

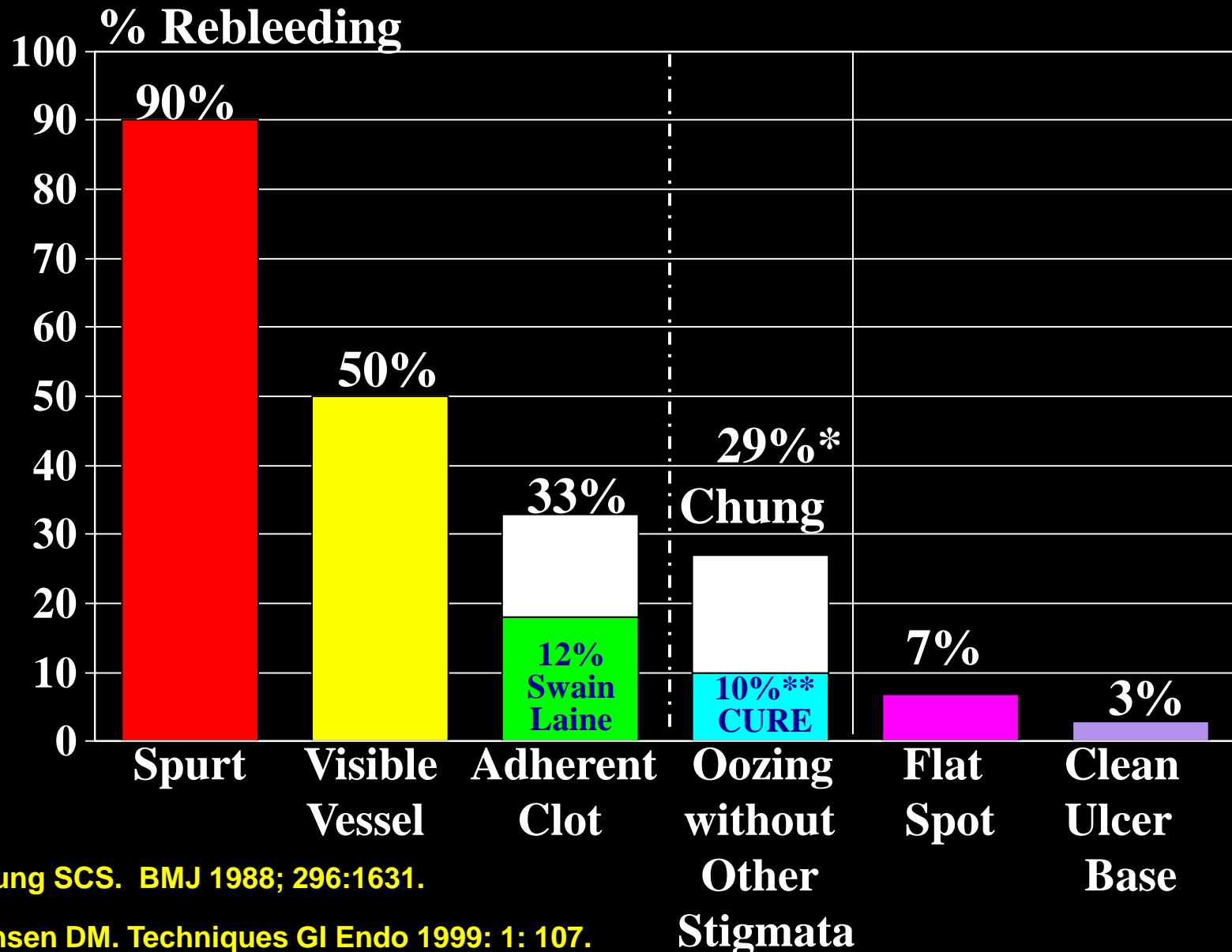
(ASGE 617b) Is There a Subgroup of Patients With Forrest Ib (Oozing) Peptic Ulcer Bleeding at Increased Risk of Rebleeding?

Dennis M. Jensen¹, Robert Stuart², Henrik Ahlbom³, Stefan Eklund³, Alan Barkun⁴, Ernst J. Kuipers⁵, Joachim Mössner⁶, James Y.W. Lau⁷, Joseph J.Y. Sung⁷

¹David Geffen School of Medicine at UCLA and CURE Digestive Diseases Research Center, Los Angeles, CA, USA; ²Glasgow Royal Infirmary, Glasgow, UK; ³AstraZeneca R&D, Mölndal, Sweden; ⁴Division of Gastroenterology, McGill University Health Center, Montreal, Canada; ⁵Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, The Netherlands; ⁶Medizinische Klinik und Poliklinik II, University of Leipzig, Leipzig, Germany; ⁷Institute of Digestive Diseases, Chinese University of Hong Kong, Shatin, Hong Kong, China

Supported by AstraZeneca R&D, Mölndal, Sweden

30 Day Ulcer Rebleeds by Stigmata on H2RA's: CURE & Others



Purposes

- 1. Determine whether there is a subgroup of oozers (Forrest 1b) with increased risk of rebleeding.**
- 2. Assess whether oozing (Forrest Ib) ulcers could be reclassified as either visible vessels (Forrest IIa) or adherent clots (Forrest IIb).**
- 3. Reanalyze rebleeding rates and other secondary outcomes based upon this reclassification of oozers.**

Overall Rebleeding Rates (Independent of Medical Therapy)

	<u>Oozing Alone</u> (N=183)	<u>Oozing & Clot or VV</u> (N=90)	<u>Spurt, VV, or Clot</u> (N=445)
72 hrs	4.4%	6.7%	10.1%
7 days	5.5%	10%	11.7%
30 days	5.5%	10%*	12.8%

