A. Effect on LFS

Strata	Control O/N	Treatment O/N	Adjusted HR (CI)
AGE ≤60			
Blaise	22 / 38	28 / 40	1.19 (0.68-2.08)
ALFA 9801	27 / 42	25 / 34	1.06 (0.61-1.84)
CALGB 19808	61 / 107	54 / 107	0.80 (0.55-1.15)
CCG 2961	59 / 145	67 / 144	1.13 (0.80-1.60)
Subtotal	169 / 332	174 / 325	1.00 (0.81-1.24)
Test of heterogeneity		P = .673	
Test of treatment effect		P = .980	
AGE >60			
ALFA 9801	28 / 42	27 / 43	1.01 (0.60-1.72)
CALGB 9720	81 / 82	79 / 81	0.90 (0.66-1.23)
Subtotal	109 / 124	106 / 124	0.93 (0.71-1.22)
Test of heterogeneity		P = .998	
Test of treatment effect		P = .591	
TOTAL	278 / 456	280 / 449	0.97 (0.82-1.15)
Test of interaction		P = .662	
Test of treatment effect		P = .754	

B. Effect on OS

Strata	Control O/N	Treatment O/N	Adjusted HR (CI)
AGE ≤60			
Blaise	21 / 38	25 / 40	1.14 (0.64-2.04)
ALFA 9801	17 / 42	17 / 34	1.35 (0.69-2.66)
CALGB 19808	45 / 107	40 / 107	0.81 (0.53-1.24)
CCG 2961	36 / 145	40 / 144	1.08 (0.69-1.70)
Subtotal	119 / 332	122 / 325	1.02 (0.79-1.31)
Test of heterogeneity		P = .733	
Test of treatment effect		P = .892	
AGE >60			
ALFA 9801	20 / 42	23 / 43	1.39 (0.76-2.54)
CALGB 9720	79 / 82	78 / 81	1.11 (0.81-1.52)
Subtotal	99 / 124	101 / 124	1.16 (0.88-1.54)
Test of heterogeneity		P = .980	
Test of treatment effect		P = .287	
TOTAL	218 / 456	223 / 449	1.08 (0.90-1.30)
Test of interaction		P = .486	
Test of treatment effect		P = .414	

Strata	Control O/N	Treatment O/N	Adjusted HR (CI)
AGE <21			
Blaise	0 / 4	1 / 3	1.00 (1.00-1.00)
CALGB 19808	2 / 3	0 / 3	1.00 (1.00-1.00)
CCG 2961	59 / 145	67 / 144	1.13 (0.80-1.60)
Subtotal	61 / 152	68 / 150	1.11 (0.78-1.57)
Test of heterogeneity		P = 1.000	
Test of treatment effect		P = .558	
AGE 21-60			
Blaise	22 / 34	27 / 37	1.06 (0.60-1.87)
ALFA 9801	27 / 42	25 / 34	1.06 (0.61-1.84)
CALGB 19808	59 / 104	54 / 104	0.83 (0.58-1.21)
Subtotal	108 / 180	106 / 175	0.93 (0.71-1.22)
Test of heterogeneity		P = .943	
Test of treatment effect		P = .613	
AGE >60			
ALFA 9801	28 / 42	27 / 43	1.01 (0.60-1.72)
CALGB 9720	81 / 82	79 / 81	0.90 (0.66-1.23)
Subtotal	109 / 124	106 / 124	0.93 (0.71-1.22)
Test of heterogeneity		P = .998	
Test of treatment effect		P = .591	
TOTAL	278 / 456	280 / 449	0.97 (0.82-1.15)
Test of interaction		P = .686	
Test of treatment effect		P = .716	

