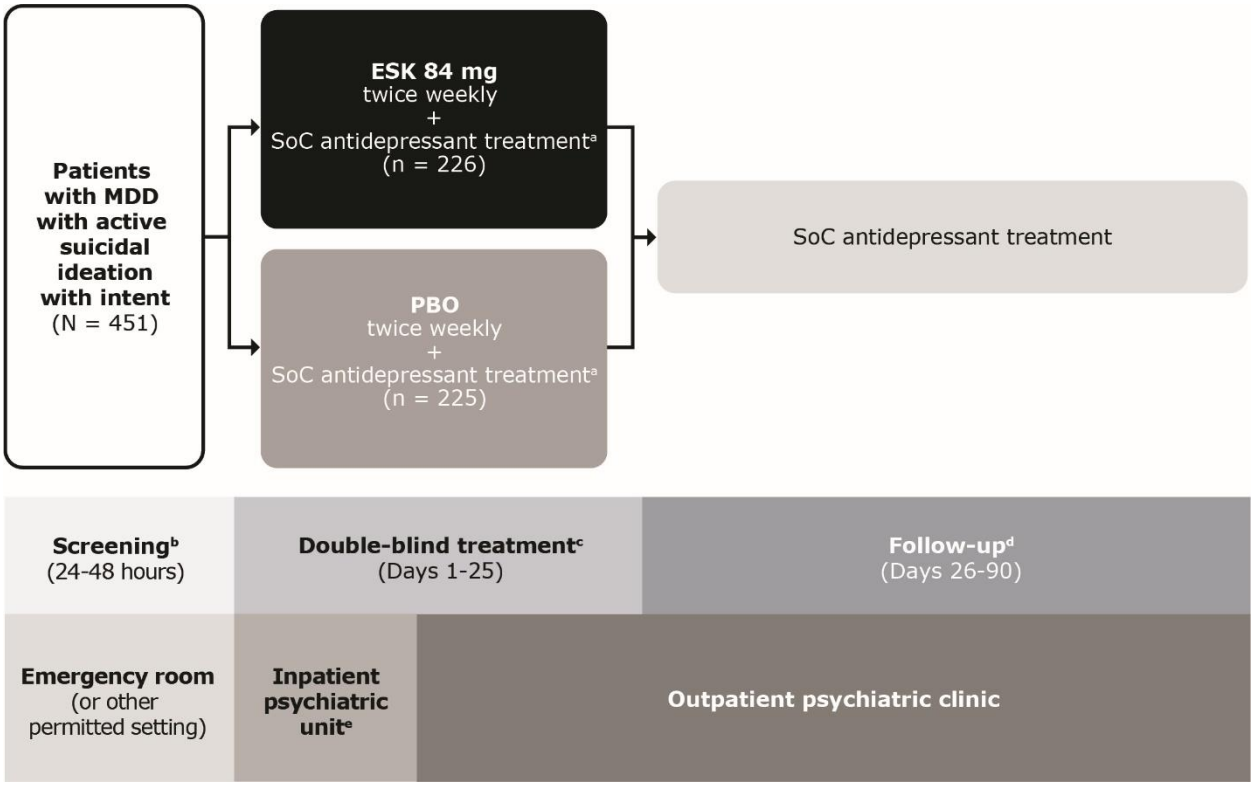
Supplemental Figure 1. ASPIRE Study Design



[a]SoC antidepressant treatment (antidepressant monotherapy or an antidepressant plus augmentation therapy) was initiated or optimized by the investigator prior to randomization.
[b]Screening was performed within 48 hours before the day 1 intranasal dose and, when possible, within 24 hours.
[c]Treatment sessions were conducted twice weekly, with dosing on days 1, 4, 8, 11, 15, 18, 22, and 25.
[d]ESK and PBO were discontinued, and SoC was continued at the discretion of the investigator; the frequency of treatment visits decreased during the course of follow up.
[e]Inpatient psychiatric care was recommended for 5 days in most countries (and for 14 days in countries in the European Union for the ASPIRE II study); discharge before 5 days was discussed with and approved by the sponsor's medical monitor.
Abbreviations: ESK = esketamine nasal spray, MDD = major depressive disorder, PBO = placebo nasal spray, SoC = standard of care.