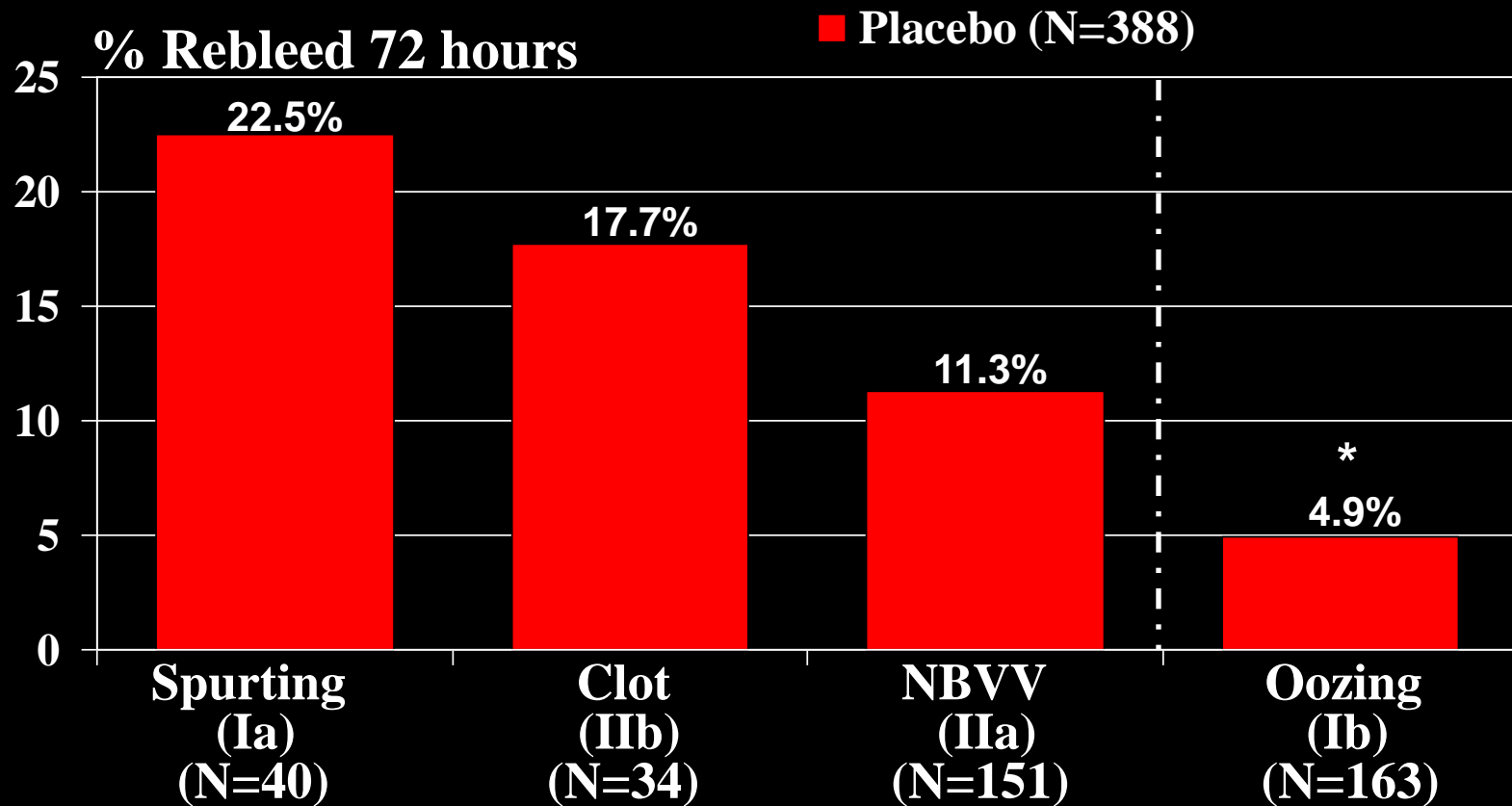
*p = 0.17 for Oozing vs. Clot or VV

30 Day Outcomes – Overall (Independent of Medical Therapy)

	<u>Oozing Alone</u> (N=183)	<u>Oozing & Clot or VV</u> (N=90)	<u>Spurt, VV, or Clot</u> (N=445)
Endo Retreatment (%)	4.9%	7.8%	10.6%
Surgery (%)	1.1%	6.7%	4.7%
Death (%)	0%	2.2%	1.6%
Hosp. days (mean)	0.4	1.1	1.2
Units RBC's (mean)	1.4	2.3	2.2

PUB Rebleeding Rates

After Endoscopic Hemostasis, at 72 hrs in Placebo Treated Patients



*p = 0.0029 for oozing vs. other stigmata of hemorrhage combined.

(ASGE 617a) Effect of Type of Endoscopic Hemostasis and Adjuvant Intravenous Esomeprazole on Peptic Ulcer Re-bleeding

Joseph J Sung¹, Alan N Barkun², Ernst J Kuipers³, Joachim Mössner⁴, Dennis M Jensen⁵, Robert Stuart⁶, James Y Lau¹, Henrik Ahlbom⁷, Tore Lind⁷, Jan Kilhamn⁷

¹Institute of Digestive Diseases, Chinese University of Hong Kong, China

²Division of Gastroenterology, McGill University, Montreal, QC, Canada

³Departments of Gastroenterology and Hepatology, and Internal Medicine, Erasmus MC University Medical Center, Rotterdam, The Netherlands

⁴Medizinische Klinik und Poliklinik II, University of Leipzig, Germany

⁵CURE Digestive Diseases Research Center, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

