

Discussion of the Phase III Study Results (DIAS-2) with Desmoteplase

Glasgow, June 1, 2007

1 p.m. BST (2 p.m. CEST, 8 a.m. EDT)



Disclaimer

It is important to note that this information contains forward-looking statements which are based on the currently held beliefs and assumptions of the management of PAION AG, which are expressed in good faith and, in its opinion, reasonable. Forward-looking statements involve known and unknown risks, uncertainties and other factors, which may cause the actual results, financial condition, performance, or achievements of PAION AG, or industry results, to differ materially from the results, financial condition, performance or achievements expressed or implied by such forward-looking statements. Given these risks, uncertainties and other factors, recipients of this information are cautioned not to place undue reliance on these forward-looking statements. PAION AG disclaims any obligation to update these forward-looking statements to reflect future events or developments.

NOTE: Generally figures are given in EUR. USD amounts were converted by using an exchange rate of 1.35 USD per EUR with the exception of the down-payment made by Forest which was received in USD and where the historical exchange rate was applied.

PAION facts

- Biopharmaceutical company based in Aachen, Germany
- Development of innovative drugs for treatment of stroke and other thrombotic diseases
- Founded in July 2000
- 84 employees (average Q1 2007)

- EUR 106m equity raised since foundation:
 - EUR 51m raised in 4 financing rounds (2000-2004)
 - EUR 46m raised with IPO in February 2005
 - EUR 9m raised in private placement in April 2006

- Partnership on Desmoteplase with Forest Labs for US and Canada
- Partnership on Desmoteplase with Lundbeck for Europe/Rest of World (RoW)



Financial Disclosure

- Co-chairman of the Steering Committee of the DIAS-2 study, with standard compensation by PAION and Forest
- No stock options held
- Chairman of other ongoing acute stroke trials, including ECASS III with standard compensation by Boehringer Ingelheim



Study Objectives and Design

- Objective: evaluate efficacy and safety of desmoteplase in the treatment of AIS 3-9 hours after stroke onset
- Randomized, double-blind, multinational, multicenter, 3-arm parallel group trial
- Treatment administered as single i.v. bolus
 - Placebo
 - Desmoteplase 90 $\mu\text{g}/\text{kg}$
 - Desmoteplase 125 $\mu\text{g}/\text{kg}$
- Multiple assessments up to 90 days post-treatment



Primary and Secondary Outcomes

- Primary efficacy parameter: clinical improvement at Day 90 defined as meeting **all** three criteria
 - ≥ 8 point improvement on NIHSS (or score ≤ 1) AND
 - Modified Rankin Scale score of 0-2 AND
 - Barthel Index score of 75-100
- Secondary efficacy parameter: change from baseline to Day 30 in infarct lesion volume
- Safety parameters
 - Rate of symptomatic ICH (confirmed by diagnostic imaging and resulting in a worsening of ≥ 4 points on the NIHSS)
 - Death
 - Major systemic bleeding



Statistical Tests

- Tests are performed for intent-to-treat population
- Global test: logistic regression models the probability of a patient being a responder with the following variables
 - Treatment group (any dose)
 - Geographic region
 - Baseline NIHSS score
 - Age
- Specific test: if the global test is significant, the logistic regression is repeated for the individual doses
- Sample size calculated to detect with 80% power a difference of 25% between active treatment (any dose) and placebo (two-sided, $\alpha = 0.05$)



