

Supplementary material

Appendix Table 1_{a-c}

List of detailed information of the 51 patients recruited in this study:

1_a: List of 25 patients with malignancy before Hymenoptera venom allergy

Age in years /Sex	Tumor Type, Year of Diagnosis	Allergy to insect venom (grade)	Atopy	VIT (cause of stopp)	VIT Side Effect	MA during VIT	Baseline serum tryptase (µg/l)
70/♂	prostate carcinoma, 2003	BV/ VV (4/4)	no	since 2007	no	remission	9.90
67/♀	breast cancer, 1998	BV (4)	yes	since 2000	no	remission	14.30, (no biopsy)
62/♂	seminoma, 1984	BV (4)	no	since 1993; 1. VIT 1993-99	LLR	remission	19.80, cutaneous mastocytosis possible (skin biopsy)
59/♀	melanoma, 1963	BV (4)	no	2002-07	unspecific (tiredness)	remission	3.42
63/♀	melanoma, 1983	BV (3-4)	no	since 2008	no	remission	4.60
56/♂	seminoma, 1987	BV (3-4)	no	since 2008	no	remission	2.99
43/♀	melanoma, around 1960	BV (3)	no	since 2008	no	remission	6.47
33/♂	angiosarcoma, 1998	BV (3)	no	since 2008	SR (maintenance dose)	remission	2.90
51/♀	breast cancer, 1996	BV (3)	yes	2002-07	LLR	remission	4.42
86/♂	prostate carcinoma, 1998	BV (3)	no	11/1998-2004	no	remission	4.26
47/♂	teratocarcinoma, 1987	BV (3)	no	1999-2004	no	remission	6.05
59/♀	breast cancer, 2001	BV (2-3)	no	since 2004	no	remission	5.36
74/♀	ovarial carcinoma, 1971	BV (2-3)	no	since 2000, follow-up refused	no	remission	7.44
65/♀	breast cancer, 2002	VV (4)	no	since 2003	LLR, unpecific (tiredness)	remission	13.10, (no biopsy)

Age in years /Sex	Tumor Type, Year of Diagnosis	Allergy to insect venom (grade)	Atopy	VIT (cause of stopp)	VIT Side Effect	MA during VIT	Baseline serum tryptase ($\mu\text{g/l}$)
73/♀	breast cancer, 1992	VV (4)	no	since 2005; 1. VIT 1985-91	no	remission	22.20, cutaneous mastocytosis possible (skin biopsy not conclusive)
72/♀	spinalioma, 2001	VV (4)	no	2003-08	no	remission	4.40
49/♂	seminoma, 1985	VV (4)	yes	since 2007	no	remission	< 1.00
54/♂	seminoma, 1995; kidney carcinoma, 1997	VV (4)	yes	since 2008	no	remission	60.20, systemic mastocytosis with involvement of skin (skin biopsy, no bone marrow biopsy)
46/♂	melanoma, ca. 1980	VV (4)	yes	since 2005	no	remission	8.51
68/♂	kidney carcinoma, 2001	VV (4)	no	since 2008	no	remission	42.20, systemic mastocytosis (bone marrow biopsy)
67/♀	breast cancer, 1997	VV (3)	no	2000-05	no	remission	4.71
42/♀	cervix carcinoma, 2006	VV (3)	yes	since 2007	no	remission	NA
38/♀	M. Hodgkin, 1992	VV (2-3)	yes	since 2004	no	remission	2.46
73/♂	prostate carcinoma, 2000	hornet (4)	no	2003-08	no	remission	6.18
63/♂	prostate carcinoma, 2001	hornet (4)	no	2003-06 (metastasis)	no	recurrence (prostat-ectomy 2001; bone metastasis 2006)	5.10