⁶Glasgow Royal Infirmary, United Kingdom

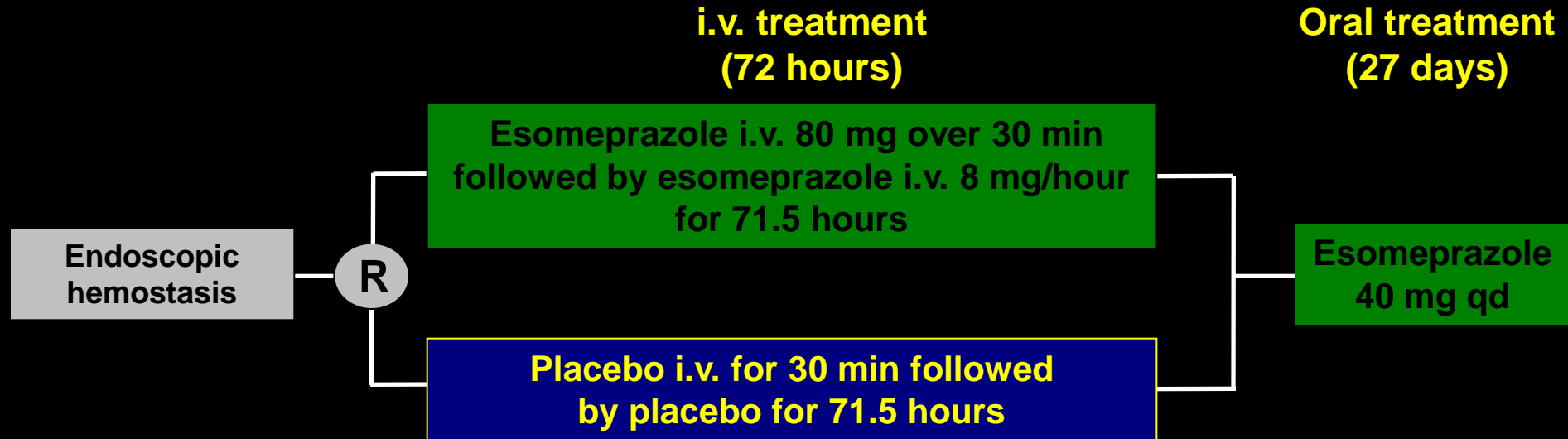
⁷AstraZeneca R&D, Mölndal, Sweden

Aim

To evaluate the effect of high-dose intravenous (i.v.) esomeprazole on re-bleeding rates in the PUB (Peptic Ulcer Bleed) study, according to type of endoscopic hemostasis (*post-hoc* analysis)

Design of the PUB Study¹

- Randomized, double-blind, placebo-controlled study at 91 centers in 16 countries



- Endoscopic therapy performed before i.v. treatment according to routine care at each center
 - Epinephrine injection (dilution 1:10,000) and/or coagulation with heater probe, or electrocoagulation, or hemoclips

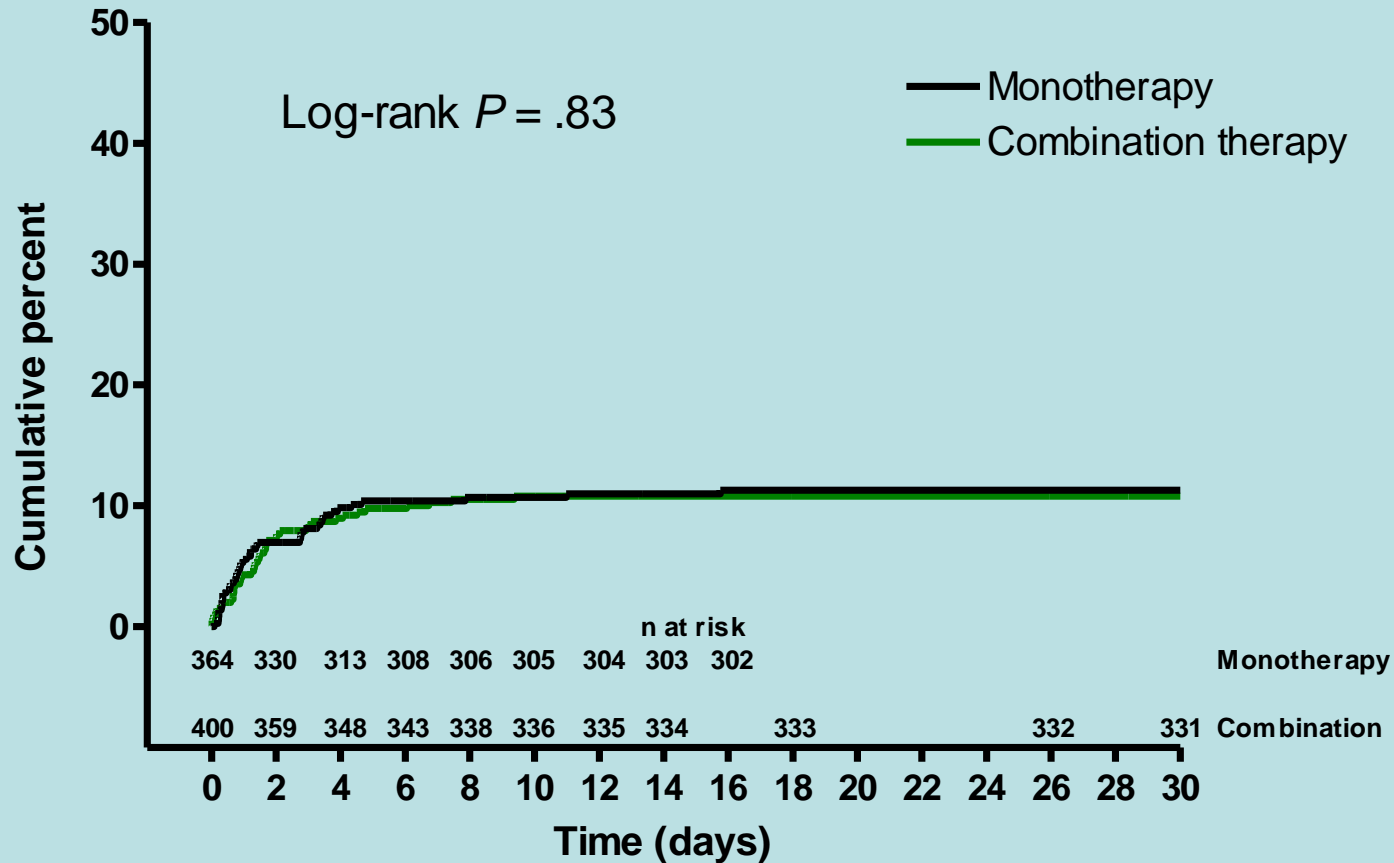
Inclusion Criteria

- Men and women aged ≥ 18 years
- Upper GI bleeding within 24 hours
 - Hematemesis, melena, or hematochezia
- One endoscopically and photographically confirmed bleeding gastric or duodenal ulcer
 - ≥ 5 mm in diameter
 - Forrest class Ia (active bleeding), Ib (oozing), IIa (visible vessel), or IIb (adherent clot)
- Successful endoscopic hemostasis

