# Phase 2b AHFIRM Topline Results

**November 2023**

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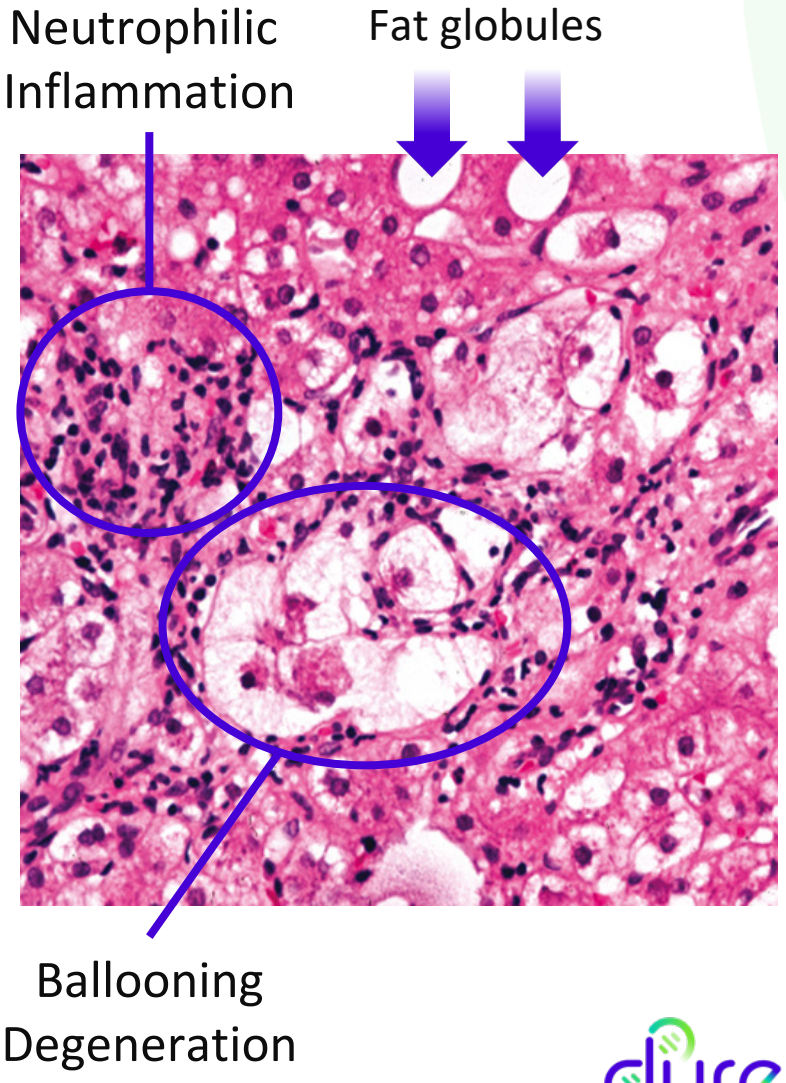
# Key Takeaways from Phase 2b AHFIRM Trial

- Compelling signal in the key secondary endpoint of mortality reduction at 90 days
  - 41% reduction with 30 mg dose
  - 35% reduction with 90 mg dose
- Numerical improvement in primary endpoint of mortality or transplant at 90 days did not achieve statistical significance
- Pronounced reduction in mortality at 90 days in U.S. population
  - 57% reduction with 30 mg dose
  - 58% reduction with 90 mg dose
- Both doses of larsucosterol were well-tolerated

**Strong rationale for advancing to a registrational Phase 3 trial with 90-day mortality as the primary endpoint**

# What is Alcohol-associated Hepatitis?

- Life-threatening form of alcohol-associated liver disease (ALD)
- Up to 30% of patients die within 90 days[1]
- Characterized by jaundice and severe inflammation – indicative of SIRS (Systemic Inflammatory Response Syndrome)
- SIRS causes a sepsis-like state that may progress to multi-organ failure and ultimately death
- **No therapies effective at reducing mortality**

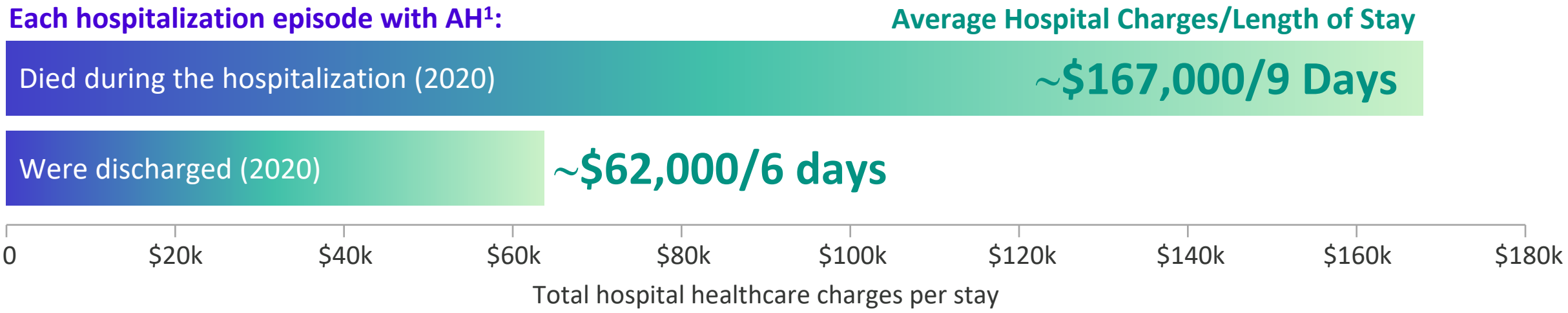





Reference:
[1] Hughes E, Hopkins LJ, Parker R. 2018. *PLOS ONE,* 13(2): e0192393

# Market Opportunity Supports >$1 Billion Peak Sales

- ~158,000 U.S. hospitalizations in 2020[1]
- Incidence may yield ~300K hospitalizations by 2034[2] based on historical rapid yearly growth rate of 5.5% between 2015-2019[3]
- 86% of hospitalized AH patients are insured[3]