Inclusion/Exclusion Criteria

Inclusion criteria

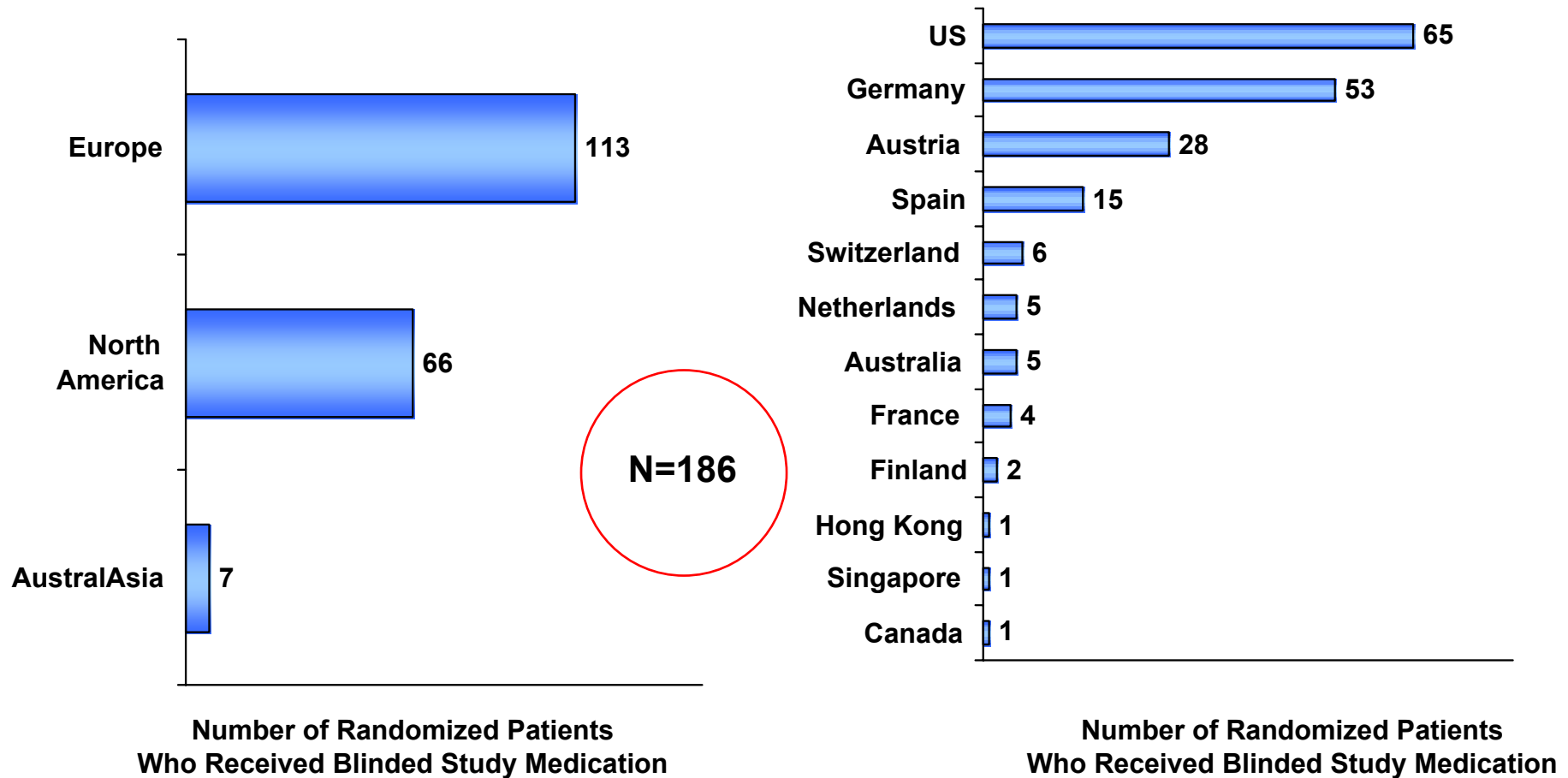
- Age 18-85 years
- Treatment within 3-9 hours after stroke onset
- Baseline NIHSS of 4-24
- $\geq 20\%$ salvageable ischemic tissue in MCA, ACA, or PCA territory as measured by imaging
 - PWI/DWI MR or perfusion CT

Exclusion criteria

- Standard clinical exclusion criteria for thrombolytic trials
- Key imaging exclusions
 - Early infarction involving $>1/3$ of MCA or entire ACA territory
 - Evidence of ICH or SAH, AV malformation, cerebral aneurysm, or cerebral neoplasm



Patient Recruitment by Region and Country





Patient Demographics and Enrollment Characteristics

Desmoteplase

	Placebo n=63	90 µg/kg n=57	125 µg/kg n=66
Age (years)			
Mean	70.0	67.9	70.0
Range	22-86	37-85	34-90
Sex (%)			
Female	58.7	47.4	43.9
Male	41.3	52.6	56.1
Imaging Modality (%)			
MRI	60.3	68.4	68.2
pCT	39.7	31.6	31.8
Time Window (%)			
3-6 h	41.3	33.3	36.4
6-9 h	58.7	66.7	63.6

