

Supplementary Tables

Beneficial effects of pumpkin seed soft extract on lower urinary tract symptoms and quality of life in men with benign prostatic hyperplasia: a meta-analysis of two randomized, placebo-controlled trials over 12 months

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Supplementary Table A

Eligibility criteria, efficacy, and safety variables of the studies

<i>Item</i>	Bach study¹	GRANU study^{2*}
<i>Inclusion criteria</i>		
IPSS	≥ 13	≥ 13 ≤ 19
Maximum urinary flow rate (Q _{max})	≤ 15 mL/sec	≤ 12 mL/sec
Prostate volume (PV)	no limits	≤ 40 mL
Post-void residual volume (PVR)	no limits	≤ 100 mL
<i>Exclusion criteria</i>		
Prostate cancer	✓	✓
Other urogenital diseases or infections	✓	✓
Insulin-dependent diabetes mellitus	✓	HbA 1c > 6
Concurrent medical conditions with impact on micturition	✓	✓
Concomitant medications known to cause micturition complaints	✓	✓
Previous surgical intervention on prostate	✓	✓
Concomitant medical treatment of BPH	✓	✓
Concomitant androgen / androgen antagonists	✓	✓
Previous surgical intervention on prostate	✓	✓
<i>Primary efficacy variable</i>		
Response rate: IPSS reduction ≥ 5 points after 12 months	✓	✓
IPSS change from baseline after 12 months	✓	✓
<i>Secondary variables</i>		
<i>At each visit</i>		
IPSS QoL index	✓	✓
<i>At baseline and study end</i>		
Q _{max}	✓	✓
PVR	✓	✓
PV	✓	✓
<i>Safety assessment</i>		
<i>At each visit</i>		
Recording and assessing adverse events	✓	✓
Blood pressure, heart rate	✓	✓
<i>At baseline and study end</i>		
Hemogram	✓	✓
Kidney and liver function laboratory tests	✓	✓
Serum PSA value	✓	✓
Urine stick test	✓	✓
Physical examination	✓	✓

*In the GRANU study, the responsible ethics committee demanded the exclusion of patients with severe symptoms (IPSS > 19) and upper limits for PV and PVR.

¹ Bach, D., 2000. Placebokontrollierte Langzeittherapiestudie mit Kürbissamenextrakt bei BPH-bedingten Miktionsbeschwerden. *Der Urologe B* 40, 437-443.

² Vahlensieck, W., Theurer, C., Pfitzer, E., Patz, B., Banik, N., Engelmann, U., 2015. Effects of Pumpkin Seed in Men with Lower Urinary Tract Symptoms due to Benign Prostatic Hyperplasia in the One-Year, Randomized, Placebo-Controlled GRANU Study. *Urologia Internationalis* 94, 286-295.

