

The effect of cannabis use on tumor response to Nivolumab in patients with advanced malignancies

- Gil Bar-Sela, Tarek Taha, Samira Talhamy, Mira Wollner, Avivit Peer, David Meiri
- Division of Oncology, Rambam Health Care Campus, Haifa, Israel
- laboratory of cancer biology and cannabinoids research, Department of Biology



2018
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MASCC/ISOO
ANNUAL MEETING
SUPPORTIVE CARE IN CANCER



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Faculty Disclosure

No, nothing to disclose regarding
Cannabis

<i>Company Name</i>	<i>Honoraria/ Expenses</i>	<i>Consulting/ Advisory Board</i>	<i>Funded Research</i>	<i>Royalties/ Patent</i>	<i>Stock Options</i>	<i>Ownership/ Equity Position</i>	<i>Employee</i>	<i>Other (please specify)</i>
Novartis	X	X						
MSD	X		X					
BMS	X							
Medison-IS	X							



Clinical use in oncology palliative care

Chemotherapy Induced Nausea and Vomiting (CINV)

Cancer-Associated Pain

Anorexia and Cachexia syndrome

Insomnia

Depression and Anxiety

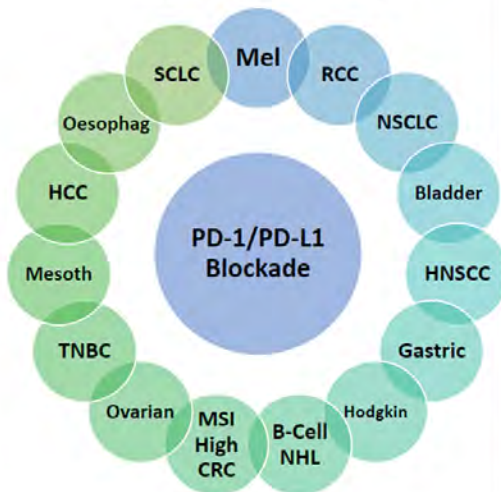


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"PDLOMAS" ACTIVITY IN 2015



Cannabis immunomodulatory effects

- Induction of apoptosis (of T cells, macrophages, splenocytes and thymocytes)
 - [Rieder SA, Immunobiology 2010 & McKallip RJ, J Pharmacol Exp Ther 2002]
- Inhibition of cell proliferation, inhibition of production of chemokines and cytokines and induction of T reg.
 - [Klein TW, J Neuroimmune Pharmacol 2006].
- **Clinical studies:**
- Cannabis for inflammatory bowel disease [Naftali T, Dig Dis. 2014]
- Cannabidiol for the Prevention of Graft-versus-Host-Disease after Allogeneic Hematopoietic Cell Transplantation: Results of a Phase II Study. [Yeshurun M, [Biol Blood Marrow Transplant](#), 2015]
- Therapeutic cannabinoids in multiple sclerosis: immunomodulation revisited [[Constantinescu CS](#), [Eur J Neurol](#). 2018]



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Study design

- A retrospective, observational study
- All patients treated with Nivolumab in the Division of Oncology from August 2015 to August 2016.
- **End points:**
 - Primary : **Response rate.**
 - Secondary : Progression Free Survival , Overall Survival.



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Results: The demographic and medical characteristics of study sample

		Immunotherapy (n=89)	Immunotherapy + Cannabis (n=51)
Age		67.7±10.2	62±10.6
Gender	Male	66 (74.2%)	40 (78.4%)
	Female	23 (25.8%)	11 (21.6%)
Type of Disease	Non-small-cell cancer	57 (64%)	41 (80.4%)
	Other malignancies	32 (36%)	10 (19.6%)
Metastasis	Brain	7 (19.1%)	9 (17.6%)
	Mediastinum	55 (61.8%)	22 (43.1%)
	Liver	13 (14.6%)	7 (13.7%)
	Adrenal	21 (23.6%)	10 (19.6%)
	Bones	28 (31.5%)	21 (41.2%)
	Other	23 (25.8%)	11 (21.6%)
Smoking	No	53 (59.6%)	22 (43.1%)
	Yes	36 (40.4%)	29 (56.9%)
Performance Status prior treatment	0	18 (26.1%)	8 (21.6%)
	1	28 (40.6%)	13 (35.1%)
	2	17 (24.6%)	10 (27%)
	3 / 4	6 (8.7%)	6 (16.2%)



