Belapectin for MASH Cirrhosis and Portal Hypertension

March 10, 2026

Today's Agenda

01	**Moderator**	Michael Cozart, LifeSci Consulting
02	**Belapectin as Galectin-3 Inhibitor for MASH cirrhosis & Portal Hypertension**	Khurram Jamil, M.D. (CMO)
03	**Current Landscape & Primary End Point Results**	Naga Chalasani, M.D.
04	**Biomarker Results**	Naim Alkhouri. M.D.
05	**Closing Remarks**	Khurram Jamil, M.D. (CMO)

Galectin Therapeutics

Belapectin a Galectin-3 Inhibitor for MASH Cirrhosis & Portal Hypertension

Khurram Jamil, M.D.
Chief Medical Officer

MASH Cirrhosis with Portal Hypertension Represents a Significant Unmet Need

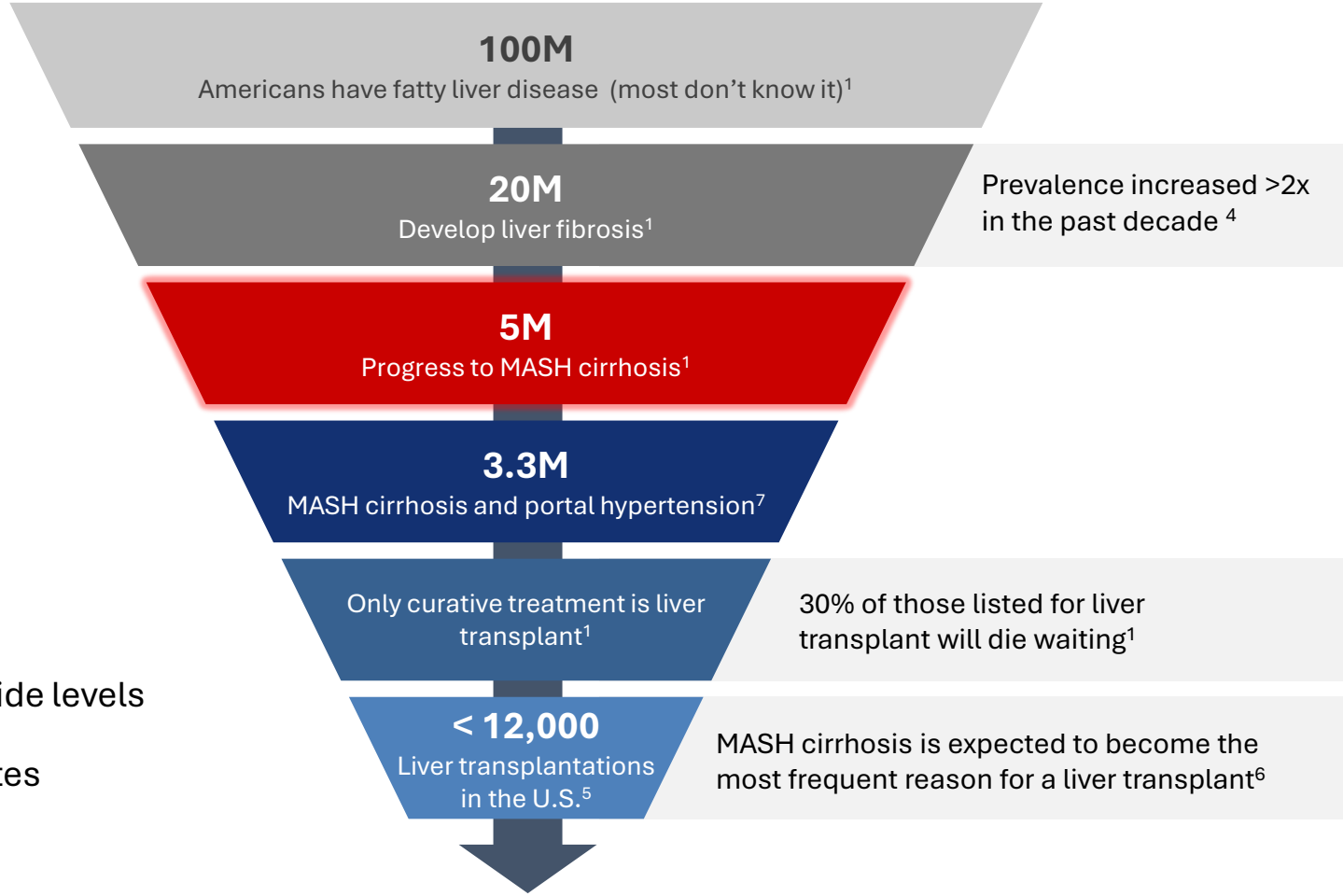
Metabolic dysfunction-associated steatohepatitis (MASH), previously known as non-alcoholic steatohepatitis (NASH), is characterized by fat accumulation, inflammation and fibrosis of the liver[1]

3%-5% of the global population is estimated to be affected by MASH, though the disease is considered to be underdiagnosed[2]

There are genetic predisposition to MASH, yet certain health conditions put patients at increased risk:[3]

- Being overweight or obese
- Having hypertension, high cholesterol or high triglyceride levels
- Having type 2 diabetes, insulin resistance or prediabetes

Addressable market in the U.S.



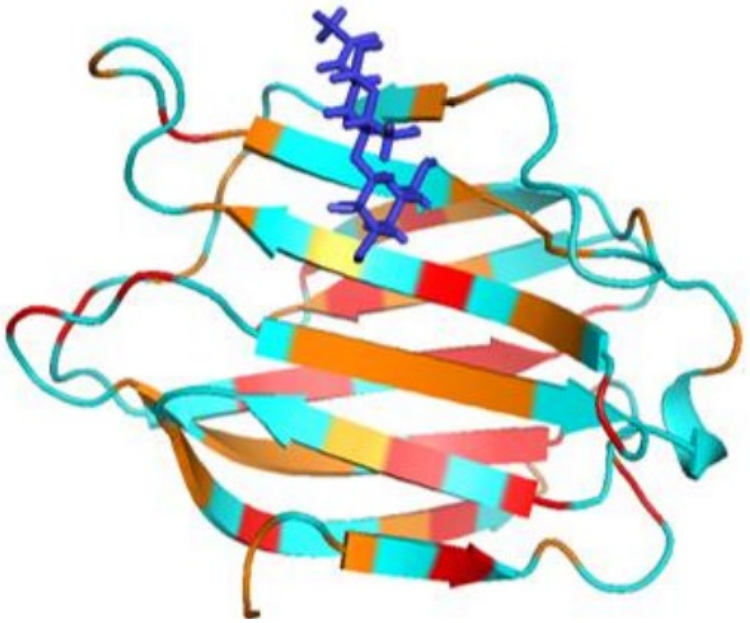
1. Fatty Liver Foundation. https://www.fattyliverfoundation.org/#gsc.tab=0. .2. Sherif ZA, et al. *Dig Dis Sci*. 2016;61(5):1214-25. 3. NIDDK. NAFLD and MASH. https://www.niddk.nih.gov/health-information/liver-disease/nafld-nash/symptoms-causes. 4. Datamonitor Healthcare. MASH Disease Analysis. 5. Scientific Registry of Transplant Recipients. OPTN/SRTR 2024 Annual Data Report: Liver. https://srtr.transplant.hrsa.gov/annual_reports/2024/Liver.aspx. 6. Stepanova M, et al. *Hepatol Commun*. 2022;6(7):1506-1515. 7. Zobair M. Younossi, et al, Prevalence and predictors of cirrhosis and portal hypertension in the United States, American Association for the Study of Liver Disease, DOI: 10.1097/HEP.0000000000001243.

Belapectin For MASH Cirrhosis and Portal Hypertension

Belapectin Preclinical Data:

Multiple animal models of MASH (streptozotocin High-Fat Diet mice[1]) and cirrhosis (thioacetamide treated rats[2]) belapectin was associated with decreased:

- Galectin-3 staining and galectin-3 expression in macrophages
- NAFLD Activity Scores
- Collagen-1 expression
- Hepatic collagen deposition
- Hepatic fibrosis
- Portal pressure



Toxicology Data

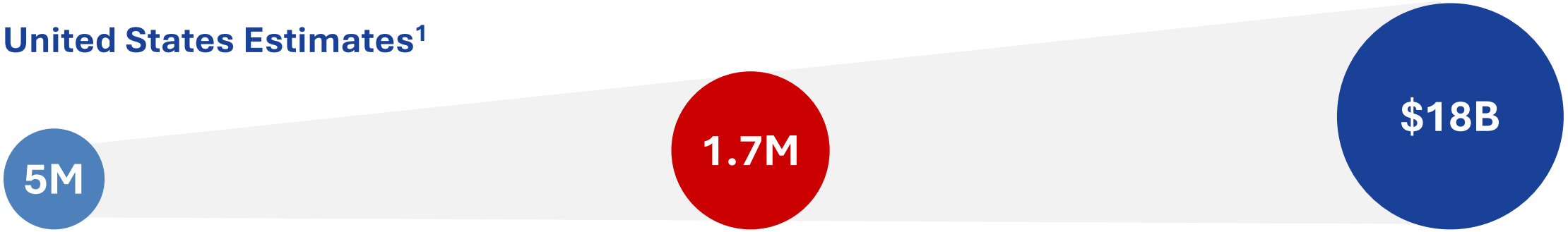
- Well-tolerated even at high doses
- Accumulated in macrophages with a residence time longer than in plasma

Belapectin is a polysaccharide polymer comprising galacturonic acid, galactose, arabinose, rhamnose and smaller amounts of other sugars. Suite of Oral Galectin-3 Inhibitor molecules as part of life cycle management plan.

1. Traber PG, et al. *PLoS One*. 2013;8(12):e83481. 2. Traber PG, et al. *PLoS One*. 2013; ;8(10):e75361.

Belapectin's Novel Mechanism Positions It to Address MASH Cirrhosis & Portal Hypertension

United States Estimates[1]



Patients with compensated MASH cirrhosis in 2024

Patients with compensated cirrhosis and portal hypertension with no varices in 2024

Peak belapectin sales in U.S.

3rd Party Market Opportunity Assessment Suggests[1]

Potential 35-100% Adoption Rate

Limited current treatment options:

- Cirrhotic management focuses on stabilization and delaying progression
- Management directed towards comorbidities

Highly favorable perception of belapectin indication, MoA and safety by HCPs

Payers believe in the high unmet need in MASH cirrhosis

A significant unmet need exists for compensated MASH cirrhosis patients with portal hypertension due to disease severity and risk of decompensation

1. LifeSci Consulting Belapectin Commercial Opportunity Assessment contracted by the Company.

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MASH Cirrhosis Landscape
Belapectin Program

Naga Chalasani, M.D.

When to Intervene in Cirrhosis- before its too late!

