Role of Image-defined risk factors in clinical practice of neuroblastoma: A systematic review and meta-analysis

Qiyang Shen¹, Qi Han¹, Hanjun Yin², Li Lu³, Tao Li¹, and Jianfeng Zhou¹

¹Children's Hospital of Nanjing Medical University ²Suqian People's Hospital of Nanjing Drum-Tower Hospital Group ³Jiangsu Provincial Hospital of Chinese Medicine

June 22, 2020

Abstract

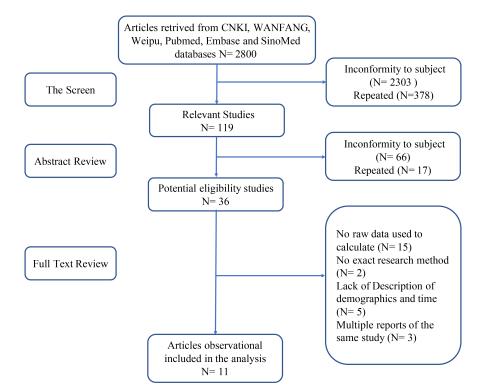
Purpose: To assess the role of image-defined risk factors in clinical practice of neuroblastoma. Methods: A systematic search was conducted to identify articles about IDRFs. Combined overall results were calculated using fixed effects models. Results: The literature search identified 11 articles including 1338 patients for analysis. There was no difference in amplification of MYCN and tumor site (abdominal tumor) between no IDRFs and any IDRFs group, but there was a significant increase of event free survival (OR: 2.43[1.69, 3.49]; P < 0.00001) and overall survival (OR: 3.15[1.68, 5.89]; P = 0.0004) in no IDRFs group. The incidence of complications (OR: 0.21[0.15, 0.30]; P < 0.00001) was higher in patients with any IDRFs. Furthermore, no IDRFs are correlated with higher rate of earlier INSS stage. Conclusions: IDRFs could be an important adjuvant image monitoring method in NB treatment. IDRFs are valuable to evaluate surgical indications for pediatric surgeon, regardless of surgical ability.

Hosted file

TitlePage.doc available at https://authorea.com/users/335737/articles/461544-role-of-image-defined-risk-factors-in-clinical-practice-of-neuroblastoma-a-systematic-review-and-meta-analysis

Hosted file

manuscript.docx available at https://authorea.com/users/335737/articles/461544-role-ofimage-defined-risk-factors-in-clinical-practice-of-neuroblastoma-a-systematic-reviewand-meta-analysis

