Cannabis-based medicines prolong survival time in patients treated under the Specialized Palliative Outpatient Care

Gastmeier K[1], Gastmeier A[2], Böhm R[3], Bimberg R[4], Herdegen T[3]

[1] Praxis für SAPV, Karl-Marx Str. 42, 14482 Potsdam
Email: knud.gastmeier@t-online.de
[2] Facharztpraxis für Innere Medizin, Lungenheilkunde und Allgemeinmedizin, Zehlendorfer Damm 217, 14532 Kleinmachnow
Email: info@praxis-baekemuehle.de
[3] Institut für Experimentelle und Klinische Pharmakologie, UKSH Campus Kiel Arnold-Heller-Straße 3, Haus U37, 24105 Kiel
[4] StatConsult IT-ServiceGmbH, am Fuchsberg 11, 39112 Magdeburg

Published 10.11.2021; Kleinmachnow

BACKGROUND

Although the 2017 Act Amending Narcotic Drugs Provisions and Other Related Provisions (Gesetz zur Änderung betäubungsmittelrechtlicher und anderer Vorschriften) explicitly aimed at improving provision of care for palliative patients, the use of cannabis-based medicines (CBM) in palliative care remains controversial due to insufficient evidence. However, many Specialized Palliative Outpatient Care (SAPV: Spezielle Ambulante Palliativversorgung) team members see in their daily practice a positive impact of the use of CBM on the four factors defined by the Institute for Quality and Efficiency in Health Care (IQWIG: Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen) as patient-relevant outcomes: morbidity, mortality, adverse events and quality of life. This led us to analyze our practice data for a potential impact of CBM therapy on the survival time of our patients. Due to the pressing relevance of our observations for palliative care patients, we are making the preliminary data from our ongoing retrospective study available in this pre-publication. Based on the current trend in the evaluation, we consider that patients could promptly benefit from a low and slowly increasing dose.

METHODS

Data of all patients under the SAPV, treated and deceased in the period from 01.04.2017 to 30.09.2021, were extracted from the Pallidoc database and analyzed statistically using R. Collected data included survival time (initiation of SAPV treatment until date of death), age, gender, and treatment with CBM. Patients with a treatment duration of less than 10 days or more than three years were excluded from the analysis.

Table 1: Descriptive statistics of the analyzed patient groups

	SAPV with CBM therapy; n (%)	SAPV without CBM therapy; n (%)
Total	137 (17.1 %)	663 (82.9 %)
Age		
> 75 years	61 (44.5 %)	416 (62.7 %)
< 75 years	76 (55.5 %)	247 (37.3 %)
Gender		
Female	62 (45.3 %)	340 (51.3 %)
Male	75 (54.7 %)	323 (48.7 %)
Dose		
> 7.5 mg THC / day	36 (26.3 %)	-
< 7.5 mg THC / day	101 (73.7 %)	-

