

Figure S2: Forest plot for haematological adverse effects.

	N+I		Norla	lone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
4.3.1 N+I Vs I alone							
Hodi 2016 (CheckMate 069)	46	95	16	47	6.7%	1.42 [0.91, 2.23]	+
Hodi 2018 (CheckMate 067)	182	313	139	311	9.7%	1.30 [1.11, 1.52]	<del></del>
Larkin 2015	175	314	139	315	9.7%	1.26 [1.08, 1.48]	
Larkin 2019	183	313	141	311	9.7%	1.29 [1.11, 1.50]	<del></del>
Postow 2015	64	95	23	45	8.1%	1.32 [0.96, 1.81]	<del>  •</del>
Wolchok 2017	182	313	140	311	9.7%	1.29 [1.11, 1.51]	
Subtotal (95% CI)		1443		1340	53.6%	1.29 [1.20, 1.39]	♦
Total events	832		598				
Heterogeneity: Tau2 = 0.00; Ch	ni² = 0.28,	df = 5 (	P = 1.00)	$  \mathbf{r}   = 0\%$	5		
Test for overall effect: $Z = 6.74$	(P < 0.00	001)					
4.3.2 N+I Vs N alone							
Amaria 2018	9	11	1	12	1.0%	9.82 [1.47, 65.45]	
Hodi 2018 (CheckMate 067)	182	313	77	313	9.2%	2.36 [1.91, 2.93]	
Larkin 2015	175	314	64	316	8.9%	2.75 [2.16, 3.50]	
Larkin 2019	183	313	78	313	9.2%	2.35 [1.89, 2.91]	
Long 2018	35	35	15	25	8.1%	1.65 [1.20, 2.28]	<del></del>
NCT02731729 (2021)	1	10	3	9	0.8%	0.30 [0.04, 2.39]	<del></del>
Wolchok 2017	182	313	74	313	9.1%	2.46 [1.97, 3.07]	
Subtotal (95% CI)		1309		1301	46.4%	2.32 [1.95, 2.75]	•
Total events	767		312				
Heterogeneity: Tau <sup>2</sup> = 0.02; Ch	$ni^2 = 12.72$	df = 6	(P = 0.06)	$(1)^2 = 5$	3%		
Test for overall effect: $Z = 9.57$	(P < 0.00	001)					
Total (95% CI)		2752		2641	100.0%	1.69 [1.39, 2.06]	•
Total events	1599		910			- ' -	
Heterogeneity: Tau <sup>2</sup> = 0.10; Ch		4. df=		.000011	: I² = 88%	1	+ + +
Test for overall effect: Z = 5.29			(, 0	,			0.2 0.5 1 2
Test for subgroup differences:		/	- 4 (D - C			-~	Favours [N+I] Favours [N or I alone]

Figure S3: Forest plot for gastrointestinal adverse effects.

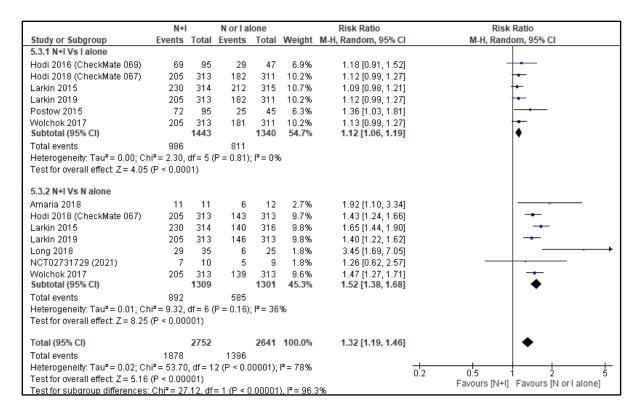


Figure S4: Forest plot for dermatological adverse effects.

	N+I N or I alone					Risk Ratio		Risk Ratio		
Study or Subgroup	<b>Events</b>	Total	<b>Events</b>	Total	Weight	M-H, Fixed, 95% CI		M-H, Fixe	d, 95% CI	
7.3.1 N+I Vs I alone										
Hodi 2016 (CheckMate 069)	10	95	1	47	3.7%	4.95 [0.65, 37.51]			-	
Hodi 2018 (CheckMate 067)	23	313	5	311	13.8%	4.57 [1.76, 11.87]			-	
Larkin 2019	23	313	5	311	13.8%	4.57 [1.76, 11.87]			-	
Postow 2015	10	95	2	45	7.5%	2.37 [0.54, 10.36]			•	
Wolchok 2017	22	313	5	311	13.8%	4.37 [1.68, 11.40]				
Subtotal (95% CI)		1129		1025	52.7%	4.23 [2.57, 6.97]				
Total events	88		18							
Heterogeneity: Chi <sup>2</sup> = 0.67, df:	= 4 (P = 0.	95); l² =	= 0%							
Test for overall effect: Z = 5.66	(P < 0.00)	001)								
7.3.2 N+I Vs N alone										
Amaria 2018	1	11	1	12	2.6%	1.09 [0.08, 15.41]	<del></del>		•	
Hodi 2018 (CheckMate 067)	23	313	5	313	13.8%	4.60 [1.77, 11.95]			-	
Larkin 2019	23	313	5	313	13.8%	4.60 [1.77, 11.95]			-	
Long 2018	5	35	1	25	3.2%	3.57 [0.44, 28.72]			•	
Wolchok 2017	22	313	5	313	13.8%	4.40 [1.69, 11.47]				
Subtotal (95% CI)		985		976	47.3%	4.28 [2.54, 7.19]				
Total events	74		17							
Heterogeneity: Chi <sup>2</sup> = 1.10, df:	= 4 (P = 0.	89); l² =	= 0%							
Test for overall effect: Z = 5.48	(P < 0.00)	001)								
Total (95% CI)		2114		2001	100.0%	4.25 [2.97, 6.10]			•	
Total events	162		35							
Heterogeneity: Chi <sup>2</sup> = 1.77, df:	= 9 (P = 0.	99); l² =	= 0%				0.1 0.	2 0.5 1	<del></del>	
Test for overall effect: Z = 7.88	(P < 0.00)	001)					0.1 0.		2 5 1 Favours [N or I alone]	
Test for subgroup differences	: Chi² = 0.0	00. df=	1 (P = 0.	98). I²=	0%			Favours [N+1]	Favours [IN OFF alone]	

