

Supplemental Table 1. <sup>131</sup>I-MIBG Therapy of patients with metastatic/inoperable pheochromocytoma/paraganglioma

Reference	PHEO/PGL Patient (n=), type of study*	Single dose (GBq or as specified), Type of <sup>131</sup> I-MIBG**	Cumulative (GBq)	Therapy # cycles	Objective CR (%) ***	Objective PR or CR+ PR (%) ***	Biochemical CR (%) ***	Biochemical PR or CR + PR(%) ***	Symptomatic CR (%)***	Symptomatic PR or CR + PR*** (%)	Duration of response or survival****
Shapiro, et al. 1991 (1)	28, NS	Mean 6.7 (3.59–11.14) LSA-MIBG	4.11–33.89 (Mean 17.72)	1–6	0	7	0	18 Catec/Metan	N/A	N/A	Partial or minor response;mean PFS 30.5 month
Safford, , et al. 2003 (2)	33, R	Mean 14.36 ±4.81 LSA-MIBG	2.59–45.25 (Mean 20.31)	1–6 (Median 1)	N/A	38	N/A	60 Catec/Metan/VMA	N/A	86 @ hypertension, pain, sweating, or anorexia	Median survival 4.7 years 5-year survival 45%
Gonias, et al. 2009 (3)	50, P	Median 32.60 (18.20– 42.92); Median 0.44 GBq/kg 18.5 if no stem cells LSA-MIBG	18.20–147.67	1–3 (Median 1)	9@ 17@@	27@ 50@@	19@ Catec/Metan 24@ CgA  57 @@ Catec/Metan 20 @@ CgA	35 @ Catec/Metan74@ CgA  71 @@ Catec/Metan 40 @@ CgA	N/A	N/A	64% 5-years OS 47% 5-year EFS
Castellani, et al. 2010 (4)	Group 1: 12  Group 2: 16 , NS	Median 5.51 (4.59–5.51)  Median 9.92 (7.4–12.95) ( LSA-MIBG	5.51–66.60 (Median 39.41)  9.21–57.20 (Median 24.09)	1-10 (Median 7)  1-6 (Median 2)	8.3  12.5	33  31	33 Catec  28 Catec	56 Catec  71 Catec	N/A	N/A	Group 1 median response duration 1.9-years  Group 2 median response duration 3-years
Wakabayashi, et al. 2013 (5)	26, R	Median 7.40 (0.07–0.21 GBq/kg), LSA-MIBG	N/A	1–6 (Median 2)	0	0	0	60	0	52 @	50% 5-year survival
Yoshinaga, et al. 2014 (6)	48, R	(3.7–14.8), Median 0.13 GBq/kg (0.049–0.21 GBq/kg)	N/A	1–4 (Median 2)	0	2	N/A	N/A	N/A	N/A	NA

		LSA-MIBG									
Rutherford, et al. 2015 (7)	22, R	Mean 9.97 (5.0–11.3), LSA-MIBG	10-50.67 (Median 20.12)	1–9 (Median 2)	5@	19@	5@	10@ Catec/Metan	5@ hypertension	23@ hypertension	Median survival 11.1-years 68 5-year survival
Noto, et al. 2018 (8)	21, P	Median 21.13 (12.02–25.75); Median 0.240 GBq/kg; (0.170.31 GBq/kg) HSA-MIBG	Same as single dose	1	0	21	47CgA 36 Metan	80 CgA 64 Metan	N/A	33 hypertension	2-year survival 62%
Wakabayashi, et al. 2019 (9)	20, P	5.55 or 7.4 LSA-MIBG	11.4 +/- 5.7	1–3	10@ 5@@	10@ 15@@	N/A	N/A	N/A	N/A	PFS at 6 month 80%
Thorpe, et al. 2020 (10)	125, R	Median 18.80 Max 19.50, LSA-MIBG	Same as single dose	1	1	34	N/A	59 defined as 20% change Catec/Metan/VMA/CgA	N/A	75 overall 14 hypertension 42 pain	Median survival 4.3 years Median PFS 2-years
Pryma, et al. 2019 (11)	68, P	(18.5 or for patients < 62.5 kg 0.296 GBq/kg, HSA-MIBG	3.8–40.5; (Med 35.7)	1–2 (Median 2)	0	23	N/A N/A N/A	31 Catec 44 Meta 68 CgA	0	25 hypertension	Median OS 37 month, single treatment Median OS 44 month, 2 treatments

