

# Can Radionuclide Therapies be used as First Line Therapy in Cancers?

Theranostics - Controversies to Consensus & Acceptance

FOR THE PROPOSAL

# Can Radionuclide Therapies be used as First Line Therapy in Cancers?



**Dr Venkatesh Rangarajan**  
**Professor of Nuclear Medicine**  
**Tata Memorial Centre**



# I-131 therapy in Ca Thyroid

## *Aim of therapy*

RRA is considered as a safe and effective method for eliminating residual thyroid tissue, as well as microscopic disease if at all present in thyroid bed

Long-term outcome of lobar ablation versus completion thyroidectomy in differentiated thyroid cancer

Santra, Amburanjan; Bal, Susan; Mahargan, Sagar; Bal, Chandrasekhar

Abstract

**Background:** Professional guidelines, both in Europe and North America, recommend completion thyroidectomy (CT) after lobe resection, except in very low-risk-differentiated thyroid cancer patients (tumor less than 1 cm; unifocal micropapillary carcinoma). Radioiodine lobar ablation (RAILA), which avoids complications associated with re-surgery, is an alternative that has been recently explored in a few international centers. However, this approach is being criticized as there are no published data available on its long-term outcomes with respect to recurrence rate, disease-free survival, and mortality compared with standard of care. This study was designed to compare the long-term outcome of RAILA with that of remnant ablation after CT.

**Methods:** Prospectively collected data were analyzed retrospectively from the case records of patients treated in our thyroid clinic in the last 25 years. The records of all patients of RAILA (364) and CT (372) were critically studied. Successful ablation rate, cumulative dose needed for complete ablation, recurrence rate, and recurrence-free survival were estimated for each group. Comparison between the two groups was made using the SPSS 11.5 statistical program.

**Results:** Radioiodine ablation rate at first dose of RAILA and remnant ablation after CT were 73 and 93.5%, respectively ( $P=0.03$ ). However, after the second dose of I-131, the former group achieved successful ablation in 92% of patients. After a median follow-up period of 5 years (range 1-23 years), seven patients developed recurrence in the CT group (1.88%) and 14 in the RAILA group (3.8%); this was not statistically significant ( $P=0.168$ ). The Kaplan-Meier disease-free survival curves between the two groups were statistically not significant ( $P=0.08$ ). No cause-specific mortality in either group has been observed till date.

**Conclusion:** Radioiodine lobar ablation is a safe, simple, effective, and less expensive alternative to CT in patients with differentiated thyroid cancer with comparable long-term outcome in terms of recurrence rate and disease-free survival.

Definite advantage in using RAIT following LOBAR RESECTION over Completion Thyroidectomy

-Avoids complications of Surgery

-No statistically significant difference in DFS

# Treatment of Painful Bone Metastases

 *Therapeutic Advances in Medical Oncology*

*Review*

## From palliative therapy to prolongation of survival: $^{223}\text{RaCl}_2$ in the treatment of bone metastases

Knut Liepe and Ajit Shinto

*Ther Adv Med Oncol*

2016, Vol. 8(4) 294–304

DOI: 10.1177/  
1758834016640494

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## High-Linear Energy Transfer Irradiation Targeted to Skeletal Metastases by the $\alpha$ -Emitter $^{223}\text{Ra}$ : Adjuvant or Alternative to Conventional Modalities?

Øyvind S. Bruland,<sup>1</sup> Sten Nilsson,<sup>3</sup> Darrell R. Fisher,<sup>4</sup> and Roy H. Larsen<sup>2</sup>

*Clin Cancer Res* 2006;12(20 Suppl) October 15, 2006 6250s

Phase II Trial of Consolidation Docetaxel and Samarium-153  
in Patients With Bone Metastases From Castration-Resistant  
Prostate Cancer

*Karim Fizazi, Philippe Beuzebec, Jean Lumbroso, Vincent Haddad, Christophe Massard, Marine Gross-Goupil,  
Mario Di Palma, Bernard Escudier, Christine Theodore, Yohann Loriot, Elodie Tournay, Jeannine Bouzy,  
and Agnes Laplanche*

All these studies have shown a significant **SIDE-EFFECT FREE CONSOLIDATION**  
OF PAINFUL Bone metastases in CRPC

Since Prostate Ca is a predominantly bone involving malignancy,

**Extrapolation of these results to an *adjuvant setting***  
**can significantly lead to improvement of QoL**

# Lu-177 PSMA Therapy in CRPC

**Table 1** Compounds approved for the treatment of CRPC: overall survival benefits versus control arms in phase III clinical studies