Allergy grade according to H.L. Mueller

VIT = Venom immunotherapy

MA = malignancy

VV = Vespula venom

BV = bee venom

SR = systemic allergic reaction

LLR = large local reaction

NA = not available

1_b: List of 16 patients with malignancy during venom immunotherapy

Age in years /Sex	Tumor Type, Year of Diagnosis	Allergy to insect venom (grade)	Atopy	VIT (cause of stop)	MA treatment during VIT	VIT Side effect	Baseline serum tryptase (µg/l)
44/♀	thyroid carcinoma, 2004	BV / VV (4/4)	yes	1997-2004, (MA)	thyroidectomy after VIT stop	SR (maintenance dose)	19.20, (skin biopsy negative)
82/♂	prostate carcinoma, 1996; colon carcinoma, 1983	BV / VV (4/4)	yes	since 1993; 1979-89 whole body extract	radiatio 1996; VIT continued	SR (maintenance dose)	33.70, cutaneous mastocytosis, systemic mastocytosis possible (skin biopsy positive, no bone marrow biopsy)
59/♀	breast cancer in situ, 2006; breast cancer 2008 (opposite side)	BV (4)	no	2003-08 (MA)	lumpectomy 2006; adjuvant chemotherapy 4 cycles (Doxorubicin, Cyclophosphamid) 03-05/2006; VIT 2006 not interrupted; ablatio mammae 2008 after VIT stop	no	4.24
73/♂	prostate carcinoma, 2008	BV (4)	no	since 2007	no specific treatment	no	NA
53/♂	seminoma, 1995	BV (3-4)	no	1993-95 (MA), 1997-98 (relapse); since 1999	semilateral orchiectomy 1995; 4 cycles chemotherapy (Cisplatin, Etoposid, Bleomycin); retroperitoneal lymphadenectomy; relapse: semilateral orchiectomy 1998; axillary lymph node dissection 1998; chemotherapy (Cisplatin, Etoposid, Ifosfamid) 03-09/1998	no	3.74

65/♂	bladder carcinoma, 2004	BV (3-4)	no	2003-07	resection 2004; VIT continued after no surgery		5.64
50/♀	Non-Hodgkin-lymphoma, 2001	BV (3)	yes	1999-2001 (MA)	no specific treatment	unspecific (Lymph node swelling, temporal dysesthesia)	3.29
50/♀	breast cancer, 2000	BV (3)	no	07-08/2000 (MA)	mastectomy, lymphangiosis carcinomatosa, chemotherapy after VIT stop	no	3.86
17/♂	melanoma, 2007	BV (2-3)	no	since 2005	local excision 2007	no	4.45
61/♀	ovarial carcinoma, 2002; breast cancer, 1988	VV (4)	no	1999-2002 (metastatic MA)	ovariectomy 2003; chemotherapy after VIT stop	no	7.88
67/♂	prostate carcinoma, 2008	VV (4)	no	since 2006	laparoscopic prostatectomy 2008, VIT continued after surgery	unspecific (tingling sensation in palms)	5.89
66/♂	prostate carcinoma, 2004	VV (3-4)	no	2001-06	prostatectomy 2004, VIT continued after surgery	no	1.93
59/♀	breast cancer, 1996	VV (3-4)	no	1991-96 (MA)	radiatio, chemotherapy after VIT stop	feeling of dizziness without blood pressure involvement during up-dosing	2.51
63/♀	breast cancer, 2000	VV (2-3)	yes	1999-2004	tumorectomy 2000; 4 cycles chemotherapy (Epirubicin, Cyclophosphamid) 07-08/2000; radiatio 2000; Tamoxifen since 2000; VIT continued after surgery	no	4.83
52/♀	breast cancer, 2006	VV (2-3)	yes	2001-06 (MA)	lumpectomy 2006; chemotherapy (Doxorubicin, Cyclophosphamid) 03-06/2006; radiatio 2006; Tamoxifen since 2006	no	3.54

75/♂	prostate carcinoma, 2006	hornet (3)	yes	2002-06 (polyneuropathy)	local radiatio 2006 after VIT stop	unspecific (polyneuropathy)	3.28
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Allergy grade according to H.L. Mueller

VIT = Venom immunotherapy

MA = malignancy

VV = Vespula venom

BV = honey bee venom

SR = systemic allergic reaction

LLR = large local reaction

NA = not available

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1c: Details of one patients with cancer after completed venom immunotherapy

Age in years /Sex	Tumor Type, Year of Diagnosis	Allergy to insect venom (grade)	Atopy	VIT	Baseline serum tryptase (µg/l)
53/♂	bladder carcinoma, 2004	BV (4)	no	2. VIT recommended; 1. VIT 1992-98	5.75

