Supplementary Materials

Spontaneous Non-Sustained Ventricular Tachycardia and Premature Ventricular Contractions and Their Prognostic Relevance in Patients with Cancer in Routine Care

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Table S1. Kind of Cancer Patients (*n* = 261).

Group	Type of Cancer	No. of Patients (*n*=261) *n*, (%)	Solid Cancer or Haematological Malignancy
Group 1—Gastrointestinal cancer (*n* = 31)	Rectal cancer	4 (2)	Solid cancer
	Colon cancer	12 (5)	Solid cancer
	Duodenal cancer	1 (<1)	Solid cancer
	Pancreatic cancer	2 (1)	Solid cancer
	Gastric cancer	4 (2)	Solid cancer
	Esophageal cancer	6 (2)	Solid cancer
	Cholangiocellular carcinoma	12 (5)	Solid cancer
Group 2—Lung cancer (*n* = 21)	Non-small-cell-lung-cancer	15 (6)	Solid cancer
	Small-cell-lung-cancer	6 (2)	Solid cancer
Group 3—Gynaecologic cancer (*n* = 35)	Cervical- / Ovarian- / Uterine cancer	12 (5)	Solid cancer
	Breast cancer	23 (9)	Solid cancer
Group 4—Other solid cancers (*n* = 42)	Tonsillar / Laryngeal / Oro- / Epi- / Hypopharyngeal carcinoma	15 (6)	Solid cancer
	Urothelial carcinoma	6 (2)	Solid cancer
	Kidney cell carcinoma	2 (1)	Solid cancer
	Prostate carcinoma	7 (3)	Solid cancer
	Sarcoma	4 (2)	Solid cancer
	Choroid melanoma	5 (2)	Solid cancer
	Thyroid cancer	1 (<1)	Solid cancer
	Thymus carcinoma	1 (<1)	Solid cancer
	Peritoneal Mesothelioma	1 (<1)	Solid cancer
Group 5—Leukaemia (*n* = 19)	Chronic myeloid leukemia	1 (<1)	Haematological malignancy
	Acute myeloid leukemia	11 (4)	Haematological malignancy
	Myeloproliferative neoplasia	3 (1)	Haematological malignancy
	Myelodysplastic syndromes	3 (1)	Haematological malignancy
	Acute lymphocytic leukemia	1 (<1)	Haematological malignancy
Group 6—Lymphoma (*n* = 113)	B-cell-Non-Hodgkin-lymphoma	82 (31)	Haematological malignancy
	T-cell-Non-Hodgkin-lymphoma	5 (2)	Haematological malignancy
	Hodgkin-lymphoma	10 (4)	Haematological malignancy
	Multiple myeloma	16 (6)	Haematological malignancy

Table S2. Baseline Medication.

