eTable 1. Search strategy.

Database	Keywords
Pubmed	
(1)	“antibody-drug conjugates”[Title/Abstract] OR “antibody-drugconjugate”[Title/Abstract] OR “ADC”[Title/Abstract] OR “ADCs”[Title/Abstract]
(2)	"neoplasms"[Mesh] OR “cancer”[Title/Abstract] OR “carcinoma”[Title/Abstract] OR “tumor”[Title/Abstract]
(3)	"clinical trials as topic"[MeSH Terms] OR "clinical trial"[Publication Type] OR "phase II "[Title/Abstract] OR "phase III"[Title/Abstract] OR "phase 2"[Title/Abstract] OR "phase 3"[Title/Abstract] OR "clinical trials"[Title/Abstract]
(4)	("2000/01/01"[Date - Publication] : "2022/06/07"[Date - Publication])
(5)	#1 AND #2 AND #3 AND #4
(6)	"review"[Article type] OR "meta"[Title] OR "meta-analysis"[Title] OR "protocol"[Title] OR "cost-effectiveness"[Title/Abstract]
(7)	#5 NOT #6
Embase	
(1)	(‘antibody-drug conjugates’ OR ‘antibody-drug conjugate’ OR ADC OR ADCs):ti,ab,kw
(2)	(neoplasms OR cancer OR carcinoma OR tumor):ti,ab,kw
(3)	trial/exp OR 'clinical trials'/exp OR 'phase 2 clinical trial'/exp OR 'phase 3 clinical trial'/exp OR 'phase II clinical trial'/exp OR 'phase III clinical trial'/exp
(4)	[article]/lim OR [article in press]/lim
(5)	[humans]/lim
(6)	[1-1-2000]/sd NOT [07-06-2022]/sd
(7)	#1 AND #2 AND #3 AND #4 AND #5 AND #6
Cochrane	
(1)	(‘antibody-drug conjugates’ OR ‘antibody-drug conjugate’ OR ADC OR ADCs) AND (neoplasms OR cancer OR carcinoma OR tumor) AND (‘clinical trials’ OR trial) NOT (conference OR review OR meta OR meta-analysis OR cost-effectiveness) (Publication date: 2000-01-01 to 2022-06-07)
Web of science	
(1)	TS=(‘antibody-drug conjugates’ OR ‘antibody-drug conjugate’ OR ADC OR ADCs)
(2)	TS=(neoplasms OR cancer OR carcinoma OR tumor)
(3)	TS=(clinical trials OR trial OR “phase II” OR “phase III” OR “phase 2” OR “phase 3”)

(4)	TS=(conference OR review OR meta OR meta-analysis OR cost-effectiveness)
(5)	#1 AND #2 AND #3 NOT #4(Publication date: 2000-01-01 to 2022-06-07)

eTable 2. Main characteristics of studies included in the meta-analysis of the profile of treatment-related adverse events.

Study	Phase	Trial name or ID	Cancer type	ADC agent	Payload type	Target agent	Total patient number, n	Patients with any grade AEs, n (%)	Patients with grade 3 or higher AEs, n (%)	Patients with AEs leading to discontinuation, n (%)	Ref.
Abraham, 2019	Ib/II	NSABP FB-10	Breast cancer	Trastuzumab Emtansine (T-DM1)	DM1	HER2	27	27 (100)	NA	NA	(1)
Advani, 2017	I	GO01295	NHL CLL	Pinatuzumab Vedotin (DCDT2980S)	MMAE	CD22	91	91 (100)	41 (45)	17 (19)	(2)
Ailawadhi, 2019	I	IMMUNO-003	MM	Lorvotuzumab Mertansine (IMGN901)	DM1	CD56	37	33 (89)	10 (27)	9 (24)	(3)
Almhanna, 2016	I	C26001	Gastrointestinal malignancies	TAK-264 (MLN0264)	MMAE	Guanylyl Cyclase C	41	36 (88)	17 (41)	3 (7)	(4)
Almhanna, 2017	II	C26002	Adenocarcinoma of the G/GEJ	TAK-264 (MLN0264)	MMAE	Guanylyl Cyclase C	38	NA	NA	3 (8)	(5)
Almhanna, 2017	II	C26003	Pancreatic adenocarcinom	TAK-264 (MLN0264)	MMAE	Guanylyl	43	32 (74)	15 (35)	4 (9)	(6)

			a			Cyclase C					
Ashkar, 2021	II	IUSCC-0568	Germ-cell tumors	Brentuximab Vedotin (SGN-35)	MMAE	CD30	18	14 (78)	2 (11)	0 (0)	(7)
Banerjee, 2018	II	GO28609	Ovarian cancer	Lifastuzumab Vedotin (DNIB0600A)	MMAE	NaPi2b	46	NA	NA	4 (9)	(8)
Banerji, 2019	I	SYD985.001	Solid tumors	Trastuzumab Duocarmazine (SYD985)	*seco*-DUBA	HER2	185	171 (92)	64 (35)	38 (21)	(9)
Bardia, 2017	I/II	IMMU-132-01	TNBC	Sacituzumab Govitecan (hRS7-SN38)	SN-38	Trop-2	69	NA	NA	3 (4)	(10)
Bardia, 2019	I/II	IMMU-132-01	TNBC	Sacituzumab Govitecan-hziy (hRS7-SN38)	SN-38	Trop-2	108	NA	NA	2 (2)	(11)
Bardia, 2021	I/II	IMMU-132-01	Epithelial cancer	Sacituzumab Govitecan-hziy (hRS7-SN38)	SN-38	Trop-2	495	483 (98)	295 (60)	19 (4)	(12)
Bardia, 2021	III	IMMU-132-05	TNBC	Sacituzumab Govitecan (hRS7-SN38)	SN-38	Trop-2	258	252 (98)	165 (64)	12 (5)	(13)
Bendell, 2014	I/II	NA	Breast cancer	Glembatumumab Vedotin (CDX-011)	MMAE	gpNMB	48	NA	NA	6 (13)	(14)

Blackhall, 2021	III	TAHOE	SCLC	Rovalpituzumab Tesirine (SC16LD6.5)	PBD	DLL3	287	NA	NA	38 (13)	(15)
Boni, 2022	I/II	CTMX-M-2009-001	Solid tumors	Praluzatamab Ravtansine (CX-2009)	DM4	CD166	99	90 (91)	37 (37)	12 (12)	(16)
Brivio, 2021	I/II	ITCC-059	Children ALL	Inotuzumab Ozogamicin (PF-5208773)	Calicheamicin	CD22	25	25 (100)	23 (92)	2 (8)	(17)
Burris, 2011	II	TDM4258g	Breast cancer	Trastuzumab Emtansine (T-DM1)	DM1	HER2	112	NA	NA	4 (4)	(18)
Caimi, 2021	II	LOTIS-2	DLBCL	Loncastuximab Tesirine (ADCT-402)	PBD	CD19	145	117 (81)	NA	34 (23)	(19)
Calvo, 2021	I	M15-891	SCLC	Rovalpituzumab Tesirine (SC16LD6.5)	PBD	DLL3	31	25 (81)	12 (39)	2 (7)	(20)
Camidge, 2021	I/Ib	M14-237	NSCLC	Telisotuzumab Vedotin (ABBV-399)	MMAE	c-Met	52	42 (81)	13 (25)	12 (23)	(21)
Cleary, 2020	I	M14-429	Solid tumors	Losatuxizumab Vedotin (ABBV-221)	MMAE	EGFR	45	NA	8 (18)	2 (4)	(22)

Coiffier, 2016	II	TCD12333	DLBCL	Coltuximab Ravtansine (SAR3419)	DM4	CD19	52	22 (42)	5 (10)	0 (0)	(23)
Coleman, 2021	II	innovaTV 204	Cervical cancer	Tisotumab Vedotin (HuMax-TF-ADC)	MMAE	TF	102	93 (92)	28 (28)	12 (12)	(24)
Cortes, 2022	III	DESTINY-Breast03	Breast cancer	Trastuzumab Deruxtecan (T-DXd)	DXd	HER2	261	256 (98)	116 (45)	33 (13)	(25)
				Trastuzumab Emtansine (T-DM1)	DM1	HER2	263	226 (87)	104 (40)	13 (5)	
Coveler, 2016	I	ASG5ME-002	Pancreatic Gastric cancers	ASG-5ME	MMAE	SLC44A4	35 15	24 (69) 14 (93)	NA	3 (9) 3 (20)	(26)
Dang, 2018	III	B1931008	B-NHL	Inotuzumab Ozogamicin (PF-5208773)	Calicheamicin	CD22	164	148 (90)	102 (62)	39 (32)	(27)
Danila, 2019	I	GO00768	CRPC	DSTP3086S	MSTP2109A	STEAP1	77	69 (90)	26 (34)	17 (22)	(28)
Daver, 2021	I	GO39902	AML	DCLL9718S	PBD	CLL-1	18	9 (50)	2 (11)	NA	(29)
De Bono, 2019	I/II	InnovaTV 201	Solid tumours	Tisotumab Vedotin (HuMax-TF-AD	MMAE	TF	147	146 (99)	61 (47)	32 (22)	(30)

				C)							
De Bono, 2021	I/Ib	D9320C 00001	CRPC	MEDI3726	PBD	PSMA	33	30 (91)	15 (46)	11 (33)	(31)
Demetri, 2021	I	M15-394	Sarcomas Solid tumors	ABBV-085	MMAE	LRRC15	78	62 (80)	19 (24)	11 (14)	(32)
Doi, 2017	I	DS8201-A-J101	Breast cancer G/GEJ tumours	Trastuzumab Deruxtecan (T-DXd)	DXd	HER2	24	NA	NA	3 (13)	(33)
Dotan, 2017	I/II	IMMU-130-02	Colorectal cancer	Labetuzumab Govitecan (hMN-14-SN38)	SN-38	CEACAM5 (CD66e)	86	NA	NA	13 (15)	(34)
Eichenauer, 2017	II	Targeted BEACOPP	Classical HL	Brentuximab Vedotin (SGN-35)	MMAE	CD30	102	NA	NA	NA	(35)
Fanale, 2012	I	SG035-0001	Lymphoma	Brentuximab Vedotin (SGN-35)	MMAE	CD30	44	NA	NA	13 (30)	(36)
Forero-Torres, 2015	II	SGN35-015	Older HL	Brentuximab Vedotin (SGN-35)	MMAE	CD30	27	NA	13 (48)	11 (41)	(37)
Forero-Torres, 2017	Ib/II	GO29044	DLBCL	Polatuzumab Vedotin	MMAE	CD79b	21	NA	NA	4 (19)	(38)
Garrido-Laguna,	I	B7521001	Solid tumors	PF-06647263	Calicheamicin	EFNA4	60	53 (88)	20 (25)	12 (38)	(39)

2019											
Geller, 2020	II	ADVL1522	Childre's tumors	Lorvotuzumab Mertansine (IMGN901)	DM1	CD56	61	22 (36)	20 (33)	NA	(40)
Gerber, 2020	I	GO27767	NSCLC Ovarian cancer	Lifastuzumab Vedotin (DNIB0600A)	MMAE	NaPi2b	87	77 (89)	41 (47)	12 (14)	(41)
Goldberg, 2020	I	ADCT-301-002	AML ALL	Camidanlumab Tesirine (ADCT-301)	PBD	CD25	35	20 (57)	11 (31)	4 (11)	(42)
Goss, 2018	II	M13-379	Solid tumors	Depatuxizumab Mafodotin (ABT-414)	MMAF	EGFR	56	NA	NA	11 (20)	(43)
Gray, 2017	I/II	IMMU-132-01	SCLC	Sacituzumab Govitecan (hRS7-SN38)	SN-38	Trop-2	53	NA	NA	NA	(44)
Hamadani, 2021	I	ADCT-402-101	B-NHL	Loncastuximab Tesirine (ADCT-402)	PBD	CD19	183	NA	NA	35 (19)	(45)
Hamadani, 2021	I	ADCT-301-001	Lymphoma	Camidanlumab Tesirine (ADCT-301)	PBD	CD25	133	116 (88)	NA	31 (23)	(46)
Hamilton, 2020	I	SCRX003-001	Ovarian cancer	Tamrintamab Pamozirine (SC-003)	PBD	DPEP3	74	64 (87)	NA	14 (19)	(47)
Hann,	I	SCRX00	Extensive-Stag	Rovalpituzumab	PBD	DLL3	26	24 (92)	NA	7 (28)	(48)

2021		1-004	e SCLC	Tesirine (SC16LD6.5)						
Hassan, 2020	I	15051	Solid tumors	Anetumab Ravtansine (BAY94-9343)	DM4	Mesothelin	148	88 (59)	26 (18)	3 (2)	(49)
Heist, 2017	I/II	IMMU-132-01	NSCLC	Sacituzumab Govitecan (hRS7-SN38)	SN-38	Trop-2	54	NA	NA	2 (4)	(50)
Herrera, 2020	II	ADCT-301-201	HL	Camidanlumab Tesirine (ADCT-301)	PBD	CD25	47	NA	NA	6 (13)	(51)
Herrera, 2022	I/Ib	GO29687	B-NHL	DCDS0780A	MMAE	CD79b	60	54 (90)	NA	21 (35)	(52)
Hong, 2021	I	BAT-8001-001-CR	Breast cancer	BAT8001	Geldanamycin	HER2	29	29 (100)	14 (48)	0 (0)	(53)
Horwitz, 2014	II	SGN35-012	TCL	Brentuximab Vedotin (SGN-35)	MMAE	CD30	35	NA	NA	7 (20)	(54)
Horwitz, 2019	III	ECHELON-2	TCL	Brentuximab Vedotin (SGN-35)	MMAE	CD30	223	NA	NA	14 (6)	(55)
Hotta, 2018	II	UMIN000017709	NSCLC	Trastuzumab Emtansine (T-DM1)	DM1	HER2	15	NA	NA	2 (13)	(56)
Hurvitz,	II	BO2197	Breast cancer	Trastuzumab	DM1	HER2	69	NA	32 (46)	5 (7)	(57)

2013		6		Emtansine (T-DM1)							
Jacobsen, 2015	II	SGN35-012	DLBCL	Brentuximab Vedotin (SGN-35)	MMAE	CD30	68	NA	NA	6 (12)	(58)
Jain, 2020	I	ADCT-402-102	B-ALL	Loncastuximab Tesirine (ADCT-402)	PBD	CD19	35	19 (54)	NA	NA	(59)
Janne, 2022	I	U31402-A-U102	NSCLC	Patritumab Deruxtecan (HER3-DXd)	DXd	HER3	81	78 (96)	38 (47)	7 (9)	(60)
Ji, 2020	I	BP29920	Breast cancer	Trastuzumab Emtansine (T-DM1)	DM1	HER2	11	11 (100)	7 (64)	1 (9)	(61)
Johnson, 2021	I	PROCLAIM-CX-2029	Solid tumors	CX-2029	MMAE	CD71	45	45 (100)	27 (60)	0 (0)	(62)
Johnson, 2021	III	MERU	Extensive-Stage SCLC	Rovalpituzumab Tesirine (SC16LD6.5)	PBD	DLL3	368	290 (79)	NA	74 (20)	(63)
Kalinsky, 2020	I/II	IMMU-132-01	Breast cancer	Sacituzumab Govitecan (hRS7-SN38)	SN-38	Trop-2	54	NA	NA	2 (4)	(64)
Kantarjian, 2016	II	EFC11603	ALL	Coltuximab Ravtansine	DM4	CD19	36	22 (61)	NA	5 (14)	(65)

				(SAR3419)						
Kantarjian, 2019	III	INO-VATE	ALL	Inotuzumab Ozogamicin (PF-5208773)	Calicheamicin	CD22	164	144 (88)	115 (70)	31 (19)	(66)
Kashiwaba, 2016	II	JO22997	Breast cancer	Trastuzumab Emtansine (T-DM1)	DM1	HER2	73	70 (96)	41 (56)	2 (3)	(67)
Kelly, 2021	I/IIa	983	MM	Indatuximab Ravtansine (BT062)	DM4	CD138	64	NA	NA	9 (14)	(68)
Khan, 2021	I	PrECOG 0504	NSCLC	Glembatumumab Vedotin (CDX-011)	MMAE	gpNMB	13	NA	NA	NA	(69)
Kim, 2015	II	IRB-21324	MF SS	Brentuximab Vedotin (SGN-35)	MMAE	CD30	32	NA	10 (31)	6 (19)	(70)
Kim, 2017	III	ALCANZA	TCL	Brentuximab Vedotin (SGN-35)	MMAE	CD30	66	57 (86)	19 (29)	16 (24)	(71)
Kim, 2019	I	16897	Solid tumors	Aprutumab Ixadotin (BAY 1187982)	MMAW	FGFR2	20	17 (85)	9 (45)	5 (25)	(72)
Kindler, 2022	II	15743	Pleural mesothelioma	Anetumab Ravtansine (BAY94-9343)	DM4	Mesothelin	163	NA	78 (48)	NA	(73)
King,	I	B740100	Solid tumors	PF-06664178	Aur0101	Trop-2	31	NA	14 (45)	3 (10)	(74)

2018		1		(RN927C)							
Kollmann sberger, 2021	II	AGS-16 C3F-15-3	RCC	AGS-16C3F	MMAF	ENPP3	67	53 (79)	17 (26)	7 (5)	(75)
Kollmann sberger, 2021	I	15383	Solid tumors	LY3076226	DM4	FGFR3	25	20 (80)	2 (8)	0 (0)	(76)
Kopp, 2019	II	AOST15 21	Osteosarcoma	Glembatumuma b Vedotin (CDX-011)	MMAE	gpNMB	22	NA	NA	NA	(77)
Krop, 2012	II	BO2285 7	Breast cancer	Trastuzumab Emtansine (T-DM1)	DM1	HER2	110	NA	NA	7 (6)	(78)
Krop, 2015	II	BO2285 7	Early-stage breast cancer	Trastuzumab Emtansine (T-DM1)	DM1	HER2	148	NA	61 (41)	20 (14)	(79)
Krop, 2017	III	TH3RES A	Breast cancer	Trastuzumab Emtansine (T-DM1)	DM1	HER2	403	NA	NA	59 (15)	(80)
Lassman, 2019	I	M12-356	Glioblastoma	Depatuxizumab Mafodotin (ABT-414)	MMAF	EGFR	60	NA	24 (40)	4 (7)	(81)
Lemech, 2020	I	M15-916	Solid tumors	ABBV-176	PBD	Prolactin receptor	19	14 (73)	6 (32)	3 (16)	(82)
Li, 2018	II	15-335	Lung cancer	Trastuzumab Emtansine	DM1	HER2	18	NA	NA	0 (0)	(83)

				(T-DM1)							
Li, 2022	II	DESTINY-Lung01	NSCLC	Trastuzumab Deruxtecan (T-DXd)	DXd	HER2	91	88 (97)	42 (46)	23 (25)	(84)
Liu, 2016	I	GO00766	Ovarian or Pancreatic cancer	DMUC5754A	MMAE	MUC16	77	71 (92)	NA	6 (8)	(85)
Liu, 2021	I	GO29213	Ovarian cancer	DMUC4064A	MMAE	MUC16	65	55 (85)	16 (25)	12 (18)	(86)
Lonial, 2021	II	DREAMM-2	MM	Belantamab Mafodotin (GSK2857916)	MMAF	CD38	95	84 (88)	54 (57)	9 (9)	(87)
Loriot, 2020	II	TROPHY-U-01	Urothelial crcinoma	Sacituzumab Govitecan (hRS7-SN38)	SN-38	Trop-2	113	107 (95)	NA	7 (6)	(88)
Lynch, 2021	I/II	RG1714038	HL	Brentuximab Vedotin (SGN-35)	MMAE	CD30	45	NA	NA	11 (24)	(89)
Maitland, 2021	I	B7661001	Solid tumors	Cofetuzumab Pelidotin (PF-06647020)	Aur0101	PTK7	112	96 (86)	44 (39)	3 (3)	(90)
Malhotra, 2021	I/II	M16-300	Extensive-Stage SCLC	Rovalpituzumab Tesirine (SC16LD6.5)	PBD	DLL3	42	41 (98)	27 (64)	6 (14)	(91)

Mansfield, 2021	I/II	SCRX001-006	Solid tumors	Rovalpituzumab Tesirine (SC16LD6.5)	PBD	DLL3	200	181 (91)	97 (49)	48 (24)	(92)
Medeiros, 2018	I/II	090516	AML	Gemtuzumab Ozogamicin	Calicheamicin	CD33	50	NA	NA	NA	(93)
Modi, 2020	Ib	DS8201-A-J101	Breast cancer	Trastuzumab Deruxtecan (T-DXd)	DXd	HER2	54	NA	NA	11 (20)	(94)
Modi, 2020	II	DESTINY-Breast 01	Breast cancer	Trastuzumab Deruxtecan (T-DXd)	DXd	HER2	184	183 (99)	89 (48)	27 (15)	(95)
Modi, 2022	III	DESTINY-Breast 04	Breast cancer	Trastuzumab Deruxtecan (T-DXd)	DXd	HER2	373	369 (99)	195 (53)	56 (15)	(96)
Moore, 2018	Ib	FORWARD II	Ovarian cancer	Mirvetuximab Soravtansine (IMGN853)	DM4	FR α	18	NA	NA	1 (6)	(97)
Moore, 2020	Ib	GO29006	Ovarian cancer	Lifastuzumab Vedotin (DNIB0600A)	MMAE	NaPi2b	41	40 (98)	30 (73)	7 (17)	(98)
Moore, 2021	III	FORWARD I	Ovarian cancer	Mirvetuximab Soravtansine (IMGN853)	DM4	FR α	243	230 (95)	61 (25)	11 (5)	(99)

Morgenszt ern, 2019	II	TRINIT Y	SCLC	Rovalpituzumab Tesirine (SC16LD6.5)	PBD	DLL3	339	308 (91)	135 (40)	33 (10)	(100)
Morgenszt ern, 2020	I/Ib	SCRX00 2-001	SCLC LCNEC	SC-002 (SC-DR002)	PBD	DLL3	35	28 (80)	NA	13 (37)	(101)
Morschha user, 2019	II	ROMUL US	DLBCL	Polatuzumab Vedotin or Pinatuzumab Vedotin	MMAE MMAE	CD79b CD22	39 42	NA	NA	12 (31) 18 (43)	(102)
Morschha user, 2019	II	ROMUL US	Follicular lymphoma	Polatuzumab Vedotin or Pinatuzumab Vedotin	MMAE MMAE	CD79b CD22	20 21	NA	NA	11 (55) 16 (76)	(102)
Narayan, 2020	I	13-040	AML	Brentuximab Vedotin (SGN-35)	MMAE	CD30	22	NA	NA	NA	(103)
Narita, 2021	I/II	INTELL ANCE-J	Malignant glioma	Depatuxizumab Mafodotin (ABT-414)	MMAF	EGFR	53	NA	NA	1 (5)	(104)
O'Brien, 2019	II	AALL16 21	B-ALL	Inotuzumab Ozogamicin (PF-5208773)	Calichea micin	CD22	48	NA	NA	NA	(105)
Ogura, 2014	I/II	JapicCTI -111650	HL sALCL	Brentuximab Vedotin (SGN-35)	MMAE	CD30	20	NA	NA	1 (5)	(106)

