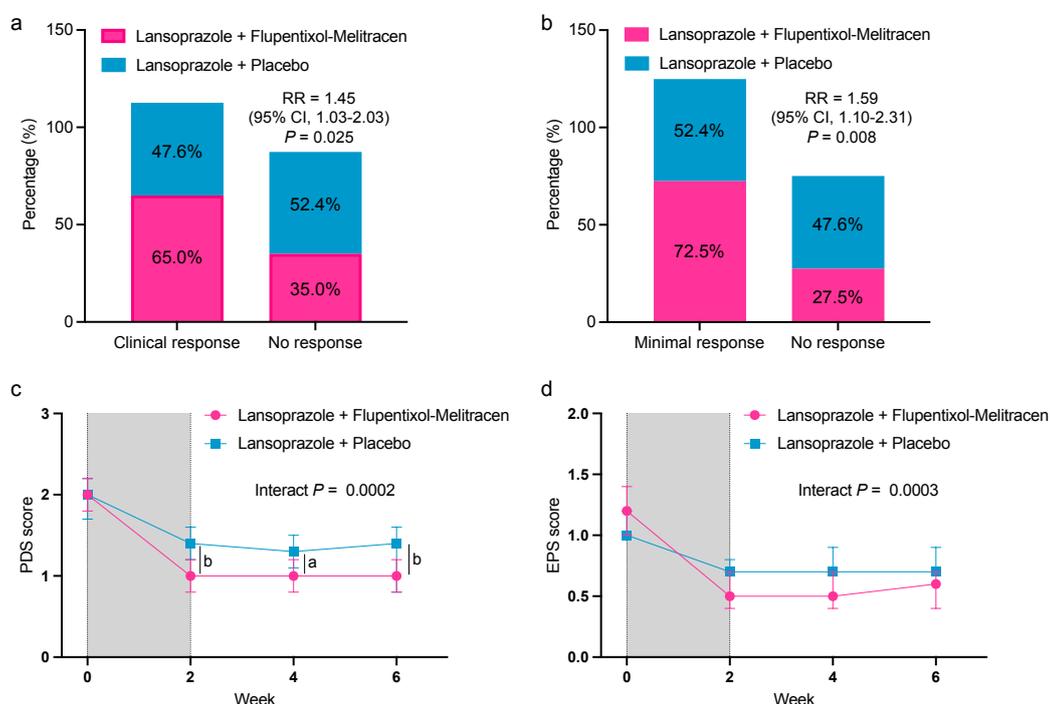


Supplementary appendix
Supplementary figure 1: Study design.



Supplementary figure 2: Percentage of treatment response and changes of estimated LPDS scores over time between lansoprazole plus flupentixol-melitracen and placebo group (Per-protocol analysis).



(a-b) Percentage of clinical response (a) and minimal clinical response (b) at the end of treatment. The relative risk (RR), along with its 95% confidence intervals (CI), was calculated to compare the lansoprazole + flupentixol-melitracen group against the lansoprazole + placebo group. (c-d) over-time model-based estimated PDS score and EPS score changes. The gray shaded area represents the treatment period. Interact *P*: group × time interaction *p*-value; ^a*P* < 0.05 and ^b*P* < 0.01.

Supplementary Table 1 Model-estimated clinical outcomes over time between Lansoprazole plus Flupentixol-melitracen and placebo groups using complete case dataset (per-protocol analysis).

Variables	Time points	LPZ + FM	LPZ + Placebo	B	95%CI	<i>p</i> value
LPDS-PDS	T1	2.0 (1.8-2.2)	2.0 (1.7-2.2)			
	T2	1.0 (0.8-1.2)	1.4 (1.2-1.6)	-0.41	-0.70 to -0.12	0.006
	T3	1.0 (0.8-1.2)	1.3 (1.1-1.5)	-0.34	-0.63 to -0.04	0.024
	T4	1.0 (0.8-1.2)	1.4 (1.2-1.6)	-0.38	-0.67 to -0.10	0.009

LPDS-EPS	T1	1.2 (1.0-1.4)	1.0 (0.8-1.2)			
	T2	0.5 (0.4-0.7)	0.7 (0.5-0.8)	-0.14	-0.35 to 0.07	0.190
	T3	0.5 (0.4-0.7)	0.7 (0.6-0.9)	-0.20	-0.41 to 0.01	0.056
	T4	0.6 (0.4-0.7)	0.7 (0.6-0.9)	-0.17	-0.38 to -0.04	0.116
SF-NDI	T1	26.9 (24.7-29.1)	28.0 (25.8-30.2)			
	T2	15.6 (13.5-17.7)	19.3 (17.3-21.4)	-3.71	-6.61 to -0.80	0.013
	T3	14.7 (12.7-16.7)	18.7 (16.7-20.7)	-4.00	-6.82 to -1.18	0.006
	T4	15.3 (13.3-17.4)	19.2 (17.2-21.3)	-3.90	-6.79 to -1.00	0.009
PHQ-9	T1	8.4 (7.0-9.8)	9.0 (7.6-10.4)			
	T2	3.2 (2.2-4.2)	5.6 (4.7-6.6)	-2.47	-3.85 to -1.09	0.001
	T3	3.1 (2.1-4.1)	5.1 (4.2-6.1)	-2.03	-3.38 to -0.69	0.003
	T4	3.2 (2.2-4.1)	5.6 (4.7-6.6)	-2.48	-3.86 to -1.10	0.000
GAD-7	T1	6.5 (5.2-7.8)	6.9 (5.6-8.2)			
	T2	2.8 (1.9-3.8)	4.6 (3.7-5.5)	-1.79	-3.11 to -0.46	0.008
	T3	2.9 (2.0-3.8)	4.3 (3.4-5.2)	-1.37	-2.66 to -0.08	0.037
	T4	3.0 (2.0-3.9)	4.7 (3.7-5.6)	-1.67	-3.02 to -0.33	0.015
PSQI	T1	8.7 (7.7-9.8)	9.0 (8.0-10.0)			
	T2	6.2 (5.2-7.1)	7.7 (6.8-8.6)	-1.52	-2.83 to -0.21	0.023
	T3	6.1 (5.2-7.0)	7.3 (6.4-8.2)	-1.22	-2.50 to 0.06	0.063
	T4	6.2 (5.3-7.1)	7.6 (6.7-8.5)	-1.37	-2.66 to 0.09	0.036

Data are estimates with 95% CI (confidence interval) for clinical outcomes at each time point for Flupentixol-melitracen and placebo groups in full analysis set. Significance is given for the between-group difference in changes at each time point. LPZ, Lansoprazole; FM, Flupentixol-Melitracen; LPDS, Leuven Postprandial Distress Scale; PDS, postprandial distress syndrome; EPS, epigastric pain syndrome; SF-NDI, Short-Form Nepean Dyspepsia Index; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder-7; PSQI, Pittsburgh Sleep Quality Index.