Phase 3 Trials of Vonapanitase to Improve Fistula Use for Hemodialysis

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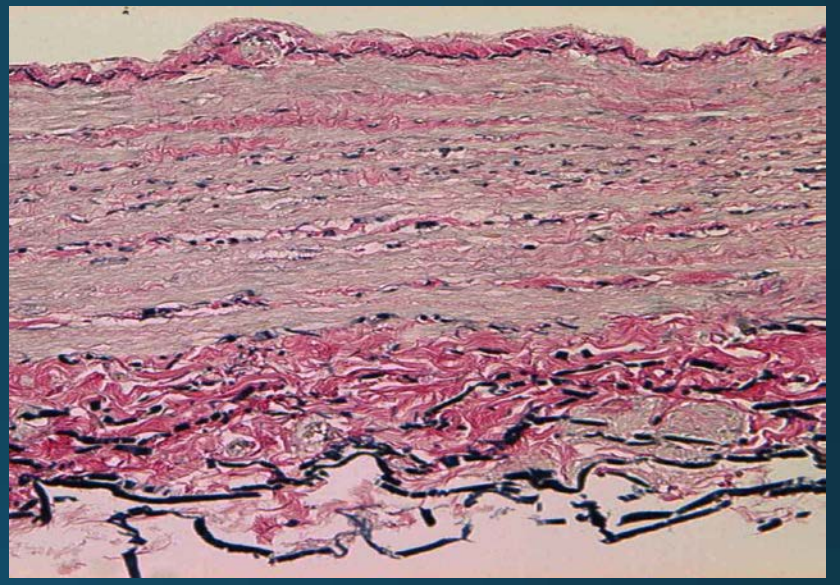
Disclosures

- Unrestricted Gift from Smith and Nephew, Inc.
- Joint Research Projects with Novartis Institutes for Biomedical Research, Inc.
- Scientific Advisory Board for Proteon Therapeutics, Inc.
- Consultant for Medtronic, Inc.
- Consultant for Humacyte, Inc.
- Consultant for Merck Sharpe & Dohme

Vonapanitase

- Investigational recombinant human chymotrypsin-like elastase family member 1
- Expressed in human dermis; Protease that cleaves peptide bonds in elastin