Reference	Investigational compound	Control arm	Hazard ratio for death (95 % CI)	Overall survival benefit (months)	P value
[3]	Docetaxel	Mitoxantrone	0.80 (0.67 – 0.94)	1.9	0.02
[4]	Docetaxel	Mitoxantrone	0.76 (0.64 – 0.94)	2.4	0.009
[5]	Cabazitaxel after docetaxel	Mitoxantrone	0.70 (0.59 – 0.83)	2.1	0.001
[6]	Abiraterone after docetaxel	Placebo	0.65 (0.54 – 0.77)	3.9	0.001
[7]	Abiraterone before docetaxel	Placebo	0.75 (0.61 – 0.93)	5.2	0.0097
[8]	Enzalutamide after docetaxel	Placebo	0.63 (0.53 – 0.75)	4.8	0.001
[9]	Enzalutamide before docetaxel	Placebo	0.71 (0.60 – 0.84)	1.8	0.001
[10]	<sup>223</sup> Ra	Placebo	0.70 (0.56 – 0.83)	3.6	0.00007

Considering the side-effect profile of all these regimens,  
*the survival offered is NOT worth the cost*

**Lutetium-177 PSMA Radioligand Therapy of Metastatic Castration-Resistant Prostate Cancer: Safety and Efficacy**

Short-running title / foot line: Lu-177 PSMA: Safety and Efficacy

Authors: Richard P. Baum<sup>1\*</sup>, Harshad R. Kulkarni<sup>1\*</sup>, Christiane Schuchardt<sup>1</sup>, Aviral Singh<sup>1</sup>, Martina Wirtz<sup>2</sup>, Stefan Wiessalla<sup>1</sup>, Margret Schottelius<sup>2</sup>, Dirk Mueller<sup>1</sup>, Ingo Klette<sup>1</sup>, Hans-Jürgen Wester<sup>2</sup>

**Median PFS – 17 months and  
Median OS was not reached at 28 months**

**This is enough evidence to say that Lu-177 PSMA is the FIRST LINE THERAPY of choice in CRPC**

**Since it's a Theranostic Agent, with imaging counterpart having high diagnostic accuracy,  
It further justifies its potential role as FIRST LINE AGENT**



# PRRT with Lu-177/Y-90

Online Submissions: [wjg.wjgnet.com](http://wjg.wjgnet.com)  
[wjg@wjgnet.com](mailto:wjg@wjgnet.com)  
doi:10.3748/wjg.15.5867



World J Gastroenterol 2009 December 14; 15(46): 5867-5870  
World Journal of Gastroenterology ISSN 1007-9327  
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*CASE REPORT*

## **Neoadjuvant peptide receptor radionuclide therapy for an inoperable neuroendocrine pancreatic tumor**

Daniel Kaemmerer, Vikas Prasad, Wolfgang Daffner, Dieter Hörsch, Günter Klöppel, Merten Hommann, Richard P Baum

PRRT can be used for downstaging disease in cases with

**Low metastatic burden, or**

**Bulky primary**

# Trans-Arterial Radio-Embolisation

VOLUME 34 · NUMBER 15 · MAY 20, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

SIRFLOX: Randomized Phase III Trial Comparing First-Line mFOLFOX6 (Plus or Minus Bevacizumab) Versus mFOLFOX6 (Plus or Minus Bevacizumab) Plus Selective Internal Radiation Therapy in Patients With Metastatic Colorectal Cancer

Presents worsening of liver-disease in Liver-predominant or Liver-only metastatic Ca

## Radioembolization of Liver Metastases in Patients With Colorectal Cancer: A Nonsurgical Treatment With Combined Modality Potential

**In patients with metastatic disease at presentation,  
SIRT serves as the first line treatment to reduce the liver tumor burden,  
And when used in combination with systemic chemotherapy,  
leads to significant improvement in survival**

## TARE in Triple Negative Breast Cancer

*J Vasc Interv Radiol.* 2014 October ; 25(10): 1523–1532.e2. doi:10.1016/j.jvir.2014.07.007.

### **Yttrium-90 radioembolization stops progression of targeted breast cancer liver metastases after failed chemotherapy:**

<sup>90</sup>Y Radioembolization for BCLM

Andrew C. Gordon<sup>1,2</sup>, William J. Gradishar<sup>3</sup>, Virginia G. Kaklamani<sup>3</sup>, Avesh J. Thuluvath<sup>1</sup>, Robert K. Ryu<sup>1</sup>, Kent T. Sato<sup>1</sup>, Vanessa L. Gates<sup>1</sup>, Riad Salem<sup>1,3,4</sup>, and Robert J. Lewandowski<sup>1</sup>

# RIT in Refractory Lymphomas

CLINICAL TRIALS AND OBSERVATIONS

## Radioimmunotherapy of relapsed indolent non-Hodgkin lymphoma with $^{131}\text{I}$ -rituximab in routine clinical practice: 10-year single-institution experience of 142 consecutive patients

