Memorial Sloan Kettering Cancer Center

Considerations on nephrotoxicity of PRRT

Monday, September 26, 2022

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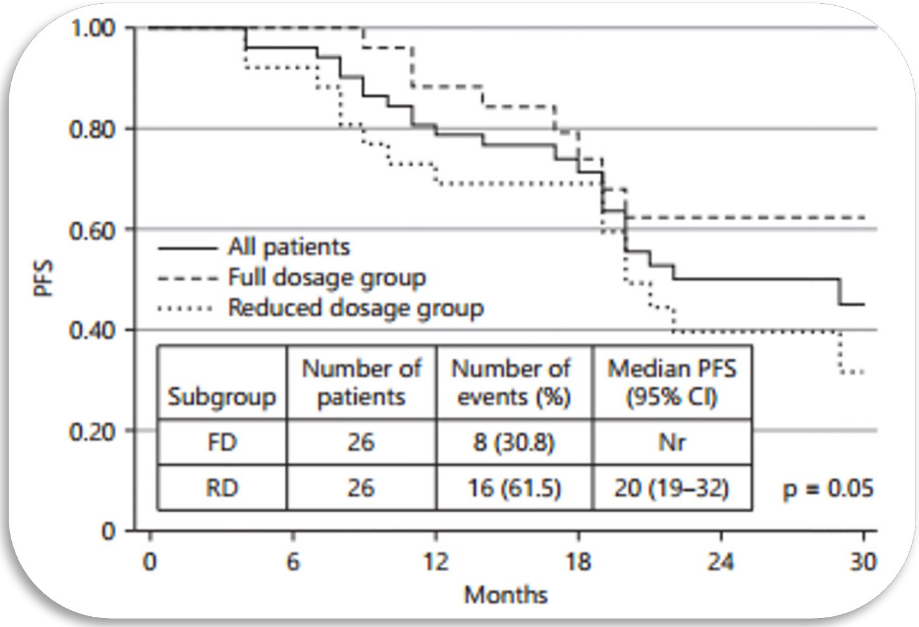
No Dosimetry, Patient-adjusted Treatments based on Risk factors

^{177}Lu-DOTATATE

P-NETs

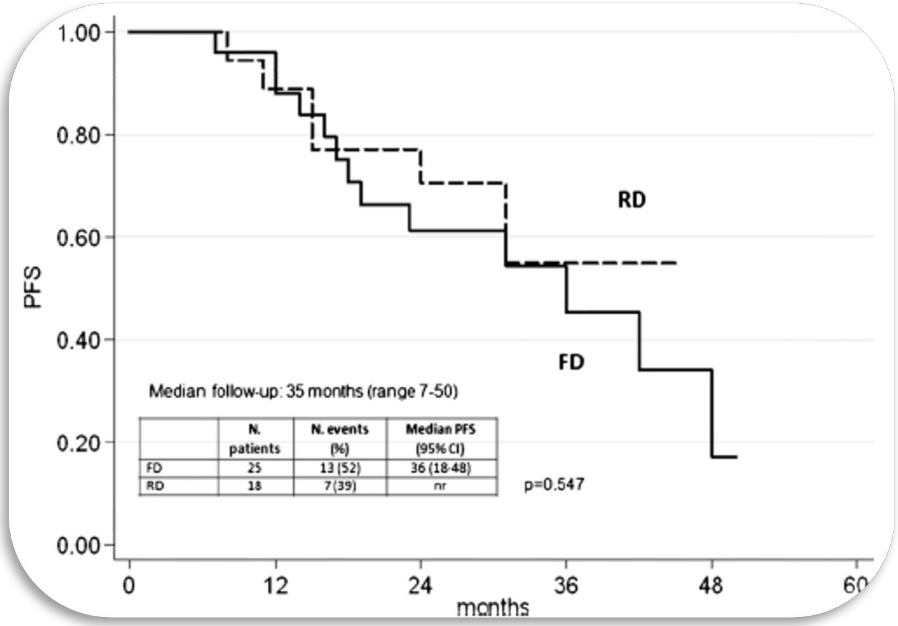


Subgroup	Number of patients	Number of events (%)	Median PFS (95% CI)
FD	26	8 (30.8)	Nr
RD	26	16 (61.5)	20 (19–32)