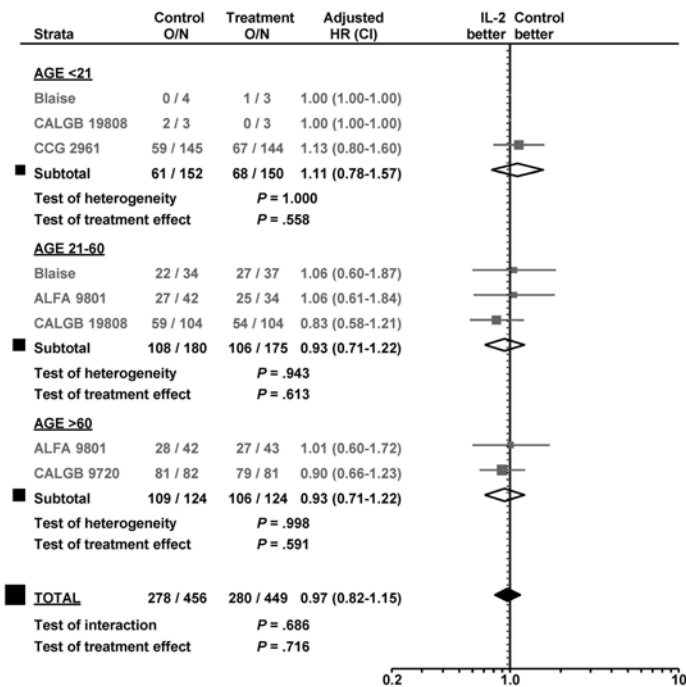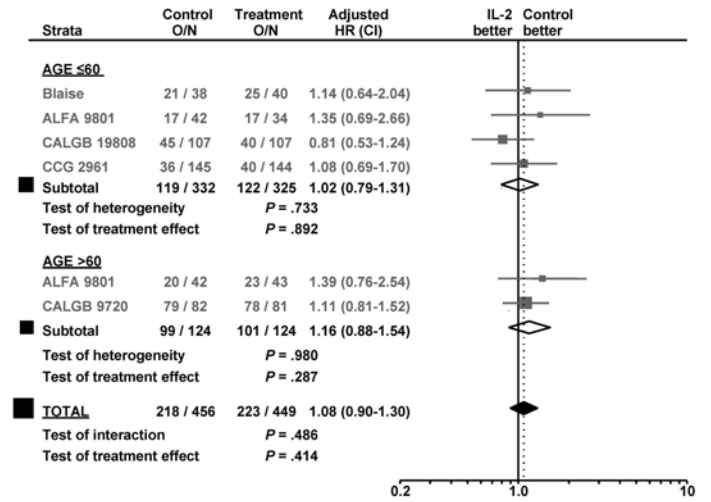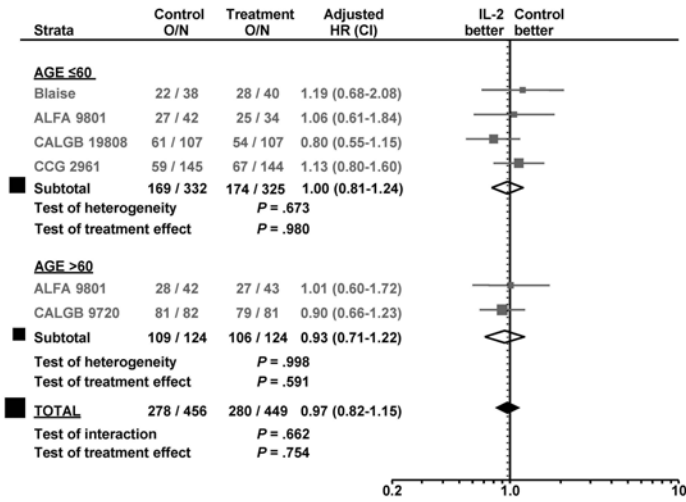| Strata	Control O/N	Treatment O/N	Adjusted HR (CI)
AGE <21			
Blaise	0 / 4	1 / 3	1.00 (1.00-1.00)
CALGB 19808	2 / 3	0 / 3	1.00 (1.00-1.00)
CCG 2961	36 / 145	40 / 144	1.08 (0.69-1.70)
Subtotal	38 / 152	41 / 150	1.05 (0.68-1.64)
Test of heterogeneity		P = 1.000	
Test of treatment effect		P = .822	
AGE 21-60			
Blaise	21 / 34	24 / 37	1.03 (0.57-1.86)
ALFA 9801	17 / 42	17 / 34	1.35 (0.69-2.66)
CALGB 19808	43 / 104	40 / 104	0.86 (0.56-1.32)
Subtotal	81 / 180	81 / 175	0.99 (0.73-1.35)
Test of heterogeneity		P = .867	
Test of treatment effect		P = .952	
AGE >60			
ALFA 9801	20 / 42	23 / 43	1.39 (0.76-2.54)
CALGB 9720	79 / 82	78 / 81	1.11 (0.81-1.52)
Subtotal	99 / 124	101 / 124	1.16 (0.88-1.54)
Test of heterogeneity		P = .980	
Test of treatment effect		P = .287	
TOTAL	218 / 456	223 / 449	1.08 (0.89-1.30)
Test of interaction		P = .746	
Test of treatment effect		P = .437	