Baseline Demographics

	Monotherapy (n = 355)	Combination therapy (n = 400)
Men	71%	67%
Age > 65 years	42%	53.5%
Forrest class		
Ia (active bleeding)	6%	12%
Ib (oozing)	48%	39%
IIa (visible vessel)	32%	42%
IIb (adherent clot)	13%	6.5%
ASA class		
1	46%	33.5%
2	44%	52%
3	11%	15%
Shock (BP)	4%	5.5%
<i>H pylori</i> -positive	63%	61%
Use of low-dose aspirin	21%	31.5%
Use of nonselective NSAID	12%	23%

Re-bleeding Within 30 Days: Monotherapy vs Combination Therapy (All Patients)



Re-bleeding Within 30 Days

Esomeprazole vs Placebo

	Esomeprazole (n = 375)	Placebo (n = 389)	P value
All patients¹	7.7%	13.6%	.01
Monotherapy (any modality; n = 355)	6.9%	13.9%	.03
Epinephrine monotherapy (n = 284)	8.4%	14.9%	.09
Combination therapy (n = 400)	8.2%	12.7%	.14

¹Sung et al. *Ann Intern Med* 2009; 150: 455–64

Outcomes After Epinephrine Injection vs. Inject Heater Probe for Spurters or Oozers on H2RA's

Spurting Bleeding

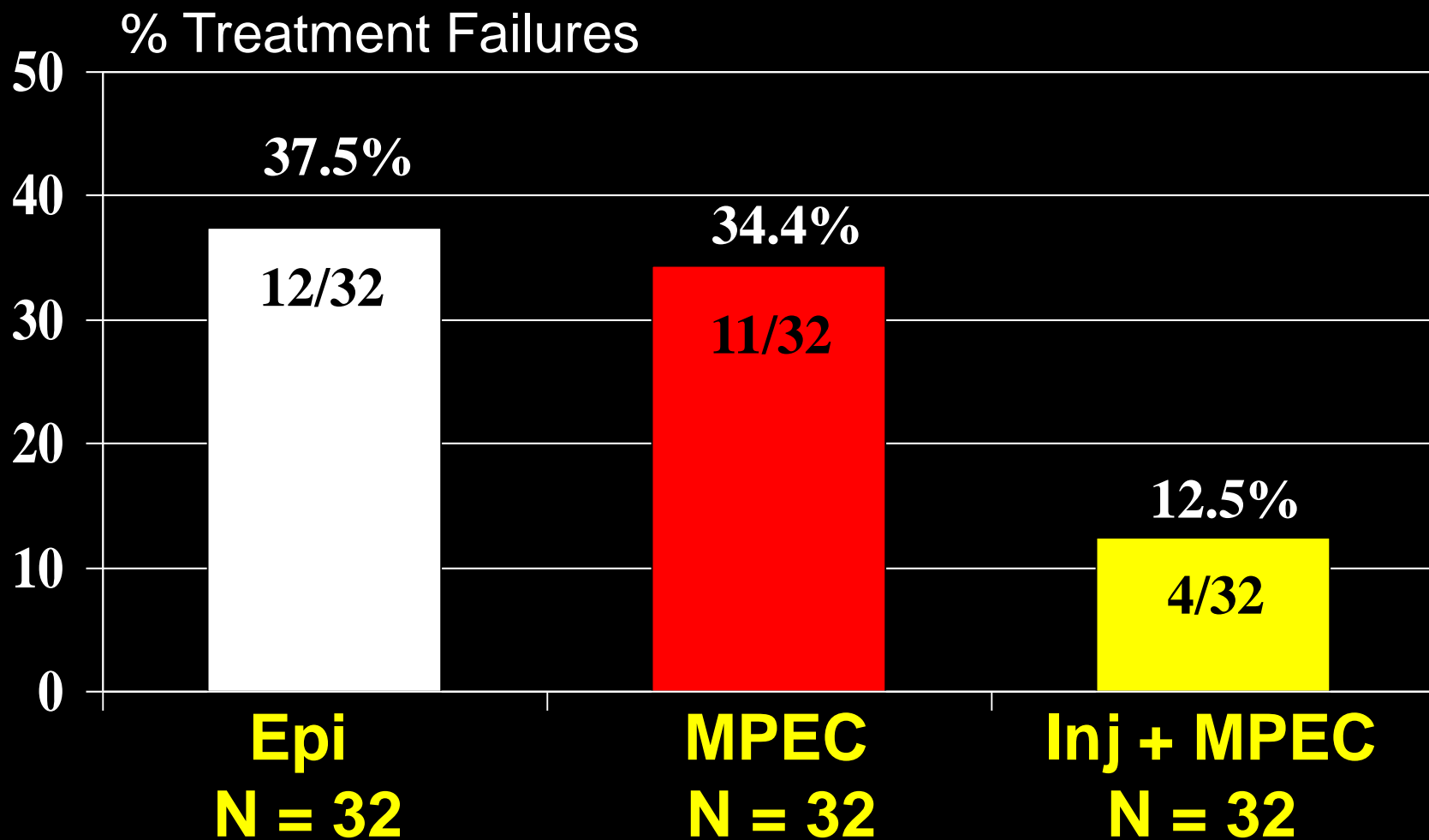
Oozing Bleeding

	<u>Epi Alone</u> (N=28)	<u>Epi + HP</u> (N=32)	<u>Epi Alone</u> (N=108)	<u>Epi + HP</u> (N=108)
Initial Success	92.6%	100%	99%	99%
Clinical Rebleed	22.2%	6.5%	5.6%	2.9%
Emergency Surgery	29.6%*	6.5%	5.6%	5.7%

*p<0.05

Chung SCS & Sung JJY. BMJ 1997; 314:1307.