Compensated cirrhosis | **Decompensated cirrhosis**

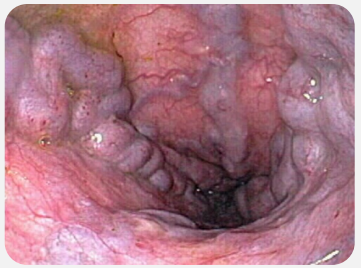
No Portal Hypertension | **Portal Hypertension**

No varices

≥6

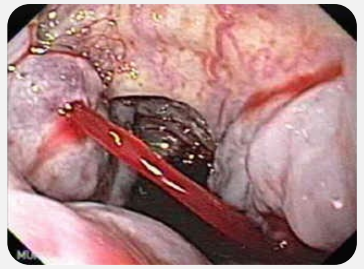
No varices

Varices,
small to large



≥10

Varices Bleeding, ascites, encephalopathy



One year mortality 1-3%

One year mortality ~50%

There are no approved therapies to reverse portal hypertension once it develops in MASH Cirrhosis

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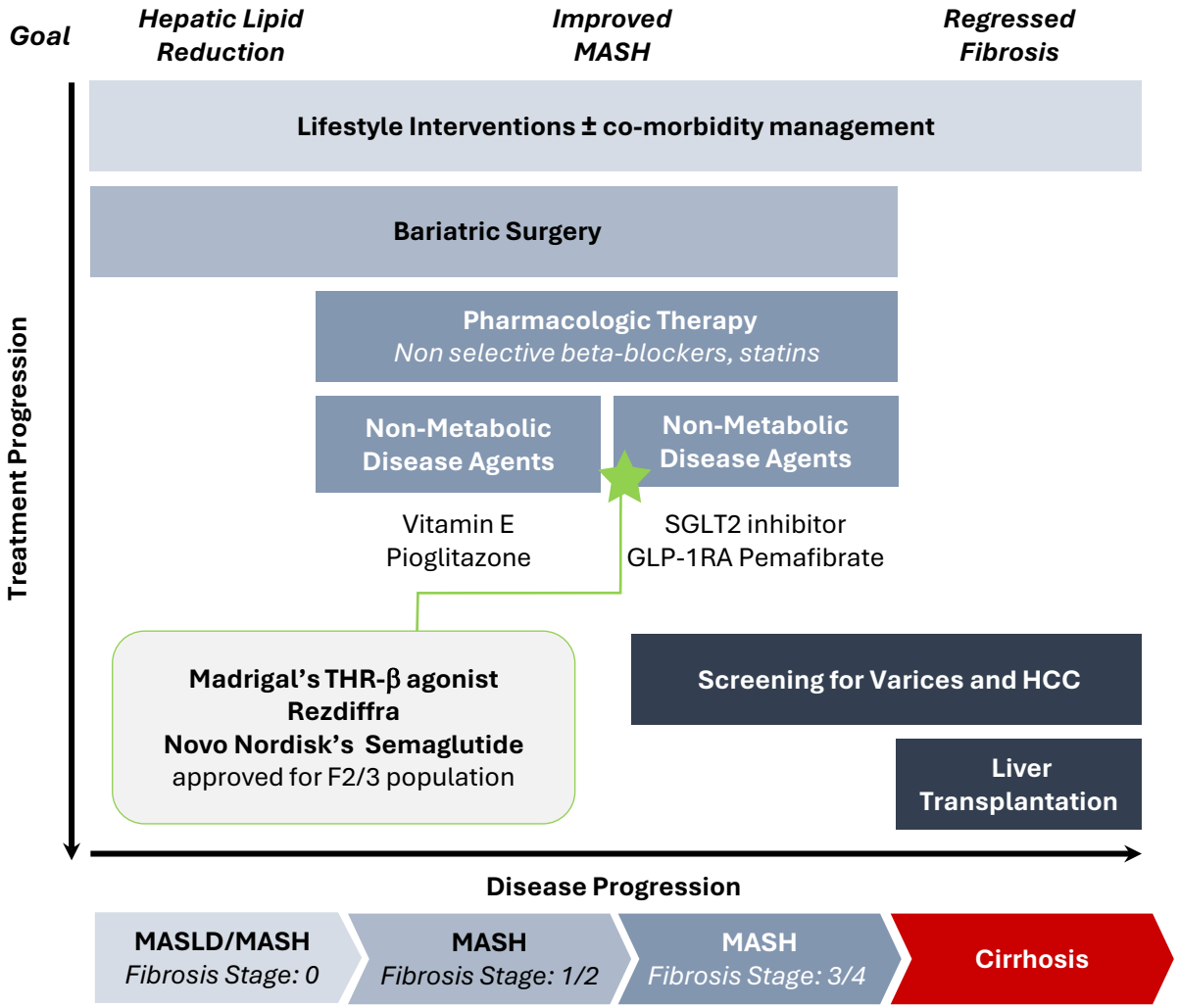
Current Treatment Paradigm

Resmetirom and Semaglutide approved for F2/3 patients; Limited options in Cirrhosis & Portal Hypertension



Lifestyle interventions are used to promote weight-loss, a key component to improve the histopathologic feature of this disease

Bariatric surgery is promising for patients who are unable to achieve sufficient weight loss at 6 months; histologic improvement has been observed post-operatively

Pharmacologic therapy Non-selective beta blockers (NSBB) and statins to manage portal hypertension.

Non-Metabolic disease agents: vitamin E may be used in patients without diabetes, data is mixed with potential safety concerns (e.g., increase in mortality); Pioglitazone has been shown to reduce the incidence of NAFLD in T2D/obese patients and improve fibrosis

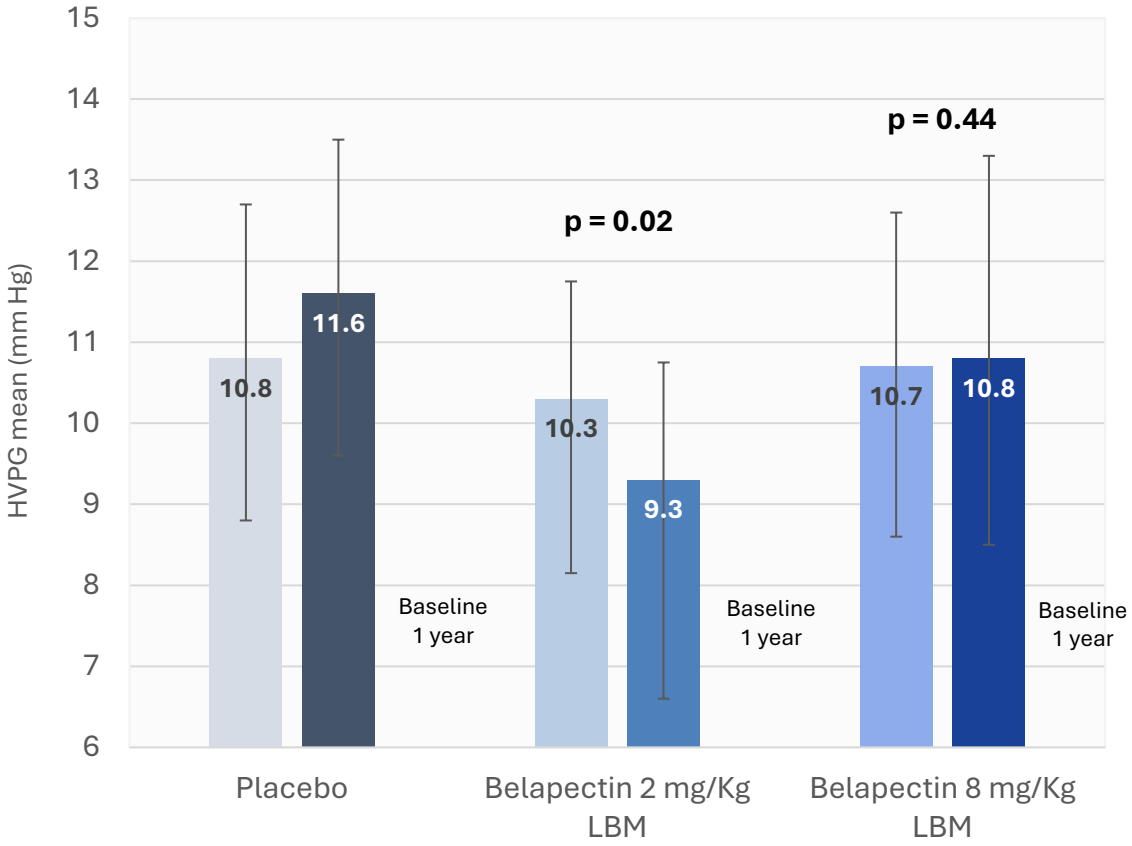
Metabolic disease agents may be prescribed to NASH patients with diabetes, depending on physician preference

Screening is recommended every 6 mos. for ≥3 fibrosis or for those with non-invasive markers highly suggestive of advanced fibrosis

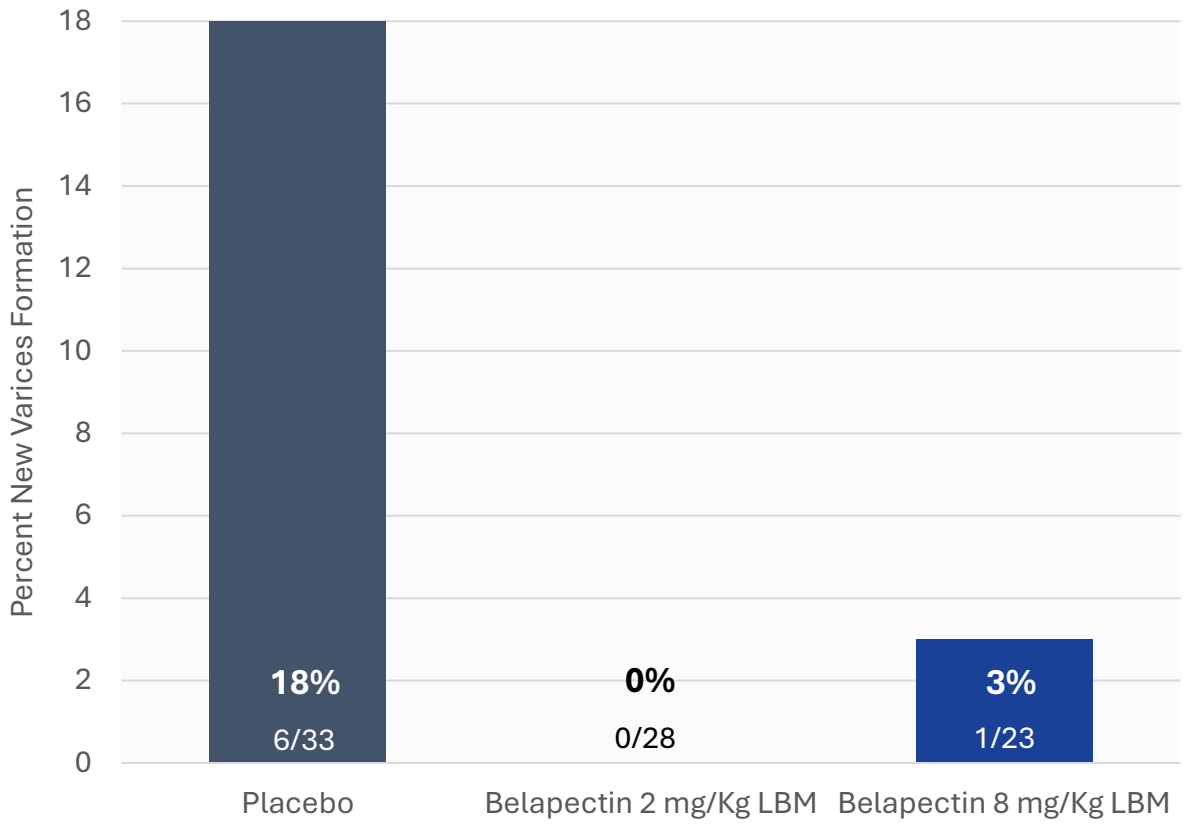
Liver transplant is typically considered when patients have developed cirrhosis, complications (e.g., ascites), or a MELD score ≥15. Transplant is currently the only option for advanced cirrhotic patients

