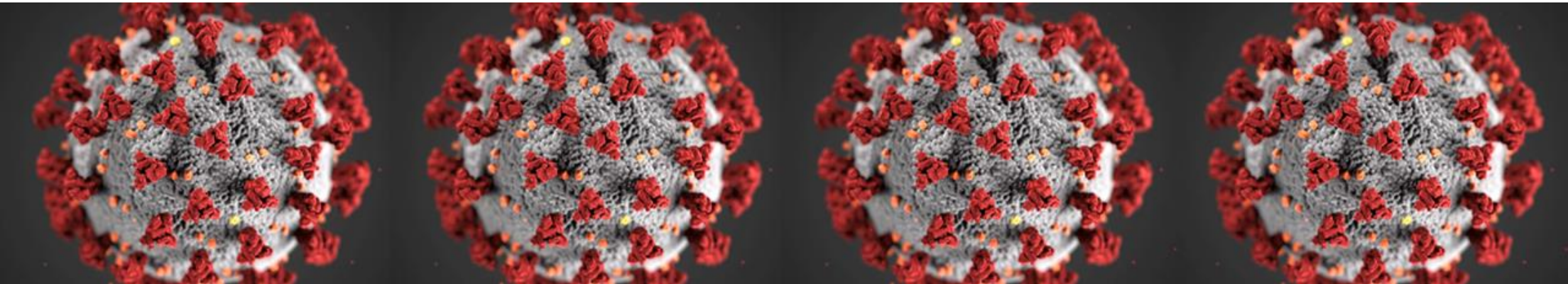
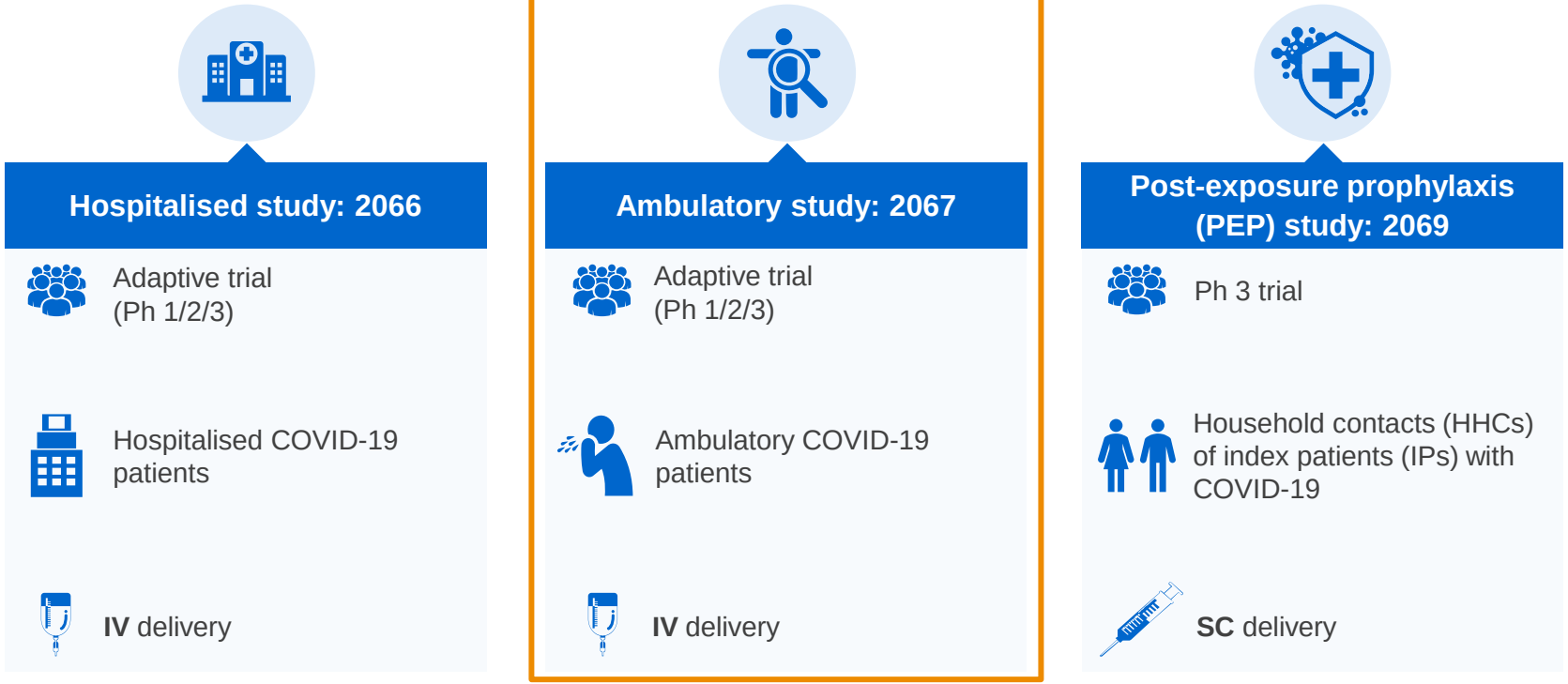
Study 2067: Cas&Im in ambulatory patients with COVID-19