Treatment Failure Rates for Ulcer Hemostasis with Epinephrine Injection, MPEC, or the Combination



Combination Treatment: Epi Injection, Cold Guillotining, Multipolar Coagulation - DU

1



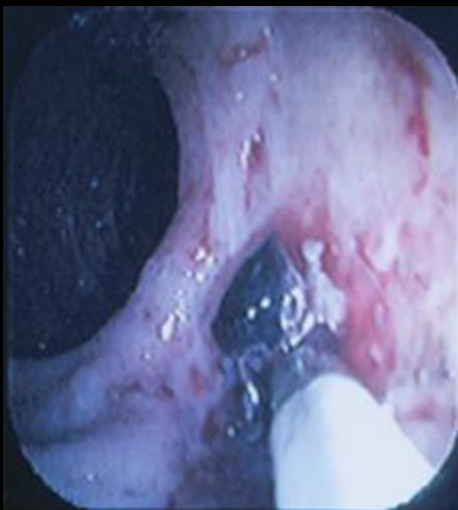
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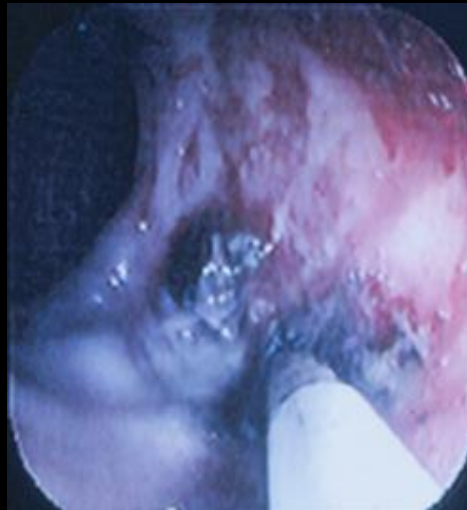
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**(ASGE 938) A Long-Term Randomized
Controlled Trial of a Novel Nanopowder
Hemostatic Agent for Control of Severe
Upper Gastrointestinal Bleeding in a
Porcine Model**

**S.A. Giday, Y. Kim, D.M. Krishnamurty, D.B. Liang,
R. Ducharme, E.J. Shin, X. Dray, G. Donatelli,
A.N. Kalloo**

Results of Nanopowder Hemostatic Agent in Gastroepiploic Artery Model

	<u>Control</u>	<u>Nanopowder</u>
Initial Hemostasis	0%	100%
Time to Hemostasis	-	13.8 minutes
Mortality from Bleeding	100%	0%
More bleeding in 24 hours	N/A	20%
Evidence of Lung or Brain Embolization	N/A	0%

(10 animals RCT)

(ASGE T1411) Doppler Ultrasound Probe (DUP) for Risk Stratification and Endoscopic Hemostasis of Bleeding Colonic Lesions

D.M. Jensen, G. Ohning, T.O.G. Kovacs, R. Jutabha, G.A. Machicado, G. Dulai

CURE Digestive Diseases Research Center; David Geffen School of Medicine at UCLA; Digestive Disease Divisions at UCLA Medical Center and VA GLA Healthcare Center; Los Angeles, CA

DUP Ultrasound Probe



DUP's are utilized to refine endoscopic risk stratification & document complete endoscopic UGI hemostasis, but there are no reports of DUP applied to bleeding colonic lesions.

Purposes

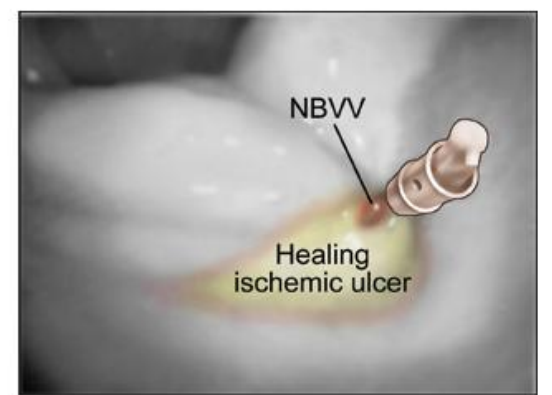
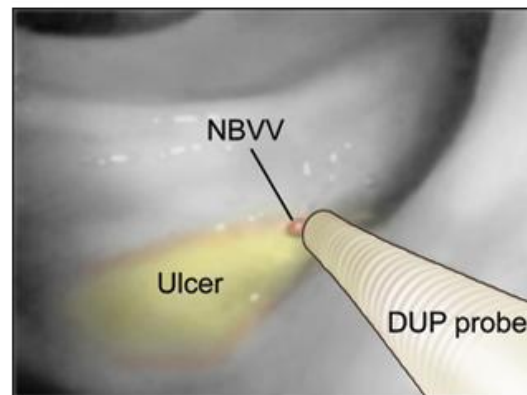
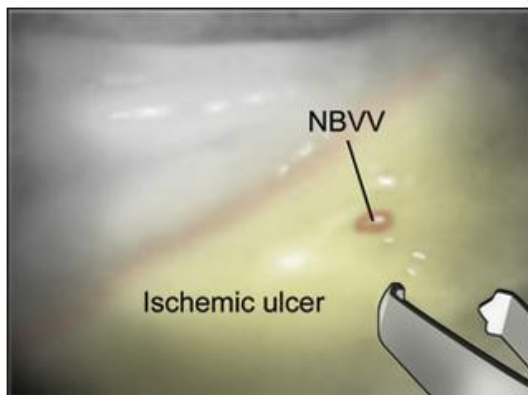
- 1. For different focal & diffuse colorectal lesions with recent hemorrhage, to assess DUP for risk stratification & treatment.**
- 2. For diverticular (TIC) hemorrhage, to compare DUP findings for definitive TIC bleeding (with stigmata) to presumptive TIC bleeding (clean TIC's).**