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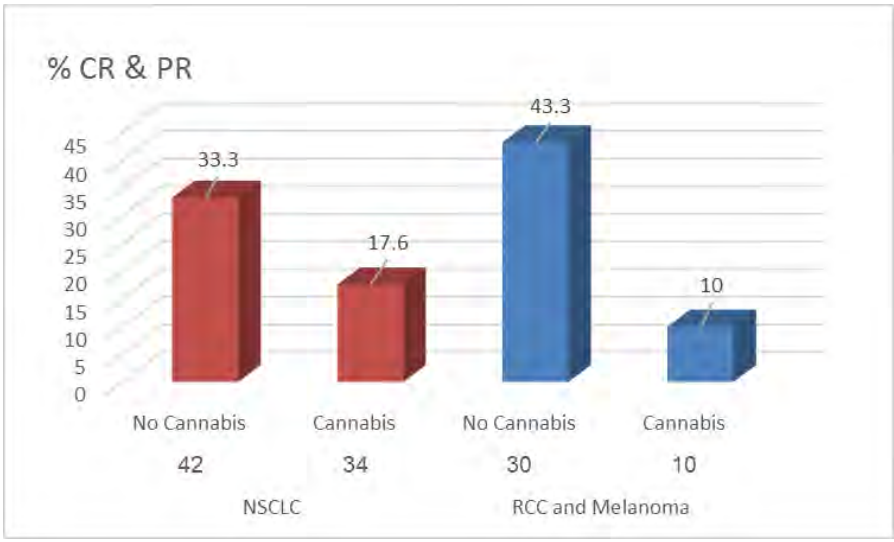
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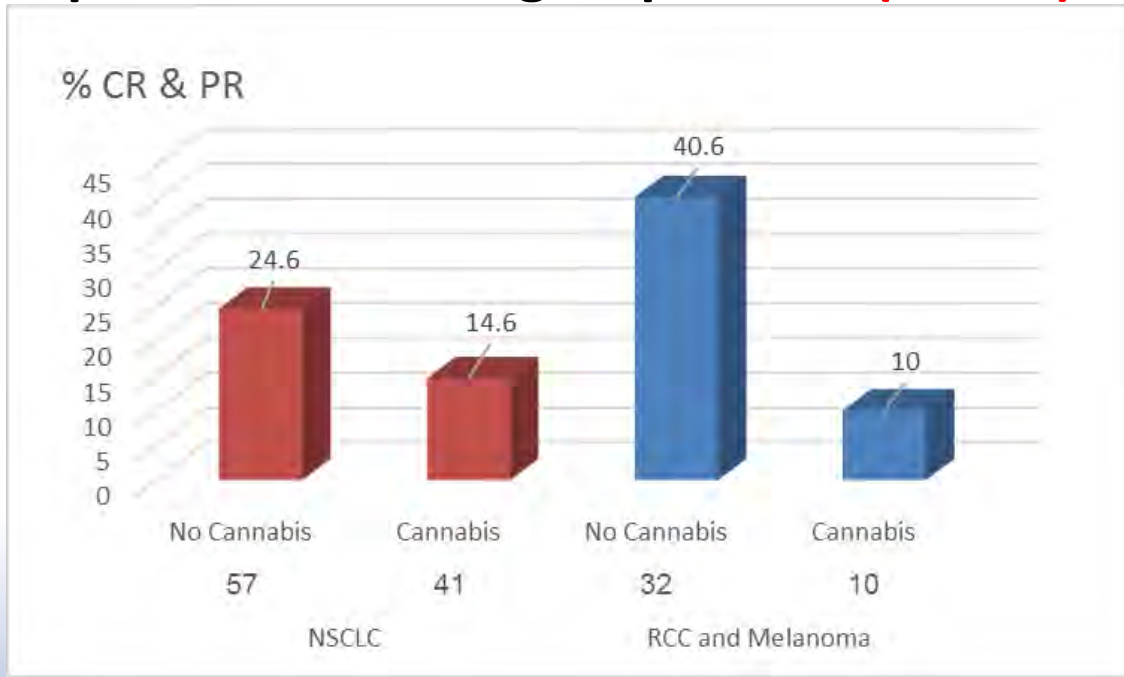
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Response rate among patients with Overall Survival ≥ 2 months (n=116)



Patients not using cannabis are **3.17** times more likely to respond to treatment ($p=0.016$, C.I 95% 1.24-8.1).