Supplementary Table B

Baseline demographic and disease characteristics of the PP set

Variable study	n	PSE (N=485) mean (SD)	Placebo (N=488) mean (SD)	Total (N=973) mean (SD)	P value
<i>Age (years)</i>					
Bach study	356	62.8 (7.4)	62.8 (7.0)	62.8 (7.1)	0.96
GRANU study	617	65.2 (6.8)	65.5 (6.7)	65.4 (6.7)	0.64
Pooled	973	64.4 (7.1)	64.5 (6.9)	64.4 (7.0)	0.73
<i>Height (cm)</i>					
Bach study	356	174.4 (6.1)	174.1 (6.5)	174.3 (6.3)	0.60
GRANU study	616	175.5 (6.6)	175.9 (6.5)	175.7 (6.5)	0.45
Pooled	972	175.1 (6.4)	175.3 (6.6)	175.2 (6.5)	0.76
<i>Weight (kg)</i>					
Bach study	356	80.7 (11.1)	80.0 (8.9)	80.3 (10.1)	0.52
GRANU study	616	84.9 (12.1)	83.8 (12.6)	84.4 (12.3)	0.27
Pooled	972	83.4 (11.9)	82.4 (11.5)	82.9 (11.7)	0.21
<i>IPSS</i>					
Bach study	356	17.8 (3.6)	17.9 (3.8)	17.8 (3.7)	0.80
GRANU study	617	16.0 (1.8)	16.1 (1.8)	16.1 (1.8)	0.49
Pooled	973	16.7 (2.8)	16.8 (2.8)	16.7 (2.8)	0.59
<i>IPSS QoL index</i>					
Bach study	355	3.3 (0.9)	3.2 (0.9)	3.2 (0.9)	0.92
GRANU study	609	3.5 (0.7)	3.5 (0.7)	3.5 (0.7)	0.45
Pooled	964	3.4 (0.8)	3.4 (0.8)	3.4 (0.8)	0.57
<i>Prostate volume (mL)</i>					
Bach study [§]	237	34.8 (16.4)	36.0 (19.6)	35.4 (18.0)	0.61
GRANU study	617	28.0 (8.5)	28.8 (7.4)	28.4 (8.0)	0.22
Pooled	854	29.9 (11.6)	30.8 (12.5)	30.3 (12.1)	0.28
<i>Q_{max} (mL/s)</i>					
Bach study	356	10.7 (2.5)	10.9 (2.6)	10.8 (2.6)	0.39
GRANU study	617	9.5 (2.0)	9.6 (1.9)	9.5 (1.9)	0.54
Pooled	973	9.9 (2.3)	10.1 (2.3)	10.0 (2.3)	0.32
<i>PVR (mL)</i>					
Bach study	356	48.2 (43.4)	48.9 (44.5)	48.6 (43.9)	0.88
GRANU study	617	33.8 (28.5)	34.9 (27.5)	34.4 (28.0)	0.61
Pooled	973	39.1 (35.4)	40.0 (35.3)	39.6 (35.3)	0.67

[§] Prostate size measurement in the Bach study was optional. PSE, pumpkin seed soft extract.

P values were calculated using a *t* test assuming equal variances.

Supplementary Table C

Mean IPSS change from baseline at all visits and differences between treatment groups after 12 months (PSE minus placebo), ITT set using LOCF

Study (N) <i>Treatment period</i>	PSE		Placebo		Difference PSE vs. placebo	
	n	Mean (SE)	n	Mean (SE)	Mean [95%CI]	<i>P</i> value
Bach study (465)						
3 months	212	-4.8 (0.3)	220	-4.2 (0.3)		
6 months	206	-5.6 (0.3)	215	-5.5 (0.3)		
9 months	201	-6.3 (0.3)	207	-5.6 (0.4)		
12 months	209	-6.8 (0.3)	217	-5.6 (0.4)		
12 months (ITT-LOCF)	227		238		-1.1 [-2.0, -0.1]	0.02
GRANU study (924)						
3 months	454	-3.1 (0.2)	460	-2.9 (0.2)		
6 months	441	-4.0 (0.2)	439	-3.9 (0.2)		
9 months	427	-4.1 (0.2)	424	-4.2 (0.3)		
12 months	404	-4.6 (0.3)	406	-4.4 (0.3)		
12 months (ITT-LOCF)	460		464		-0.3 [-1.0, 0.4]	0.37
Pooled (1389)						
3 months	666	-3.7 (0.2)	689	-3.3 (0.2)		
6 months	647	-4.5 (0.2)	654	-4.4 (0.2)		
9 months	628	-4.8 (0.2)	631	-4.6 (0.2)		
12 months	613	-5.3 (0.2)	623	-4.8 (0.2)		
12 months (ITT-LOCF)	687		702		-0.6 [-1.1, 0.0]	0.05

CI, Confidence intervals calculated using *t*-distribution: *P* values were calculated using a *t* test assuming equal variances. PSE, pumpkin seed soft extract.

Supplementary Table D

IPSS QoL scores and changes from baseline at all visits (ITT set).