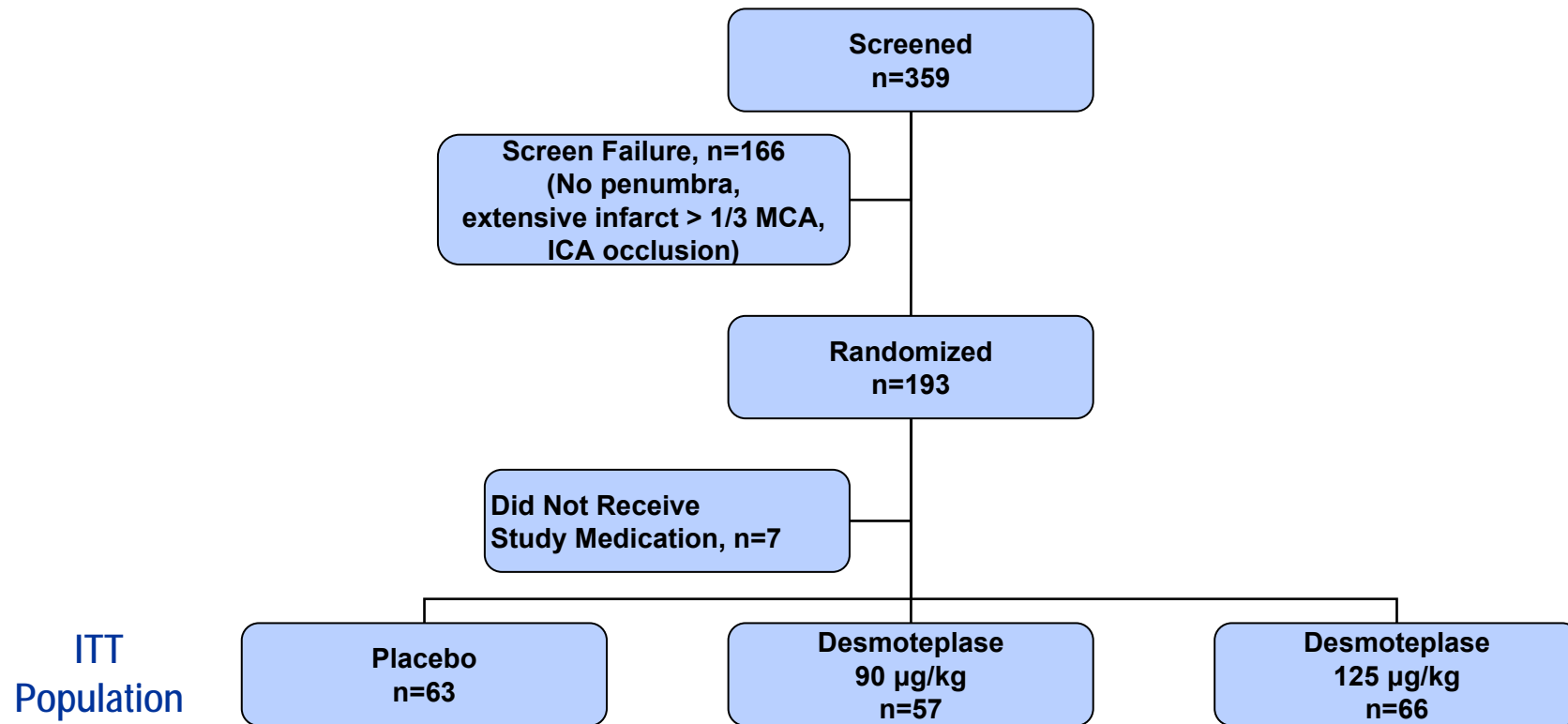


Clinical Characteristics at Baseline

	Placebo n=63	Desmoteplase	
		90 µg/kg n=57	125 µg/kg n=66
NIHSS			
Median	9.0	9.0	9.0
Mean ± SD	10.3 ± 5.0	10.7 ± 5.6	10.4 ± 4.6
Time to treatment			
Mean ± SD (min)	391 ± 92	388 ± 88	402 ± 88
Diabetics			
n (%)	12 (19%)	16 (28%)	15 (23%)
Blood Pressure (mm Hg)			
systolic, Mean ± SD	156 ± 21	150 ± 22	152 ± 19
diastolic, Mean ± SD	84 ± 14	80 ± 12	81 ± 12