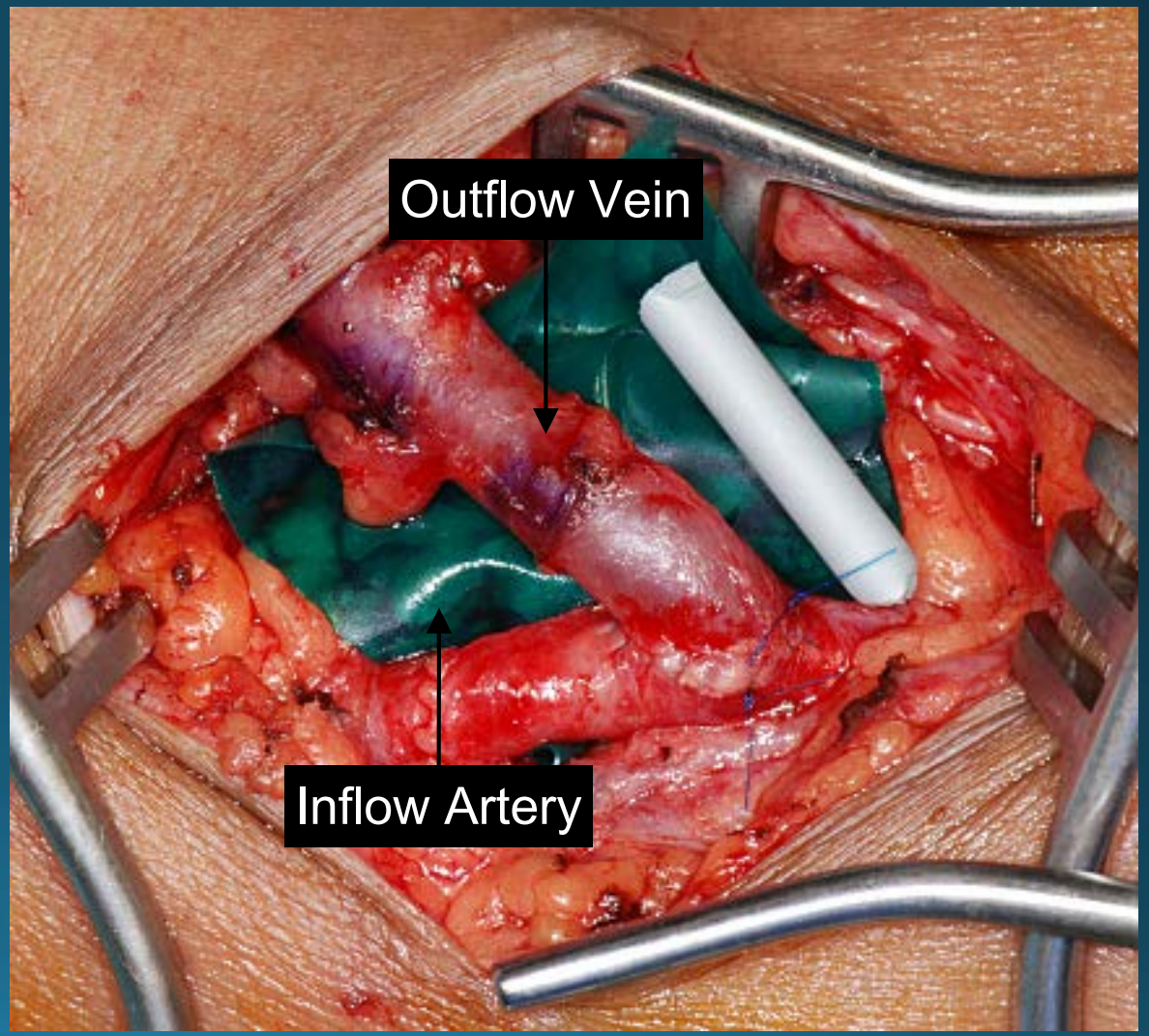
Vonapanitase



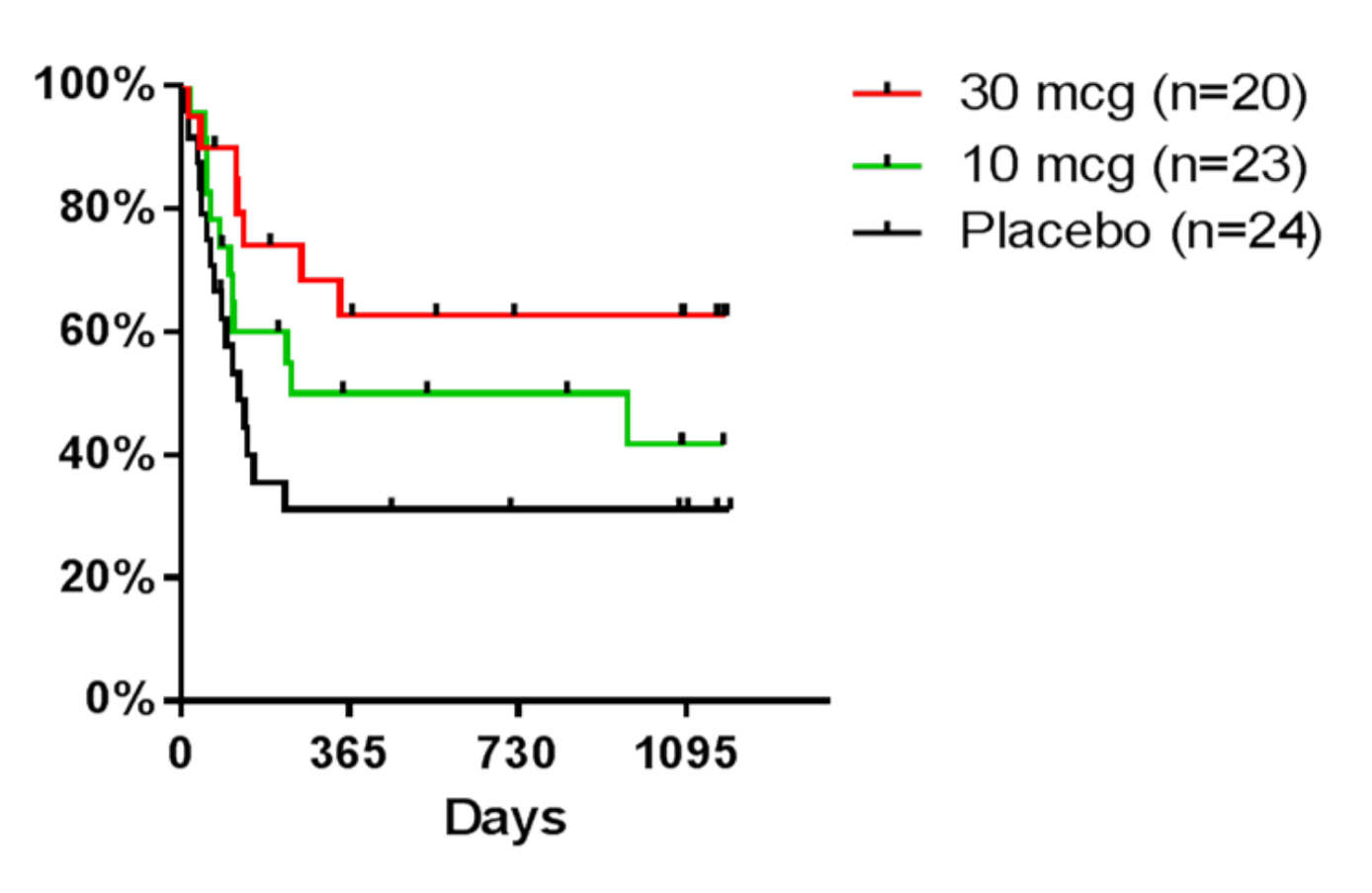
- Investigational recombinant human chymotrypsin-like elastase family member 1
- Expressed in human dermis; Protease that cleaves peptide bonds in elastin
- Elastin fragments know to be chemotactic for the cells that cause intimal hyperplasia
- Endogenous elastases involved in remodeling
- Fast Track designation in the US; Orphan Drug designation in the US and EU for AVFs