O'Malley, 2020	Ib	IMGN853-0402	Ovarian cancer	Mirvetuximab Soravtansine (IMGN853)	DM4	FR α	66	65 (98)	NA	19 (29)	(107)
Ott, 2014	I/II	CR011-CLN-11	Melanoma	Glembatumumab Vedotin (CDX-011)	MMAE	gpNMB	117	NA	NA	11 (9)	(108)
Ott, 2019	II	CDX011-05	Melanoma	Glembatumumab Vedotin (CDX-011)	MMAE	gpNMB	62	55 (89)	21 (34)	4 (6)	(109)
Owonikoko, 2016	I	MDX1203-01	RCC B-NHL	BMS-936561 (MDX-1203)	Calicheamicin	CD70	26	26 (26)	9 (35)	11 (42)	(110)
Ozcan, 2021	IV	B1931030	ALL	Inotuzumab Ozogamicin (PF-5208773)	Calicheamicin	CD22	22	13 (59)	NA	2 (9)	(111)
Pal, 2019	I	SGN70A-001	RCC	SGN-CD70A	PBD	CD70	18	NA	NA	5 (28)	(112)
Palanca-Wessels, 2015	I	GO01294	NHL CLL	Polatuzumab Vedotin	MMAE	CD79b	95	NA	NA	23 (51)	(113)
Pegram, 2021	I/II	D5760C00001	Breast cancer Gastric cancer	MEDI4276	DM1	HER2	47	43 (92)	17 (36)	5 (11)	(114)
Peng, 2021	II	RC48-C008	G/GEJ cancer	RC48-ADC	MMAE	HER2	125	122 (98)	40 (32)	18 (14)	(115)
Perez, 2017	III	MARIANNE	Breast cancer	Trastuzumab Emtansine	DM1	HER2	361	357 (99)	164 (45)	66 (18)	(116)

				(T-DM1)							
Perez, 2017	III	MARIANNE	Breast cancer	Trastuzumab Emtansine (T-DM1)	DM1	HER2	366	361 (98)	169 (46)	70 (19)	(116)
Peters, 2019	II	BO29389	NSCLC	Trastuzumab Emtansine (T-DM1)	DM1	HER2	49	NA	NA	1 (2)	(117)
Petrylak, 2019	I	PSMA ADC 1301	CRPC	PSMA ADC	MMAE	PSMA	52	NA	NA	0 (0)	(118)
Ribrag, 2014	I	TED6828	B-NHL	SAR3419	DM4	CD19	69	NA	NA	NA	(119)
Rosen, 2020	I	B7501001	Solid tumors	PF-06650808	Auristatin-based cytotoxic	Notch3	40	35 (88)	21 (53)	3 (8)	(120)
Rosenberg, 2019	II	SGN22E-001	Urothelial carcinoma	Enfortumab Vedotin (ASG-22CE)	MMAE	Nectin-4	125	117 (94)	68 (54)	15 (12)	(121)
Rosenberg, 2020	I	EV-101	Urothelial carcinoma	Enfortumab Vedotin (ASG-22CE)	MMAE	Nectin-4	155	145 (94)	53 (34)	16 (10)	(122)
Rosenthal, 2019	I	20090505	Malignant glioma	AMG 595	DM1	EGFR	32	28 (88)	17 (53)	3 (9)	(123)

Ross, 2006	II	SG0002-015	NSCLC	SGN-15 (cBR96-Doxorubicin)	Doxorubicin	Le^y	59	NA	NA	(124)
Rottey, 2022	I/IIa	CA008-002	Solid tumors	BMS-986148	DM4	Mesothelin	96 30	83 (86) 27 (90)	45 (47) 10 (33)	17 (13)	(125)
Rudin, 2017	I/II	SCRX16-001	SCLC	Rovalpituzumab Tesirine (SC16LD6.5)	PBD	DLL3	74	65 (88)	28 (38)	18 (22)	(126)
Sandhu, 2020	I	GO27935	Melanoma	DEDN6526A	MMAE	ET_BR	53	51 (96)	22 (42)	5 (9)	(127)
Sehn, 2020	Ib/II	GO29365	DLBCL	Polatuzumab Vedotin	MMAE	CD79b	39	NA	NA	NA	(128)
Shah, 2016	I	IMGN-002	Solid tumors	Lorvotuzumab Mertansine (IMGN901)	DM1	CD56	97	73 (75)	36 (37)	6 (6)	(129)
Shapiro, 2017	I	B4481001	Solid tumors	PF-06263507	MMAF	5T4	26	22 (85)	3 (12)	3 (12)	(130)
Sharman, 2019	II	SGN35-013	Solid tumors	Brentuximab Vedotin (SGN-35)	MMAE	CD30	63	46 (73)	NA	6 (10)	(131)
Sheng, 2021	II	RC48-C005	Urothelial carcinoma	RC48-ADC	MMAE	HER2	43	43 (100)	25 (58)	11 (26)	(132)

Shimizu, 2021	I	MORAb-202-J0811-101	Solid tumors	MORAb-202	Eribulin	FR α	22	21 (95)	3 (14)	1 (5)	(133)
Shitara, 2019	I	DS8201-A-J101	Gastric cancer	Trastuzumab Deruxtecan (T-DXd)	DXd	HER2	44	43 (98)	28 (64)	5 (11)	(134)
Shitara, 2020	II	DESTINY-Gastric01	Gastric cancer	Trastuzumab Deruxtecan (T-DXd)	DXd	HER2	125	122 (98)	94 (75)	12 (10)	(135)
Siena, 2021	II	DESTINY-CRC01	Colorectal cancer	Trastuzumab Deruxtecan (T-DXd)	DXd	HER2	78	73 (94)	38 (49)	2 (3)	(136)
Socinski, 2017	I/II	Immunogen 0007	Extensive-Stage SCLC	Lorvotuzumab Mertansine (IMGN901)	DM1	CD56	33 94	NA 90 (96)	30 (91) 83 (88)	37 (29)	(137)
Starodub, 2015	I/II	IMMU-132-01	Solid tumors	Sacituzumab Govitecan (hRS7-SN38)	SN-38	Trop-2	25	NA	NA	NA	(138)
Stathis, 2018	I	IMGN0301	B-NHL	IMGN529	DM1	CD37	49	NA	NA	5 (10)	(139)
Stein, 2018	I	SGN33A-001	AML	Vadastuximab Talirine (SGN-CD33A)	PBD	CD33	131	NA	NA	34 (26)	(140)
Stewart, 2019	I	GO27825	MM	DFRF4539A	MMAE	FcRH5	39	30 (77)	9 (23)	7 (18)	(141)

Straus, 2021	III	ECHELON-1	Classical HL	Brentuximab Vedotin (SGN-35)	MMAE	CD30	662	641 (97)	549 (83)	88 (13)	(142)
Strickler, 2018	I/Ib	M14-237	Solid tumors	Telisotuzumab Vedotin (ABBV-399)	MMAE	c-Met	48	34 (71)	8 (17)	11 (23)	(143)
Takahashi, 2020	I	7465-CL-0101	Urothelial carcinoma	Enfortumab Vedotin (ASG-22CE)	MMAE	Nectin-4	17	15 (88)	NA	3 (18)	(144)
Takahashi, 2021	I	DS8201-A-A104	Solid tumors	Trastuzumab Deruxtecan (T-DXd)	DXd	HER2	40	38 (95)	17 (43)	7 (18)	(145)
Tamura, 2019	I	DS8201-A-J101	Breast cancer	Trastuzumab Deruxtecan (T-DXd)	DXd	HER2	115	113 (98)	57 (50)	13 (11)	(146)
Tannir, 2014	I	SGN75-001	NHL RCC	SGN-75	MMAF	CD70	47	38 (81)	NA	14 (24)	(147)
Terui, 2021	II	JO40762	DLBCL	Polatuzumab Vedotin	MMAE	CD79b	35	33 (94)	NA	7 (20)	(148)
Thompson, 2018	I	2009002	RCC	AGS-16M8F	MMAF	ENPP3	26	26 (100)	16 (62)	1 (4)	(149)
Thungappa, 2022	III	CTRI/2018/07/014881	Breast cancer	Trastuzumab Emtansine (ZRC-3256) Trastuzumab	DM1	HER2	168	NA	NA	0 (0)	(150)

				Emtansine (T-DM1)							
Tilly, 2022	III	POLARIX	DLBCL	Polatuzumab Vedotin	MMAE	CD79b	435	426 (98)	264 (61)	27 (6)	(151)
Tolaney, 2020	I	GO29146	Solid tumors	DLYE5953A	MMAE	LY6E	68	63 (93)	17 (25)	5 (7)	(152)
Trněný, 2018	II	ARD10248	DLBCL	Coltuximab Ravtansine (SAR3419)	DM4	CD19	61	33 (54)	NA	4 (7)	(153)
Trudel, 2019	I	117159	MM	GSK2857916	MMAF	BCMA	35	NA	NA	4 (11)	(154)
Tsurutani, 2020	I	DS8201-A-J101	Solid tumors	Trastuzumab Deruxtecan (T-DXd)	DXd	HER2	59	NA	NA	5 (9)	(155)
Udagawa, 2019	I	SCRX001-008	SCLC	Rovalpituzumab Tesirine (SC16LD6.5)	PBD	DLL3	29	29 (100)	15 (52)	4 (14)	(156)
Vahdat, 2021	IIb	METRIC	TNBC	Glembatumumab Vedotin (CDX-011)	MMAE	gpNMB	213	211 (99)	150 (70)	31 (15)	(157)
Van Den Bent, 2020	II	EORTC 1410	Glioblastoma	Depatuxizumab Mafodotin (ABT-414)	MMAF	EGFR	84 88	NA	NA	12 (7)	(158)

Verma, 2012	III	EMILIA	Breast cancer	Trastuzumab Emtansine (T-DM1)	DM1	HER2	490	470 (96)	200 (41)	29 (6)	(159)
Vij, 2020	I/Ib	M14-467	MM	ABBV-838	MMAE	SLAMF 7/CS1	75	55 (71)	30 (40)	16 (21)	(160)
Von Minckwitz, 2019	III	KATHERINE	Breast cancer	Trastuzumab Emtansine (T-DM1)	DM1	HER2	740	731 (99)	190 (26)	133 (18)	(161)
Waqar, 2021	II	S1400K	Lung Cancer	Telisotuzumab Vedotin (ABBV-399)	MMAE	c-Met	23	NA	7 (30)	NA	(162)
Weekes, 2016	I	DMO4993g	Ovarian Cancer	DMOT4039A	MMAE	Mesothelin	71	39 (72)	14 (26)	4 (6)	(163)
Yardley, 2015	II	EMERGE	Breast cancer	Glembatumumab Vedotin (CDX-011)	MMAE	gpNMB	96	87 (91)	39 (40)	8 (8)	(164)
Younes, 2010	I	SG035-0001	Lymphomas	Brentuximab Vedotin (SGN-35)	MMAE	CD30	45	NA	NA	12 (27)	(165)
Yu, 2021	II	EV-201	Urothelial carcinoma	Enfortumab Vedotin (ASG-22CE)	MMAE	Nectin-4	89	86 (97)	49 (55)	14 (16)	(166)
Zhang, 2022	I	ACE-Breast-01	Breast cancer	ARX788	AS269	HER2	69	67 (97)	8 (12)	2 (3)	(167)

Zinzani, 2019	I/II	CheckMate 436	Mediastinal B-cell lymphoma	Brentuximab Vedotin (SGN-35)	MMAE	CD30	30	25 (83)	16 (53)	5 (17)	(168)

Abbreviation: ID, Identification; ADC, antibody-drug conjugate; AEs, Adverse Events; BHL, non-Hodgkin lymphoma; CLL, chronic lymphocytic leukemia; MM, multiple myeloma; G/GEJ, the stomach or gastroesophageal junction; TNBC, Triple-Negative Breast Cancer; ALL, acute lymphoblastic leukemia; DLBCL, diffuse large B-cell lymphoma; SCLC, small cell lung cancer; NSLCL, non–small cell lung cancer; B-NHL, B-cell non-Hodgkin lymphoma; CRPC, castration-resistant prostate cancer; AML, Acute myeloid leukemia; PBD, pyrrolobenzodiazepine; HL, Hodgkin's lymphoma; TCL, T-cell lymphomas; B-ALL, B-cell acute lymphoblastic leukemia; MF, mycosis fungoides; SS, Sézary syndrome; RCC, renal cell carcinoma; LCNEC, large cell neuroendocrine carcinoma; MEC, mitoxantrone+etoposide+cytarabine; RT, radiotherapy; sALCL, systemic anaplastic large-cell lymphoma; PSMA, prostate-specific membrane antigen; ET_BR, endothelin B receptor.

eTable 3. Main characteristics of randomized controlled trials included in the meta-analysis of comparison of treatment-related adverse events.

Study	Phase	Trial name or ID	Cancer type	ADC agent	Payload type	Target agent	Controlled agent	Total patient number in ADC arm, n	Patients with any grade AEs in ADC arm, n (%)	Patients with grade 3 or higher AEs in ADC arm, n (%)	Total patient number in controlled arm, n	Patients with any grade AEs in controlled arm, n (%)	Patients with grade 3 or higher AEs in controlled arm, n (%)	Ref.
Banerjee, 2018	II	GO28609	Ovarian cancer	Lifastuzumab vedotin (DNIB0600A)	MMAE	NaPi2b	Pegylated, liposomal, doxorubicin	46	NA	NA	47	NA	NA	(8)
Bardia, 2021	III	IMMU-132-05	TNBC	Sacituzumab Govitecan (hRS7-SN38)	SN-38	Trop-2	Chemotherapy	258	252 (98)	165 (64)	224	192 (86)	104 (47)	(13)
Blackhall, 2021	III	TAHOE	SCLC	Rovalpituzumab Tesirine (SC16LD6.5)	SG3199	DLL3	Topotecan	287	NA	NA	129	NA	NA	(15)

Cortes, 2022	III	DESTINY-Breast03	Breast cancer	Trastuzumab Deruxtecan (T-DXd)	DXd	HER2	Trastuzumab emtansine	257	256 (98)	116 (45)	261	228 (87)	105 (40)	(25)
Dang, 2018	III	B1931008	B-NHL	Inotuzumab Ozogamicin (PF-5208773)	Caliche-amicin	CD22	Rituximab plus bendamustin Rituximab plus gemcitabine	164	148 (90)	102 (62)	167	146 (87)	107 (64)	(27)
Eichenauer, 2017	II	Targeted BEACOPP	Classical HL	Brentuximab Vedotin (SGN-35)	MMAE	CD30	BrECADD	50	NA	NA	52	NA	NA	(35)
Horwitz, 2019	III	ECHELON-2	TCL	Brentuximab Vedotin (SGN-35)	MMAE	CD30	CHOP	223	NA	NA	226	NA	NA	(55)
Hurvitz, 2013	II	BO21976	Breast cancer	Trastuzumab Emtansine (T-DM1)	DM1	HER2	Trastuzumab plus docetaxel	69	NA	32 (46)	66	NA	60 (91)	(57)
Johnson, 2021	III	MERU	Extensive-Stage SCLC	Rovalpituzumab Tesirine (SC16LD6.5)	PBD	DLL3	Placebo	368	290 (79)	NA	373	145 (39)	NA	(63)

Kantarjian, 2019	III	INO-VATE	ALL	Inotuzumab Ozogamicin (PF-5208773)	Calicheamicin	CD22	Chemotherapy	164	144 (88)	115 (70)	143	130 (91)	114 (80)	(66)
Kim, 2017	III	ALCANZA	TCL	Brentuximab Vedotin (SGN-35)	MMAE	CD30	Methotrexate or bexarotene	66	57 (86)	19 (29)	62	44 (71)	18 (29)	(71)
Kindler, 2022	II	15743	Pleural mesotheli-oma	Anetumab Ravtansine (BAY94-9343)	DM4	Mesoth-elin	Vinorelbine	163	NA	78 (48)	72	NA	53 (74)	(73)
Kollmannsberger, 2021	II	AGS-16C3F-15-3	RCC	AGS-16C3F	MMAF	ENPP3	Axitinib	67	53 (79)	17 (26)	66	61 (92)	30 (45)	(75)
Krop, 2017	III	TH3RESA	Breast cancer	Trastuzumab Emtansine (T-DM1)	DM1	HER2	Treatment of physician's choice	403	NA	NA	184	NA	NA	(80)
Modi, 2022	III	DESTINY-Breast04	Breast cancer	Trastuzumab Deruxtecan (T-DXd)	DXd	HER2	Treatment of physician's choice	371	369 (99)	195 (53)	172	169 (98)	116 (67)	(96)
Moore, 2021	III	FORWARD I	Ovarian cancer	Mirvetuximab Soravtansine (IMGN853)	DM4	FR α	Chemotherapy	243	230 (95)	61 (25)	109	98 (90)	48 (44)	(99)
Morschhauser,	II	ROMULUS	DLBCL	Polatuzumab Vedotin	MMAE	CD79b	Pinatuzumab vedotin	39	NA	NA	42	NA	NA	(100)

2019							plus Rituximab							
Morschhauser, 2019	II	ROMULUS	Follicular lymphoma	Polatuzumab Vedotin	MMAE	CD79b	Pinatuzumab vedotin plus rituximab	20	NA	NA	21	NA	NA	(102)
Perez, 2017	III	MARIANNE	Breast cancer	Trastuzumab Emtansine (T-DM1)	DM1	HER2	Trastuzumab plus taxane	361 366	357 (99) 361 (98)	164 (45) 169 (46)	353	348 (99)	191 (54)	(116)
Sehn, 2020	Ib/II	GO29365	DLBCL	Polatuzumab Vedotin	MMAE	CD79b	Bendamustine plus rituximab	39	NA	NA	39	NA	NA	(128)
Shitara, 2020	II	DESTINY-Gastric01	Gastric cancer	Trastuzumab Deruxtecan (T-DXd)	DXd	HER2	Physician's choice of chemotherapy	125	122 (98)	94 (75)	62	56 (90)	27 (44)	(169)
Socinski, 2017	I/II	Immunogen 0007	Extensive-stage SCLC	Lorvotuzumab Mertansine (IMGN901)	DM1	CD56	EC	94	90 (96)	83 (88)	47	39 (83)	33 (70)	(137)
Straus, 2021	III	ECHELON-1	Classical HL	Brentuximab Vedotin (SGN-35)	MMAE	CD30	ABVD	662	641 (97)	549 (83)	659	617 (94)	389 (59)	(142)
Thungappa, 2021	III	CTRI/2018/0	Breast cancer	Trastuzumab Emtansine	DM1	HER2	Trastuzumab emtansine	113	NA	NA	55	NA	NA	(150)

		7/014881		(ZRC-3256)										
Tilly, 2022	III	POLARIX	DLBCL	Polatuzumab Vedotin	MMAE	CD79b	Rituximab plus CHOP	435	426 (98)	264 (61)	438	431 (98)	262 (60)	(151)
Vahdat, 2021	IIb	METRIC	TNBC	Glembatumumab Vedotin (CDX-011)	MMAE	gpNMB	Capecitabine	213	211 (99)	150 (70)	92	92 (100)	52 (57)	(157)
Van Den Bent, 2020	II	EORTC 1410	Glioblastoma	Depatuxizumab Mafodotin (ABT-414)	MMAF	EGFR	Lomustine or temozolomide	8488	NA	NA	77	NA	NA	(158)
Verma, 2012	III	EMILIA	Breast cancer	Trastuzumab Emtansine (T-DM1)	DM1	HER2	Lapatinib plus capecitabine	490	470 (96)	200 (41)	488	477 (98)	278 (57)	(159)
Von Minckwitz, 2019	III	KATHERINE	Breast cancer	Trastuzumab Emtansine (T-DM1)	DM1	HER2	Trastuzumab	740	731 (99)	190 (26)	720	672 (93)	111 (15)	(161)
Yardley, 2015	II	EMERGE	Breast cancer	Glembatumumab Vedotin (CDX-011)	MMAE	gpNMB	Investigator's choice chemotherapy	96	87 (91)	39 (40)	41	37 (90)	16 (36)	(164)

Abbreviation: ID, Identification; ADC, antibody-drug conjugate; AEs, Adverse Events; TNBC, Triple-Negative Breast Cancer; SCLC, small cell lung cancer; NHL, non-Hodgkin lymphoma; HL, Hodgkin's lymphoma; BrECADD, brentuximab vedotin+etoposide+cyclophosphamid+doxorubicin+dexamethason+dacarbazine; CHOP, cyclophosphamide+doxorubicin+vincristine+prednisone; EC, cisplatin or carboplatin combined with etoposide; ABVD, doxorubicin+bleomycin+vinblastine+dacarbazine

eTable 4. Risk of bias of each randomized controlled trial included for comparison.

Study	Randomization	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selecting report	Other sources of bias
Banerjee, 2018	unclear	unclear	high	unclear	low	low	low
Bardia, 2021	unclear	unclear	high	low	low	low	low
Blackhall, 2021	unclear	unclear	high	unclear	low	low	low
Cortes, 2022	unclear	unclear	high	low	low	low	low
Dang, 2018	unclear	unclear	high	unclear	low	low	low
Eichenauer, 2017	low	low	high	low	low	low	low
Horwitz, 2019	low	low	low	low	low	low	low
Hurvitz, 2013	low	low	high	high	low	low	low
Johnson, 2021	unclear	unclear	low	low	low	low	low
Kantarjian, 2019	unclear	unclear	high	high	low	low	low
Kim, 2017	low	low	high	low	low	low	low
Kindler, 2022	low	low	high	low	low	low	low
Kollmannsberger, 2021	unclear	unclear	high	low	low	low	low
Krop, 2017	low	low	high	high	low	low	low
Modi, 2022	low	low	high	low	low	low	low
Moore, 2021	low	low	high	low	low	low	low
Morschhauser, 2019	low	low	high	high	low	low	low
Perez, 2017	low	low	high	low	low	low	low
Sehn, 2020	unclear	unclear	high	low	low	low	low
Shitara, 2020	unclear	unclear	high	low	low	low	low

Socinski, 2017	unclear	unclear	high	unclear	low	low	low
Straus,2021	low	low	high	low	low	low	low
Thungappa, 2021	low	low	high	low	low	low	low
Tilly, 2022	low	low	low	low	low	low	low
Vahdat, 2021	low	low	high	low	low	low	low
Van Den Bent, 2020	low	low	high	low	low	low	low
Verma, 2012	low	low	high	low	low	low	low
Von Minckwitz, 2019	low	low	high	low	low	low	low
Yardley, 2015	unclear	unclear	high	low	low	low	low

Low indicates no risk, high indicates high risk and unclear indicates unknown risk.

eTable 5. Patients with adverse events leading to treatment discontinuation.

