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Somatostatin analogs (SSA) were increasingly used as bridging strategy for delaying surgery (32%), and were self-injected or delivered by home care service in 36% and 49% of cases respectively. Treatment breaks of targeted therapies (17%), PRRT (13%), or chemotherapy (9%) were also proposed. Patients with advanced NET were considered a priority group for vaccination (94%), but not those with resected NET (19%).

Conclusions: COVID-19 pandemic paved the way towards telemedicine in many institutions. While systemic treatments were generally continued, surgical interventions were delayed in 55% of cases. Regarding SSA, home care service or self-injections have been used more frequently. As the pandemic evolves, new data will be needed to design future health policy measures.

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New prognostic frontiers for lung neuroendocrine tumors: An Italian-Spanish multicentric study of 200 cases

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Background: Well-differentiated neuroendocrine tumors of the lung (Lung NET) are classified as typical (TC) and atypical (AC) carcinoids, on the basis of mitotic count and presence of necrosis. However, the identification of prognostic factors, other than TNM stage and histopathological diagnosis of AC versus TC, are still lacking.

Methods: We assessed the association of clinical and pathological data with survival in a multicenter retrospective series of 200 surgically resected lung NET from 8 Italian & 1 Spanish Institutions. Patients data were collected and analysed by SPSS program.

Results: The study population presented a median age of 60 years (13-86), 40.0% presented a male gender, 31.5% were smokers, 31.0% AC, 40.5% left-sided tumors, 36.5% with a peripheral location. I&II TNM stages at diagnosis were present in 84.5% of cases, with 25% nodal positive status. Mitotic count \geq 2/10 HPF in 31%, necrosis in 17.5%, Ki67 >20% in 8 patients (4%). The population had a median OS of 49 months (0.6-323), and a median PFS of 36.0 months (0.5-323). At Cox univariate regression model, male gender (p=0.0001, p=0.001), left side (p=0.001, p=0.015), nodal positive status (p=0.0001, p=0.0001), advanced TNM stage (p<0.0001, p<0.0001), mitotic count $\geq 2/10$ HPF (p=0.001, p=0.031), Ki67 > 20% (p=0.017, p=0.001), presence of necrosis (p=0.001, p=0.04), and AC histotype (p=0.0001, p=0.006), correlated with shorter PFS and OS, respectively. Tumoral peripheral location (p=0.038) correlated with shorter OS. At Cox multivariate regression analysis, gender (male vs female) (p=0.0057), tumor side (left vs right) (p=0.0118), advanced stage (p=0.0206), a Ki67 >20% and/or a mitotic count >10/10 HPF (p=0.0109), and the presence of necrosis (p=0.0010) were confirmed as independent prognostic factors in terms of PFS. Gender (male vs female) (p=0.0127), tumor side (left vs right) (p=0.0669) and advanced stage (p=0.0208) were independent negative prognostic factors for OS

Conclusions: This study confirm the prognostic relevance of TNM stage and of the diagnosis of AC, to stratify NET patients. Additionally, our analysis suggests a potential prognostic value for new clinical and pathological features, as male gender, left-sided primary tumor and high proliferation index.

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Modified TGR: A new strong radiological marker to accurately predict early response to PRRT in GEPNETs

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Background: To investigate the value of modified TGR (tumor growth rate) as radiological predictor of early response to PRRT, in GEPNET patients.

Methods: G1-G2 GEPNET patients treated with PRRT (177Lu-Oxodotreotide, 4 administrations, 7.4 GBq) at our centre from 04/2019 to 10/2020 were considered. Three CT/MRI scans per patient were collected: one performed within 3 months before PRRT, one interim evaluation after 2 PRRT and one within 4 months after the end of treatment to assess early response, according to RECIST1.1. All the scans were centrally re-evaluated by 2 dedicated radiologists. TGR was calculated in 2 ways: assuming the volume of lesions can be calculated applying the volume of a sphere formula (TGR_sphere, classical TGR formula, Dromain, BMC 2019) or the volume of an elliptical cylinder (TGR_ elliptical, new model). In both cases, to assess TGR, baseline versus interim evaluations were compared and the values were expressed as % increase/month. Patients were subdivided as responders (CR, PR, SD) and non-responders (PD), according to RECIST. Previous therapy lines were calculated as possible confounders. Fisher and K-Wallis test were applied to assess independence between response to treatment and patient characteristics. Logistic regression was performed to determine predictability of both TGR models, ROC analysis was applied to assess the performance of the 2 models and evaluate optimal TGR cut-off.

Results: Twenty-seven patients (12 males, 15 females, mean age 63.9, range 37-80) were evaluated. 15 (55.6%) were midgut, 12 (44.4%) foregut, 24 (88.8%). PRRT was applied in second line in 18 (66.6%), in third or further in 9 (33.4%). Considering RECIST, 4 (14.8%) were non-responders. Logist regression showed OR equal to 5.9 with AUC 0.95 (Sensitivity 75%, Specificity 95%) for TGR_elliptical model and OR 1.05 with AUC 0.75 (Sensitivity 25%, Specificity 75%), for TGR_spherical. The optimal cutoff value for progression prediction was 5.5% increase/month for TGR_elliptical (Sensitivity 100%, Specificity 86.4%) and 5.3%/month for TGR_sphere (Sensitivity 75%, Specificity 81.8%).

Conclusions: Interim TGR_elliptical is a strong and accurate predictor of early progression of GEPNET disease after PRRT. External validation is on course.

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