Figure S1. Forest plots of HRs for the benefit of IL-2 monotherapy in terms of LFS (A) and OS (B) by age category (<21 vs 21-60 vs >60 years)
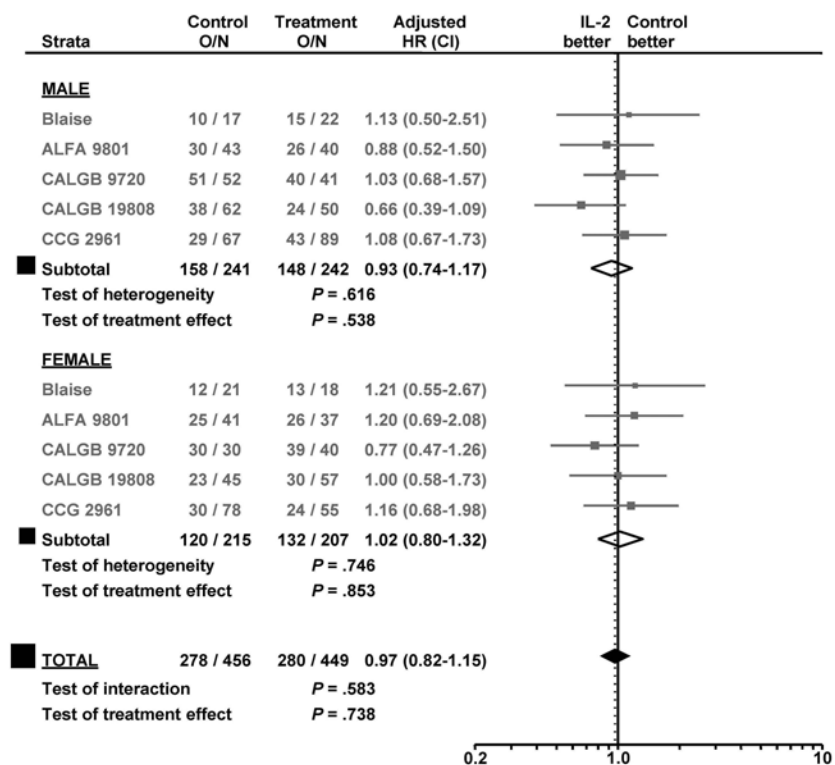
CI = confidence interval; HR = hazard ratio; IL-2 = interleukin-2; LFS = leukemia-free survival; O/N = event rate per arm where O is the number of observed events (relapse or death) and N is the sample size; OS = overall survival; RCTs = randomized controlled trials.
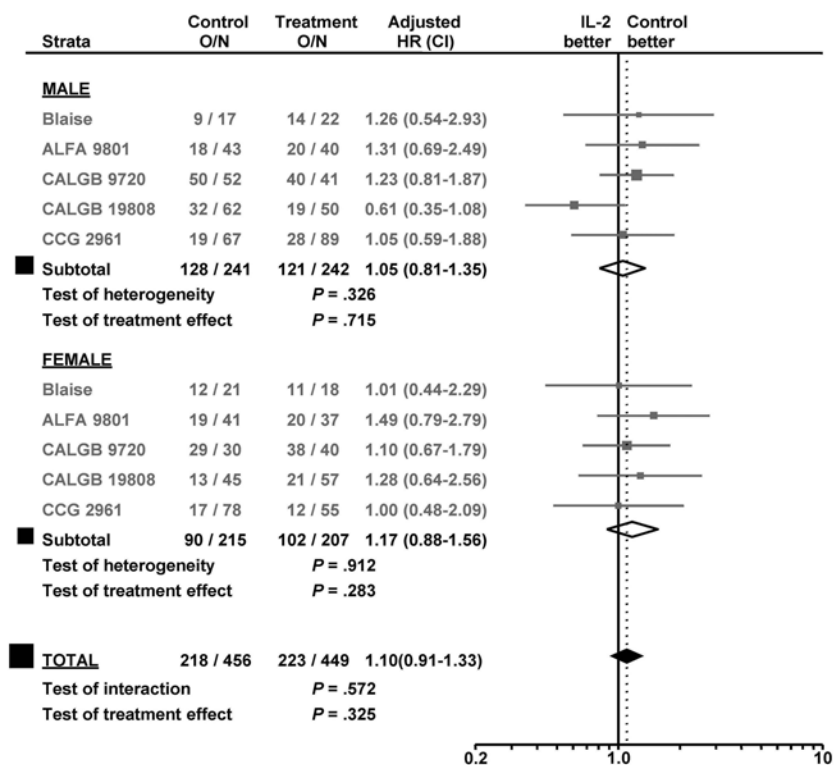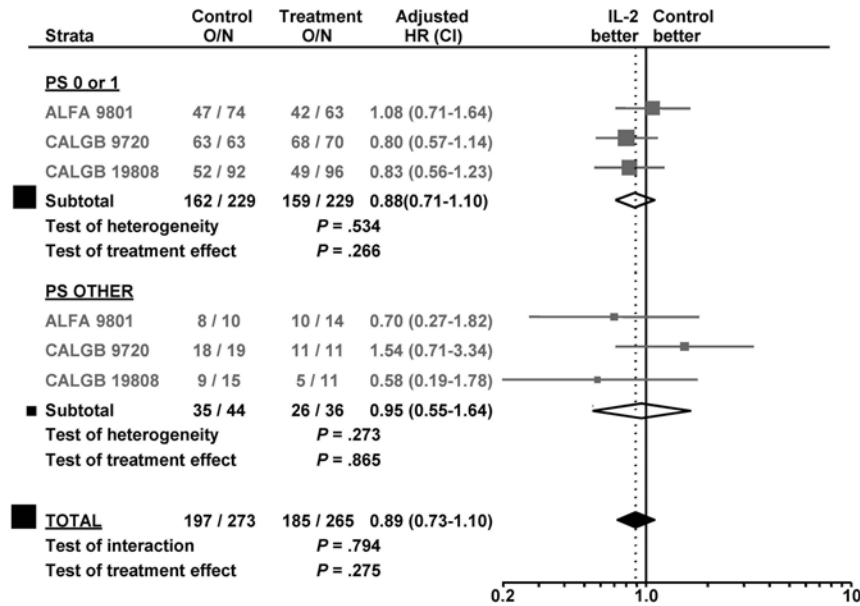
Figure S2. Forest plots of HRs for the benefit of IL-2 monotherapy in terms of LFS (A) and OS (B) by gender (male vs female)
CI = confidence interval; HR = hazard ratio; IL-2 = interleukin-2; LFS = leukemia-free survival; O/N = event rate per arm where O is the number of observed events (relapse or death) and N is the sample size; OS = overall survival; RCTs = randomized controlled trials.

A. Effect on LFS

Strata	Control O/N	Treatment O/N	Adjusted HR (CI)
PS 0 or 1			
ALFA 9801	47 / 74	42 / 63	1.08 (0.71-1.64)
CALGB 9720	63 / 63	68 / 70	0.80 (0.57-1.14)
CALGB 19808	52 / 92	49 / 96	0.83 (0.56-1.23)
Subtotal	162 / 229	159 / 229	0.88(0.71-1.10)
Test of heterogeneity		P = .534	
Test of treatment effect		P = .266	
PS OTHER			
ALFA 9801	8 / 10	10 / 14	0.70 (0.27-1.82)
CALGB 9720	18 / 19	11 / 11	1.54 (0.71-3.34)
CALGB 19808	9 / 15	5 / 11	0.58 (0.19-1.78)
Subtotal	35 / 44	26 / 36	0.95 (0.55-1.64)
Test of heterogeneity		P = .273	
Test of treatment effect		P = .865	
TOTAL	197 / 273	185 / 265	0.89 (0.73-1.10)
Test of interaction		P = .794	
Test of treatment effect		P = .275	

