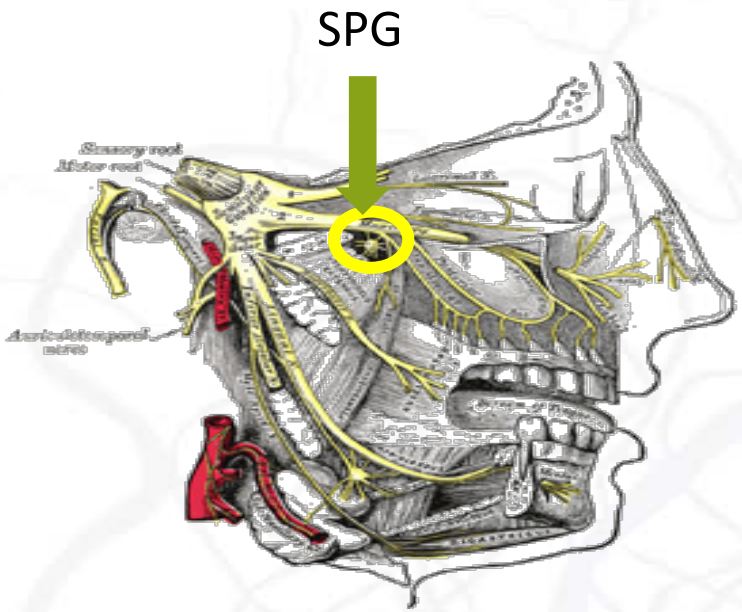
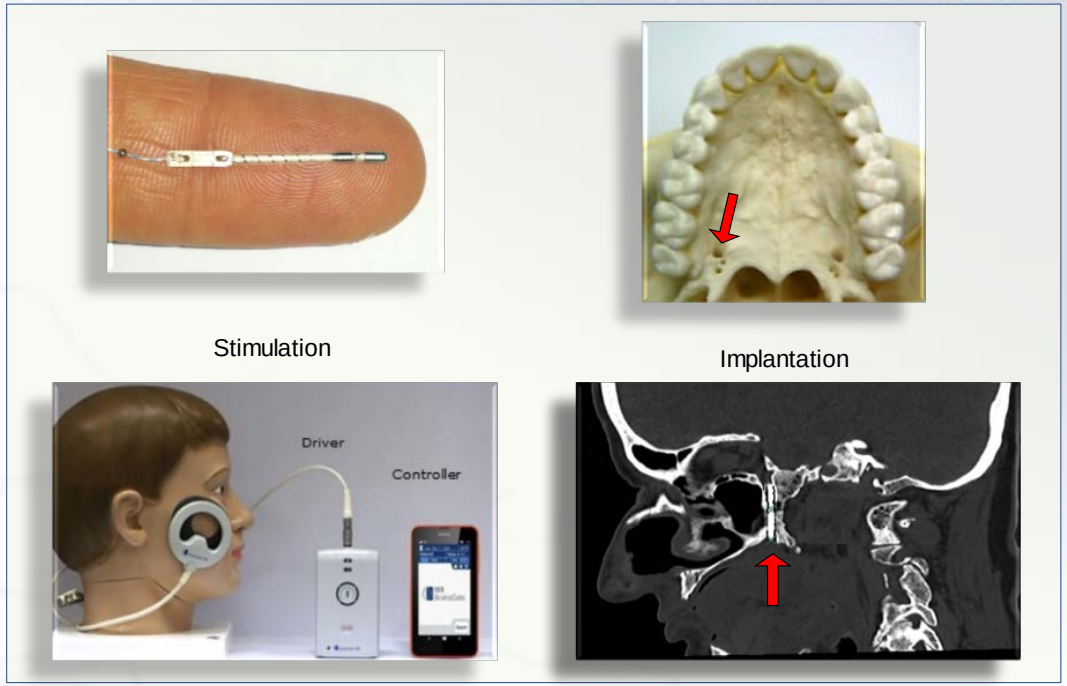
Sphenopalatine Ganglion Stimulation Improves Outcome from Acute Ischemic Stroke in a Dose-Dependent Manner: Further Insights from the Pivotal ImpACT-24B Trial