Variable	Healthy Controls (*n* = 35)	Cancer Patients (*n* = 261)	*p*-Value	Cancer Deaths (*n* = 158)	Cancer Survivors (*n* = 103)	*p*-Value
Aspirin, *n* (%)	2 (6)	63 (24)	0.07	39 (25)	24 (23)	0.80
Angiotensin-converting enzyme inhibitor, *n* (%)	2 (6)	57 (22)	0.11	40 (25)	17 (17)	0.09
Calcium channel blocker, *n* (%)	0	37 (14)	**0.0025**	20 (13)	17 (17)	0.38
Angiotensin II receptor blocker, *n* (%)	0	36 (14)	**0.0028**	16 (10)	20 (19)	**0.033**
Beta-blocker, *n* (%)	5 (14)	117 (45)	**0.0001**	74 (47)	43 (42)	0.42
Spironolactone, *n* (%)	0	7 (3)	0.23	5 (3)	2 (2)	0.61
Diuretics, *n* (%)	0	71 (27)	**<0.0001**	45 (28)	26 (25)	0.57
Anticoagulants, *n* (%)	1 (3)	93 (36)	**0.0002**	61 (39)	32 (31)	0.21
Antidiabetics or Insulin, *n* (%)	0	28 (11)	**0.0099**	17 (11)	11 (11)	0.98
Proton pump inhibitors, *n* (%)	1 (3)	167 (64)	**<0.0001**	98 (62)	69 (67)	0.41
Opioids, *n* (%)	0	46 (18)	**0.0006**	32 (20)	14 (14)	0.17
Antidepressants, *n* (%)	0	23 (9)	**0.021**	19 (12)	4 (4)	**0.013**
Corticosteroids, *n* (%)	0	73 (28)	**<0.0001**	51 (32)	22 (21)	0.055
Prior chemotherapy, *n* (%)	–	199 (76)	–	127 (80)	72 (70)	0.052
Prior immunotherapy, *n* (%)	–	125 (48)	–	75 (47)	50 (49)	0.87
Alkylating agents, *n* (%)	–	113 (43)	–	64 (41)	49 (48)	0.26
Platins, *n* (%)	–	74 (28)	–	56 (35)	18 (17)	**0.0016**
Anti-metabolites, *n* (%)	–	98 (38)	–	64 (41)	34 (33)	0.22
Topoisomerase inhibitors, *n* (%)	–	47 (18)	–	28 (18)	19 (18)	0.88
Antracyclines, *n* (%)	–	79 (30)	–	45 (28)	34 (33)	0.44
Antimitotics, *n* (%)	–	60 (23)	–	30 (19)	30 (29)	0.06
Taxanes, *n* (%)	–	30 (11)	–	24 (15)	6 (6)	**0.020**
Histone deacetylase inhibitors, *n* (%)	–	1 (<1)	–	0	1 (1)	0.34
Antibodies/ Immunotherapy, *n* (%)	–	105 (40)	–	63 (40)	42 (41)	0.88
Thyrosin kinase inhibitors, *n* (%)	–	13 (5)	–	11 (7)	2 (2)	**0.043**
Other kinase inhibitors, *n* (%)	–	3 (1)	–	3 (2)	0	0.77
Proteasom inhibitors, *n* (%)	–	17 (7)	–	9 (6)	8 (8)	0.51
Other chemotherapeutic agents, *n* (%)	–	16 (6)	–	11 (7)	5 (5)	0.51

Significant p-values ($p < 0.05$) are bold.

Table S3. Prior Chemotherapy, Immunotherapy and Targeted Therapy.