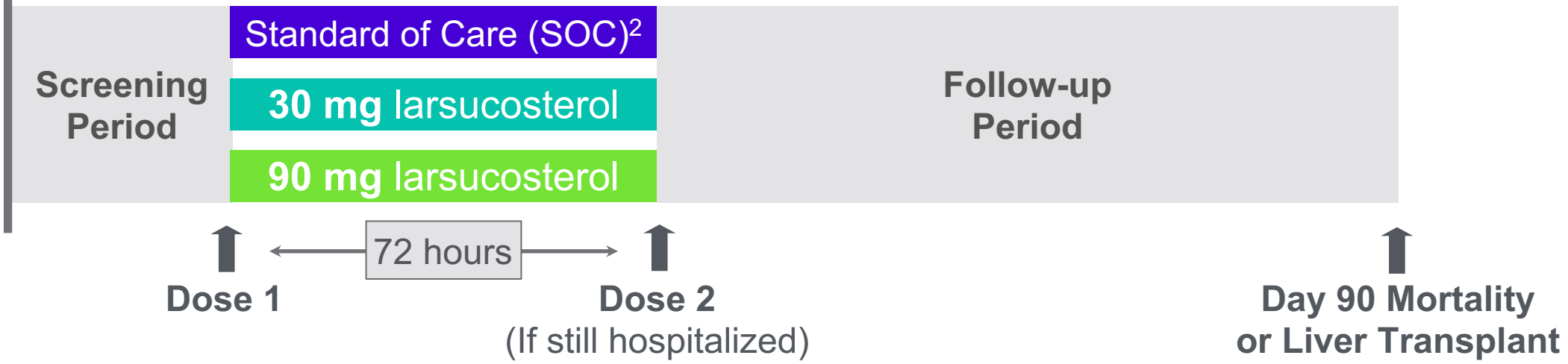

References:
[1] Marlowe N, Lam D, Liangpunsakul S. 2023. *Alcohol Clin Exp Res,* 00:1-7; [2]Market Research – ClearView Analysis 2023; [3]Marlowe N et al. 2022. *Alcohol Clin Exp Res,* 46(8):1472-1481.

# Phase 2b AHFIRM Trial Design

**Trial Overview**

**Severe AH patients** with MDF[1] score ≥ 32 and MELD[1] score 21-30
**307 subjects** randomized to three groups in a 1:1:1 ratio
**Global trial** conducted in U.S., E.U., Australia and U.K.

**Study Design**




[1] Maddrey's Discriminant Function (MDF); Model for End-Stage Liver Disease (MELD)
[2] All patients receive supportive care, which for standard of care (SOC) patients may include methylprednisolone capsules at the investigators' discretion. In order to maintain blinding, patients in the two larsucosterol arms receive matching placebo capsules if the investigator prescribes steroids.

# Median Baseline Characteristics and Trial Outcome by Arm

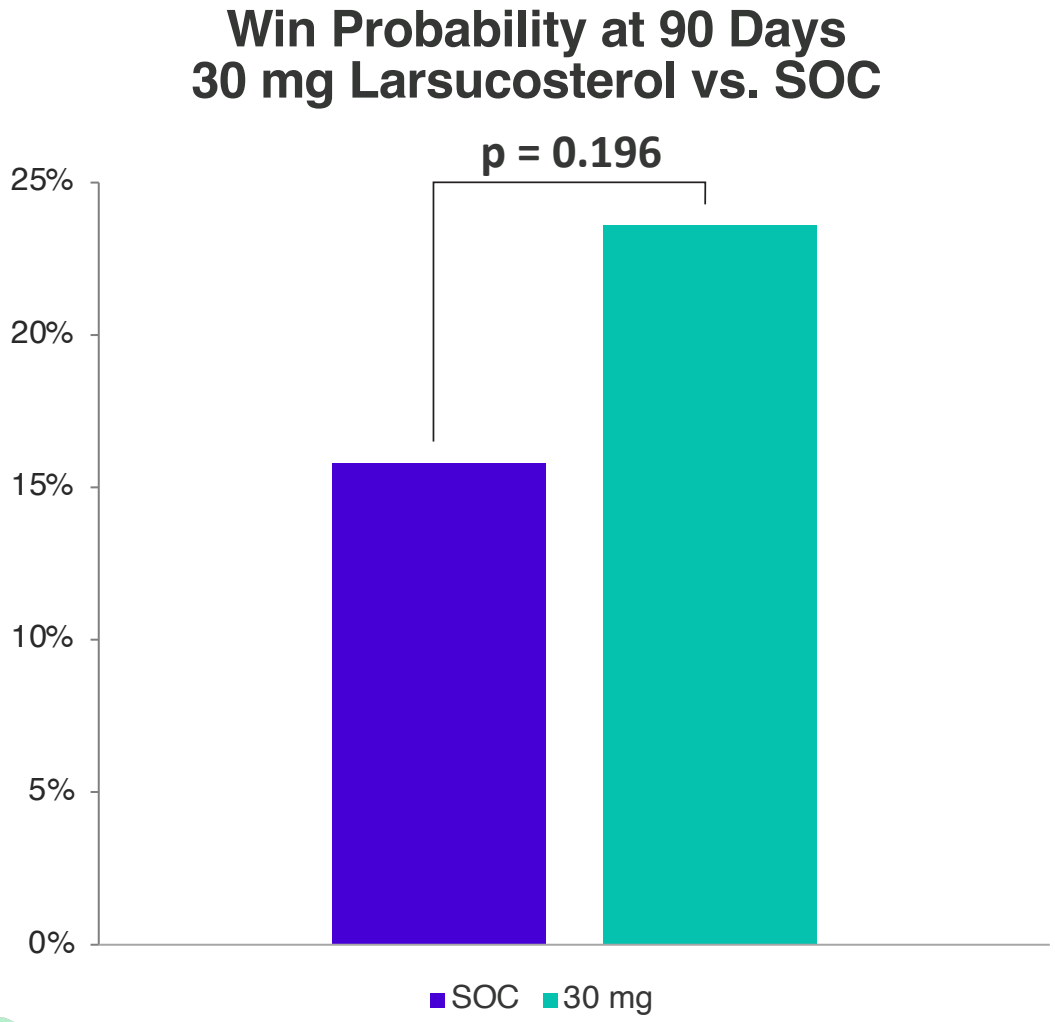
| | SOC | Larsucosterol 30 mg | Larsucosterol 90 mg |
|---|---|---|---|
| Number of patients randomized | 103 | 102 | 102 |
| Number of patients with 90-day outcome data | 102 | 99 | 101 |
| | | | |
| MELD[1] | 25.0 | 24.0 | 25.0 |
| MDF | 61.50 | 57.20 | 63.00 |
| Age | 47.0 | 44.0 | 43.0 |
| | | | |
| Deaths (%) | 25 (24.5%) | 15 (15.2%) | 17 (16.8%) |
| Transplants (%) | 4 (3.9%) | 6 (6.1%) | 9 (8.9%) |
| Alive & Transplant-free (%) | 73 (71.6%) | 78 (78.8%) | 75 (74.3%) |