JL Saver, NM Bornstein, H-C Diener, PB Gorelick, T Janelidze, M Savic, N Zarqua, A Shuaib, D Yarnitsky, CA Molina

for the ImpACT-24B Trial Investigators

ImpACT-24B Pivotal Trial

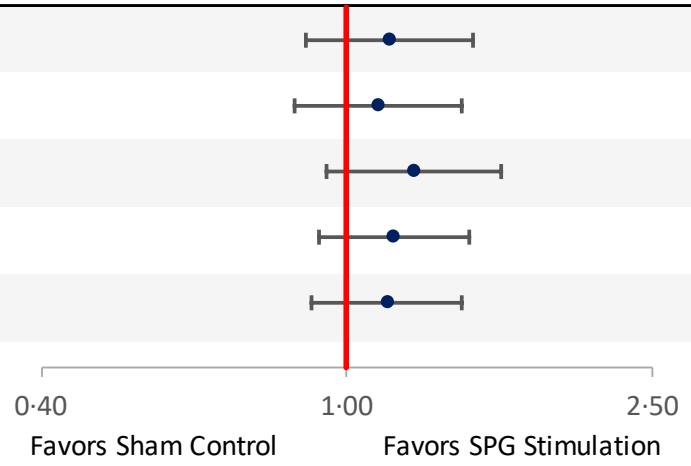




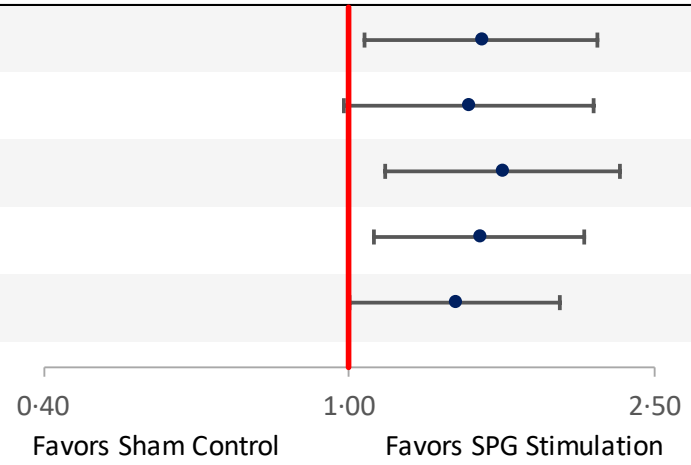
	Study Design
Objective	Safety & efficacy in anterior circulation stroke started 8-24h after onset
Design	Randomized, Double-Blind, Sham-Controlled
Primary Endpoint	mRS improvement beyond expectations at 3 months (sliding dichotomy)
Two Primary Analysis Populations	• mITT – all patients receiving at least one active/sham SPG stimulation • Confirmed Cortical Involvement (CCI) - NIHSS ≥ 10, at least one cortical ASPECTS region

Efficacy Results

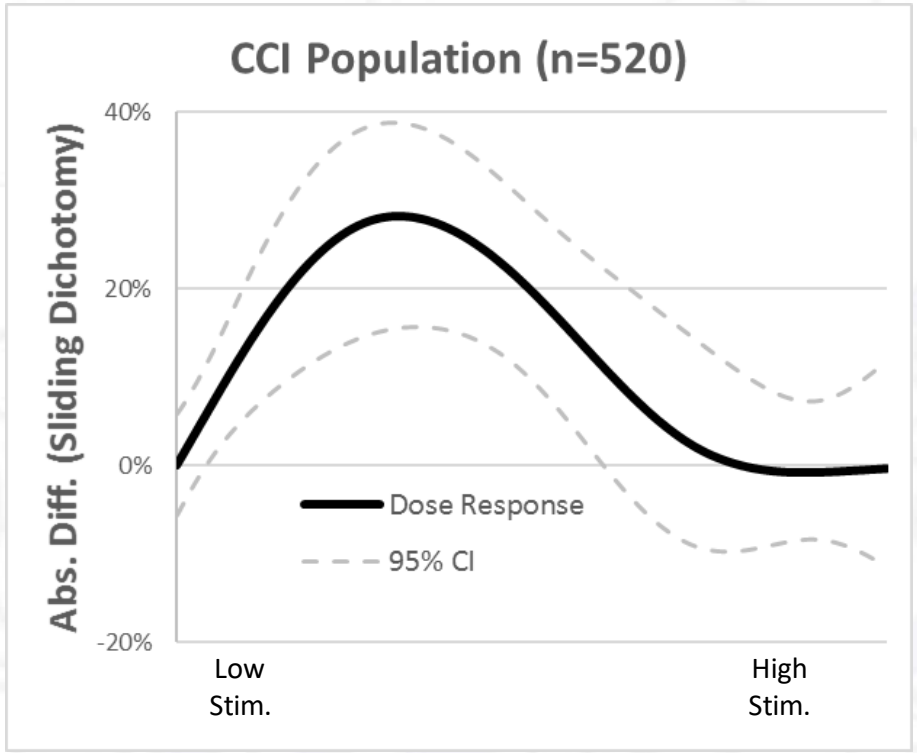
mITT	SPG Stimulation	Sham Control	Odds Ratio	Odds Ratio	P Value
Sliding Dichotomy	48·6%	45·5%	1·14 [0·89, 1·46]		0·31
Dichotomy 0-2	44·1%	41·8%	1·10 [0·85, 1·41]		0·47
Dichotomy 0-3	67·6%	63·0%	1·22 [0·94, 1·59]		0·13
SIS-16	57·7	54·7	1·15 [0·92, 1·44]		0·23
Utility weighted mRS	55·83	53·18	1·13 [0·90, 1·41]		0·24