p = 0.05

Paganelli G Neuroendocrinology 2013

GI-NETs



	N. patients	N. events (%)	Median PFS (95% CI)
FD	25	13 (52)	36 (18-48)
RD	18	7 (39)	nr

p=0.547

Paganelli G EJNMMI 2014

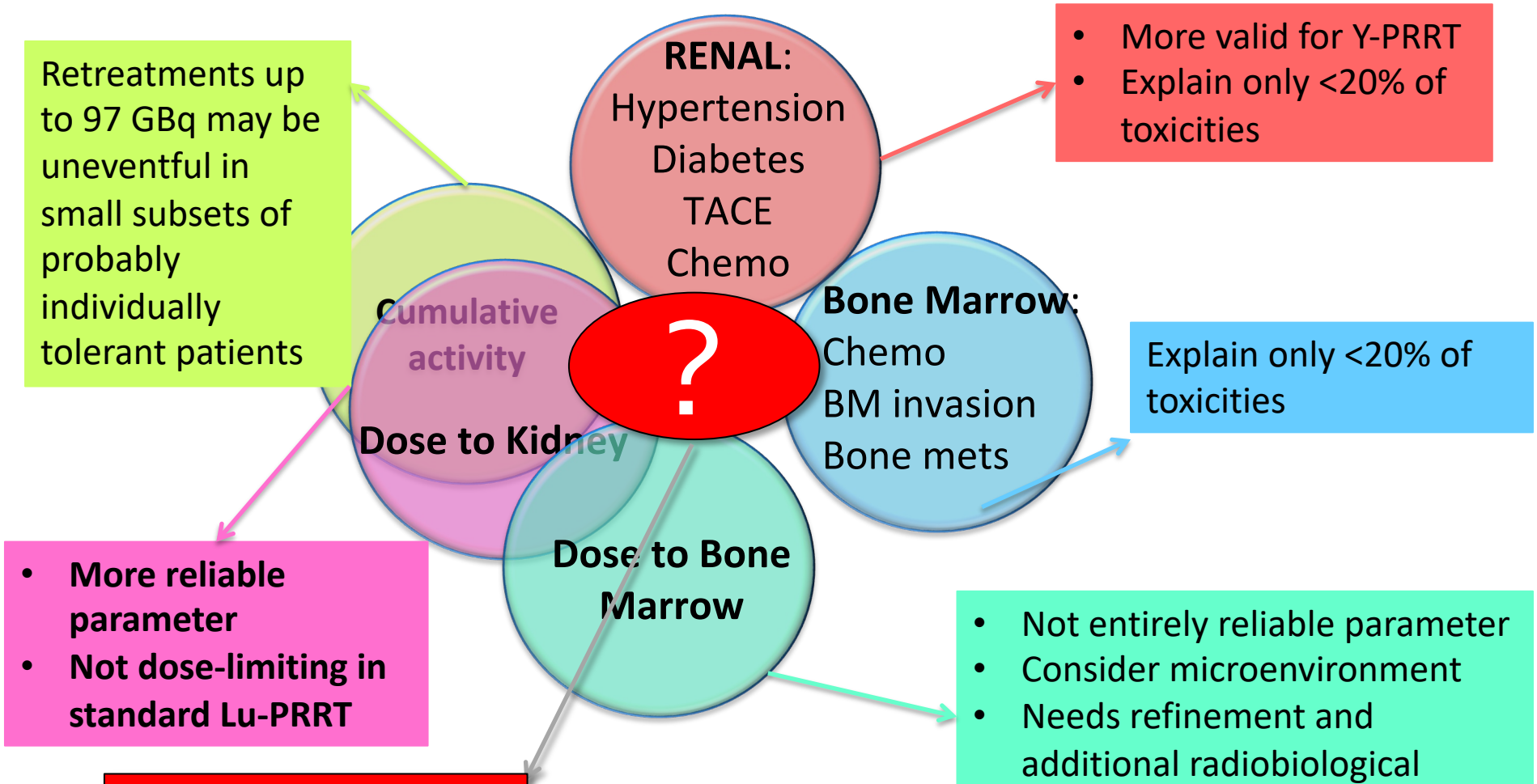
Lower PFS in lower PRRT dosages

Full dose scheme recommended

No difference between dose regimens

Risk pts may benefit from PRRT

Predicting Toxicity to PRRT



Bodei L et al. 2014, 2015
Cremonesi et al. 2011
Ahmadzadehfar H et al 2017
Sandstrom et al. 2013

G3 and G4 toxicity in 807 pts treated at IEO Milan (1997-2013)

Median cumulative activity:

