

Uptake and Extent Scale

The intensity of tumor uptake on OctreoScan® and the extent of tumor burden is to be scored according to simple scaling systems, see supplemental figs. 1 and 2.

The Netherlands Cancer Registry

The expected number of patients with dysfunction of the hematopoietic system was calculated using the website of Dutch cancer figures (www.cijfersoverkanker.nl).

The incidence (number of cancers per 100,000 persons a year) was used for four categories with the following selection criteria:

1. Myelodysplastic Syndrome (MDS) – the selected tumor group was “MDS and Myelodysplastic/myeloproliferative disorders” with subgroup “Myelodysplastic Syndrome”.
2. Acute myeloid leukaemia (AML) – the selected tumor group was “Acute Myeloid Leukaemia” including all subgroups.
3. Myeloproliferative disorders (MPN) - the selected tumor group was “Myeloproliferative disorders” with subgroup “Myeloproliferative neoplasm, other”.
4. Myelodysplastic/myeloproliferative neoplasms (MDS/MPN) - the selected tumor group was “MDS and Myelodysplastic/myeloproliferative disorders” with subgroup “Myelodysplastic/Myeloproliferative disorders” plus tumor group “Myeloproliferative disorders” with subgroup “Chronic Myeloid Leukaemia”.

Incidence data extracted from the website, sorted by 5-years age category and sex can be found in supplemental table 1 - 10. Expected numbers were adjusted for sex, age and duration of follow-up period.

Patient age, sex and follow-up characteristics in all 367 and 274 Gastroenteropancreatic Neuroendocrine tumors (GEP-NETs) patients with expected number of expected number of hematopoietic neoplasms can be found in supplemental table 11 - 14.

Relative Risk

The Relative risk (RR), it's standard error and 95% confidence interval are calculated according to Altman (1).

The relative risk or risk ratio is given by

$$RR = \frac{a/(a+b)}{c/(c+d)}$$

where a is the number of exposed patients with a positive (bad) outcome, b is the number of exposed patients with a negative (good) outcome, c is the number of non-exposed patients with a positive (bad) outcome and d is the number of non-exposed patients with a negative (good) outcome.

The standard error of the log relative risk is

$$SE\{\ln(RR)\} = \sqrt{\frac{1}{a} + \frac{1}{c} - \frac{1}{a+b} - \frac{1}{c+d}}$$

with a 95% confidence interval of

$$95\%CI = \exp(\ln(RR) - 1.96 \cdot SE\{\ln(RR)\}) \text{ to } \exp(\ln(RR) + 1.96 \cdot SE\{\ln(RR)\})$$

Where zeros cause problems with computation of the relative risk or its standard error, 0.5 is added to all cells (a,b,c,d) (2,3).

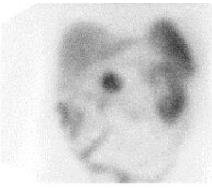
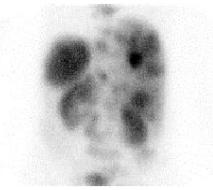
Supplemental Results

In total 367 patients were treated of whom 324 patients met the inclusion criteria. Forty-three patients were off-protocol for various reasons (see table 15). The tumor type of 93 non GEP-NET patients can be found in supplemental table 16.

Patient characteristics of all 13 patients with persistent hematological dysfunction (PHD) can be found in table 17. Calculations of the relative risk can be found in table 18.

			
1) <Liver (Excluded)	2) ≈ Liver	3) > Liver	4) Very intense (>>Kidneys, spleen)

Supplemental Fig. 1 - Tumor uptake scaling system; 1. Uptake less than the liver (excluded) 2. Uptake equal to the liver 3. Uptake more than the liver 4. Uptake more than kidneys and/or spleen.

		
1) Limited	2) Moderate	3) Extensive
Up to 5 sites in one part of the body (head/neck, chest, upper abdomen, lower abdomen)	Multiple sites in up to 2 sites of the body. Neither qualifying for limited nor for extensive.	Many tumor sites in ≥ 2 parts of the body.

Supplemental Fig. 2 - Tumor mass on OctreoScan; 1. Limited tumor mass is up to 5 sites in one part of the body (head/neck, chest, upper abdomen, lower abdomen) 2. Moderate tumor mass is multiple sites in up to 2 sites of the body, neither qualifying for limited nor for extensive 3. Extensive tumor mass is many tumor sites in ≥ 2 parts of the body. Usually a combination of extensive liver and lymph node involvement or diffuse skeletal metastases. Diffuse liver metastasis with limited abdominal involvement does not qualify.

REFERENCES

1. Altman D. Practical Statistics for Medical Research Chapman & Hall London Google Scholar. 1991.
2. Pagano M, Gauvreau K. Comparison of two means. *Principles of Biostatistics*, edited by Pagano M and Gauvreau K Belmont, CA: Duxbury Thompson Learning. 2000.
3. Deeks JJ, Higgins JP. Statistical algorithms in review manager 5. *Statistical Methods Group of The Cochrane Collaboration*. 2010:1-11.

Supplemental Table 1 – Incidence of Myeloproliferative Neoplasms (MPN) in males per age category from 2001-2011 in The Netherlands, obtained from the Netherlands Cancer Registry (www.cijfersoverkanker.nl).