M-XX-00005666



Cas&Im: under clinical investigation for the treatment and prevention of COVID-19



IV, intravenous; SC, subcutaneous

NCT04426695; NCT04425629; NCT04452318

Cas&Im in ambulatory patients with COVID-19

Adaptive trial Phase 3 portion

- **Aged ≥18 years**
- Ambulatory patients with COVID-19
- Confirmation of SARS-CoV-2 infection by molecular testing ≤72 hours from randomisation
- COVID-19 symptom onset ≤7 days from randomisation
- Not on any COVID-19 therapies

Ph 3, N=4,567

R 1:1:1

Original Ph 3 part protocol

Cas&Im 2,400 mg IV
or
Cas&Im 8,000 mg IV
or
Placebo IV

Patients with or without risk factors

Protocol update

- **Dosing change**
- **All patients required to have ≥1 risk factor for severe COVID-19**

Amended Ph 3 part protocol

Cas&Im 2,400 mg IV
or
Cas&Im 1,200 mg IV
or
Placebo IV

Only patients with risk factors

Home-based visits
Electronic survey results

Day 1 3 5 7 9 11 13 15 18 22 25 29

Baseline visit
End of study
NP swab – original protocol
NP swab – amended protocol

Primary endpoint

- COVID-19–related hospitalisations or all-cause deaths through Day 29

Adaptive Phase 1/2/3 trial (2067)
Ph 3 portion of study also included children and pregnant women (data not yet available)

Weinreich DM, et al. 2021; NCT04425629

Baseline characteristics in high-risk patients

Baseline characteristic	1,200 mg IV N=736	Corresponding placebo N=748	2,400 mg IV (pooled) N=1,355	Corresponding placebo N=1,341
Median age (IQR), years	48.5 (37.0–57.5)	48.0 (35.0–57.0)	50.0 (39.0–60.0)	50.0 (37.0–58.0)
Age ≥50 years, %	48.5	47.6	52.8	50.6
Male, %	49.5	47.1	48.4	47.2
Hispanic/Latino, %	42.4	39.4	34.2	35.1
Black/African American, %	5.2	5.1	4.9	4.9
BMI ≥30kg/m^2, %	55.7	57.1	58.1	57.6
Median days of symptoms prior to baseline (IQR)	3 (2–4)	3 (2–5)	3 (2–5)	3 (2–5)
Median viral load, log_{10} copies/mL	6.92	6.85	7.01	6.95
Median viral load, million copies/mL	8.4	7.1	10.3	9.0
Viral load >10^6, %	65	63	68	65
Seronegative, %	68	69	69	69
Seropositive, %	24	22	24	22

IQR, interquartile range

Weinreich DM, et al. 2021

Primary endpoint met: Cas&Im reduced the risk of hospitalisation or death by ~70% compared to placebo