IL-2 better / Control better — axis: 0.2, 1.0, 10

B. Effect on OS

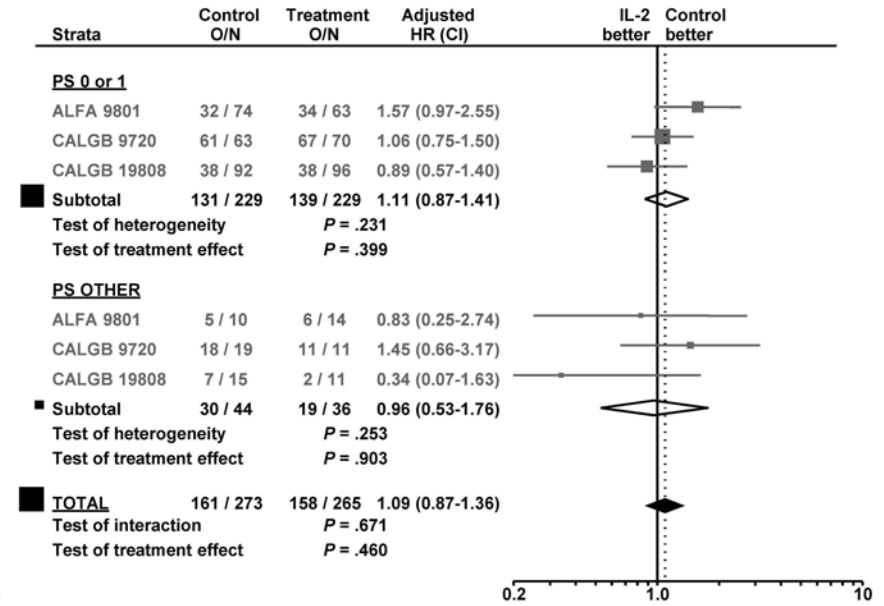| Strata	Control O/N	Treatment O/N	Adjusted HR (CI)
PS 0 or 1			
ALFA 9801	32 / 74	34 / 63	1.57 (0.97-2.55)
CALGB 9720	61 / 63	67 / 70	1.06 (0.75-1.50)
CALGB 19808	38 / 92	38 / 96	0.89 (0.57-1.40)
Subtotal	131 / 229	139 / 229	1.11 (0.87-1.41)
Test of heterogeneity		P = .231	
Test of treatment effect		P = .399	
PS OTHER			
ALFA 9801	5 / 10	6 / 14	0.83 (0.25-2.74)
CALGB 9720	18 / 19	11 / 11	1.45 (0.66-3.17)
CALGB 19808	7 / 15	2 / 11	0.34 (0.07-1.63)
Subtotal	30 / 44	19 / 36	0.96 (0.53-1.76)
Test of heterogeneity		P = .253	
Test of treatment effect		P = .903	
TOTAL	161 / 273	158 / 265	1.09 (0.87-1.36)
Test of interaction		P = .671	
Test of treatment effect		P = .460	

