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Supplementary Data

Supplementary Tables

Supplementary Table 1. Search strategy for Embase

#1	Cytokine-Induced Killer Cells/
#2	cytokine induced killer cell*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
#3	(cytokine induced adj6 killer cell*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
#4	2 or 3
#5	1 or 4
#6	*colorectal cancer*/ or colorectal neoplasm*.mp. or colon cancer*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
#7	exp colon tumor/
#8	exp rectum tumor/
#9	6 or 7 or 8
#10	5 or 9

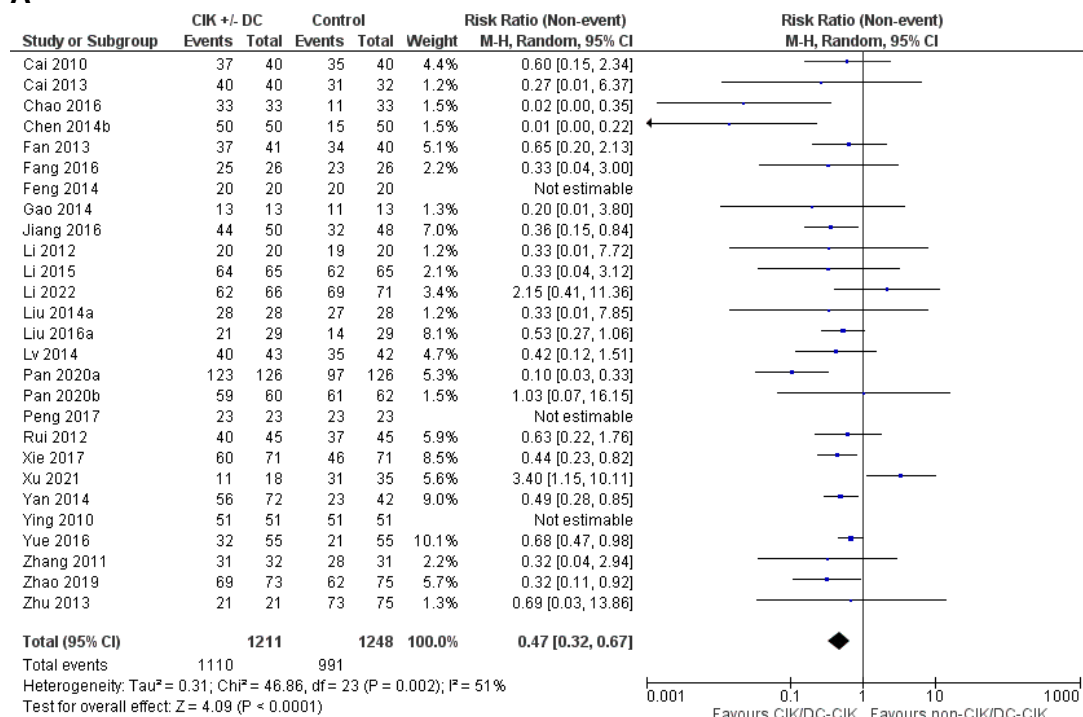**Supplementary Table 2.** Search strategy for MEDLINE

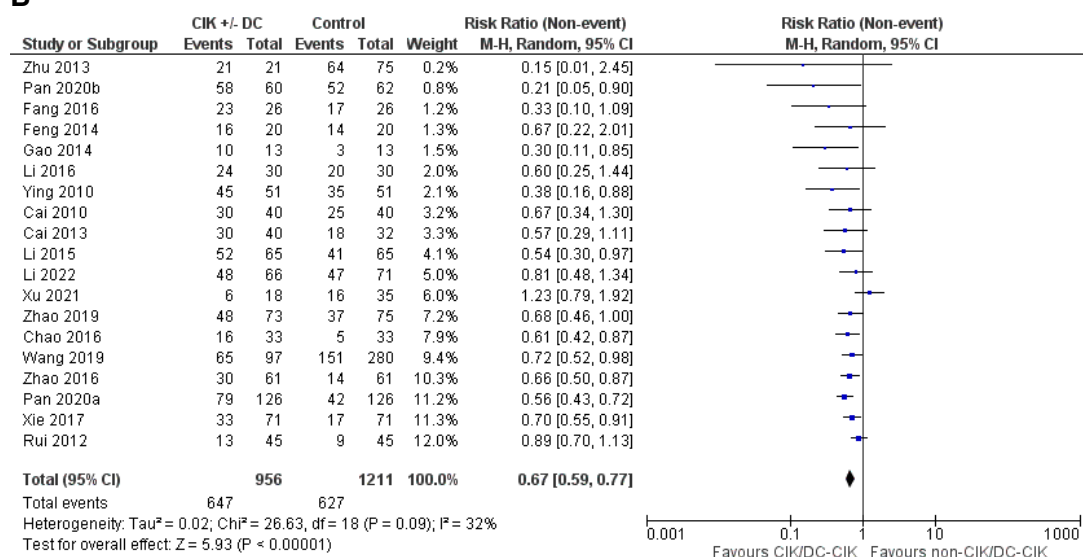|	
#1	Cytokine-Induced Killer Cells/
#2	cytokine induced killer cell*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol
#3	(cytokine induced adj6 killer cell*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
#4	2 or 3
#5	1 or 4
#6	exp Colorectal Neoplasms/
#7	*colorectal cancer*/ or colorectal neoplasm*.mp. or colon cancer*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
#8	6 or 7
#9	5 and 8