\*R = retrospective, P = prospective. NS = not specified, PHEO=pheochromocytoma, PGL=paraganglioma

\*\* LSA-MIBG= low specific activity LSA-<sup>131</sup>I-MIBG, HSA = high specific activity HSA-<sup>131</sup>I-MIBG

\*\*\* CR = complete response, PR = partial response, N/A= not available, CgA = chromogranin A, Catec = catecholamine, Metan = metanephrines, VMA= Vanillylmandelic acid

\*\*\*\*OS = overall survival, PFS = progression free survival, EFS = event free survival, TTP = time to progression

@ not well defined criteria

@ @ After second treatment

Supplemental Table 2. PRRT of patients with metastatic/inoperable pheochromocytoma/paraganglioma.

Reference	PHEO/PGL Patient (n=); type of study*	Radiopharmaceutical single injected activity GBq treatment interval	Cumulative injected mean/median(range)GBq	Therapy # cycles	Objective CR (%) ***	Objective PR or CR+ PR (%) ***	Biochemical CR (%) ***	Biochemical PR or CR + PR(%) ***	Symptomatic CR (%)***	Symptomatic PR or CR + PR*** (%)	Duration of response or survival****	Adverse events
van Essen, et al. 2006 (12)	12 (1 PHEO, 6 sPGL, 5 HNPG, 9 metastatic, 3 inoperable); P	<sup>177</sup> Lu-DOTATATE 7.4 GBq/cycle ×4; 6–10 weeks	(14.8–29.6)	2-4	0	9	N/A	N/A	N/A	N/A	N/A	1 MDS  1 Grade 4 hematotoxicity
Forrer, et al. 2008 (13)	28 (5 PHEO, 23 PGL,incurable); R	<sup>90</sup> Y-DOTATOC 7.4GBq/m2/cycle x2; every 8 weeks (n = 19) or 1.35GBq/m2/cycle,x4; every 6 weeks (n = 6) <sup>90</sup> Y-DOTATOC/ <sup>177</sup> Lu--DOTATOC 3.7 GBq/m <sup>2</sup> × 1 cycle/7.4 GBq × 2 cycles; every 8 weeks (n=3)	N/A	1-4	0	7 all groups	N/A	N/A	N/A	N/A	TTP > 18m	No Grade 2 or greater hematotoxicity, no renal toxicity
Imhof, et al. 2011 (14)	39 (11 PHEO, 28 PGL); P	<sup>90</sup> Y-DOTATOC 3.7 GBq/m2/cycle	N/A	Median 2 (1–10)*	0	36 for PHEO, 11 for PGL #	N/A	18 for PHEO, 14 for PGL#	N/A	46 for PHEO, 21 for PGL#	Mean survival: PHEO 32m /PGL82 m	***12.8% Grade 3-4 hemaotoxicity 9.2% Grade 4–5 nephrotoxicity

Puranik, et al. 2015 (15)	9 HNPGL (2 metastatic, 7 inoperable); P	<sup>90</sup> Y-DOTATOC alone (n=5) 1.5–5.7  Or combined <sup>177</sup> Lu-DOTATATE 5.4-7.5 (n=4) every 3–6 months	N/A	Median 2 (2–4)	0  @@@ <sup>68</sup> Ga-DOTATOC: N/A	0  @@@ <sup>68</sup> Ga-DOTATOC: 44	N/A	N/A	N/A	N/A		No renal or hematological toxicity.
Pinato et al. 2016 (16)	5 PGL (all <i>SDHB</i> and metastatic); R	<sup>177</sup> Lu-DOTATATE 6.6–7.6 GBq/cycle every 12 weeks	N/A	Median 3 (1–4 cycles)	N/A	20 PR	N/A	N/A	N/A	N/A	Mean OS 53 months Mean PFS 36 months	20% Pulmonary toxicity possibly related
Kong, et al. 2017 (17)	20 (8 PHEO, 12 PGL)  (8 <i>SDHx</i> ) 14 uncontrolled HTN; 6 metastatic or recurrent; R	<sup>177</sup> Lu-DOTATATE N/A 9 with radiosensitizer chemotherapy every 6–10 weeks	Median 22	Median 4 cycles	0  @@@ <sup>68</sup> Ga-DOTATOC: 0	29  @@@ <sup>68</sup> Ga-DOTATOC: 47	0 Metan  0 CgA	57 Metan  54CgA	15symptom# 0hypertension#	76symptom# 62hypertension#	Median PFS 39 m, medianOS 29m	10% Grade 3 thrombocytopenia
Nastos, et al. 2017 (18)	11 (1 PHEO, 10 PGL; locally	<sup>90</sup> Y-DOTATATE (n=8) 3.2 GBq/cycle		3–4 cycles	N/A	100	N/A	N/A	N/A	N/A	Mean OS 61 months	Grade 3–4 renal toxicity 9%