IL-2 better / Control better — axis: 0.2, 1.0, 10

Figure S3. Forest plots of HRs for the benefit of IL-2 monotherapy in terms of LFS (A) and OS (B) by baseline performance status (PS 0-1 vs other)
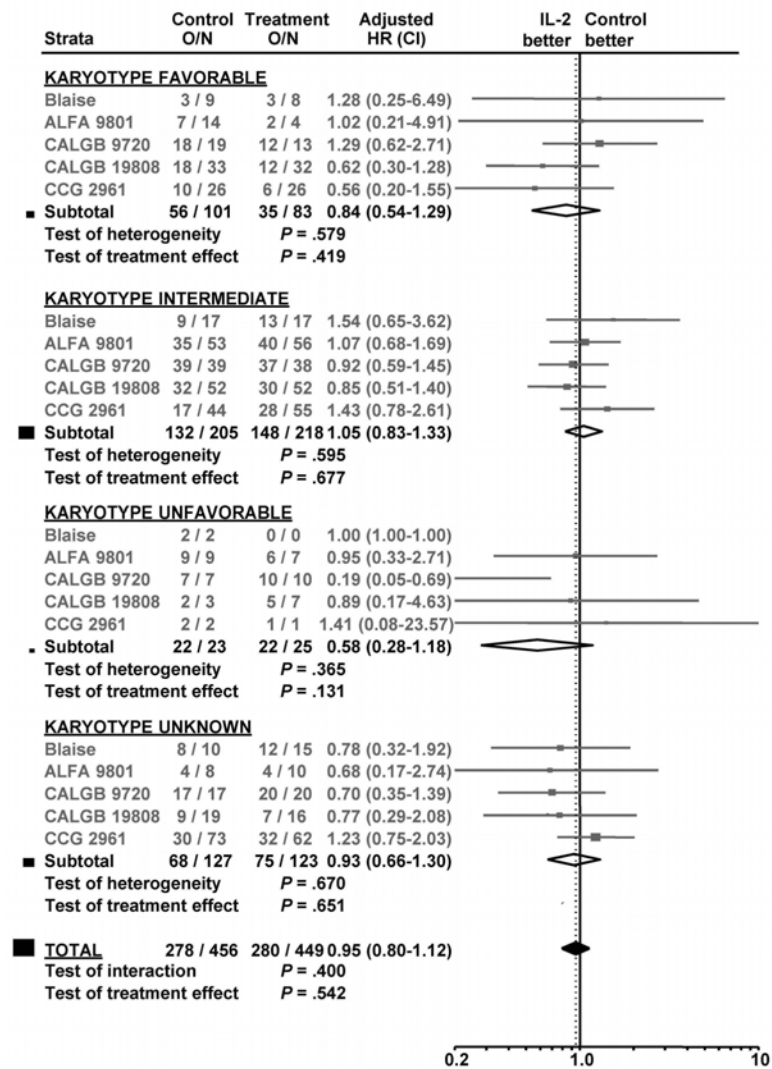
CI = confidence interval; HR = hazard ratio; IL-2 = interleukin-2; LFS = leukemia-free survival; O/N = event rate per arm where O is the number of observed events (relapse or death) and N is the sample size; OS = overall survival; RCTs = randomized controlled trials.
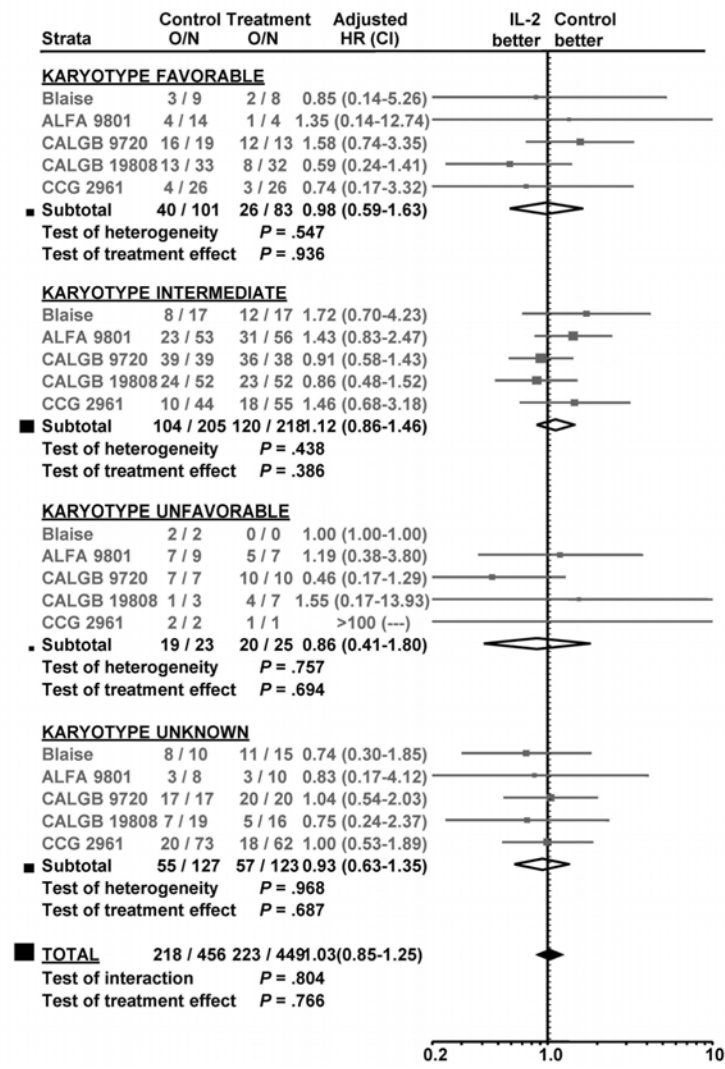
Figure S4. Forest plots of HRs for the benefit of IL-2 monotherapy in terms of LFS (A) and OS (B) by four karyotype categories (favorable vs intermediate vs unfavorable vs unknown)
CI = confidence interval; HR = hazard ratio; IL-2 = interleukin-2; LFS = leukemia-free survival; O/N = event rate per arm where O is the number of observed events (relapse or death) and N is the sample size; OS = overall survival; RCTs = randomized controlled trials.
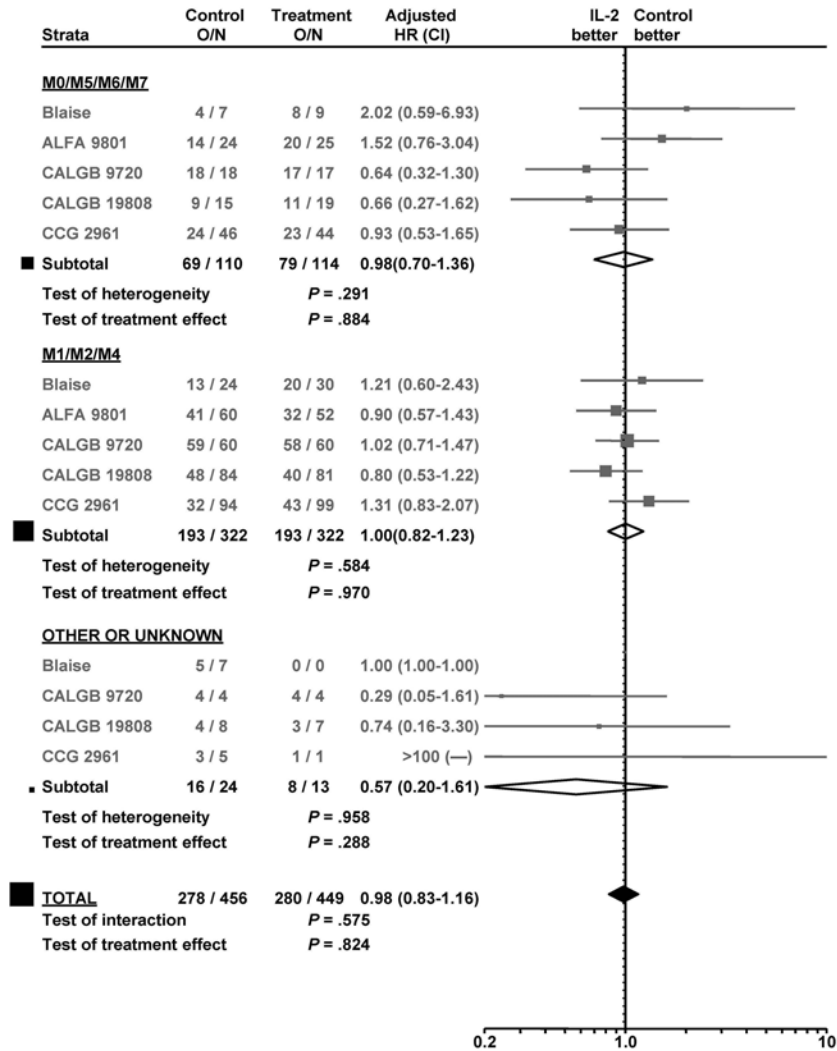
A. Effect on LFS

