Supplementary Information

Mirikizumab Pharmacokinetics in Patients With Moderately-to-Severely Active Ulcerative Colitis: Results From Phase III LUCENT Studies

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LIST OF TABLES AND FIGURES

Online Resource 2: Table 1 PK sampling schedule for AMAC, LUCENT 1, and LUCENT 2

AMAC primary study			
	W	V	S
	Screening	V1	
	Baseline	V2	✓[b]
Induction	W2	V3	✓
	W4	V4	✓[b]
	W6	V5	✓
	W8	V6	✓[b]
	W11–12	V7[c]	✓
Maintenance[a]	W12–13	V8	✓
	W16	V9	✓
	W20	V10	✓
	W24	V11	✓
	W28	V12	
	W32	V13	✓
	W36	V14	
	W40	V15	✓
	W44	V16	
	W48	V17	✓
	W52	V18	
	W56	V19	✓
	W60	V20	
	W64	V21	✓
	W68	V22	
	W72	V23	✓
	W76	V24	
	W80	V25	✓
	W84	V26	
	W88	V27	✓
	W92	V28	
	W96	V29	✓
	W100	V30	
	W104	V31	✓
Follow-up	W108	V801	
	W112	V802	✓
	W116	V803	
	W120	V804[d]	✓

AMAC extension study			
	W	V	S
Induction	W0	V1	✓[b]
	W2	V2	✓
	W4	V3	✓[b]
	W6	V4	✓
	W8	V5	✓[b]
	W11–12	V6[e]	✓
Maintenance[a]	W12–13	V7	✓
	W16	V8	✓
	W20	V9	✓
	W24	V10	✓
	W28	V11	
	W32	V12	✓
	W36	V13	
	W40	V14	✓
	W44–45	V15	
	W48	V16	✓
	W52	V17	
	W56	V18	✓
	W60	V19	
	W64	V20	✓
	W68	V21	
	W72	V22	✓
	W76	V23	
	W80	V24	✓
	W84	V25	
	W88	V26	
	W92	V27	✓
Follow-up	W96	V805	
	W100	V806	✓
	W104	V807	
	W108	V808[f]	✓

LUCENT 1			
	W	V	S
		V0	
Treatment	W0	V1	✓[g]
	W2	V2	
	W4	V3	✓[g]
	W8	V4	✓[h]
	W12	V5	✓
		ETV[i]	✓
		V997 (UV)	✓
Follow-up	LV +4	V801	
	±4	V802	✓

LUCENT 2			
	W	V	S
Maintenance	W0	V1	✓[j]
	W4	V2	✓
	W8	V3	
	W12	V4	✓
	W16	V5	✓[k]
	W20	V6	✓[k]
	W24	V7	✓
	W28	V8	✓[k]
	W32	V9	✓[k]
	W36	V10	✓[k]
	40 LV	V11	✓
	ETV	N/A	✓
	UV	V997	✓[k]
Follow-up	LV or ETV +4	801	
	LV or ETV +12/16[l]	802	✓

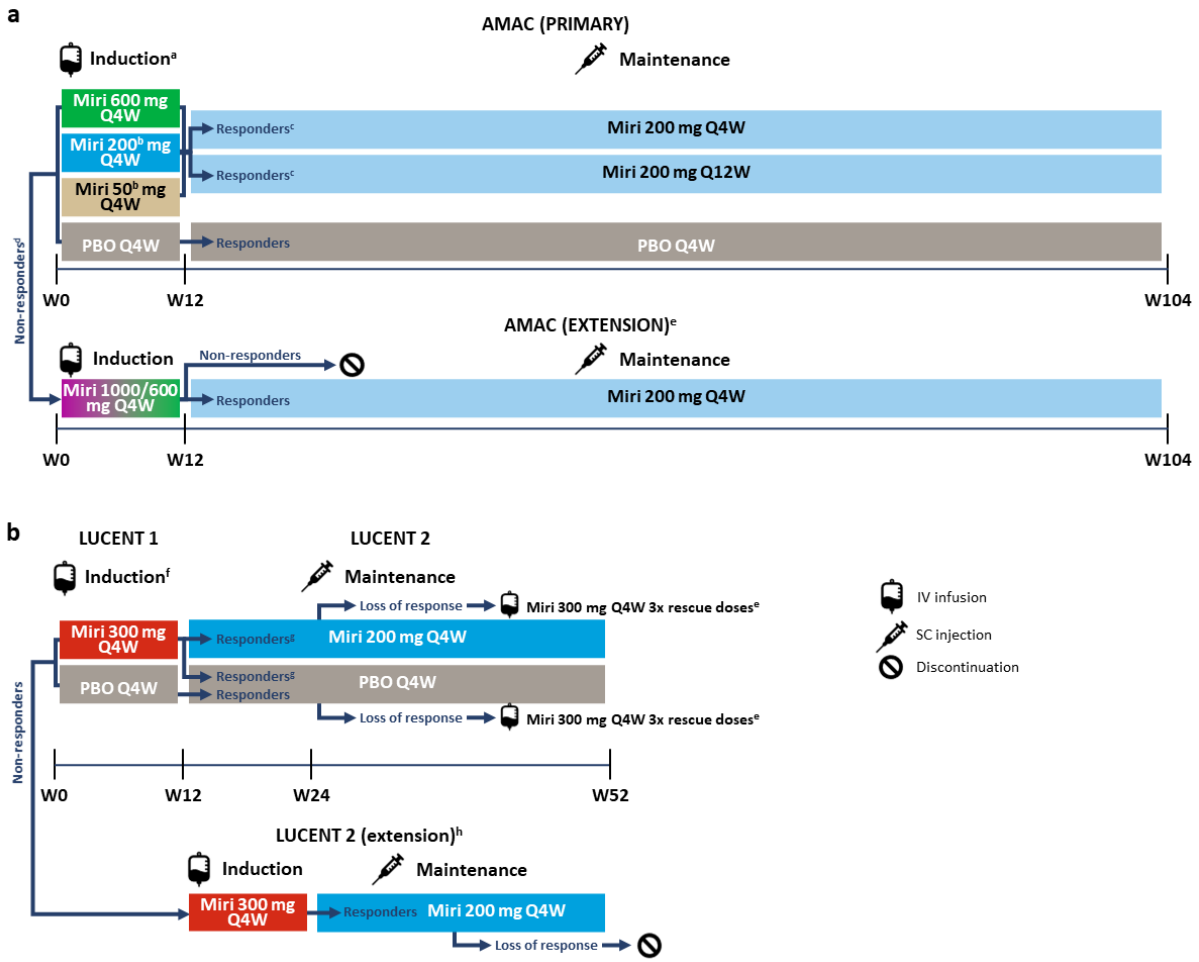
C_{max} maximum concentration, *ETV* early termination visit, *IV* intravenous(ly), *LOR* loss of response, *LV* last visit, *N/A* not applicable, *PK* pharmacokinetic, *S* sampling for PK analysis, *SC* subcutaneously, *UV* unscheduled visit, *V* Visit, *W* Week