Cause of discontinuationa	ADC therapy/No. (%) (N, 1,113)
Neurologic	
Peripheral sensory neuropathy	161 (14.5)
Peripheral neuropathy	122 (11.0)
Peripheral motor neuropathy	18 (1.6)
Hypoesthesia	12 (1.1)
Peripheral sensorimotor neuropathy	5 (0.5)
Hypoxic ischemic encephalopathy	2 (0.2)
Gait disturbance	2 (0.2)
Dizziness	2 (0.2)
Hypersensitivity	2 (0.2)
Cerebral ischemia	1 (0.1)
Brain edema	1 (0.1)
Vertigo	1 (0.1)
Memory impairment	1 (0.1)
Confusional state	1 (0.1)
Hematologic	
Thrombocytopenia	125 (11.2)
Neutropenia	47 (4.2)
Increased gamma-glutamyl transferase	30 (2.7)
Increased blood bilirubin	29 (2.6)
Increased aspartate transaminase	25 (2.3)
Increased alanine aminotransferas	18 (1.6)
Febrile neutropenia	14 (1.3)
Neutrophil count decrease	5 (0.5)
Hypoalbuminemia	4 (0.4)
Anemia	3 (0.3)
Increased blood creatinine phosphokinase	2 (0.2)
Alkaline Phosphatase Increased	1 (0.1)
Lipase increase	1 (0.1)
Troponin increased	1 (0.1)
Pulmonary	
Pneumonitis	64 (5.8)
Interstitial lung disease	39 (3.5)
Pleural effusion	22 (2.0)
Pneumonia	7 (0.6)
Dyspnoea	6 (0.5)
Hypoxia	2 (0.2)
Respiratory failure	2 (0.2)
Pneumothorax	1 (0.1)
Acute respiratory distress syndrome	1 (0.1)

Upper respiratory tract infection	1 (0.1)
Bronchopneumonia	1 (0.1)
Hemoptysis	1 (0.1)
Aspiration reaction	1 (0.1)
Respiratory tract hemorrhage	1 (0.1)
Pneumocystis jiroveci pneumonia	1 (0.1)
Cough	1 (0.1)
Other	4 (0.4)
Cardiovascular	
Decreased left-ventricular ejection fraction	12 (1.1)
Pericardial effusion	6 (0.5)
Hypotension	2 (0.2)
Sinus tachycardia	2 (0.2)
Coronary artery disease	1 (0.1)
Pericarditis	1 (0.1)
QT prolonged	1 (0.1)
Paroxysmal atrial tachycardia	1 (0.1)
Atrial fibrillation anaemia	1 (0.1)
Cardiac arrest	1 (0.1)
Renal	
Proteinuria	6 (0.5)
Acute kidney injury	4 (0.4)
Renal failure	2 (0.2)
Worsening chronic renal disease	1 (0.1)
Gastrointestinal	
Hepatotoxicity	12 (1.1)
Gastrointestinal hemorrhage	6 (0.5)
Nausea	5 (0.5)
Abdominal pain	4 (0.4)
Vomiting	3 (0.3)
Diarrhea	2 (0.2)
Small intestinal obstruction	2 (0.2)
Ascites	2 (0.2)
Immune-mediated hepatitis	2 (0.2)
Hypoalbuminemia	1 (0.1)
Hyperbilirubinemia	1 (0.1)
Bile duct obstruction	1 (0.1)
Musculoskeletal	
Myalgia	2 (0.2)
Muscular weakness	2 (0.2)
Muscle spasms	1 (0.1)
Arthralgia	1 (0.1)
Hip fracture	1 (0.1)
Joint crepitation	1 (0.1)

Metabolism and nutrition	
Decreased appetite	8 (0.7)
Dehydration	4 (0.4)
Hypophosphatemia	2 (0.2)
Hypercalcemia	2 (0.2)
Hypomagnesemia	1 (0.1)
Failure to thrive	1 (0.1)
Constitutional	
Fatigue	17 (1.5)
Asthenia	4 (0.4)
Pyrexia	3 (0.3)
Disturbance	2 (0.2)
Malaise	2 (0.2)
Physical health deterioration	1 (0.1)
Fluid retention	1 (0.1)
Metabolic acidosis	1 (0.1)
Malnutrition	1 (0.1)
Oedema	
Peripheral oedema	8 (0.7)
Localised oedema	5 (0.5)
Face oedema	2 (0.2)
Ocular	
Corneal deposits	12 (1.1)
Keratitis	9 (0.8)
Vision blurred	7 (0.6)
Corneal epithelial microcysts	6 (0.5)
Reduced visual acuity	3 (0.3)
Ulcerative keratitis	2 (0.2)
Corneal scar	2 (0.2)
Visual distortions	1 (0.1)
Limbal stem cell deficiency	1 (0.1)
Photophobia	1 (0.1)
Blepharitis	1 (0.1)
Conjunctivitis	1 (0.1)
Entropion	1 (0.1)
Erythema	1 (0.1)
Trichiasis	1 (0.1)
Cataract	1 (0.1)
Other	37 (3.3)
Dermatologic	
Rash	22 (2.0)
Dermatologic bullae	2 (0.2)
Hyperpigmentation	2 (0.2)
Mucositis	1 (0.1)

Lichenoid keratosis	1 (0.1)
Pruritus	1 (0.1)
Urticaria	1 (0.1)
Herpes zoster	1 (0.1)
Infecious	
Sepsis	18 (1.6)
Septic shock	3 (0.3)
Urosepsis	1 (0.1)
Neutropenic sepsis	1 (0.1)
Fungal infection	1 (0.1)
Other	
Stomatitis	4 (0.4)
Infusion reaction	2 (0.2)
Paraesthesia	2 (0.2)
Tumor lysis syndrome	2 (0.2)
Decreased DLCO	2 (0.2)
Tumour haemorrhage	1 (0.1)
Capillary leak syndrome	1 (0.1)
Glucose intolerance	1 (0.1)
Anal Fistula	1 (0.1)
Back pain	1 (0.1)
Pleuritic pain	1 (0.1)
Influenza	1 (0.1)
Graft-versus-host disease reactivatio	1 (0.1)
Drug specific antibody titre present	1 (0.1)
Clear cell renal cell carcinoma	1 (0.1)
Erythroleukemia	1 (0.1)
Radiation necrosis	1 (0.1)
Multiple organ dysfunction syndrome	1 (0.1)

[a] Unknown were not included (1030 cases).

Abbreviation: DLCO, diffusing capacity of the lung for carbon monoxide.

eTable 6. Incidences of grade 3 or higher adverse events in main payload-conjugates ADCs (N≥200).

Endpoint	MMAE (%, 95% CI)	DM1 (%, 95% CI)	DXd (%, 95% CI)	PBD (%, 95% CI)	SN-38 (%, 95% CI)	DM4 (%, 95% CI)	Calicheamicin (%, 95% CI)	MMAF (%, 95% CI)
Hematologic								
Neutropenia	37.0 (34.9, 39.2)	29.9 (25.1, 34.8)	18.8 (14.7, 22.8)	15.7 (9.2, 22.2)	42.8 (39.9, 45.7)	23.9 (16.2, 31.7)	13.7 (10.2, 17.2)	-
Thrombocytopenia	28.8 (16.5, 41.2)	22.2 (19.7, 24.6)	-	14.4 (11.3, 17.5)	24.4 (17.8, 31.0)	22.6 (13.7, 31.6)	56.0 (42.2, 69.8)	12.9 (7.4, 18.5)
Lymphopenia	22.6 (11.4, 33.9)	27.3 (12.1, 42.5)	-	-	11.6 (6.7, 16.5)	36.5 (23.5, 49.6)	-	-
Febrile neutropenia	17.1 (14.9, 19.4)	-	-	25.7 (11.2, 40.2)	12.3 (8.4, 16.1)	-	-	-
Anemia	15.3 (12.2, 18.4)	19.7 (12.8, 26.6)	9.9 (3.8, 16.0)	12.8 (5.7, 19.8)	11.3 (9.1, 13.4)	-	-	-
WBC count decreased	11.2 (8.1, 14.4)	15.2 (2.9, 27.4)	-	-	13.8 (10.9, 16.8)	-	-	-
Gastrointestinal								
Nausea	27.5 (18.3, 36.6)	22.2 (6.5, 37.9)	-	-	10.1 (5.1, 15.2)	-	-	-
Decreased appetite	24.3 (10.5, 38.1)	11.1 (0.7, 23.0)	-	-	-	-	-	-
Neurologic								
Peripheral neuropathy	10.0 (-0.7, 20.7)	-	-	-	-	-	-	-
Hepatorenal								
AST increased	17.5 (10.8, 24.1)	13.7 (5.8, 21.6)	-	18.4 (9.7, 27.1)	-	-	-	-
ALT increased	15.9 (9.5, 22.3)	-	-	14.9 (4.7, 25.1)	-	-	-	-
GGT increased	-[a]	-	-	16.2 (7.4, 24.9)	-	-	-	-
Hypoalbuminemia	-	-	-	13.8 (1.2, 26.3)	-	-	-	-
Liver function test abnormalities	-	18.2 (-4.6, 41.0)	-	-	-	-	-	-
Ocular toxicities								
Keratitis	13.3 (4.7, 21.9)	-	-	-	-	-	-	-

Pulmonary								
Pneumonia	6.3 (-2.1, 14.6)	-	-	-	-	-	-	-
Constitutional								
Fatigue	15.9 (6.8, 24.9)	16.0 (5.8, 26.2)	-	-	12.0 (-0.7, 24.7)	-	-	-
Hypokalemia	10.8 (0.8, 20.8)	NA	-	-	-	-	-	-
Hypophosphatemia	8.7 (-2.8, 20.2)	NA	-	11.4 (0.9. 22.0)	-	-	-	-
Dehydration	-	-	-	-	-	-	-	-
Skin								
Rash	-	-	-	-	-	21.4 (13.9, 28.8)	-	-
Skin reactions and nail disorders	-	-	-	19.1 (7.9, 30.4)	-	-	-	-
Other								
Hypertension	-	-	-	-	-	13.6 (5.4, 21.9)	-	-

[a] Unreported.

Abbreviation: WBC, white blood cell; AST, aspartate transaminase; ALT, alanine aminotransferas; GGT, gamma-glutamyl transferase.

eTable 7. Incidences of grade 3 or higher adverse events in main anti-target monoclonal antibody ADCs (N≥200).

Endpoint[a]	Anti-HER2 (%, 95% CI)	Anti-DLL3 (%, 95% CI)	Anti-CD30 (%, 95% CI)	Anti-Trop-2 (%, 95% CI)	Anti-CD79b (%, 95% CI)	Anti-CD22 (%, 95% CI)	Anti-Nectin-4 (%, 95% CI)	Anti-gpNMB (%, 95% CI)	Anti-FRα (%, 95% CI)	Anti-CD19 (%, 95% CI)	Anti-CD56 (%, 95% CI)
Hematologic											
Neutropenia	18.7 (15.8, 21.5)	13.8 (1.2, 26.3)	61.5 (58.0, 65.0)	40.3 (37.0, 43.6)	28.3 (24.0, 32.5)	-	-	-	15.4 (8.8, 21.9)	-	43.4 (34.7, 51.9)
Thrombocytopenia	23.2 (20.6, 25.8)	12.9 (9.9, 15.9)	23.1 (11.6, 34.5)	24.4 (17.8, 31.0)	-	-	-	24.6 (20.5, 28.7)	43.8 (26.6, 60.9)	9.6 (1.6, 17.6)	18.1 (11.4, 24.8)
Anemia	9.9 (3.8, 16.0)	10.3 (-0.7, 21.4)	-	11.3 (9.1, 13.4)	12.0 (8.9, 15.0)	-	-	-	-	-	19.7 (12.8, 26.6)
WBC count decreased	14.4 (8.2, 20.6)	-	-	13.8 (10.9, 16.8)	-	-	-	9.4 (5.5, 13.3)	-	-	15.2 (2.9, 27.4)
Febrile neutropenia	-[b]	-	19.3 (16.3, 22.3)	12.3 (8.4, 16.1)	13.8 (10.6, 17.0)	-	-	-	-	-	-
Lymphopenia	-	-	-	11.6 (6.7, 16.5)	-	-	-	-	-	36.5 (23.5, 49.6)	27.3 (12.1, 42.5)
Gastrointestinal											
Diarrhoea	22.2 (6.5, 37.9)	-	-	10.1 (5.1, 15.2)	-	-	-	-	-	-	-
Nausea	11.1 (-0.7,23.0)	-	-	-	-	27.5 (18.3, 36.6)	-	-	-	-	-
Neurologic											
Hypoesthesia	23.3 (10.6, 35.9)	-	-	-	-	-	-	-	-	-	-
Hepatorenal											
AST increased	13.7 (7.0, 20.4)	13.8 (1.2, 26.3)	-	-	-	-	17.5 (10.8, 24.1)				
ALT increased	-	-	-	-	-	-	15.9 (9.5, 22.3)				

Liver function test abnormalities	18,2 (-4.6, 41.0)	-	-	-	-	-	-	-	-	-	-
Hypoalbuminemia	-	13.8 (1.2, 26.3)	-	-	-	-	-	-	-	-	-
Pulmonary											
Pleural effusion	-	10.3 (-0.7, 21.4)	-	-	-	-	-	-	-	-	-
Constitutional											
Fatigue	16.0 (5.8, 26.2)	7.7 (0.4, 14.9)	15.9 (6.8, 24.9)	-	-	-	-	-	-	-	-
Dehydration	11.1 (-0.7, 23.0)	-	-	-	-	-	-	-	-	-	-
Other											
Hypertension	-	-	-	-	-	13.6 (5.4, 21.9)	-	13.6 (5.4, 21.9)			

[a] Grade 3 treatment-related adverse events not associated with anti-Mesothelin ADCs in the included studies (incidence > 10%).

[b] Unreported.

Abbreviation: WBC, white blood cell; AST, aspartate transaminase; ALT, alanine aminotransferas; GGT, gamma-glutamyl transferase

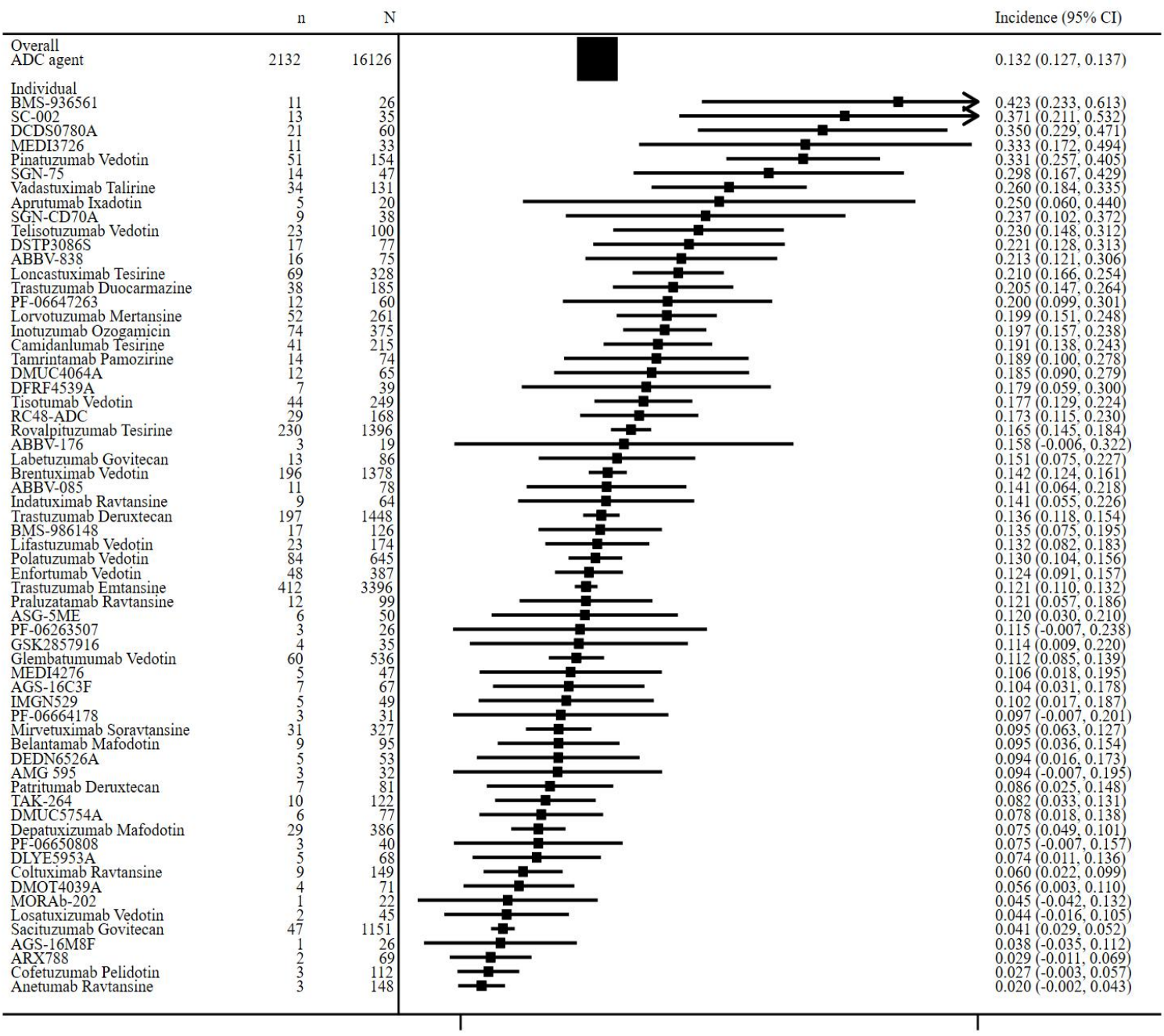
eTable 8. Indirect comparison of RCTs.

Subgroup	All gradae		Grade 3 or higher	
	Odds ratio [95% CI]	*P*-value	Odds ratio [95% CI]	*P*-value
ADC agent				
AGS-16C3F	0.31 [0.11, 0.92]	0.0346	0.41 [0.20, 0.85]	0.0166
Trastuzumab Deruxtecan	0.61 [0.47, 0.79]	0.0003	0.80 [0.64, 0.99]	0.0374
Polatuzumab Vedotin	0.77 [0.28, 2.08]	0.6051	1.04 [0.79, 1.36]	0.7923
Glembatumumab Vedotin	0.84 [0.26, 2.69]	0.7689	1.51 [1.00; 2.27]	0.0504
Inotuzumab Ozogamicin	1.00 [0.61, 1.64]	0.9975	0.78 [0.56, 1.10]	0.1629
Trastuzumab Emtansine	1.26 [0.89, 1.77]	0.1894	0.93 [0.82, 1.06]	0.2813
Mirvetuximab Soravtansine	1.99 [0.86, 4.57]	0.1082	0.43 [0.27, 0.69]	0.0004
Brentuximab Vedotin	2.11 [1.34, 3.31]	0.0012	2.74 [2.18, 3.44]	< 0.0001
Lorvotuzumab Mertansine	4.62 [1.31, 16.23]	0.0172	**3.20** [**1.32, 7.77**]	**0.0101**
Rovalpituzumab Tesirine	5.85 [4.22, 8.09]	< 0.0001	NA	NA
Sacituzumab Govitecan	**10.94** [**4.59, 26.04**]	**< 0.0001**	2.05 [1.42, 2.95]	0.0001
Anetumab Ravtansine	NA	NA	0.33 [0.18, 0.60]	0.0003
Payload type				
MMAF	0.31 [0.11, 0.92]	0.0346	0.41 [0.20, 0.85]	0.0166
DM1	0.80 [0.69, 0.92]	0.0019	0.86 [0.76; 0.97]	0.0148
Calicheamicin	1.00 [0.61, 1.64]	0.9975	0.78 [0.56, 1.10]	0.1629
MMAE	1.65 [1.14, 2.39]	0.0077	1.71 [1.46, 1.99]	< 0.0001
DM4	1.99 [0.86, 4.59]	0.1082	0.41 [0.29, 0.59]	< 0.0001
PBD	5.85 [4.22, 8.09]	< 0.0001	NA	NA
SN-38	7.00 [2.87, 17.08]	< 0.0001	**2.05** [**1.42, 2.95**]	**0.0001**
DXd	**27.67** [**12.00, 63.78**]	**< 0.0001**	1.50 [1.20, 1.89]	0.0005
Target agent				
ENPP3	0.31 [0.11, 0.92]	0.0346	0.41 [0.20, 0.85]	0.0166
CD79b	0.77 [0.28, 2.08]	0.6051	1.04 [0.79, 1.36]	0.7923
gpNMB	0.84 [0.26, 2.69]	0.7689	1.51 [1.00, 2.27]	0.0504
CD22	1.00 [0.61, 1.64]	0.9975	0.79 [0.56, 1.10]	0.1629
FRα	1.99 [0.86, 4.59]	0.1082	0.43 [0.27, 0.67]	0.0004
CD30	2.11 [1.35, 3.32]	0.0012	**2.74** [**2.18, 3.44**]	**< 0.0001**
DLL3	5.85 [4.22, 8.09]	< 0.0001	NA	NA
Trop-2	7.00 [2.87, 17.08]	< 0.0001	2.05 [1.42, 2.95]	0.0001
HER2	**7.53** [**5.92, 9.58**]	**< 0.0001**	1.19 [1.07, 1.33]	0.0017
Mesothelin	NA	NA	0.33 [0.18, 0.60]	0.0003

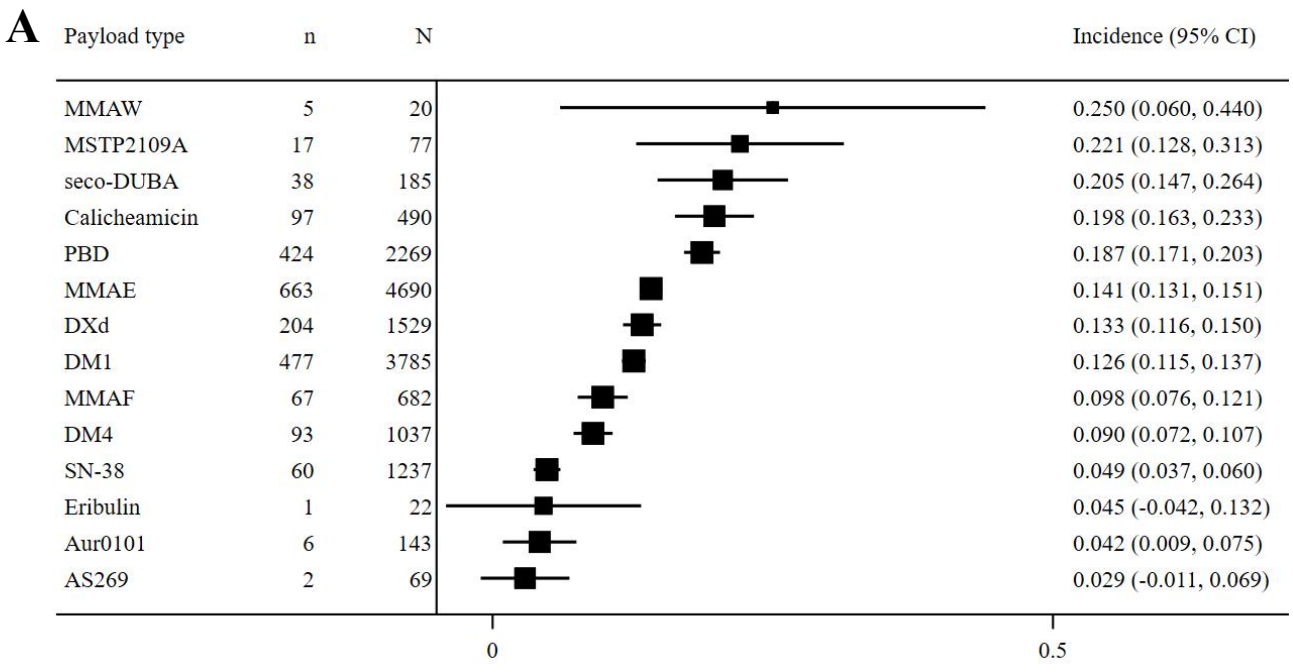
eTable 9. Result of heterogeneity test.