Supplementary Figures

Supplementary Figure 1. Risk of bias assessment summary

A

Study or Subgroup	CIK +/- DC Events	Total	Control Events	Total	Weight	Risk Ratio (Non-event) M-H, Random, 95% CI
Cai 2010	37	40	35	40	4.4%	0.60 [0.15, 2.34]
Cai 2013	40	40	31	32	1.2%	0.27 [0.01, 6.37]
Chao 2016	33	33	11	33	1.5%	0.02 [0.00, 0.35]
Chen 2014b	50	50	15	50	1.5%	0.01 [0.00, 0.22]
Fan 2013	37	41	34	40	5.1%	0.65 [0.20, 2.13]
Fang 2016	25	26	23	26	2.2%	0.33 [0.04, 3.00]
Feng 2014	20	20	20	20		Not estimable
Gao 2014	13	13	11	13	1.3%	0.20 [0.01, 3.80]
Jiang 2016	44	50	32	48	7.0%	0.36 [0.15, 0.84]
Li 2012	20	20	19	20	1.2%	0.33 [0.01, 7.72]
Li 2015	64	65	62	65	2.1%	0.33 [0.04, 3.12]
Li 2022	62	66	69	71	3.4%	2.15 [0.41, 11.36]
Liu 2014a	28	28	27	28	1.2%	0.33 [0.01, 7.85]
Liu 2016a	21	29	14	29	8.1%	0.53 [0.27, 1.06]
Lv 2014	40	43	35	42	4.7%	0.42 [0.12, 1.51]
Pan 2020a	123	126	97	126	5.3%	0.10 [0.03, 0.33]
Pan 2020b	59	60	61	62	1.5%	1.03 [0.07, 16.15]
Peng 2017	23	23	23	23		Not estimable
Rui 2012	40	45	37	45	5.9%	0.63 [0.22, 1.76]
Xie 2017	60	71	46	71	8.5%	0.44 [0.23, 0.82]
Xu 2021	11	18	31	35	5.6%	3.40 [1.15, 10.11]
Yan 2014	56	72	23	42	9.0%	0.49 [0.28, 0.85]
Ying 2010	51	51	51	51		Not estimable
Yue 2016	32	55	21	55	10.1%	0.68 [0.47, 0.98]
Zhang 2011	31	32	28	31	2.2%	0.32 [0.04, 2.94]
Zhao 2019	69	73	62	75	5.7%	0.32 [0.11, 0.92]
Zhu 2013	21	21	73	75	1.3%	0.69 [0.03, 13.86]
Total (95% CI)		**1211**		**1248**	**100.0%**	**0.47 [0.32, 0.67]**
Total events	1110		991			

Heterogeneity: Tau² = 0.31; Chi² = 46.86, df = 23 (P = 0.002); I² = 51%
Test for overall effect: Z = 4.09 (P < 0.0001)