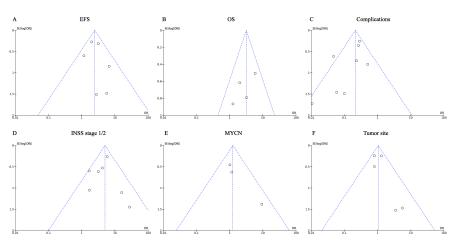


Study or Subgroup	No IDR		Any IDR		Weight	Odds Ratio M-H, Fixed, 95% CI	Vear		Odds Ratio M-H, Fixed, 95% Cl	
imon, T	195	227	105	139	50.0%	1.97 [1.15, 3.38]				
Aonclair, T	268	291	93	118	28.5%	3.13 [1.70, 5.78]				
ehara, T	30	32	18	26	3.4%	6.67 [1.27, 34.92]	2019		· · · · · · · · · · · · · · · · · · ·	_
ucas, J. T., Jr	9	9	52	67	1.8%	5.61 [0.31, 101.92]				
helps, H. M	36	41	56	65	14.4%	1.16 [0.36, 3.73]				
hang, A. A	6	6	44	53	2.0%	2.78 [0.14, 53.58]	2019			
otal (95% CI)		606		468	100.0%	2.43 [1.69, 3.49]			•	
otal events	544		368						•	
leterogeneity: Chi ² =				$^{2} = 0\%$				0.01	0.1 1 10	10
Test for overall effect:	: Z = 4.76	(P < 0	.00001)						No IDRFs Any IDRFs	
OS		_		_						
Study or Subgroup	No IDR Events		Any IDR Events		Weight	Odds Ratio M-H, Fixed, 95% CI	Year		Odds Ratio M-H, Fixed, 95% Cl	
Simon, T	222	227	133	139	31.9%	2.00 [0.60, 6.69]				
Monclair, T	285	291	105	118	27.1%	5.88 [2.18, 15.87]				
Pohl, A	14	16	59	86	20.3%	3.20 [0.68, 15.09]			+	
ehara, T	32	32	26	26		Not estimable	2019			
Phelps, H. M	28	31	22	25	20.7%	1.27 [0.23, 6.93]	2019			
Fotal (95% CI)		507		204	100.0%	3 15 [1 68 5 80]				
fotal (95% CI) Fotal events	581	597	345	594	100.0%	3.15 [1.68, 5.89]				
lotal events leterogeneity: Chi ² =		= 3 (P		² = 5%				H		
Test for overall effect:				/0				0.01	0.1 İ 10 No IDRFs Any IDRFs	10
									NO IDRES ANY IDRES	
Complications										
	No IDF		Any IDF			Odds Ratio			Odds Ratio	
Study or Subgroup	Events		Events			M-H, Fixed, 95% CI			M-H, Fixed, 95% Cl	
Simon, T	34	227	53	139	39.7%	0.29 [0.17, 0.47]				
Günther, P	0	21	7	39	3.7%	0.10 [0.01, 1.86]		•		
Monclair, T Yoneda. A	15 0	291 21	20 17	118 61	19.2% 6.4%	0.27 [0.13, 0.54] 0.06 [0.00, 1.03]		•		
Pohl, A	2	16	19	86	3.7%	0.50 [0.11, 2.41]				
Tanaka, Y	ō	15	4	5	4.5%	0.01 [0.00, 0.31]		←		
Phelps, H. M	3	49	8	37	6.1%	0.24 [0.06, 0.96]				
Chenji	7	29	40	46	16.7%	0.05 [0.01, 0.16]				
Total (05%/ Ct)				F 7 -	100 001	0.21 /0.15 0.2-1				
Fotal (95% CI)	~ ~	669	168	531	100.0%	0.21 [0.15, 0.30]			-	
Heterogeneity: Chi ² = Test for overall effect:			^o = 0.08);	I ² = 4	5%			0.01	0.1 1 10 No IDRFs Any IDRFs	10
Total events Heterogeneity: Chi ² = Test for overall effect: INSS stage 1/2 Study or Subgroup	12.81, d Z = 8.67	' (P < 0 Fs	P = 0.08); 0.00001) Any IDR	Fs		Odds Ratio M-H Fixed 95% Cl	Year	0.01	No IDRFs Any IDRFs Odds Ratio	10
Heterogeneity: Chi ² = Test for overall effect: INSS stage 1/2 Study or Subgroup	12.81, d Z = 8.67 No IDR Events	' (P < 0 Fs Total	P = 0.08); 0.00001) Any IDR Events 1	Fs Fotal	Weight	M-H, Fixed, 95% Cl		0.01	No IDRFs Any IDRFs	10
Heterogeneity: Chi ² = Fest for overall effect: INSS stage 1/2 Study or Subgroup Simon, T	12.81, d Z = 8.67	' (P < 0 Fs Total 227	P = 0.08); 0.00001) Any IDR Events 1 75	Fs Fotal	<u>Weight</u> 46.5%	M-H, Fixed, 95% Cl 5.83 [3.49, 9.73]	2008	0.01	No IDRFs Any IDRFs Odds Ratio	10
Heterogeneity: Chi ² = Fest for overall effect: INSS stage 1/2 Study or Subgroup Simon, T Sünther, P	= 12.81, d : Z = 8.67 No IDR Events 198 7	' (P < 0 Fs Total 227 21	P = 0.08); 0.00001) Any IDRI Events 1 75 9	Fs Fotal 139 39	Weight 46.5% 16.4%	М-H, Fixed, 95% Cl 5.83 [3.49, 9.73] 1.67 [0.52, 5.39]	2008 2011	0.01	No IDRFs Any IDRFs Odds Ratio	10
Heterogeneity: Chi ² = Test for overall effect:	12.81, d Z = 8.67 No IDR Events 198	' (P < 0 Fs Total 227	P = 0.08); 0.00001) Any IDR Events 1 75	Fs Fotal	<u>Weight</u> 46.5%	M-H, Fixed, 95% Cl 5.83 [3.49, 9.73]	2008 2011 2016	0.01	No IDRFs Any IDRFs Odds Ratio	10
Heterogeneity: Chi ² = Fest for overall effect: INSS stage 1/2 Study or Subgroup Jimon, T Jünther, P Yohl, A Fanaka, Y	12.81, d Z = 8.67 No IDR Events 198 7 12	r (P < 0 Fs Total 227 21 16	P = 0.08); 0.00001) Any IDR Events 1 75 9 42	Fs Total 139 39 86	Weight 46.5% 16.4% 12.9% 5.5%	M-H, Fixed, 95% Cl 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52]	2008 2011 2016 2016	0.01	No IDRFs Any IDRFs Odds Ratio	10
Heterogeneity: Chi ² = Test for overall effect: INSS stage 1/2 Study or Subgroup Jannon, T Janther, P John, A Tanaka, Y Yoneda, A Chang, A, A	12.81, d Z = 8.67 No IDR Events 198 7 12 8 31 7	r' (P < 0 Fs Total 227 21 16 15 31 8	P = 0.08); 0.00001) Any IDR Events 1 75 9 42 2 53 18	Fs Total 139 39 86 5 76 59	Weight 46.5% 16.4% 12.9% 5.5% 1.9% 2.1%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27]	2008 2011 2016 2016 2016 2019	0.01	No IDRFs Any IDRFs Odds Ratio	
Heterogeneity: Chi ² = Test for overall effect: INSS stage 1/2 Study or Subgroup Jannon, T Janther, P John, A Tanaka, Y Yoneda, A Chang, A, A	12.81, d Z = 8.67 No IDR Events 198 7 12 8 31	r (P < 0 Fs Total 227 21 16 15 31	P = 0.08); 0.00001) Any IDR Events 1 75 9 42 2 53	Fs Fotal 139 39 86 5 76	Weight 46.5% 16.4% 12.9% 5.5% 1.9%	M-H, Fixed, 95% Cl 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52]	2008 2011 2016 2016 2016 2019	0.01	No IDRFs Any IDRFs Odds Ratio	10
Heterogeneity: Chi ² = Test for overall effect: INSS stage 1/2 Study or Subgroup Jimon, T Günther, P Yohl, A Ganaka, Y Yoneda, A Yhang, A. A Yhelps, H. M	12.81, d Z = 8.67 No IDR Events 198 7 12 8 31 7	Y (P < 0 Fs Total 227 21 16 15 31 8 49	P = 0.08); 0.00001) Any IDR Events 1 75 9 42 2 53 18	Fs Total 139 39 86 5 76 59 37	Weight 46.5% 16.4% 12.9% 5.5% 1.9% 2.1% 14.7%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91]	2008 2011 2016 2016 2016 2019	0.01	No IDRFs Any IDRFs Odds Ratio	