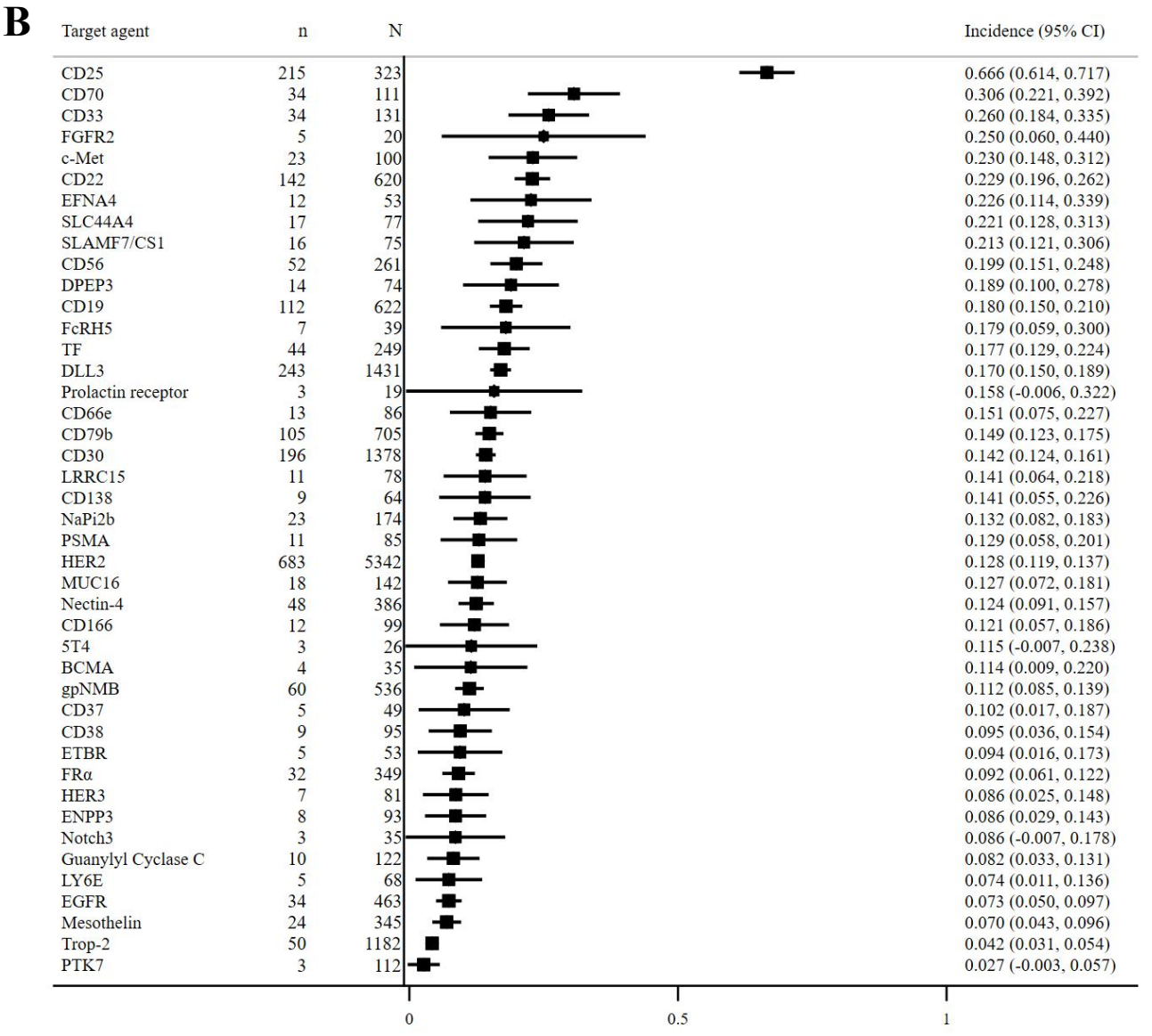
Coefficients	I^2 [95% CI]	*P*-value	Egger's test (*P*)
ADC agent			
All-grade	95.9% [94.9%, 96.7%]	＜0.0001	0
Grade 3 or higher	96.3% [95.4%, 97.0%]	＜0.0001	0.452
Payload type			
All-grade	95.6% [94.0%, 96.7%]	＜0.0001	0.08
Grade 3 or higher	95.7% [94.1%, 96.8%]	＜0.0001	0.382
Target agent			
All-grade	95.3% [94.4%, 96.2%]	＜0.0001	0
Grade 3 or higher	94.8% [93.6%, 95.7%]	＜0.0001	0.13
Caner type			
All-grade	96.7% [95.4%, 97.6%]	＜0.001	0.01
Grade 3 or higher	97.0% [95.9%, 97.8%]	＜0.001	0.8

eFigure 1. Incidences of treatment-related adverse events leading to treatment discontinuation in each ADC.



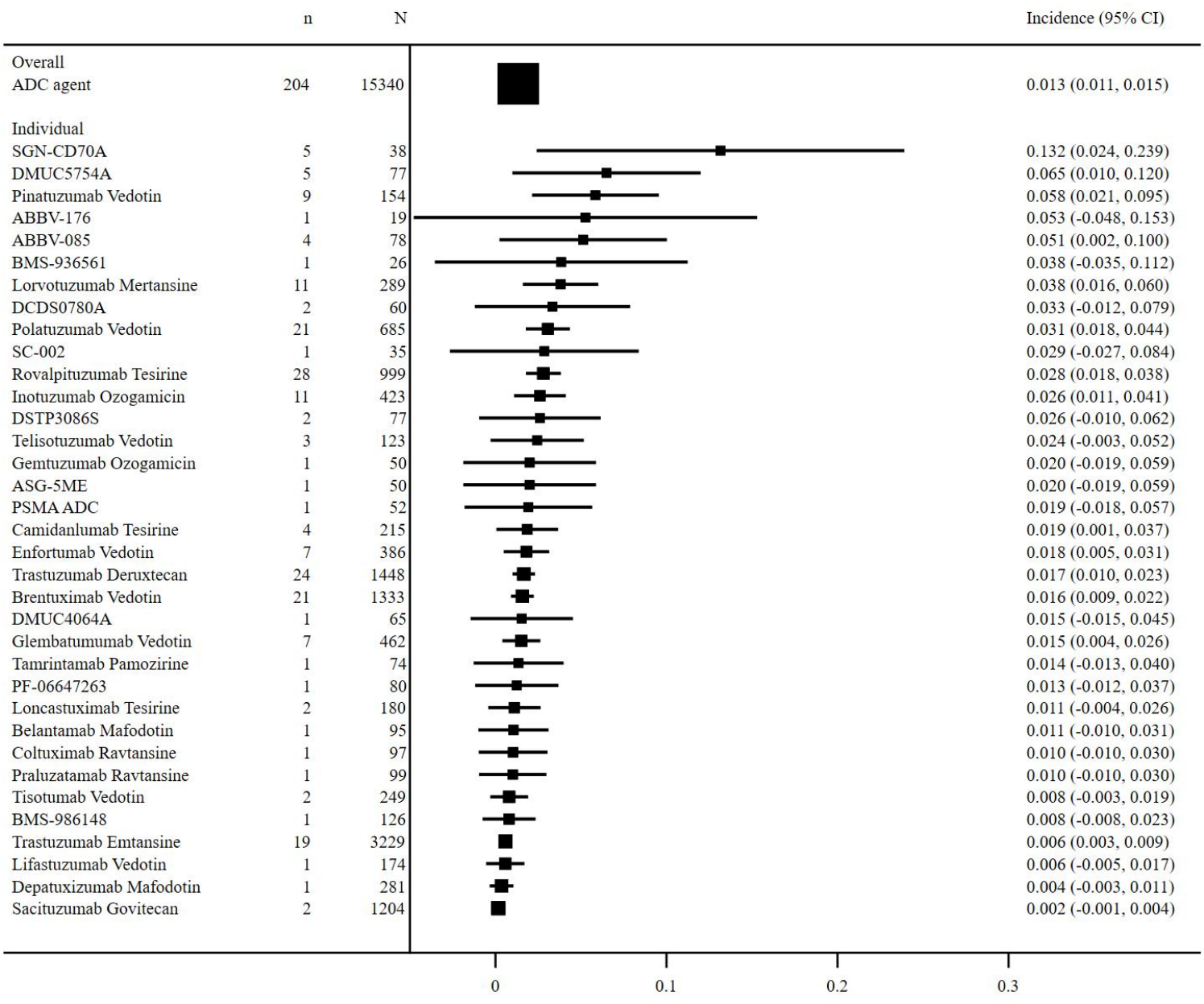
eFigure 2. Incidences of treatment-related adverse events leading to treatment discontinuation in each payload and target-containing ADC.



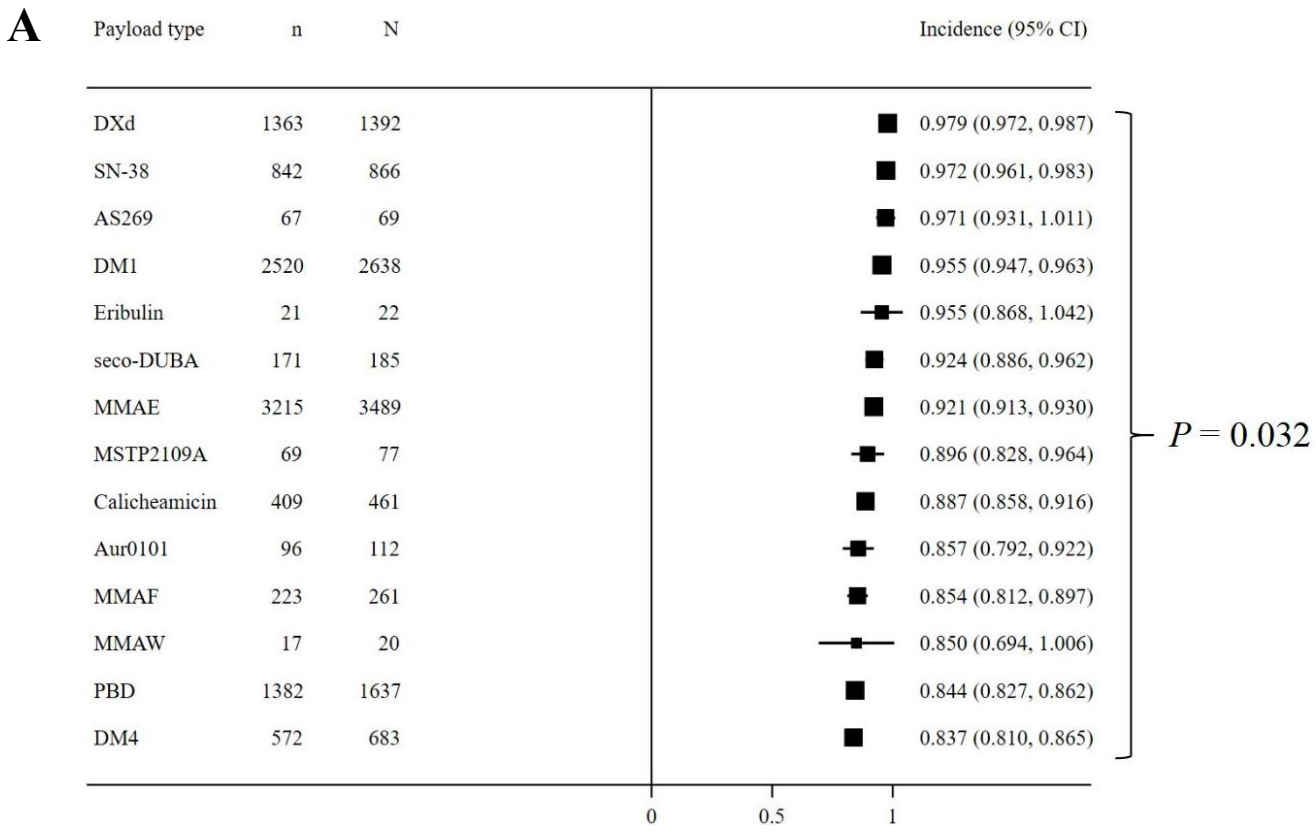


A, Incidences of treatment-related adverse events leading to treatment discontinuation in each payload-conjugates ADC. B, Incidences of treatment-related adverse events leading to treatment discontinuation in each anti-target monoclonal antibody ADC.

eFigure 3. Incidences of treatment-related adverse events deaths in each ADC.

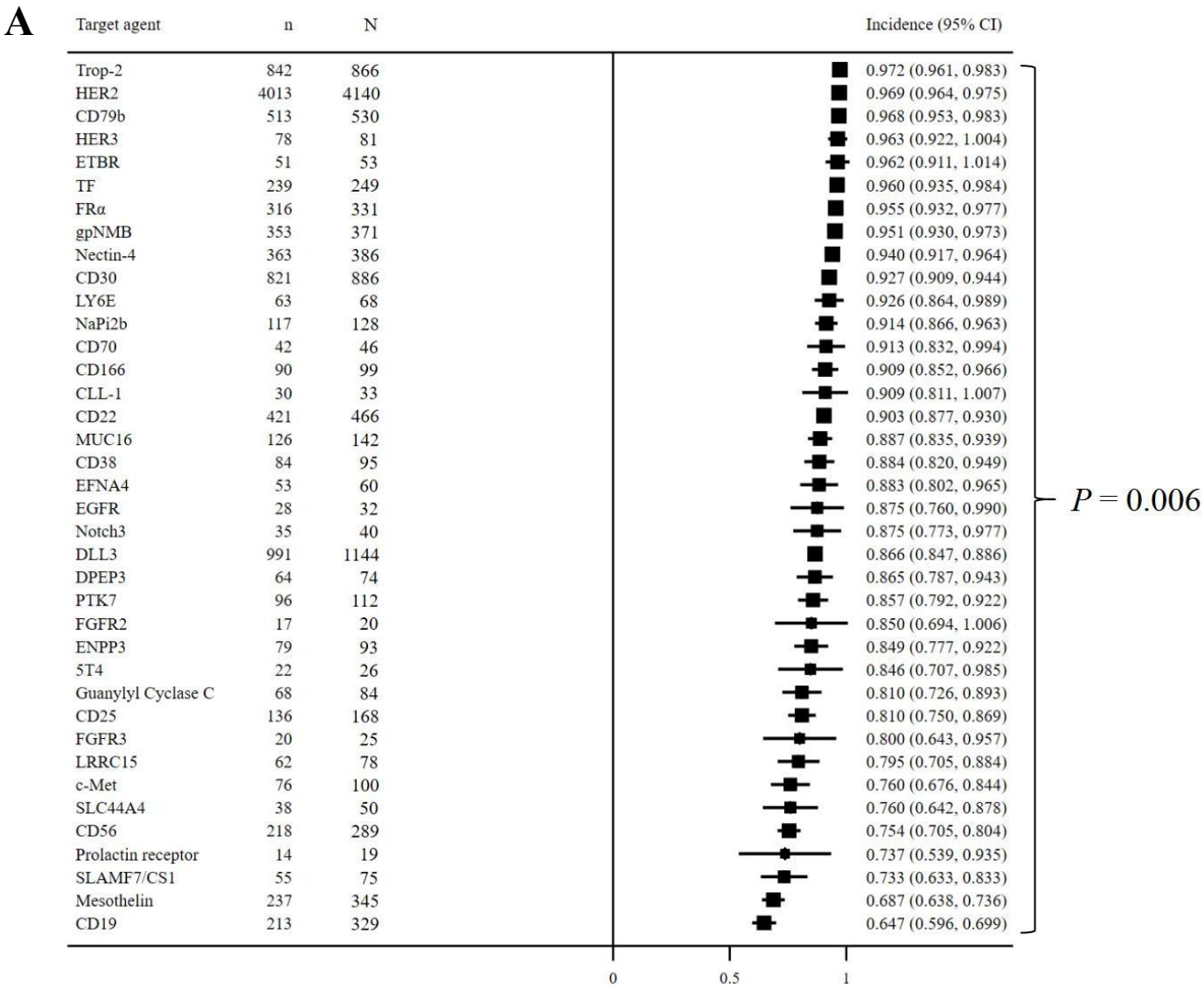


eFigure 4. Subgroup analysis of overall adverse event incidence in each payload-conjugates ADC.



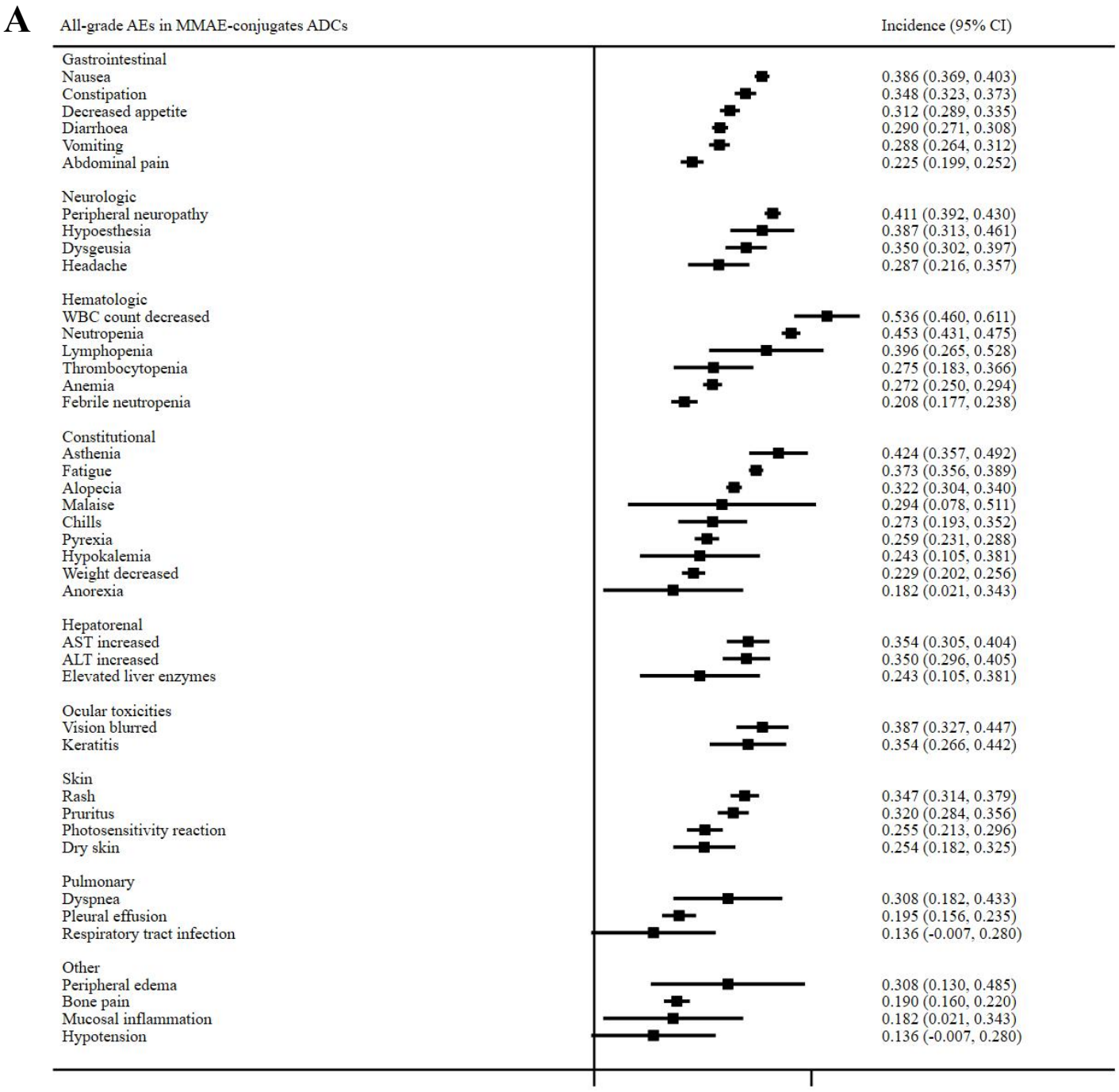
A, All-grade adverse event in each payload-conjugates ADC. B, Grade 3 or higher adverse event in each payload-conjugates ADC. *P*-value is Anova test result.

eFigure 5. Subgroup analysis of overall adverse event incidence in each anti-target monoclonal antibody ADC.