DUP for Focal vs. Diffuse Colon Lesions

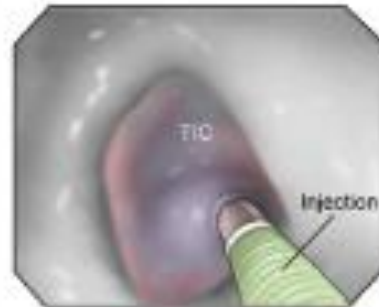
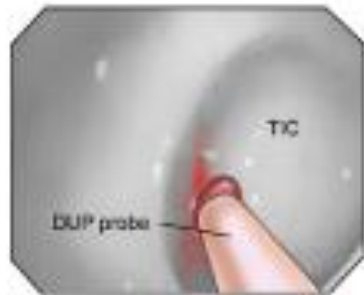
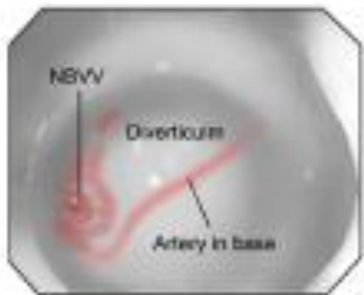
Lesion Type	Focal	Diffuse
# Patients	27	8
# Lesions	32	8
Lesions DUP+	75% (24/32)	87.5% (7/8)
Change in patient risk stratification or Rx	70.4% (19/27)	37.5% (3/8)*
Overall 30d Rebleed	3.7% (1/27)	50% (4/8)*

*p < 0.05

Ischemic Ulcer with NBVV



Diverticulum with NBVV



Blood Flow with Doppler Ultrasound Probe for Diverticular Hemorrhage: Definitive vs. Presumptive

Stigmata of Hemorrhage	Number	+ DUP	Totals (Rate + DUP)	30 day Rebleeding
<u>Definitive TIC Bleeds</u>				
Clot	4	3	3/4	0/4
NBVV	4	4	4/4	0/4
Ooze	2	2	2/2	0/2
Definitive TIC Bleed	10	9	9/10 (90%)*	0/10 (0%)
<u>Clean TIC (Presumptive TIC Bleed)</u>				
	10	0	0/10 (0%)	0/10 (0%)

***p < 0.05**

Treatment Results

- For focal lesions with major SRH, endoscopic hemostasis (MPEC or hemoclip with or without epinephrine injection) controlled active bleeding, rendered DUP negative with major SRH, & yielded a 30 day rebleed rate of 4.2% (1/24).
- For diffuse lesions or tumors, DUP often indicated underlying blood flow, which could be temporarily halted by endoscopic treatments, but 30 day rebleed rates were high (4/8 = 50%).
- After combination therapy or definitive TIC bleeds, DUP was – and no patients rebled.

**(ASGE T1345) Increasing Prevalence of
Delayed Post-Polypectomy Induced Ulcer
(DPPIU) Hemorrhage as a Cause of Severe
Hematochezia and Its Potential Risk Factors**

**K.A. Ghassemi, D.M. Jensen, T.O.G. Kovacs, G.V.
Ohning, R. Jutabha, G.S. Dulai,
G.A. Machicado**

**Division of Digestive Diseases, David Geffen School of
Medicine at UCLA, & CURE Hemostasis Research
Group, VA GLAHC, Los Angeles, CA**

Purposes

In patients with severe hematochezia, to:

- 1. Quantify the change in local prevalence of hematochezia due to DPPIU vs. other colon causes (OTHER) in the past 20 years.**
- 2. Compare clinical features and 30-day outcomes of DPPIU vs. OTHERS (colon diagnoses).**
- 3. Identify potential risk factors for DPPIU hemorrhage.**

Clinical and Endoscopic Features, and 30-day Outcomes of DPPIU vs. OTHER Colon Diagnoses

	DPPIU	OTHER
# of Patients	39	484
Stigmata	92.3%*	40.2%
Endoscopic Hemostasis	87.2%*	26.5%
Rebleed	7.7%	12.0%
Surgery	5.1%	6.2%
Death	0%	4.3%

*p < 0.05

Bivariate Analysis of Risk Factors for DPPIU vs. OTHER Colon Dx

<u>Risk factor</u>	<u>DPPIU</u> <u>(N=39)</u>	<u>OTHER</u> <u>(N=484)</u>	<u>P</u>
Acute ASA use	18.8%	5.3%	0.0703
ASA + warfarin	10.3%	2.3%	0.0199
Antihypertensive meds	46.2%	22.7%	0.0011
Asian race	18%	7.9%	0.0305
Severe heart disease	41%	21%	0.0094

Risk Factors for DPPIU Hemorrhage vs. OTHER Colon Dx by Multivariate Analysis

Risk Factor	Odds Ratio	95% Confidence Interval	<i>P</i>
Asian race vs. other race	2.52	1.02-6.23	0.0455
Antihypertensive med use	2.66	1.34-5.25	0.0050
ASA + warfarin	3.45	0.99-11.96	0.0510

Overall Results

- **Prevalence of DPPIU hemorrhage as a cause of colonic hematochezia markedly increased from 1.3% (2/150) 20 years ago to 7.4% (39/523) within the last 12 years ($p=0.0057$).**
- **Presence of stigmata and endoscopic hemostasis rates were significantly higher in DPPIU patients than OTHER colon Dx.**
- **There was a trend toward decreased rebleed rate, surgery, and death in DPPIU patients.**