Heterogeneity: Chi ² = Test for overall effect: INSS stage 1/2 Study or Subgroup Jannon, T Janther, P John, A Fanaka, Y Goneda, A Chang, A. A Phelps, H. M Fotal (95% CI)	: 12.81, d : Z = 8.67 No IDR <u>Events</u> 198 7 12 8 31 7 22	r' (P < 0 Fs Total 227 21 16 15 31 8	P = 0.08); 0.00001) Any IDR Events 7 9 42 2 53 18 6	Fs Total 139 39 86 5 76 59 37	Weight 46.5% 16.4% 12.9% 5.5% 1.9% 2.1%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27]	2008 2011 2016 2016 2016 2019	0.01	No IDRFs Any IDRFs Odds Ratio	
Heterogeneity: Chr ² = Frest for overall effect: INSS stage 1/2 itudy or Subgroup jimon, T Jönther, P Yohl, A Granaka, Y Yoneda, A A Ahang, A. A Yhelps, H. M Frotal (95% CI) Total events	: 12.81, d : Z = 8.67 No IDR Events 198 7 12 8 31 7 22 285	Y (P < 0 Fs Total 227 21 16 15 31 8 49 367	P = 0.08); 0.00001) Any IDR Events 1 75 9 42 2 53 18 6 205	Fs Total 139 39 86 5 76 59 37 441	Weight 46.5% 16.4% 12.9% 5.5% 1.9% 2.1% 14.7% 100.0%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91]	2008 2011 2016 2016 2016 2019		No IDRFs Any IDRFs Odds Ratio M-H, Fixed, 95% CI	-
Heterogeneity: Chi ² = Test for overall effect: INSS stage 1/2 Study or Subgroup Simon, T Guinther, P Yohl, A Granaka, Y Yoneda, A Yhapg, A, A Yhelps, H. M Total (95% Cl) Total events Heterogeneity: Chi ² =	: 12.81, d : Z = 8.67 No IDR Events 198 7 12 8 31 7 22 285 7.89, df =	r (P < 0 Fs Total 227 21 16 15 31 8 49 367 = 6 (P =	P = 0.08); 0.00001) Any IDRI Events 1 75 9 42 2 53 18 6 205 = 0.25); I ²	Fs Total 139 39 86 5 76 59 37 441	Weight 46.5% 16.4% 12.9% 5.5% 1.9% 2.1% 14.7% 100.0%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91]	2008 2011 2016 2016 2016 2019	0.01	Odds Ratio M-H, Fixed, 95% CI	-
Heterogeneity: Chi ² = Test for overall effect: INSS stage 1/2 Study or Subgroup Simon, T Zointher, P Pohl, A	: 12.81, d : Z = 8.67 No IDR Events 198 7 12 8 31 7 22 285 7.89, df =	r (P < 0 Fs Total 227 21 16 15 31 8 49 367 = 6 (P =	P = 0.08); 0.00001) Any IDRI Events 1 75 9 42 2 53 18 6 205 = 0.25); I ²	Fs Total 139 39 86 5 76 59 37 441	Weight 46.5% 16.4% 12.9% 5.5% 1.9% 2.1% 14.7% 100.0%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91]	2008 2011 2016 2016 2016 2019		No IDRFs Any IDRFs Odds Ratio M-H, Fixed, 95% CI	
Heterogeneity: Chi ² = fest for overall effect: INSS stage 1/2 itudy or Subgroup imon, T jünther, P ohl, A inana, A inang, A. A helps, H. M foral (95% CI) oral events Heterogeneity: Chi ² = fest for overall effect:	: 12.81, d : Z = 8.67 No IDR Events 198 7 12 8 31 7 22 285 7.89, df =	r (P < 0 Fs Total 227 21 16 15 31 8 49 367 = 6 (P =	P = 0.08); 0.00001) Any IDRI Events 1 75 9 42 2 53 18 6 205 = 0.25); I ²	Fs Total 139 39 86 5 76 59 37 441	Weight 46.5% 16.4% 12.9% 5.5% 1.9% 2.1% 14.7% 100.0%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91]	2008 2011 2016 2016 2016 2019		Odds Ratio M-H, Fixed, 95% CI	
Heterogeneity: Chi ² = Test for overall effect: INSS stage 1/2 Study or Subgroup Jimon, T Jünther, P Jönh, A Granaka, Y Goneda, A Chang, A. A helps, H. M Total (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect:	12.81, d Z = 8.67 No IDR Events 198 7 12 8 31 7 22 285 7.89, df Z = 8.30	r' (P < 0 Fs Total 227 21 16 15 31 8 49 367 = 6 (P = (P < 0.	P = 0.08); 0.00001) Any IDR Events 1 75 9 42 2 53 18 6 205 = 0.25); ² 00001)	Fs Total 139 86 5 76 59 37 441 = 249	Weight 46.5% 16.4% 12.9% 5.5% 1.9% 2.1% 14.7% 100.0%	 M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 1.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] 	2008 2011 2016 2016 2016 2019		No IDRFs Any IDRFs Odds Ratio M-H, Fixed, 95% CI	-
Heterogeneity: Ch ² = Fest for overall effect: INSS stage 1/2 itudy or Subgroup jimon, T Jünther, P Yohl, A (ranaka, Y Yoneda, A A Arhang, A. A Yhelps, H. M Fotal (95% Cl) Total events Heterogeneity: Chi ² = Fest for overall effect:	* 12.81, d : Z = 8.67 No IDR Events 198 7 12 8 31 7 22 285 7.89, df = Z = 8.30	Y (P < 0 Fs Total 227 21 16 15 31 8 49 367 = 6 (P = (P < 0.) Fs	P = 0.08); .00001) Any IDR <u>Events 1</u> 75 9 42 2 53 18 6 205 = 0.25); I ² .00001) Any IDR	Fs <u>fotal</u> 139 86 5 76 59 37 441 = 249 Fs	Weight 46.5% 16.4% 5.5% 1.9% 2.1% 14.7% 100.0%	M-H, Fixed, 95% C1 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] Odds Ratio	2008 2011 2016 2016 2019 2019		No IDRFs Any IDRFs Odds Ratio M-H, Fixed, 95% CI	
Heterogeneity: Chi ² = Test for overall effect: INSS stage 1/2 Study or Subgroup Jimon, T Jinther, P Pohl, A Granaka, Y Yoneda, A A Phelps, H. M Total (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect: MYCN Study or Subgroup	* 12.81, d : Z = 8.67 No IDR Events 198 7 22 8 31 7 22 285 7.89, df Z = 8.30 No IDR Events	Y (P < 0 Fs Total 227 21 16 15 31 8 49 367 = 6 (P = (P < 0). Fs Total	P = 0.08); 0.00001) Any IDR Events 1 75 9 42 2 53 18 6 205 = 0.25); I ² .00001) Any IDR Events	Fs 139 39 86 59 37 441 = 249 Fs Total	Weight 46.5% 16.4% 12.9% 2.1% 14.7% 100.0%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 1.41 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] Odds Ratio M-H, Fixed, 95% CI	2008 2011 2016 2016 2019 2019 2019		No IDRFs Any IDRFs Odds Ratio M-H, Fixed, 95% CI	