Vonapanitase Administration

- Single treatment applied topically to adventitial surface immediately after AVF creation
- Delivered as a series of drops over 10 minutes
- Irrigation of surgical site with saline lavage after treatment
- Inactivated by blood



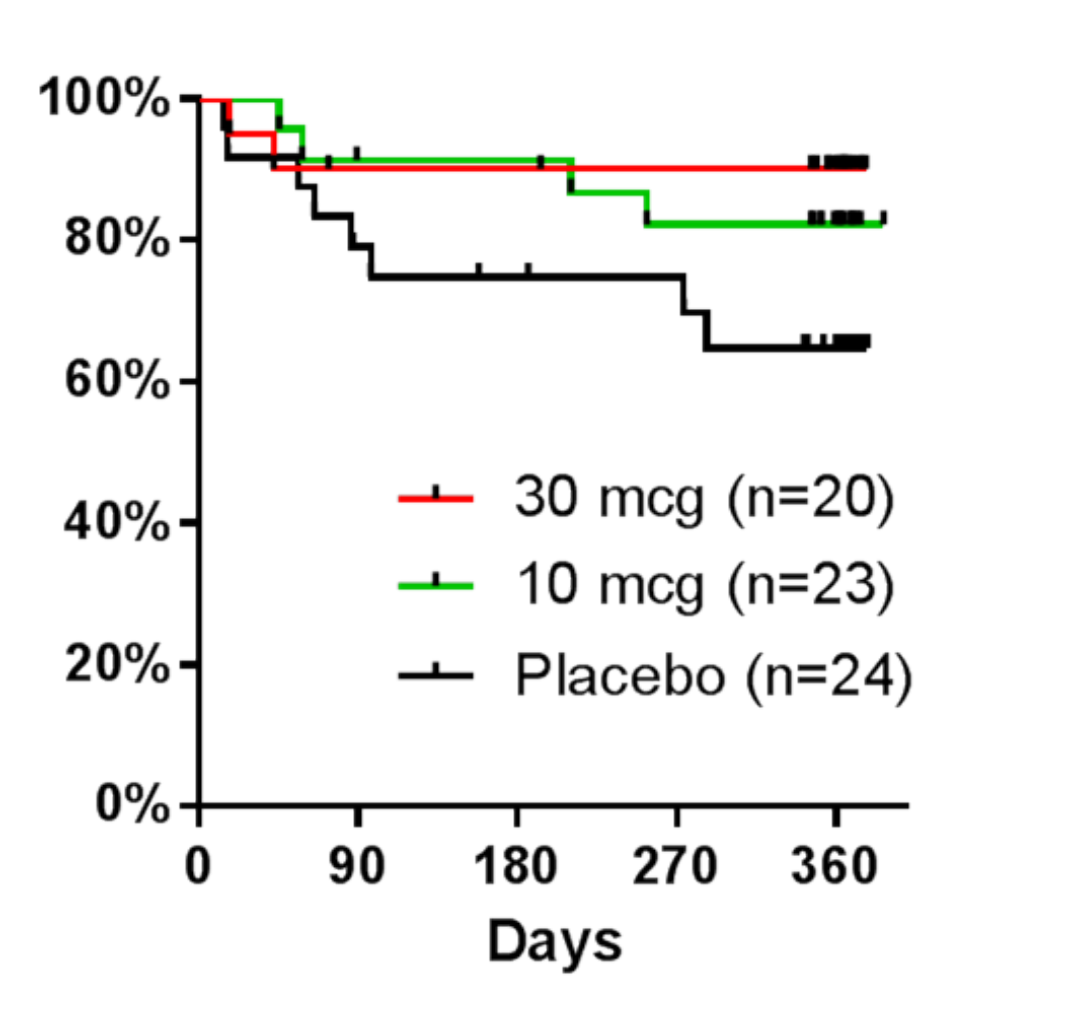
Primary Unassisted Patency In Radiocephalic AVFs—Phase II



Vonapanitase reduced the risk of primary patency loss by 63%[1]
The proportion without patency loss increased from 31% to 63%

Not pre-specified for RC AVF subset. [1] 30 mcg group – RC AVFs. Hazard ratio 0.37 (Log-rank, p=0.02). Peden JVA 2016.

Secondary Patency--Radiocephalic



Vonapanitase reduced the risk of secondary patency loss by 76%[1]

The proportion without patency loss increased from 59% to 90%

Not pre-specified for RC AVF subset. [1] 30 mcg group – RC AVFs. Hazard ratio 0.24 (Log-rank, p=0.046). Peden JVA 2016.

Clinical Development Program

Study	Follow-up	N	Clinical Sites	Status
Phase 1	One year	66	10	Completed
Phase 2	One year	151	27	Completed
Phase 3 (PATENCY-1)	One year	313	31	Completed (registry ongoing)
Phase 3 (PATENCY-2)	One year	603	39	Fully enrolled Data March 2019.