Phase 2b Study of Belapectin in Patients with MASH Cirrhosis: GT-026 Trial

HVPG Change at Week 52
Second Incidence of Varices at week 52



Belapectin Reduced Emergence of Varices in Patients with MASH Cirrhosis[1,*]



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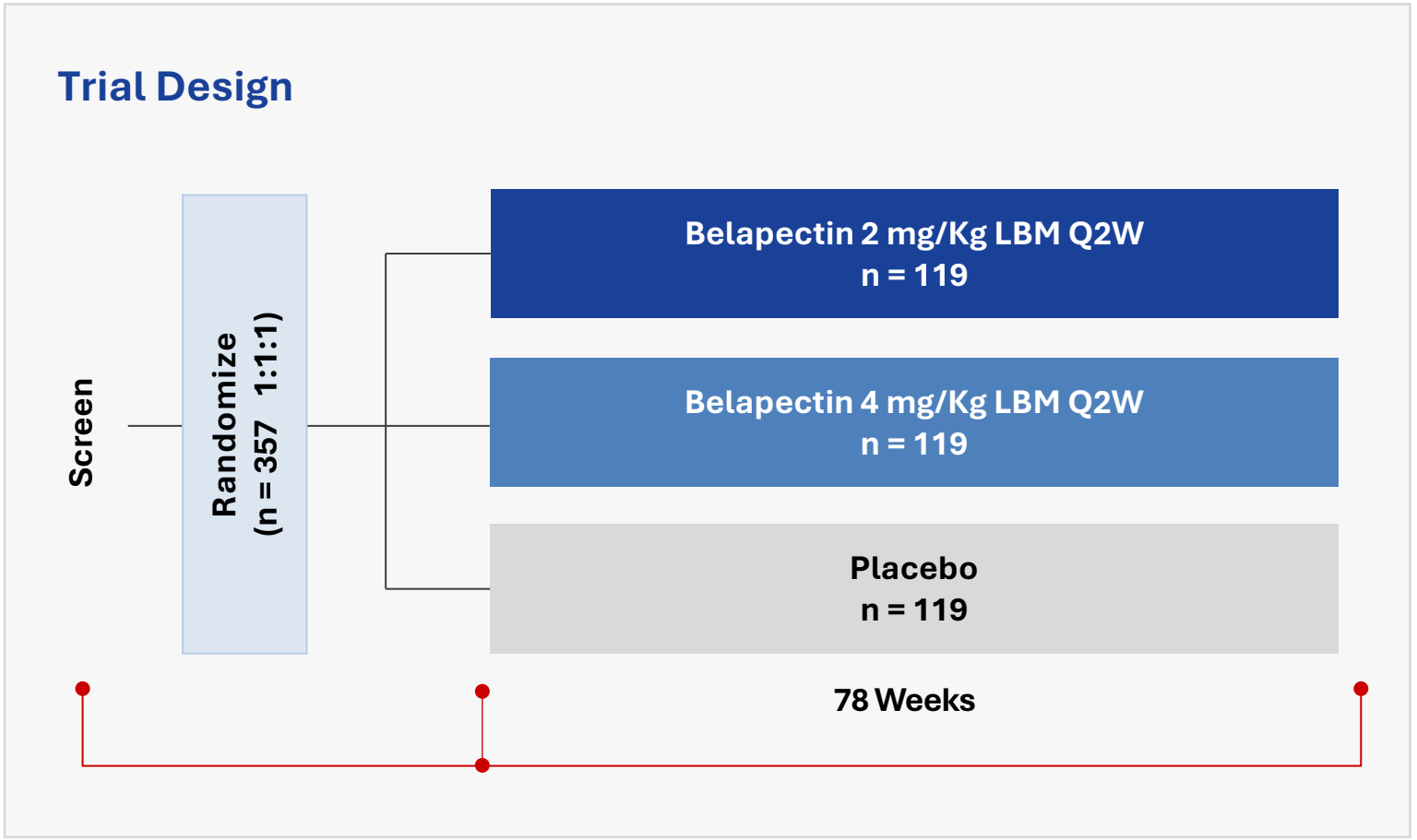
HVPG = Hepatic Venous Pressure Gradient; LBM = lean body mass
*ITT with LOCF, ANCOVA with baseline as covariate and treatment as factors, Bonferroni-Holm.
1. Chalasani N, et al. *Gastroentrol.* 2020;158:1334-45.

NAVIGATE Trial Design

Patient Population

- MASH cirrhosis based on Liver Forum Recommended Criteria for Clinical Trials
- Diagnosis of Portal Hypertension as per Baveno VI criteria (via non-invasive markers)
- No gastroesophageal varices by endoscopy at baseline
- Assessment of Varices thru central adjudication of endoscopy videos by multiple blinded reviewers based on standardized protocol.



NAVIGATE Study: Patient Population and Efficacy Endpoints

Key inclusion criteria

MASH cirrhosis

No varices on EGD

CTP Scores <7

Evidence of Portal hypertension:

Platelet count <150,000/mm3 or at least two of the following

I. AST/ALT > 1
II. Spleen ≥ 14 cm
III. Collaterals by imaging
IV. Stiffness ≥ 20 kPa

Primary endpoint

Composite primary end point in ITT population

Incidence of Varices in per protocol population

Composite secondary endpoint

Hepatic decompensation events

All-cause mortality

Proportion of patients with large varices or red wale sign

Varices requiring treatment

MELD ≥ 15

Liver transplant

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ALT = alanine aminotransferase ; AST = aspartate transaminase; CTP = Child-Turcotte-Pugh; EGD = Esophagogastroduodenoscopy; MELD = model for end-stage liver disease.
*Intercurrent events include; Liver related clinical events, any AE leading to discontinuation, TIPS = Trans-jugular intrahepatic portosystemic shunt; ≥12-month use of GLP-1 or NSBB
ITT- Intent to Treat

Key Populations for Assessment of Varices Outcome

- **ITT** All randomized subjects minus two subjects who had varices at baseline;
- **Per Protocol** All subjects who completed 18 month of therapy and had an EGD at baseline and 18 month
  - Subject were required to complete the study even after development of varices unless subject dropped out for other reasons
- **Composite Primary End point** Any subject who developed esophageal varices or had an intercurrent event or dropouts without an EGD/intercurrent event
  - Intercurrent events included;
    - Liver related clinical events,
    - AE leading to discontinuation
    - TIPS-Trans-jugular intrahepatic portosystemic shunt
    - ≥12-month use of GLP-1 or NSBB

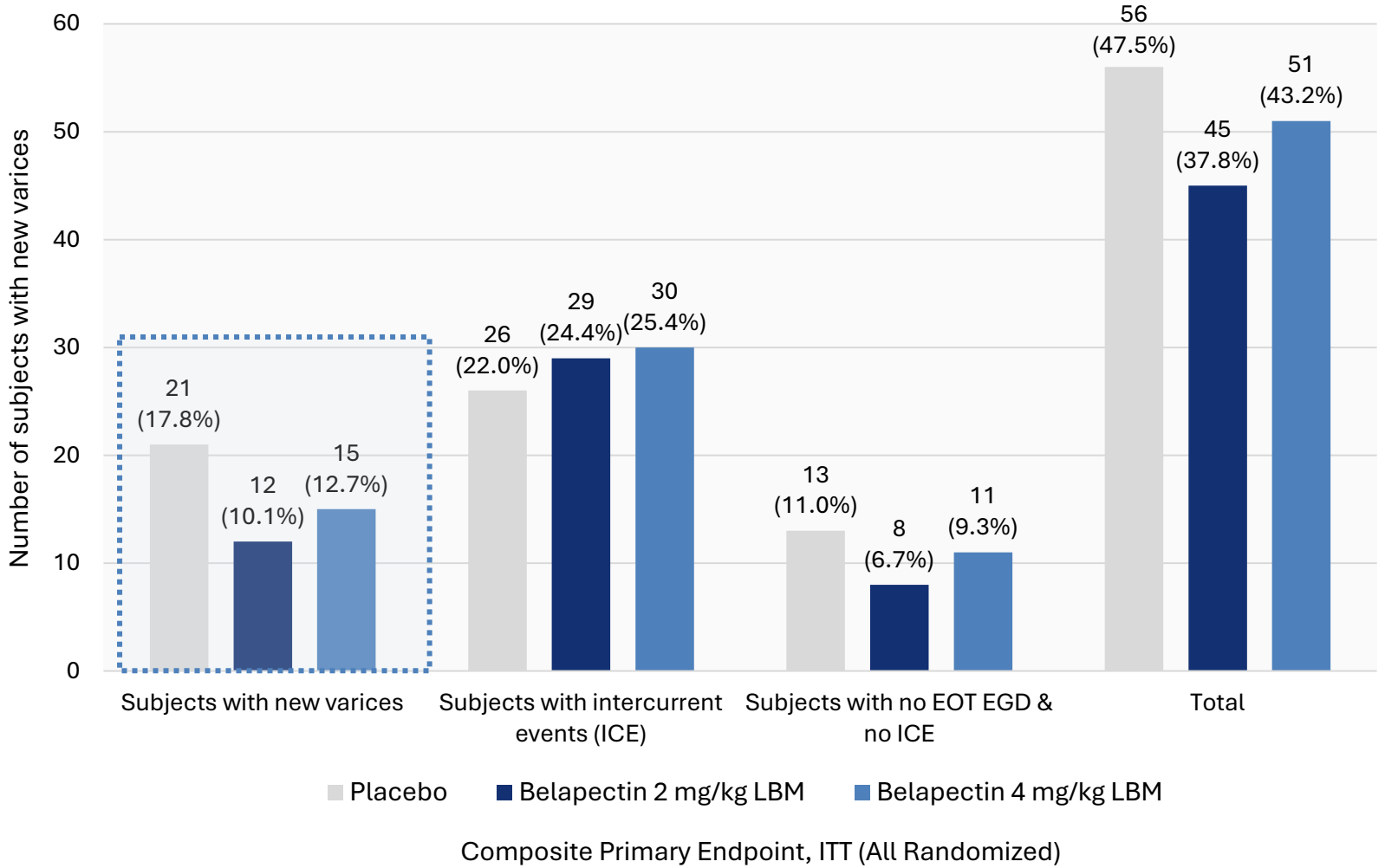
NAVIGATE Trial: Baseline Demographics

n = 355

	Placebo (n = 118	Belapectin 2 mg (n = 119)	Belapectin 4 mg (n = 118)
	Mean (Standard Deviation)	Mean (Standard Deviation)	Mean (Standard Deviation)
Age (years)	60.4 (8.50)	60.6 (8.82)	59.0 (9.14)
Gender (female), n	72 (61.0)	75 (63.0)	83 (70.3)
Ethnicity (Hispanic), n	34 (28.8)	39 (32.8)	33 (28.0)
Race (white), n	104 (88.1)	107 (89.9)	111 (94.1)
Weight (kg)	94.2 (21.68)	98.1 (24.30)	94.6 (20.95)
BMI (Kg/m^2)	33.82 (6.46)	34.88 (6.68)	34.53 (6.22)
Hypertension	89 (75.4)	89 (74.8)	82 (69.5)
Type 2 Diabetes	80 (67.8)	79 (66.4)	79 (66.9)
HbA1C %	6.4 (1.27)	6.3 (1.13)	6.4 (1.09)
Alanine Aminotransferase (ALT), U/L	46.3 (29.92)	38.9 (26.88)	39.7 (20.22)
Aspartate Aminotransferase (AST), U/L	46.7 (23.52)	41.8 (24.40)	43.6 (21.90)
Platelets (per µL)	130.1 (39.66)	127.6 (48.39)	136.4 (53.62)
Liver Stiffness Measurement (kPa)	23.6 (11.44)	25.1 (15.04)	25.8 (12.91)
Spleen (cm)	13.79 (2.7)	13.97 (2.6)	13.87 (2.4)
MELD Score	7.6 (1.65)	7.9 (2.46)	7.5 (1.55)
Child Pugh Score	5.1 (0.29)	5.1 (0.31)	5.0 (0.18)
Statins (n)	49 (41.5)	55 (46.2)	47 (39.8)
GLP-1 agonist (n)	24 (20.3)	26 (21.8)	27 (22.9)

NAVIGATE: Composite Primary End Point Results

Intent to Treat



Key points

- Intent to Treat (ITT) -All randomized subjects
- Primary end point composite strategy i.e. new varices and/or intercurrent events or drop out
- Intercurrent events (ICEs) include; Liver related clinical events, AE leading to discontinuation, TIPS; ≥12-month use of GLP-1 or NSBB
- Overall Target Significance level– 2-sided p value of 0.05; using CMH test, stratified by Type 2 diabetes status at randomization.