Heterogeneity: Chi ² = Test for overall effect: INSS stage 1/2 HNSS stage 1/2 HINSS st	* 12.81, d : Z = 8.67 No IDR Events 198 7 12 8 31 7 22 285 7.89, df Z = 8.30 No IDR Events 12	Fs Total 227 21 16 31 8 49 367 = 6 (P = (P < 0.))	2 = 0.08); 0.00001) Any IDRI Events 1 75 9 42 2 3 3 18 6 205 = 0.25); l ² .00001) Any IDR 205 = 0.25); l ² .00001)	Fs Total 139 39 86 59 37 441 = 24% SFs Total 86	Weight 46.5% 16.4% 2.9% 5.5% 1.9% 2.1% 14.7% 100.0% 6 Weight 33.2%	M-H, Fixed, 95% C1 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] Odds Ratio M-H, Fixed, 95% C1 1.16 [0.34, 3.96]	2008 2011 2016 2016 2019 2019 <i>Year</i> 2016		No IDRFs Any IDRFs Odds Ratio M-H, Fixed, 95% CI	
Heterogeneity: Chi ² = Fest for overall effect: INSS stage 1/2 itudy or Subgroup imon, T Jonther, P Yohl, A Chang, A. A Yhelps, H. M Frotal (95% Cl) Total events Heterogeneity: Chi ² = Fest for overall effect: MYCN Study or Subgroup Yohl, A Tanaka, Y	* 12.81, d : Z = 8.67 No IDR <u>Events</u> 198 7 12 8 31 7 22 285 7.89, df Z = 8.30 No IDR <u>Events</u> 12 14	Y (P < 0 Fs Total 227 21 16 15 31 8 49 367 = 6 (P = (P < 0). Fs Total	P = 0.08); 0.00001) Any IDR Events 1 75 9 42 2 53 18 6 205 = 0.25); I ² .00001) Any IDR Events	Fs Total 139 86 5 76 59 37 441 = 249 SFs Total 86 5 5 5 5 5 5 5 5 5 5 5 5 5	Weight 46.5% 16.4% 2.9% 5.5% 1.9% 2.1% 14.7% 100.0% 6 Weight 33.2%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] Odds Ratio M-H, Fixed, 95% CI 1.16 [0.34, 3.96] 9.33 [0.62, 139.57]	2008 2011 2016 2016 2019 2019 2019 Year 2016 2016		No IDRFs Any IDRFs Odds Ratio M-H, Fixed, 95% CI	-
Heterogeneity: Chi ² = Fest for overall effect: INSS stage 1/2 itudy or Subgroup imon, T jonther, P Yohl, A franka, Y Yohelys, H. M Fotal (95% Cl) Total events Heterogeneity: Chi ² = Fest for overall effect: MYCN Study or Subgroup Yohl, A Fanaka, Y Yhelps, H. M	* 12.81, d : Z = 8.67 No IDR Events 198 7 12 8 31 7 22 285 7.89, df Z = 8.30 No IDR Events 12	Y (P < 0 Fs Total 227 21 16 15 31 8 49 367 = 6 (P = 0. Fs Total 16 15 31 8 49 367 Fs Total 16 15 31 8 49 367 15 31 8 49 367 15 31 15 31 8 49 367 15 31 15 15 15 15 15 15 15 15 15 1	Any IDR Events 1 75 9 42 2 53 18 6 205 = 0.25); ² 00001) Any IDR Events 2 6 205 = 0.25); ² 00001)	Fs Total 139 86 5 76 59 37 441 = 249 SFs Total 86 5 37	Weight 46.5% 16.4% 12.9% 5.5% 1.9% 2.1% 14.7% 100.0% 6	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] Odds Ratio M-H, Fixed, 95% CI 1.16 [0.34, 3.96] 9.33 [0.62, 13.957] 1.02 [0.42, 2.50]	2008 2011 2016 2016 2019 2019 2019 Year 2016 2016		No IDRFs Any IDRFs Odds Ratio M-H, Fixed, 95% CI	-
Heterogeneity: Chi ² = Fest for overall effect: INSS stage 1/2 Study or Subgroup Jimon, T Jinther, P Johl, A Granaka, Y Orola, A, A Phelps, H. M Fotal (95% Cl) Orola events Heterogeneity: Chi ² = Fest for overall effect: MYCN Study or Subgroup Johl, A Tanaka, Y Phelps, H. M Fotal (95% Cl)	12.81, d Z = 8.67 No IDR Fvents 198 7 12 8 31 7 22 285 7.89, df = Z = 8.30 No IDR Events 12 4 32 12 8 31 7 22 285 7.89, df = 285 7.89, df = 295 7.89, df = 202 7.89, df = 202 7.8	Fs Total 227 21 16 15 31 8 49 367 = 6 (P = (P < 0.)	2 = 0.08); 0.00001) Any IDRI Events 1 75 9 42 2 53 18 6 205 = 0.25); l ² 0.0001) Any IDR Events 62 3 24	Fs Total 139 86 5 76 59 37 441 = 249 SFs Total 86 5 37	Weight 46.5% 16.4% 12.9% 2.1% 14.7% 100.0% 6 Weight 33.2% 2.0%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] Odds Ratio M-H, Fixed, 95% CI 1.16 [0.34, 3.96] 9.33 [0.62, 139.57]	2008 2011 2016 2016 2019 2019 2019 Year 2016 2016		No IDRFs Any IDRFs Odds Ratio M-H, Fixed, 95% CI	10
Heterogeneity: Chi ² = Fest for overall effect: INSS stage 1/2 Study or Subgroup Jimon, T Jonther, P John, A Fanaka, Y fortal (95% CI) Fotal events Heterogeneity: Chi ² = Fest for overall effect: MYCN Study or Subgroup John, A Fanaka, Y Phelps, H. M Fotal (95% CI) Fotal (95% CI) Fotal events	* 12.81, d : Z = 8.67 No IDR <u>Events</u> 198 7 12 8 8 31 7 22 285 7.89, df = Z = 8.30 No IDR <u>Events</u> 14 32 58	Fs Total 227 21 16 15 31 6 49 367 = 6 (P = 0. Fs Total 16 15 31 16 15 31 16 15 31 16 15 367 Fs Total 8 49 367 5 367 8 49 367 5 5 367 5 5 367 5 5 367 5 5 367 5 5 367 5 5 367 5 5 5 5 5 5 5 5 5 5 5 5 5	2 = 0.08); 0.00001) Any IDR Events 1 75 9 42 2 53 18 6 205 = 0.25); l ² 0.0001) Any IDR Events 2 3 24 89	Fs Total 139 39 86 59 37 441 = 249 Fs Total 86 5 37 128	Weight 46.5% 16.4% 12.9% 5.5% 1.9% 1.9% 2.1% 14.7% 100.0%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] Odds Ratio M-H, Fixed, 95% CI 1.16 [0.34, 3.96] 9.33 [0.62, 13.9.57] 1.02 [0.42, 2.50]	2008 2011 2016 2016 2019 2019 2019 Year 2016 2016		No IDRFs Any IDRFs Odds Ratio M-H, Fixed, 95% CI	-
Heterogeneity: Chi ² = Fest for overall effect: INSS stage 1/2 itudy or Subgroup imon, T Jonther, P Yohl, A Chang, A. A Yhelps, H. M Fotal (95% CI) Total events Heterogeneity: Chi ² = Fest for overall effect: MYCN Study or Subgroup Yohl, A Cinanaka, Y Yhelps, H. M Fotal (95% CI) Fotal events Heterogeneity: Chi ² =	* 12.81, d : Z = 8.67 No IDR <u>Events</u> 198 7 12 8 31 7 22 285 7.89, df Z = 8.30 No IDR <u>Events</u> 12 14 4 32 58 2.33, df	Fs = 6 (P < 0) $Fs = 6 (P < 0)$ $Fs = 6 (P < 0)$ $Fs = 70 (P < 0)$ $Fs = 70 (P < 0)$ $Fs = 80$ $Fs = 2 (P < 0)$	2 = 0.08); 0.00001) Any IDR Events 1 75 9 42 25 18 6 205 = 0.25); l ² 00001) Any IDR Events 2 62 3 24 89 = 0.31); l ²	Fs Total 139 39 86 59 37 441 = 249 Fs Total 86 5 37 128	Weight 46.5% 16.4% 12.9% 5.5% 1.9% 1.9% 2.1% 14.7% 100.0%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] Odds Ratio M-H, Fixed, 95% CI 1.16 [0.34, 3.96] 9.33 [0.62, 13.9.57] 1.02 [0.42, 2.50]	2008 2011 2016 2016 2019 2019 2019 Year 2016 2016		Odds Ratio M-H, Fixed, 95% CI	