Allergy grade according to H.L. Mueller

VIT = Venom immunotherapy

MA = malignancy

BV = honey bee venom

1a: List of 9 patients with malignancy and Hymenoptera venom allergy without venom immunotherapy

Age in years/Sex	Tumor Type, Year of Diagnosis	Allergy to insect venom (grade)	Atopy	VIT status	Baseline serum tryptase ($\mu\text{g/l}$)
62/♀	breast cancer, 1995	BV / VV (4/4)	no	VIT recommended	14.30 (no biopsy)
39/♂	M. Hodgkin, 2008	BV (3-4)	no	VIT recommended	2.12
62/♀	breast cancer, 1999	VV (3)	no	VIT recommended	5.26
51/♂	seminoma, 1997	VV (2-3)	no	VIT recommended	9.06
61/♀	colon carcinoma (peritoneal metastasis), 2003	VV (2)	no	VIT not recommended	2.27
56/♂	seminoma, 1996	BV (2)	yes	VIT not recommended	5.54
63/♀	breast cancer, 2001	VV (2)	no	VIT not recommended	1.69
49/♂	kidney carcinoma, 2001	BV (2)	no	VIT not recommended	8.58
62/♂	prostate carcinoma, 2003	VV (2)	yes	VIT not recommended	3.21

Allergy grade according to H.L. Mueller

VIT = Venom immunotherapy

VV = Vespula venom

BV = bee venom

Appendix table 2_a

Statistics of MA incidence in patients with VIT versus Swiss population of 2008 including subgroups according to age [15]

Age	HVA with VIT 5-year-incidence	MA in HVA with VIT 5-year-incidence	rate	Swiss population 1-year	MA in Swiss population 1-year-incidence	expected MA in HVA with VIT 5-year-incidence	p-value
0-14	73	0	0	1'179'744	152	0.05	1
15-39	456	1	0.0022	2'516'729	1'496	1.36	1
40-44	192	1	0.0052	649'072	1'040	1.54	1
45-49	177	0	0	614'756	1'647	2.37	0.1828
50-54	152	4	0.0263	534'363	2'355	3.35	0.7225
55-59	123	2	0.0163	477'116	3'591	4.63	0.2215
60-64	128	2	0.0156	453'631	4'976	7.02	0.0501
65-69	97	3	0.0309	366'691	5'381	7.12	0.1202
70-74	62	1	0.0161	296'797	5'061	5.26	0.0632
75+	36	2	0.0556	612'957	11'911	3.5	0.5761
Sum	1495	16	0.0113	7'701'856	37'611	36.23	0.0001

HVA = Hymenoptera venom allergy

VIT = venom immunotherapy

MA = malignancy

Appendix table 2_b

Statistics of malignancy incidence of different tumor sites in patients with VIT versus mean annual incidence in Swiss population 2003-2007 [15]

Cancer	MA in HVA with VIT 5-year-incidence	rate	MA in Swiss population 1-year-incidence	rate Swiss population	p-value
Prostate	5	0.0033	5901	0.0038	1
Breast	5	0.0033	5175	0.0034	1
melanoma	1	0.0007	1930	0.0013	1
Non-Hodgkin	1	0.0007	1400	0.0009	1
bladder	1	0.0007	1083	0.0007	1
Ovary	1	0.0007	593	0.0004	0.438
thyroid	1	0.0007	492	0.0003	0.380
Testis	1	0.0007	402	0.0003	0.323
other sites	0	0	16113	0.0105	0.000
Sum	16	0.0107	33089	0.02148	0.002

HVA = Hymenoptera venom allergy

VIT = venom immunotherapy

MA = malignancy

Appendix table 3

Statistics of 51 patients with HVA and MA compared to 758 patients with HVA [20]

	present study	Blum et al.	Confidence Interval	p-value
bT \geq 11.4 μg/l	9/49*	44/758	[0.086 - 0.314]	0.002
Atopy	15/51	253/731	[0.162 - 0.425]	0.374
Side effects to VIT	11/51	-	[0.142 - 0.429]	-

HVA = Hymenoptera venom allergy

VIT = venom immunotherapy

MA = malignancy

*bT not available in 2 patients