Variables	All Cancer Patients *n* = 261	GI Cancer *n* = 31	Lung Cancer *n* = 21	Gynaecologic Cancer *n* = 35	Other solid Cancers *n* = 42	Leukaemia *n* = 19	Lymphoma *n* = 113
Alkylating agents, *n*	113	0	1	13	2	4	93
Cyclophosphamide, *n**	77	0	1	10	0	2	64
Ifosfamide, *n**	15	0	0	0	1	0	14
Melphalan, *n*	14	0	1	0	0	0	13
Temozolomide, *n*	1	0	0	0	1	0	0
Dacarbazine, *n*	6	0	0	0	0	0	6
Procarbazine, *n*	3	0	0	0	0	0	3
Carmustine, *n*	7	0	0	0	0	0	7
Chlorambucil, *n*	3	0	0	0	0	0	3
Thiotepa, *n*	3	0	0	0	0	0	3
Treosulfan, *n*	3	0	0	3	0	0	0
Busulfan, *n*	2	0	0	0	0	2	0
Bendamustine, *n*	24	0	0	0	0	0	24
Platins, *n*	74	18	16	13	15	1	11
Carboplatin, *n*	26	1	8	12	2	0	2
Cisplatin, *n**	40	4	7	4	13	1	11
Oxaliplatin, *n*	13	12	0	0	0	0	1
Anti-metabolites, *n*	98	22	8	8	9	10	41
High-dose Methotrexate, *n*	24	0	0	0	1	1	22
Fluorouracil, *n*	27	18	0	2	6	0	1
Pemetrexed, *n*	1	0	0	0	1	0	0
Tioguanine, *n*	1	0	1	0	0	0	0
Capecitabine, *n*	13	7	1	5	0	0	0
Gemcitabine, *n*	18	1	7	4	1	1	4
Fludarabine, *n*	7	0	0	0	0	4	3
Trifluridine/Tipiracil, *n*	1	1	0	0	0	0	0
Clofarabine, *n**	0	0	0	0	0	0	0
Cytarabine, *n*	32	0	1	0	0	9	22
Topoisomerase inhibitors, *n*	47	8	8	1	2	3	25
Irinotecan, *n*	8	8	0	0	0	0	0
Topotecan, *n*	3	0	1	1	0	0	1
Mitoxantrone, *n*	5	0	0	0	0	3	2
Pixantrone, *n*	6	0	0	0	0	0	6
Etoposide, *n*	29	1	8	0	2	0	18
Antracyclines, *n*	79	0	1	13	3	7	55
Doxorubicin / Adriamycin, *n**	70	0	1	9	3	3	54
Pegylated liposomal Doxorubicin, *n**	3	0	0	3	0	0	0
Daunorubicin, *n**	5	0	1	0	0	3	1
Epirubicin, *n**	5	0	0	4	1	0	0
Idarubicin, *n**	3	0	0	0	0	2	1
Antimitotics, *n*	60	0	1	2	1	2	54
Vincristine, *n*	54	0	0	0	1	2	51
Vinorelbine, *n*	3	0	1	1	0	0	1
Vinblastine, *n*	6	0	0	0	0	0	6
Taxanes, *n*	30	5	2	18	5	0	0
Docetaxel, *n**	11	4	0	3	4	0	0