Male		Incidence Myeloproliferative Neoplasms (MPN) (excluding CML) per year											Average Incidence MPN (excluding CML)
Cat	Age	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	
1	0-4	0	0	0	0	0	0	0	0	0	0	0	0.0
2	5-9	0	0	0	0	0	0	0	0	0	0	0	0.0
3	10-14	0	0	0	0	0	0	0	0	0	0	0	0.0
4	15-19	0	0	0	0	0	0	0	0	0	0	0	0.0
5	20-24	0	0	0	0	0	0	0	0	0	0.19	0	0.0
6	25-29	0	0	0	0	0	0	0	0	0.2	0	0	0.0
7	30-34	0	0	0	0.16	0	0	0	0	0	0.6	0	0.1
8	35-39	0	0.15	0	0.15	0	0	0	0.32	0.17	0.17	0	0.1
9	40-44	0.16	0	0	0.46	0	0.3	0.15	0.15	0	0.31	0	0.1
10	45-49	0	0	0	0.17	0.33	0.16	0.16	0	0.46	0.31	0.46	0.2
11	50-54	0	0.35	0.35	0.71	1.07	0.35	0.35	0	0.51	1.17	0.5	0.5
12	55-59	0	1.38	1.67	1.44	1.05	1.75	0.9	0.55	2.02	0.73	0.73	1.1
13	60-64	0.81	0.79	0.76	0.49	1.2	1.58	1.66	1.96	1.7	1.65	1.47	1.3
14	65-69	1.95	2.25	2.53	0.92	2.4	2.04	2.28	2.21	4.26	2.58	2.67	2.4
15	70-74	2.4	0.39	3.48	2.29	1.89	2.61	4.77	3.94	4.52	3.03	4.57	3.1
16	75-79	3.85	4.91	2.7	3.19	2.59	5.05	5.4	3.36	3.75	5.98	4.06	4.1
17	80-84	4.93	3.76	1.79	2.57	4.18	4.93	3.22	1.57	4.57	4.4	5.64	3.8
18	85-89	2.24	0	4.42	4.38	2.07	0	0	0	4.73	1.52	5.86	2.3
19	90-94	0	0	0	0	6.86	0	0	0	0	5.64	0	1.1
20	95-99	0	0	0	0	0	0	0	0	0	0	0	0.0
Total	0-99												1.0

Supplemental Table 2 – Incidence of Chronic Myeloid Leukemia (CML) in males per age category from 2001-2011 in The Netherlands, obtained from the Netherlands Cancer Registry (www.cijfersoverkanker.nl).

Male		Incidence Chronic Myeloid Leukemia (CML) per year											Average Incidence CML
Cat	Age	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	
1	0-4	0	0	0.19	0.19	0	0	0	0	0	0	0	0.0
2	5-9	0.2	0.2	0	0.2	0	0.2	0	0	0.19	0	0.4	0.1
3	10-14	0.4	0	0.39	0	0.19	0.39	0.2	0	0.2	0	0	0.2
4	15-19	0	0.21	0.61	0	0.2	0	0.39	0.39	0.19	0	0	0.2
5	20-24	0	0.41	0.41	0.2	0.2	0	1.02	0.6	0.79	0.39	0.19	0.4
6	25-29	0.18	0.57	1.36	0.6	0	1.01	0.2	0.8	0.8	0.2	0.79	0.6
7	30-34	0.6	0	0.93	0.81	0.17	1.46	0.38	0.59	0.6	1.59	0.2	0.7
8	35-39	0.59	0.44	1.04	0.45	0.75	0.15	1.24	0.63	0.66	1.22	1.46	0.8
9	40-44	0.79	1.72	0.46	1.21	0.45	0.6	1.06	1.37	0.61	1.07	1.38	1.0
10	45-49	0.52	0.68	1.85	0.5	1.15	0.81	1.91	1.1	1.55	1.23	0.61	1.1
11	50-54	0.51	1.74	0.88	1.07	1.07	1.23	1.22	0.87	0.85	0.5	1.98	1.1
12	55-59	1.29	2.36	1.3	0.54	1.92	0.88	1.44	1.46	0.92	1.28	2	1.4
13	60-64	2.42	1.05	1.53	0.74	0.96	1.81	2.08	1.17	1.32	2.2	1.65	1.5
14	65-69	2.92	1.61	0.32	4	2.1	2.34	2.56	2.21	1.06	2.58	1.94	2.1
15	70-74	1.2	3.14	1.55	2.67	1.51	1.49	2.57	2.51	2.09	4.71	2.29	2.3
16	75-79	6.6	6	7.57	2.66	4.15	5.05	5.4	4.79	1.88	2.76	3.61	4.6
17	80-84	4.93	5.63	3.58	5.99	5.85	4.93	6.43	1.57	6.09	2.2	4.23	4.7
18	85-89	0	6.65	4.42	4.38	2.07	3.82	0	1.67	4.73	0	0	2.5
19	90-94	15.83	7.68	0	14.22	0	0	0	0	6.15	0	5.03	4.4
20	95-99	42.46	0	0	0	0	0	37.64	0	0	0	0	7.3
Total	0-99												1.9

Supplemental Table 3 – Incidence of Myelodysplastic/myeloproliferative neoplasms (MDS/MPN) in males per age category from 2001-2011 in The Netherlands, obtained from the Netherlands Cancer Registry (www.cijfersoverkanker.nl).