CCI	SPG Stimulation	Sham Control	Odds Ratio	Odds Ratio	P Value
Sliding Dichotomy	49·6%	39·9%	1·48 [1·05, 2·10]		0·0258
Dichotomy 0-2	34·8%	27·2%	1·43 [0·99, 2·08]		0·06
Dichotomy 0-3	62·3%	51·1%	1·58 [1·11, 2·25]		0·01
SIS-16	52·2	43·9	1·48 [1·08, 2·02]		0·01
Utility weighted mRS	50·00	43·89	1·37 [1·00, 1·87]		0·05



Relation Between Stimulation Level and Clinical Outcomes



Inverted U-Shaped Dose Effect Curve (IUSDEC)

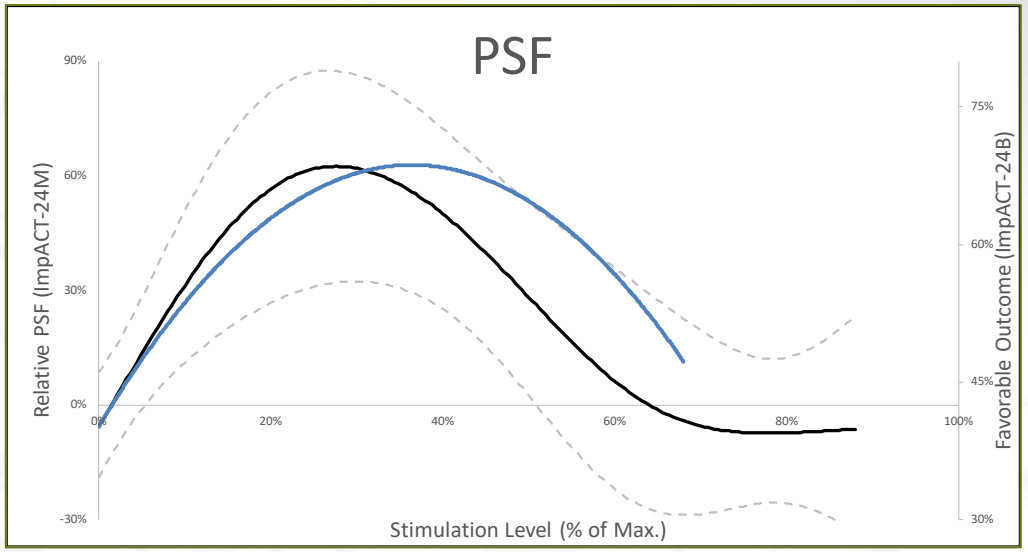
Endpoint	CCI	Non-CCI
Favorable Outcome (mRS Sliding Dichotomy)	0·003	0·54
Independence (mRS 0-2)	0·02	0·67
Self-Care or Better (mRS 0-3)	0·01	0·88
Stroke-Related QOL (SIS-16)	0·02	0·67
Disability level (UW-mRS)	0·03	0·95