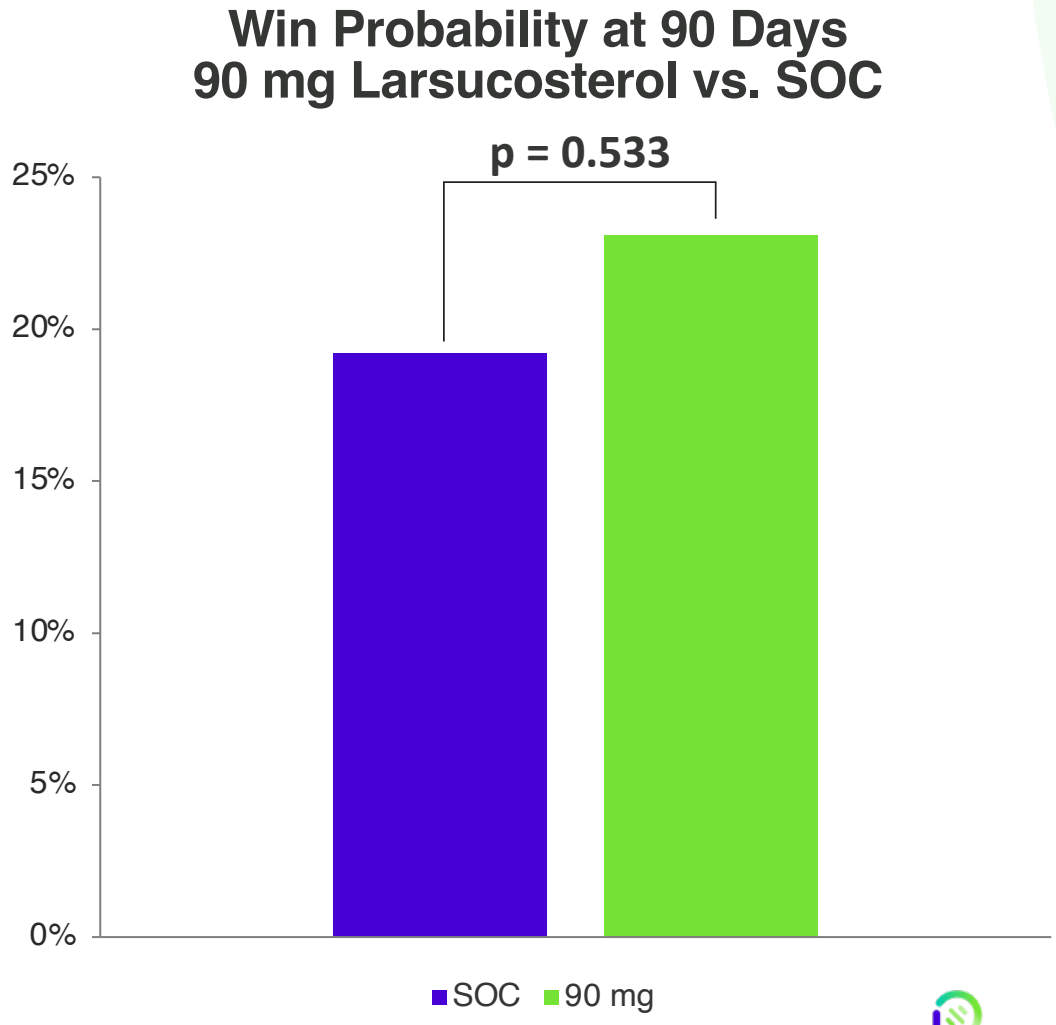


[1] Based on central lab MELD score

# Numerical Improvement in Primary Endpoint

## Did not achieve statistical significance

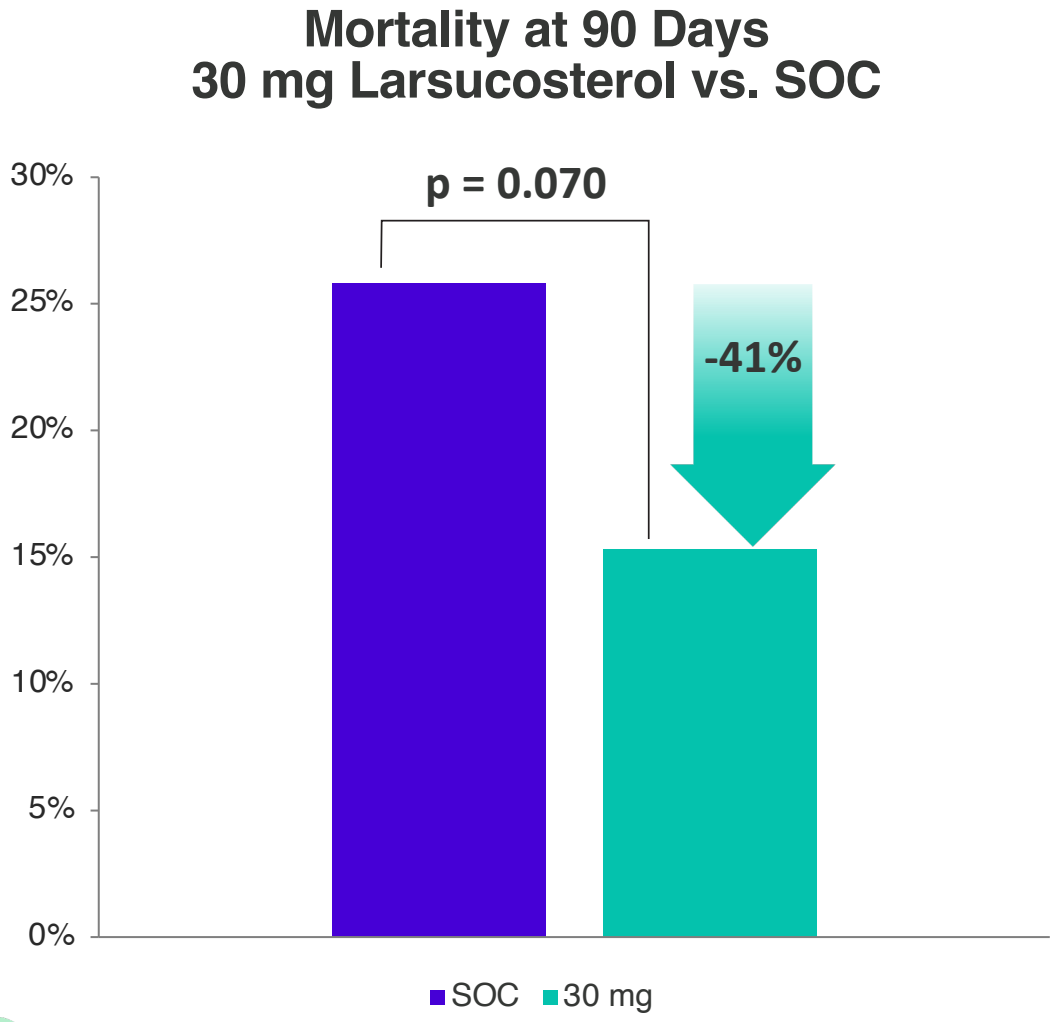


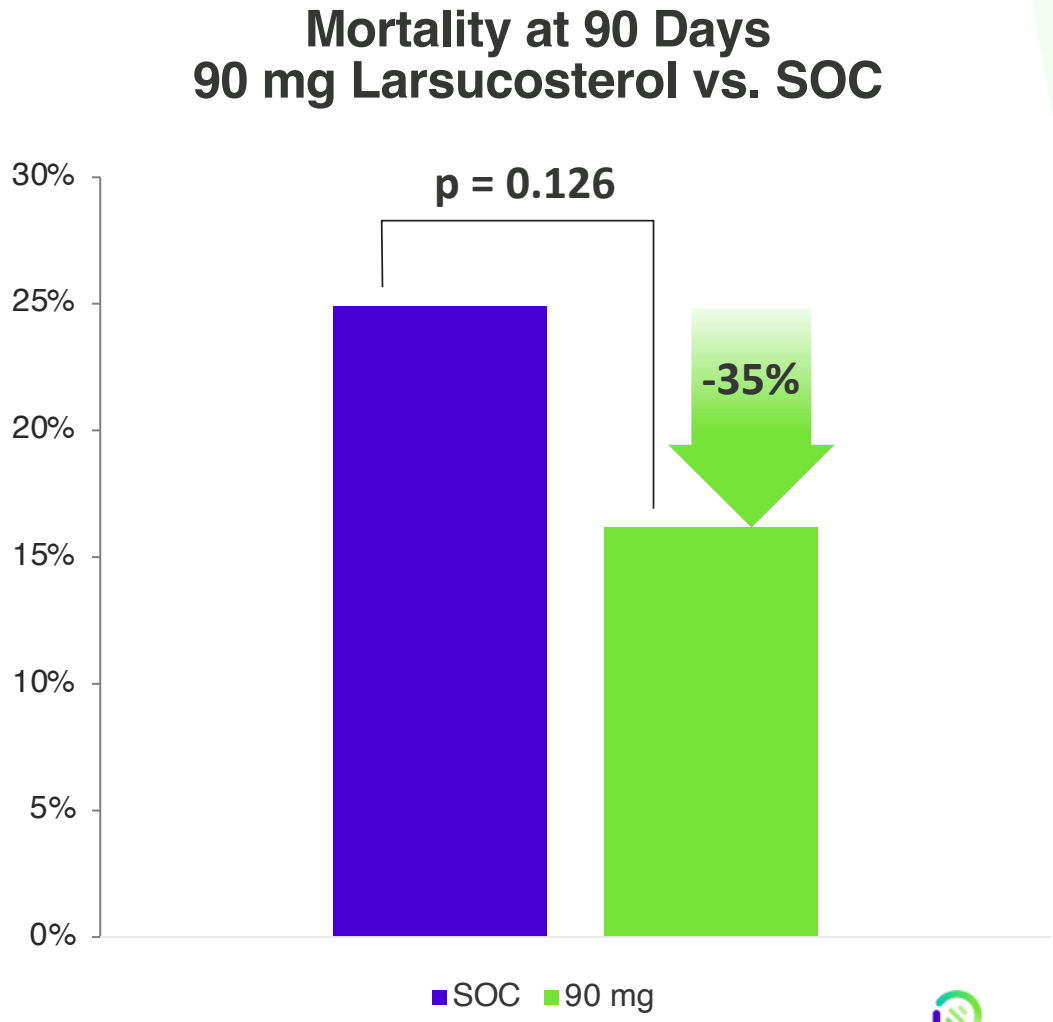