Michael F. Leahy<sup>1</sup> and J. Harvey Turner<sup>2</sup>

Departments of <sup>1</sup>Hematology and <sup>2</sup>Nuclear Medicine, The University of Western Australia, Fremantle Hospital, Fremantle, Australia

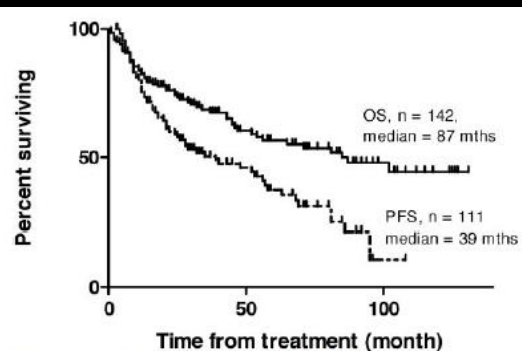


Figure 1. Kaplan-Meier plots of overall survival (OS) and progression-free survival (PFS) in 142 consecutive patients receiving  $^{131}\text{I}$ -rituximab radioimmunotherapy for relapsed indolent lymphoma.

Radioimmunotherapy is a safe, effective treatment of low-grade lymphoma and increases OS while preserving quality of life. Radioiodinated rituximab offers practical, cost-effective radioimmunotherapy for routine clinical applications where regulatory or cost constraints limit the availability of proprietary radiolabeled murine anti-CD20 mAbs, and it also has the potential for safe, effective repeated radioimmunotherapy upon relapse.

## Radioimmunotherapy with $^{177}\text{Lu}$ -DOTA-Rituximab: Final Results of a Phase I/II Study in 31 Patients with Relapsing Follicular, Mantle Cell, and Other Indolent B-Cell Lymphomas

Flavio Forrer<sup>1,2</sup>, Catharina Oechsli-Oberholzer<sup>3</sup>, Benedetta Campana<sup>3</sup>, Richard Herrmann<sup>4</sup>, Helmut R. Maecke<sup>5,6</sup>, Jan Mueller-Brand<sup>1,2</sup>, and Andreas Lohri<sup>3</sup>

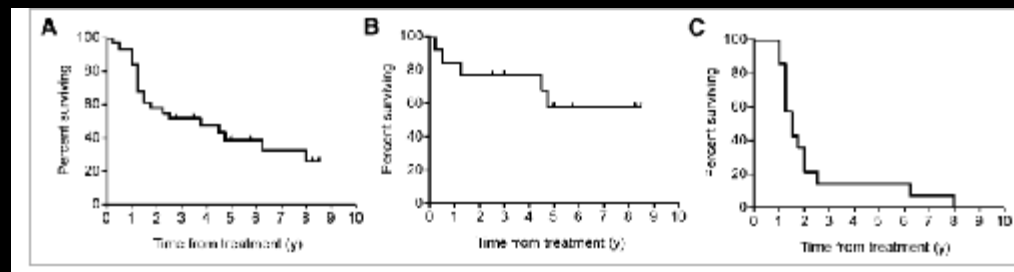


FIGURE 2. Kaplan–Meier survival curves of all patients, patients with follicular lymphoma, and patients with MCL. (A) Overall survival of 31 patients receiving  $^{177}\text{Lu}$ -DOTA-rituximab. (B) Overall survival of 13 patients with follicular lymphoma receiving  $^{177}\text{Lu}$ -DOTA-rituximab. (C) Overall survival of 14 patients with MCL receiving  $^{177}\text{Lu}$ -DOTA-rituximab.

In conditions like refractory FL, where there is no treatment option following ASCT, RIT is the available option.

On similar lines, RIT can be used upfront in refractory lymphomas.. considering the lower toxicity profile and since sustained remissions are achieved.

## MIBG Therapy in Neuroblastoma

Nucl Med Commun. 1994 Sep;15(9):712-7.

**$^{131}\text{I}$ -MIBG as a first-line treatment in high-risk neuroblastoma patients.**

Hoefnagel CA<sup>1</sup>, De Kraker J, Valdés Olmos RA, Voûte PA.

**Down staging of disease**  
**Reducing tumor bulk**

Eur J Nucl Med Mol Imaging (2013) 40:1711–1717  
DOI 10.1007/s00259-013-2510-z

ORIGINAL ARTICLE

**Toxicity of upfront  $^{131}\text{I}$ -metaiodobenzylguanidine ( $^{131}\text{I}$ -MIBG) therapy in newly diagnosed neuroblastoma patients: a retrospective analysis**

**Relatively safe ...bearing isolated incidence of hematotoxicity**

# Isotope therapy as first line

- There is solid scientific and conceptual basis
- Lack of evidence/RCT
- Must be given a fair chance
- Conflict of interest appears to be the most important challenge