, 48 LBP-TOP) extracted from the images, and adding 15 clinical features. We defined the final performance. To the best of our knowledge, this is the first study for feasibility and hypothesis generation of a radiomic strategy to predict early progression in LAPC and our data suggests that a specific signature can be identified (AUC 0.83; prediction accuracy 80.7%).

Conclusions: This model based on clinical and PET/CT radiomic features assessed before treatment can predict the early progression in LAPC patients. It could be a promising pre-treatment, non-invasive, approach that can assist physicians in evaluating the risk of early progression in patients individually, and thus achieving a personalized treatment and better clinical outcomes. The identification of the external validation dataset is actually ongoing.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosures: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.156

P-67 Comparison of the malignant predictors in intrahepatic and extrahepatic intraductal papillary neoplasm of bile duct

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Background: Intraductal papillary neoplasm of the bile duct (IPNB) is a precancerous lesion of cholangiocarcinoma, for which surgical resection is the most effective treatment. We evaluated the predictors of malignancy in IPNB according to anatomical location and the prognosis without surgery.

Methods: A total of 196 IPNB patients who underwent pathologic confirmation by surgical resection or endoscopic retrograde cholangiography or percutaneous transhepatic cholangioscopic biopsy were included. Clinicopathological findings of IPNB with invasive carcinoma or mucosal dysplasia were analyzed according to anatomical location.

Results: Of the 116 patients with intrahepatic IPNB (I-IPNB) and 80 patients with extrahepatic IPNB (E-IPNB), 62 (53.4%) and 61 (76.3%) were diagnosed with invasive carcinoma, respectively. Multivariate analysis revealed that mural nodule $>$ 12 mm ($p=0.043$) in I-IPNB and enhancement of mural nodule ($p=0.044$) in E-IPNB were predictive factors for malignancy. Pathology discrepancy before and after surgery, IPNB has 71.2% of sensitivity and 82.3% of specificity. In the non-surgical IPNB group, composed of nine I-IPNB and seven E-IPNB, 43.7% progressed to IPNB with invasive carcinoma within 876 days.

Conclusions: E-IPNB has a higher rate of malignancy than I-IPNB. The predictive factor for malignancy is mural nodule $>$ 12 mm in I-IPNB and mural nodule enhancement in E-IPNB.

Legal entity responsible for the study: The author.

Funding: Has not received any funding.

Disclosures: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.157

P-68 Regorafenib monotherapy as second-line treatment of patients with RAS-mutant advanced colorectal cancer (STREAM): An academic, multicenter, single-arm, two-stage, phase 2 study

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Background: Therapeutic options after first-line treatment in patients with RAS mutant metastatic colorectal cancer (mCRC) are limited by poor clinical outcomes and lack of activity of anti-epidermal growth factor receptor drugs. Maintaining angiogenesis inhibition and switching the chemotherapy backbone represents the current therapeutic strategy of second-line mCRC therapy. Regorafenib, an oral broad-spectrum multikinase inhibitor targeting angiogenesis, has been shown to prolong overall survival (OS) and is approved after progression on chemotherapy.

Methods: STREAM trial was an academic, multicentric, phase 2, single-arm, Simon's two-stage design, aimed to establish the activity of regorafenib, defined as the rate of patients alive and progression free after 6months from study entry (6mo-PFS) in patients with RAS mutant mCRC, after progression on fluoropyrimidine, oxaliplatin and bevacizumab.Setting α and β errors at 0.10, defining a 6mo-PFS rate of 30% as p0 and 50% as p1, to consider the study positive $\geqq$8 patients without progression at 6mo, were needed in the first stage (N=22) and $\geqq$18 in the overall population (N=46). Regorafenib was administered orally at the approved schedule of 160mg day1-21 q28. Secondary endpoints were the evaluation of toxicity, objective response rate (ORR), progression-free survival (PFS), OS. Early metabolic response assessed by PET-CT scan after 2 weeks of treatment was an exploratory endpoint. Translational analyses are ongoing and will be presented at a later stage.

Results: Between November 2015, and December 2020, 46 patients were enrolled. median age was 67ys; 80.4% had ECOG performance status 0, 32.6% single organ involvement, 26% lung-limited disease. The study did not meet its predefined primary endpoint. Eight of the first 22 patients and 14 in the overall population were 6mo-PFS, as compared to the 18 required by the study protocol. At a median follow-up of 50.2 months (95%CI=24.2-56.3), ORR was 10.9%, Disease Control Rate (DCR) was 54.6%, median (m)PFS was 3.6mo (95%CI=1.9-6.7).Despite the short mPFS, regorafenib did not preclude a subsequent treatment: mPFS2 (from study entry to progression to subsequent treatment line) was 13.3mo (95%CI=8.4-19.7) and mOS was 18.9mo (95%CI=10.3-35.3). No unexpected toxicity was reported. Grade$\geq$3 AEs occurred in 18 patients(39.1%), mostly hand foot syndrome(13%), fatigue and bilirubin increase(6.5%). Early metabolic response with PET/CT was not associated with ORR, mPFS and mOS. Baseline metabolic assessment, not predictive of ORR and mPFS, was significantly associated with mOS. A subgroup of patients, with single organ involvement, mostly lung-limited disease, low baseline PET-CT parameters, a low rate of early progression in first line ($<$6months=21.4%) and a long mPFS2 (23.3mo 95%CI=13.3-39.9), reported a long disease control with regorafenib: ORR=35.7%; mPFS=10.2mo (95%CI =8.6-13.5), mOS=38.8mo (95%CI=23.9-NR). Conversely, patients with higher radiological and metabolic burden of disease, higher rate of early progression in first-line ($<$6months=56.3%) and a shorter mPFS2 (8.4mo CI95%=6.1-13.3), reported unfavorable outcomes.

Conclusions: Despite the study did not meet its primary endpoint, treatment with regorafenib had no unexpected toxicity and did not preclude efficacy of subsequent treatments. A subgroup of patients characterized by good prognostic features (limited disease, lung metastasis and low metabolic burden) had clinical benefit with regorafenib. Appropriate patients selection might guide the clinical development of regorafenib in an earlier setting, ensuring a chemotherapy-free interval in the treatment sequence.

Clinical trial identification: EudraCT Number: 2015-001105-13.

Legal entity responsible for the study: The authors.

Funding: Partially supported by Bayer.

Disclosures: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.158