ITT Totals		
Placebo	**2 mg/kg**	**4 mg/kg**
118	119	118
-	p = 0.278	p = 0.522

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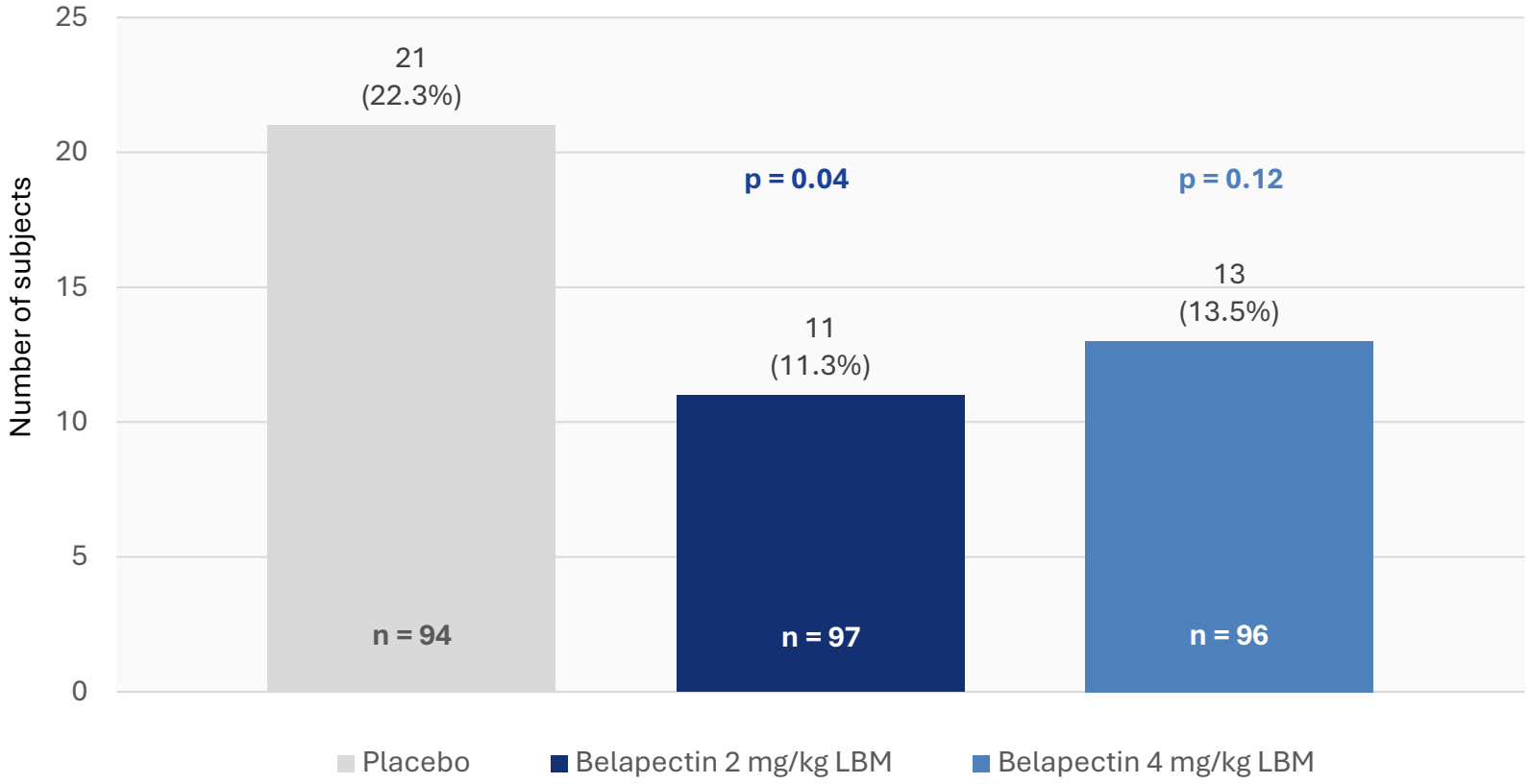
NAVIGATE: Significantly Lower Incidence of Varices in Completer Population

Per Protocol

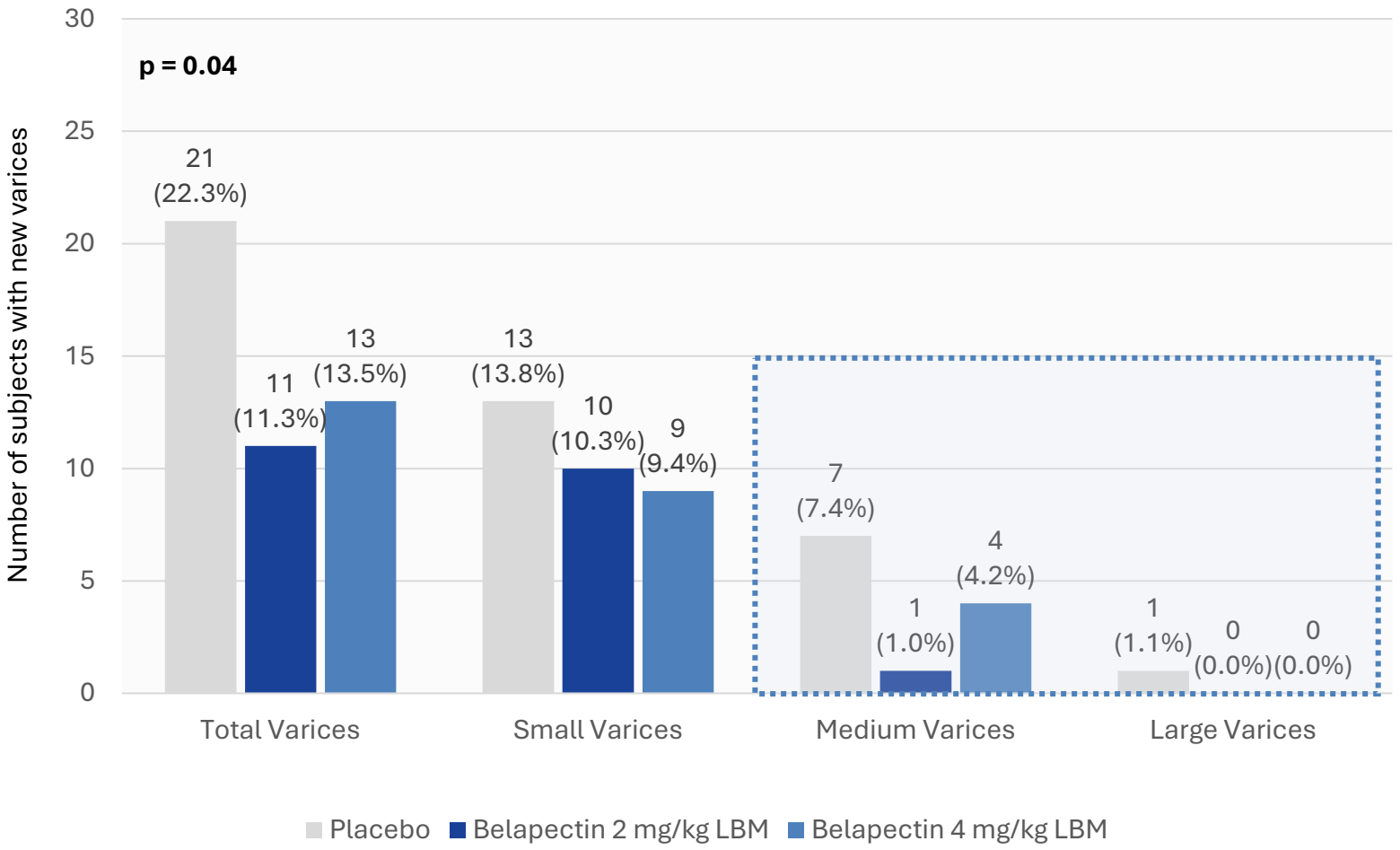


Key points

- NAVIGATE 18-month Primary Analyses Result; Per protocol population n= 287
- Per Protocol Population: All ITT subjects who completed 18 months of treatment with an end of treatment (EOT) EGD
- Overall Target Significance level – 2-sided p value of 0.05; using CMH test, stratified by Type 2 diabetes status at randomization.

NAVIGATE: Reduced Incidence of Medium/Large Varices with Belapectin

Per Protocol



Key points

Placebo Treatment Group: n = 94

2 mg/kg LBM Belapectin Treatment Group: n = 97

4 mg/kg LBM Belapectin Treatment Group: n = 96

Varices grade definition

- Large > 5 mm in diameter, occupying more than 1/3 of esophageal lumen
- Medium >5 mm in diameter, occupying less than 1/3 of esophageal lumen
- Small <5 mm in diameter, minimally elevated above esophageal mucosa.

Lowest Rates of Liver-Related Events and MACE Observed with the 2 mg Dose

Per Protocol

		Belapectin	
	Placebo (n = 94) n (%)	2mg/kg LBM (n = 97) n (%)	4mg/kg LBM (n = 96) n (%)
Subjects with Composite Clinical Outcomes, n (%)	**5 (5.3)**	**3 (3.1)**	**9 (9.4)**
Varices (Esophageal or Gastric) Requiring Treatment	3 (3.2)	3 (3.1)	4 (4.2)
Variceal Bleed Requiring Hospitalization	0	0	0
Clinically Significant Ascites Requiring Hospitalization	0	0	1 (1.0)
Spontaneous Bacterial Peritonitis	0	0	1(1.0)
Overt Hepatic Encephalopathy (West Haven Score ≥2 and Requiring Hospitalization)	1(1.1)	0	1 (1.0)
Liver Transplant	0	0	0
Model End Stage Liver Disease (MELD) Score ≥ 15	1(1.1)	0	2 (2.1)
MI or Hospitalization for Unstable Angina	0	0	1 (1.0)
Stroke or Transient Ischemic Attack	1 (1.1)	0	1 (1.0)

MACE- major adverse cardiovascular events; subjects with multiple events counted once

Safety Summary

Adverse Events

Discontinuation of the study due to Adverse Events was similar across 3 cohorts:

- 7 (5.9%) in the Placebo
- 5 (4.2%) in 2 mg/kg LBM Belapectin
- 8 (6.7%) in 4 mg/kg LBM Belapectin
- One subject in each of the three cohorts discontinued the study due to death

- No drug related SAE reported in the entire trial
- No Adjudicated Drug-Induced Liver Injury (DILI) Events.