- All studies multicenter, randomized, double-blind, placebo-controlled
- All studies include an additional 2 years of possible follow-up in a registry

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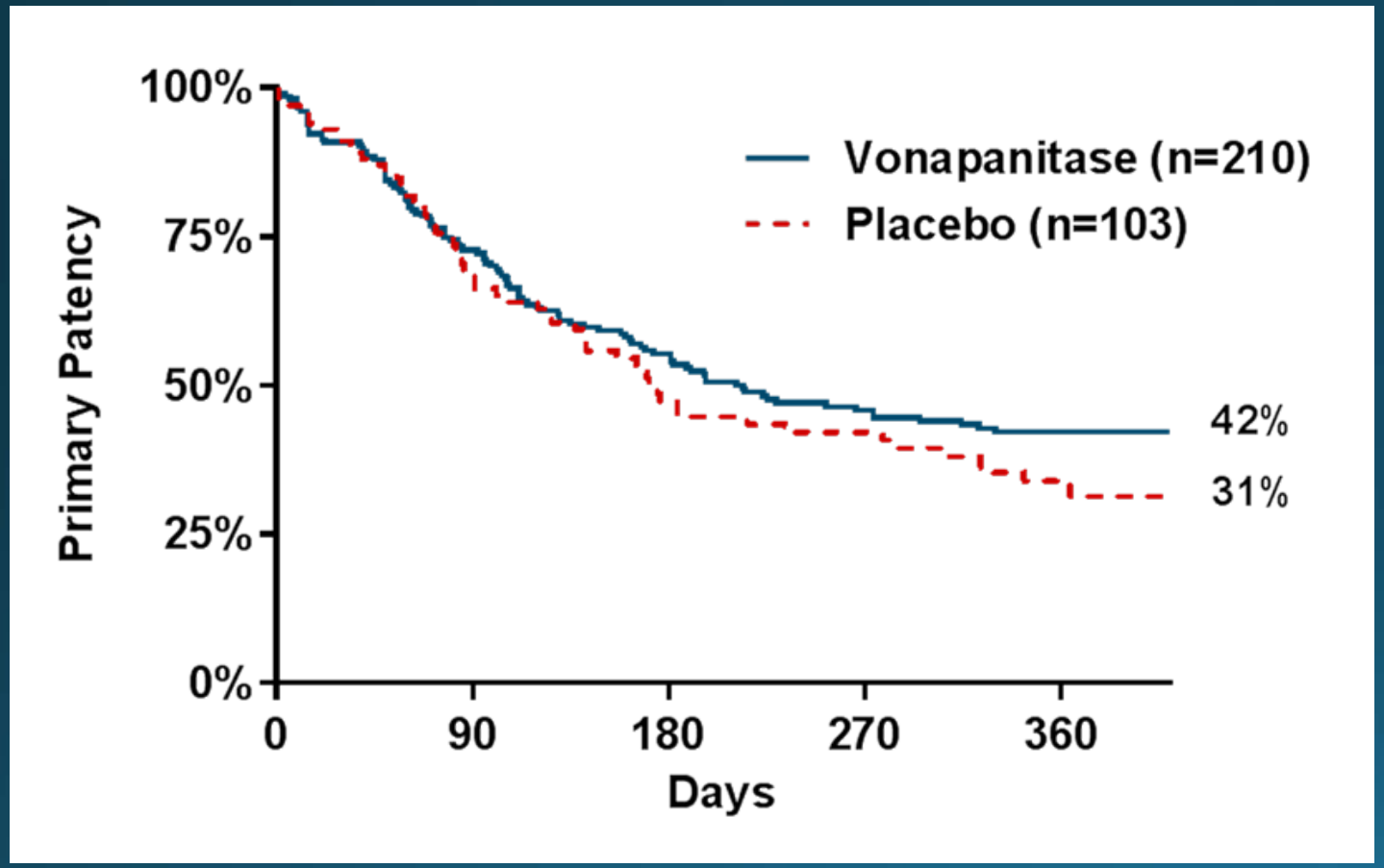
Phase 3 PATENCY-1 Trial (In press, *Journal of Vascular Surgery*)

Design	Multicenter, randomized, double-blind, placebo-controlled
N	313 patients in U.S.
Patients	Patients with CKD on or expecting to initiate hemodialysis and undergoing surgical creation of a radiocephalic fistula
Dose	Vonapanitase 30 mcg vs. placebo (2:1 randomization)
Primary Endpoint	Primary unassisted patency (time from fistula surgical creation until first thrombosis or procedure to restore or maintain patency)
Secondary Endpoint	Secondary patency (time from fistula surgical creation until fistula abandonment)
Tertiary Endpoints	Use for hemodialysis Fistula maturation by ultrasound criteria Rate of procedures