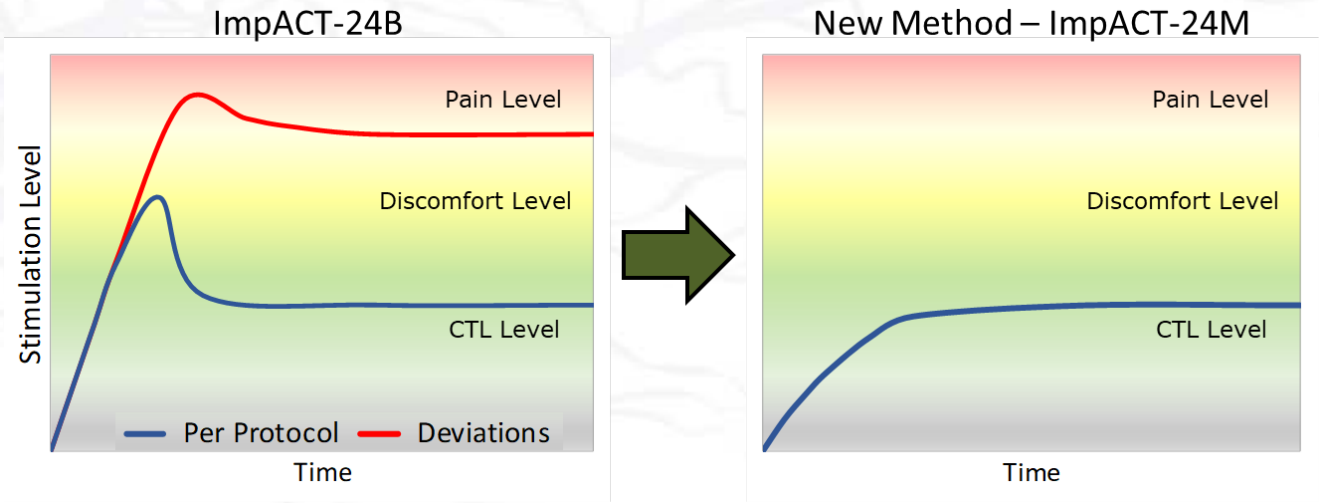
*Adjusted for: age, sex, NIHSS, side, ASPECTS, OTT, DM, AF. and predicted mRS mean-median difference

ImpACT-24B Efficacy in Optimal Dose Range (1%-38% of Max Dose)

Outcome	SPG stim (N=61)	Sham stim (N=276)	Odds ratio (95% CI)	p-value
Favorable Outcome (mRS Sliding Dichotomy)	68·9%	39·9%	3·34 (1·84-6·04)	<0·0001
Independence (mRS 0-2)	54·1%	27·2%	3·16 (1·79-5·58)	<0·0001
Self-Care or Better (mRS 0-3)	82·0%	51·1%	4·35 (2·17-8·71)	<0·0001
	SPG stim (N=61)	Sham stim (N=276)	Diff. (95% CI)	p-value
Stroke-Related QoL (SIS-16)	67·3	43·9	23·5 (12·7-34·2)	<0·0001
Disability level (UW-mRS)	64·6	43·9	20·7 (10·8-30·6)	<0·0001

Clinical Dose-Response in 24B Trial Matches Physiologic Dose-Resp in Later 24M Trial*





*ImpACT-24M presented at ISC 2019

Discussion

- SPG stimulation was safe in all patients and showed evidence of benefit in patients with confirmed cortical involvement up to 24h from onset. Results further supported by:
  - Consistent beneficial effects on all secondary efficacy endpoints
  - Similar findings in preceding pilot ImpACT-24A trial
  - Increased and robust statistical significance in individual-patient-data pooled meta-analysis
  - Strong dose-response relationship, with inverted U-shaped dose-effect curve (IUSDEC)
- ImpACT-24B benefit magnitude - for every 100 patients treated with SPG stimulation:
  - 10 more will have a favorable long-term disability outcome
  - At optimal stimulation levels, potentially 29 more will have a favorable long-term disability outcome

Conclusion

- “The cumulative evidence indicates that sphenopalatine ganglion stimulation is an efficacious therapy for patients with cortical acute ischaemic stroke 8–24 hours after onset who are ineligible for intravenous thrombolytic therapy.”

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