Strata	Control O/N	Treatment O/N	Adjusted HR (CI)	IL-2 better	Control better
M0/M5/M6/M7					
Blaise	4 / 7	8 / 9	2.02 (0.59-6.93)		
ALFA 9801	14 / 24	20 / 25	1.52 (0.76-3.04)		
CALGB 9720	18 / 18	17 / 17	0.64 (0.32-1.30)		
CALGB 19808	9 / 15	11 / 19	0.66 (0.27-1.62)		
CCG 2961	24 / 46	23 / 44	0.93 (0.53-1.65)		
■ Subtotal	69 / 110	79 / 114	0.98 (0.70-1.36)		
Test of heterogeneity			P = .291		
Test of treatment effect			P = .884		
M1/M2/M4					
Blaise	13 / 24	20 / 30	1.21 (0.60-2.43)		
ALFA 9801	41 / 60	32 / 52	0.90 (0.57-1.43)		
CALGB 9720	59 / 60	58 / 60	1.02 (0.71-1.47)		
CALGB 19808	48 / 84	40 / 81	0.80 (0.53-1.22)		
CCG 2961	32 / 94	43 / 99	1.31 (0.83-2.07)		
■ Subtotal	193 / 322	193 / 322	1.00 (0.82-1.23)		
Test of heterogeneity			P = .584		
Test of treatment effect			P = .970		
OTHER OR UNKNOWN					
Blaise	5 / 7	0 / 0	1.00 (1.00-1.00)		
CALGB 9720	4 / 4	4 / 4	0.29 (0.05-1.61)		
CALGB 19808	4 / 8	3 / 7	0.74 (0.16-3.30)		
CCG 2961	3 / 5	1 / 1	>100 (—)		
▪ Subtotal	16 / 24	8 / 13	0.57 (0.20-1.61)		
Test of heterogeneity			P = .958		
Test of treatment effect			P = .288		
TOTAL	278 / 456	280 / 449	0.98 (0.83-1.16)		
Test of interaction			P = .575		
Test of treatment effect			P = .824		