Male		Incidence Myelodysplastic/myeloproliferative neoplasms (MDS/MPN) per year											Average Incidence MDS/MPN
Cat	Age	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	
1	0-4	0	0.19	0.38	0	0.39	0.2	0.82	0.62	0.63	0.21	0.21	0.3
2	5-9	0	0	0	0	0	0	0	0	0	0	0	0.0
3	10-14	0	0	0	0	0	0	0	0	0	0	0	0.0
4	15-19	0	0	0	0	0	0	0	0	0	0.19	0	0.0
5	20-24	0	0	0	0	0	0.2	0	0	0	0	0	0.0
6	25-29	0	0	0	0	0	0	0	0	0	0	0	0.0
7	30-34	0.15	0	0	0	0.34	0	0	0	0.2	0	0	0.1
8	35-39	0	0	0	0.15	0	0	0	0	0	0	0	0.0
9	40-44	0	0	0	0.15	0	0.15	0	0	0	0	0	0.0
10	45-49	0	0.17	0.51	0	0.16	0	0.32	0	0	0.15	0.15	0.1
11	50-54	0.34	0.17	0.35	0.53	0.36	0	0	0.17	0	0	0	0.2
12	55-59	0.21	0.59	0.56	0.9	0.7	0.35	0.36	0.73	0.55	0.92	0.73	0.6
13	60-64	0.54	1.05	1.27	2.22	1.2	0.68	1.04	2.15	1.13	1.1	1.1	1.2
14	65-69	2.27	2.57	2.84	2.16	3.3	3.21	1.42	3.31	3.99	3.36	2.43	2.8
15	70-74	3.2	3.93	3.48	4.2	4.91	2.98	5.13	5.74	7.3	4.04	4.9	4.5
16	75-79	3.3	4.91	4.33	5.85	6.22	10.6	8.84	6.71	5.63	7.36	5.86	6.3
17	80-84	6.9	8.45	5.37	7.7	5.01	8.22	4.82	5.49	10.66	13.19	9.87	7.8
18	85-89	6.72	4.43	0	10.95	0	5.73	7.15	10.03	11.04	7.58	11.72	6.9
19	90-94	0	0	0	0	0	0	0	0	12.3	5.64	10.07	2.5
20	95-99	0	0	0	0	0	0	0	0	0	0	0	0.0
Total	0-99												1.7

Supplemental Table 4 – Incidence of Myelodysplastic syndrome (MDS) in males per age category from 2001-2011 in The Netherlands, obtained from the Netherlands Cancer Registry (www.cijfersoverkanker.nl).

Male		Incidence Myelodysplastic syndrome (MDS) per year											Average Incidence MDS
Cat	Age	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	
1	0-4	0	0.38	0.38	0	0.2	0	0.41	0.42	0	0	0	0.2
2	5-9	0.2	0	0	0.4	0	0	0	0.39	0	0.2	0.4	0.1
3	10-14	0	0	0.58	0.97	0	0.2	0	0	0	0	0.58	0.2
4	15-19	0	0	0	1	0.2	0.2	0.39	0.39	0	0.39	0.19	0.3
5	20-24	0	0	0	0.2	0	0	0.2	0.2	0.2	0	0	0.1
6	25-29	0	0.19	0.39	0.4	0.2	0	0.4	0	0.4	0.2	0.2	0.2
7	30-34	0.15	0.15	0.31	0.16	0.34	0.18	0.19	0	0	0.2	0.2	0.2
8	35-39	0.15	0.3	0.15	0.15	0.6	0.15	0	0.16	0.33	0.52	0.37	0.3
9	40-44	0	0.31	0.46	0.15	0.15	0.45	0.6	0.46	0.92	0.61	0.31	0.4
10	45-49	1.03	0.68	0.84	0.83	0.98	0.49	0.8	0.79	0.77	1.07	0.76	0.8
11	50-54	1.35	1.91	3.35	1.42	1.6	2.29	2.1	2.77	2.22	0.84	1.32	1.9
12	55-59	1.29	2.76	2.98	3.24	1.75	2.81	3.6	2.93	3.86	3.3	2.54	2.8
13	60-64	5.1	4.99	3.82	5.42	6.47	5.88	5.81	7.64	6.8	8.07	4.96	5.9
14	65-69	10.71	12.53	13.59	12.01	11.09	11.39	13.11	14.91	14.91	14.99	15.3	13.1
15	70-74	19.59	23.17	27.07	19.86	21.51	18.62	25.67	30.83	25.73	25.91	22.85	23.7
16	75-79	34.12	32.75	31.37	41.5	42.53	37.86	45.69	41.7	49.75	39.58	42.38	39.9
17	80-84	33.49	50.71	62.62	53.03	54.3	56.7	54.67	72.97	62.43	63.04	51.45	55.9
18	85-89	51.54	68.69	66.36	70.08	47.55	61.14	71.46	61.84	64.66	72.79	54.22	62.8
19	90-94	39.57	46.1	51.95	85.35	75.5	53.8	65.34	44.55	67.65	39.48	75.52	58.6
20	95-99	84.93	0	42.4	41.72	40.63	39.39	0	71.29	33.08	31.38	60.79	40.5
Total	0-99												15.4

Supplemental Table 5 – Incidence of Acute myeloid Leukemia (AML) in males per age category from 2001-2011 in The Netherlands, obtained from the Netherlands Cancer Registry (www.cijfersoverkanker.nl).