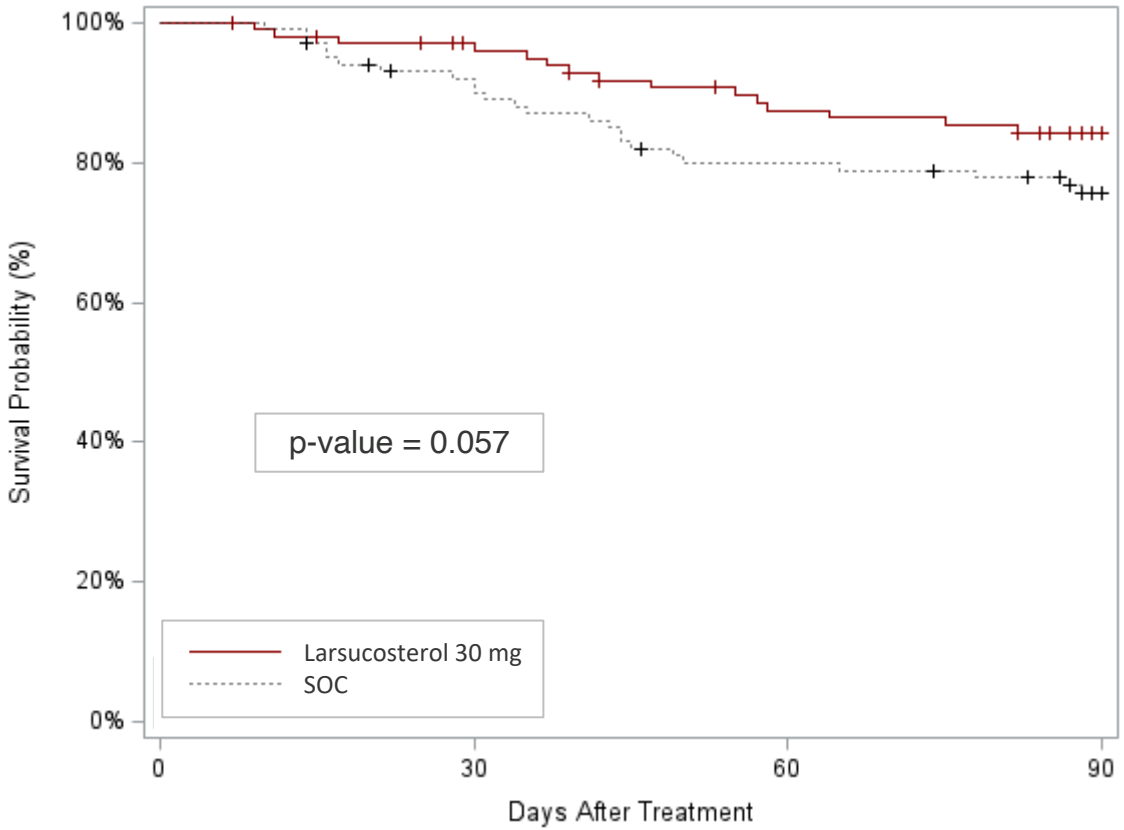

Primary endpoint was analyzed using a hierarchical assessment of patient outcomes to calculate a win probability for each of the 30 mg and 90 mg dose of larsucosterol compared with standard of care. Win probability was calculated on the hierarchy of