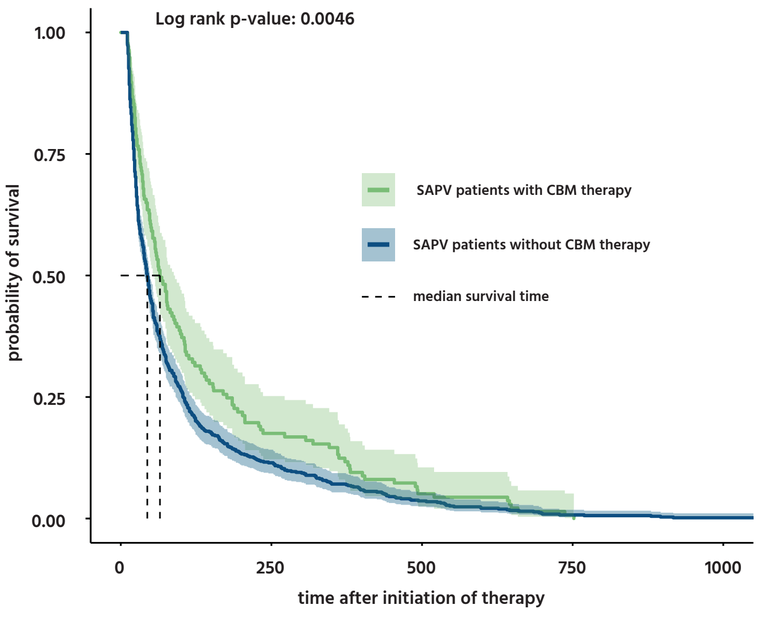
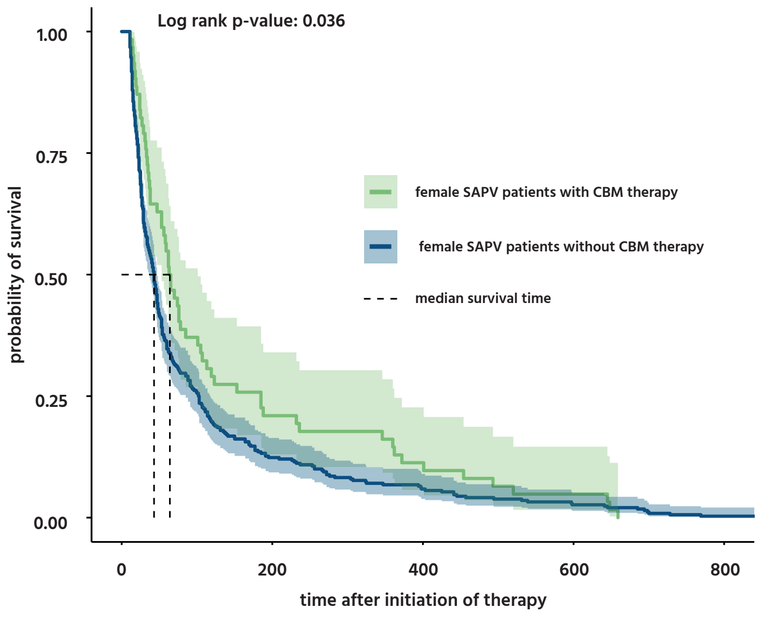


Figure 1: Kaplan-Meier curves of SAPV patients with and without CBM therapy



Fiigure 2: Kaplan-Meier curves of female SAPV patients with and without CBM therapy

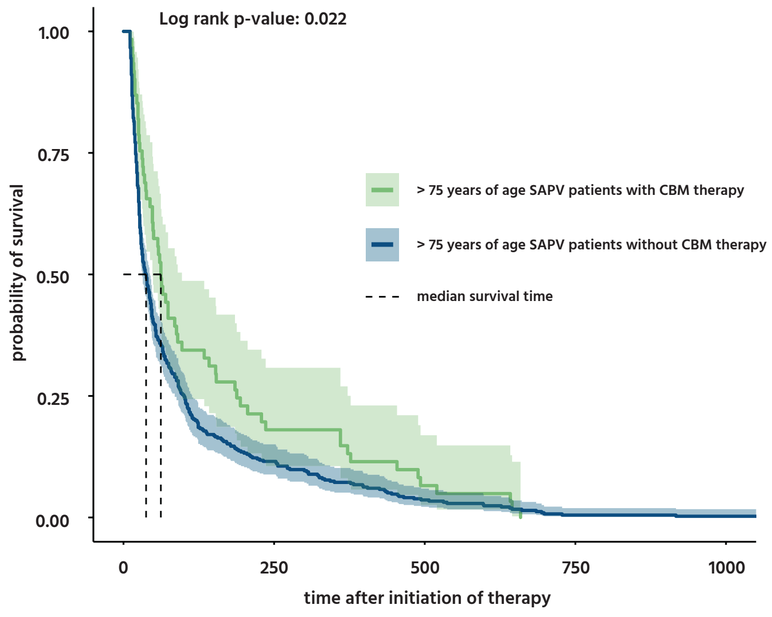


Figure 3: Kaplan-Meier curves of > 75 years of age SAPV patients with and without CBM therapy

Table 2: Comparison of median survival time of SAPV patients by treatment, gender and age, and multivariate analysis