Patient Disposition





Results

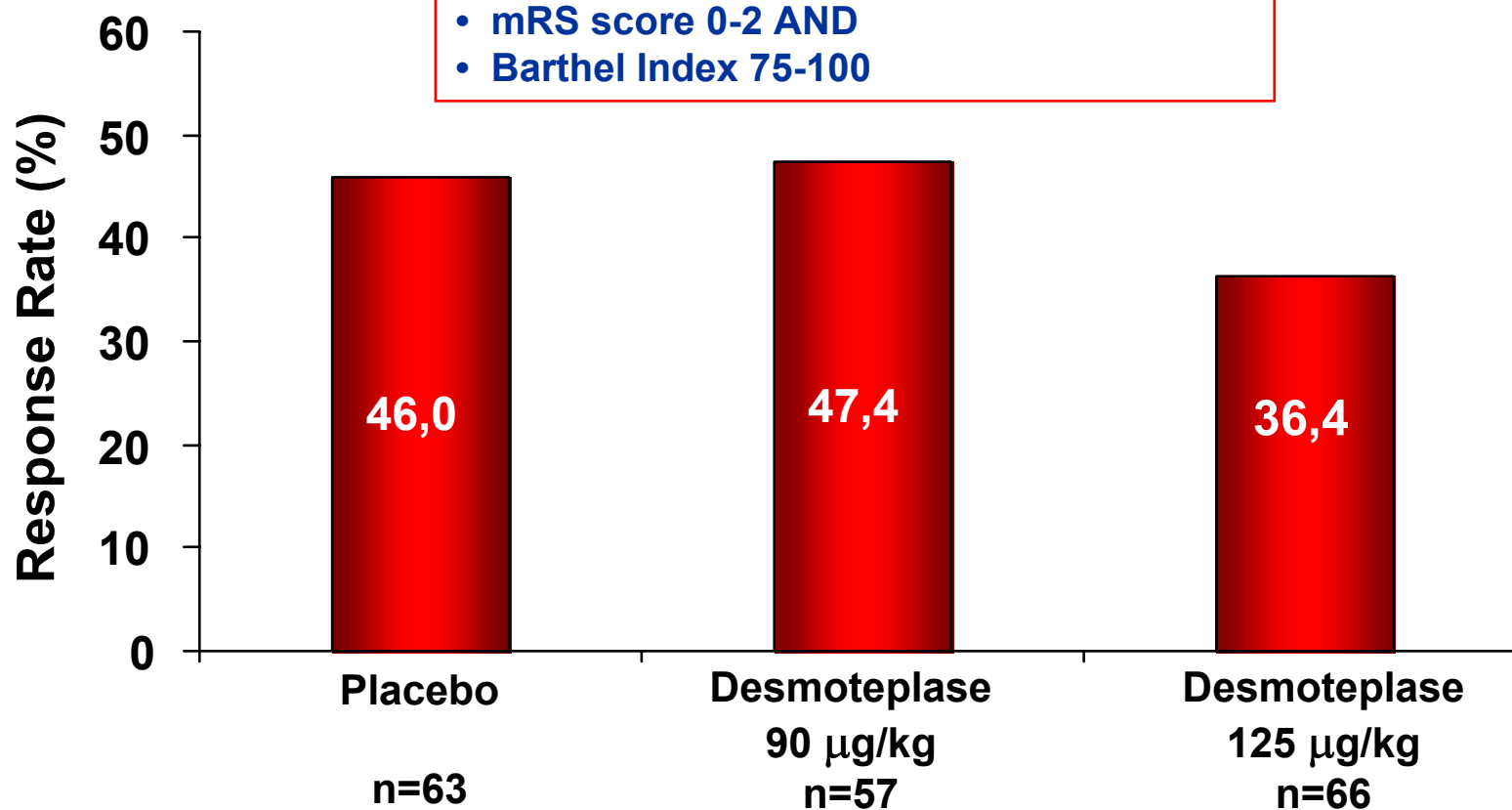
ITT only
per protocol in progress

Clinical Response at Day 90, ITT

Response defined as achieving

all 3 of the following:

- ≥ 8 point NIHSS improvement or 0-1 AND
- mRS score 0-2 AND
- Barthel Index 75-100



