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Patients and methods

This retrospective study involved 116 consecutive patients surgically treated (R0) between 1998 and 2008 for AC and LCNEC in two Italian and French expert networks. Slides were reviewed by two expert pathologists to validate the histological definition (WHO 2004).

Results

The files of 86 patients were reviewed (49 males and 37 females). Mean age at diagnosis was 58 ± 15 years for AC and 63 ± 15 years for LCNEC. The most frequent presenting symptom was respiratory infection (AC: 24%, LCNEC: 31%); endocrine syndrome occurred in only one AC patient (Cushing's syndrome). Mean follow-up time was 80.6 months in AC and 50.6 months in LCNEC. The most used surgery was lobectomy (AC: 81%, LCNEC: 59%). N-positive status was found in 29 and 57% of AC and LCNEC respectively. The rate of recurrence was 39% among AC (15% local, 24% distant metastasis) and 41% in LCNEC (27% local, 14% distant metastasis). The mean time of recurrence from surgery was 24.6 months in AC and 15 months in LCNEC. Median OS was 5.4 years in LCNEC (not reached in AC). Median DFS was not reached in both histotypes. Recurrence rate was higher in N+ AC patients than in N0 ones (76 vs 24%).

Conclusion

Patients with lung AC and LCNEC experience a high rate of recurrence after surgery. Beside LCNEC patients, N-positive AC patients should be considered for adjuvant therapy and be subjected to an intensive monitoring on. A better definition of lung NETs prognosis and natural history is expected from large collaborative studies.

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P519**mTOR, AKT, p70S6K and ERK1/2 levels predict sensitivity to mTOR and PI3K/mTOR inhibitors in human bronchial carcinoids**

Teresa Gagliano¹, Mariaenrica Bellio¹, Erica Gentilin^{1,3}, Daniela Molè¹, Federico Tagliati¹, Marco Schiavon², Narciso Giorgio Cavallusco¹, Fiorella Calabrese², Maria Rosaria Ambrosio¹, Federico Rea², Ettore degli Uberti^{1,3} & Maria Chiara Zatelli^{1,3}

¹Section of Endocrinology, University of Ferrara, Ferrara, Italy; ²University of Padua, Padua, Italy; ³Laboratorio in rete del Tecnopolo "Tecnologie delle terapie avanzate" (LTTA) of the University of Ferrara, Ferrara, Italy.

Background

Bronchial carcinoids (BCs) are rare neuroendocrine tumors that are still orphan of medical treatment. Human BC primary cultures may display resistance to everolimus, an inhibitor of the mammalian target of rapamycin (mTOR), in terms of cell viability reduction.

Aim

To assess whether the novel dual PI3K/mTOR inhibitor, NVP-BEZ235, may be effective in everolimus-resistant human BC tissues and cell lines. In addition, we search for possible markers of mTOR inhibitors efficacy, that may help in identifying the patients that may benefit from mTOR inhibitors treatment, sparing them from ineffective therapy.

Results

NVP-BEZ235 is twice as potent as everolimus in reducing cell viability and activating apoptosis in human BC tissues that display sensitivity to mTOR inhibitors, but is not effective in everolimus-resistant BC tissues and cell lines, that by-pass cyclin D1 down-regulation and escape G0/G1 blockade. Rebound AKT activation was not observed in response to treatment with either mTOR inhibitor in 'resistant' BC cells. We also show that, in addition to total mTOR levels, putative markers of BC sensitivity to mTOR inhibitors are represented by higher AKT, p70S6K and ERK1/2 protein levels.

Conclusion

These data indicate that the dual PI3K/mTOR inhibitor NVP-BEZ235 is more potent than everolimus in reducing human BC cell proliferation. 'Resistant' cells display lower levels of mTOR, AKT, p70S6K and ERK1/2, indicating that these proteins may be useful as predictive markers of resistance to mTOR and PI3K/mTOR inhibitors in human BC.

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P520**Assessment of fatal events in patients with radio-active iodine (RAI)-refractory differentiated thyroid cancer responsive to treatment with sorafenib**

Vincenzo Marotta¹, Michela Del Prete¹, Valeria Ramundo¹, Francesca Marciello¹, Antonella Di Sarno², Raffaella Esposito¹, Annachiara Carratù¹, Chiara de Luca di Roseto¹, Luigi Camera³, Annamaria Colao¹ & Antongiulio Faggiano⁴

¹Department of Clinical Medicine and Surgery, Federico II University, Naples, Italy; ²IX Infectious Disease and Interventional Ultrasound Unit, "D. Cotugno" Hospital, Naples, Italy; ³Department of Biomorphological and Functional Sciences, Federico II University, Naples, Italy; ⁴Endocrinology, National Cancer Institute, "Fondazione G. Pascale", Naples, Italy.

Introduction

Targeted therapy with the multi-kinase inhibitor sorafenib is effective for treatment of differentiated thyroid cancer (DTC) unresponsive to RAI. Although kinase-inhibitors (KIs) are usually well tolerated, severe and even fatal adverse events are reported. Aim of the study was to assess incidence and characteristics of fatal events in patients with RAI-refractory DTC responsive to treatment with sorafenib.

Design

A retrospective analysis of patients with progressive iodine-refractory DTC subjected to off-label treatment with sorafenib in our centre was performed. Radiological response was assessed according to RECIST criteria version 1.1.

Results

From March 2010, 17 patients affected with RAI-refractory DTC were subjected to treatment with sorafenib. Of them, 12 subjects were responsive to treatment (seven achieved stable disease and five partial response). Median time of treatment for responding patients was 14 months. Fatal events were reported in five of 12 patients (42%). Three patients died from severe haemorrhage of the upper respiratory tract after 4 months of treatment. They had a wide tracheo-oesophageal neoplastic infiltration previously treated with external beam irradiation. Two subjects died from cardiac arrest after 10 months of treatment. They had developed a moderate hypertension after starting treatment with sorafenib.

Conclusions

Although treatment with sorafenib is effective in most patients affected with RAI-refractory DTC, it could be responsible of fatal events. Particularly, bleeding events and cardiac damage are considered as specific adverse events in subjects treated with KIs. In light of this, we suggest to exclude from treatment, or to use a reduced dosage, in those patients with mucosal neoplastic infiltration and those previously treated with radiotherapy. Furthermore, a careful and individualized cardiovascular management is mandatory.

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P521**Diagnosis of endogenous hyperinsulinism through arterial calcium stimulation with hepatic venous sampling**

Paloma Moreno Moreno¹, María Rosa Alhambra Exposito¹, Luis Zurera Tintero^{1,2}, Rafael Palomares Ortega¹, María Angeles Gálvez Moreno¹ & Pedro Benito López¹

¹Servicio de Endocrinología y Nutrición. Reina Sofia University Hospital, Córdoba, Spain; ²UGC de Radiodiagnóstico. Reina Sofia University Hospital, Córdoba, Spain.

Objective

The aim of this study was to assess the utility of arterial calcium stimulation with hepatic venous sampling (ASVS) in the localization of tumors in patients with endogenous hyperinsulinism not detected with other methods.

Patients and methods

We performed a retrospective study of 30 patients admitted to our hospital for hypoglycemia who underwent ASVS because the source of hyperinsulinism was not clearly identified by other imaging techniques. The histopathological results in patients who underwent a surgical procedure were considered the reference for statistical study of the accuracy of this technique. Statistical analysis was performed by comparing proportions with the χ^2 test with Yates' correction for contingency tables, and *Cohen's κ* coefficient as a measure of interrater agreement between two observations.

Results

Surgery was performed in 21 patients, 20 with positive ASVS and the remaining