Patients with ≥1 COVID-19-related hospitalisation or death through Day 29

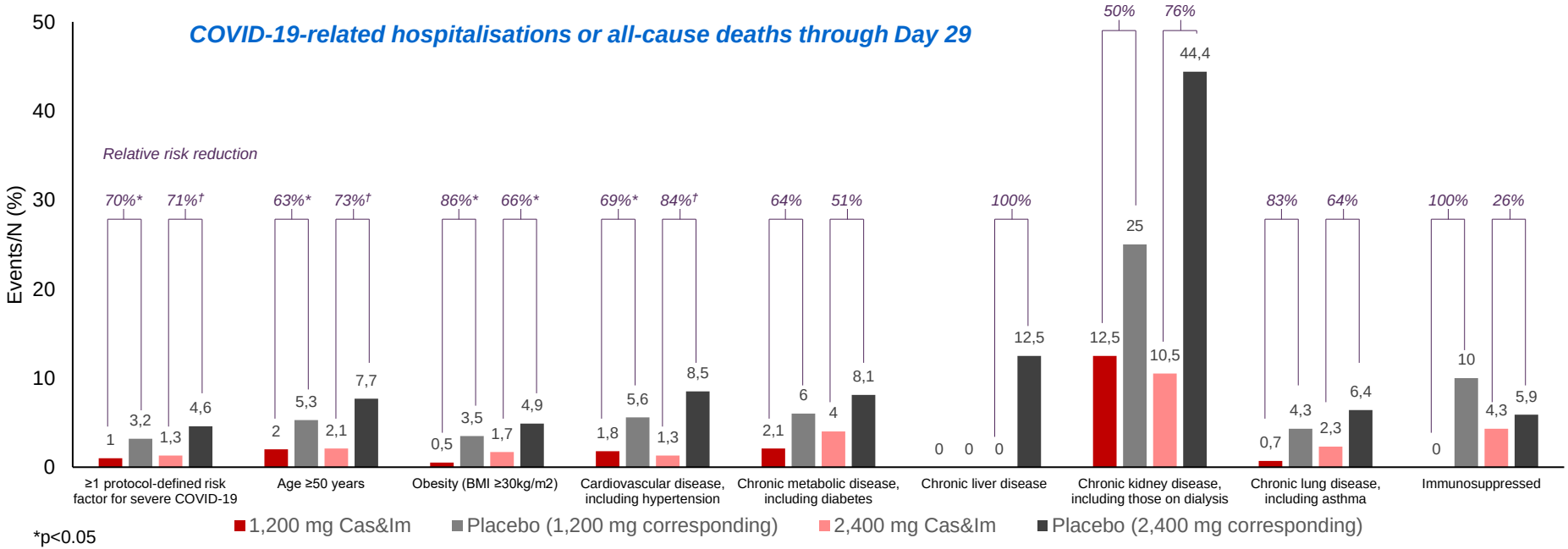
	1,200 mg IV n=736	Placebo n=748	2,400 mg IV n=1,355	Placebo n=1,341
n (%)	7 (1.0)	24 (3.2)	18 (1.3)	62 (4.6)
Risk reduction relative	**70%** (p=0.002)		**71%** (p<0.001)	

	Placebo n=1,843	1,200 mg IV n=827	2,400 mg IV n=1,849
Deaths, n	5	1	1

mFAS (Modified Full Analysis Set – all randomised patients with a positive SARS-CoV-2 RT-qPCR test from NP swabs at randomisation and ≥1 risk factor for severe COVID-19)

Weinreich DM, et al. 2021

Reduction in risk of hospitalisation or death across high-risk subgroups and dose



*p<0.05
†p<0.001
CDC, Centers for Disease Control and Prevention

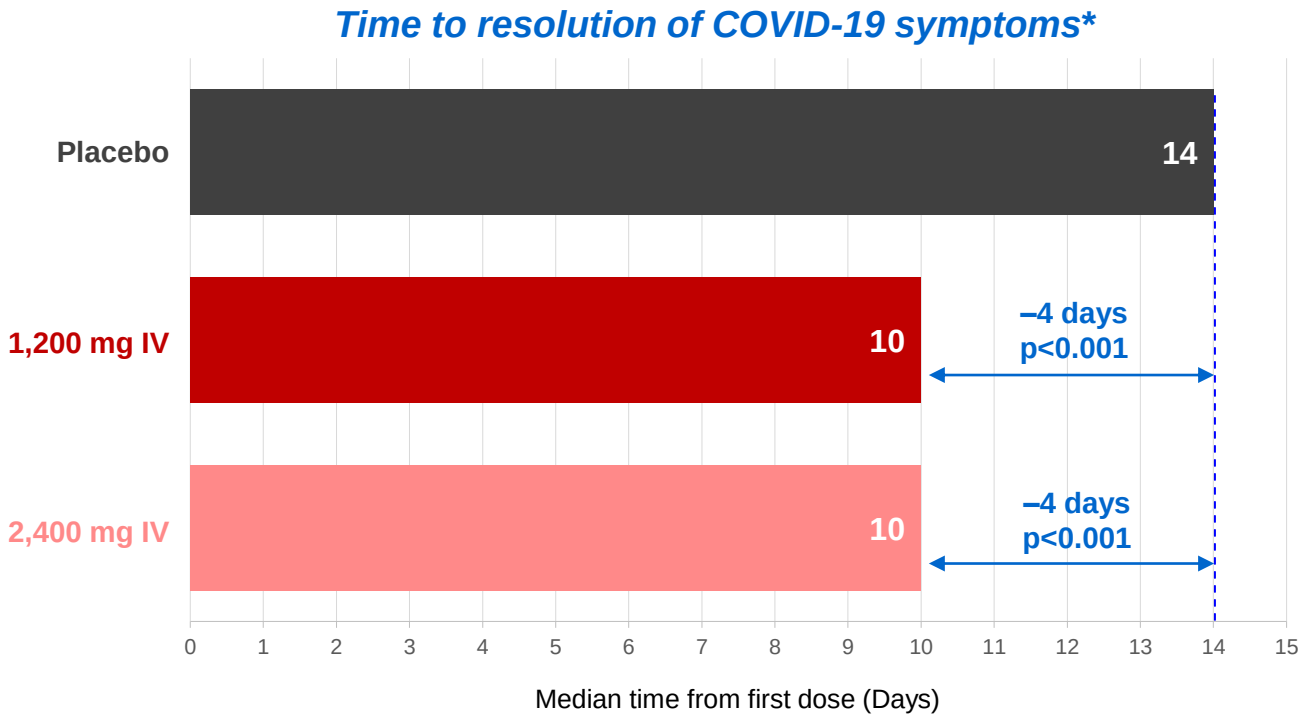
Shorter hospital stays and lower rate of both admission to ICUs and ventilator support