A, All-grade adverse event in each anti-target monoclonal antibody ADC. B, Grade 3 or higher adverse event in each anti-target monoclonal antibody ADC. *P*-value is Anova test result.

eFigure 6. Incidences of all-grade adverse events in main payload-conjugates ADCs (N≥200).



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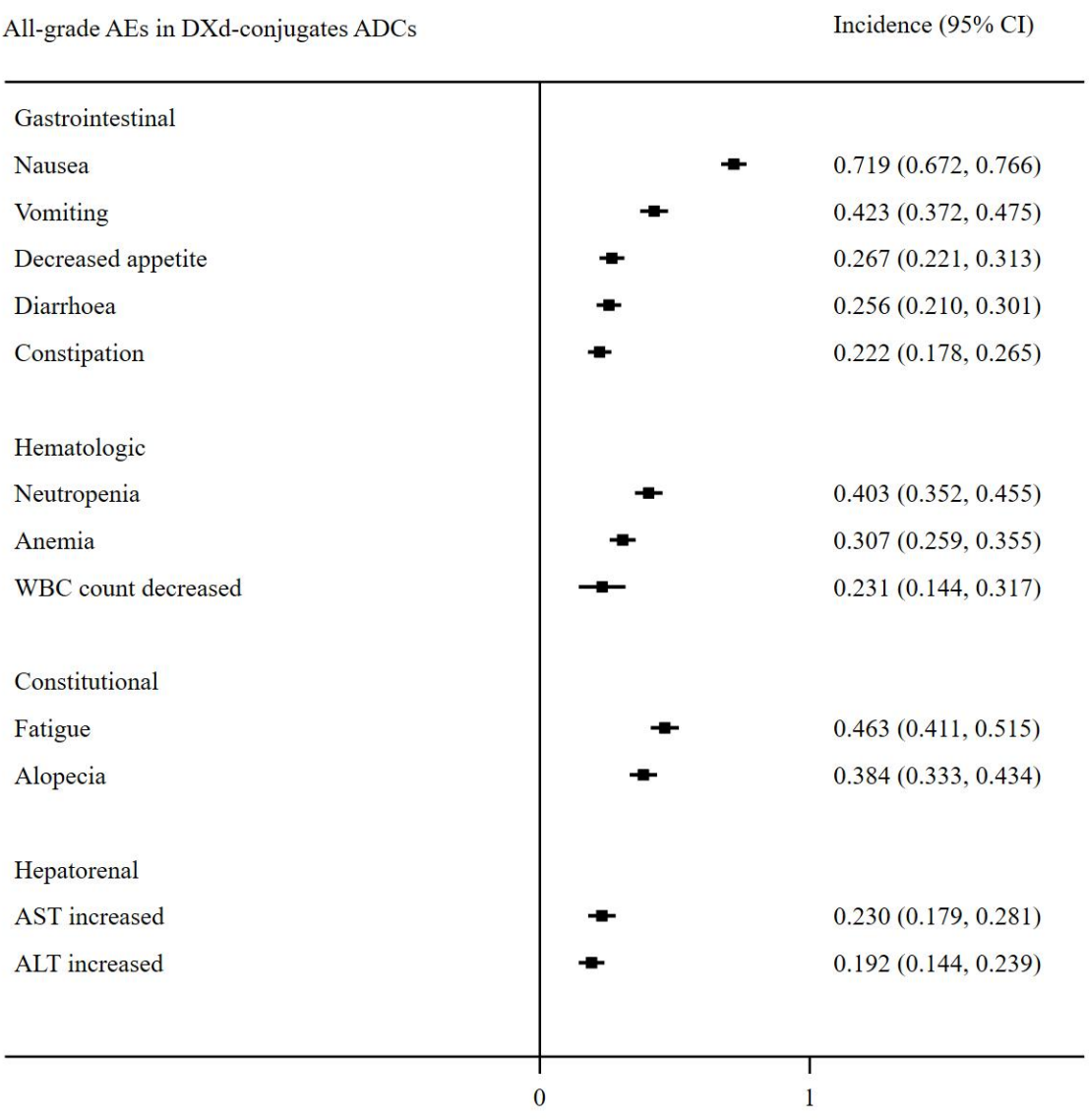
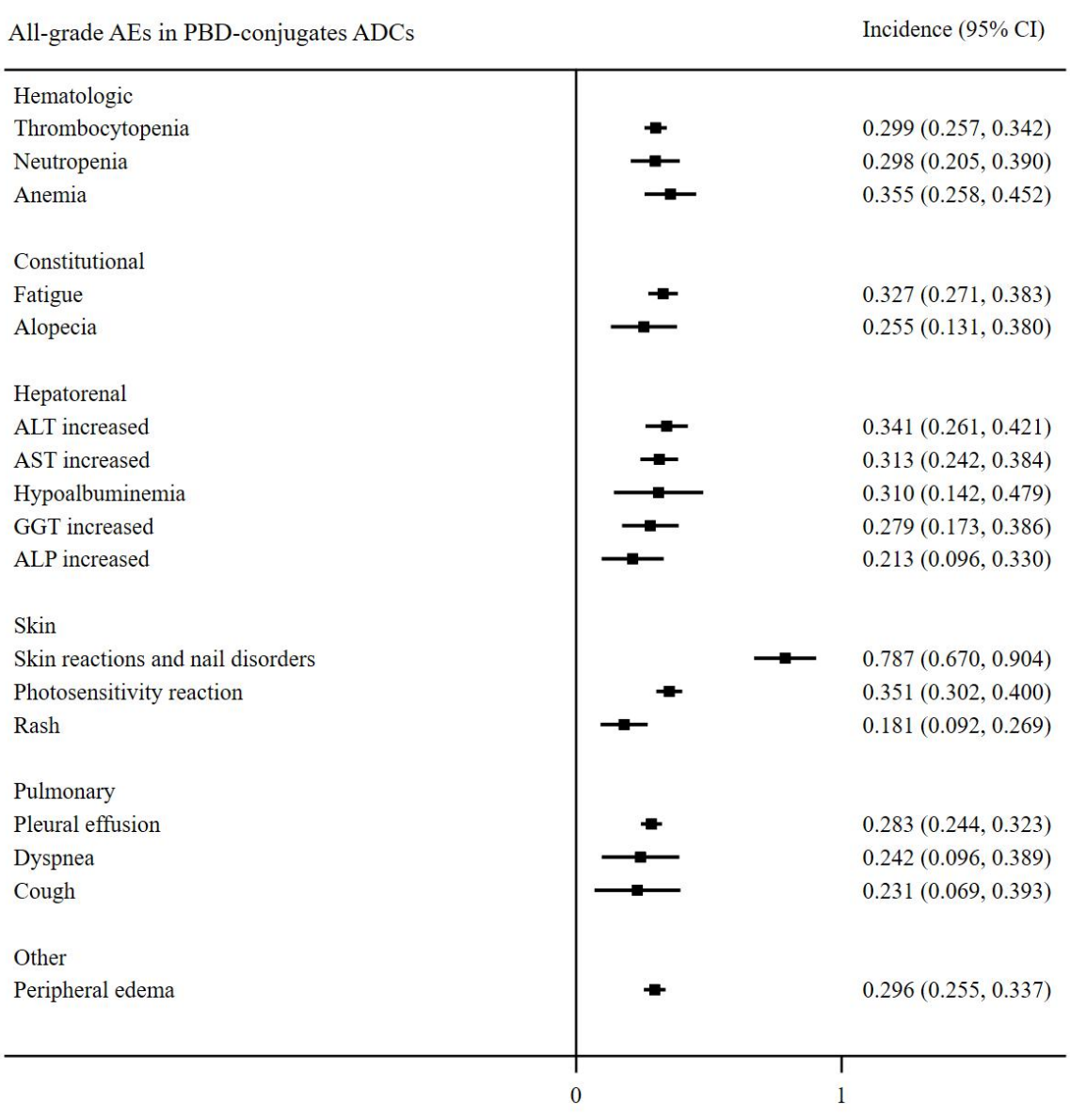
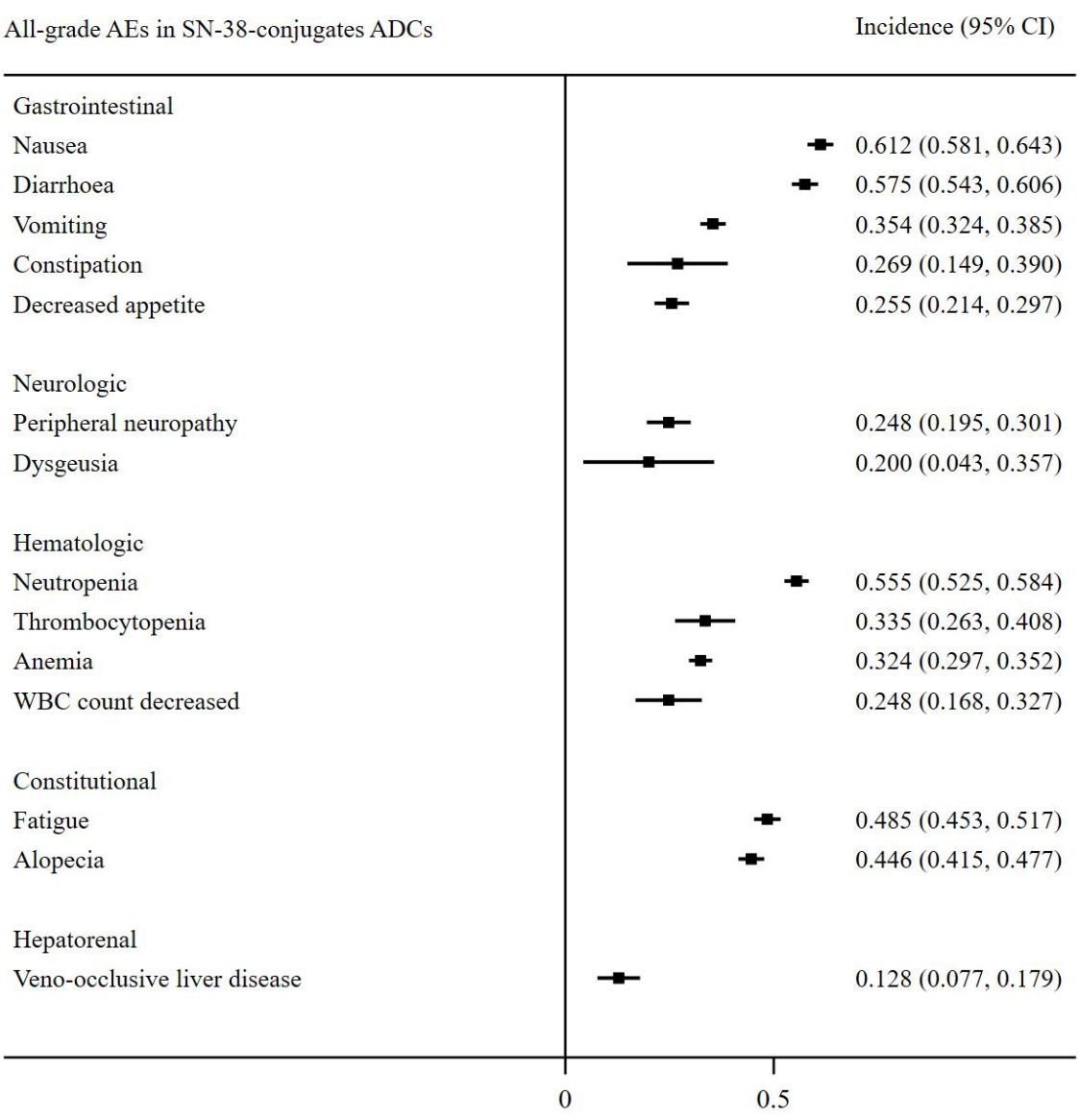

All-grade AEs in DXd-conjugates ADCs
Incidence (95% CI)
Gastrointestinal
Nausea
0.719 (0.672, 0.766)
Vomiting
0.423 (0.372, 0.475)
Decreased appetite
0.267 (0.221, 0.313)
Diarrhoea
0.256 (0.210, 0.301)
Constipation
0.222 (0.178, 0.265)
Hematologic
Neutropenia
0.403 (0.352, 0.455)
Anemia
0.307 (0.259, 0.355)
WBC count decreased
0.231 (0.144, 0.317)
Constitutional
Fatigue
0.463 (0.411, 0.515)
Alopecia
0.384 (0.333, 0.434)
Hepatorenal
AST increased
0.230 (0.179, 0.281)
ALT increased
0.192 (0.144, 0.239)
0
1

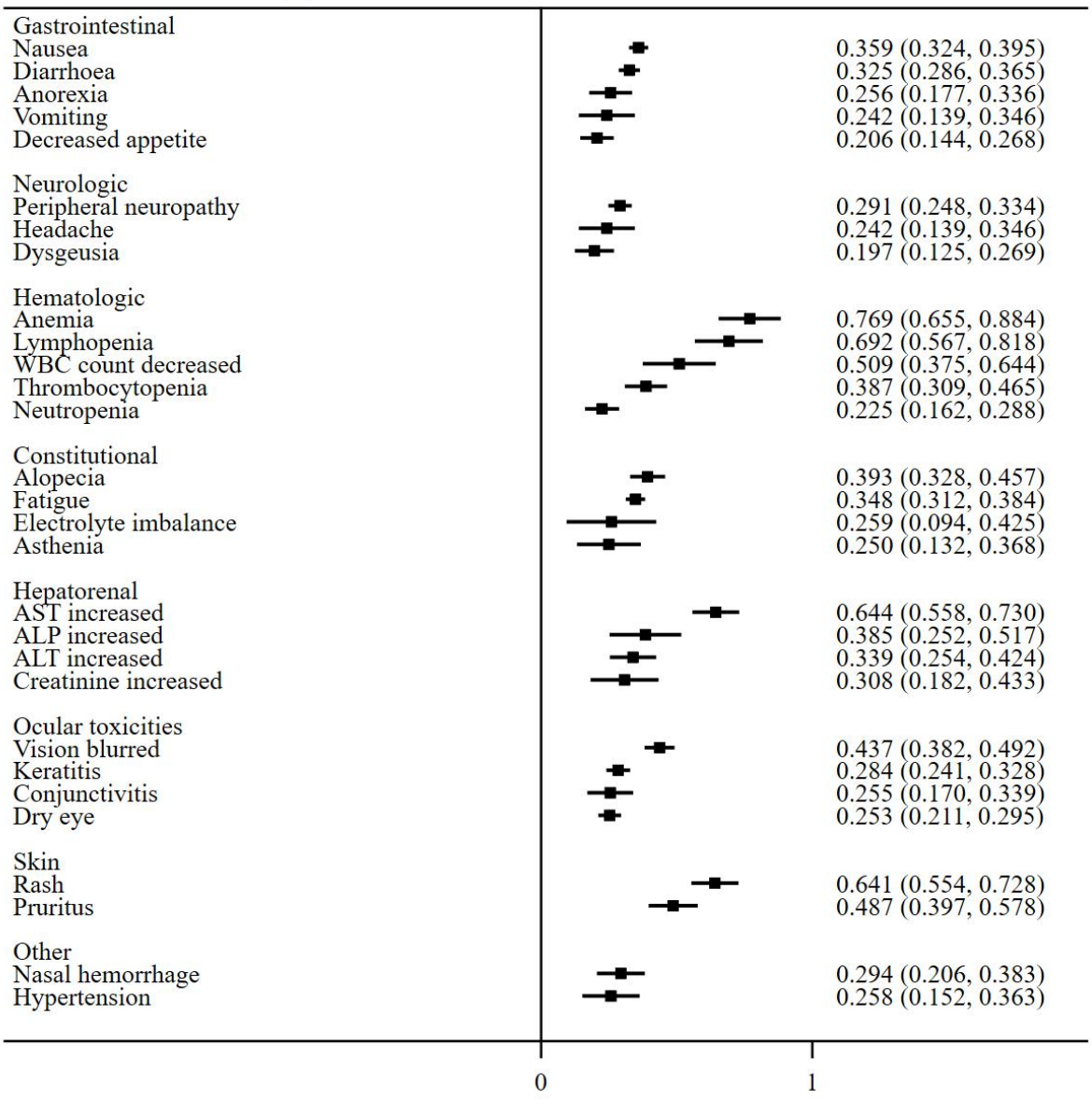
D

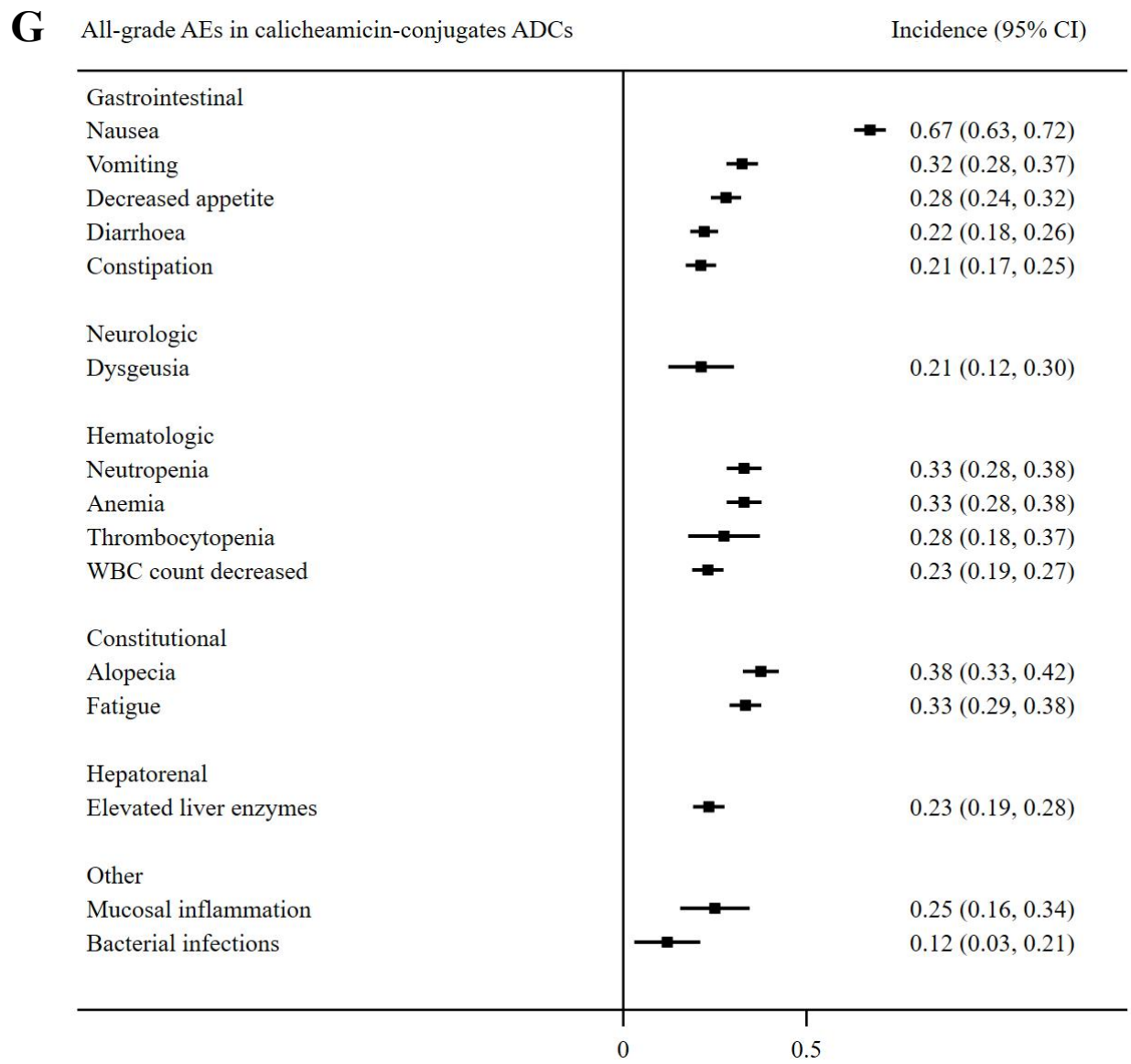

All-grade AEs in PBD-conjugates ADCs
Incidence (95% CI)
Hematologic
Thrombocytopenia
0.299 (0.257, 0.342)
Neutropenia
0.298 (0.205, 0.390)
Anemia
0.355 (0.258, 0.452)
Constitutional
Fatigue
0.327 (0.271, 0.383)
Alopecia
0.255 (0.131, 0.380)
Hepatorenal
ALT increased
0.341 (0.261, 0.421)
AST increased
0.313 (0.242, 0.384)
Hypoalbuminemia
0.310 (0.142, 0.479)
GGT increased
0.279 (0.173, 0.386)
ALP increased
0.213 (0.096, 0.330)
Skin
Skin reactions and nail disorders
0.787 (0.670, 0.904)
Photosensitivity reaction
0.351 (0.302, 0.400)
Rash
0.181 (0.092, 0.269)
Pulmonary
Pleural effusion
0.283 (0.244, 0.323)
Dyspnea
0.242 (0.096, 0.389)
Cough
0.231 (0.069, 0.393)
Other
Peripheral edema
0.296 (0.255, 0.337)
0
1