B. Effect on OS

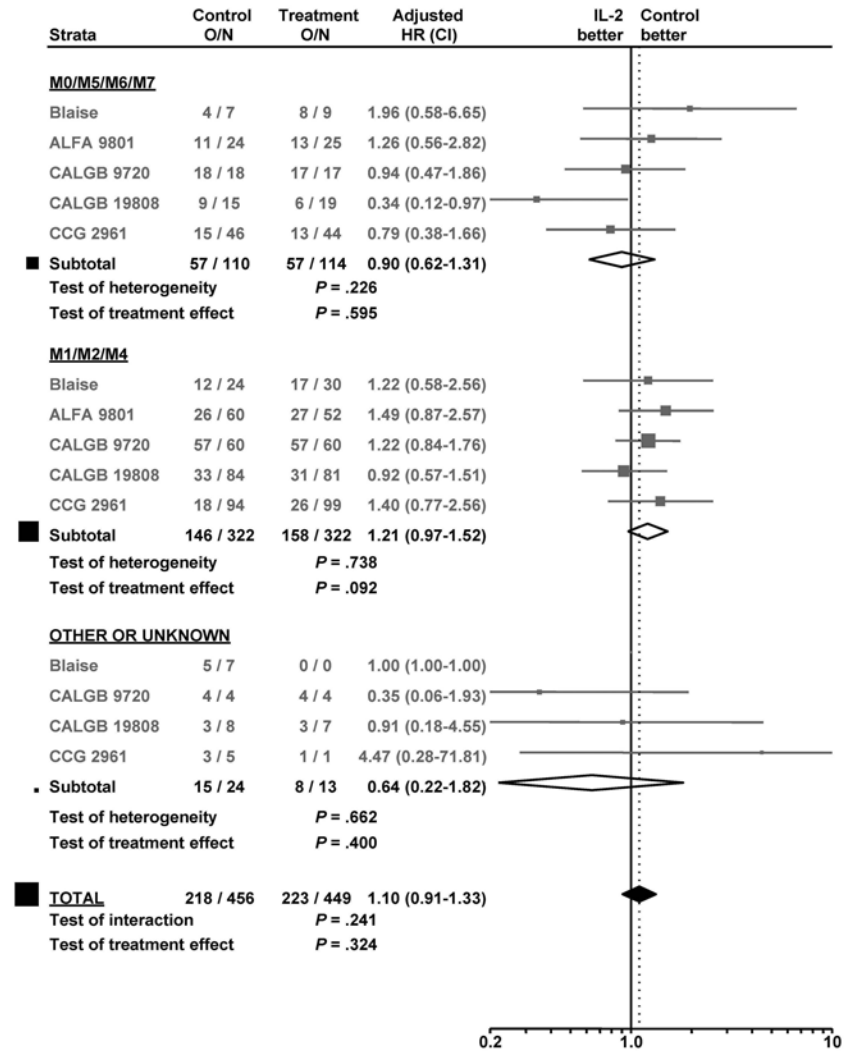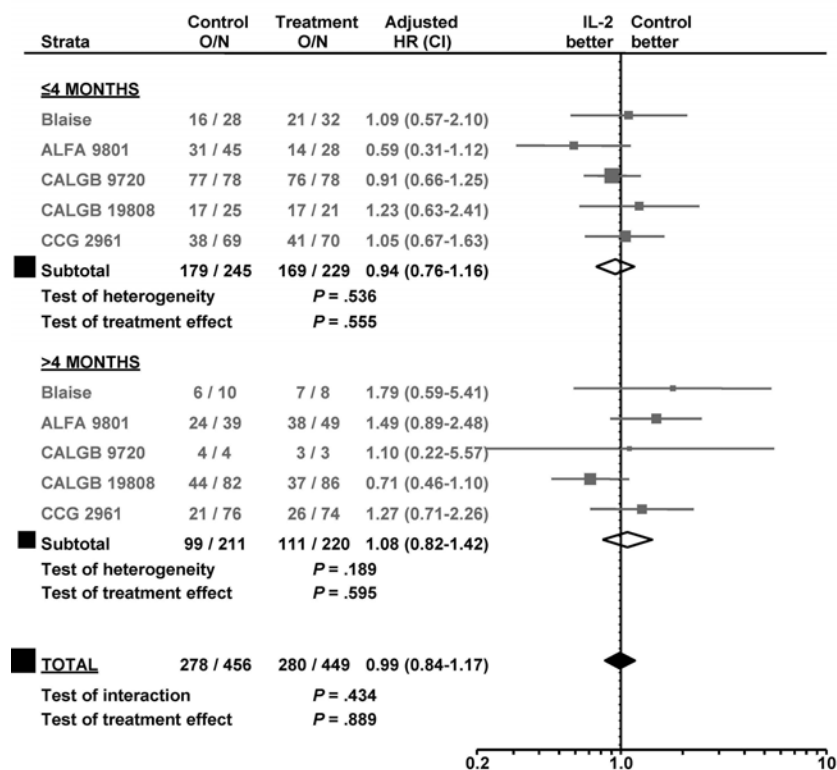| Strata	Control O/N	Treatment O/N	Adjusted HR (CI)	IL-2 better	Control better
M0/M5/M6/M7					
Blaise	4 / 7	8 / 9	1.96 (0.58-6.65)		
ALFA 9801	11 / 24	13 / 25	1.26 (0.56-2.82)		
CALGB 9720	18 / 18	17 / 17	0.94 (0.47-1.86)		
CALGB 19808	9 / 15	6 / 19	0.34 (0.12-0.97)		
CCG 2961	15 / 46	13 / 44	0.79 (0.38-1.66)		
■ Subtotal	57 / 110	57 / 114	0.90 (0.62-1.31)		
Test of heterogeneity			P = .226		
Test of treatment effect			P = .595		
M1/M2/M4					
Blaise	12 / 24	17 / 30	1.22 (0.58-2.56)		
ALFA 9801	26 / 60	27 / 52	1.49 (0.87-2.57)		
CALGB 9720	57 / 60	57 / 60	1.22 (0.84-1.76)		
CALGB 19808	33 / 84	31 / 81	0.92 (0.57-1.51)		
CCG 2961	18 / 94	26 / 99	1.40 (0.77-2.56)		
■ Subtotal	146 / 322	158 / 322	1.21 (0.97-1.52)		
Test of heterogeneity			P = .738		
Test of treatment effect			P = .092		
OTHER OR UNKNOWN					
Blaise	5 / 7	0 / 0	1.00 (1.00-1.00)		
CALGB 9720	4 / 4	4 / 4	0.35 (0.06-1.93)		
CALGB 19808	3 / 8	3 / 7	0.91 (0.18-4.55)		
CCG 2961	3 / 5	1 / 1	4.47 (0.28-71.81)		
▪ Subtotal	15 / 24	8 / 13	0.64 (0.22-1.82)		
Test of heterogeneity			P = .662		
Test of treatment effect			P = .400		
TOTAL	218 / 456	223 / 449	1.10 (0.91-1.33)		
Test of interaction			P = .241		
Test of treatment effect			P = .324		

Figure S5. Forest plots of HRs for the benefit of IL-2 monotherapy in terms of LFS (A) and OS (B) by three AML subtype categories (M0-M5-M6-M7 vs M1-M2-M4 vs other or unknown)
AML = acute myeloid leukemia; CI = confidence interval; HR = hazard ratio; IL-2 = interleukin-2; LFS = leukemia-free survival; O/N = event rate per arm where O is the number of observed events (relapse or death) and N is the sample size; OS = overall survival; RCTs = randomized controlled trials.