[a]A single sample was drawn prior to study drug administration, if occurring on a dosing day
[b]On the day of dosing, PK samples were drawn before each IV infusion (trough) and at the end of each IV infusion (C_{max})
[c]For patients who discontinued during the induction period, V7 (W12) served as the ETV
[d]V804 (W120) served as the end-of-study visit or ETV if a patient prematurely discontinued from the study at any time during the maintenance or follow-up periods
[e]For patients who were non-responders at the end of the induction phase, V6 (W12) served as the end-of-study visit
[f]V808 (W108) served as the end-of-study visit or ETV if a patient prematurely discontinued from the study at any time during the maintenance phase or follow-up period
[g]Pre-dose and post-dose sampling
[h]Pre-dose sampling only
[i]ETV could occur on any day without regard to visit interval
[j]Results from W12 of the LUCENT 1 study were used for W0 of this study
[k]Patients with confirmed secondary LOR should have samples taken prior to mirikizumab IV rescue dosing and 4 and 12 weeks after rescue initiation
[l]Patients who discontinued study drug with last dose administered IV returned for a last visit + 16-week post-treatment follow-up visit without a 12-week follow-up. Patients who discontinued study drug with last dose administered SC returned for a last visit + 12-week post-treatment follow-up visit without a 16-week follow-up

Online Resource 4: Table 2 List of covariates tested with the model generated using the AMAC and LUCENT 1+2 results for their impact on mirikizumab PK

	AMAC	LUCENT 1+2
Age	✓	✓
Sex	✓	✓
Race		✓
Ethnic origin	✓	
Baseline body weight	✓	✓
Baseline body mass index	✓	✓
Prior biologic therapy		✓
Smoking		✓
Cockroft-Gault creatinine clearance		✓
Baseline albumin		✓
Time-varying albumin	✓	✓
Baseline C-reactive protein	✓	✓
Time-varying C-reactive protein		✓
Baseline bilirubin		✓
Baseline fecal calprotectin	✓	✓
Duration of disease		✓
Extent of disease	✓	
SC injection site		✓
Baseline modified Mayo score	✓	✓
Baseline stool frequency Mayo subscore		✓
Baseline rectal bleeding Mayo subscore	✓	✓
Baseline endoscopic findings Mayo subscore		✓
Baseline corticosteroid or immunomodulator use		✓
Baseline ASA use		✓
Baseline ASA and similar agents		✓
Immunogenicity (ADA+/-, TE-ADA+/-, ADA titer, neutralizing ADA+/-)	✓	✓

ADA antidrug antibody, *ASA* aminosalicyclic acid, *PK* pharmacokinetics, *SC* subcutaneous, *TE-ADA* treatment-emergent antidrug antibody