alive and transplant-free being superior to transplant and death and transplant being superior to death. Comparisons of the same outcome were included in the denominator as ties.

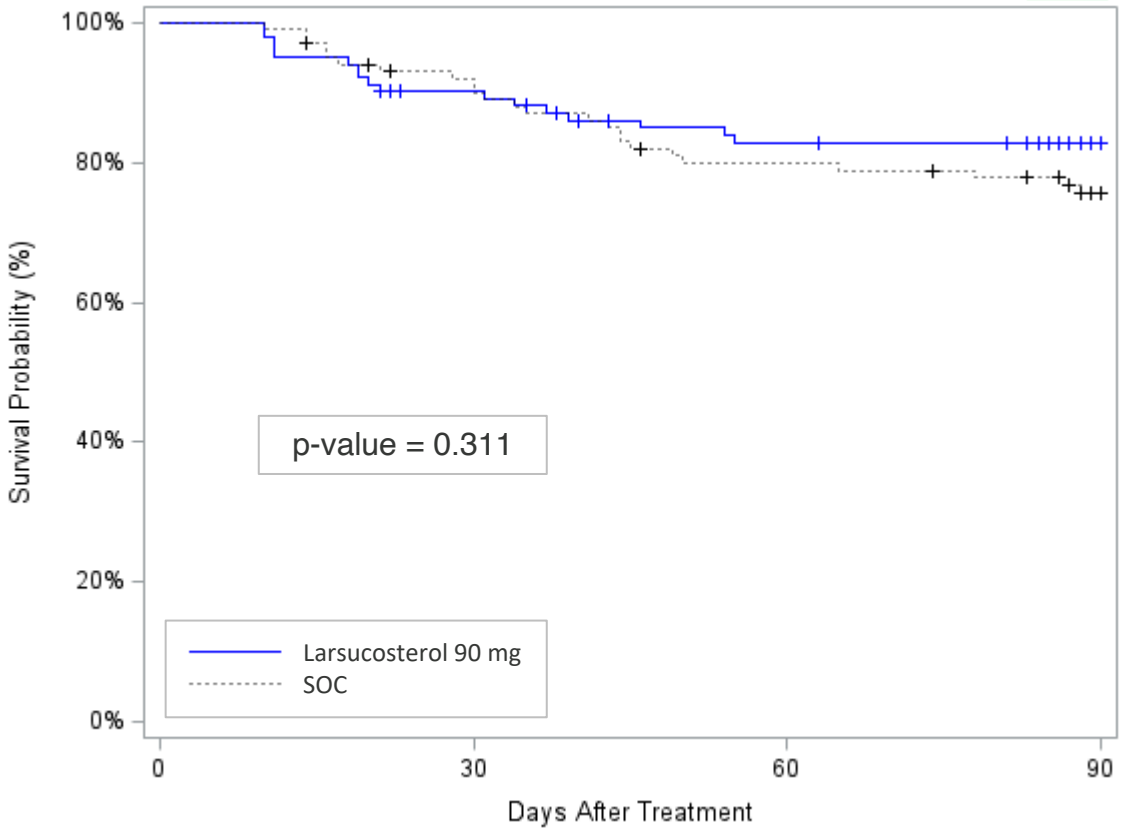
# Clinically Meaningful Trend Toward Reduced Mortality