Study (N) Visit	IPSS QoL Score				Change from baseline			
	PSE		Placebo		PSE		Placebo	
	<i>n</i>	Mean (SD) [95% CI]	<i>n</i>	Mean (SD) [95% CI]	<i>n</i>	Mean (SD) [95% CI]	<i>n</i>	Mean (SD) [95% CI]
Bach study (465)								
Baseline	227	3.2 (0.9) [3.1, 3.3]	237	3.2 (0.9) [3.1, 3.3]				
3 months	212	2.1 (0.9) [2.0, 2.2]	220	2.3 [1.0] [2.2, 2.5]	212	-1.1 (1.0) [-1.2, -0.9]	219	-0.9 (1.1) [-1.0, -0.7]
6 months	206	2.0 (0.9) [1.9, 2.1]	215	2.1 (1.0) [2.0, 2.2]	206	-1.2 (1.1) [-1.4, -1.1]	214	-1.1 (1.1) [-1.3, -1.0]
9 months	201	1.9 (1.0) [1.8, 2.1]	207	2.0 (1.0) [1.9, 2.2]	201	-1.3 (1.1) [-1.4, -1.1]	206	-1.2 (1.2) [-1.3, -1.0]
12 months	209	1.9 (1.0) [1.8, 2.0]	217	2.1 (1.1) [1.9, 2.2]	209	-1.3 (1.2) [-1.5, -1.1]	216	-1.1 (1.2) [-1.3, -1.0]
GRANU study (924)								
Baseline	452	3.5 [0.7] [3.4, 3.6]	461	3.5 (0.7) [3.4, 3.6]				
3 months	459	2.7 (1.1) [2.6, 2.8]	464	2.8 (1.1) [2.7, 2.9]	451	-0.8 (1.1) [-0.9, -0.7]	461	-0.7 (1.1) [-0.8, -0.6]
6 months	439	2.5 (1.1) [2.4, 2.6]	440	2.6 (1.1) [2.5, 2.7]	432	-1.0 (1.1) [-1.1, -0.9]	437	-0.9 (1.1) [-1.1, -0.8]
9 months	430	2.3 (1.1) [2.2, 2.5]	421	2.5 (1.2) [2.4, 2.6]	422	-1.1 (1.2) [-1.3, -1.0]	418	-1.0 (1.2) [-1.1, -0.9]
12 months	403	2.3 (1.1) [2.2, 2.4]	407	2.5 (1.2) [2.3, 2.6]	397	-1.2 (1.2) [-1.3, -1.1]	404	-1.0 (1.2) [-1.2, -0.9]
Pooled (1389)								
Baseline	679	3.4 (0.8) [3.3, 3.5]	698	3.4 (0.8) [3.4, 3.5]				
3 months	671	2.5 (1.1) [2.5, 2.6]	684	2.6 (1.1) [2.6, 2.7]	663	-0.9 (1.1) [-0.9, -0.8]	680	-0.8 (1.1) [-0.9, -0.7]
6 months	645	2.3 (1.1) [2.2, 2.4]	655	2.4 (1.1) [2.3, 2.5]	638	-1.1 (1.1) [-1.2, -1.0]	651	-1.0 (1.1) [-1.1, -0.9]
9 months	631	2.2 (1.1) [2.1, 2.3]	628	2.3 (1.1) [2.2, 2.4]	623	-1.2 (1.2) [-1.3, -1.1]	624	-1.1 (1.2) [-1.2, -1.0]
12 months*	612	2.2 (1.1) [2.1, 2.2]	624	2.3 (1.2) [2.2, 2.4]	606	-1.2 (1.2) [-1.3, -1.1]	620	-1.1 (1.2) [-1.2, -1.0]

Confidence intervals (CI) were calculated using *t*-distribution. **P* = 0.02 for the difference between PSE and placebo group after 12-month treatment, calculated using a *t* test assuming equal variances. PSE, pumpkin seed soft extract.