Advanced Thoracic NET Clinical Cases: PRRT in Lung NEN

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ESMO Preceptorship Prague 2017
TTP 71 Months
Survival 80+ Months
8e december 2012

177Lu-DOTA-octreotate
Radionuclide Therapy of
Neuroendocrine Tumours
Dosimetry-Based Therapy Planning and Outcome
Bronchial carcinoids: 13 patients with advanced disease

Median time to progression 44 months

Median overall survival 44 months

Ulrike Garske-Román, Dissertation Uppsala University 2012
<table>
<thead>
<tr>
<th>Bronchial carcinoids</th>
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<tr>
<td><strong>Median Time to Progression 44 Months</strong></td>
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<td><strong>Percent of Patients</strong></td>
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<tr>
<td><strong>Time to Progression (Months)</strong></td>
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**Median Overall Survival 44 Months**

**Patients Alive**

**Survival after Start of 177Lu-DOTA-octreotate**

(Months)
Lung NET & PRRT

- Sabet, Haug, Eiden et al JNM May 2014, supplement 1, 394
- 22 patients Bronchial NETs G1&2: $^{177}$Lu-DOTA-octreotate 4 cycles, intended 3 months interval, mean activity 7.8 GBq
- PFS 31, median OS 42
This publication should have been mentioned in this place:

- Long-term results of PRRT in advanced bronchopulmonary carcinoid

- Retrospective analysis of 114 patients with advanced stages of BPC treated in Milan from 1997-2012, follow-up until 2014 with three different PRRT protocols

- $^{90}\text{Y-DOTATOC}$ vs $^{177}\text{Lu-DOTATATE}$ vs $^{90}\text{Y-DOTATOC}+^{177}\text{Lu-DOTATATE}$

- Rating of objective responses, overall survival (OS) and progression-free survival (PFS)
• Median OS (evaluated in 94 patients) 58.8 months
• Median PFS 28 months
• The $^{177}$Lu-DOTATATE protocol resulted in the highest 5-year OS (61.4 %). Morphological responses (partial responses+ minor responses) were obtained in 26.5 % of the cohort and were associated with longer OS and PFS.
• The $^{90}$Y- DOTATOC+$^{177}$Lu-DOTATATE protocol provided the highest response rate (38.1 %).
• Adverse events were mild in the majority of patients. However, haematological toxicity negatively affected survival.
• Patients treated with $^{90}$Y- DOTATOC alone more frequently showed a mild/moderate decrease in renal function. In patients treated with chemotherapy before PRRT had a shorter OS and PFS, and a higher risk of developing nephrotoxicity.
• Conclusion:
• PRRT proved to be promising in prolonging survival and delaying disease progression
• Despite the potential selection biases, considering the risk-benefit ratio, $^{177}$Lu-DOTATATE monotherapy seems the best option for PRRT.
• Our results indicate that the use of PRRT in earlier stages of the disease could provide a more favorable outcome.
Leukemia and PRRT: Uppsala experience

- 485 patients with data (++)
- 6 leukemia (bony mets in at least 5)
- 1 ALL: Lung NET, BM mets +, previous temozolomide
- 1 CML: SI-NET (unconfirmed) G2/G3; BM mets +++ previous temozolomide (4 mo)
- 4 AML:
  - 1 Lung: Paraplatin Vepesid before, 3 years Temozolomide after PRRT,
  - 2 SI-NET (1 no chemo; BM mets ++, 1 unknown treatment)
  - 1 EPT (Strepto/5FU: intolerance r/t declined kidney function)
- Absorbed BM doses: 0.2-0.5 Gy blood dose; 0.47-0.64 Gy total accumulated dose
This publication should have been mentioned in this place:


• Long-term tolerability of PRRT in 807 patients with neuroendocrine tumours: the value and limitations of clinical factors

  • Bodei, L, Kidd, M, Paganelli, G, Grana, CM, Drozdov, I, Cremonesi, M, Lepensky, C, Kwekkeboom, DJ, Baum, RP, Krenning, EP, Modlin, IM
  • 807 patients studied at IEO Milan (1997-2013)
  • 177Lu: 34.4%/ 90Y: 44.4% 177Lu&90Ycombined (19.5%)/ 2% PRRT combined with other agents

• **Results:** Treatment with $^{90}$Y and $^{90}$Y+$^{177}$Lu was more likely to result in nephrotoxicity than treatment with $^{177}$Lu alone (33.6 %, 25.5 % and 13.4 % of patients, respectively; p < 0.0001)
Results: Nephrotoxicity (any grade), transient and persistent, occurred in 279 patients (34.6 %) and was severe (grade 3+4) in 12 (1.5 %).

Myelodysplastic syndrome occurred in 2.35 % of patients... Platelet toxicity grade (......) and longer PRRT duration (......) were relevant. Acute leukaemia occurred in 1.1 % of patients (....).

Myelodysplastic syndrome occurred in 2.35 % of patients ... Platelet toxicity grade ....and longer PRRT duration .......were relevant. Acute leukaemia occurred in 1.1 % of patients.

Conclusion Identified risk factors provide a limited (<30 %) risk estimate even with target tissue dosimetry.

These data strongly suggest the existence of unidentified individual susceptibilities to radiation-associated disease.
PRRT and chemotherapy

• More data need to be collected regarding late bone marrow toxicity
• Combination of especially alkylating agents or cisplatinum and radiation (PRRT) reported problematic
• Brieau et al 2016 (20% 4/20 3 MDS, 1 AML) all had had alkylating agents
• Kesavan et al 2014 (2/65 patients (3%) PRRT with tem/cap) MDS
Risk factors and open questions

- Presence of BM mets: Can they increase the stochastic risk? What about small volume disease in skeleton?
- Early hematotoxicity after treatment: indicator?
- Bone marrow absorbed doses? Blood doses? Accumulated activity?
Getting back to PRRT in lung NETs......

• Promising
• A place for 1st line therapy in progressive patients with advanced disease?
• A randomised study would be nice: against .....???
Open questions!

• The future is yours to ask the right questions to provide new concepts and to come up with new ideas!
The aim of therapy
• Thank you for your attention!
• Hopefully, your stay in Prague was fruitful!