		1,200 mg IV n=736	Placebo n=748	2,400 mg IV n=1,355	Placebo n=1,341
Days of hospitalisation due to COVID-19	No. of hospitalised patients	7 (1.0%)	24 (3.2%)	18 (1.3%)	62 (4.6%)
	No. of days of hospitalisation per patient, Median (IQR)	**4.0** (3.0–6.0)	**5.5** (4.0–10.5)	**6.0** (3.0–11.0)	**7.0** (5.0–13.0)
Proportion of patients admitted to an intensive care unit (ICU)	No.of patients admitted to ICU within 29d	3 (0.4%)	7 (0.9%)	6 (0.4%)	18 (1.3%)
	Relative risk vs placebo (95% CI)	**56.4% reduction** (-67.8, 88.7)		**67.0% reduction** (17.2, 86.9)	
Proportion of patients requiring mechanical ventilation (MV)	No. of patients requiring MV within 29d	1 (0.1%)	2 (0.3%)	1 (<0.1%)	6 (0.4%)
	Relative risk vs placebo (95% CI)	**49.2% reduction** (-459.2, 95.4)		**83.5% reduction** (-36.8, 98.0)	

Cas&Im was also associated with a lower proportion of patients with COVID-19-related hospitalisation, emergency room visits, or all-cause death through Day 29 and patient requiring any medically-attended visit for worsening COVID-19 (hospitalisation, emergency room visit, urgent care visit or physician office/telemedicine visit) or all-cause death

Weinreich DM, et al. 2021 appendix

Cas&Im reduced duration of symptoms by 4 days compared to placebo



mFAS. *From treatment initiation (Day 0), median time from symptom onset was 3 days in each arm

Weinreich DM, et al. 2021

Safety profile

Adverse events, n (%)	Placebo (N=1,843)	1,200 mg IV (N=827)	2,400 mg IV (N=1,849)	8,000 mg IV (N=1,012)
AESI: infusion-related reaction Grade ≥2 through Day 4	0	2 (0.2)	1 (<0.1)	3 (0.3)
AESI: hypersensitivity reaction Grade ≥2 through Day 29	1 (<0.1)	0	1 (<0.1)	0
Patients with any SAE (occurring in >1 patient)*	74 (4.0)	9 (1.1)	24 (1.3)	17 (1.7)
Respiratory, thoracic and mediastinal disorders	22 (1.2)	1 (0.1)	7 (0.4)	5 (0.5)
Infections and infestations	48 (2.6)	5 (0.6)	14 (0.8)	12 (1.2)
Metabolism and nutrition disorders	4 (0.2)	0	0	0
Deaths	5 (0.3)	1 (0.1)	1 (<0.1)	0

Includes all patients enrolled in study
*SAEs occurred more frequently in the placebo group as compared to any Cas&Im dose group and were consistent with COVID-19 and associated complications
SAE, serious adverse event; AESI Adverse events of special interest

Weinreich DM, et al. 2021

Key messages

In high-risk ambulatory patients, Cas&Im led to significant improvements in all key clinical and virological endpoints

- Reduced risk of hospitalisation or death by ~70%
- Reduced duration of symptoms by 4 days vs placebo
- Reduced viral load more rapidly than placebo

Benefits were observed regardless of serostatus or baseline viral load

Cas&Im was generally well tolerated

Weinreich DM, et al. 2021

References

- NCT04425629. Available at: https://clinicaltrials.gov/ct2/show/NCT04425629.
- NCT04426695. Available at: https://clinicaltrials.gov/ct2/show/NCT04426695.
- NCT04452318. Available at: https://clinicaltrials.gov/ct2/show/NCT04452318.
- Weinreich DM, et al. *N Engl J Med* 2021; https://www.nejm.org/doi/full/10.1056/NEJMoa2108163
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