Vonapanitase Increased Primary Patency – Not Statistically Significant

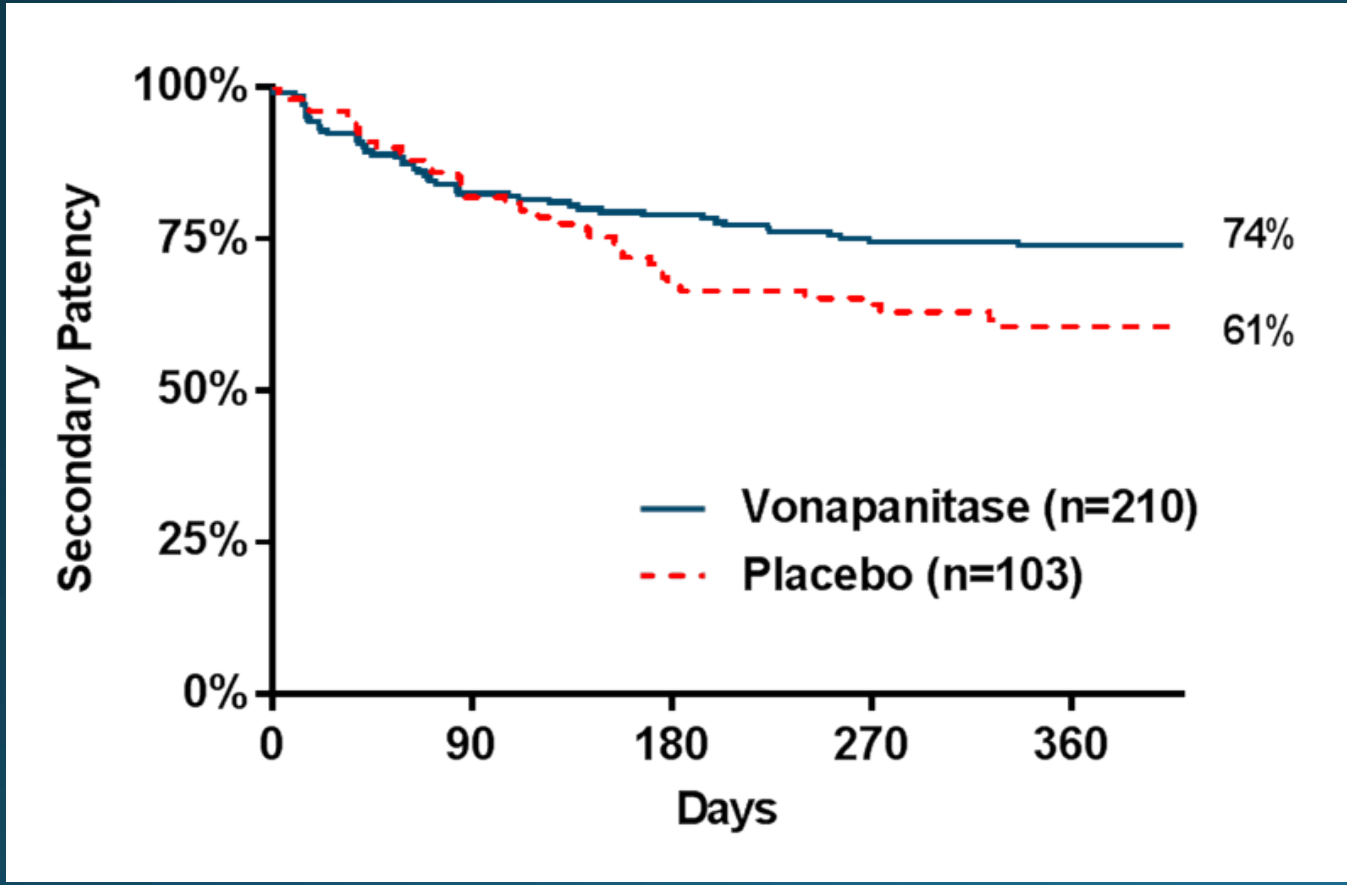


17% reduction in risk of primary unassisted patency loss (thrombosis or procedure to restore or maintain patency)
Hazard ratio 0.83, 95% CI 0.61 – 1.14, p=0.254
Bleyer JVS 2018 in press

Numbers at risk for patency loss:

Vonapanitase	210	139	96	77	40
Placebo	103	66	37	32	19

Vonapanitase Increased Secondary Patency

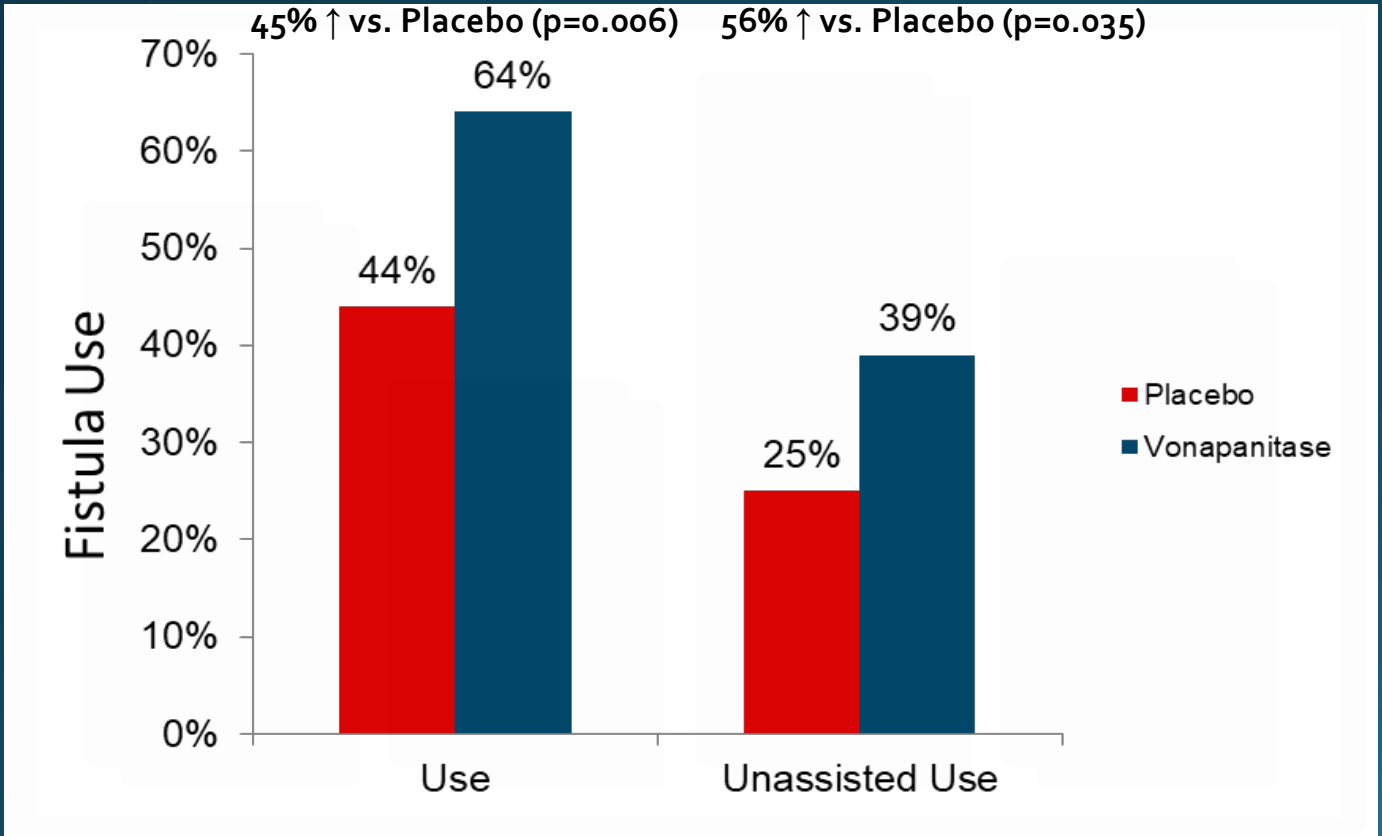


34% reduction in risk of secondary patency loss (abandonment)
Hazard ratio 0.66,
95% CI 0.43 – 1.00,
p=0.048
Bleyer JVS 2018 in press

Number at risk for patency loss:

Vonapanitase	210	163	147	135	82
Placebo	103	80	60	55	39

Vonapanitase Increased Use of the Fistula for Hemodialysis



Definition of fistula use:

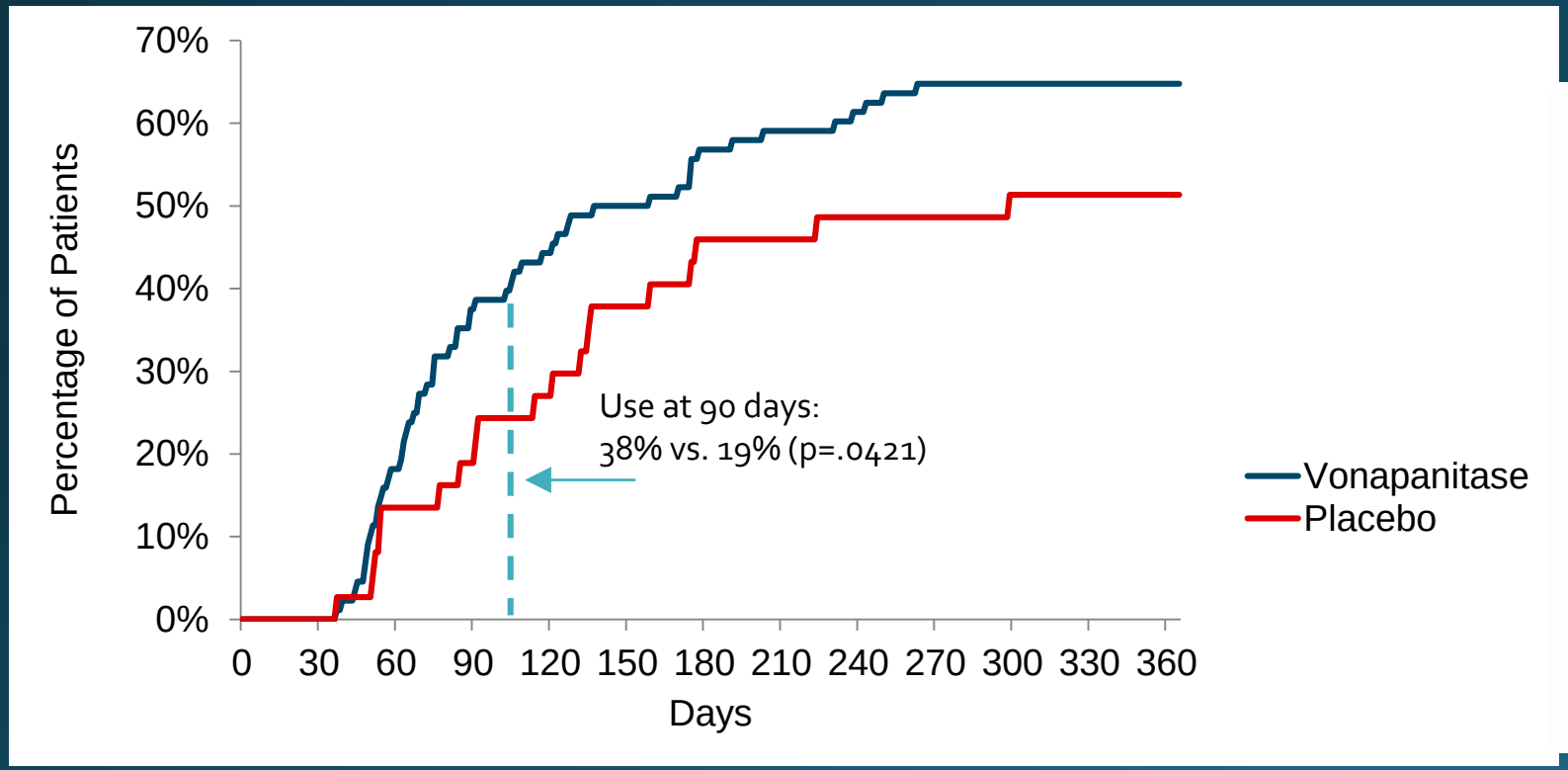
Use for hemodialysis for ≥ 90 days or for patients not on hemodialysis ≥ 90 days prior to last study visit, ≥ 30 days of use including the last visit