Heterogeneity: Chi ² = Fest for overall effect: INSS stage 1/2 Study or Subgroup Jimon, T Jonther, P John, A Fanaka, Y foreda, A A Chang, A. A Phelps, H. M Total (95% CI) Total events Heterogeneity: Chi ² = Fest for overall effect: MYYCN Study or Subgroup John, A Fanaka, Y Phelps, H. M Total (95% CI) Total events Heterogeneity: Chi ² = Fest for overall effect: Phelps, H. M	* 12.81, d : Z = 8.67 No IDR <u>Events</u> 198 7 12 8 31 7 22 285 7.89, df Z = 8.30 No IDR <u>Events</u> 12 14 4 32 58 2.33, df	Fs = 6 (P < 0) $Fs = 6 (P < 0)$ $Fs = 6 (P < 0)$ $Fs = 70 (P < 0)$ $Fs = 70 (P < 0)$ $Fs = 80$ $Fs = 2 (P < 0)$	2 = 0.08); 0.00001) Any IDR Events 1 75 9 42 25 18 6 205 = 0.25); l ² 00001) Any IDR Events 2 62 3 24 89 = 0.31); l ²	Fs Total 139 39 86 59 37 441 = 249 Fs Total 86 5 37 128	Weight 46.5% 16.4% 12.9% 5.5% 1.9% 1.9% 2.1% 14.7% 100.0%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] Odds Ratio M-H, Fixed, 95% CI 1.16 [0.34, 3.96] 9.33 [0.62, 13.9.57] 1.02 [0.42, 2.50]	2008 2011 2016 2016 2019 2019 2019 Year 2016 2016	0.01	Odds Ratio M-H, Fixed, 95% CI	10
Heterogeneity: Chi ² = Fest for overall effect: INSS stage 1/2 Study or Subgroup Jimon, T Jonther, P John, A Fanaka, Y foreda, A A Chang, A. A Phelps, H. M Total (95% CI) Total events Heterogeneity: Chi ² = Fest for overall effect: MYYCN Study or Subgroup John, A Fanaka, Y Phelps, H. M Total (95% CI) Total events Heterogeneity: Chi ² = Fest for overall effect: Phelps, H. M	* 12.81, d : Z = 8.67 No IDR <u>Events</u> 198 7 12 8 31 7 22 285 7.89, df Z = 8.30 No IDR <u>Events</u> 12 12 8 31 7 22 285 7.89, df 2 2,83, df 22 2,83, df 2 2,83, df 2 2,83, df 2 2,83, df 2 2,83, df 2 2,83, df 2 2,83, df 2,23, df 2,33, df 2,23, df 2,33, df 2,23, df 2,33, df 3,33, df 2,33,	Fs = 6 (P < 0) $Fs = 10 (P < 0)$ $Fs = 10 (P = 0)$	2 = 0.08); 0.00001) Any IDR Events 1 75 9 42 25 18 6 205 = 0.25); l ² 00001) Any IDR Events - 62 3 24 89 = 0.31); l ²	Fs $\frac{139}{39}$ 86 5 59 37 441 = 24% Fs $\frac{124}{37}$ 86 5 37 128 $\frac{2}{2}$ = 14%	Weight 46.5% 16.4% 12.9% 5.5% 1.9% 1.9% 2.1% 14.7% 100.0%	 M-H, Fixed, 95% CI 5.83 [3.49, 9,73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] Odds Ratio M-H, Fixed, 95% CI 1.16 [0.34, 3.96] 9.33 [0.62, 139.57] 1.02 [0.42, 2.50] 1.24 [0.62, 2.46] 	2008 2011 2016 2016 2019 2019 2019 Year 2016 2016	0.01	Odds Ratio M-H, Fixed, 95% CI 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.1	
Heterogeneity: Chi ² = Frest for overall effect: INSS stage 1/2 itudy or Subgroup imon, T jünther, P ohl, A inanaka, Y ioneda, A thang, A. A thang, A. A thang, A. A thelps, H. M Total (95% CI) otal events Heterogeneity: Chi ² = fest for overall effect: itudy or Subgroup bohl, A inanaka, Y helps, H. M Total (95% CI) otal events Heterogeneity: Chi ² = fest for overall effect: Eventor site	* 12.81, d : Z = 8.67 No IDR Events 198 7 12 8 31 7 22 285 7.89, df = Z = 8.30 No IDR Events 12 12 4 4 32 285 7.89, df = Z = 0.60 No IDR	Y (P < 0 Fs Total 227 21 16 5 31 8 49 367 = 6 (P = (P < 0. Fs Total 16 (P < 0. Fs Total 16 5 49 367 = 6 (P = (P < 0. Fs (P < 0.) (P = 0.	P = 0.08); 0.00001) Any IDRI Events 1 75 9 42 2 53 18 6 205 = 0.25); I ² 00001) Any IDR Events 2 62 324 89 = 0.31); I ² .55) Any IDR	Fs $\frac{139}{39}$ 86 5 76 59 37 441 $= 249$ Fs $\frac{128}{37}$ 128 $2^2 = 14^2$ RFs	Weight 46.5% 16.4% 2.9% 5.5% 1.9% 4.7% 100.0% 6 Weight 33.2% 2.0% 6 8 8	M-H, Fixed, 95% CI 5.83 [3.49, 9.75] 1.67 [0.52, 5.39] 1.47 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] Odds Ratio M-H, Fixed, 95% CI 1.16 [0.34, 3.96] 9.33 [0.62, 139.57] 1.02 [0.42, 2.50] 1.24 [0.62, 2.46]	2008 2011 2016 2016 2019 2019 2019 2019 2019 2019 2019 2019	0.01	Odds Ratio M-H, Fixed, 95% CI	10
Heterogeneity: Chi ² = Fest for overall effect: INSS stage 1/2 itudy or Subgroup imon, T jonther, P Yohl, A Fanaka, Y foreda, A A A A helps, H. M Fotal (95% Cl) Total events Heterogeneity: Chi ² = Fest for overall effect: MYCN itudy or Subgroup YCN itudy or Subgroup YCN iterogeneity: Chi ² = Fest for overall effect: Total effect: Fotal (95% Cl) Total events Heterogeneity: Chi ² = Fest for overall effect: Tumor site Study or Subgroup	* 12.81, d : Z = 8.67 No IDR Events * 198 7 7 12 8 31 7 22 285 7.89, df = Z = 8.30 No IDR Events 12 8 2.33, df : Z = 0.60 No IDR	Fs = 5 + 227 + 21 + 16 + 227 + 21 + 16 + 16 + 16 + 16 + 16 + 16 + 16	2 = 0.08); 0.00001) Any IDR Events 1 75 9 42 253 18 205 = 0.25); I ² 00001) Any IDR Events 89 = 0.31); I ² 55)	Fs [otal 139 86 59 37 441 = 249 (Fs Total 86 5 37 128 87 128 87 128 87 128 87 128 87 128 128 128 129 129 129 139 139 139 139 139 139 139 13	Weight 46.5% 16.4% 2.9% 12.9% 5.5% 1.9% 2.1% 1.9% 2.1% 1.9% 33.2% 2.0% 64.8% 100.0% % Weight 34.2% Weight 35.2% 2.0% 64.8% Weight 35.2%	M-H, Fixed, 95% CT 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] 0dds Ratio M-H, Fixed, 95% CT 1.24 [0.62, 2.46] Odds Ratio M-H, Fixed, 95% CT	2008 2011 2016 2016 2019 2019 2019 2019 2019 2016 2016 2019	0.01	Odds Ratio M-H, Fixed, 95% CI 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.1	10