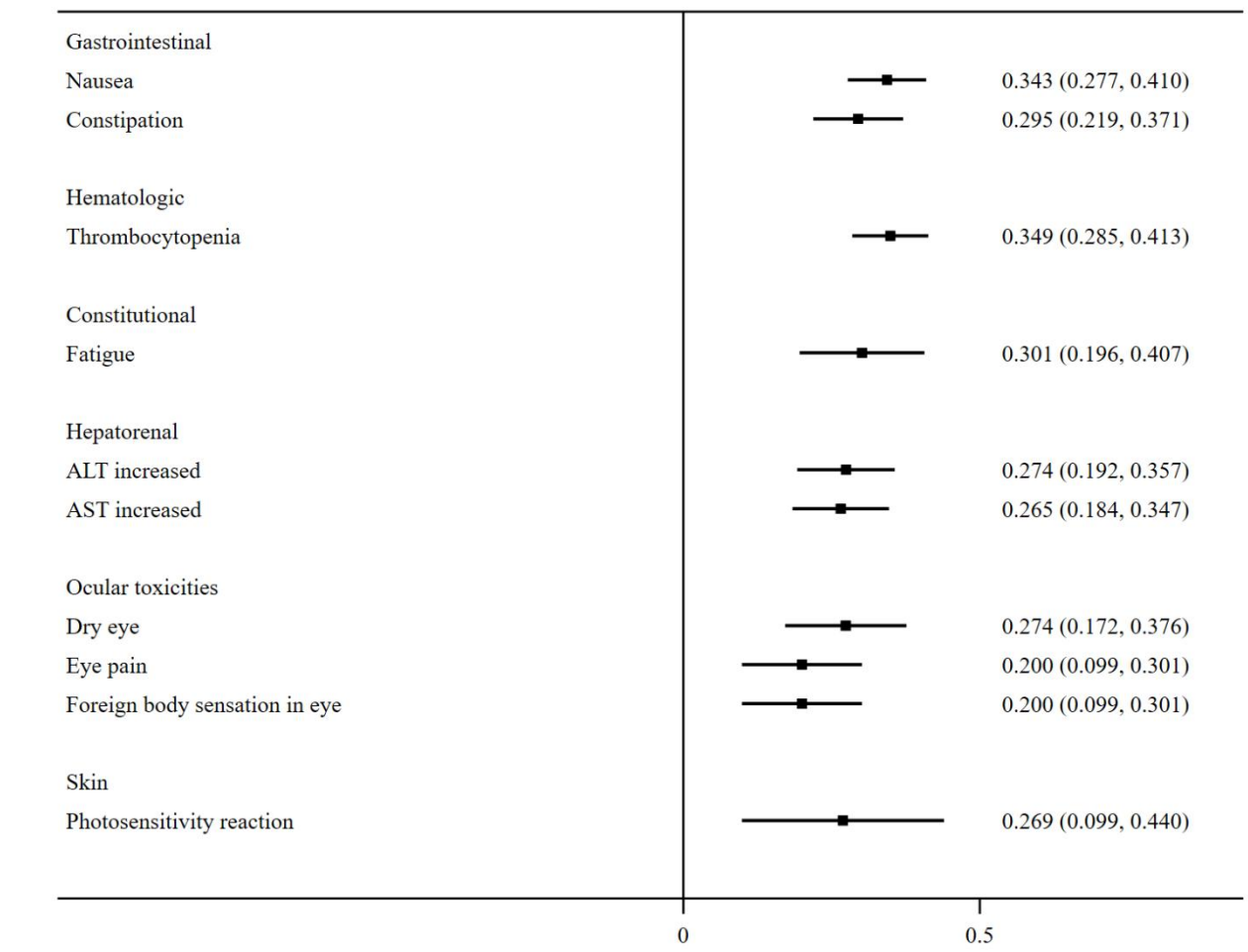
E


All-grade AEs in SN-38-conjugates ADCs
Incidence (95% CI)
Gastrointestinal
Nausea 0.612 (0.581, 0.643)
Diarrhoea 0.575 (0.543, 0.606)
Vomiting 0.354 (0.324, 0.385)
Constipation 0.269 (0.149, 0.390)
Decreased appetite 0.255 (0.214, 0.297)
Neurologic
Peripheral neuropathy 0.248 (0.195, 0.301)
Dysgeusia 0.200 (0.043, 0.357)
Hematologic
Neutropenia 0.555 (0.525, 0.584)
Thrombocytopenia 0.335 (0.263, 0.408)
Anemia 0.324 (0.297, 0.352)
WBC count decreased 0.248 (0.168, 0.327)
Constitutional
Fatigue 0.485 (0.453, 0.517)
Alopecia 0.446 (0.415, 0.477)
Hepatorenal
Veno-occlusive liver disease 0.128 (0.077, 0.179)
0
0.5

F


All-grade AEs in DM4-conjugates ADCs
Incidence (95% CI)
Gastrointestinal
Nausea 0.359 (0.324, 0.395)
Diarrhoea 0.325 (0.286, 0.365)
Anorexia 0.256 (0.177, 0.336)
Vomiting 0.242 (0.139, 0.346)
Decreased appetite 0.206 (0.144, 0.268)
Neurologic
Peripheral neuropathy 0.291 (0.248, 0.334)
Headache 0.242 (0.139, 0.346)
Dysgeusia 0.197 (0.125, 0.269)
Hematologic
Anemia 0.769 (0.655, 0.884)
Lymphopenia 0.692 (0.567, 0.818)
WBC count decreased 0.509 (0.375, 0.644)
Thrombocytopenia 0.387 (0.309, 0.465)
Neutropenia 0.225 (0.162, 0.288)
Constitutional
Alopecia 0.393 (0.328, 0.457)
Fatigue 0.348 (0.312, 0.384)
Electrolyte imbalance 0.259 (0.094, 0.425)
Asthenia 0.250 (0.132, 0.368)
Hepatorenal
AST increased 0.644 (0.558, 0.730)
ALP increased 0.385 (0.252, 0.517)
ALT increased 0.339 (0.254, 0.424)
Creatinine increased 0.308 (0.182, 0.433)
Ocular toxicities
Vision blurred 0.437 (0.382, 0.492)
Keratitis 0.284 (0.241, 0.328)
Conjunctivitis 0.255 (0.170, 0.339)
Dry eye 0.253 (0.211, 0.295)
Skin
Rash 0.641 (0.554, 0.728)
Pruritus 0.487 (0.397, 0.578)
Other
Nasal hemorrhage 0.294 (0.206, 0.383)
Hypertension 0.258 (0.152, 0.363)
0
1

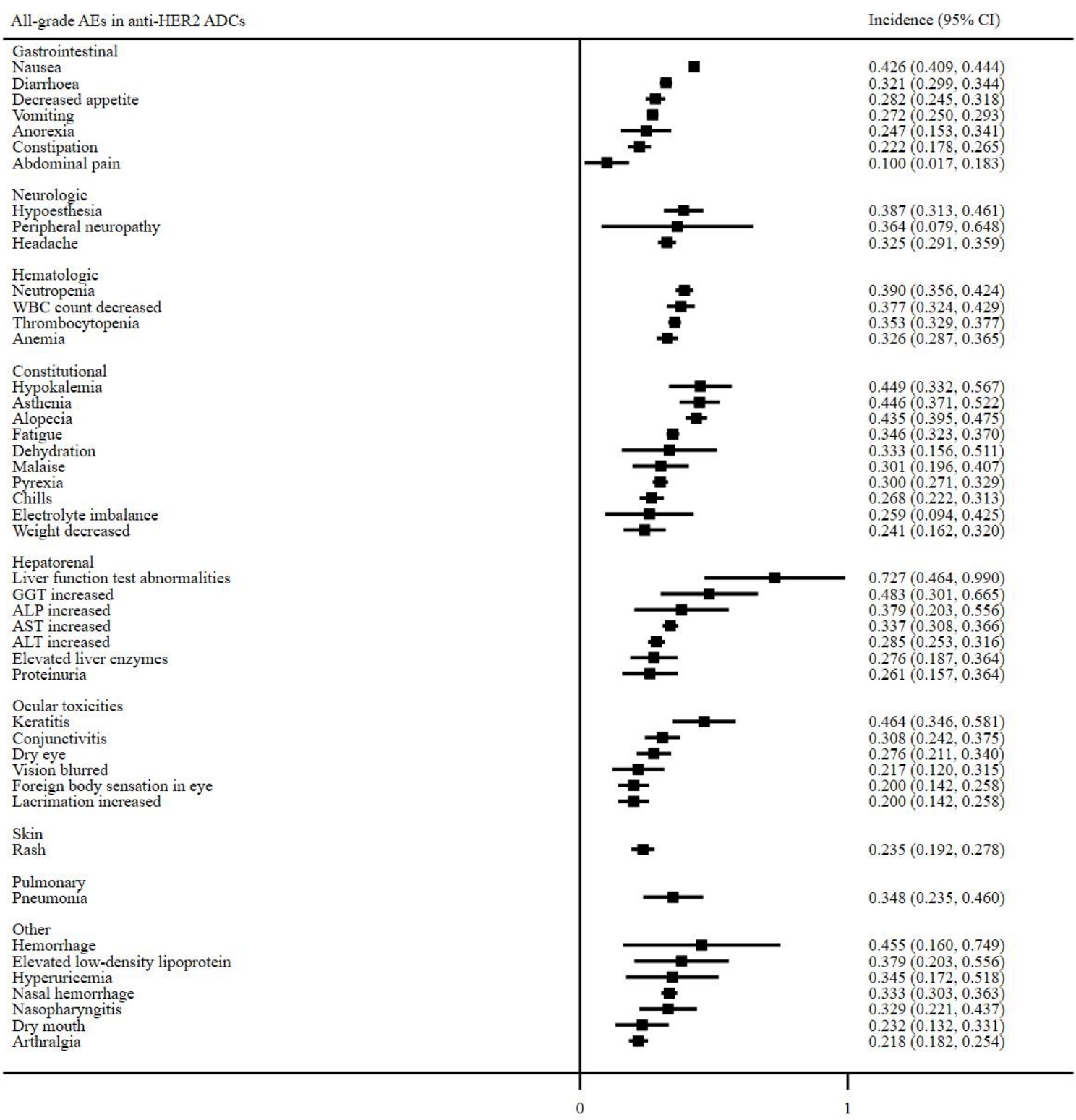


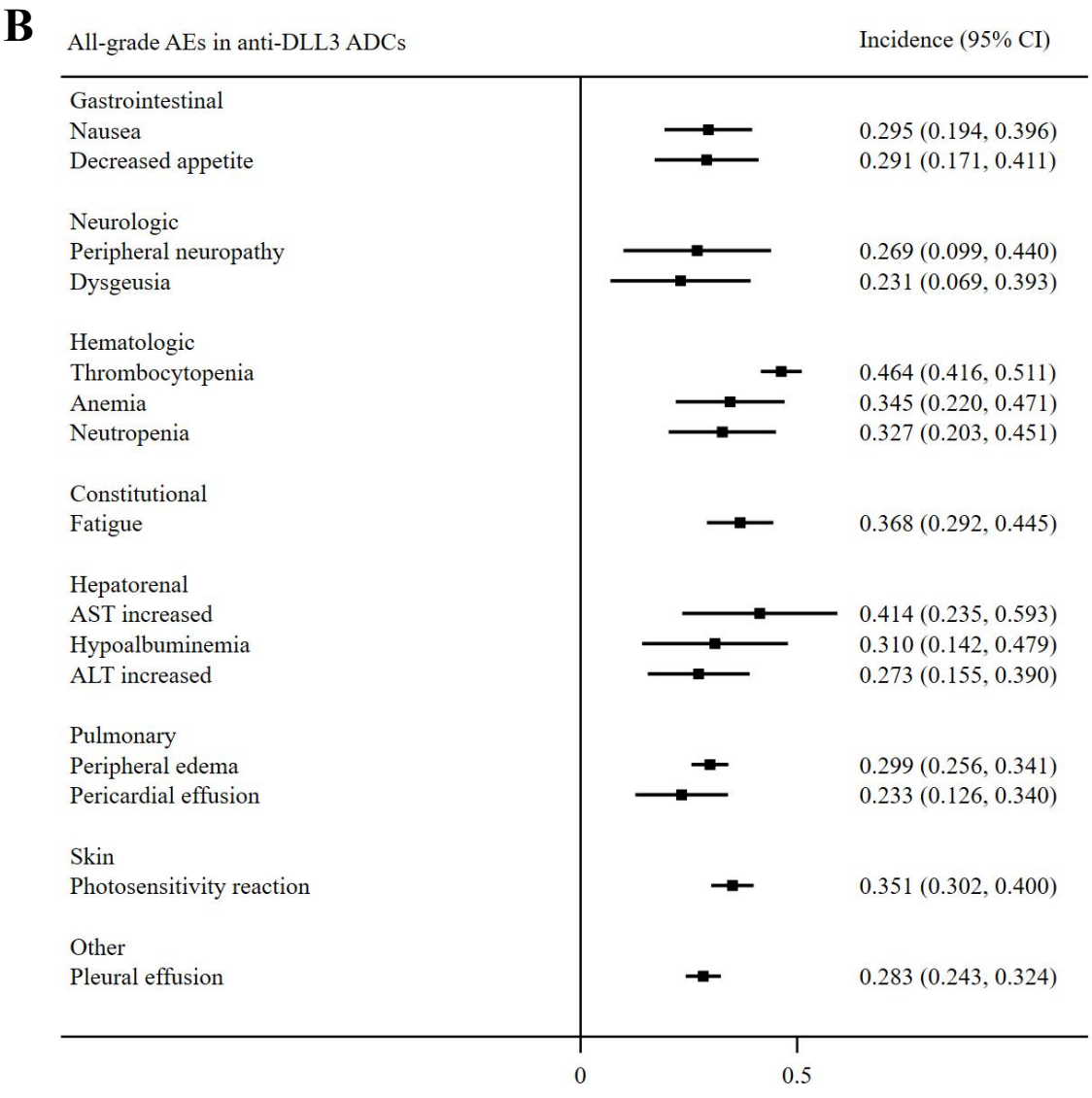


Abbreviation: WBC, white blood cell; GGT, gamma-glutamyl transpeptidase; AST, alanine aminotransferase; ALT, aspartate transaminase; ALP, alkaline phosphatase.

A, Incidences of all-grade adverse events in MMAF-conjugates ADCs. B, Incidences of all-grade adverse events in DM1-conjugates ADCs. C, Incidences of all-grade adverse events in DXd-conjugates ADCs. D, Incidences of all-grade adverse events in PBD-conjugates ADCs. E, Incidences of all-grade adverse events in SN-38-conjugates ADCs. F, Incidences of all-grade adverse events in DM4-conjugates ADCs. G, Incidences of all-grade adverse events in calicheamicin-conjugates ADCs. H, Incidences of all-grade adverse events in MMAF-conjugates ADCs.

eFigure 7. Incidences of all-grade adverse events in main anti-target monoclonal antibody ADCs (N≥200).





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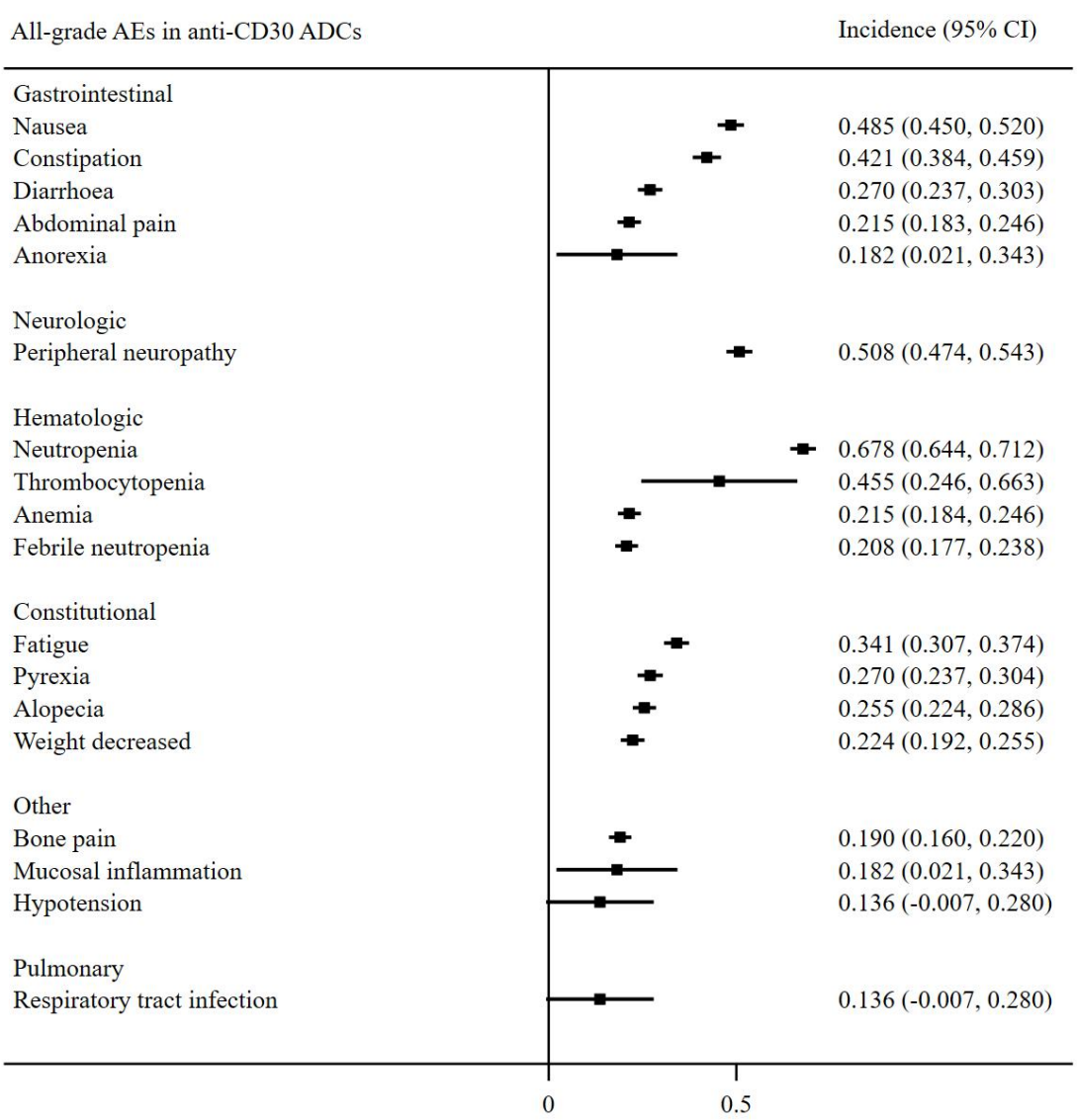
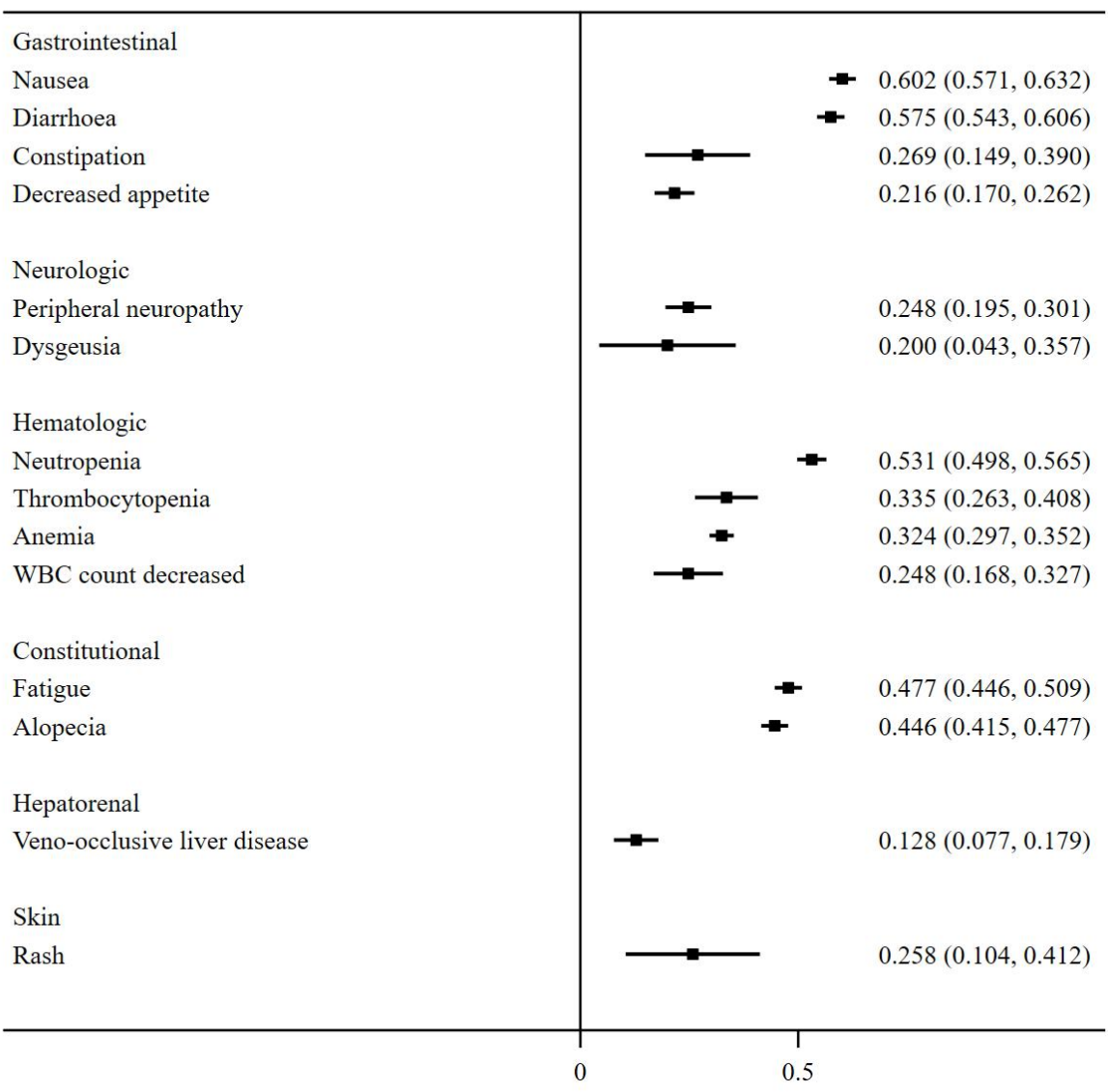
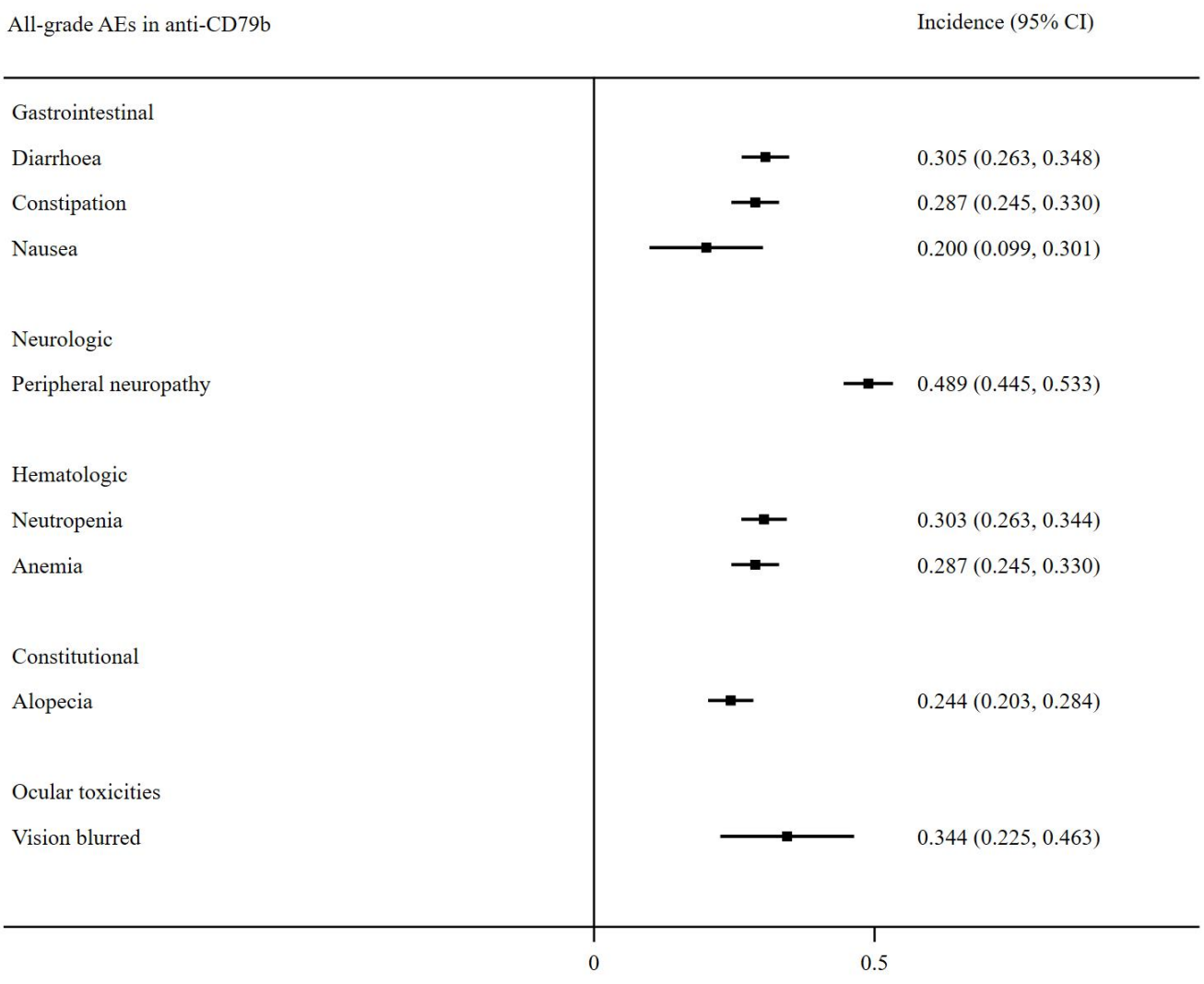