Favours CIK/DC-CIK   Favours non-CIK/DC-CIK

B

Study or Subgroup	CIK +/- DC Events	Total	Control Events	Total	Weight	Risk Ratio (Non-event) M-H, Random, 95% CI
Zhu 2013	21	21	64	75	0.2%	0.15 [0.01, 2.45]
Pan 2020b	58	60	52	62	0.8%	0.21 [0.05, 0.90]
Fang 2016	23	26	17	26	1.2%	0.33 [0.10, 1.09]
Feng 2014	16	20	14	20	1.3%	0.67 [0.22, 2.01]
Gao 2014	10	13	3	13	1.5%	0.30 [0.11, 0.85]
Li 2016	24	30	20	30	2.0%	0.60 [0.25, 1.44]
Ying 2010	45	51	35	51	2.1%	0.38 [0.16, 0.88]
Cai 2010	30	40	25	40	3.2%	0.67 [0.34, 1.30]
Cai 2013	30	40	18	32	3.3%	0.57 [0.29, 1.11]
Li 2015	52	65	41	65	4.1%	0.54 [0.30, 0.97]
Li 2022	48	66	47	71	5.0%	0.81 [0.48, 1.34]
Xu 2021	6	18	16	35	6.0%	1.23 [0.79, 1.92]
Zhao 2019	48	73	37	75	7.2%	0.68 [0.46, 1.00]
Chao 2016	16	33	5	33	7.9%	0.61 [0.42, 0.87]
Wang 2019	65	97	151	280	9.4%	0.72 [0.52, 0.98]
Zhao 2016	30	61	14	61	10.3%	0.66 [0.50, 0.87]
Pan 2020a	79	126	42	126	11.2%	0.56 [0.43, 0.72]
Xie 2017	33	71	17	71	11.3%	0.70 [0.55, 0.91]
Rui 2012	13	45	9	45	12.0%	0.89 [0.70, 1.13]
Total (95% CI)		**956**		**1211**	**100.0%**	**0.67 [0.59, 0.77]**
Total events	647		627			

Heterogeneity: Tau² = 0.02; Chi² = 26.63, df = 18 (P = 0.09); I² = 32%
Test for overall effect: Z = 5.93 (P < 0.00001)

Favours CIK/DC-CIK   Favours non-CIK/DC-CIK

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Study or Subgroup	CIK +/- DC Events	Total	Control Events	Total	Weight	Risk Ratio (Non-event) M-H, Random, 95% CI
Chao 2016	10	33	20	33	10.1%	1.77 [1.10, 2.86]
Gao 2014	10	13	2	13	4.2%	0.27 [0.10, 0.76]
Li 2015	43	65	29	65	11.4%	0.61 [0.41, 0.92]
Li 2022	44	66	32	71	11.5%	0.61 [0.41, 0.91]
Pan 2020a	63	126	33	126	15.0%	0.68 [0.55, 0.83]
Pan 2020b	53	60	45	62	5.8%	0.43 [0.19, 0.95]
Wang 2019	72	97	142	280	12.3%	0.52 [0.37, 0.75]
Xie 2017	30	71	14	71	14.6%	0.72 [0.57, 0.91]
Xu 2021	3	18	4	35	14.5%	0.94 [0.74, 1.19]
Zhu 2013	21	21	57	75	0.7%	0.09 [0.01, 1.49]
Total (95% CI)		570		831	100.0%	0.69 [0.54, 0.88]
Total events	349		378			