Heterogeneity: Chi ² = Fest for overall effect: INSS stage 1/2 Study or Subgroup Jonner, P Jonh, A Jonner, P John, A Jonner, P John, A Jonner, P John, A Johner, P John, A Johner, P John, A Johner, A MYCN Study or Subgroup John, A Total (95% CI) Total events Heterogeneity: Chi ² = Fest for overall effect: MYCN Study or Subgroup Johner, T Johner, B Johner, Johner, B Johner, B Johner, Johner, B Johner, Johner, B Johner, Johner, B Johner, Johner, Joh	 12.81, di Z = 8.67 No IDR Events 198 7 12 8 31 7 22 285 7.89, df = 2 = 8.30 No IDR Events 12 14 32 58 2.33, df = 2 = 0.600 No IDR Events 12 14 32 	$Fs = \frac{1}{227}$ $227 = 227$ $211 = 16$ $8 = 49$ $367 = 6 (P = 0$ $Fs = Total = 16$ $166 = 15$ $49 = 80$ $80 = 2 (P = 0$ $Fs = Total = 227$	2 = 0.08); 0.00001) Any IDRI Events 1 75 9 42 2 53 18 6 205 = 0.25); I ² 00001) Any IDR Events 2 3 24 89 = 0.31); I ² .55) Any IDR Events 1 101	Fs Total 139 39 86 59 37 441 = 24% Fs Total 86 57 37 128 2 = 14% RFs Total 139 139	Weight 46.5% 16.4% 5.5% 1.9% 5.5% 1.9% 5.1 1.9% 5.5% 1.9% 6 Weight 33.2% 2.0% 64.8% 100.0% % Weight 36.5%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] 0/dds Ratio M-H, Fixed, 95% CI 1.30 [0.80, 2.11]	2008 2011 2016 2019 2019 2019 2019 2019 2019 2016 2016 2016 2016 2019 2019	0.01	Odds Ratio M-H, Fixed, 95% CI	10
Heterogeneity: Chi ² = Fest for overall effect: INSS stage 1/2 Study or Subgroup Jimon, T Jinther, P Johl, A Fanaka, Y fordad, A A A A A A A A A A A A A A	* 12.81, d : Z = 8.67 No IDR Events 198 7 12 8 31 7 22 285 7.89, df = Z = 8.30 No IDR Events 12 285 7.89, df = Z = 8.30 No IDR Events 12 58 2.33, df : Z = 0.600 No IDR Events 176 196 198 176 198 176 198 176 198 176 198 176 198 176 198 176 198 176 198 176 176 176 176 176 176 176 176	Fs = 7 (P < 0) $Fs = 70 tal = 1227 (P < 1) (P < 0)	2 = 0.08); 0.00001) Any IDR Events 1 75 9 42 2 53 18 6 205 = 0.25); 1 ² 0.0001) Any IDR Events 3 24 89 = 0.31); 1 ² .55) Any IDR Events 101 86	Fs = 139 $39 = 86$ $59 = 37$ $441 = 249$ $Fs = 142$ $8Fs = 142$ $8Fs = 142$ $8Fs = 139$ 118	Weight 46.5% 16.4% 12.9% 5.5% 1.9% 1.17% 100.0% 6 Weight 33.2% 2.0% 64.8% 100.0% % Weight 36.5% 50.2%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] M-H, Fixed, 95% CI 1.16 [0.34, 3.96] 9.33 [0.62, 139.57] 1.02 [0.42, 2.50] 1.24 [0.62, 2.46] Odds Ratio M-H, Fixed, 95% CI 1.30 [0.80, 2.11] 0.50 [0.50, 1.29]	2008 2011 2016 2019 2019 2019 2019 2019 2019 2016 2016 2016 2016 2019 Year Year 2016 2016 2019	0.01	Odds Ratio M-H, Fixed, 95% CI 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.1	
Heterogeneity: Chi ² = Fest for overall effect: INSS stage 1/2 itudy or Subgroup imon, T Jonther, P Yohl, A Trata (4, Y Yohl, A, A A A A A A A A A A Costal events Heterogeneity: Chi ² = Fest for overall effect: MYCN Study or Subgroup Yohl, A Cinanka, Y Yohl, A Cinanka, Y Yohl, A Cinanka, Y Yohl, A Cinanka, Y Yohl, A Cinanka, Y Total events Heterogeneity: Chi ² = Fest for overall effect: Cumor site Study or Subgroup Simon, T Wonclair, T Cinanka, Y Simon, T Wonclair, T Cinanka, Y	* 12.81, d : Z = 8.67 No IDR Events 7 12 8 31 7 22 285 7.89, df = Z = 8.30 No IDR Events 12 14 32 58 2.33, df = Z = 0.60 No IDR Events 176 199 14	r (P < 0 Fs Total 227 21 16 15 31 8 49 367 = 6 (P = (P < 0.) Fs Total 16 15 49 80 = 2 (P + (P = 0) 80 = 2 (P + (P = 0) 80 = 2 (P + (P = 0) 80 80 = 2 (P + (P = 0) 80 = 2 (P + (P = 0)) 80 = 2 (P + (P = 0)) = 2 (P + (P + (P = 0))) = 2 (P + (P	2 = 0.08); 0.00001) Any IDR Events 1 75 9 42 25 18 6 205 = 0.25); l ² 00001) Any IDR Events 2 6 205 = 0.25); l ² 00001) Any IDR Events 2 3 24 89 = 0.31); l ² .55) Any IDR Events 2 101 86 4	Fs $\frac{1}{139}$ 39 86 59 441 = 249 Fs $\frac{1}{128}$ $2^{2} = 14^{2}$ 128 $2^{2} = 14^{2}$ 139 1139 139 139	Weight 46.5% 16.4% 5.5% 1.9% 5.5% 1.9% 2.1% 1.4.7% 100.0% 6 Weight 33.2% 2.6 44.8% 100.0% % Weight 36.5% 50.2% 0.2%	M-H, Fixed, 95% CT 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] 0dds Ratio M-H, Fixed, 95% CT 1.24 [0.62, 2.46] 0dds Ratio M-H, Fixed, 95% CT 1.30 [0.80, 2.11] 0.80 [0.50, 1.29] 0.80 [0.50, 1.21] 0.80 [0.50, 1.2	2008 2011 2016 2019 2019 2019 2019 2019 2019 2016 2016 2019 2019 2019	0.01	Odds Ratio M-H, Fixed, 95% CI 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.1	