Response rate among all patients (n=140)

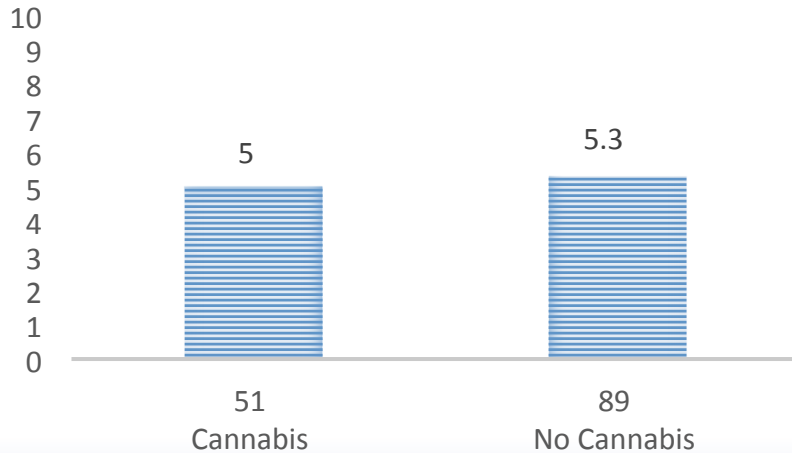




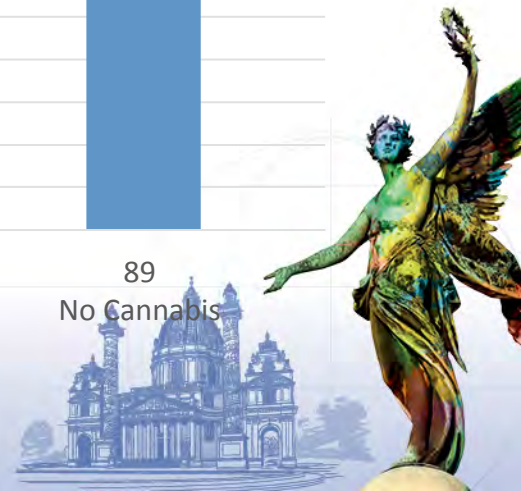
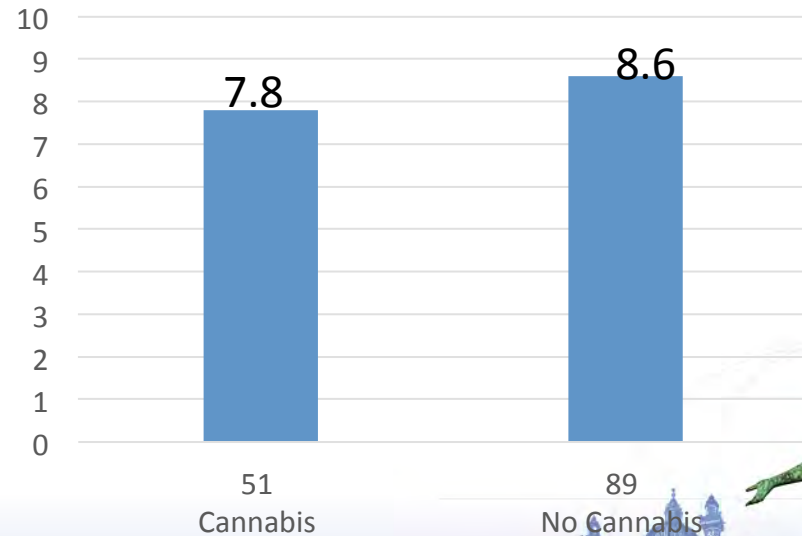
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- Cannabis use was not a significant factor for PFS or OS.
- A multivariate analysis showed that factors affecting PFS and OS were: smoking status, brain metastases, low performance status.

MEAN PFS (MONTHS) 140PTS.



Mean OS (months) 140pts.



Cannabis compounds and response type

6/8 companies, 37/51 patients.

- ▶ There was no significant impact of cannabis composition on response.