Treatment-Emergent Adverse Events (TEAEs)

Similar proportion of subjects reported **Treatment-Emergent Adverse Events TEAEs** across 3 cohorts:

- 112 (94.9%) in Placebo
- 116 (97.5%) in 2 mg/kg LBM Belapectin
- 116 (96.7%) in 4 mg/kg LBM Belapectin

Treatment-Emergent Serious Adverse Events (TESAEs)

Similar proportion of subjects reported **Treatment-Emergent Serious Adverse Events** across 3 cohorts:

- 23 (19.5%) in Placebo
- 27 (22.7%) in 2 mg/kg LBM Belapectin
- 25 (20.8%) in 4 mg/kg LBM Belapectin

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NAVIGATE
Biomarker Results at 18 Months

Naim Alkhouri, M.D.

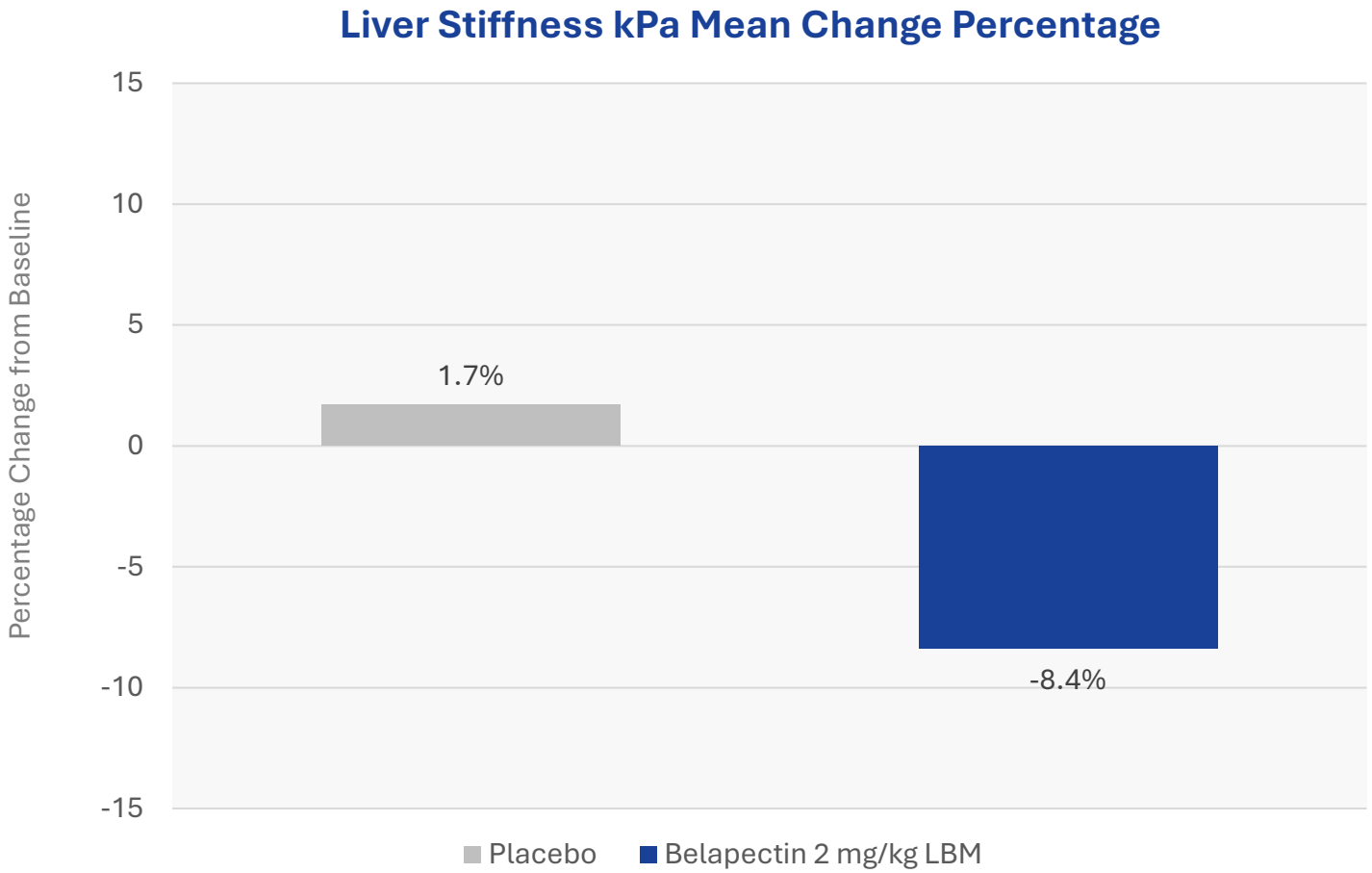
NAVIGATE Enrolled Subject with Advanced Cirrhosis & Portal Hypertension

Key Baseline Characteristics, Per Protocol

	Placebo (n = 94)	Belapectin 2 mg (n = 97)
	Mean (Standard Deviation)	Mean (Standard Deviation)
Platelets (per µL)	132.3 (40.73)	125.8 (48.52)
Liver Stiffness Measurement (kPa)	23.4 (11.39)	23.7 (13.19)
Spleen size (cm)	13.7 (2.92)	13.9 (2.52)
MELD Score	7.5 (1.68)	8.0 (2.65)
Child Pugh Score	5.1 (0.29)	5.1 (0.31)
CSPH / Probable CSPH	55.3%	58%
FIB-4	3.56 (1.99)	3.73 (2.11)
ELF score	10.7 (1.17)	10.6 (0.99)
AGILE- 4 score	0.66 (0.24)	0.69 (0.22)

NAVIGATE: Belapectin Treatment Associated with Decreased Liver Stiffness

Per Protocol

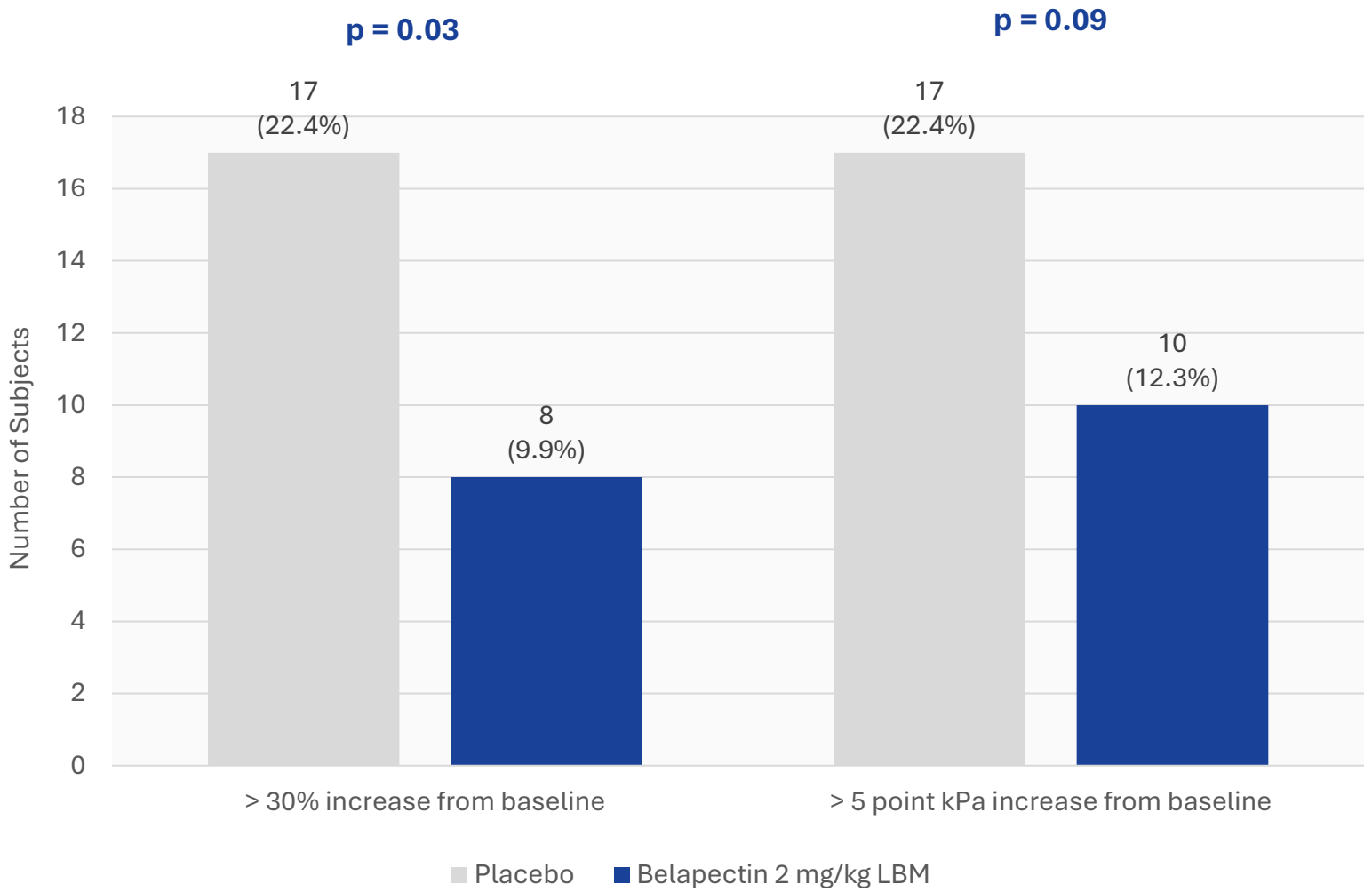


	Belapectin	
	Placebo (n = 76)	**2 mg/kg LBM** (n = 81)
Mean	22.6	24.6
Standard Deviation	10.31	13.971
Median	22.4	21.8