	SAPV with CBM therapy		SAPV without CBM therapy		SAPV without CBM vs with CBM	Multivariate analysis
	n	median survival time (days, 95 % CI)	n	median survival time (days, 95 % CI)	Log Rank p-value	REF/CBM HR (95 % CI; p-value)
CBM therapy						
SAPV with CBM	137	65 (53-88)			0.0046	Reference
SAPV without CBM (REF)			663	44 (39-48)		1.29 (1.07-1.5; 0.008)
Gender						
Female	62	64 (53-101)	340	43 (36-47)	0.036	Reference
Male	75	74 (48-107)	323	47 (39-58)	0.066	0.96 (0.83-1.1; 0.545)
Age						
> 75 years	61	62 (48-97)	416	37.5 (31-44)	0.022	1.10 (0.95-1.3; 0.201)
< 75 years	76	76 (53-106)	247	53 (48-60)	0.16	Reference
Groups by gender and age						
Female, > 75 years	32	62.5 (37-185)	231	33 (29-43)	0.041	
Female, < 75 years	30	70.5 (53-113)	109	53 (48-62)	0.66	
Male, > 75 years	29	60 (48-142)	185	39 (32-54)	0.27	
Male, < 75 years	46	76.5 (42-132)	138	53.5 (42-70)	0.13	

Table 3: SAPV patients with < 7.5 mg THC / day (low-dose) or > 7.5 mg THC / day compared to SAPV patients without CBM therapy

	n	Median survival time, days (95 % CI)	CBM/REF HR (95 % CI; p-value)
SAPV with > 7.5 mg THC / day	36	104 (70-185)	0.56 (0.40-0.79; < 0.001)
SAPV with < 7.5 mg THC / day	101	57 (44-76)	0.88 (0.71-1.09; 0.233)
SAPV without CBM (REF)	663	44 (39-48)	Reference

RESULTS

A total of 800 SAPV patients were included in the analysis, of which 137 received THC (Δ-9-Tetrahydrocannabinol)-containing CBM (17.1 %, female: 45.3 %; > 75 years of age: 44.5 %), and 663 patients (82.9 %, female: 51.3 %; > 75 years of age: 62.7 %) were provided SAPV without the use of CBM (**Table 1**).

The therapy with CBM was associated with prolonged median survival after initiation of SAPV treatment from 44 to 65 days (log rank p = 0.0046) (**Figure 1**).

The assessment of the influence of gender and age on prolonged median survival time with CBM therapy showed that women (64 days with CBM vs 43 days without CBM; log rank p = 0.036; **Figure 2**) and elderly patients (> 75 years of age: 62 days with CBM vs 37.5 days without CBM; log rank p = 0.022; women > 75 years of age: 62.5 days with CBM vs 33 days without CBM; log rank p = 0.041) particularly benefited from CBM therapy (**Table 2, Figure 3**).

For men, prolonged median survival time was observed with CBM therapy but this did not reach statistical significance (**Table 2**).

A multivariate analysis confirmed the observed positive association between CBM therapy and median survival time of SAPV patients (REF/CBM HR: 1.29; p = 0.008) when age and gender were included as influencing factors (**Table 2**).

CBM therapy was initiated at the lowest dose which was then gradually increased until the first effect was observed. After a short observation period, a decision was made whether a further dose increase was required. By using this approach, patients generally received low-dose CBM therapy. A subdivision of CBM therapy into low-dose (< 7.5 mg THC / day; median daily dose 3.2 ± 2.1 mg THC) and patients with higher-dose (> 7.5 mg THC / day; median daily dose 12.0 ± 8.4 mg THC) suggested a superiority of the higher-dose therapy in terms of median survival time (104 days > 7.5 mg THC vs 57 days < 7.5 mg THC) (**Table 3**).

It is worth noting that even in the patient group with > 7.5 mg THC / day, the median daily dose was relatively low. Men under 75 years of age took the highest median daily doses (6.4 ± 9.08 mg THC / day), whereas for the other groups the median daily dose was 4.8 mg THC / day (data not shown).

CONCLUSION

The current trend in the evaluation of patient data from our SAPV team indicates an overall positive association between CBM therapy and prolonged median survival time of SAPV patients. Women and elderly patients appear to be particularly likely to benefit from such therapy. From the available data, we can conclude that current prescribing practices deprive patients of days of life and that CBM therapy should be included as first line therapy for the patient groups considered due to the significant prolongation of survival time.

Since these observations are highly relevant for palliative care clinical practice, we are currently working in cooperation with other SAPV teams to expand and validate the present dataset.