	advanced or metastatic)  11 PHEO/PGL treated with MIBG; R	or <sup>177</sup> Lu-DOTATATE (n=1) 7.4 GBq/cycle or Y-90 or <sup>177</sup> Lu-DOTATATE with-131 MIBG (n = 2) every 10–12 weeks	(3.6–17.7)  N/A								PFS 38.5 months EFS 17.9 months	Grade 3–4 Neutropenia 9%  Thrombocytopenia 9%
Hamiditabar, et al. 2017 (19)	5 (1PHEO, 4PGL)  P	<sup>177</sup> Lu-DOTATATE 7.4 GBq/cycle	N/A	1–6 cycles	0	0	N/A	N/A	N/A	N/A	N/A	No Grade 3–4 renal toxicity  Hematologic toxicity ***
Demirci, et al. 2018 (20)	12 PHEO/PGL; R	<sup>177</sup> Lu-DOTATATE Median 5.04 GBq (3.7–8.1 GBq)	N/A	Median 6 cycles (2–12)***	0	50 PR	N/A	N/A	N/A	N/A	Mean PFS 31 months, Mean OS 52 months	2%Gr3 ***hematologic 1% Creatinine > 2 mg/dl
Zandee, et al. 2019 (21)	30 (3 PHEO, 10 PGL, 17 HNPGL) 16 SDHx (inoperable or metastatic); R	<sup>177</sup> Lu-DOTATATE 7.4 GBq/cycle Every 6–12 weeks	14.8–29.6	1–4	0	23	33	50	N/A	N/A	Median PFS: 91 months HNPGL 10 months PHEO 18 months sPGL	Grade 3 anemia 6.7%  20% Grade 3–4 hematotoxicity MDS 3% Catecholamine release 6.7%
Yadav, et al. 2019 (22)	25 (8 sPGL, 17HNPGL; 20 metastatic, 5 localized); R	<sup>177</sup> Lu-DOTATATE + capecitabine 5.5–7.4 GBq/cycle every 3 months	Mean 22.9 (14.4–50)	Median 3 (2–8)	0	28	0	CgA 28	N/A	43 hypertension	Median PFS 32m	No Gr 2 or greater toxicity

Vyakarana m, et al. 2019 (23)	22 (19 PHEO, 13 PGL; 2 localized, 20 metastatic, 7 <i>SDHx</i> );  R	<sup>177</sup> Lu-DOTATATE  7.4 GBq/cycle x4m(n=3)  7.4 GBq/cycle until renal dose 23 Gy or 2 Gy whole body(n=19)  Every 6-8 wks	Median 29.6 (22.2–81.4)	Median 4 cycles (range 3– 11)	0  @@@ <sup>177</sup> Lu- DOTAT ATE imaging:  0	9  @@@  <sup>177</sup> Lu- DOTATATE imaging:  47	N/ACatec  N/A CgA	25 Catec  40 CgA	N/A	40#	Median OS 49.6 months (Range 8– 139), PFS 21.6 months (3.7–138)	No Grade 3- 4 hematologic or renal
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\*PHEO= pheochromocytoma, PGL=paraganglioma, HNPG= head neck paraganglioma, sPGL= sympathetic paraganglioma, R = retrospective, P = prospective, NA= not available, SDH= succinate dehydrogenase complex

\*\*\* based on anatomical imaging PR = partial response, CgA = chromogranin A,

@@@functional imaging response EORTC criteria (CR complete disappearance on functional imaging, PR ≥50% reduction in SUV. Other used improvement by 1 point in Krenning score.

\*\*\*\*OS = overall survival, PFS = progression free survival, EFS = event free survival

#not well defined criteria

## SUPPLEMENTAL TABLE REFERENCES

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