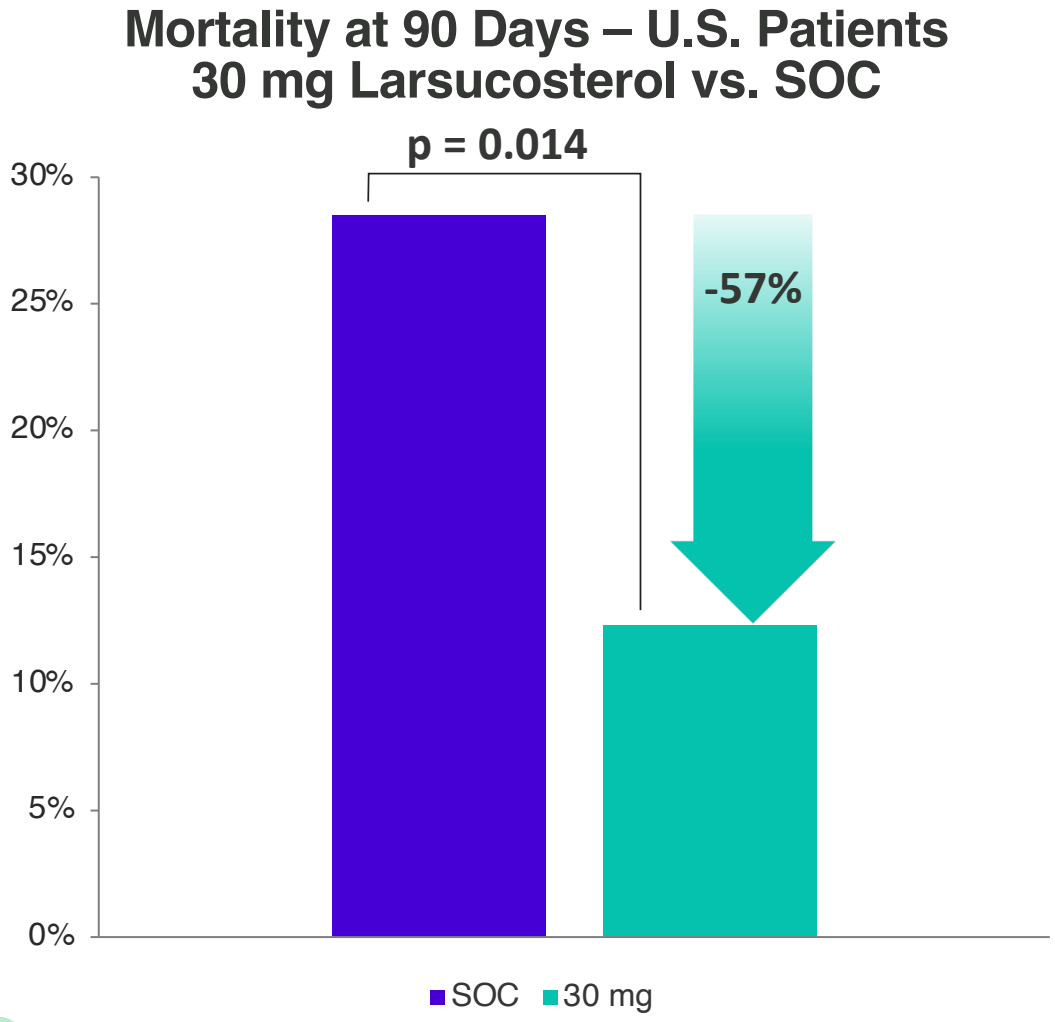



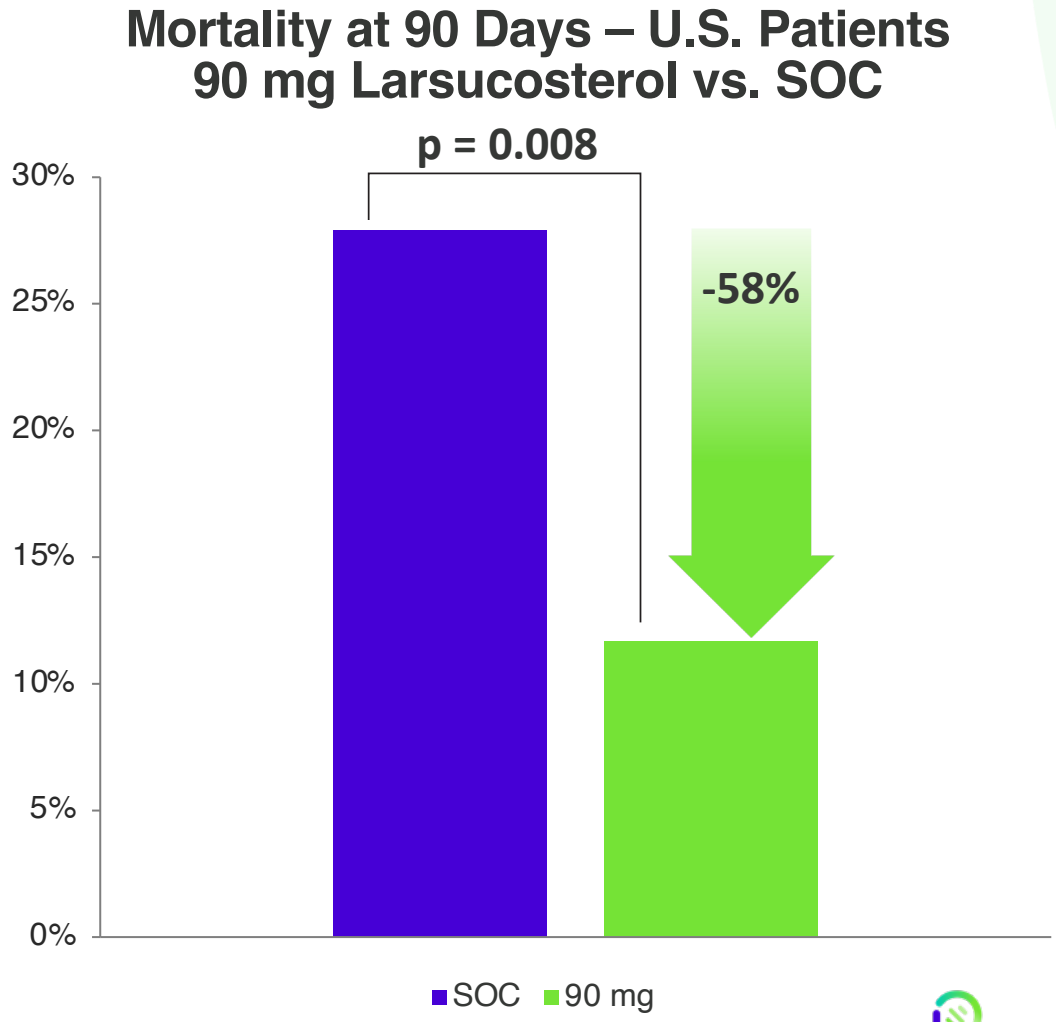
# Kaplan-Meier Analysis of Mortality