Values based on Per Protocol Set for Subjects with all Phase 2b assessments

Significantly Less Progression of Liver Stiffness on Belapectin

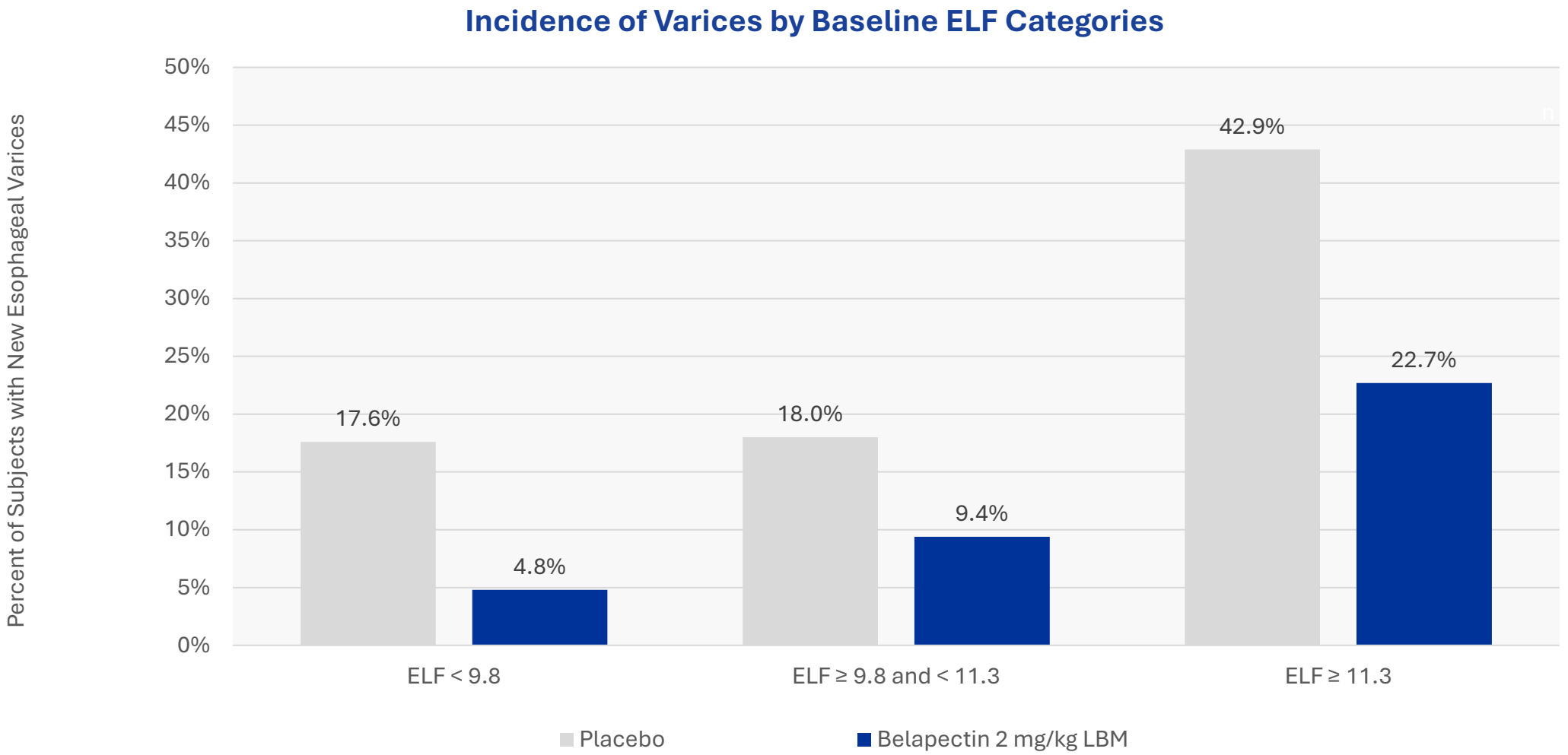
Per Protocol



Belapectin	
Placebo	**2mg/kg LBM**
76	81

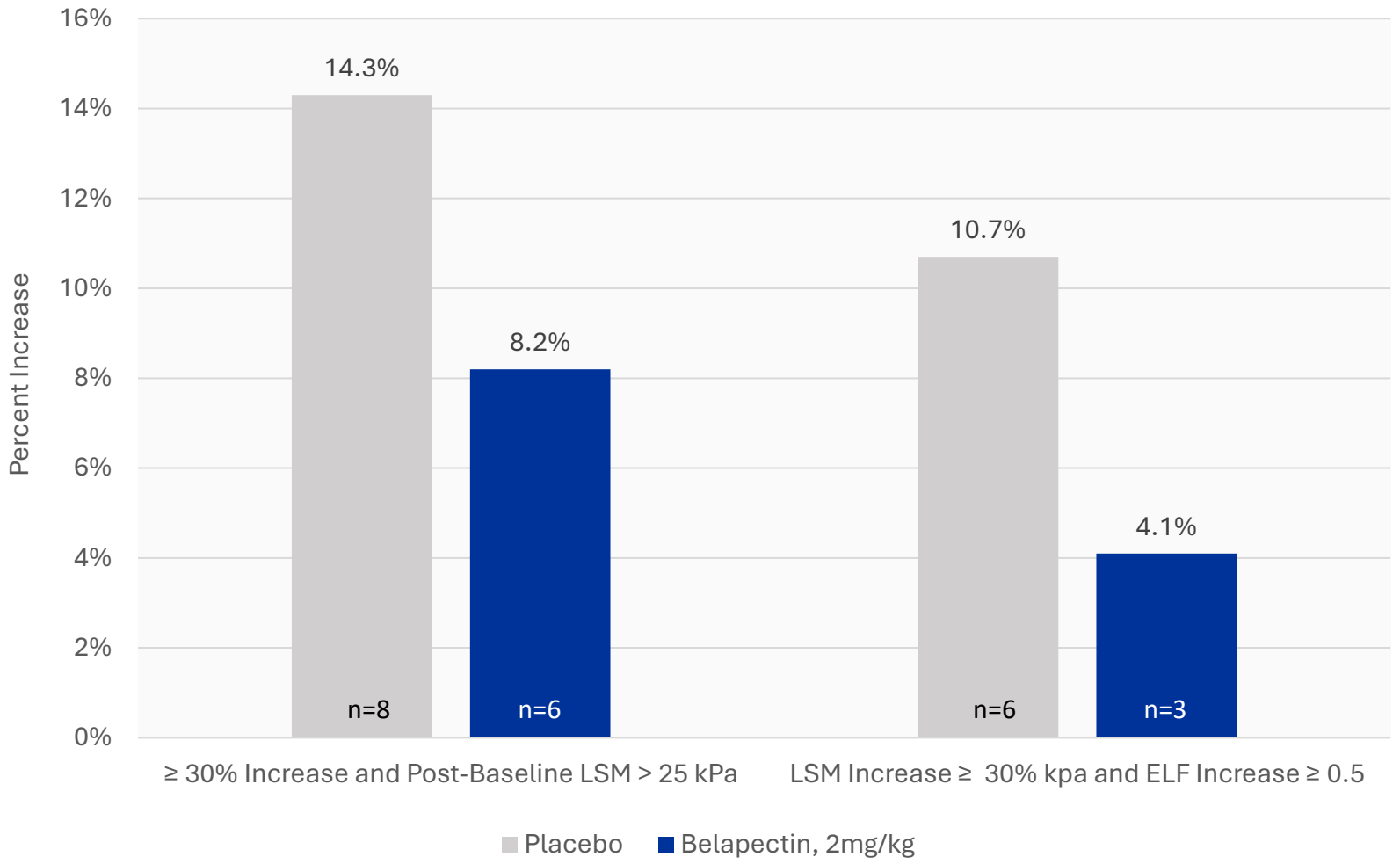
ELF Score Stratification Reveals Greater Variceal Benefit of Belapectin in Highest-Risk Patients

Per Protocol



Concordant Fibrosis Biomarkers Support Belapectin's Effect on Stopping Disease Progression

Per Protocol

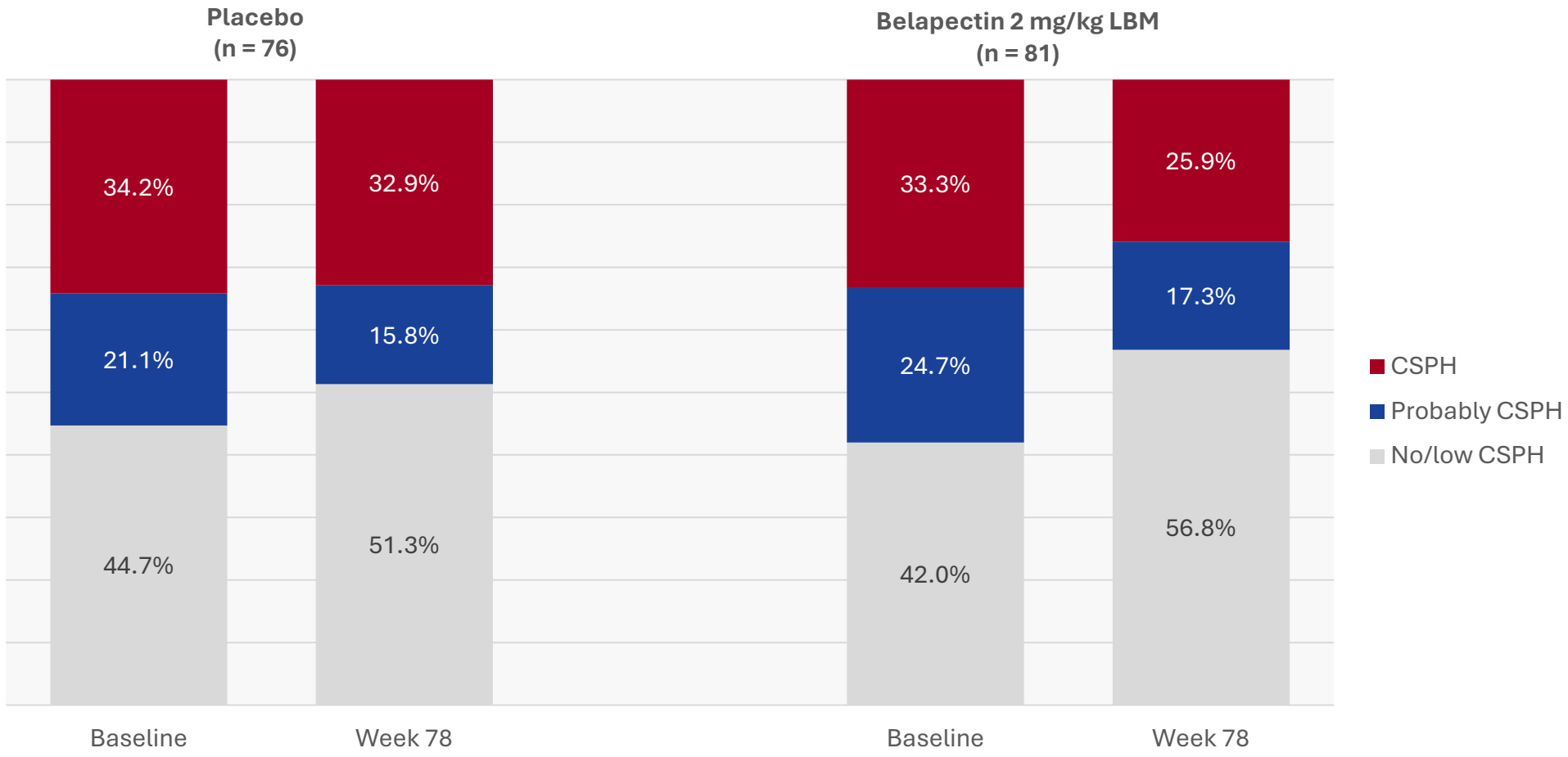


	Belapectin
Placebo	**2mg/kg LBM**
56	73

Values based on Per Protocol Set, Subjects with all scheduled Phase 2b and ELF assessments