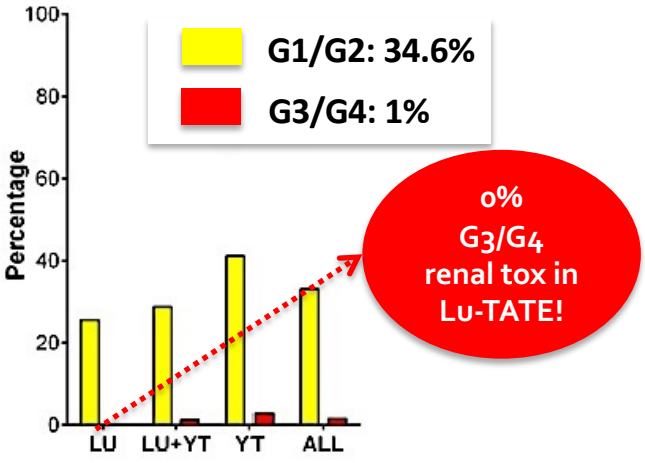
- ^{90}Y-TOC : 10.1 GBq
- ^{90}Y-TOC+^{177}Lu-TATE : 6.4+12.7 GBq
- ^{177}Lu-TATE : 22.9 GBq

Grade[a]	All		^{90}Y		^{90}Y+^{177}Lu		^{177}Lu	
	No. of patients	Percent of patients	No. of patients	Percent of patients	No. of patients	Percent of patients	No. of patients	Percent of patients
0	67	8.3	33	9.2	11	7.0	23	7.9
1	410	50.8	147	40.8	75	47.8	188	64.8
2	253	31.4	129	35.8	54	34.4	70	24.1
3	63	7.8	39	10.8	15	9.6	9	3.1
4	14	1.7	12	3.3	2	1.3	0	0
Total	807	100	360	100	157	100	290	100
1/2		82.2		76.7		82.2		89.0
3/4		9.5		14.2		10.8		3.1