Unassisted means without a prior corrective procedure to restore or maintain patency

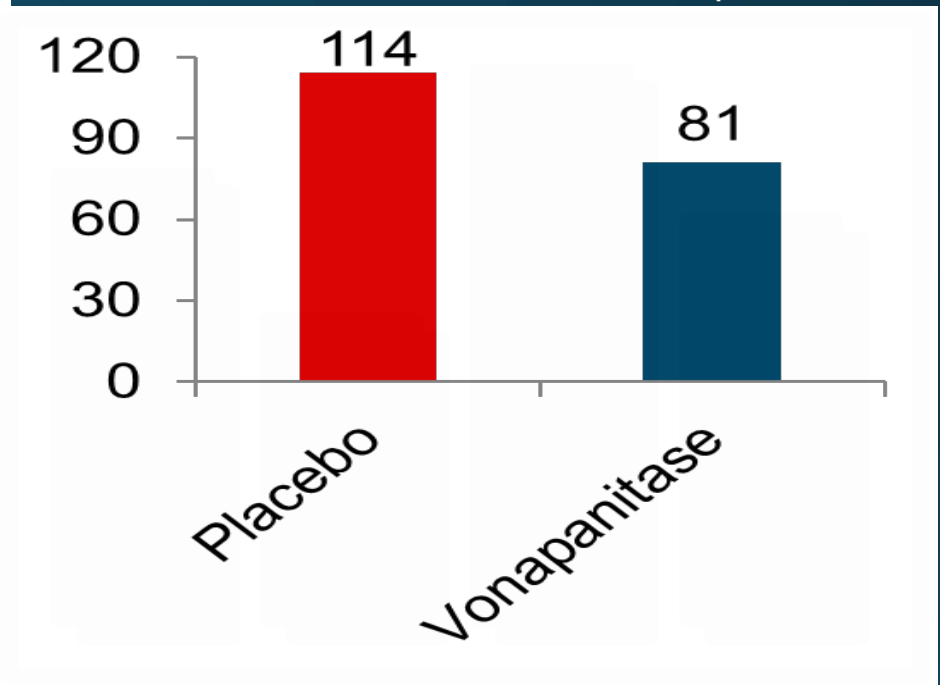
Bleyer JVS 2018 in press

Reduced Time to AVF Use

Evaluated in Patients on HD at Study Initiation



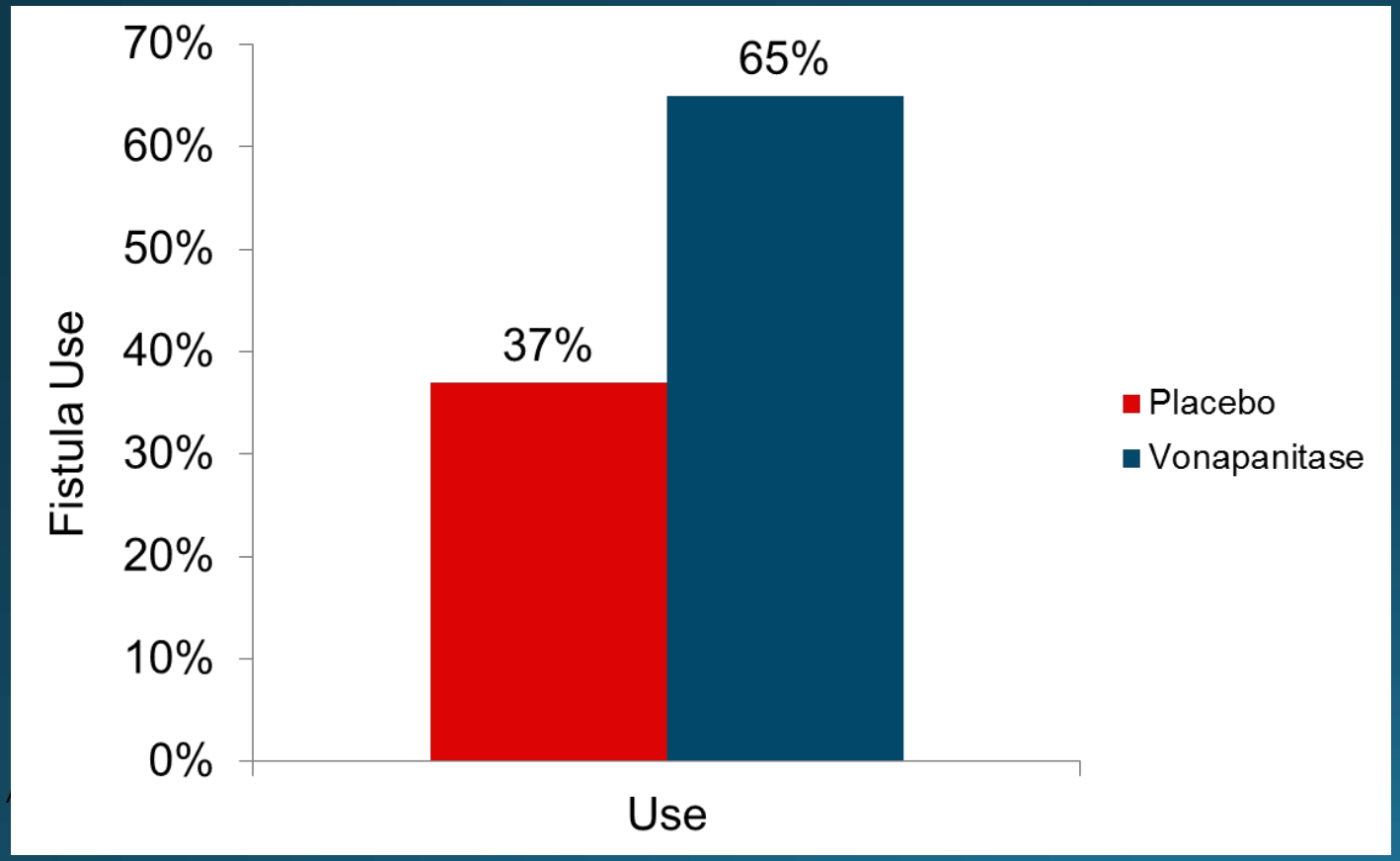
Median Time to AVF Use
41% Greater for Placebo (p=ns)



AVF Use defined using the same definition as the tertiary endpoint. Chi-square test for 90 day analysis. Analysis of median time to use includes all patients on HD at study initiation with successful use (vonapanitase n=57, placebo n=19). Bleyer JVS 2018 in press

Increase in Patients Initiating HD Using the AVF

Evaluated in Patients Pre-hemodialysis at Study Initiation Who Progressed to HD



Analysis includes patients who had their AVF created at least 6 weeks prior to HD initiation (excludes patients who remained predialysis during the study). Bleyer JVS 2018 in press

Vonapanitase Phase 3 Safety Profile

- No evidence of immunogenicity
- Adverse events consistent with underlying condition
- Adverse events comparable for vonapanitase and placebo

Adverse Events	Placebo (n=102)	Vonapanitase (n=209)
Vascular stenosis	40.2%	38.3%
Fistula thrombosis	26.5%	19.6%
Hypoaesthesia (numbness)	4.9%	5.3%
Procedural pain	5.9%	4.8%

Includes any adverse event that occurred in at least 5% of patients in either treatment group
Analysis excludes 2 patients who were randomized but not treated. Bleyer JVS 2018 in press

Ongoing Phase 3 PATENCY-2 Trial

Design	Multicenter, randomized, double-blind, placebo-controlled