Heterogeneity: Chi ² = Test for overall effect: INSS stage 1/2 Study or Subgroup Jimon, T Jinther, P Pohl, A Tanaka, Y Yhelps, H. M Total (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect: MYCN Study or Subgroup Pohl, A Tanaka, Y Phelps, H. M Total (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect: Tumor Site Study or Subgroup Study or Subgroup	* 12.81, d : Z = 8.67 No IDR Events 198 7 12 8 31 7 22 285 7.89, df = Z = 8.30 No IDR Events 12 285 7.89, df = Z = 8.30 No IDR Events 12 58 2.33, df : Z = 0.600 No IDR Events 176 196 198 176 198 176 198 176 198 176 198 176 198 176 198 176 198 176 198 176 176 176 176 176 176 176 176	Fs = 7 (P < 0) $Fs = 70 tal = 1227 (P < 1) (P < 0)	2 = 0.08); 0.00001) Any IDR Events 1 75 9 42 2 53 18 6 205 = 0.25); 1 ² 0.0001) Any IDR Events 3 24 89 = 0.31); 1 ² .55) Any IDR Events 101 86	Fs = 139 $39 = 86$ $59 = 37$ $441 = 249$ $Fs = 142$ $8Fs = 142$ $8Fs = 142$ $8Fs = 139$ 118	Weight 46.5% 16.4% 12.9% 2.9% 1.9% 1.9% 4.1% 100.0% 6 Weight 100.0% % Weight 33.2% 50.2% 50.2% 50.2% 0.9%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] 0/dds Ratio M-H, Fixed, 95% CI 1.16 [0.34, 3.96] 9.33 [0.62, 129.57] 1.02 [0.42, 2.50] 1.24 [0.62, 2.46] 0/dds Ratio M-H, Fixed, 95% CI 1.30 [0.80, 2.11] 0.80 [0.51, 0.93] 3.50 [0.18, 69.34] 3.54 [0.31, 98.30]	2008 2011 2016 2016 2019 2019 2019 2019 2019 2019 2016 2016 2016 2016 2019 2019	0.01	Odds Ratio M-H, Fixed, 95% CI 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.1	
Heterogeneity: Chi ² = Test for overall effect: INSS stage 1/2 Study or Subgroup Jimon, T Jönther, P Johl, A Granaka, Y Orolal avents Heterogeneity: Chi ² = Test for overall effect: MYCN Study or Subgroup Johl, A Tanaka, Y Phelps, H. M Fotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Tumor Site Study or Subgroup Simon, T Monclair, T Fanaka, Y Phelps, H. M	12.81, d Z = 8.67 No IDR 7 198 7 12 8 311 7 22 285 7.89, df = Z = 8.30 No IDR Events 12 14 32 58 2.33, df = Z = 0.60 No IDR Events 12 14 32 14 32 14 12 12 12 12 12 12 12 12 12 12	Fs = Total = (P < 0) $Fs = 0$ $Fs =$	2 = 0.08); 0.00001) Any IDRI Events 1 75 9 42 2 53 18 6 205 = 0.25); ² 0.0001) Any IDR Events 62 3 24 89 = 0.31); ³ 55) Any IDR Events 10,25	Fs Total 139 86 5 59 37 441 = 24% Fs Total 86 5 37 128 Fs Total 139 118 5 86 86	Weight 46.5% 16.4% 5.5% 1.9% 5.5% 1.9% 2.1% 1.4.7% 100.0% 6 Weight 33.2% 2.6 44.8% 100.0% % Weight 36.5% 50.2% 0.2%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] 0/dds Ratio M-H, Fixed, 95% CI 1.61 [0.34, 3.96] 9.33 [0.62, 2.46] 0/dds Ratio M-H, Fixed, 95% CI 1.30 [0.80, 2.11] 0.80 [0.50, 1.29] 3.50 [0.18, 69.34] 5.54 [0.31, 98.30] 0.80 [0.30, 2.13]	2008 2011 2016 2016 2019 2019 2019 2019 2019 2019 2016 2016 2016 2016 2019 2019	0.01	Odds Ratio M-H, Fixed, 95% CI 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.1	10
Heterogeneity: Chi ² = Test for overall effect: INSS stage 1/2 Study or Subgroup Jimon, T Jinther, P Pohl, A Tanaka, Y Yhelps, H. M Total (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect: MYCN Study or Subgroup Pohl, A Tanaka, Y Phelps, H. M Total (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect: Tumor Site Study or Subgroup Study or Subgroup	12.81, d Z = 8.67 No IDR 7 198 7 12 8 311 7 22 285 7.89, df = Z = 8.30 No IDR Events 12 14 32 58 2.33, df = Z = 0.60 No IDR Events 12 14 32 14 32 14 12 12 12 12 12 12 12 12 12 12	Fs = Total = (P < 0) $Fs = 0$ $Fs =$	2 = 0.08); 0.00001) Any IDRI Events 1 75 9 42 2 53 18 6 205 = 0.25); ² 0.0001) Any IDR Events 62 3 24 89 = 0.31); ³ 55) Any IDR Events 10,25	Fs Total 139 86 5 59 37 441 = 24% Fs Total 86 5 37 128 Fs 128 Fs 128 Fs 139 118 5 86 37	Weight 46.5% 16.4% 12.9% 2.9% 1.9% 1.9% 4.1% 100.0% 6 Weight 100.0% % Weight 33.2% 50.2% 50.2% 50.2% 0.9%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] 0/dds Ratio M-H, Fixed, 95% CI 1.16 [0.34, 3.96] 9.33 [0.62, 129.57] 1.02 [0.42, 2.50] 1.24 [0.62, 2.46] 0/dds Ratio M-H, Fixed, 95% CI 1.30 [0.80, 2.11] 0.80 [0.51, 0.93] 3.50 [0.18, 69.34] 3.54 [0.31, 98.30]	2008 2011 2016 2016 2019 2019 2019 2019 2019 2019 2016 2016 2016 2016 2019 2019	0.01	Odds Ratio M-H, Fixed, 95% CI 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.1	10
Heterogeneity: Chi ² = Frest for overall effect: INSS stage 1/2 itudy or Subgroup imon, T jonther, P tohl, A inaka, Y foreda, A. A thelps, H. M Total (95% CI) otal events Heterogeneity: Chi ² = Test for overall effect: WYCN itudy or Subgroup tohl, A inaka, Y thelps, H. M Total (95% CI) otal events Heterogeneity: Chi ² = Test for overall effect: Tumor Site itudy or Subgroup imon, T donclair, T Fanaka, Y bohl, A inaka, Y inaka, Y bohl, A inaka, Y bohl, A inaka, Y bohl, A inaka, Y bohl, A inaka, Y bohl, A inaka, Y inaka, Y inaka, Y inaka, Y inaka, Y inaka, Y inaka, Y inaka, Y inaka, Y	* 12.81, d : Z = 8.67 No IDR Events 7 12 8 31 7 22 285 7.89, df Z = 8.30 No IDR Events 12 14 32 58 2.33, df Z = 0.60 No IDR Events 176 199 14 35 440	Fs = Total = 0 $Fs = Total = 0$ $Fs	2 = 0.08); 0.00001) Any IDR Events 1 75 9 42 2 53 18 6 205 = 0.25); l ² 00001) Any IDR Events 2 6 2 3 24 89 = 0.31); l ² .55) Any IDR Events 1 6 2 3 24 89 = 0.31); l ² .55) Any IDR Events 2 .55)	Fs 139 39 86 5 57 76 59 37 441 = 24% Fs Total 128 85 37 128 85 37 128 85 37 128 85 37 385 86 86 86 86 86 86 86 86 86 86	Weight 46.5% 16.4% 5.5% 1.9% 5.5% 1.9% 5.1 1.9% 6 Weight 33.2% 2.6% 64.8% Weight 36.5% 50.2% 0.9% 36.5% 0.9% 11.8% 100.0%	M-H, Fixed, 95% CI 5.83 [3.49, 9.73] 1.67 [0.52, 5.39] 3.14 [0.94, 10.52] 1.71 [0.22, 13.41] 27.67 [1.62, 471.52] 15.94 [1.83, 139.27] 4.21 [1.49, 11.91] 4.97 [3.40, 7.25] 0/dds Ratio M-H, Fixed, 95% CI 1.61 [0.34, 3.96] 9.33 [0.62, 2.46] 0/dds Ratio M-H, Fixed, 95% CI 1.30 [0.80, 2.11] 0.80 [0.50, 1.29] 3.50 [0.18, 69.34] 5.54 [0.31, 98.30] 0.80 [0.30, 2.13]	2008 2011 2016 2016 2019 2019 2019 2019 2019 2019 2016 2016 2016 2016 2019 2019	0.01	Odds Ratio M-H, Fixed, 95% CI 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.1	