Heterogeneity: Tau² = 0.09; Chi² = 33.52, df = 9 (P = 0.0001); I² = 73%
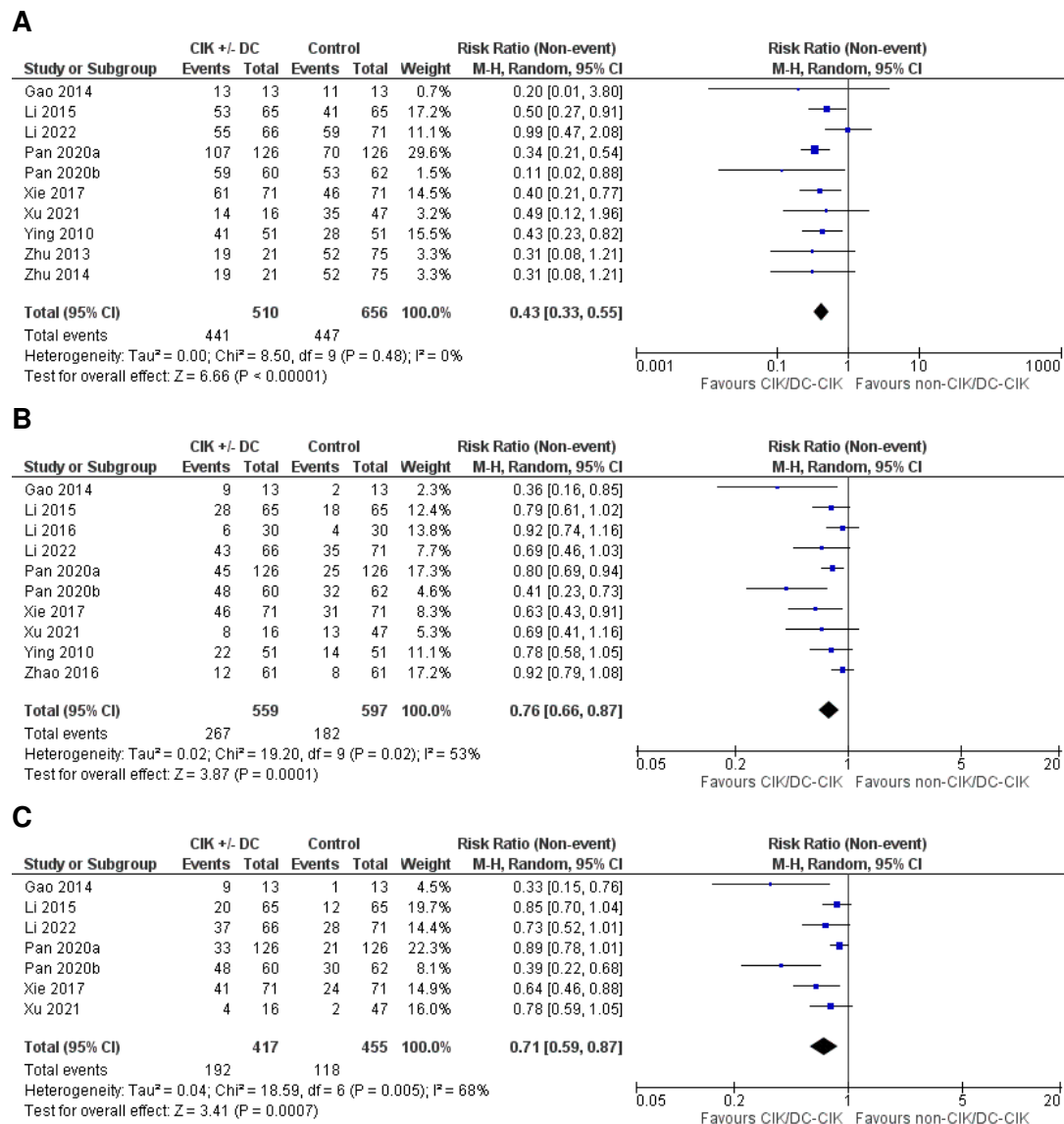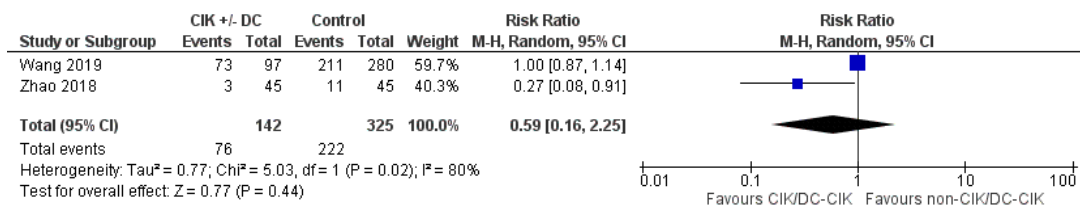Test for overall effect: Z = 3.04 (P = 0.002)

Supplementary Figure 2. CIK/DC-CIK therapy versus non-CIK/DC-CIK therapy for (A) 1-year, (B) 3-year and (C) 5-year overall survival (OS) rates. Twenty-seven studies involving 2,459 patients, nineteen studies involving 2,167 patients and ten studies involving 1,401 patients contributed data to 1-, 3- and 5-year OS rate analysis respectively. CIK, cytokine-induced killer cell; DC, dendritic cell.

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A

B

C

Supplementary Figure 3. CIK/DC-CIK therapy versus non-CIK/DC-CIK therapy for (A) 1-year, (B) 3-year and (C) 5-year progression-free survival (PFS) rates. Ten studies involving 1,166 patients, ten studies involving 1,156 patients and seven studies involving 872 patients contributed data to 1-, 3- and 5-year PFS rate analysis respectively. CIK, cytokine-induced killer cell; DC, dendritic cell.

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Supplementary Figure 4. CIK/DC-CIK therapy versus non-CIK/DC-CIK therapy on any adverse events. Two studies involving 467 patients contributed data to any adverse events analysis. CIK, cytokine-induced killer cell; DC, dendritic cell.