LOCF

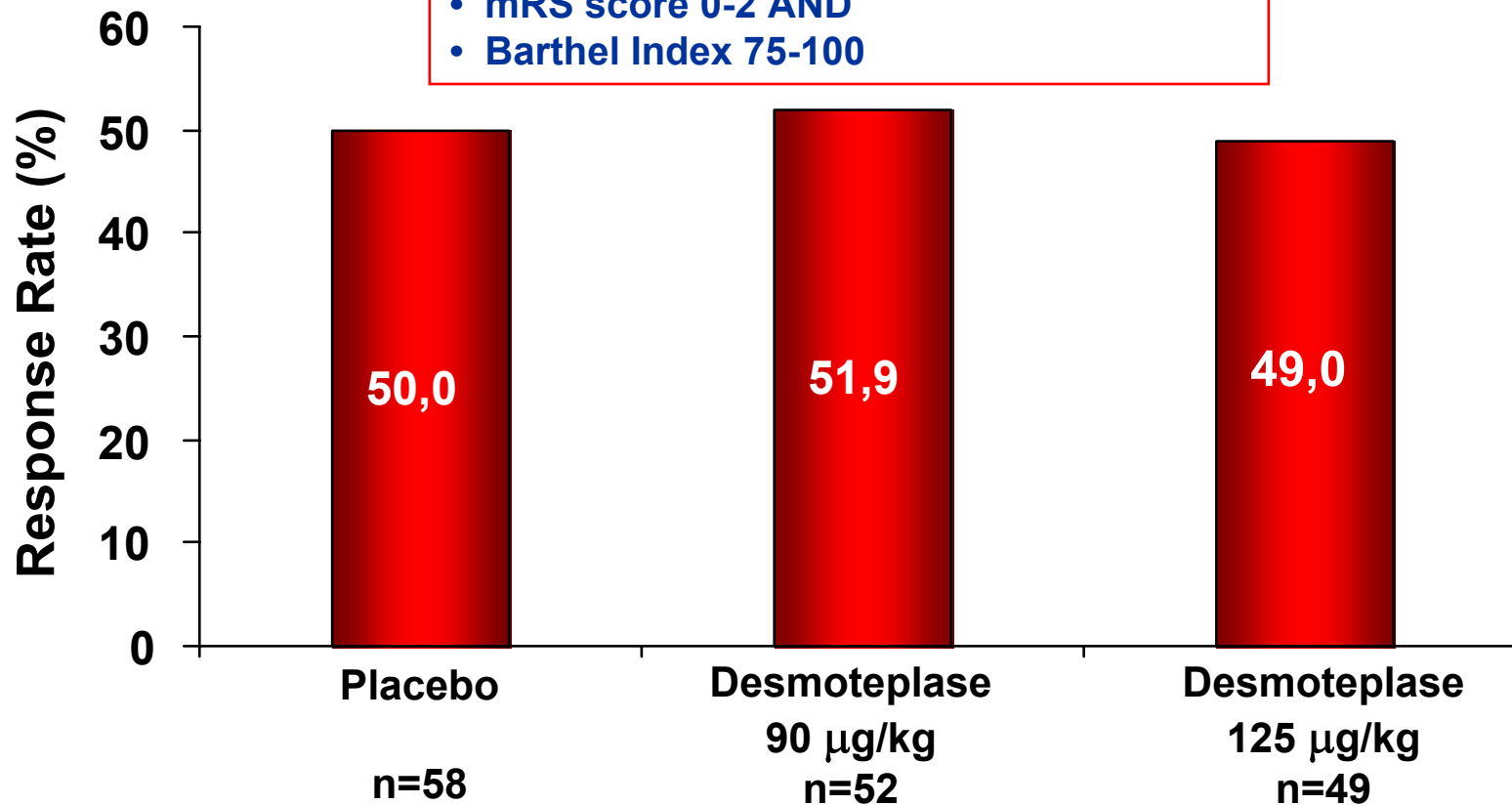


Clinical Response at Day 90 without Dropouts

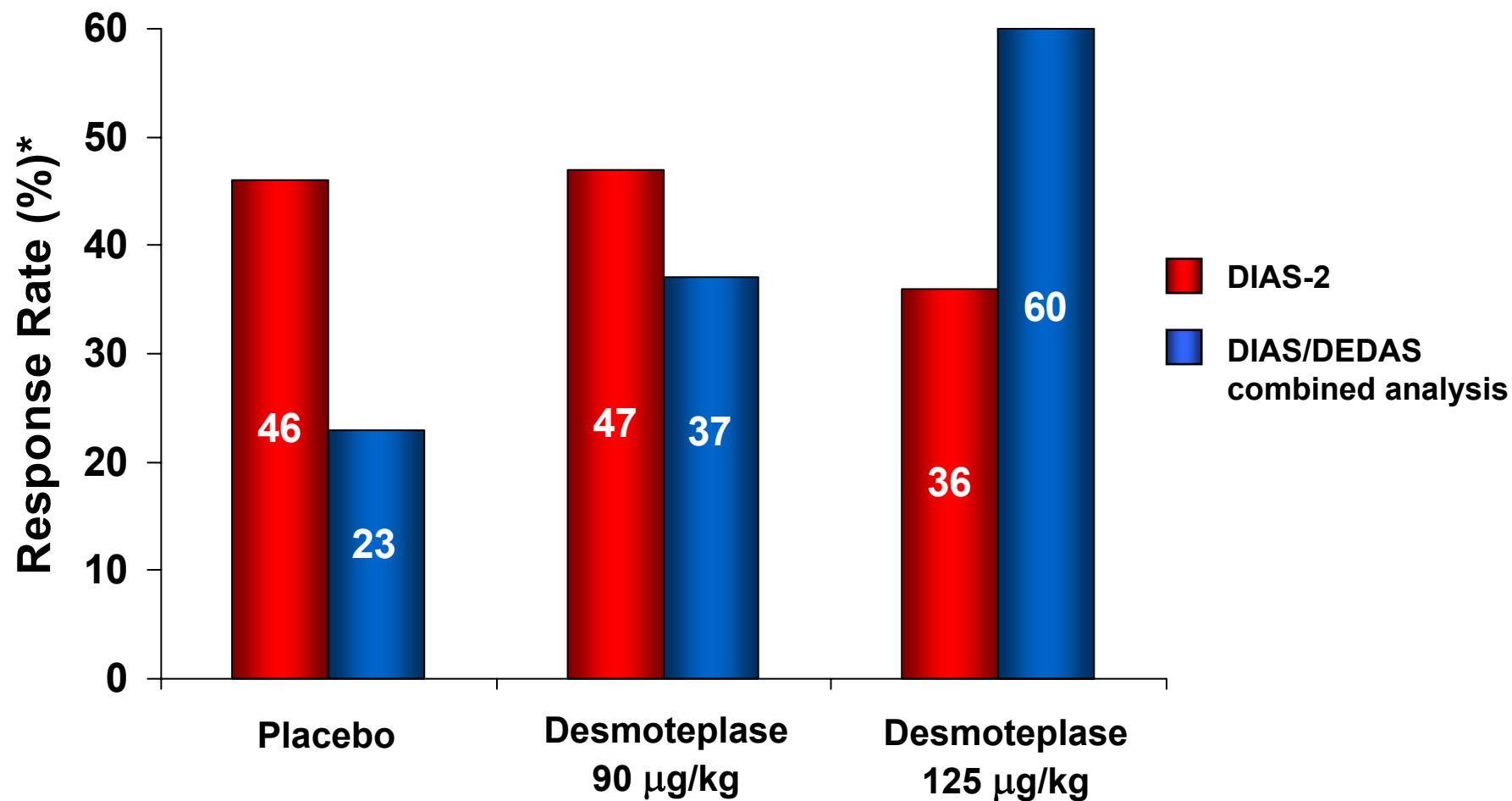
Response defined as achieving

all 3 of the following:

- ≥ 8 point NIHSS improvement or 0-1 AND
- mRS score 0-2 AND
- Barthel Index 75-100