Male		Incidence Acute myeloid Leukemia (AML) per year											Average Incidence
Cat	Age	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	AML
1	0-4	1.75	1.54	1.15	1.15	1.76	1.2	1.23	1.67	1.05	1.27	1.06	1.3
2	5-9	0.2	0.59	0.6	0.4	0.59	0.39	0.19	0.97	0.58	0.59	0.4	0.5
3	10-14	0.99	1.57	1.36	0.58	0.97	0.79	0.99	0.4	0.6	0.59	0.39	0.8
4	15-19	0.83	1.03	1.41	0.6	0.99	0.59	0.59	0.39	0.58	0.39	0.58	0.7
5	20-24	0.2	0.41	1.22	0.82	0.2	0.61	1.22	0.2	0.39	1.16	1.14	0.7
6	25-29	1.09	1.32	1.75	0.8	1.21	1.01	0.61	1.41	0.8	1.59	0.99	1.1
7	30-34	1.49	1.06	0.78	0.65	1.2	0.91	0.76	1.57	1.39	1	0.99	1.1
8	35-39	1.18	1.33	1.34	1.2	1.5	1.06	0.62	0.79	0.99	2.26	1.46	1.2
9	40-44	1.27	1.4	1.69	1.52	1.2	1.65	1.06	0.91	2.44	1.22	1.54	1.4
10	45-49	2.41	3.91	2.7	2.99	1.48	2.59	2.55	2.99	2.01	2.3	2.44	2.6
11	50-54	4.06	4.17	3.35	4.44	2.84	2.29	3.15	4.15	2.73	3.36	3.14	3.4
12	55-59	5.36	5.32	6.7	5.03	5.42	5.44	6.12	4.94	6.61	6.41	4.72	5.6
13	60-64	6.99	7.35	9.69	7.39	8.39	8.14	5.6	7.44	8.88	8.25	10.28	8.0
14	65-69	15.25	13.17	13.27	13.86	9.89	14.02	13.11	10.49	11.98	11.63	12.14	12.6
15	70-74	15.19	22.38	17.4	17.57	18.12	15.64	16.5	20.08	15.99	14.8	19.91	17.6
16	75-79	31.92	23.47	20.01	16.49	27.49	22.72	23.09	27.32	22.53	18.87	29.3	23.9
17	80-84	32.51	19.72	27.73	33.36	29.24	17.26	28.94	29.03	34.26	31.52	28.9	28.4
18	85-89	29.13	24.37	19.91	32.85	14.47	26.75	17.86	16.71	20.5	18.2	27.84	22.6
19	90-94	15.83	23.05	29.69	35.56	13.73	20.18	19.6	6.36	43.05	22.56	15.1	22.2
20	95-99	42.46	42.46	0	0	81.27	39.39	0	0	33.08	0	0	21.7
Total	0-99												8.9

Supplemental Table 6 – Incidence of Myeloproliferative Neoplasms (MPN) in females per age category from 2001-2011 in The Netherlands, obtained from the Netherlands Cancer Registry (www.cijfersoverkanker.nl).

Female		Incidence Myeloproliferative Neoplasms (MPN) (excluding CML) per year										Average Incidence MPN (excluding CML)
Cat	Age	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
1	0-4	0	0	0	0	0	0	0	0	0	0	0
2	5-9	0	0	0	0	0	0	0	0	0	0	0
3	10-14	0	0	0	0	0	0	0	0	0	0	0
4	15-19	0	0	0	0	0	0	0	0	0	0	0
5	20-24	0	0	0	0	0.21	0	0	0	0	0	0.19
6	25-29	0	0	0	0	0	0	0	0	0	0	0
7	30-34	0.31	0.16	0.16	0	0.17	0	0	0	0.2	0	0.1
8	35-39	0	0	0.15	0	0.15	0	0	0	0.17	0	0.18
9	40-44	0	0.16	0	0	0.31	0	0	0.16	0	0.16	0.16
10	45-49	0.18	0.17	0	0.17	0.17	0	0	0.32	0	0	0.16
11	50-54	0.35	0	0.18	0.18	0	0.18	0	0.17	0.17	0.17	0.17
12	55-59	0.44	0.81	0.57	0.55	0.18	0.36	0.18	0.19	0.56	0.18	0.73
13	60-64	0.27	0.26	0.51	0.25	0.72	0.23	0.63	0.79	0.76	1.29	0.55
14	65-69	1.18	1.78	0.88	1.45	1.7	2.23	1.37	1.34	1.55	0.76	0.48
15	70-74	0.32	0.96	0.64	1.91	1.28	2.55	3.18	2.52	2.78	2.42	2.96
16	75-79	1.46	1.47	1.85	0.37	1.84	1.1	2.53	1.8	3.58	2.5	1.78
17	80-84	1.55	0	1.45	3.75	0.92	0.93	4.16	1.85	2.76	1.82	3.14
18	85-89	1.75	0	0	0.88	0.85	3.23	1.54	0.74	0	2.08	1.37
19	90-94	2.21	0	0	2.08	0	0	0	0	0	0	1.68
20	95-99	0	0	0	0	0	0	0	0	0	0	0.0
Total	0-99											0.5

Supplemental Table 7 – Incidence of Chronic Myeloid Leukemia (CML) in females per age category from 2001-2011 in The Netherlands, obtained from the Netherlands Cancer Registry (www.cijfersoverkanker.nl).