Hosted file

Table 1.docx available at https://authorea.com/users/335737/articles/461544-role-of-image-

defined-risk-factors-in-clinical-practice-of-neuroblastoma-a-systematic-review-and-metaanalysis



		Representative cases	Selection of controls	Ascertainment of exposure	Outcome not present at start	Comparability of groups	Outcome assessment
g, A. A.2019		•	+	•	•		
os, H. M.2019	1	•	+	+	+	+	
s, J. T., Jr.2019		•	•	•	+	+	
a, T.2019		•	•	•	+	+	
da, A.2016	÷	•	•	•	+	•	
ka, Y.2016		•	•	•	+	+	
A.2016		•	•	•	+	Ŧ	
clair, T.2015		•	+	•	+	+	
ner, P.2011		•	+	•	+	+	
n, T.2008		•	•	•	+	•	

Follow-up completeness

Follow-up duration

+

Ŧ

Ŧ

Ŧ

÷

+

Ŧ

Ŧ

+

÷

Zhang Phelps Lucas Iehara Yoned Tanak Pohl, Moncl Günth Simon

n'a'
inai
prel
pe
ay
Ĩ
ata
\square
ed.
iewe
revi
GL
pe
een
t D
no
has
[p
ar
rint
tep
a pr
his a
EI -
149
426
115
91
3219
9282
15
au
241
2252
10
rg/
oi.o
ttps:/
121
ht1
Ē.
- h
n. — h
ission. — h
ermission. — h
tt permission. — h
hout permission. — h
without permission. — h
use without permission. — h
without permission. — h
use without permission. — h
d. No reuse without permission. — h
srved. No reuse without permission. — h
d. No reuse without permission. — h
ts reserved. No reuse without permission. — h
ights reserved. No reuse without permission. — h
rights reserved. No reuse without permission. — h
ights reserved. No reuse without permission. — h
der. All rights reserved. No reuse without permission. — h
rights reserved. No reuse without permission. — h
der. All rights reserved. No reuse without permission. — h
/funder. All rights reserved. No reuse without permission. — h
or/funder. All rights reserved. No reuse without permission. — h
or/funder. All rights reserved. No reuse without permission. — h
is the author/funder. All rights reserved. No reuse without permission. — h
the author/funder. All rights reserved. No reuse without permission. — h
is the author/funder. All rights reserved. No reuse without permission. — h
is the author/funder. All rights reserved. No reuse without permission. — h
right holder is the author/funder. All rights reserved. No reuse without permission. $$ h
pyright holder is the author/funder. All rights reserved. No reuse without permission. $$ h
copyright holder is the author/funder. All rights reserved. No reuse without permission. $$ h
The copyright holder is the author/funder. All rights reserved. No reuse without permission. — h
The copyright holder is the author/funder. All rights reserved. No reuse without permission. $$ h
The copyright holder is the author/funder. All rights reserved. No reuse without permission. — h
2020 - The copyright holder is the author/funder. All rights reserved. No reuse without permission. $-h$
020-The copyright holder is the author/funder. All rights reserved. No reuse without permission. $-h$
Jun 2020 — The copyright holder is the author/funder. All rights reserved. No reuse without permission. — h
$J_{ m un}$ 2020 — The copyright holder is the author/funder. All rights reserved. No reuse without permission. — h
orea 22 Jun 2020 — The copyright holder is the author/funder. All rights reserved. No reuse without permission. — h
$^{+}$ 22 Jun 2020 — The copyright holder is the author/funder. All rights reserved. No reuse without permission. — h
orea 22 Jun 2020 — The copyright holder is the author/funder. All rights reserved. No reuse without permission. — h
orea 22 Jun 2020 — The copyright holder is the author/funder. All rights reserved. No reuse without permission. — h