N	603 patients in U.S. and Canada
Patients	Patients with CKD on or expecting to initiate hemodialysis and undergoing surgical creation of a radiocephalic fistula
Dose	Vonapanitase 30 mcg vs. placebo (2:1 randomization)
Co-Primary Endpoints	Fistula use for hemodialysis Secondary patency
Other Efficacy Endpoints	Primary unassisted patency Procedure rate Fistula maturation

clinicaltrials.gov (NCT 02414841). Endpoint definitions same as PATENCY-1.

Program Status

- Results from PATENCY-1 supported FDA Breakthrough Therapy Designation
  - FDA's criteria for BTD: potential treatment for serious or life-threatening condition and preliminary clinical evidence indicates drug may offer substantial improvement (clear advantage) over available therapies on one or more clinically significant endpoints
- FDA agreement on filing strategy with co-primary endpoints in PATENCY-2
  - Endpoint definitions same as PATENCY-1
  - If each successful at $p<0.05$, BLA can be filed without additional trials
  - Data expected March 2019; BLA filing expected in 2019

www.proteontherapeutics.com . Press release May 10, 2017

Summary – Vonapanitase Data to Date

- Evidence of biologic signal in radiocephalic fistulas
- Secondary and tertiary endpoints suggest positive impact on clinically meaningful outcomes
  - Use for hemodialysis (p=0.006)
  - Unassisted use for hemodialysis (0.035)
  - Secondary patency (p=0.048) and in efficacy analysis set (p=0.007)
- PATENCY-2 Trial data available in 1st Quarter of 2019
- *Potential novel adjunct to enhance AVF outcomes*