A
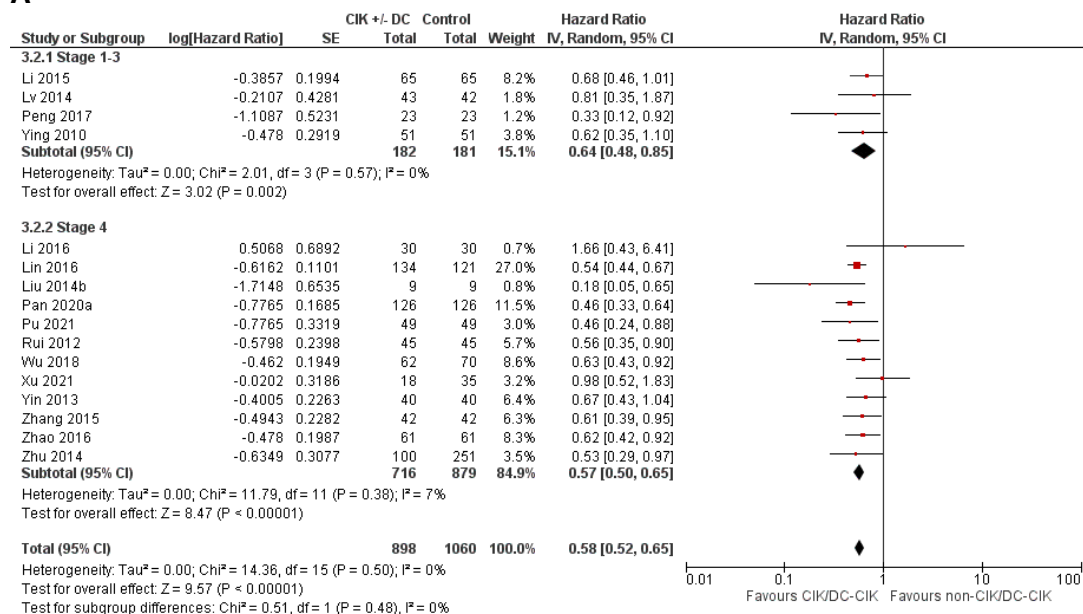
B
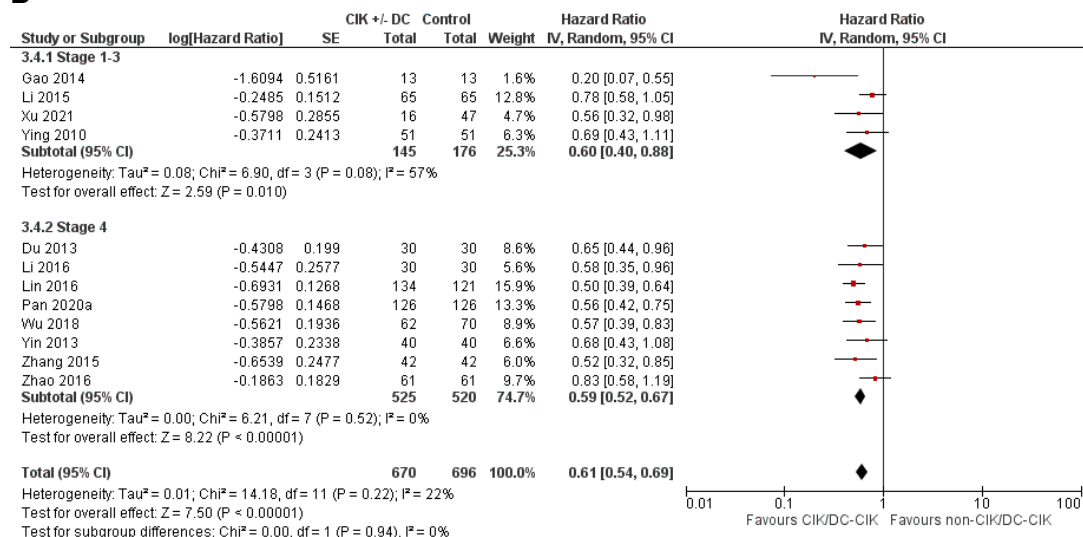
Supplementary Figure 5. Subgroup analysis by disease stage for (A) overall survival (OS) and (B) progression-free survival (PFS) between CIK/DC-CIK therapy versus non-CIK/DC-CIK therapy. Sixteen studies involving 1,958 patients and twelve studies involving 1,366 patients contributed data to OS and PFS analysis respectively. CIK, cytokine-induced killer cell; DC, dendritic cell.