Risk Factors for Delayed Post-Polypectomy Bleeding (Multivariate Analyses Results)

	Adjusted Odds Ratio	(95% CI)
Hypertension¹	5.6	(1.8-17.2)
Warfarin Anticoagulation Resumption²	5.2	(2.2-12.5)
[Aspirin & Warfarin³]	3.45	(0.99-11.96)
Antihypertensive med use³	2.66	(1.3-5.3)
Asian vs. Other race³	2.52	(1.02-6.23)
For each mm increase in polyp size, ↑ 9% risk	1.09	(1.0-1.2)

1. Watabe H. GIE 2006;64:73.

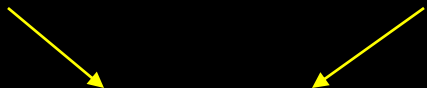
2. Sawhney MS. Endosc 2008;40:115

3. Ghassemi KA. GIE 2009;69:AB275.

**(ASGE 514) Safety and Efficacy of
Colonoscopy to Treat Diverticular Bleeding
– Long-Term Outcomes of a Large
Multicenter Cohort**

**T. Kaltenbach, R.R. Watson, J.N. Shah, S.
Friedland, K.R. Mcquaid, T. Sato, A.K. Shergill,
R.M. Soetikno**

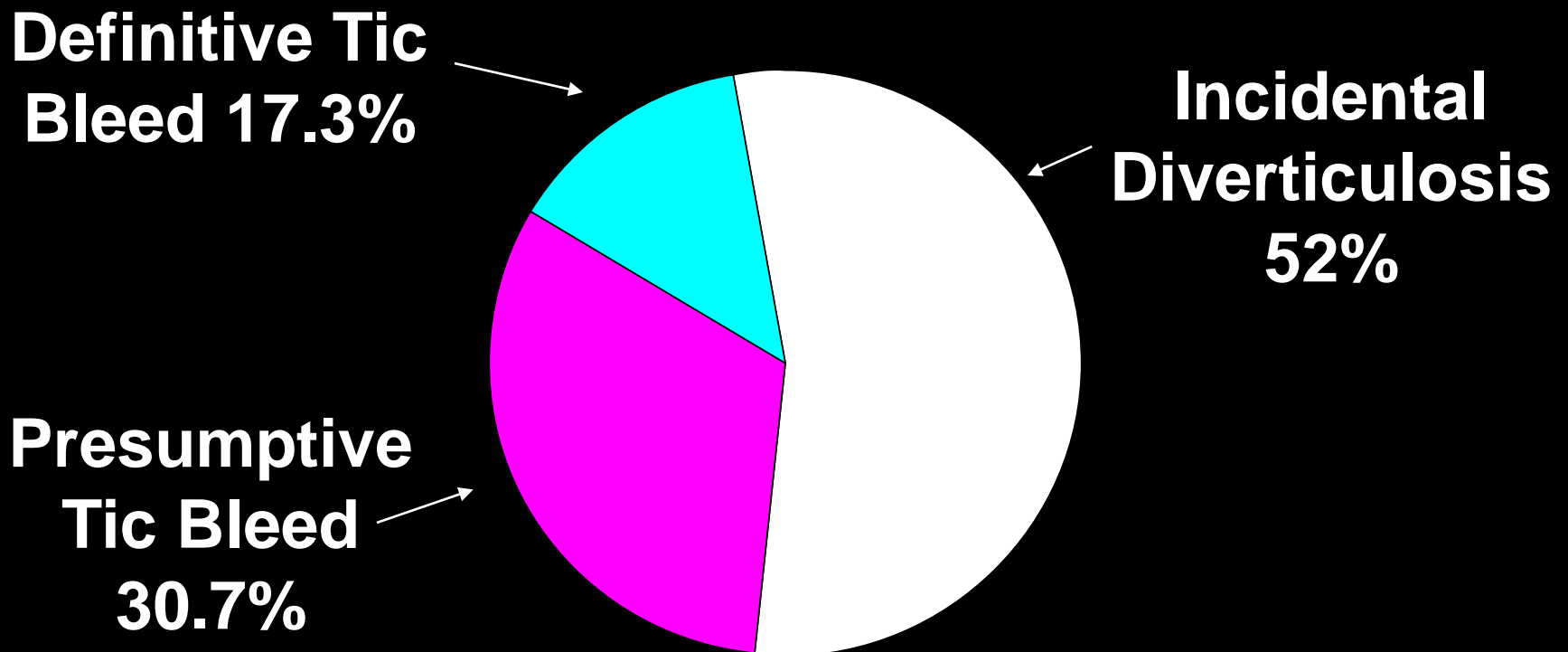
Definitive* vs. Presumptive Diverticular Hemorrhage

	<u>Endo Hemostasis</u>	<u>IR/Surgery</u>	<u>Presumptive</u>
Patients	25	3	36
Mean Hosp. Days	5.6 ± 5.3	36 ± 6.0	8.3 ± 21.4
30d Rebleed	0	0	?
Delayed Rebleed (Mean 37 months)	 21.4% (6/28)		22% (8/36)