Figure S5: Forest plot for pulmonary adverse effects.

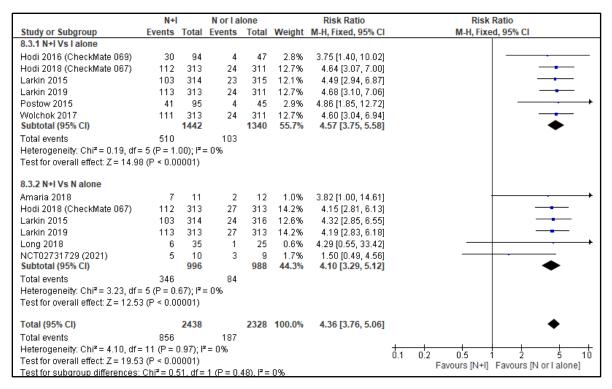


Figure S6: Forest plot for liver adverse effects.

	N+l		Norla	lone		Risk Ratio	Risk Ratio		
Study or Subgroup	<b>Events Total</b>		Events Total		Weight	M-H, Random, 95% CI	M-H, Random, 95% CI		
9.3.1 N+I Vs I alone									
Hodi 2016 (CheckMate 069)	30	94	4	47	3.3%	3.75 [1.40, 10.02]	· · · · · · · · · · · · · · · · · · ·		
Hodi 2018 (CheckMate 067)	117	313	40	311	12.1%	2.91 [2.10, 4.01]	<del></del>		
Larkin 2015	47	314	13	315	6.8%	3.63 [2.00, 6.57]			
Larkin 2019	114	313	29	311	10.8%	3.91 [2.68, 5.69]			
Postow 2015	26	95	10	45	6.2%	1.23 [0.65, 2.33]			
Wolchok 2017	111	313	29	311	10.8%	3.80 [2.61, 5.55]			
Subtotal (95% CI)		1442		1340	50.0%	3.08 [2.29, 4.14]	•		
Total events	445		125						
Heterogeneity: Tau² = 0.07; Cl			(P = 0.05)	5); I² = 5	5%				
Test for overall effect: Z = 7.47	(P < 0.00	001)							
9.3.2 N+I Vs N alone									
Amaria 2018	8	11	1	12	1.0%	8.73 [1.29, 59.00]			
Hodi 2018 (CheckMate 067)	117	313	52	313	13.0%	2.25 [1.69, 3.00]	_ <del>-</del>		
Larkin 2015	47	314	27	316	9.3%	1.75 [1.12, 2.74]	<del></del>		
Larkin 2019	114	313	48	313	12.7%	2.38 [1.76, 3.20]	_ <del></del>		
Long 2018	13	35	1	15	1.0%	5.57 [0.80, 38.85]	+		
NCT02731729 (2021)	0	10	1	9	0.4%	0.30 [0.01, 6.62]	+ -		
Wolchok 2017	111	313	49	313	12.7%	2.27 [1.68, 3.05]			
Subtotal (95% CI)		1309		1291	50.0%	2.24 [1.91, 2.62]	•		
Total events	410		179						
Heterogeneity: Tau <sup>2</sup> = 0.00; Cl	$ni^2 = 5.73$ ,	df = 6 (	P = 0.45)	$     ^2 = 0 \%$	6				
Test for overall effect: Z = 10.0	4 (P < 0.0	0001)							
Total (95% CI)		2751		2631	100.0%	2.63 [2.16, 3.21]	•		
Total events	855		304						
Heterogeneity: Tau² = 0.06; Cl	ni² = 25.25	i, df = 1	2 (P = 0.0	01); l² =	52%		0.2 0.5 1 2 5		
Test for overall effect: Z = 9.65			,				0.2		
Test for subgroup differences	•		1 (P = 0.1	06). I²=	71.3%		ravours (in+i) Favours (in or raione)		

Figure S7: Forest plot for endocrine adverse effect