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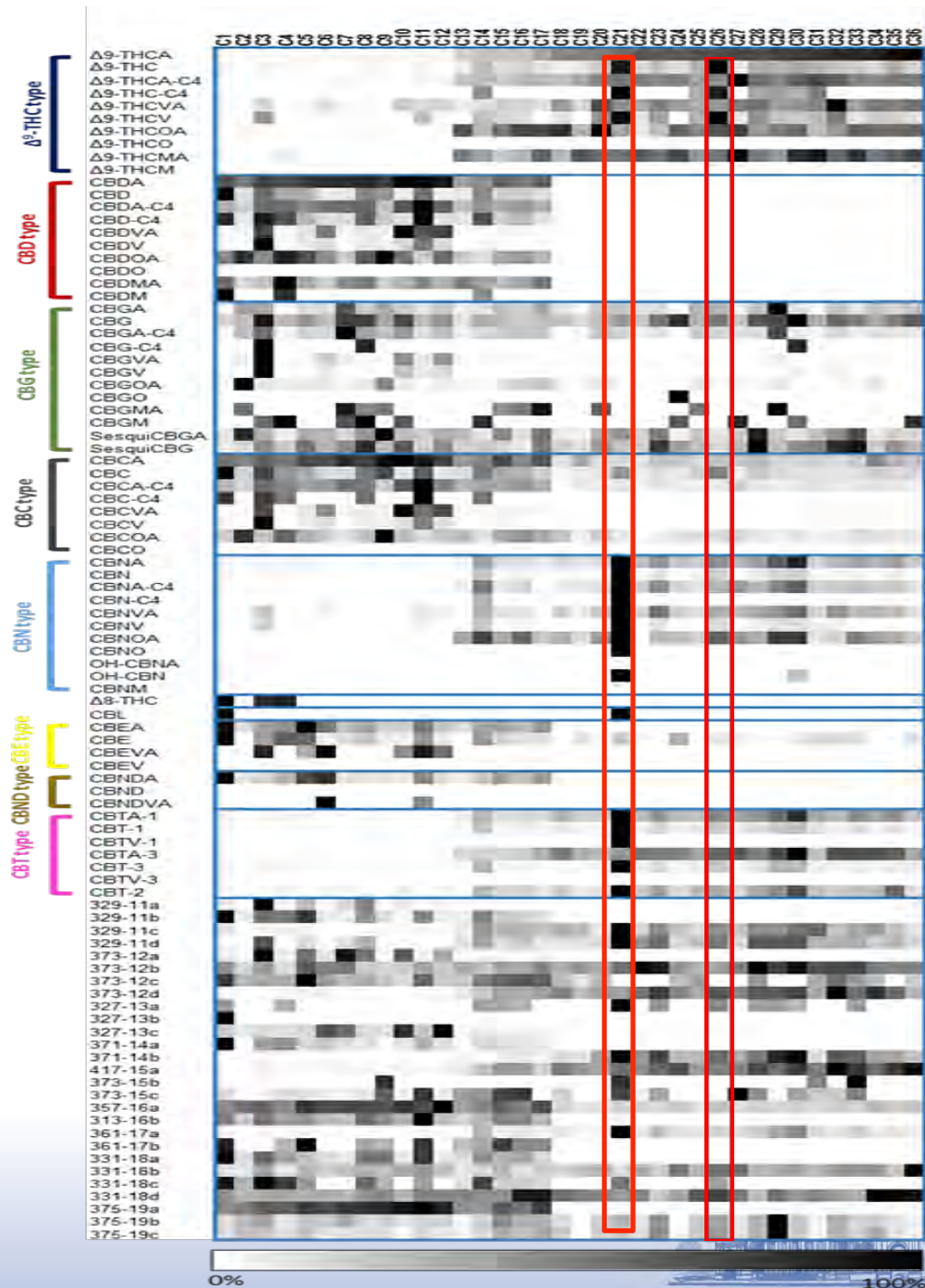
Cannabis type	Partial Response Complete Response Stable Disease	Disease Progression	p value
	(n=9)	(n=28)	
THC > 10%	8 (29.6%)	19 (70.4%)	p=0.393
THC < 10%	1 (10%)	9 (90%)	
CBD >= 1%	4 (16%)	21 (84%)	p=0.116
CBD < 1%	5 (41.7%)	7 (58.3%)	



Cannabis Strains:

Phytocannabinoids profiling of 36 different medical *Cannabis* strains.

The mass-spectrometry coupled with liquid chromatography (LC-MS) concentrations of each phytocannabinoid were normalized to the highest value and compared per phytocannabinoid in a heat map. Strains were arranged according to increasing Δ^9 -THCA content (first line) and phytocannabinoids by subclasses.



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Conclusions

In this retrospective analysis, the use of cannabis during immunotherapy treatment decreased RR, without affecting PFS or OS and without relation to cannabis composition. This information can be critical for a large group of patients and requires caution when starting immunotherapy.



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