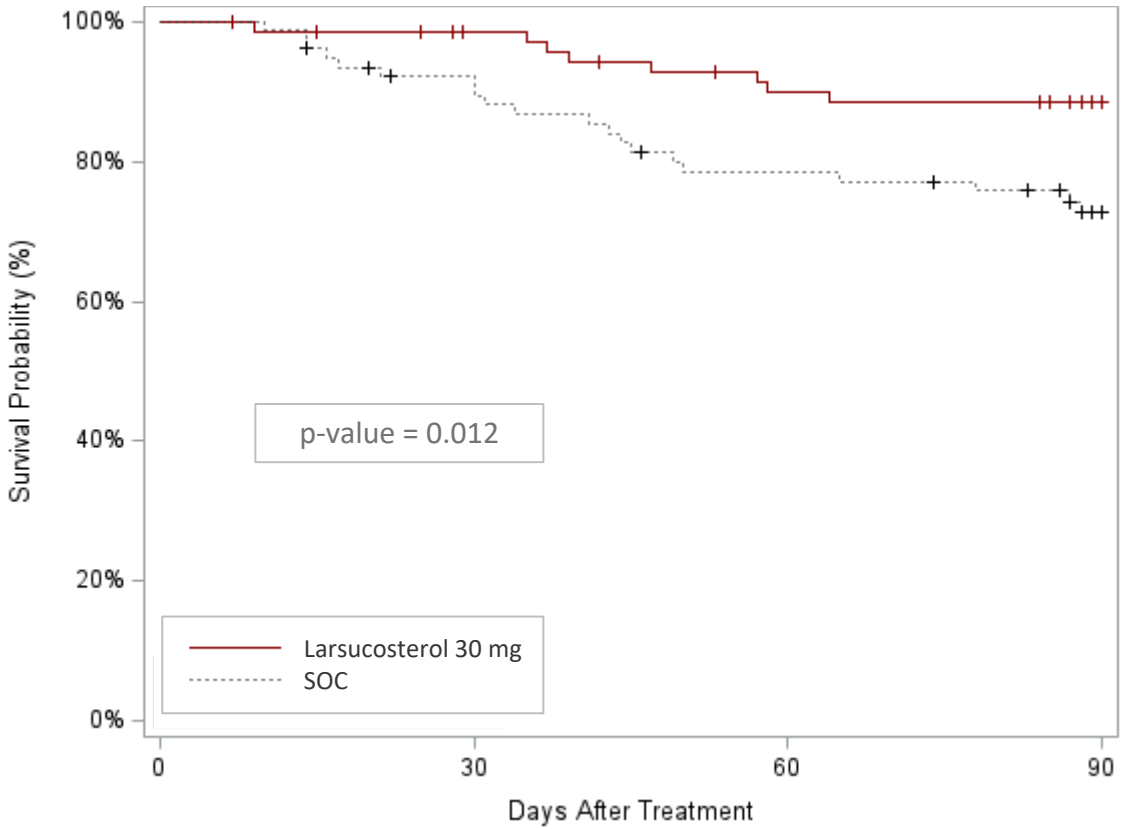



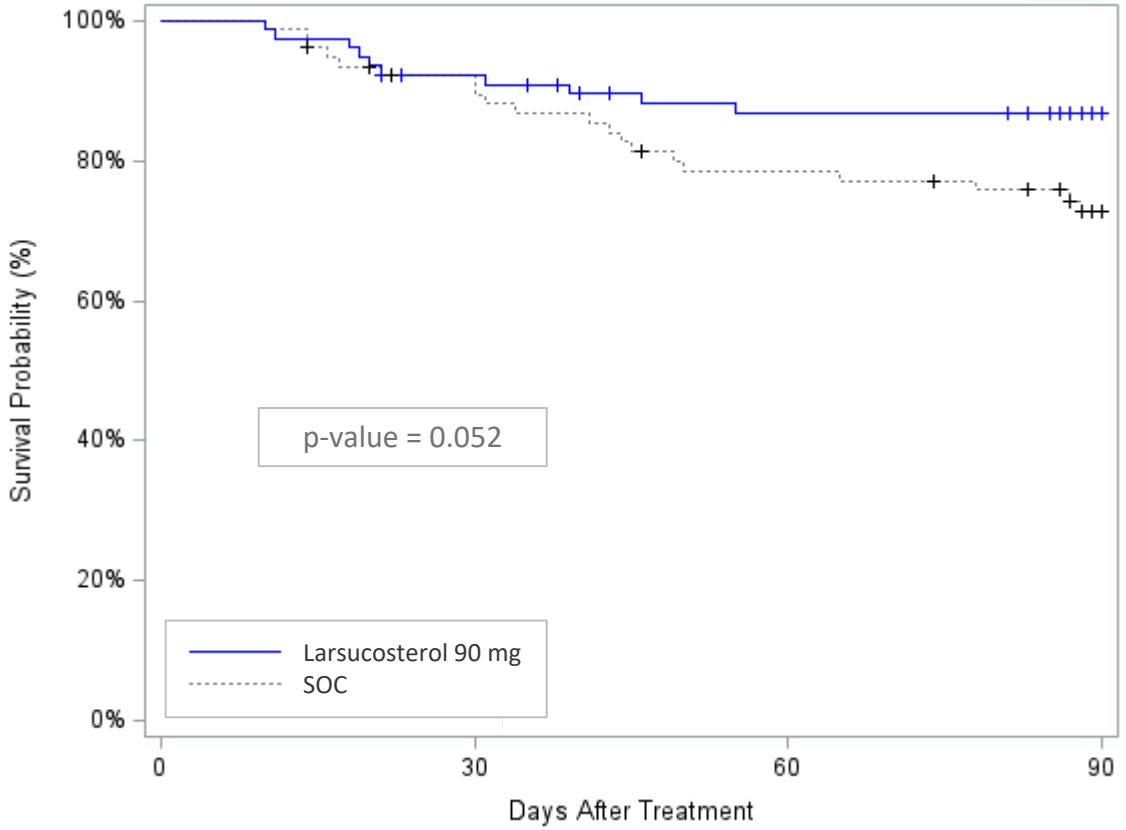
# More Pronounced Reduction in Mortality Observed in U.S.



