Efficacy, Safety and Tolerability of Nangibotide in Patients with Septic Shock.

A Randomized, Double-blind, Placebo Controlled Dose Selection Study

The ASTONISH Study (MOT-C-203)

Table 1: Study Schedule

	SCR									EoS	FU unblinded[2]		
Assessment / Study Day[1]	**≤24H**	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**28 +4d**	**90 ±4d**	**6m ±1w**	**12m ±1w**
Informed consent	X[11]												
Inclusion/exclusion criteria	X												
Medical history and demographics	X												
Previous therapies[3]	X												
APACHE II Score	X												
Pregnancy test[4]	X												
Height and weight[5]	X												
Physical Examination	X									X[14]			
Vital Signs	X	X[12]	X	X	X	X	X			X			
ECG	X	X[12,15]	X[13]	X[13]	X[13]	X[13]	X[13]			X			
Organ dysfunction / SOFA Score[6]	X	X[12]	X	X	X	X	X	X	X				
Charlson Comorbidity Index CCI)	X												
Call to the CCC	X												
Randomization	X												
Study Drug Infusion[7]		X	X	X	X	X	X						
Prior and concomitant Therapies	X	X	X	X	X	X	X	X	X	X			
Vasopressor	X	X	X	X	X	X	X	X	X	X			
IMV	X	X	X	X	X	X	X	X	X	X			
RRT	X	X	X	X	X	X	X	X	X	X			
Mortality		X	X	X	X	X	X	X	X	X	X	X	X
Adverse Events[16]	X	X	X	X	X	X	X	X	X	X			
Clinical Laboratory (see table 2)	X	X[12]	X	X	X	X	X	X	X	X			
Anti-drug antibodies (ADA)		X[12]								X			
PK[17]		X[12]	X[13]	X[13]	X[13]	X[13]	X[13]						
Biomarker samples (see table 2)		X[12]	X	X	X	X	X	X	X	X			
EuroQol (EQ 5D)										X	X	X	X
Healthcare resource utilization[8]										X	X	X	X
Secondary infections[9]										X			
Discharge letter collection[10]										X			

SCR: screening; EoS: end of study; FU: Follow-up; CCC: Clinical coordination center; d: day; w: week; m: month

1: Study days refer to calendar days, day 0 is defined as the calendar day of first study drug administration
2: By phone only
3: All medication taken within the last 24 hours before start of treatment should be documented
4: Women of childbearing potential
5: Estimate in case measurement is not feasible
6: Daily up to day 7, even in case of intensive care unit (ICU) discharge
7: Patients will be treated for at least 3 days (72 ±2 hours) with study drug. After the first 3 days of treatment, patients still requiring vasopressor will be treated until 24 (±2) hours after vasopressor withdrawal with a maximum treatment duration of 5 days (120 ±2 hours)
8: Day 28 completed at site (including duration of hospitalization and ICU stay, discharge location); 90 days, 6 and 12 months via phone call
9: Day 28 completed by site
10: Discharge letters from ICU discharge, hospital discharge and for every hospitalization starting before day 28 (where permissible)
11: In case of emergency consent, confirmation of consent as soon as patient is capable
12: Before first treatment administration
13: Daily until end of infusion
14: Brief physical examination
15: In triplicate, at least 1 minute apart
16: AEs will be collected until day28 as specified in section
17: For sites where it is not technically feasible, the collection of PK samples may be waived by the sponsor