All-grade AEs in anti-CD30 ADCs
Incidence (95% CI)
Gastrointestinal
Nausea
0.485 (0.450, 0.520)
Constipation
0.421 (0.384, 0.459)
Diarrhoea
0.270 (0.237, 0.303)
Abdominal pain
0.215 (0.183, 0.246)
Anorexia
0.182 (0.021, 0.343)
Neurologic
Peripheral neuropathy
0.508 (0.474, 0.543)
Hematologic
Neutropenia
0.678 (0.644, 0.712)
Thrombocytopenia
0.455 (0.246, 0.663)
Anemia
0.215 (0.184, 0.246)
Febrile neutropenia
0.208 (0.177, 0.238)
Constitutional
Fatigue
0.341 (0.307, 0.374)
Pyrexia
0.270 (0.237, 0.304)
Alopecia
0.255 (0.224, 0.286)
Weight decreased
0.224 (0.192, 0.255)
Other
Bone pain
0.190 (0.160, 0.220)
Mucosal inflammation
0.182 (0.021, 0.343)
Hypotension
0.136 (-0.007, 0.280)
Pulmonary
Respiratory tract infection
0.136 (-0.007, 0.280)
0
0.5

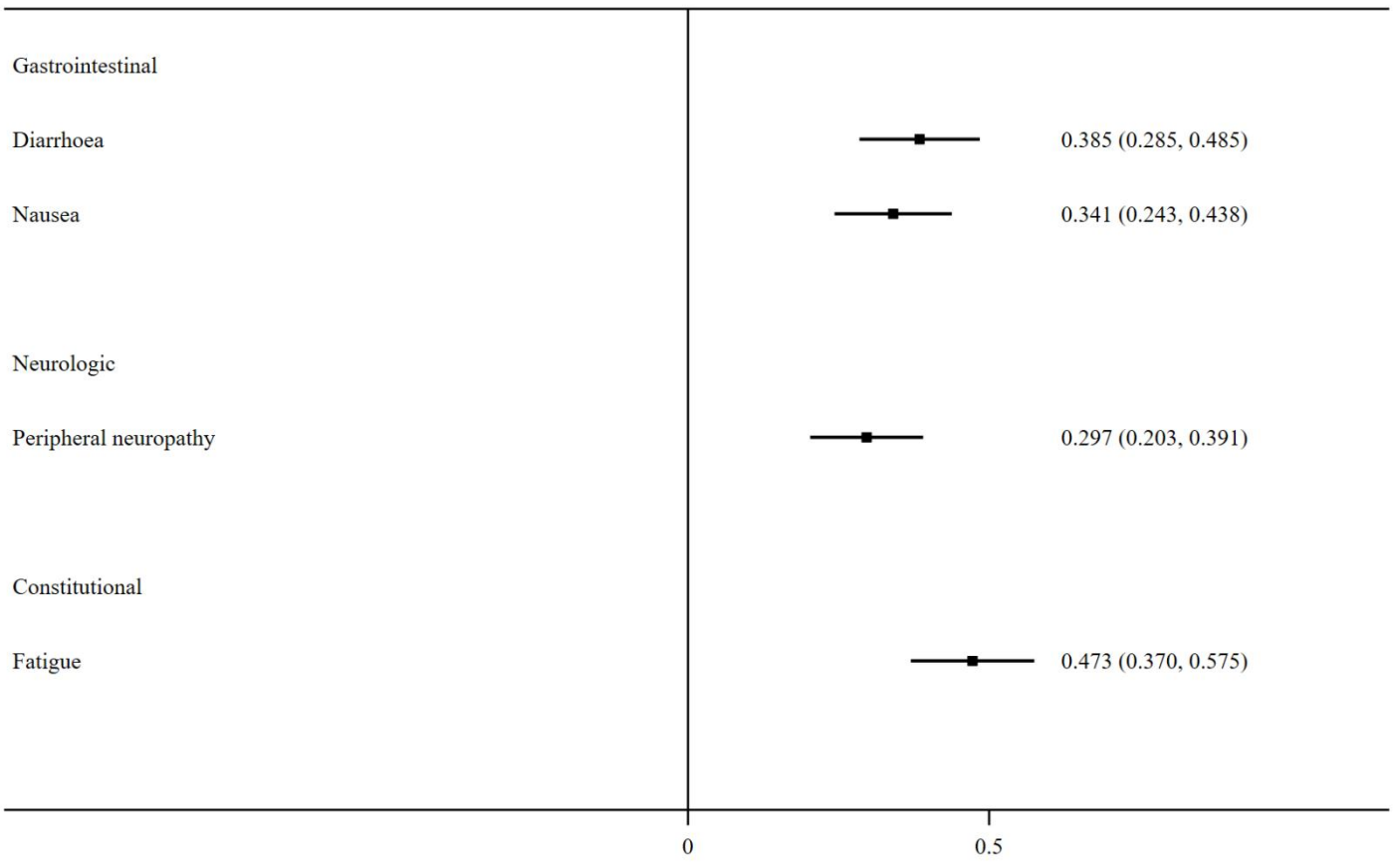
D


All-grade AEs in anti-Trop-2 ADCs
Incidence (95% CI)
Gastrointestinal
Nausea
0.602 (0.571, 0.632)
Diarrhoea
0.575 (0.543, 0.606)
Constipation
0.269 (0.149, 0.390)
Decreased appetite
0.216 (0.170, 0.262)
Neurologic
Peripheral neuropathy
0.248 (0.195, 0.301)
Dysgeusia
0.200 (0.043, 0.357)
Hematologic
Neutropenia
0.531 (0.498, 0.565)
Thrombocytopenia
0.335 (0.263, 0.408)
Anemia
0.324 (0.297, 0.352)
WBC count decreased
0.248 (0.168, 0.327)
Constitutional
Fatigue
0.477 (0.446, 0.509)
Alopecia
0.446 (0.415, 0.477)
Hepatorenal
Veno-occlusive liver disease
0.128 (0.077, 0.179)
Skin
Rash
0.258 (0.104, 0.412)
0
0.5

E All-grade AEs in anti-CD79b



F All-grade AEs in anti-CD22 ADCs



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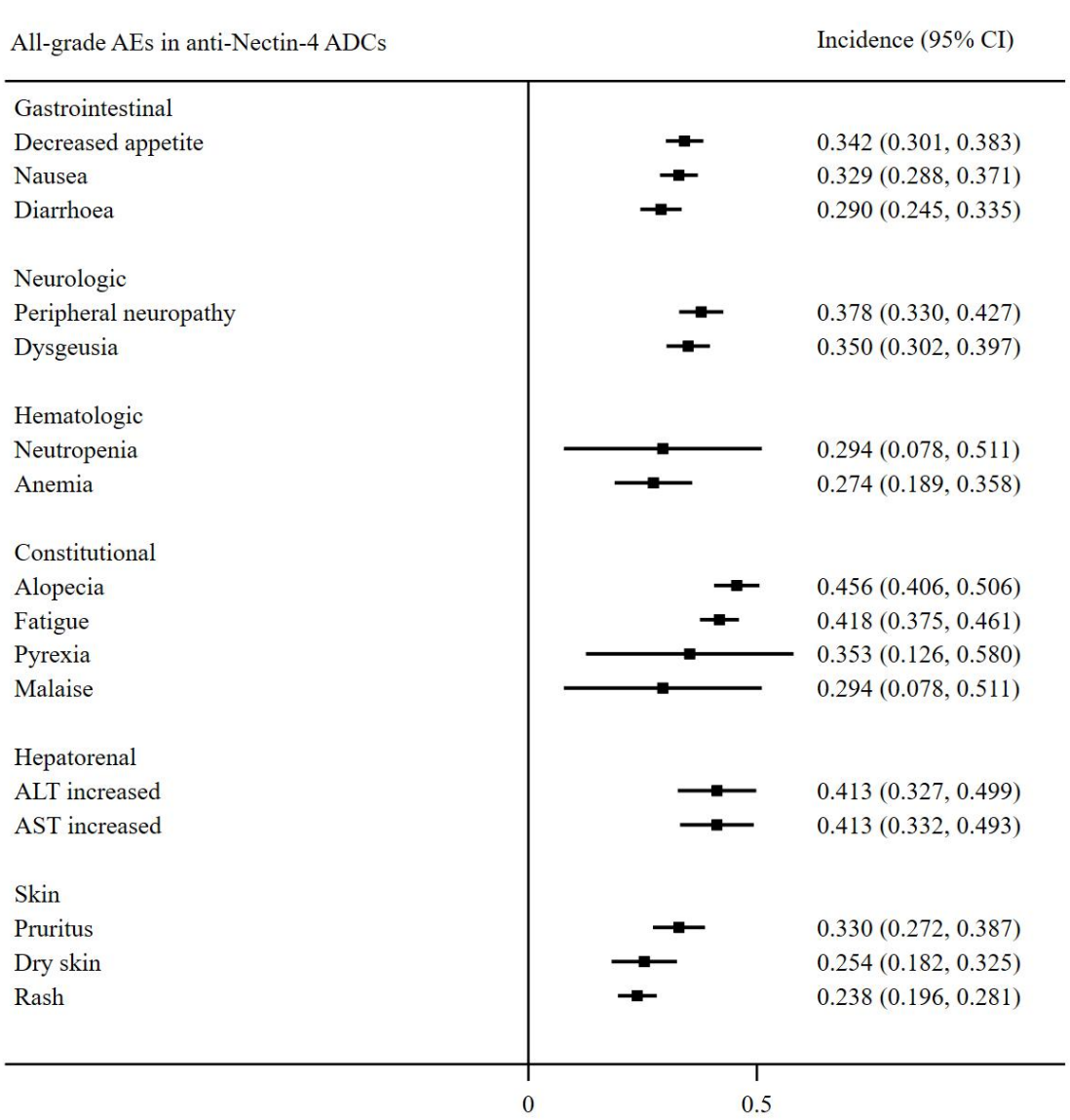
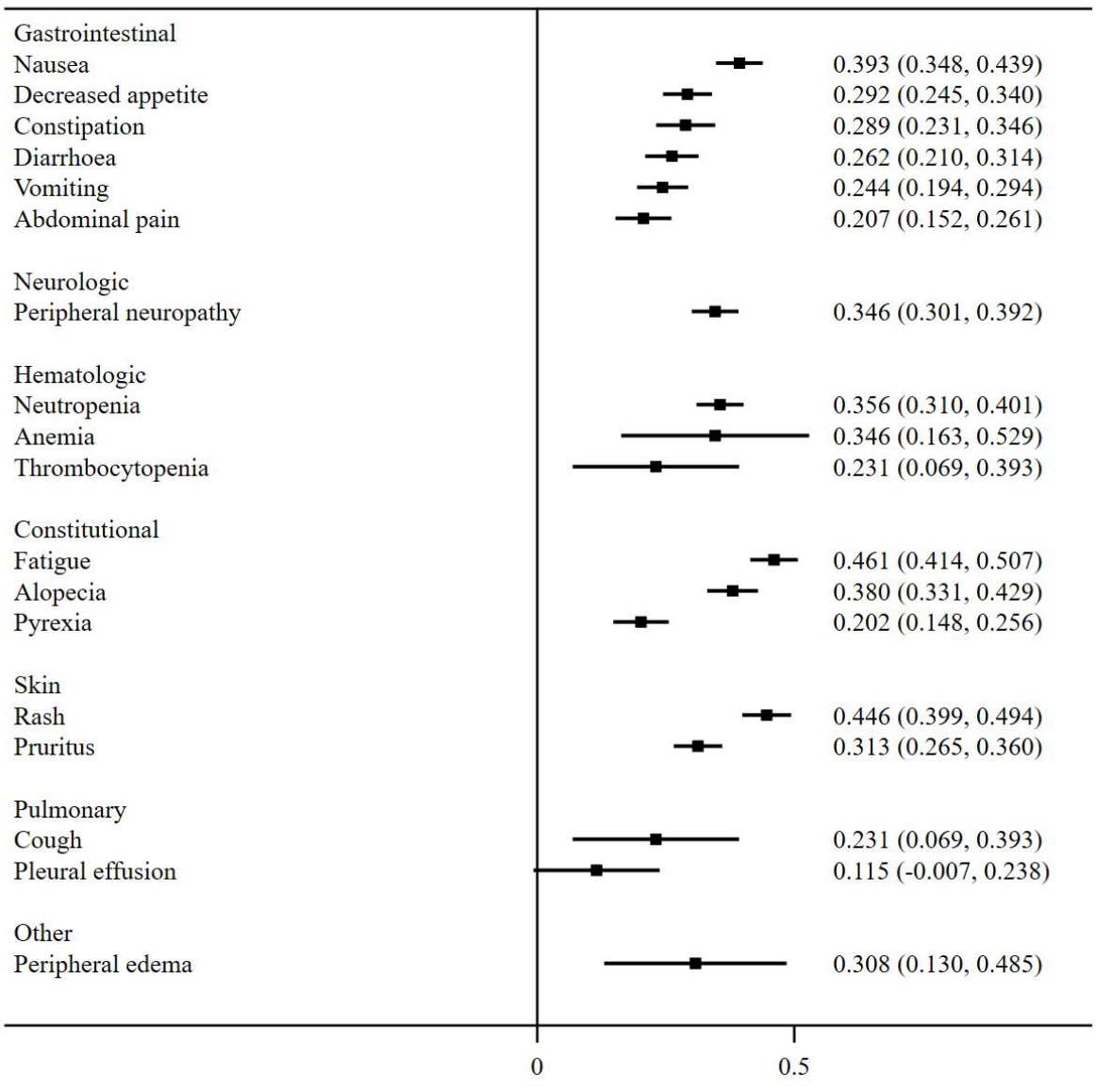
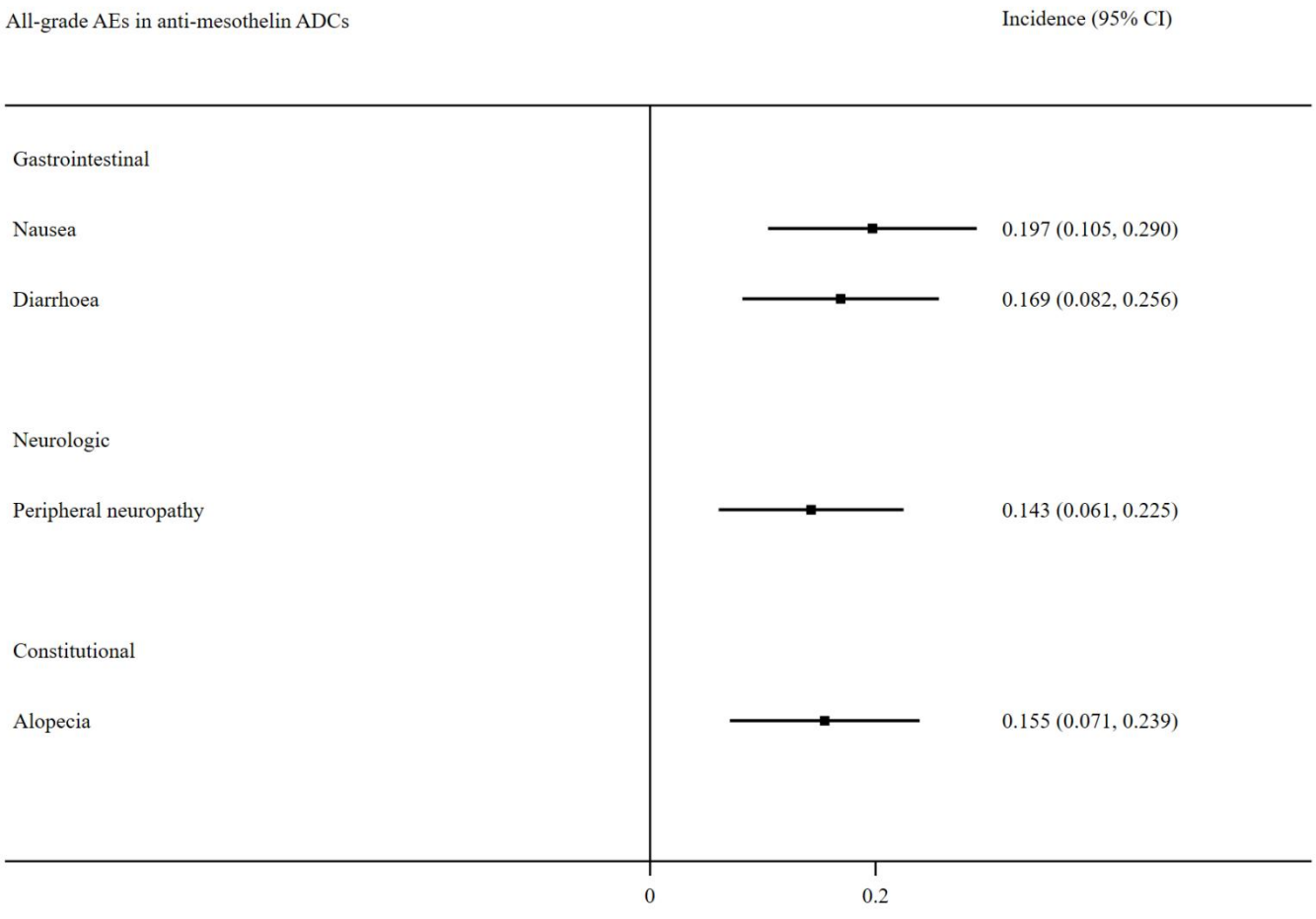

All-grade AEs in anti-Nectin-4 ADCs
Incidence (95% CI)
Gastrointestinal
Decreased appetite 0.342 (0.301, 0.383)
Nausea 0.329 (0.288, 0.371)
Diarrhoea 0.290 (0.245, 0.335)
Neurologic
Peripheral neuropathy 0.378 (0.330, 0.427)
Dysgeusia 0.350 (0.302, 0.397)
Hematologic
Neutropenia 0.294 (0.078, 0.511)
Anemia 0.274 (0.189, 0.358)
Constitutional
Alopecia 0.456 (0.406, 0.506)
Fatigue 0.418 (0.375, 0.461)
Pyrexia 0.353 (0.126, 0.580)
Malaise 0.294 (0.078, 0.511)
Hepatorenal
ALT increased 0.413 (0.327, 0.499)
AST increased 0.413 (0.332, 0.493)
Skin
Pruritus 0.330 (0.272, 0.387)
Dry skin 0.254 (0.182, 0.325)
Rash 0.238 (0.196, 0.281)
0
0.5