A. Effect on LFS

Strata	Control O/N	Treatment O/N	Adjusted HR (CI)	IL-2 better / Control better
≤4 MONTHS				
Blaise	16 / 28	21 / 32	1.09 (0.57-2.10)	
ALFA 9801	31 / 45	14 / 28	0.59 (0.31-1.12)	
CALGB 9720	77 / 78	76 / 78	0.91 (0.66-1.25)	
CALGB 19808	17 / 25	17 / 21	1.23 (0.63-2.41)	
CCG 2961	38 / 69	41 / 70	1.05 (0.67-1.63)	
Subtotal	179 / 245	169 / 229	0.94 (0.76-1.16)	
Test of heterogeneity		$P = .536$		
Test of treatment effect		$P = .555$		
>4 MONTHS				
Blaise	6 / 10	7 / 8	1.79 (0.59-5.41)	
ALFA 9801	24 / 39	38 / 49	1.49 (0.89-2.48)	
CALGB 9720	4 / 4	3 / 3	1.10 (0.22-5.57)	
CALGB 19808	44 / 82	37 / 86	0.71 (0.46-1.10)	
CCG 2961	21 / 76	26 / 74	1.27 (0.71-2.26)	
Subtotal	99 / 211	111 / 220	1.08 (0.82-1.42)	
Test of heterogeneity		$P = .189$		
Test of treatment effect		$P = .595$		
TOTAL	278 / 456	280 / 449	0.99 (0.84-1.17)	
Test of interaction		$P = .434$		
Test of treatment effect		$P = .889$		

Scale: 0.2 — 1.0 — 10

B. Effect on OS

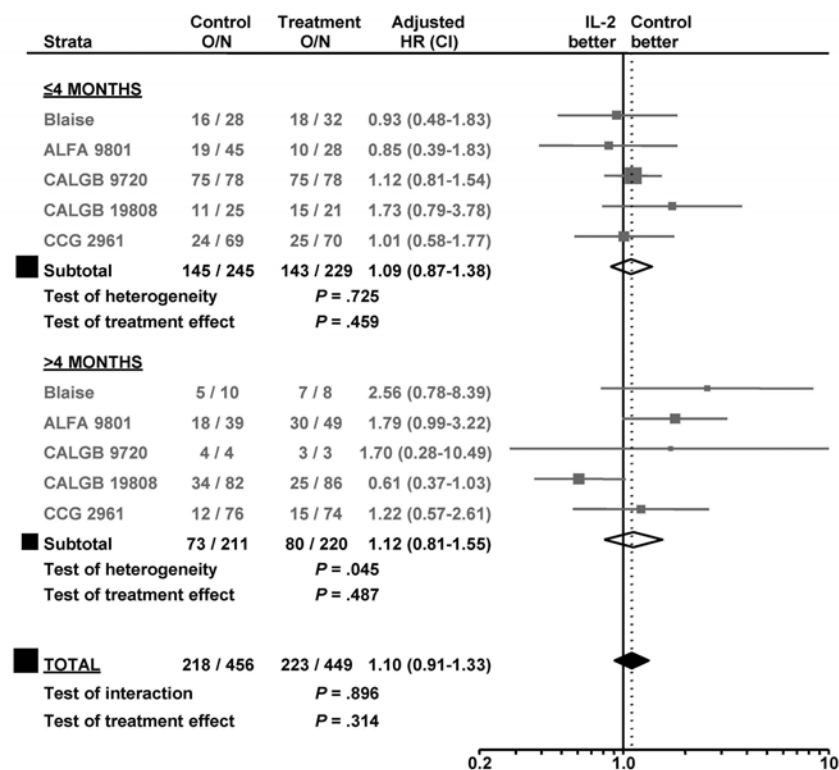| Strata	Control O/N	Treatment O/N	Adjusted HR (CI)	IL-2 better / Control better
≤4 MONTHS				
Blaise	16 / 28	18 / 32	0.93 (0.48-1.83)	
ALFA 9801	19 / 45	10 / 28	0.85 (0.39-1.83)	
CALGB 9720	75 / 78	75 / 78	1.12 (0.81-1.54)	
CALGB 19808	11 / 25	15 / 21	1.73 (0.79-3.78)	
CCG 2961	24 / 69	25 / 70	1.01 (0.58-1.77)	
Subtotal	145 / 245	143 / 229	1.09 (0.87-1.38)	
Test of heterogeneity		$P = .725$		
Test of treatment effect		$P = .459$		
>4 MONTHS				
Blaise	5 / 10	7 / 8	2.56 (0.78-8.39)	
ALFA 9801	18 / 39	30 / 49	1.79 (0.99-3.22)	
CALGB 9720	4 / 4	3 / 3	1.70 (0.28-10.49)	
CALGB 19808	34 / 82	25 / 86	0.61 (0.37-1.03)	
CCG 2961	12 / 76	15 / 74	1.22 (0.57-2.61)	
Subtotal	73 / 211	80 / 220	1.12 (0.81-1.55)	
Test of heterogeneity		$P = .045$		
Test of treatment effect		$P = .487$		
TOTAL	218 / 456	223 / 449	1.10 (0.91-1.33)	
Test of interaction		$P = .896$		
Test of treatment effect		$P = .314$		

Scale: 0.2 — 1.0 — 10

Figure S6. Forest plots of HRs for the benefit of IL-2 monotherapy in terms of LFS (A) and OS (B) by time from CR (≤4 months vs >4 months)

CI = confidence interval; CR = complete remission; HR = hazard ratio; IL-2 = interleukin-2;
LFS = leukemia-free survival; O/N = event rate per arm where O is the number of observed events (relapse or death) and N is the sample size; OS = overall survival; RCTs = randomized controlled trials.