Female		Incidence Chronic Myeloid Leukemia (CML) per year											Average Incidence
Cat	Age	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	CML
1	0-4	0.2	0	0	0	0	0	0	0	0	0	0	0.0
2	5-9	0.21	0	0	0	0	0	0.2	0	0	0	0	0.0
3	10-14	0	0	0	0	0	0	0	0.21	0	0.21	0.41	0.1
4	15-19	0	0	0	0	0.21	0	0	0.2	0.2	0	0.2	0.1
5	20-24	0.21	0.21	0.21	0	0.42	0	0	0	0.4	0.2	0	0.2
6	25-29	0.37	0.77	0.39	0.2	0	0	0.61	0.41	0.2	0.2	0.4	0.3
7	30-34	0.15	0.31	0.48	0.33	0.35	0	0.76	0.59	1	0	0.6	0.4
8	35-39	0.61	0.77	0.62	0.31	0.46	0.47	1.1	1.44	0.66	0.52	0.91	0.7
9	40-44	0.98	0.96	0.16	0.47	0.77	0.77	0.47	0.47	0.78	0.94	0.62	0.7
10	45-49	1.41	1.04	0.86	1.01	1.33	0.99	1.46	0.64	0.63	0.94	0.47	1.0
11	50-54	0.87	1.43	0.18	1.45	1.08	1.25	1.59	2.1	0.34	0.68	1.17	1.1
12	55-59	0.44	0.2	1.53	2.21	1.97	1.07	1.65	1.11	1.3	0.92	2.19	1.3
13	60-64	0.53	2.09	1.02	1.49	2.41	1.37	1.05	1.18	1.52	0.37	2.03	1.4
14	65-69	1.78	3.55	1.47	2.31	1.42	1.95	0.82	0.8	2.07	1.26	1.66	1.7
15	70-74	2.89	2.55	2.55	1.59	1.28	2.55	2.23	0.63	2.47	1.21	2.08	2.0
16	75-79	2.92	1.47	3.7	2.22	4.06	2.56	1.81	2.51	1.43	3.21	1.78	2.5
17	80-84	3.63	4.51	2.42	2.81	2.31	3.24	3.7	2.31	2.3	0.91	0.9	2.6
18	85-89	3.5	1.74	3.51	5.28	4.26	2.42	1.54	4.43	1.42	2.77	1.37	2.9
19	90-94	2.21	6.55	0	2.08	4.06	0	1.95	0	0	0	1.68	1.7
20	95-99	0	0	0	8.6	0	0	7.69	0	0	0	0	1.5
Total	0-99												1.1

Supplemental Table 8 – Incidence of Myelodysplastic/Myeloproliferative Neoplasms (MDS/MPN) in females per age category from 2001-2011 in The Netherlands, obtained from the Netherlands Cancer Registry (www.cijfersoverkanker.nl).

Female		Incidence Myelodysplastic/myeloproliferative neoplasms (MDS/MPN) per year										Average Incidence MDS/MPN
Cat	Age	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
1	0-4	0	0	0.2	0.2	0.2	0.21	0.21	0.44	0	0.22	0.22
2	5-9	0	0	0	0	0	0	0	0	0	0	0
3	10-14	0	0	0	0	0.2	0	0.21	0	0	0	0
4	15-19	0	0	0	0	0	0	0	0	0	0	0
5	20-24	0.21	0	0	0	0	0.21	0	0	0	0	0
6	25-29	0	0	0	0	0	0.2	0	0	0	0	0.2
7	30-34	0	0	0	0	0	0	0	0	0	0	0
8	35-39	0	0	0	0.15	0	0	0	0.16	0	0	0
9	40-44	0.16	0	0	0	0	0	0.16	0.31	0	0.16	0
10	45-49	0	0	0	0	0	0.49	0	0.16	0	0.16	0
11	50-54	0.35	0	0.36	0.18	0	0	0.18	0.52	0.69	0.34	0.17
12	55-59	0.22	0	0.19	0.18	0.36	0.18	1.1	0.19	0.37	0.37	0.18
13	60-64	0.53	0.78	0.26	0.5	0.72	0.68	0.84	0.39	0.38	0.37	0.5
14	65-69	0.89	1.48	1.47	1.45	1.98	0.83	0.27	1.07	1.55	1.26	1.66
15	70-74	0.32	0.64	1.91	2.55	2.87	2.23	2.23	0.95	3.09	2.12	2.96
16	75-79	2.56	1.1	2.59	2.22	1.48	3.29	3.62	3.23	1.07	3.57	2.85
17	80-84	2.07	2.51	2.91	3.28	2.31	3.24	3.24	6.01	2.76	4.55	4.04
18	85-89	3.5	1.74	1.75	1.76	5.11	6.46	2.32	4.43	4.95	3.46	2.06
19	90-94	0	2.18	0	0	2.03	3.99	0	0	0	3.62	0
20	95-99	0	0	0	0	0	0	7.69	7.32	0	0	1.4
Total	0-99											0.8

Supplemental Table 9 – Incidence of Myelodysplastic syndrome (MDS) in females per age category from 2001-2011 in The Netherlands, obtained from the Netherlands Cancer Registry (www.cijfersoverkanker.nl).