Eribulin, *n*	3	0	0	3	0	0	0
Paclitaxel, *n**	19	1	2	15	1	0	0
Protein-bound paclitaxel, *n**	1	0	0	1	0	0	0
Histone deacetylase inhibitor, *n*	1	0	0	0	0	0	1
Belinostat, *n*	1	0	0	0	0	0	1
Antibodies/ Immunotherapy, *n*	105	5	6	9	10	1	74

Alemtuzumab, *n*	1	0	0	0	0	0	1
Bevacizumab, *n**	10	3	0	6	0	0	1
Brentuximab, *n*	7	0	0	0	0	0	7
Cetuximab, *n*	13	4	0	0	9	0	0
Daratumumab, *n*	1	0	0	0	0	0	1
Isatuximab, *n*	1	0	0	0	0	0	1
Nivolumab, *n*	6	0	4	0	1	0	1
Olaratumab, *n*	1	0	0	0	1	0	0
Panitumumab, *n*	1	1	0	0	0	0	0
Pertuzumab, *n**	1	0	0	1	0	0	0
Pembrolizumab, *n*	2	0	1	1	0	0	0
Rituximab, *n*	71	0	0	0	0	1	70
Tomuzotuximab, *n*	1	0	0	0	1	0	0
Ofatumumab, *n*	1	0	0	0	0	0	1
Trastuzumab, *n**	2	0	0	2	0	0	0
Programmed death-ligand 1-Antibody, *n*	1	0	1	0	0	0	0
Thyrosin kinase inhibitors, *n*	13	1	2	1	3	1	5
Afatinib, *n**	2	0	2	0	0	0	0
Axitinib, *n**	0	0	0	0	0	0	0
Ibrutinib, *n**	5	0	0	0	0	0	5
Imatinib, *n**	1	0	0	0	0	1	0
Osimertinib, *n**	2	0	2	0	0	0	0
Pazopanib, *n**	1	0	0	0	1	0	0
Sunitinib, *n**	1	0	0	0	1	0	0
Sorafenib, *n**	2	0	0	0	2	0	0
Nilotinib, *n**	1	0	0	0	0	1	0
Lapatinib, *n**	1	0	0	1	0	0	0
Regorafenib, *n**	1	1	0	0	0	0	0
Other Kinase inhibitors, *n*	3	0	0	1	0	0	2
Idelalisib, *n*	2	0	0	0	0	0	2
Palbociclib, *n*	0	0	0	0	0	0	0
Ribociclib, *n*	1	0	0	1	0	0	0
Proteasom inhibitors, *n*	17	0	1	0	0	0	16
Bortezomib, *n**	17	0	1	0	0	0	16
Ixazomib, *n*	1	0	0	0	0	0	1
Other chemotherapeutic agents, *n*	16	0	0	0	4	1	11
Tretinoin (ATRA), *n*	1	0	0	0	0	1	0
Everolimus, *n**	1	0	0	0	1	0	0
Temsirolimus, *n**	3	0	0	0	0	0	3
Mitomycin, *n*	4	0	0	0	3	0	1
Bleomycin, *n*	4	0	0	0	0	0	4
Venetoclax, *n*	1	0	0	0	0	0	1
Lenalidomide, *n*	2	0	0	0	0	0	2
Pomalidomide, *n*	1	0	0	0	0	0	1
Romidepsin, *n*	1	0	0	0	0	0	1
Azacitidine, *n*	1	0	0	0	0	1	0