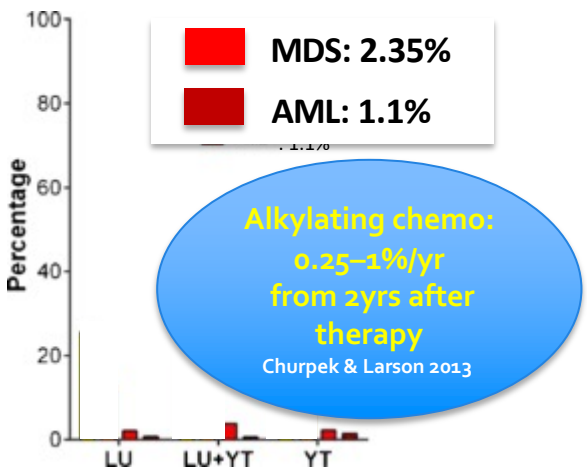
Bodei L et al. EJNMMI 2015

Permanent toxicity after PRRT is low and comparable to other treatments
n=807

Renal Toxicity



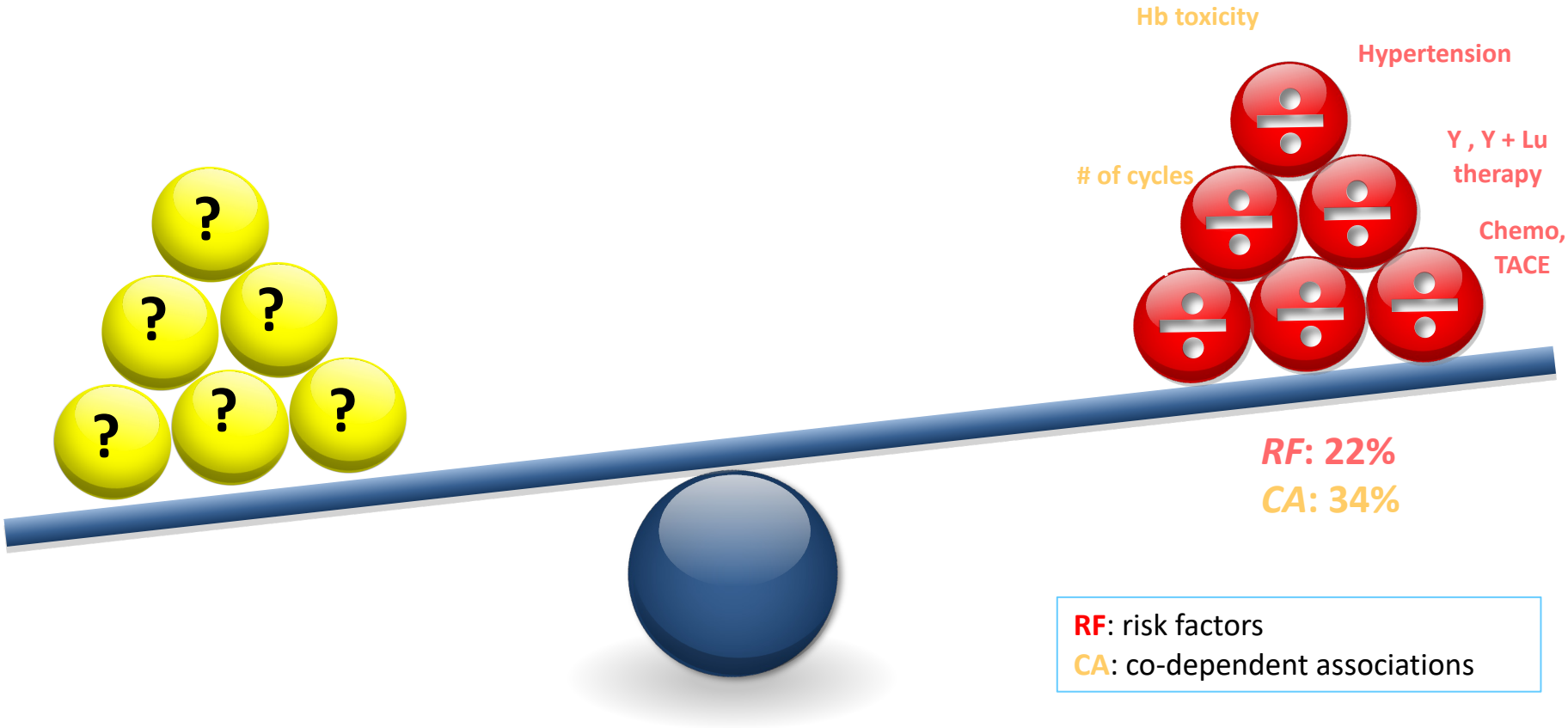
Bone Marrow Toxicity



- Severe nephrotoxicity was virtually absent after ^{177}Lu-peptides
- Bone marrow toxicity low and comparable with other anti neoplastic therapies

Bodei L et al. EJNMMI 2015

Nephrotoxicity: Comparative Analysis of Clinical Factor Weight
n=807



RF: risk factors
CA: co-dependent associations

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Bodei L et al. EJNMMI 2015

Dosimetry isn't all…

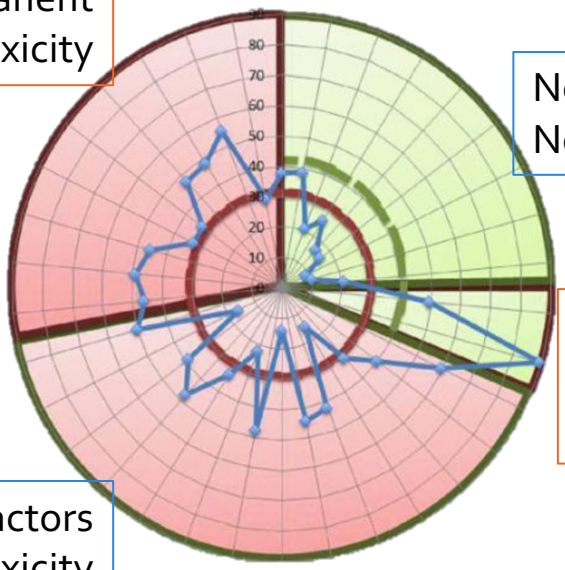
^{90}Y- and ^{177}Lu-PRRT

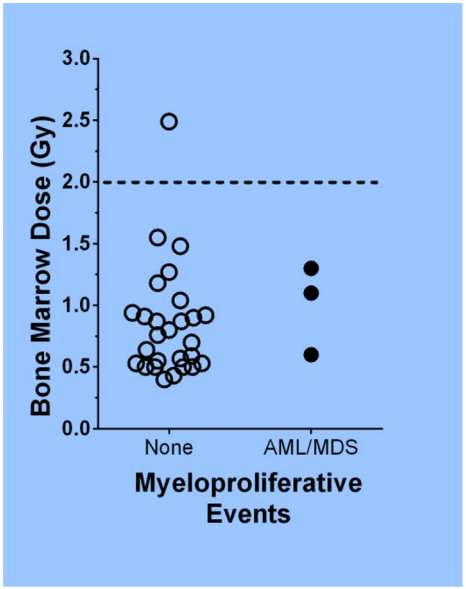
Risk factors
Permanent
toxicity

No risk factors
No toxicity

No risk factors
Permanent
toxicity

Risk factors
No toxicity





Unless very high doses are administered, there is a grey zone of unpredictable outcome around the thresholds

Individual susceptibility to adverse *sequelae* of PRRT is likely to have an individual genetic basis.

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Bodei L et al. EJNMMI 2015