Female		Incidence Myelodysplastic syndrome (MDS) per year										Average Incidence	
Cat	Age	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	
1	0-4	0.2	0.2	0	0	0.2	0.21	0	0	0	0	0.22	0.1
2	5-9	0	0.41	0	0	0.21	0	0	0.41	0.2	0.21	0	0.1
3	10-14	0	0	0	0	0	0.21	0.42	0.21	0	0.21	0	0.1
4	15-19	0	0.43	0	0	0	0.21	0	0.61	0.2	0.2	0.2	0.2
5	20-24	0.42	0	0.62	0	0	0.21	0.21	0	0.2	0.2	0.19	0.2
6	25-29	0.37	0.38	0.39	0.2	0.2	0.4	0.2	0	0.4	0.2	0	0.2
7	30-34	0	0.31	0.32	0.33	0.17	0.18	0.19	0	0	0	0	0.1
8	35-39	0.61	0.15	0.46	0.15	0.31	0.16	0.16	0.32	0.5	0.35	0.18	0.3
9	40-44	0.49	0.64	0.47	0.62	0.62	0.31	0.62	0.47	0.62	0.78	0.31	0.5
10	45-49	0.53	1.04	0.69	0.51	0.33	0.33	0.65	0.96	0.79	1.4	1.09	0.8
11	50-54	1.22	1.25	1.09	0.73	0.72	1.07	1.06	1.05	1.03	1.18	1	1.0
12	55-59	1.76	2.23	1.91	1.47	3.4	2.5	1.83	2.04	2.05	1.85	2.56	2.1
13	60-64	3.45	2.35	4.34	3.47	3.86	5.01	6.07	4.14	3.8	3.88	2.77	3.9
14	65-69	4.74	9.18	8.23	7.23	4.53	8.07	8.48	5.87	7.25	6.81	8.56	7.2
15	70-74	10.29	13.73	10.19	13.38	8.93	11.48	11.45	13.86	10.51	15.11	12.75	12.0
16	75-79	16.8	12.13	24.03	15.93	20.29	12.79	18.09	17.6	28.26	22.12	22.41	19.1
17	80-84	18.14	21.57	25.68	19.21	25.89	29.62	33.77	24.49	30.84	25.04	23.34	25.2
18	85-89	24.52	20.93	29.82	24.62	34.9	30.7	29.34	24.35	26.18	28.37	26.07	27.3
19	90-94	17.69	17.47	17.12	16.64	22.33	21.94	15.64	32.75	15.19	25.31	16.84	19.9
20	95-99	0	9.12	17.82	8.6	8.24	0	15.38	0	6.95	6.65	19.26	8.4
Total	0-99												6.4

Supplemental Table 10 – Incidence of Acute Myeloid Leukemia (AML) in females per age category from 2001-2011 in The Netherlands, obtained from the Netherlands Cancer Registry (www.cijfersoverkanker.nl).

Female		Incidence Acute myeloid Leukemia (AML) per year											Average Incidence
Cat	Age	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	AML
1	0-4	1.02	1.21	1	1.41	1.64	1.26	1.07	1.09	0.88	0.44	1.33	1.1
2	5-9	0.21	0.41	0	0.62	0.21	0.41	0.2	0.2	0.41	0.21	0.21	0.3
3	10-14	0.41	0.82	0.61	0.61	0.41	0.41	0.42	0.84	0.42	0	0.41	0.5
4	15-19	0.22	0.86	0	0	2.28	1.23	1.23	0.41	0.4	1.01	0.61	0.8
5	20-24	1.26	1.04	0.62	1.04	0.42	0.42	1.67	0.61	0.4	1.18	0.78	0.9
6	25-29	0.74	0.96	1.58	0.6	1.62	1.01	0.81	1.42	2.02	0.6	1	1.1
7	30-34	1.24	1.09	1.11	1.15	0.35	1.83	0.76	1.38	1.99	1.2	0.99	1.2
8	35-39	1.69	1.38	1.54	1.86	1.24	2.17	2.04	1.76	1	2.09	2	1.7
9	40-44	2.11	1.6	1.58	3.12	3.4	2.16	1.86	1.87	2.19	1.71	1.56	2.1
10	45-49	2.11	3.48	1.72	3.72	2.33	2.46	2.91	2.24	2.36	2.65	3.27	2.7
11	50-54	3.49	1.97	2.17	2.54	1.63	4.83	2.3	3.15	2.92	3.39	2.5	2.8
12	55-59	3.53	5.67	5.34	4.97	3.93	4.83	4.77	4.46	4.28	4.99	3.29	4.6
13	60-64	3.99	6.27	7.65	4.95	6.52	3.65	3.35	5.72	5.9	4.43	4.61	5.2
14	65-69	4.15	6.52	9.41	10.41	5.95	8.35	6.57	7.48	8.8	9.33	9.75	7.9
15	70-74	9.97	12.45	10.5	12.42	9.56	8.61	7	9.45	9.89	14.81	10.97	10.5
16	75-79	9.86	13.24	15.9	13.34	12.17	14.26	13.39	13.65	16.81	14.98	13.87	13.8
17	80-84	12.96	16.55	16.48	18.27	12.48	17.58	15.27	15.25	13.35	18.21	19.75	16.0
18	85-89	10.51	11.34	14.04	14.07	14.47	10.5	15.44	20.66	21.94	13.15	19.21	15.0
19	90-94	8.84	6.55	4.28	16.64	10.15	15.96	9.77	9.63	9.5	9.04	10.1	10.0
20	95-99	9.4	0	8.91	0	8.24	0	7.69	0	0	0	0	3.1
Total	0-99												5.1

Supplemental Table 11 – Patient age, sex and follow-up characteristics in 367 patients. Age category (Age-Cat), Follow-up (FU)

Age-Cat	Age	Total no.	Male	Female	FU in yrs.	FU-Male	FU-Female
1	0-4	0	0	0	0.0	0.0	0.0
2	5-9	0	0	0	0.0	0.0	0.0
3	10-14	0	0	0	0.0	0.0	0.0
4	15-19	0	0	0	0.0	0.0	0.0
5	20-24	0	0	0	0.0	0.0	0.0
6	25-29	0	0	0	0.0	0.0	0.0
7	30-34	14	7	7	20.6	7.1	13.4
8	35-39	12	2	10	28.2	7.0	21.3
9	40-44	29	14	15	53.9	15.3	38.5
10	45-49	38	20	18	228.2	59.9	168.3
11	50-54	44	23	21	135.8	68.0	67.8
12	55-59	66	33	33	173.6	85.3	88.3
13	60-64	62	34	28	317.7	108.3	209.4
14	65-69	34	14	20	145.2	73.5	71.7
15	70-74	39	19	20	104.2	51.2	53.0
16	75-79	22	13	9	73.5	42.9	30.6
17	80-84	6	4	2	20.9	11.9	9.0
18	85-89	1	0	1	7.0	4.3	2.7
19	90-94	0	0	0	0.0	0.0	0.0
20	95-99	0	0	0	0.0	0.0	0.0
Total	0-99	367	183	184	1308.8	534.7	774.1

Supplemental Table 12 - Expected number of hematological malignancies in 367 patients; Myeloproliferative Neoplasms (MPN), Chronic Myeloid Leukemia (CML), Myelodysplastic/Myeloproliferative neoplasms (MDS/MPN). Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML).