* Active bleed 42%; NBVV 10.7%; Clot 32%; Erosion 14%

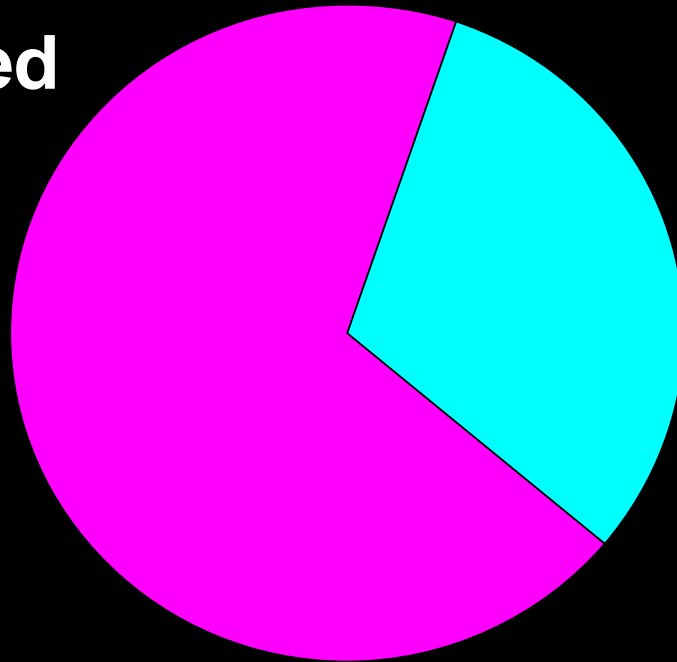
Prevalence of Definitive, Presumptive, & Incidental Diverticular Hemorrhage

(323 patients with diverticulosis & severe hematochezia)



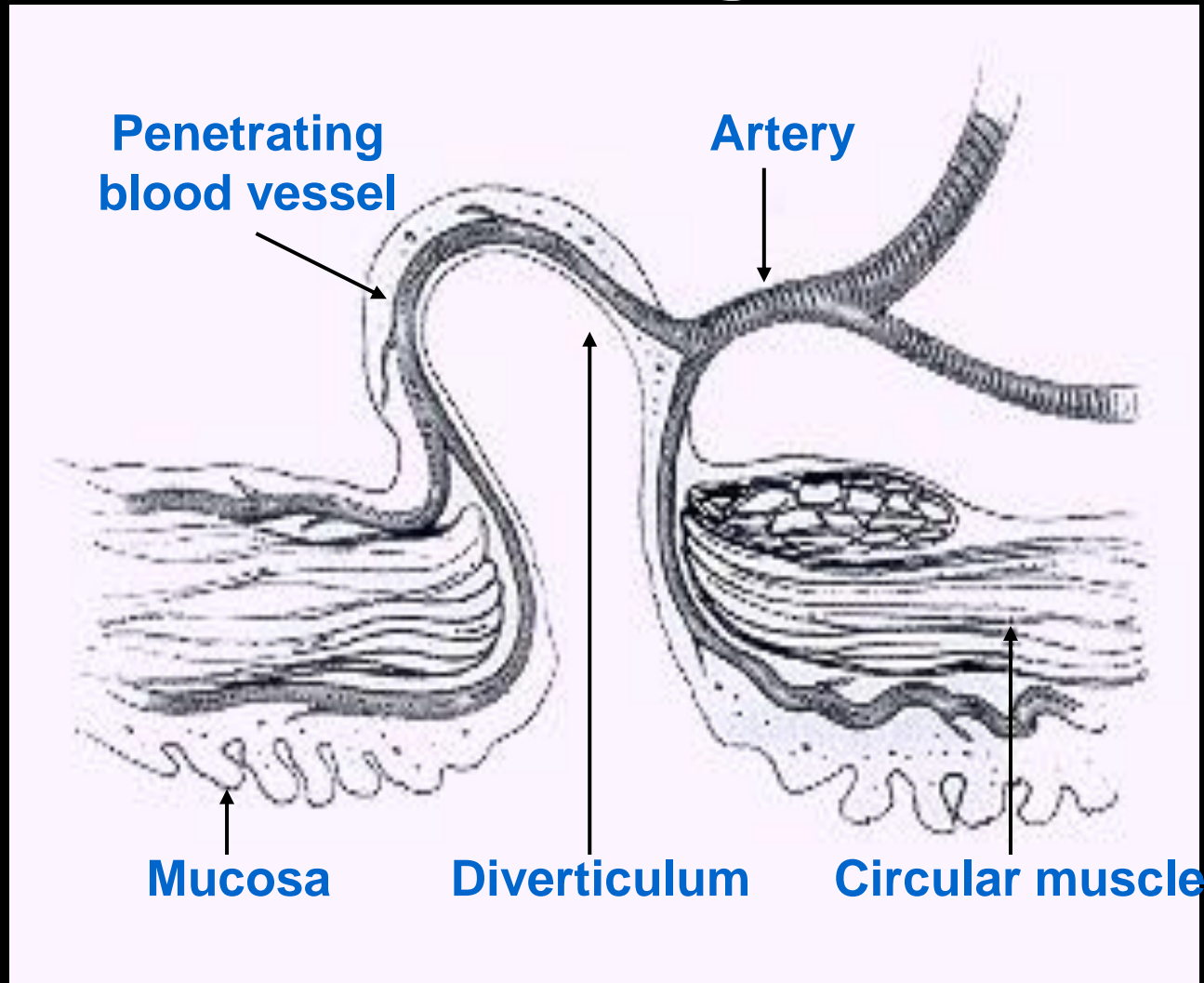
True Diverticular Hemorrhage: Prevalences of Definitive & Presumptive Bleeding (N=155)

**Presumptive
Diverticular Bleed**
63.9%
(N=99)



**Definitive
Diverticular Bleed**
36.1%
(N=56)

Location of Diverticular Vessels & Stigmata



**CURE (vs. #514)
53% (vs. 32%)**

47% (vs. 68%)

Jensen DM. CURE DDRC 2009.

Outcomes by Initial Treatment After 60 days

(Mean F/U 3.2 ± 0.2 yrs)

	<u>MED</u> N=85	<u>ENDO</u> N=35	<u>SURG</u> N=8	<u>TOTALS</u> N=128
TIC Rebleed	10.6%	8.6%	0%	9.4%
Other Bleeds	7.1%	11.4%	25%	9.4%
Other TIC Complications	2.4%	0%	0%	1.6%

No significant differences

D. Jensen. Gastro 2008; 134: A122 (#846).