Belapectin Drives Meaningful Improvement in Portal Hypertension Risk Category

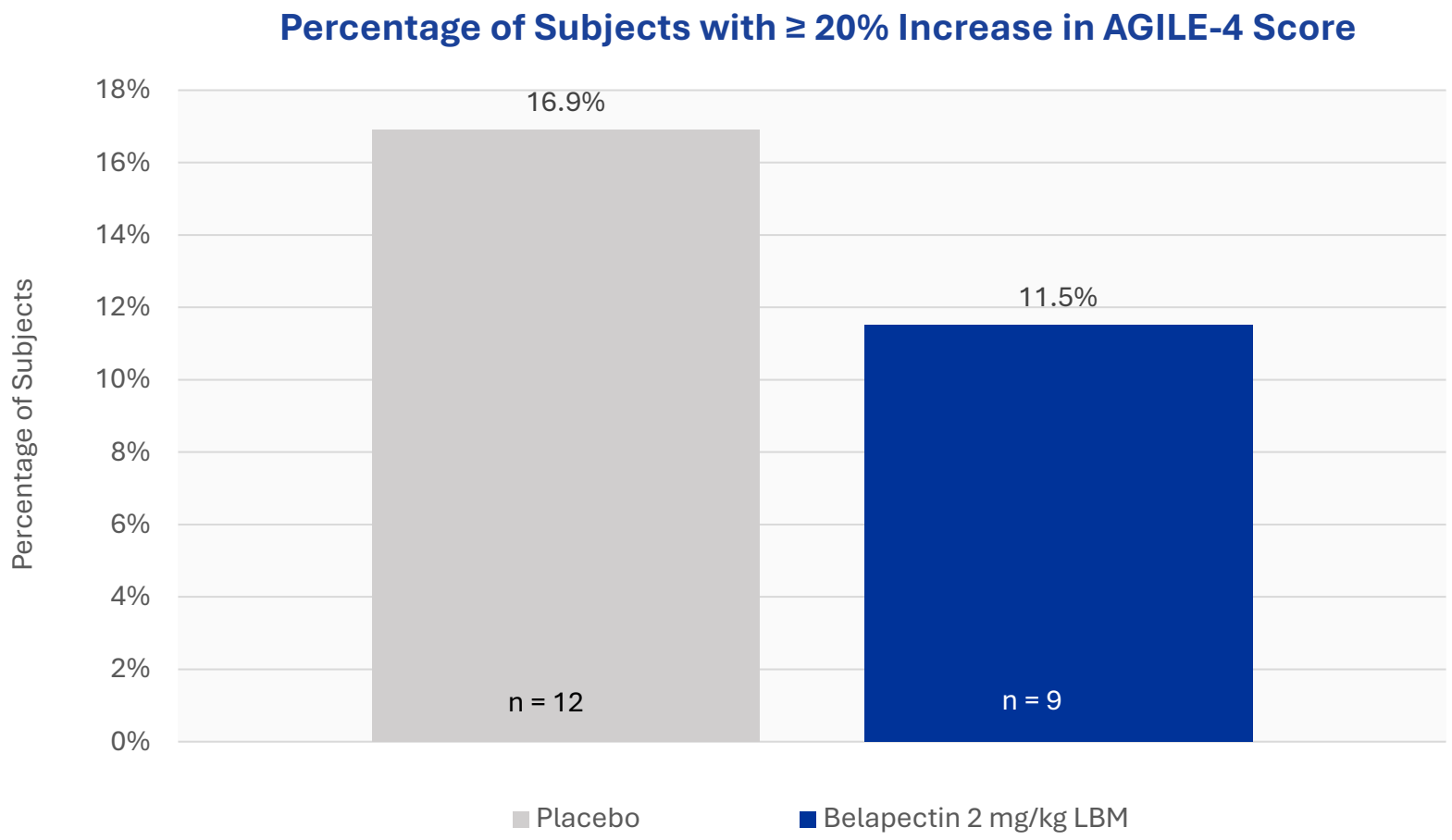
Per Protocol



CSPH LSM ≥ 25 kPa; Probable CSPH LSM ≥20 & platelet <150 or LSM 15-20 & platelet <110; no/low CSPH LSM≤ 15 and platelet≥ 150;
Baveno VII Guidelines de Franchis 2022 Jhep
Values based on Per Protocol Set, Subjects with all scheduled Phase 2b and ELF assessments

Belapectin Reduces Worsening in AGILE-4 Score Across Treated Patients

Per Protocol



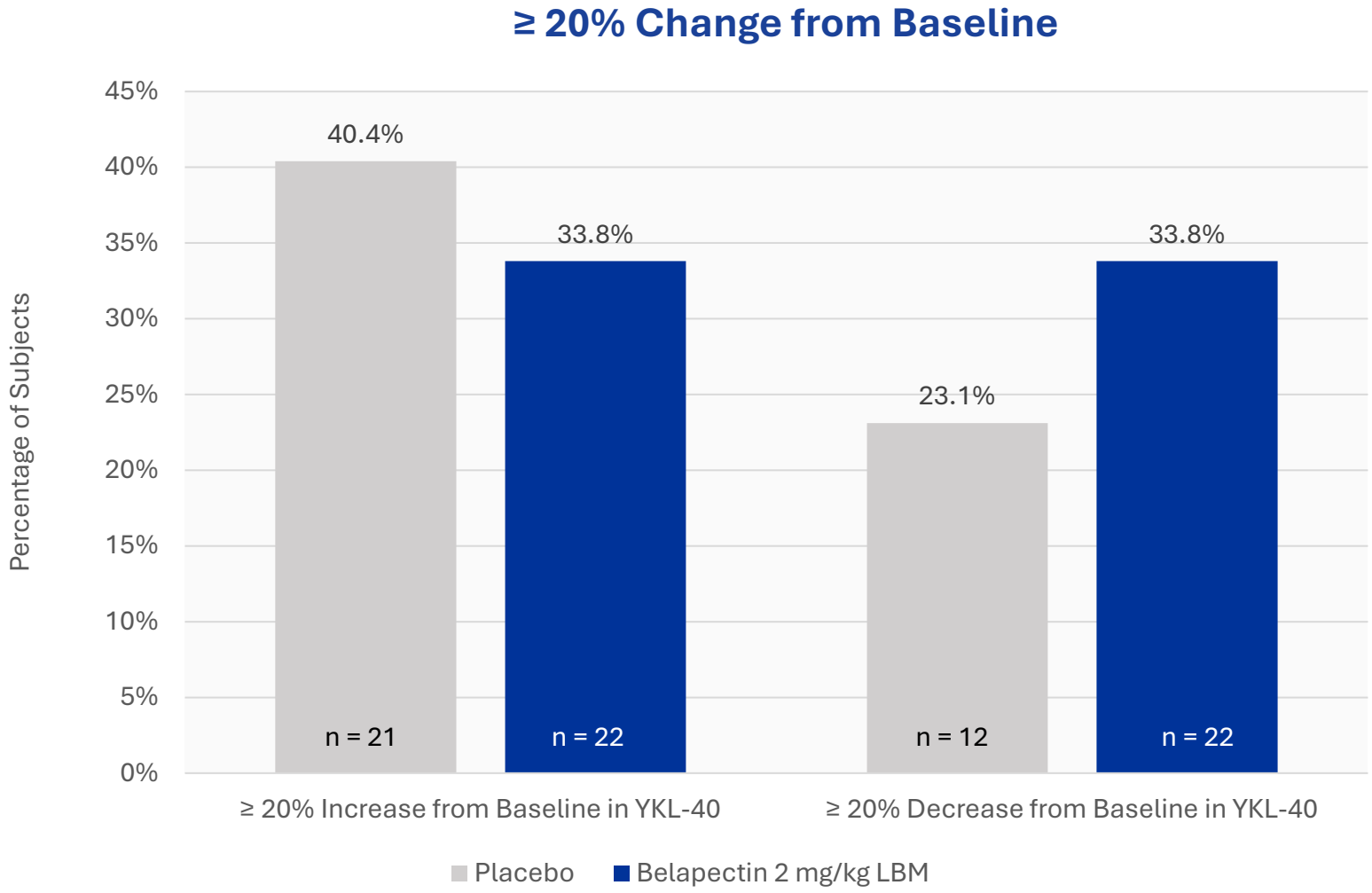
	Belapectin	
	Placebo n = 71	**2mg/kg LBM** n = 78
Baseline Mean	0.66	0.68
Standard Deviation	0.24	0.23

AGILE-4 incorporates LSM, Age, Sex, AST/ALT, Platelet, Diabetes status
Data values for populations where subjects had all 4 Phase 2b assessments.

Belapectin Treatment Associated with Meaningful Changes in YKL-40

Per Protocol

YKL-40 is a circulating marker of inflammation, also part of NIS-4



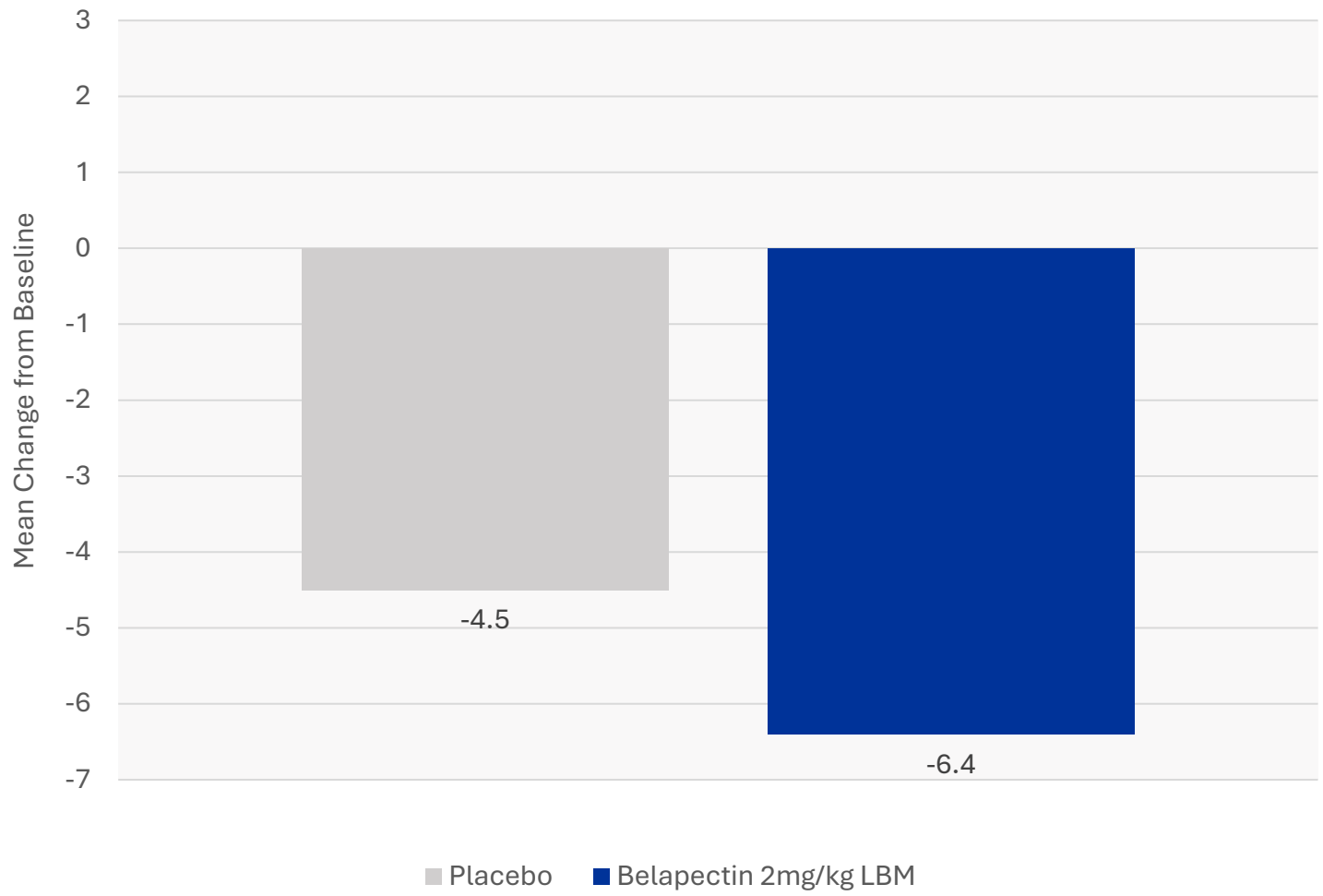
	Belapectin	
	Placebo (n = 52)	**2mg/kg LBM** (n = 65)
Baseline Mean	5.11	4.95
Standard Deviation	0.945	0.837