GI, gastrointestinal. * anti-cancer drugs that may cause left ventricular dysfunction (according to the "2016 ESC Position Paper on cancer treatments and cardiovascular toxicity" – Zamorano et al. EHJ. 2016).

Table S4. Association of NSVT ≥4 Beats & ≥100 bpm with Relevant Variables in all Cancer Patients (n = 261).

Variable	No NSVT ≥4 Beats & ≥100 bpm (*n* = 236)	NSVT ≥4 Beats & ≥100 bpm (*n* = 25)	*p*-value
Clinical characteristics			
Age (year)	67 ± 12	65 ± 13	0.30
Female sex, *n* (%)	123 (52)	9 (36)	0.13
BMI (kg/m²)	25 ± 5	26 ± 7	0.26
Cancer stage ≥III, *n* (%)	166 (70)	22 (88)	0.33
Cancer type: solid, *n* (%)	116 (49)	13 (52)	0.74
ECOG performance status ≥2, *n* (%)	100 (42)	11 (44)	0.88
Prior potentially cardiotoxic anti-cancer drugs, *n* (%)	147 (62)	15 (60)	0.82
Left ventricular ejection fraction (%)	65 ± 7 (*n*=163)	63 ± 10 (*n*=18)	0.41
Laboratory parameters			
Haemoglobin (g/dL)	10.9 ± 2.0	10.4 ± 1.9	0.33
Leucocytes (/nL)	6.3 (4.4 – 9.7)	6.9 (3.9 – 9.5)	0.97
Platelets (/nL)	228 ± 170	204 ± 117	0.50
Sodium (mmol/L)	139 ± 4	138 ± 3	0.64
Potassium (mmol/L)	3.9 ± 0.5	3.9 ± 0.5	0.99
Creatinine (mg/dL)	0.98 ± 0.53	1.16 ± 1.01	0.15
GOT (U/L)	26 (19 – 36) (*n*=161)	33 (23 – 66) (*n*=10)	0.27
Secondary diagnoses			
Arterial hypertension, *n* (%)	119 (50)	13 (52)	0.88
Coronary artery disease, *n* (%)	27 (11)	7 (28)	**0.019**
Atrial fibrillation, *n* (%)	12 (5)	2 (8)	0.91
Previous myocardial infarction, *n* (%)	16 (7)	4 (16)	0.61
Diabetes mellitus type 2, *n* (%)	46 (19)	4 (16)	0.92
Chronic kidney disease, *n* (%)	38 (16)	3 (12)	0.89
Previous stroke, *n* (%)	26 (11)	1 (4)	0.52
Current use of antibiotics, *n* (%)	42 (18)	3 (12)	0.79
Medication at study entry			
Aspirin, *n* (%)	56 (24)	7 (28)	0.64
Angiotensin-converting enzyme inhibitor, *n* (%)	46 (19)	11 (44)	**0.0048**
Calcium channel blocker, *n* (%)	33 (14)	4 (16)	0.93
Angiotensin II receptor blocker, *n* (%)	33 (14)	3 (12)	0.93
Beta-blocker, *n* (%)	107 (45)	10 (40)	0.61
Spironolactone, *n* (%)	5 (2)	2 (8)	0.64
Diuretics, *n* (%)	66 (28)	5 (20)	0.39
Anticoagulants, *n* (%)	82 (35)	11 (44)	0.36
Antidiabetics or Insulin, *n* (%)	27 (11)	1 (4)	0.52
Proton pump inhibitors, *n* (%)	152 (64)	15 (60)	0.66
Opioids, *n* (%)	44 (19)	2 (8)	0.44
Antidepressants, *n* (%)	21 (9)	2 (8)	0.97
Corticosteroids, *n* (%)	69 (29)	4 (16)	0.52
Anti-cancer therapy			
Prior chemotherapy, *n* (%)	178 (75)	21 (84)	0.62
Prior immunotherapy, *n* (%)	116 (49)	9 (36)	0.21
Alkylating agents, *n* (%)	103 (44)	10 (40)	0.73
Platins, *n* (%)	67 (28)	7 (28)	0.97
Anti-metabolites, *n* (%)	90 (38)	8 (32)	0.55
Topoisomerase inhibitors, *n* (%)	42 (18)	5 (20)	0.79
Antracyclines, *n* (%)	72 (31)	7 (28)	0.80
Antimitotics, *n* (%)	55 (23)	5 (20)	0.71
Taxanes, *n* (%)	28 (12)	2 (8)	0.89
Histone deacetylase inhibitor, *n* (%)	1 (<1)	0	0.76
Antibodies/ Immunotherapy, *n* (%)	96 (41)	9 (36)	0.65
Thyrosin kinase inhibitors, *n* (%)	13 (6)	0	0.14
Other kinase inhibitors, *n* (%)	3 (1)	0	0.52
Proteasom inhibitor, *n* (%)	16 (7)	1 (4)	0.89
Other chemotherapeutic agents, *n* (%)	13 (6)	3 (12)	0.75
24h-ECG			
Average 24h heart rate (bpm)	78 ± 13	85 ± 20	**0.016**
No. of premature atrial contraction / 24h	185 (27 – 1028)	690 (51 – 2073)	0.09