Age-Cat	Age	MPN (without CML)	CML	MDS/MPN	MDS	AML
1	0-4	0.000	0.000	0.000	0.000	0.000
2	5-9	0.000	0.000	0.000	0.000	0.000
3	10-14	0.000	0.000	0.000	0.000	0.000
4	15-19	0.000	0.000	0.000	0.000	0.000
5	20-24	0.000	0.000	0.000	0.000	0.000
6	25-29	0.000	0.000	0.000	0.000	0.000
7	30-34	0.000	0.001	0.000	0.000	0.002
8	35-39	0.000	0.002	0.000	0.000	0.004
9	40-44	0.001	0.006	0.000	0.002	0.015
10	45-49	0.005	0.043	0.004	0.042	0.111
11	50-54	0.010	0.033	0.006	0.035	0.094
12	55-59	0.044	0.078	0.026	0.146	0.291
13	60-64	0.080	0.137	0.076	0.345	0.600
14	65-69	0.044	0.047	0.047	0.280	0.243
15	70-74	0.051	0.044	0.065	0.358	0.283
16	75-79	0.028	0.033	0.042	0.298	0.171
17	80-84	0.002	0.003	0.004	0.029	0.016
18	85-89	0.000	0.000	0.000	0.001	0.000
19	90-94	0.000	0.000	0.000	0.000	0.000
20	95-99	0.000	0.000	0.000	0.000	0.000
Total	0-99	0.265	0.425	0.271	1.536	1.831

Supplemental Table 13 – Patient age, sex and follow-up characteristics in 274 Gastroenteropancreatic Neuroendocrine tumors (GEP-NETs) patients.

Patient Characteristics								Expected number of hematopoietic neoplasms				
Age-Cat	Age	Total no.	Male	Female	FU in yrs	FUMale	FUFemale	MPN (without CML)	CML	MDS/MPN	MDS	AML
1	0-4	0	0	0	0.0	0.0	0.0	0.000	0.000	0.000	0.000	0.000
2	5-9	0	0	0	0.0	0.0	0.0	0.000	0.000	0.000	0.000	0.000
3	10-14	0	0	0	0.0	0.0	0.0	0.000	0.000	0.000	0.000	0.000
4	15-19	0	0	0	0.0	0.0	0.0	0.000	0.000	0.000	0.000	0.000
5	20-24	0	0	0	0.0	0.0	0.0	0.000	0.000	0.000	0.000	0.000
6	25-29	0	0	0	0.0	0.0	0.0	0.000	0.000	0.000	0.000	0.000
7	30-34	6	3	3	9.4	5.8	3.6	0.000	0.000	0.000	0.000	0.000
8	35-39	7	1	6	23.1	6.3	16.8	0.000	0.001	0.000	0.000	0.002
9	40-44	19	10	9	38.3	9.7	28.6	0.000	0.003	0.000	0.002	0.007
10	45-49	26	13	13	203.2	45.7	157.5	0.003	0.027	0.002	0.020	0.070
11	50-54	36	19	17	108.2	49.4	58.8	0.006	0.021	0.004	0.028	0.060
12	55-59	47	23	24	144.6	75.5	69.1	0.026	0.046	0.015	0.085	0.173
13	60-64	53	29	24	298.0	94.8	203.2	0.063	0.109	0.060	0.354	0.474
14	65-69	28	12	16	125.9	63.6	62.4	0.031	0.034	0.034	0.172	0.175
15	70-74	29	15	14	87.8	46.9	40.9	0.033	0.028	0.043	0.235	0.184
16	75-79	18	11	7	54.1	36.5	17.6	0.019	0.022	0.028	0.184	0.113
17	80-84	5	3	2	16.2	9.5	6.8	0.001	0.002	0.003	0.019	0.010
18	85-89	0	0	0	4.3	3.8	0.5	0.000	0.000	0.000	0.000	0.000
19	90-94	0	0	0	0.0	0.0	0.0	0.000	0.000	0.000	0.000	0.000
20	95-99	0	0	0	0.0	0.0	0.0	0.000	0.000	0.000	0.000	0.000
Total	0-99	274	139	135	1113.2	447.3	665.8	0.183	0.292	0.190	1.100	1.268

Supplemental Table 14 – Expected number of hematological malignancies in 274 patients; Myeloproliferative Neoplasms (MPN), Chronic Myeloid Leukemia (CML), Myelodysplastic/Myeloproliferative neoplasms (MDS/MPN). Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML).

