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ABSTRACT FINAL ID: 172;
TITLE: High dose Y-90-Ibritumomab-Tiuxetan with autologous stem cell transplantation in refractory-resistant NHL patients
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ABSTRACT BODY:
Objectives: Therapeutic options are limited for aggressive high-grade NHL pts not suitable to high dose chemotherapy. Y-90-Ibritumomab-Tiuxetan has already been demonstrated active in elderly pts with resistant-refractory DLBCL at standard activity, however response is usually of short duration. Increasing RIT dose-intensity could improve and prolong efficacy. We evaluated feasibility and toxicity of HD-Y-90-Ibritumomab-Tiuxetan with PBSC (peripheral blood stem cells) support in resistant-refractory NHL pts in a phase I/II study.

Methods: We enrolled 39 pts and treated 28 pts, as 11 of them failed stem cell mobilization. Median age was 68 yrs. 34/39 pts had advanced stage disease at diagnosis.

Three activity-levels were fixed: 30, 45, 56 MBq/kg. 4 pts received 30, 4 pts 45 and 20 pts 56 MBq/kg.

All pts underwent dosimetry: if no abnormal uptake was observed, they received the planned activity and then reinfused with PBSC previously harvested.

Results: Dosimetry showed acceptable radiation-absorbed doses to normal organs in all cases, except in 2 pts, both planned to receive 56 MBq/Kg and therefore excluded from the treatment.

All patients engrafted promptly without differences among the 3 activity levels.

Median adsorbed doses were (mGy/MBq): 0.8-0.2(RM), 3.0-1.7(heart wall), 1.7-0.8(lungs), 3.9-2.3(liver), 2.5-1.6(spleen), 2.2-1.1(kidneys), 3.0-1.0(testes), 0.6-0.1(total-body). At present 24/28 pts are evaluable for response after a median follow up of 14 months: 10 pts showed CR, 4 pts reached a PR. 6/10 CR patients were treated at the highest activity level.

Conclusions: Y-90-Ibritumomab-Tiuxetan at myeloblative activity is feasible with PBSC support and it could be safely delivered in elderly and heavily pretreated pts.

It is mandatory to perform dosimetry in order to prevent toxicity. Clinical efficacy and mild treatment-related toxicities suggest further investigation.

References: The role of dosimetry in the high activity 90Y-ibritumomab tiuxetan regimens: two cases of abnormal biodistribution.

High activity 90Y-ibritumomab tiuxetan (Zevalin) with peripheral blood progenitor cells support in patients with refractory/resistant B-cell non-Hodgkin lymphomas.


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Objectives: Incorporation of biological information from PET/CT imaging into tumor volume delineation will potentially improve radiation treatment planning (RTP) and treatment outcomes. We investigated the feasibility of using parametric images derived from dynamic $^{18}$F-fluorodeoxyglucose (FDG) and $^{18}$F-fluoromisonidazole (FMISO) studies to improve the distinction between cancerous and normal tissue and to generate dose-escalated IMRT plans to hypoxic sub-volumes.

Methods: FDG flux ($K_{FDG}$) and FMISO flux ($K_{FMISO}$) images were generated using a 2-tissue compartmental model for an advanced head and neck cancer patient and were co-registered to the treatment planning CT using the Philips PINNACLE® RTP software. IMRT plans were generated with 7 coplanar 6-MV photon beams in a half-beam blocked arrangement with supraclavicular AP fields to deliver an initial dose of 70 Gy to the primary PTV, 63 Gy to affected nodes, and a simultaneous integrated boost of 10 Gy to the FMISO sub-volume without added morbidity to surrounding normal tissues. The primary PTV was defined with a customized 1-cm margin around the GTV defined by an iso-contour (35% of maximum) of the $K_{FDG}$ image. The boost targets were defined by an iso-contour (50% of maximum) of the $K_{FMISO}$ image with no margin.

Results: Primary PTV dose coverage was mean 76 Gy, D95 of 69 Gy. FMISO GTV dose coverage was mean 81 Gy, D95 of 80 Gy. Both parotid glands were spared with mean doses of 24 and 23 Gy. The cord dose was below 45 Gy.

Conclusions: We demonstrate the feasibility of using parametric imaging from dynamic FDG and FMISO studies for delineating gross tumor volume and in directing dose-escalated IMRT to hypoxic sub-volumes of head and neck cancer. Further studies are needed to compare static imaging and dynamic imaging to influence RTP decisions in patients with head and neck cancer.

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SESSION TITLE: Oncology: Image Guided Therapy
OBJECTIVES: 89Zr-ibritumomab-tiuxetan-PET can be used to monitor biodistribution of 90Y-ibritumomab-tiuxetan (Zevalin) as shown in mice. The aim of the present study was to assess biodistribution and radiation dosimetry of Zevalin in humans and to evaluate whether co-injection of a therapeutic dose of Zevalin influences biodistribution of 89Zr-ibritumomab-tiuxetan.

METHODS: Six patients with relapsed B cell NHL scheduled for autologous stem cell transplantation underwent PET scans at 1, 72 and 144 h after injection of 74 MBq 89Zr-ibritumomab-tiuxetan and again after co-injection of 14.8 MBq/kg Zevalin, both times pretreated with 250 mg/m² rituximab. Volumes of interest were drawn over liver, kidneys, lungs, spleen and tumors. Zevalin absorbed doses were calculated using Olinda. Red marrow dosimetry was based on blood samples. Tumor doses were calculated using an exponential fit. Agreement between uptake prior to and during therapy was assessed using intraclass correlation coefficients (ICC).

RESULTS: Highest 90Y absorbed dose was seen in the liver (4.4±2.5 mGy/MBq), followed by spleen, kidneys and lungs. Red marrow dose was 0.7±0.1 mGy/MBq. Effective dose was 0.7±0.2 mSv/MBq. Tumor doses ranged from 9 to 29 mGy/MBq. Pre-therapy and therapy uptake in source organs showed a high agreement (ICC = 0.97, mean difference 5 ± 15%). Agreement between predicted 90Y effective doses was high as well (ICC = 0.91). No significant difference between pre-therapy and therapy tumor doses was found, but correlation was lower (ICC 0.75, mean difference 5 ± 33%).

CONCLUSIONS: Biodistribution of 89Zr-ibritumomab-tiuxetan is not influenced by simultaneous therapy with Zevalin. Absorbed doses to kidney and spleen were significantly higher and lower, respectively, than those previously estimated using 111In-ibritumomab-tiuxetan. Dose-limiting organ in patients undergoing stem cell transplantation is the liver.

REFERENCES: