

**Updates on Gene and Cell Therapy for Critical Limb Threatening Ischemia (CLTI): Options for the No-option Patient**

Richard J. Powell MD

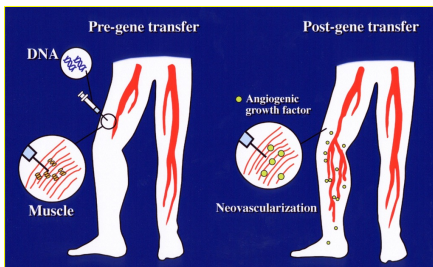
Section of Vascular Surgery  
Dartmouth-Hitchcock Medical Center



**Presenter Disclosure Information**

Richard J Powell, MD  
FINANCIAL DISCLOSURE:  
None

**Gene or Cell Therapy by Intramuscular Injection**



Pre-gene transfer: DNA injection into Muscle.

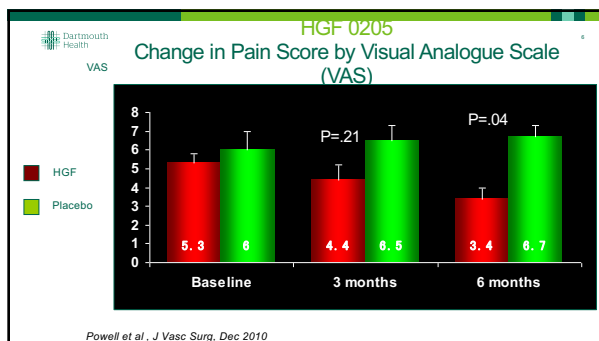
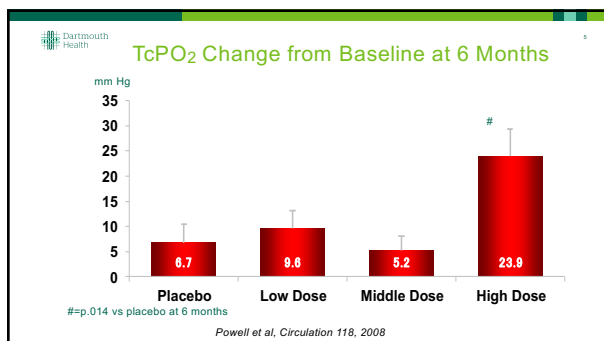
Post-gene transfer: Angiogenic growth factor leads to Neovascularization.

**A Phase II Double Blind Placebo-Controlled Study to Assess the Safety and Efficacy of AMG0001 to Improve Perfusion in Critical Limb Ischemia**

**HGF-STAT Trial**

Richard Powell, M.D.  
Principle Investigator  
Professor of Surgery  
Section of Vascular Surgery  
Dartmouth Medical School

*Powell et al. Circulation 118, 2008*



**Safety and efficacy of prolonged administration of hepatocyte growth factor (HGF) plasmid (AMG0001) in patients with chronic limb threatening ischemia (CLTI)**

Richard Powell, MD; David G. Armstrong, DPM, MD, PhD; Michael S. Conte, MD; Charles M. Zelen, DPM; Ruixi Luo, PhD; Jonathan Wright, DrPH, MBA; Yoshiyuki Takasu, MS; Susan W. Pitman Lowenthal, MD, MPH

DFCON, October 2020

**HGF plasmid in CLTI patients: safety and efficacy of prolonged AMG0001 administration**

	AMG0001			Placebo			P-value
	n	mean	SD	n	mean	SD	
TBI	17	0.168	0.2692	14	-0.044	0.1846	0.033
AP (dorsalis pedis)	14	32.9	41.55	12	16.7	34.25	0.324
AP (posterior tibial)	12	35.1	33.97	11	13.2	24.98	0.051
Pain (VAS)	16	-1.61 (34%)	2.86	11	-0.20 (3%)	3.09	0.002

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**QOL (SF-36): Comparison of Change between pre and post Treatment**

Health Concept	Amount of Change		Difference in Average	95%CI	*p < 0.05
	Placebo	AMG0001			
Physical Functioning	11.25	13.33	2.08	-11.93-16.10	
Role physical	15.91	9.26	-6.65	-38.47-25.17	
Bodily pain	6.58	20.63	14.05*	1.00-27.10	
General Health Perceptions	1.25	6.78	5.53	-6.93-17.99	
Mental Health	-12.00	11.69	23.69*	3.44-43.94	
Role Emotional	0.00	18.52	18.52	-3.39-40.42	
Social Functioning	8.33	15.28	6.94	-25.91-39.80	
Vitality	-3.33	12.31	15.64	-1.64-32.92	
Summary Score :					
Physical Component Summary	8.68	6.79	-1.89	-9.85-6.08	
Mental Component Summary	-4.49	5.70	10.18	-0.54-20.91	

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#AHA24

### ANATOMICALLY DIRECTED LOWER EXTREMITY GENE THERAPY FOR ULCER HEALING: A DOUBLE BLIND, RANDOMIZED, PLACEBO CONTROLLED STUDY

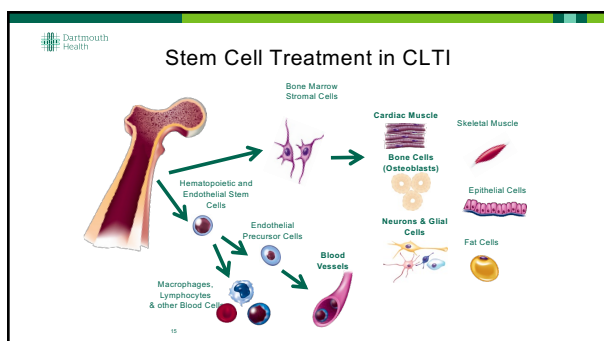
David G. Armstrong, DPM, MD, PhD\*, Michael S. Conte, MD#, Joseph L. Mills, MD, Matthew T. Menard, MD, Dennis P. Orgill, MD, PhD, Robert D. Gallano, MD, Robert S. Kirsner, MD, PhD, Alik Farber, MD, MBA, John C. Lantis, MD, Charles M. Zelen, DPM, Marissa J. Carter, PhD, MA, Caitlin W. Hicks, MD, MS, Richard J. Powell, MD

\* Division of Surgery, Keck School of Medicine of USC, Division of Surgery, University of California, San Francisco, Brigham and Women's Hospital, Harvard Medical School, Boston Medical Center, Feinberg School of Medicine, Northwestern University, Icahn School of Medicine, University of Miami, Johns Hopkins University School of Medicine, Dartmouth Geisel School of Medicine

Dartmouth Health November 21, 2024 14

### HGF gene therapy: Collatagene TM (Anges Inc)

- 2020 conditional, time-limited approval by Japanese Ministry of Health and Welfare for CLTI in patients with no surgical or endovascular option
- Performed in the setting of multidisciplinary teams
- Physicians with experience in treatment of CLTI



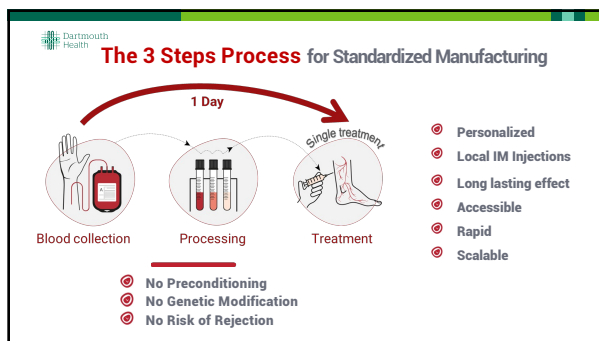
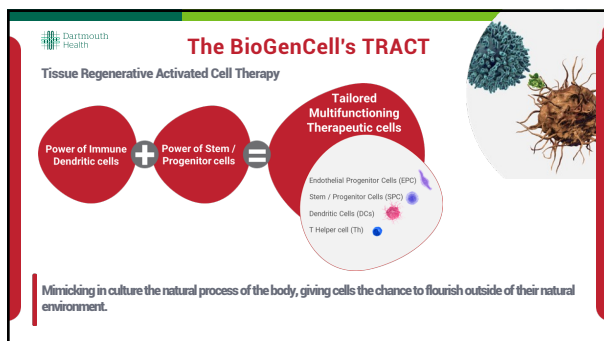
Dartmouth Health

## BioGenCell

Unique Therapy for Unique People

Phase 1/2, Open label & double-blind randomized placebo-controlled study to assess the feasibility of BGC101 (EnEPC) in the treatment of peripheral arterial disease (PAD) with critical limb ischemia (CLI)

Global PI – Prof. Michael Conte  
 U.S. FDA IND [A1202805023](#) ; CTR (Belgium) [EUCT024-516665-3E-001](#)



### EnEPC-CLI-01 Phase 1

Open labelled, Single Dose

**Efficacy Results:**

Objective	Subjective
✓ 6-Month Amputation Free Survival	✓ VAS Pain relief (4/4)
✓ Leg blood flow – ABI (3/4)	✓ Pain control – weaned off narcotic medication (2/2)
✓ Healing of wounds – (2/3) [only 3 had wounds]	✓ GMWT Walking (3/3) [only 3 had 2 legs]
	✓ Improved Quality of life (4/4)

Legend: PTA: Percutaneous Transluminal Angioplasty; ABI: Ankle/Brachial Index; GMWT: 6-minute walking test; VAS: Visual Analog Scale

- ✓ BGC101 achieved 100% survival and >80% at 12 months
- ✓ Durable therapeutic effect beyond 7 years

### EnEPC-CLI-01 Phase 2

Double Blinded, Single Dose

**Study Design**

- Population: Rutherford 4 & 5 with no revascularization option (N=40)
- Randomization: 2:1 between BGC101 and placebo
- Stratification for Diabetic Patients (N=23)
- Follow-up: 1 Year Active at the Hospital + 2 Years telephonic communication
- Administration:
  - Patient awake ; lidocaine cream
  - Single dose, 30 x 0.5 mL IM injections (<10 minutes)

**Visits' Timeline**

**Patient recruitment completed**

### 6-Month Follow-up Interim Analysis

Major Amputation or Death Free Survival (AFS) Rate ITT Cohort  
Blinded Data

Amputations rates in patients with:	N	No. of AMP	AMP Rate
Total	18	6	33%
Rutherford's 5	12	5	42%
Rutherford's 4	6	1	17%
WHI 4	2	2	100%
WHI 3	10	3	30%
WHI 2	6	1	17%
Diabetic	10	3	30%
Hypertension	13	5	38%
High Cholesterol	4	4	29%
Diabetic + Hypertension	7	3	43%
Diabetic + High Cholesterol	9	3	33%
Diabetic + Hypertension + High Cholesterol	7	3	43%

### Conclusions

- Phase 2 data have been promising
- Pivotal trials are ongoing
- Trial enrollment remains challenging
- Remains an unmet need for effective medical therapy for “no-option” CLTI