Age-Cat	Age	MPN (without CML)	CML	MDS/MPN	MDS	AML
1	0-4	0.000	0.000	0.000	0.000	0.000
2	5-9	0.000	0.000	0.000	0.000	0.000
3	10-14	0.000	0.000	0.000	0.000	0.000
4	15-19	0.000	0.000	0.000	0.000	0.000
5	20-24	0.000	0.000	0.000	0.000	0.000
6	25-29	0.000	0.000	0.000	0.000	0.000
7	30-34	0.000	0.000	0.000	0.000	0.000
8	35-39	0.000	0.001	0.000	0.000	0.002
9	40-44	0.000	0.003	0.000	0.002	0.007
10	45-49	0.003	0.027	0.002	0.020	0.070
11	50-54	0.006	0.021	0.004	0.028	0.060
12	55-59	0.026	0.046	0.015	0.085	0.173
13	60-64	0.063	0.109	0.060	0.354	0.474
14	65-69	0.031	0.034	0.034	0.172	0.175
15	70-74	0.033	0.028	0.043	0.235	0.184
16	75-79	0.019	0.022	0.028	0.184	0.113
17	80-84	0.001	0.002	0.003	0.019	0.010
18	85-89	0.000	0.000	0.000	0.000	0.000
19	90-94	0.000	0.000	0.000	0.000	0.000
20	95-99	0.000	0.000	0.000	0.000	0.000
Total	0-99	0.183	0.292	0.190	1.100	1.268

Supplemental Table 15 - 43 out of 367 off-protocol with reason:

Reason:	Number of patients
Low uptake (on first post therapy scan)	14
Concomitant Radiotherapy	6
Diagnostic	4
Previous ^{111}In -PRRT	3
Low Karnofsky score	3
Poor renal function	3
Low baseline Hb, platelets or WBC	3
Previous ^{90}Y -PRRT	2
No pathology available	2
Hb transfusion prior to PRRT	1
Previous ^{131}I -therapy	1
Patient was not able to give fully consent	1
Total	43

Supplemental Table 16 - 93 out of 367 patients with Non GEP-NETs:

Type of tumor	Number of patients
NET - thorax/chest	2
NET - unknown primary	28
NET - other locations	4
Tyroid carcinoma	19
Paraganglioma	14
Feochromocytoma	2
Meningioma	4
Hurthe cell carcinoma	6
SCLC	1
Grawitz pancreas	1
Mamma carcinoma	3
Erdheim chester	1
HCC	2
Prostate carcinoma	1
Esthesioneuroblastoma	1
Melanoma	2
Medulloblastoma	1
Rectum carcinoma	1
Total	93

Supplemental Table 17 – Characteristics of 13 patients with persistent hematological dysfunction (PHD) after peptide receptor radiotherapy (PRRT) with ^{177}Lu -DOTATATE (^{177}Lu). Neuroendocrine tumor (NET), Neuroendocrine tumor of the pancreas (PNET), Radioactive iodine I-131 therapy (^{131}I), cold Octreotide (Octreotide), External beam radiotherapy (EBRT), PRRT with ^{177}Lu -Hemoglobin (Hb), Platelets (PLT), White Blood Cells (WBC).

Patient		Administered						Bone marrow					Diagnosis
no.	sex	Age	Diagnosis	Previous therapy	Activity (GBq)	PRRT interrupted	Reason	Blood work	1. Aspirate	2. Flow	3. Cytogenetics	4. Biopsy	
359	f	70	NET	Octreotide	30.0	no	-	Hb	yes	no	no	yes	MDS, RARS
297	f	60	NET	Octreotide	18.6	yes	Maximum kidney dose	Hb, PLT, WBC	yes	no	no	yes	Hypoplasia
293	m	61	PNET	chemo-embolisation	29.3	no	-	Hb, PLT	yes	yes	46,XY, t(9;22)	yes	CML
284	m	57	PNET	-	29.7	no	-	Hb	yes	no	-5,-7,del(12p), +mar	yes	MDS, RAEB-II
252	f	64	NET	Octreotide	30.0	no	-	Hb, WBC	no	no	no	no	Pancytopenia
241	f	41	PNET	-	26.3	yes	Hematological toxicity	Hb, PLT, WBC	yes	no	no	yes	Aplasia
185	m	74	PNET	-	26.4	no		Hb, PLT	yes	yes	45,XY,-7 [20]	yes	MDS/MPN: CMML-1
158	m	62	NET	Octreotide	22.2	yes	Maximum kidney dose	Hb, PLT, WBC	yes	yes	no	yes	MDS, RAEB-II
105	v	67	NET	-	22.3	yes	Hematological toxicity	WBC	yes	no	no	yes	Hypoplasia
102	m	68	NET	-	30.0	no	-	Hb, PLT, WBC	yes	yes	no	yes	MDS, Hypocellular
91	f	59	NET	Octreotide, local EBRT	22.7	yes	Maximum kidney dose	Hb, PLT, WBC	yes	yes	46,XX	yes	AML
81	f	58	NET	Octreotide	22.3	yes	Maximum kidney dose	Hb, PLT, WBC	yes	no	no, JAK2 neg	yes	Myelofibrosis/ MPN
45	f	58	Thyroid cancer	Radioactive iodine therapy	16.7 (^{131}I) & 15.2 (^{177}Lu)	no	-	Hb, PLT	yes	no	no	yes	Hypoplasia

Supplemental Table 18 – Calculations for the relative risk (RR) in all 367 patients and 274 Neuroendocrine gastroenteropancreatic tumors (GEP-NETs).

	All 367 patients	274 GEP-NET patients
Exposed group		
Number with positive (bad) outcome (a):	8	8
Number with negative (good) outcome (b):	359	266
Control group		
Number with positive (bad) outcome (c):	4.4	3
Number with negative (good) outcome (d):	362.6	271
Relative Risk	1.82	2.67
95% Confidence Interval	1.26 to 2.62	0.72 to 9.95
Z statistic	3.22	1.46
Significance level	P = 0.0013	P = 0.1442
NNT (Harm)	101.81	54.800
95% Confidence Interval	254.25 (Harm) to 63.65 (Harm)	23.99 (Harm) to ∞ to 192.77 (Harm)