Chart values for subjects with all Phase2b YKL-40 assessments; table presents log transformed values

Trend Toward Reduced Pro-C3 with Belapectin

Pro-C3 is a marker fibrosis or scar tissue build up

Per Protocol



	Belapectin	
	Placebo n = 79	**2mg/kg LBM** n = 81
Baseline Mean	50.19	45.91
Standard Deviation	38.45	31.58

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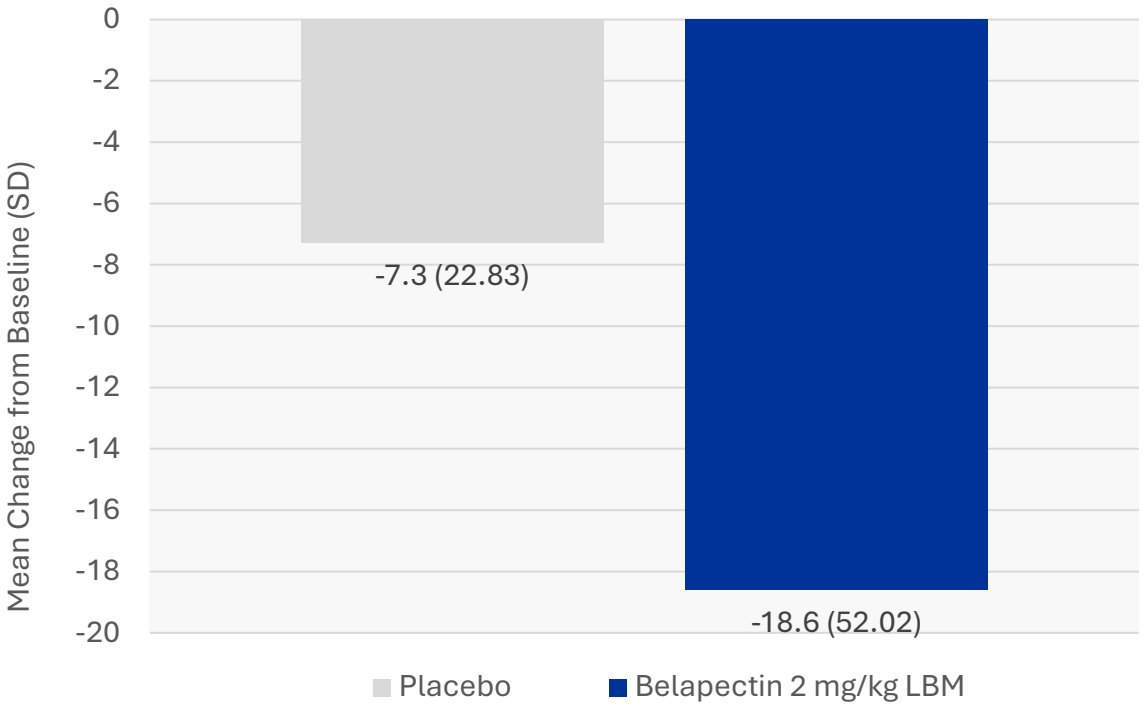
Chart values for subjects with all Phase2b YKL-40 assessments; ; table presents raw values; Pro-C3 unit ng/mL

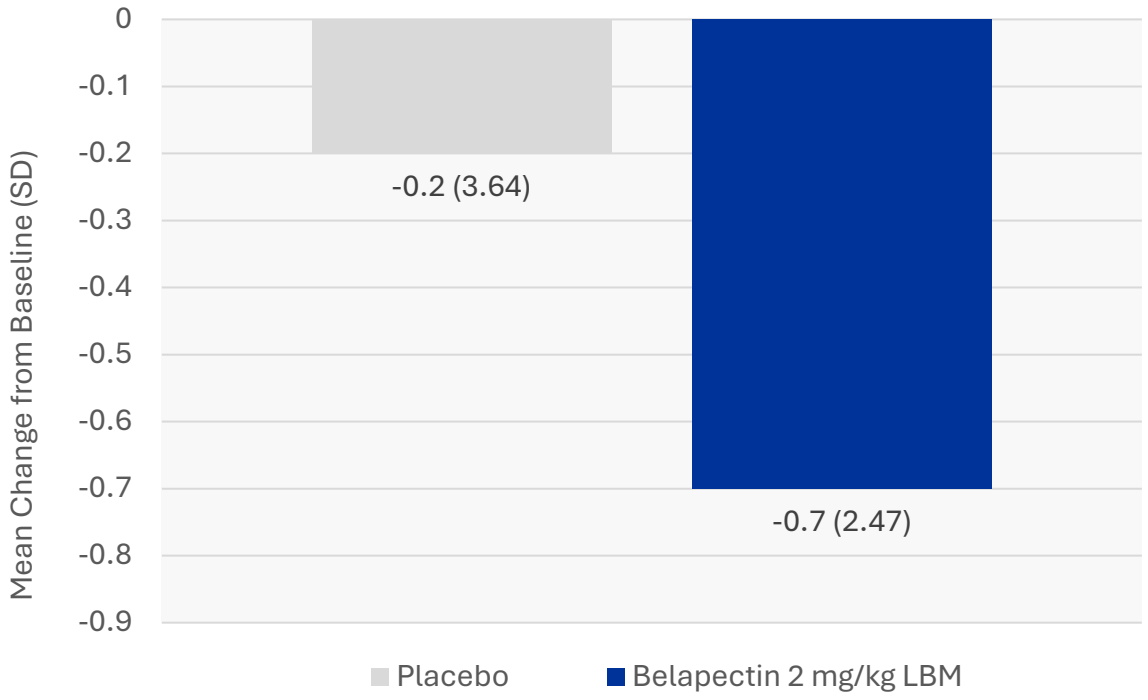
Belapectin Reduces Fibrogenesis in Highest-Risk Patients (ELF ≥ 11.3)

Change in Pro-C3



	Placebo n = 15	2mg/kg LBM n = 17
Baseline Mean	81.3	73.5
Standard Deviation (SD)	71.75	58.86

Change in Pro-C3/CTX-III ratio

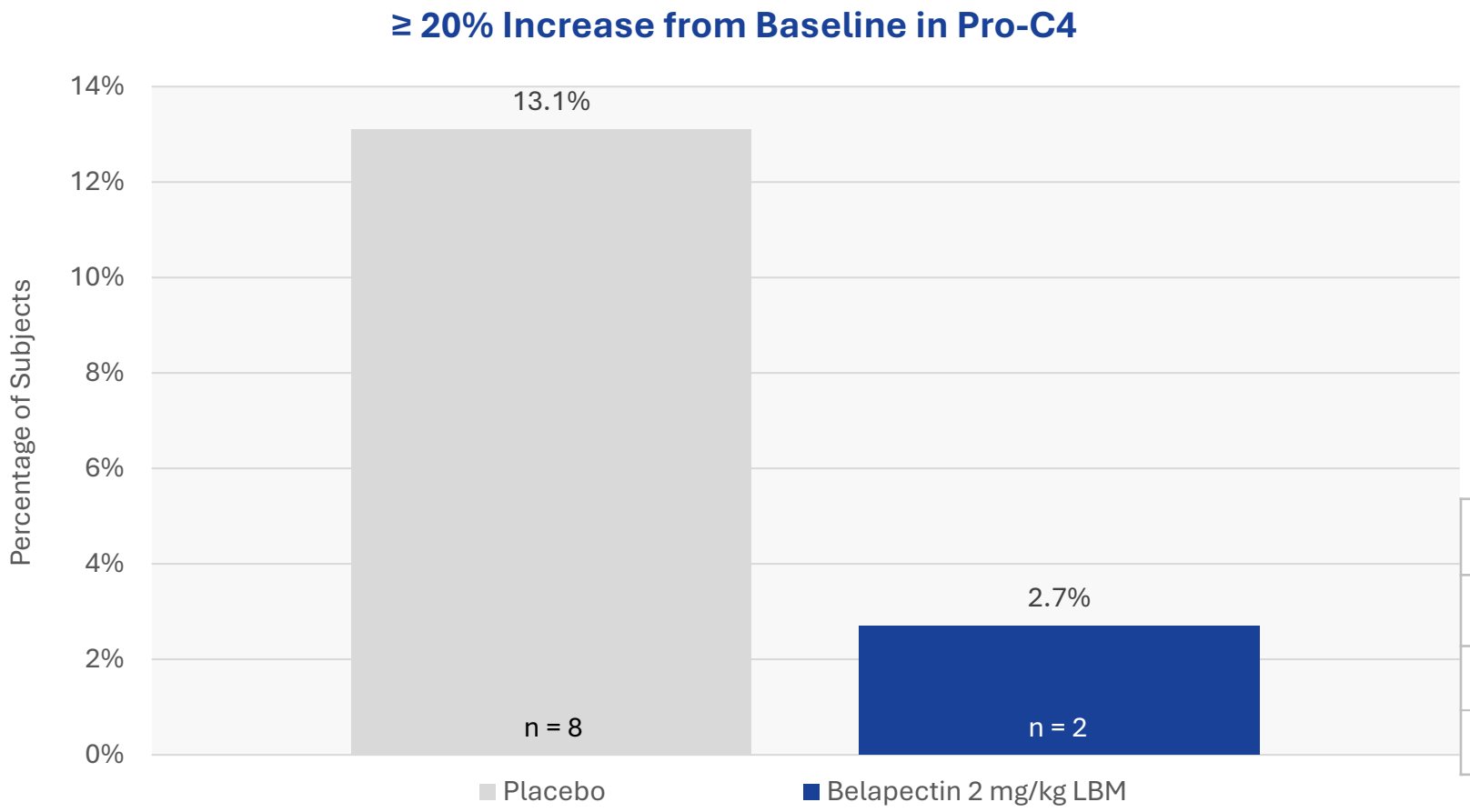


	Placebo n = 17	2mg/kg LBM n = 19
Baseline Mean	4.7	5.6
Standard Deviation (SD)	5.38	3.07

Lower Rate of Pro-C4 Worsening with Belapectin Treatment

Pro-C4 is a marker of type-IV collagen build-up indicates increase in fibrosis and disease progression

Per Protocol



	Belapectin	
	Placebo n = 61	**2mg/kg LBM** n = 73
Baseline Mean	8.61	8.62
Standard Deviation	0.207	0.212

Table presents log transformed values for subjects with baseline and week 78 assessments

Key Takeaways

01 Belapectin 2 mg/kg LBM significantly reduced the incidence of new esophageal varices at 18 months in patients with MASH cirrhosis and portal hypertension

02 Biomarkers results provide supportive evidence of the clinically meaningful results

03 These findings validate prior favorable observations from the GT-026 trial[1].

04 Favorable safety profile with adverse events, serious adverse events, and discontinuation rates comparable to placebo.

05 Belapectin has the potential to address the critical unmet need of patients with MASH cirrhosis and portal hypertension

1. Chalasani N, et al. Gastroentrol. 2020;158:1334-45.

Galectin Therapeutics

Thank you!