No. of premature ventricular contraction / 24h	20 (2 – 279)	439 (114 – 3263)	**0.0001**
≥20 Premature ventricular contractions / 24h, *n* (%)	118 (50)	21 (84)	0.09
≥50 Premature ventricular contractions / 24h, *n* (%)	97 (41)	20 (80)	**0.0002**

Values are means ± SD or n (%). 24h, 24 hours; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; bpm, beats per minute; GOT, glutamic oxaloacetic transaminase; no., number; NSVT, non-sustained ventricular tachycardia. *P*-values are determined using the unpaired *t*-test.

Table S5. Association of <20 PVC & ≥20 PVC with Relevant Variables in all Cancer Patients (*n* = 261).

Variable	<20 PVC (*n* = 122)	≥20 PVC (*n* = 139)	*p*-Value
Clinical characteristics			
Age (year)	65 ± 13	70 ± 11	**0.0018**
Female sex, *n* (%)	73 (60)	59 (42)	**0.0051**
BMI (kg/m²)	21 ± 5	25 ± 5	0.94
Cancer stage ≥III, *n* (%)	93 (76)	95 (68)	0.16
Cancer type: solid, *n* (%)	61 (50)	68 (49)	0.86
ECOG performance status ≥2, *n* (%)	56 (46)	55 (40)	0.30
Prior potentially cardiotoxic anti-cancer drugs, *n* (%)	71 (58)	91 (65)	0.23
Left ventricular ejection fraction (%)	65 ± 7 (*n*=89)	64 ± 8 (*n*=92)	0.38
Laboratory parameters			
Haemoglobin (g/dL)	10.9 ± 2.1	10.7 ± 2.0	0.52
Leucocytes (/nL)	6.1 (4.3 – 9.1)	6.8 (4.4–9.6)	0.36
Platelets (/nL)	218 ± 121	232 ± 197	0.52
Sodium (mmol/L)	139 ± 4	139 ± 4	0.86
Potassium (mmol/L)	3.9 ± 0.5	4.0 ± 0.6	0.12
Creatinine (mg/dL)	1.01 ± 0.66	0.99 ± 0.52	0.83
GOT (U/L)	24 (18–36) (*n*=83)	28 (20–37) (*n*=88)	0.12
Secondary diagnoses			
Arterial hypertension, *n* (%)	55 (45)	87 (63)	**0.0046**
Coronary artery disease, *n* (%)	8 (7)	26 (19)	**0.0036**
Atrial fibrillation, *n* (%)	4 (3)	10 (7)	0.17
Previous myocardial infarction, *n* (%)	4 (3)	16 (12)	**0.010**
Diabetes mellitus type 2, *n* (%)	22 (18)	28 (20)	0.67
Chronic kidney disease, *n* (%)	15 (12)	26 (19)	0.16
Previous stroke, *n* (%)	13 (11)	14 (10)	0.88
Current use of antibiotics, *n* (%)	19 (16)	26 (19)	0.50
Medication at study entry			
Aspirin, *n* (%)	27 (22)	36 (26)	0.48
Angiotensin-converting enzyme inhibitor, *n* (%)	20 (16)	37 (27)	**0.046**
Calcium channel blocker, *n* (%)	18 (15)	19 (14)	0.80
Angiotensin II receptor blocker, *n* (%)	12 (10)	24 (17)	0.08
Beta-blocker, *n* (%)	53 (43)	64 (46)	0.67
Spironolactone, *n* (%)	3 (2)	4 (3)	0.85
Diuretics, *n* (%)	32 (26)	39 (28)	0.74
Anticoagulants, *n* (%)	39 (32)	54 (39)	0.25
Antidiabetics or Insulin, *n* (%)	17 (14)	11 (8)	0.12
Proton pump inhibitors, *n* (%)	80 (66)	87 (63)	0.62
Opioids, *n* (%)	19 (16)	27 (19)	0.42
Antidepressants, *n* (%)	13 (11)	10 (7)	0.32
Corticosteroids, *n* (%)	34 (28)	39 (28)	0.97
Anti-cancer therapy			
Prior chemotherapy, *n* (%)	87 (71)	112 (81)	0.08
Prior immunotherapy, *n* (%)	59 (48)	66 (47)	0.89
Alkylating agents, *n* (%)	48 (39)	65 (47)	**0.021**
Platins, *n* (%)	37 (30)	37 (27)	0.56
Anti-metabolites, *n* (%)	47 (39)	51 (37)	0.56
Topoisomerase inhibitors, *n* (%)	26 (21)	21 (15)	0.38
Antracyclines, *n* (%)	35 (29)	44 (32)	0.60
Antimitotics, *n* (%)	28 (23)	32 (23)	0.31
Taxanes, *n* (%)	12 (10)	18 (13)	0.39
Histone deacetylase inhibitor, *n* (%)	0	1 (1)	0.46
Antibodies/ Immunotherapy, *n* (%)	53 (43)	52 (37)	0.27

Thyrosin kinase inhibitors, *n* (%)	9 (7)	4 (3)	0.12
Other kinase inhibitors, *n* (%)	3 (2)	0	0.09
Proteasom inhobitors, n (%)	6 (5)	11 (8)	0.71
Other chemotherapeutic agents, *n* (%)	6 (5)	10 (7)	0.95
24h-ECG			
Average 24h heart rate (bpm)	77 ± 15	80 ± 13	**0.042**
No. of premature atrial contraction / 24h	53 (20–353)	543 (100–2287)	**<0.0001**
No. of premature ventricular contraction / 24h	2 (0–7)	297 (87–1312)	**<0.0001**
NSVT ≥4 beats & ≥100 bpm, *n* (%)	4 (3)	21 (15)	**<0.0001**
NSVT ≥6 beats & ≥100 bpm, *n* (%)	2 (2)	10 (7)	**0.028**

Values are means ± SD or n (%). 24h, 24 hours; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; bpm, beats per minute; GOT, glutamic oxaloacetic transaminase; no., number; NSVT, non-sustained ventricular tachycardia. Significant p-values ($p < 0.05$) are bold.