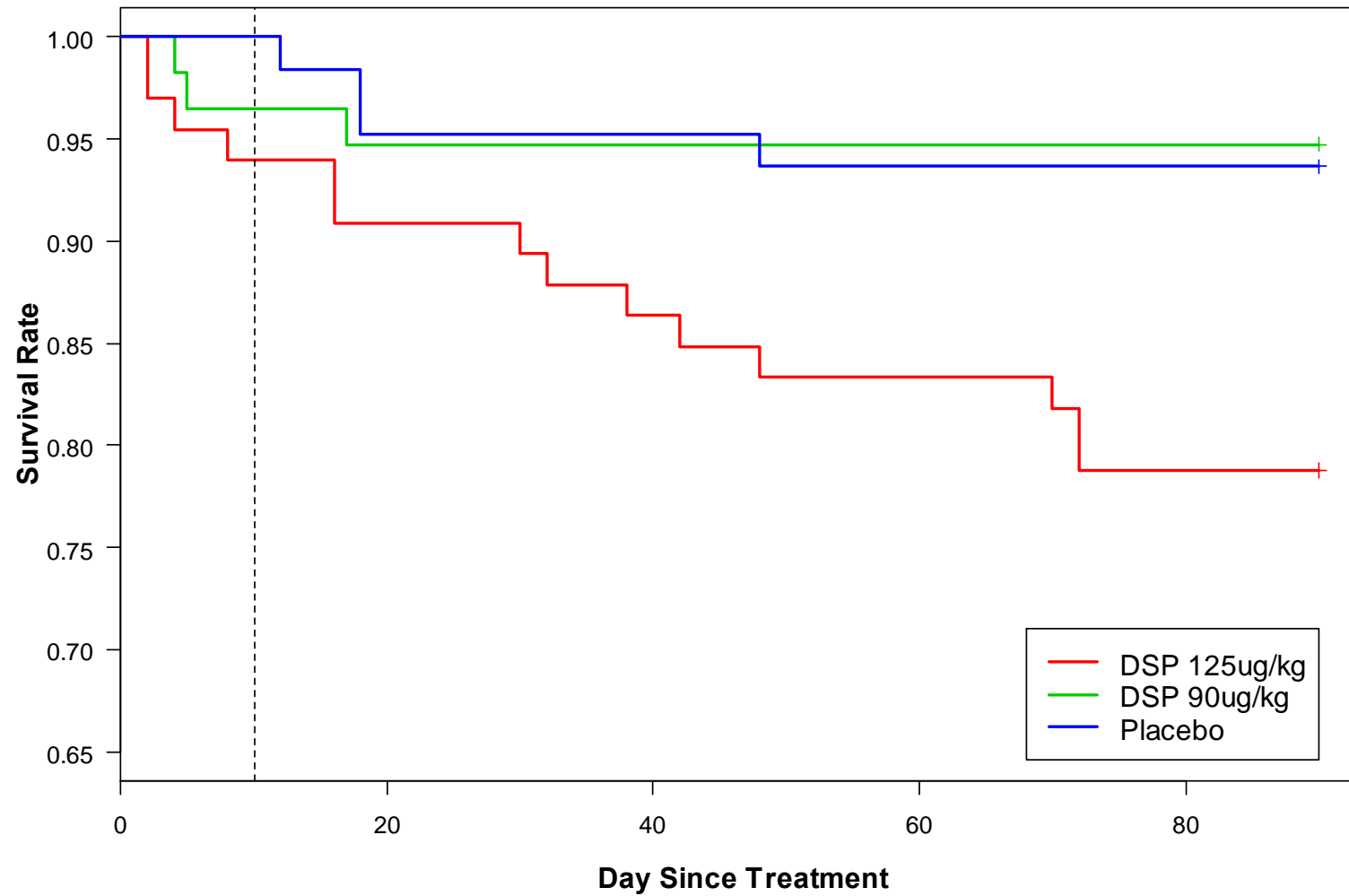
DIAS-2 compared to DIAS/DEDAS



* As defined previously



Kaplan-Meier Estimate of Survival Curve by Treatment Group





Other Safety Results

		Desmoteplase	
	Placebo n=63	90 µg/kg n=57	125 µg/kg n=66
<i>All-Cause 90-Day Death</i>			
n (%)	4 (6.3%)	3 (5.3%)	14 (21.2%)
<i>Major Systemic Bleeding</i>			
n (%)	1 (1.6%)	1 (1.8%)	1 (1.5%)

No anaphylactoid reactions were reported



Symptomatic ICH

	Desmoteplase		
	Placebo n=63	90 µg/kg n=57	125 µg/kg n=66
<i>sICH within 36 h</i>			
n (%)	0	2 (3.5%)*	2 (3.0%)
<i>sICH within 72 h</i>			
n (%)	0	2 (3.5%)*	3 (4.5%)

* One patient had baseline ICH present prior to receiving study medication



Conclusions

- No significant difference in clinical outcome between desmoteplase and placebo
- Higher than expected placebo response rate
 - responder rate in placebo group as high as in desmoteplase groups
- Increased mortality in the 125 $\mu\text{g}/\text{kg}$ dose group
 - predominantly late death rate (>10 days)
- sICH rate is low in all treatment groups



Next Steps

- In depth per protocol analysis
- PK and antibody analyses
- Analysis of placebo response
- Imaging analysis
- Adjudication of late death cases

Thank you very much for your
attention

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