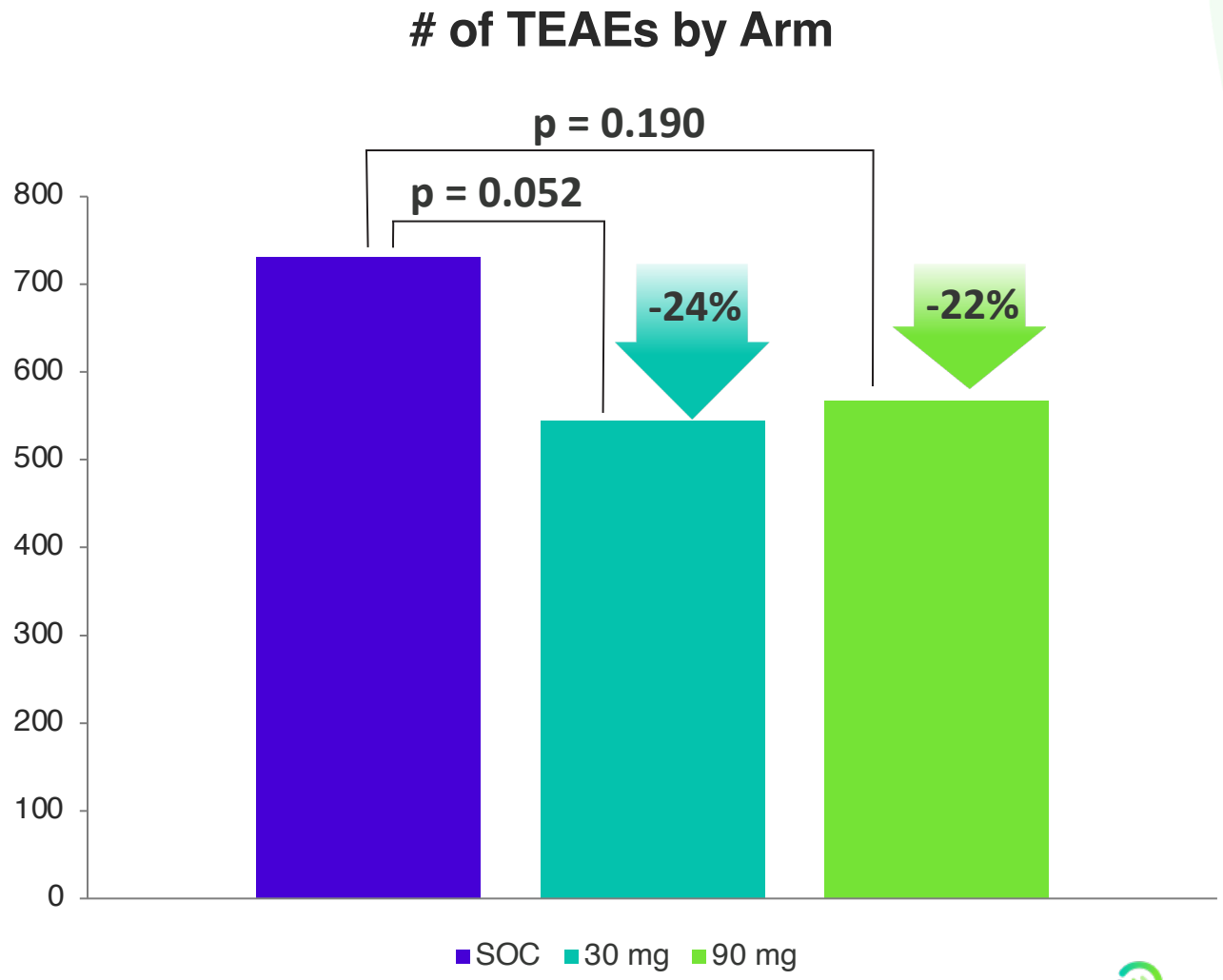
# Kaplan-Meier Analysis of Mortality (U.S. Patients)



# Larsucosterol Was Well-Tolerated

- Numerically fewer TEAEs in both 30 mg and 90 mg arms compared with SOC
- No meaningful difference in serious AEs and none attributed to larsucosterol




TEAEs = Treatment Emergent Adverse Events

# Conclusions and Next Steps for Larsucosterol in AH

- Compelling efficacy signal in favor of larsucosterol in key secondary endpoint of reduced mortality at 90 days; 41% for the 30 mg dose and 35% for the 90 mg dose compared with SOC
- In U.S. patients, larsucosterol treatment reduced mortality at 90 days by 57% for the 30 mg dose (p=0.014) and by 58% for the 90 mg dose (p=0.008) compared with SOC
- Larsucosterol was well-tolerated; both dose groups had numerically fewer adverse events than standard of care

## NEXT STEPS

- Discuss AHFIRM data with FDA in first quarter of 2024
- Strong rationale for advancing larsucosterol to a registrational Phase 3 trial with 90-day mortality as the primary endpoint
- AHFIRM data to be presented at upcoming scientific meeting

# Q&A