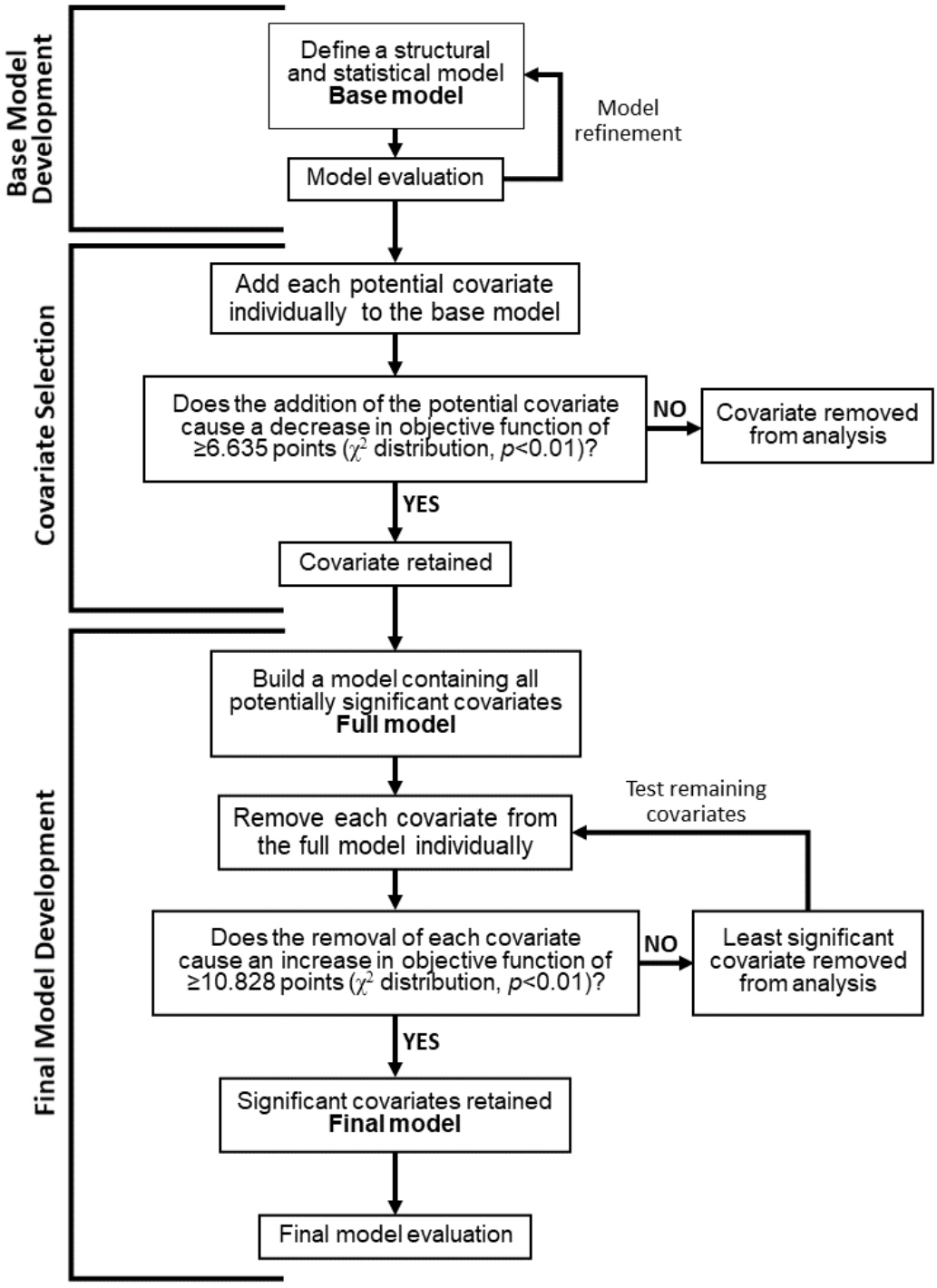


Online Resource 1: Fig. 1 Design of AMAC, LUCENT 1, and LUCENT 2 trials

Response was characterized by a decrease in MMS of ≥2 points and a ≥30% (AMAC) or ≥30% (LUCENT 1+2) decrease from baseline, and a decrease of ≥1 point in the RB subscore from baseline or an RB subscore of 0 or 1. Loss of response was defined as a ≥2-point increase from maintenance baseline in the combined SF+RB scores and a combined SF+RB score of ≥4 on two consecutive visits, confirmed by an endoscopic subscore of 2 or 3

[a]1:1:1:1 randomization; [b]doses after the first one were adjusted based on exposure, resulting in an average group dose of Miri 250 mg and 100 mg for the 200-mg and 50-mg groups, respectively; [c]1:1 randomization; [d]non-responders to induction regimens had the option to discontinue from the study or enter the open-label extension period; [e]open-label; [f]3:1 randomization to Miri 300 mg or PBO IV Q4W; [g]2:1 randomization to Miri 200 mg or PBO SC Q4W; [h]open-label

IV intravenous, *Miri* mirikizumab, *MMS* modified Mayo score, *PBO* placebo, *Q4W* every 4 weeks, *Q12W* every 12 weeks, *RB* rectal bleeding, *SC* subcutaneous, *SF* stool frequency, *W* Week, LUCENT 1+2



Online Resource 3: Fig. 2 General process for PK modeling. *PK* pharmacokinetic