Role of nuclear medicine in the treatment of GEP-NETs. The brazilian experience with PRRT: a first line therapeutic option?

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After the very encouraging results with more than 500 patients, obtained at the Erasmus University in Rotterdam, after our own experience with more than 30 patients who participated in the initial protocol, adding the availability of peptides, aminoacids that were necessary to

protect the kidneys, and radioisotope 177Lu, and after acquiring the labelling expertise of peptides with 177Lu at our national atomic energy agency (IPEN/CNEN) in Sao Paulo; learning from our oncologists about the need for better therapeutic options for treatment of metastatic GEP-NETs; we decided to start our treatment program for GEP-NETs in October 2006.

Initially, we used the same inclusion criteria used in the Netherlands, that means metastatic tumors, carcinoids or NETs of unknown origin, NE differentiation, Ki67 <10%, inoperable GEP-NETs. So surgery was not a therapeutic option, progressive disease since the goal of our therapy was palliation and not cure. Progressive disease was defined as such based on symptoms (including weight loss), tumor markers, or imaging. Also patients who had tachyphylaxis for somatostatin analogues were included.

Inclusion criteria were: tumor uptake on OctreoScan equas or higher than liver uptake (life expectancy at least 12 months), normal blood and kidney function (Hb ≥ 8.9 g/dl, WBC ≥ 2,000/mm^3, platelet count ≥ 80.000/mm^3, plasma creatinine ≤ 1.7 mg/dl, creatinine clearance >50 ml/min, Karnofsky Performance Status ≥ 50, and of course, a signed informed consent.

The administration protocol included 4 cycles of 177Lu-Octreotate with an interval ranging between 6 and 10 weeks. A rather long interval is due to logistics. Having the materials prepared in Sao Pablo is sometimes as complicated as the disease itself since we got the materials from the Netherlands. We pretreated the patients with antiemetics (Granisetron 1mg i.v.), 4-hour infusions of aminoacids to protect the kidneys, and 177Lu-Octreotate i.v. 30 min after the infusion. Patients were hospitalized for 24 hours.

Between October 2006 and May 2008, we treated 34 patients who received 107 doses. Thirty one patients were treated according to this protocol; twenty nine patients had GEP tumors, and 17 of them had a 3 months follow –up. At this point we performed an evaluation to compare our results with the Dutch results.

For acute toxicity, our results were very similar. We observed nausea (27%), vomiting (7%) and abdominal pain (24%). Also, 13% of patients had hair loss (grade 1 according to the WHO criteria).

As serious side effect, we analysed the hematological toxicity. One patient treated with a cumulative dose of 400 mCi developed grade IV (WHO criteria) pancitopenia. After the second dose this patient also presented a breast invasive ductal carcinoma that was simultaneously treated with chemotherapy.

Regarding to liver toxicity, 1 female patient (treated with one 100 mCi dose) who had hepatic failure and rapidly growing diffuse liver metastases, was treated outside the protocol. This patient died within weeks. So far we have not had any cases of renal failure.

At 3 -month follow up we can conclude that our results are comparable to those obtained in Rotterdam, in spite of our small amount of data.

In order to administer therapies like this in countries like ours, it is very important to consider the availability of the peptide and of lutetium, to have an isolation ward although with this kind of isotopes and the kind of radiation emitted this is not necessary. Disposal of radioactive waste might be a problem depending on the facilities in your hospital. Tumor dosimetry is always a complicated issue. A multidisciplinary team including surgeons, oncologists, nurses, and physicists is absolutely essential. Moreover, costs are expected to be high, mainly as for lutetium production.

In summary, the PRRT Rotterdam protocol was used in all patients. The PRRT in Brazil lead to good results with few side effects, in a disease with few therapeutic options. Using the same selection criteria and the same treatment protocol we obtained results similar to those presented by the Rotterdam group.

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