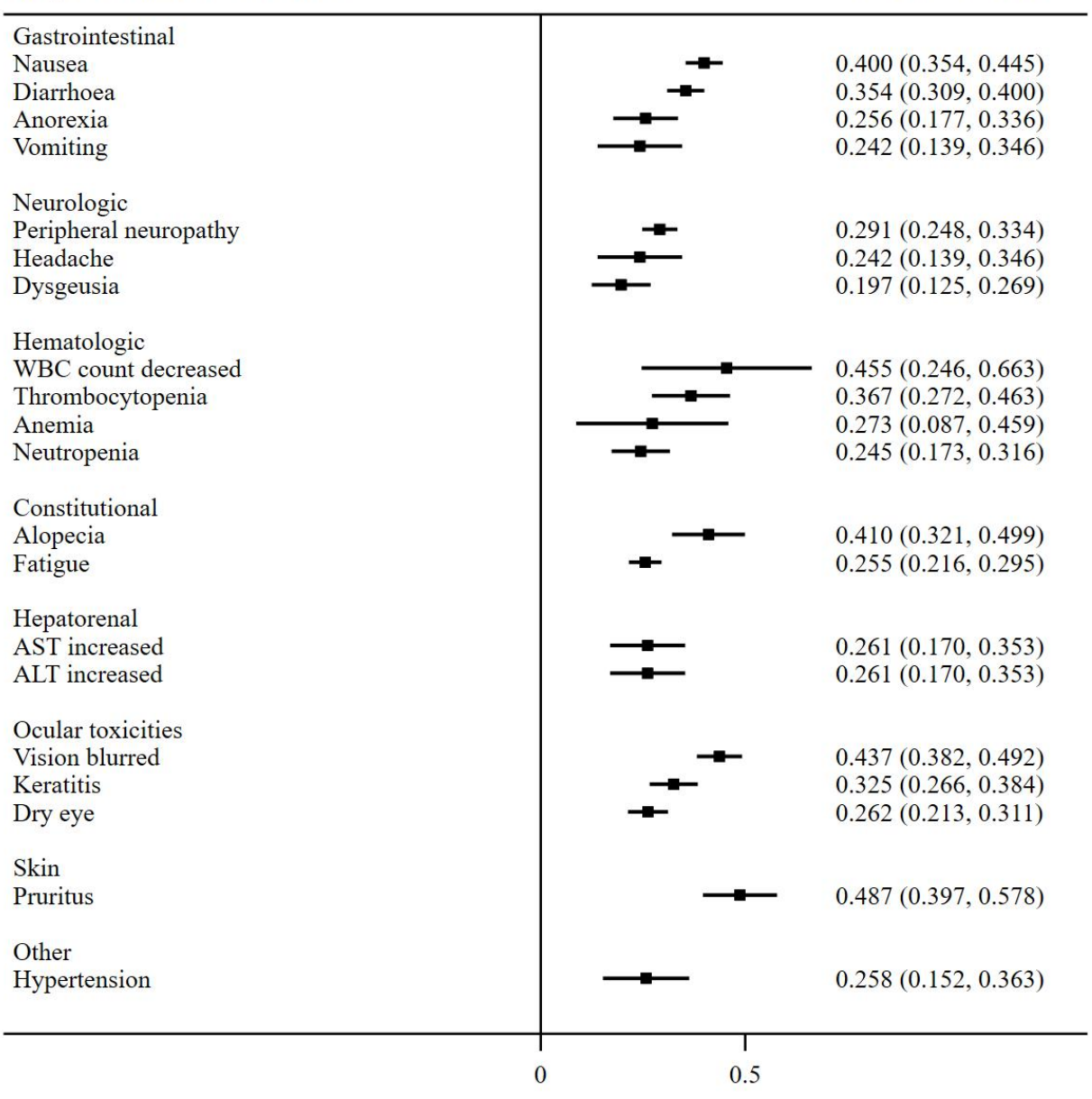
H

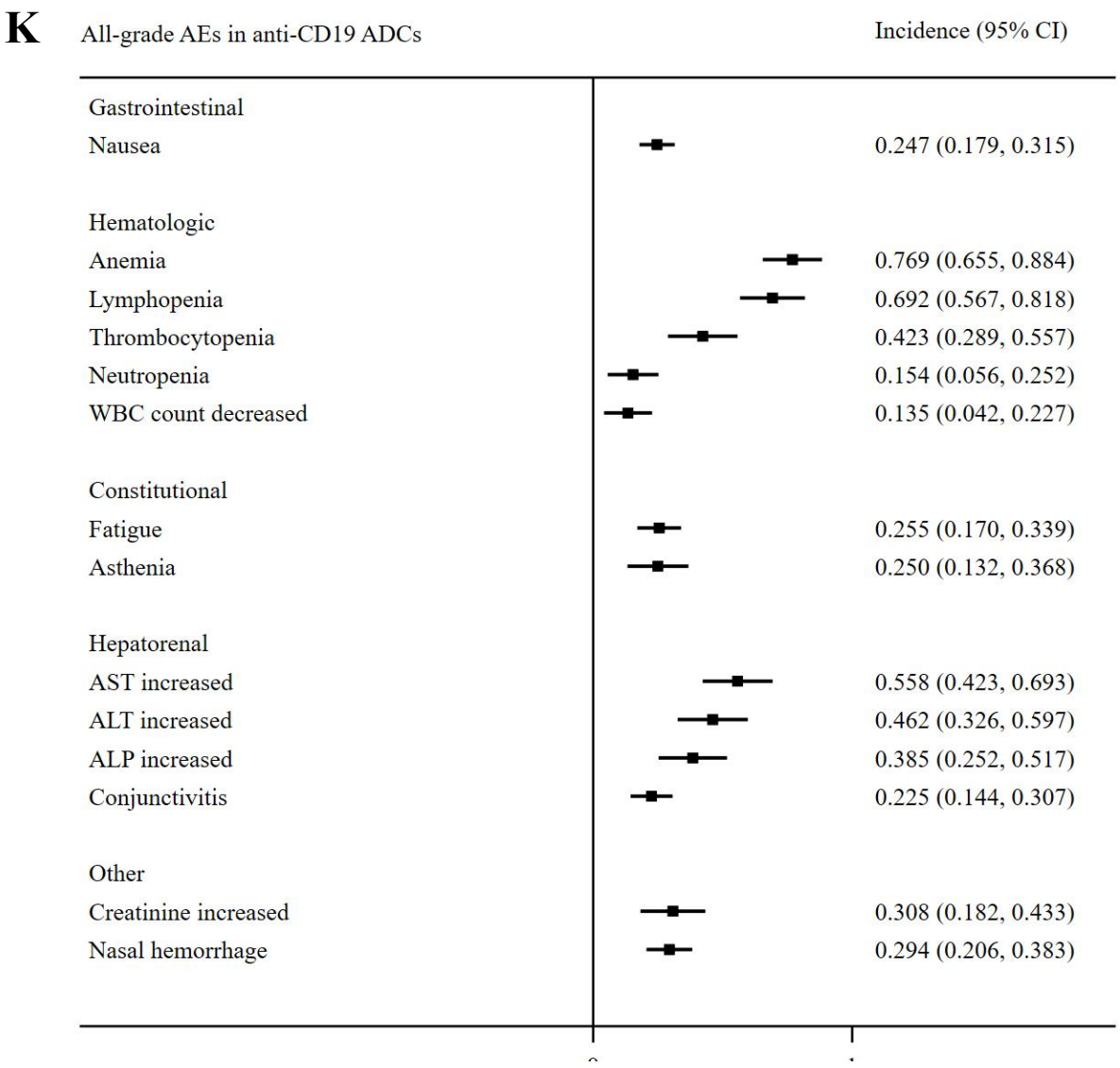

All-grade AEs in anti-gpNMB ADCs
Incidence (95% CI)
Gastrointestinal
Nausea 0.393 (0.348, 0.439)
Decreased appetite 0.292 (0.245, 0.340)
Constipation 0.289 (0.231, 0.346)
Diarrhoea 0.262 (0.210, 0.314)
Vomiting 0.244 (0.194, 0.294)
Abdominal pain 0.207 (0.152, 0.261)
Neurologic
Peripheral neuropathy 0.346 (0.301, 0.392)
Hematologic
Neutropenia 0.356 (0.310, 0.401)
Anemia 0.346 (0.163, 0.529)
Thrombocytopenia 0.231 (0.069, 0.393)
Constitutional
Fatigue 0.461 (0.414, 0.507)
Alopecia 0.380 (0.331, 0.429)
Pyrexia 0.202 (0.148, 0.256)
Skin
Rash 0.446 (0.399, 0.494)
Pruritus 0.313 (0.265, 0.360)
Pulmonary
Cough 0.231 (0.069, 0.393)
Pleural effusion 0.115 (-0.007, 0.238)
Other
Peripheral edema 0.308 (0.130, 0.485)
0
0.5

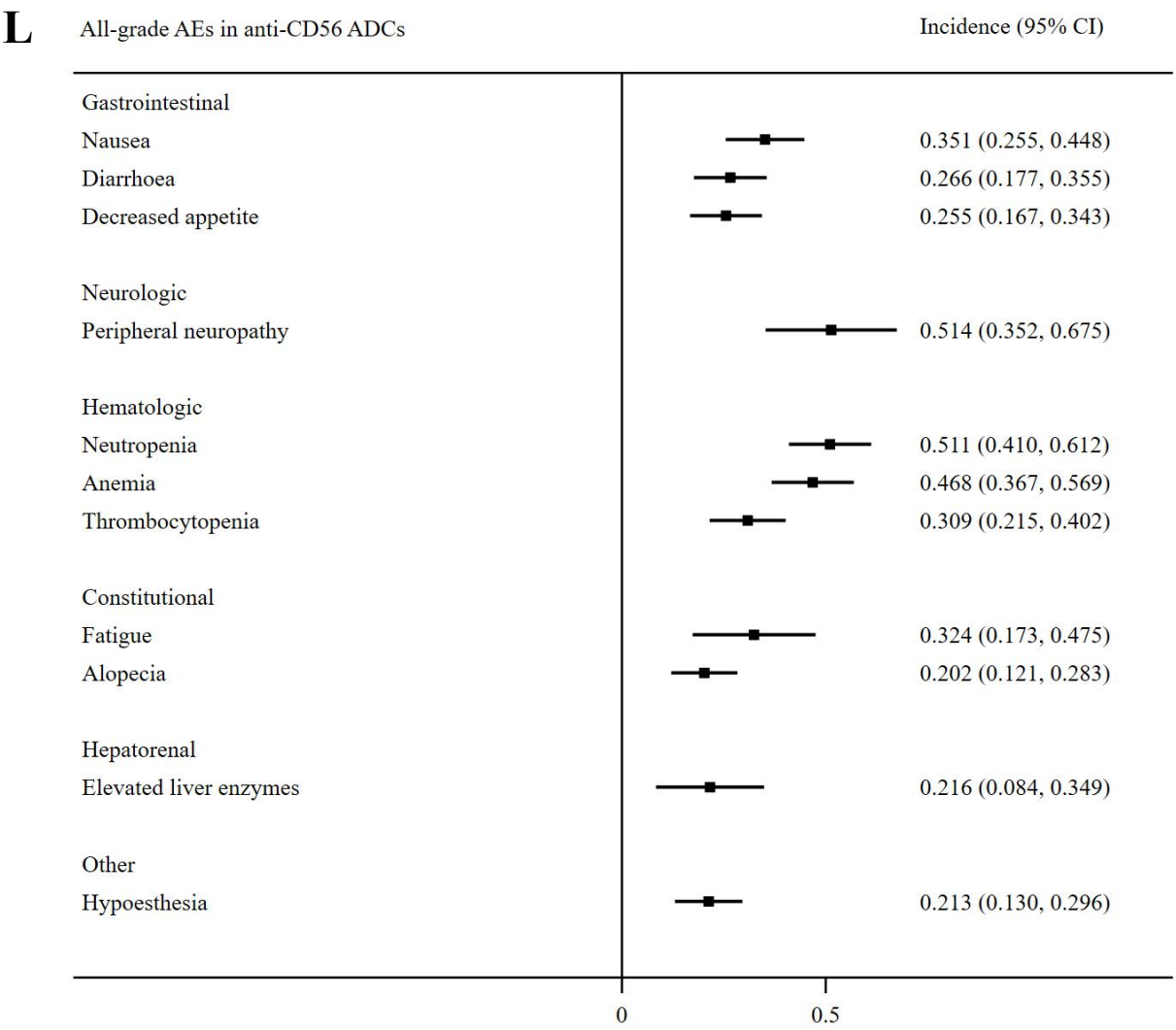
I All-grade AEs in anti-mesothelin ADCs



J All-grade AEs in anti-FRα ADCs



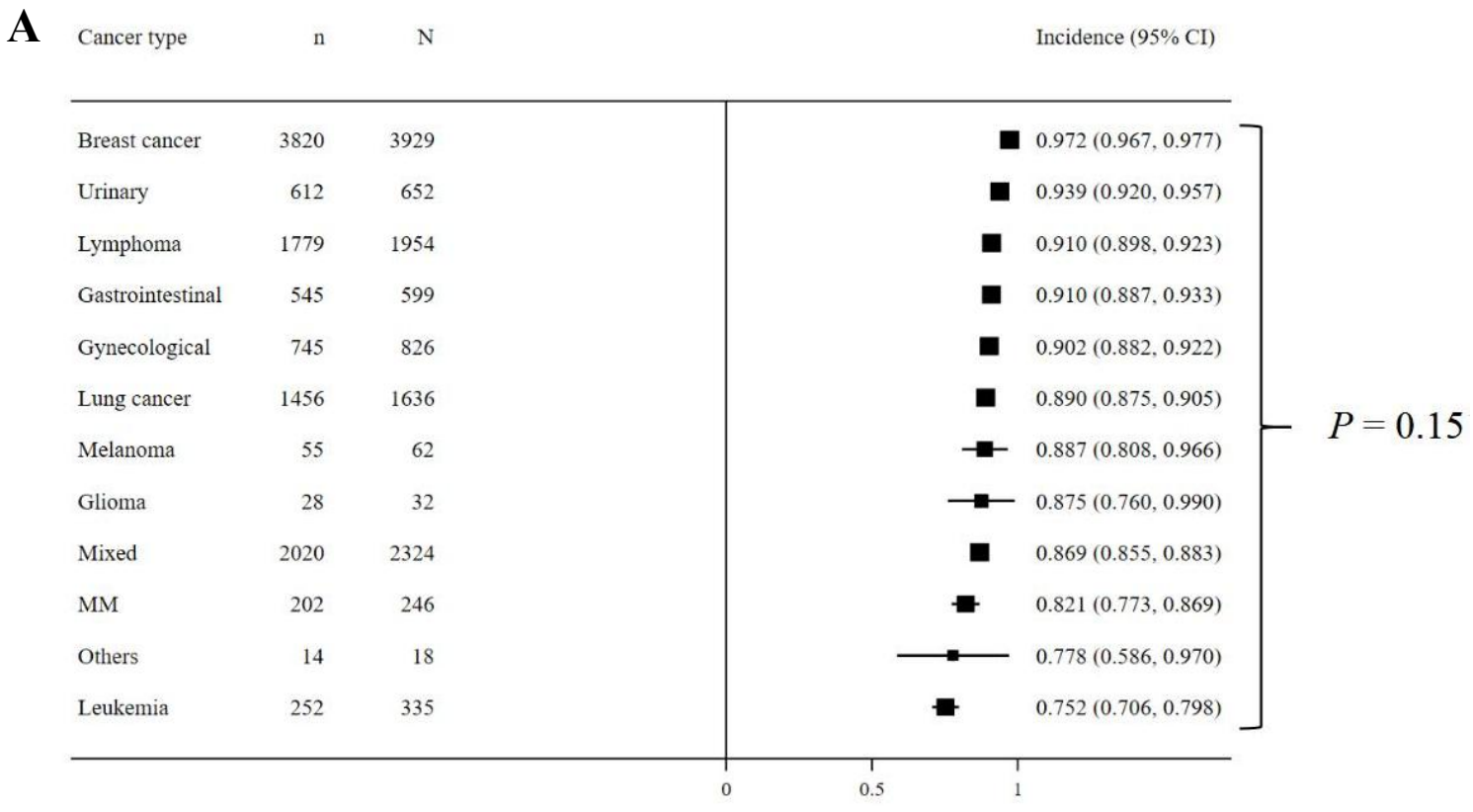


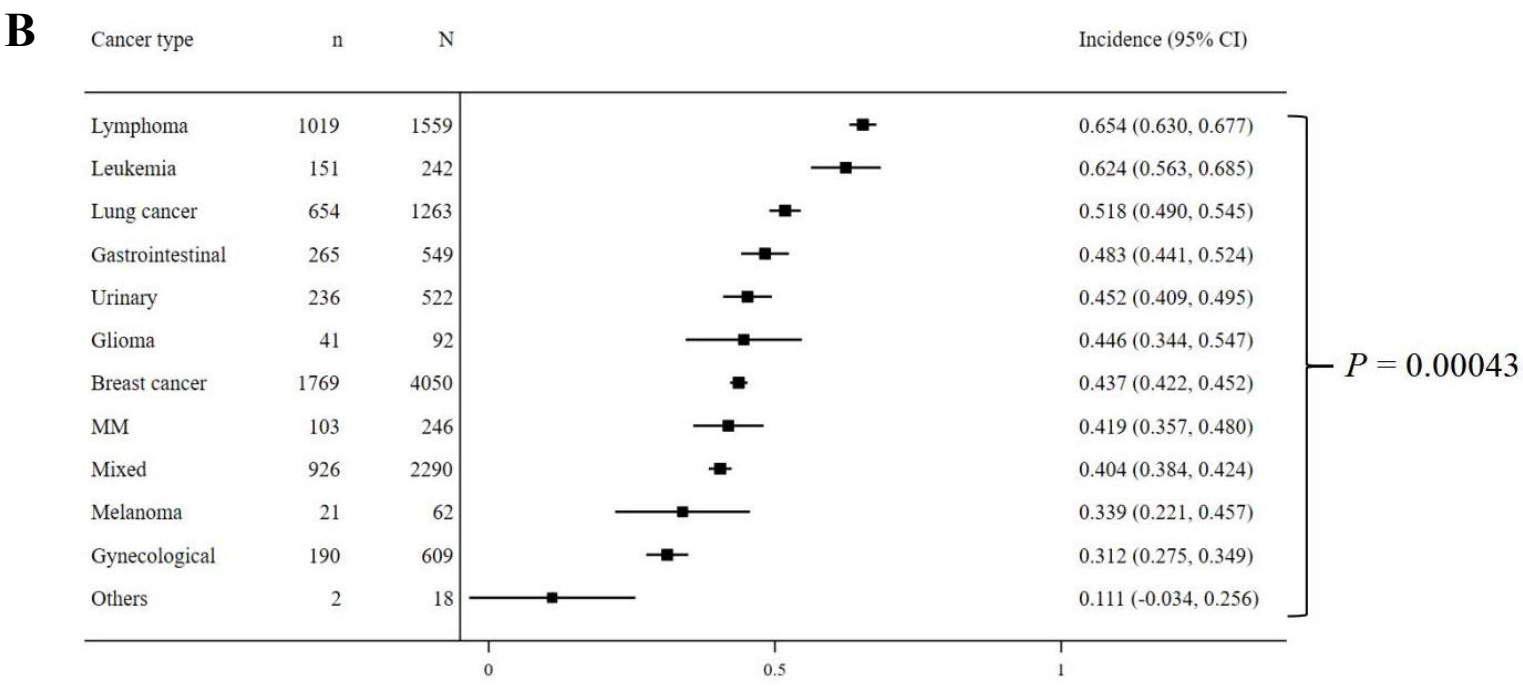


Abbreviation: WBC, white blood cell; GGT, gamma-glutamyl transpeptidase; AST, alanine aminotransferase; ALT, aspartate transaminase; ALP, alkaline phosphatase.

A, Incidences of all-grade adverse events in anti-HER2 mAb ADCs. B, Incidences of all-grade adverse events in anti-DLL3 mAb ADCs. C, Incidences of all-grade adverse events in anti-CD30 mAb ADCs. D, Incidences of all-grade adverse events in anti-Trop-2 mAb ADCs. E, Incidences of all-grade adverse events in anti-CD79b mAb ADCs. F, Incidences of all-grade adverse events in anti-CD22 mAb ADCs. G, Incidences of all-grade adverse events in anti-Nectin-4 mAb ADCs. H, Incidences of all-grade adverse events in anti-gpNMB mAb ADCs. I, Incidences of all-grade adverse events in anti-mesothelin mAb ADCs. J, Incidences of all-grade adverse events in anti-FRa mAb ADCs. K, Incidences of all-grade adverse events in anti-CD19 mAb ADCs. L, Incidences of all-grade adverse events in anti-CD56 mAb ADCs.

eFigure 8. Subgroup analysis of overall adverse event incidence by cancer type.

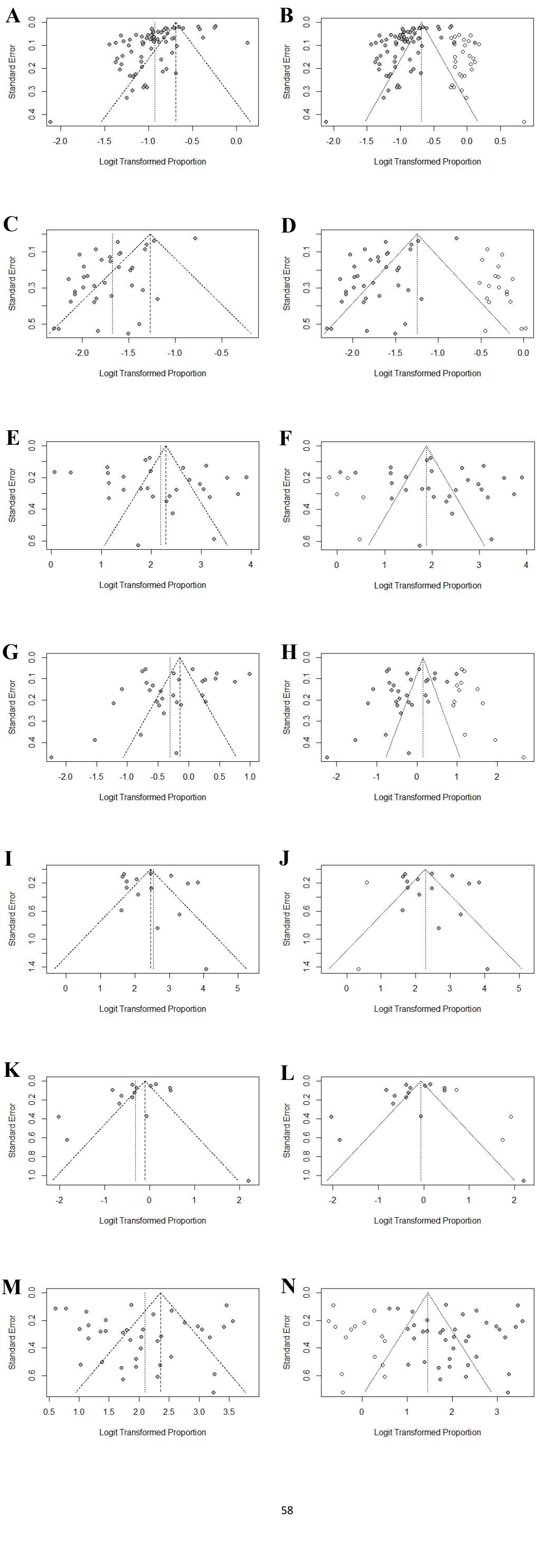


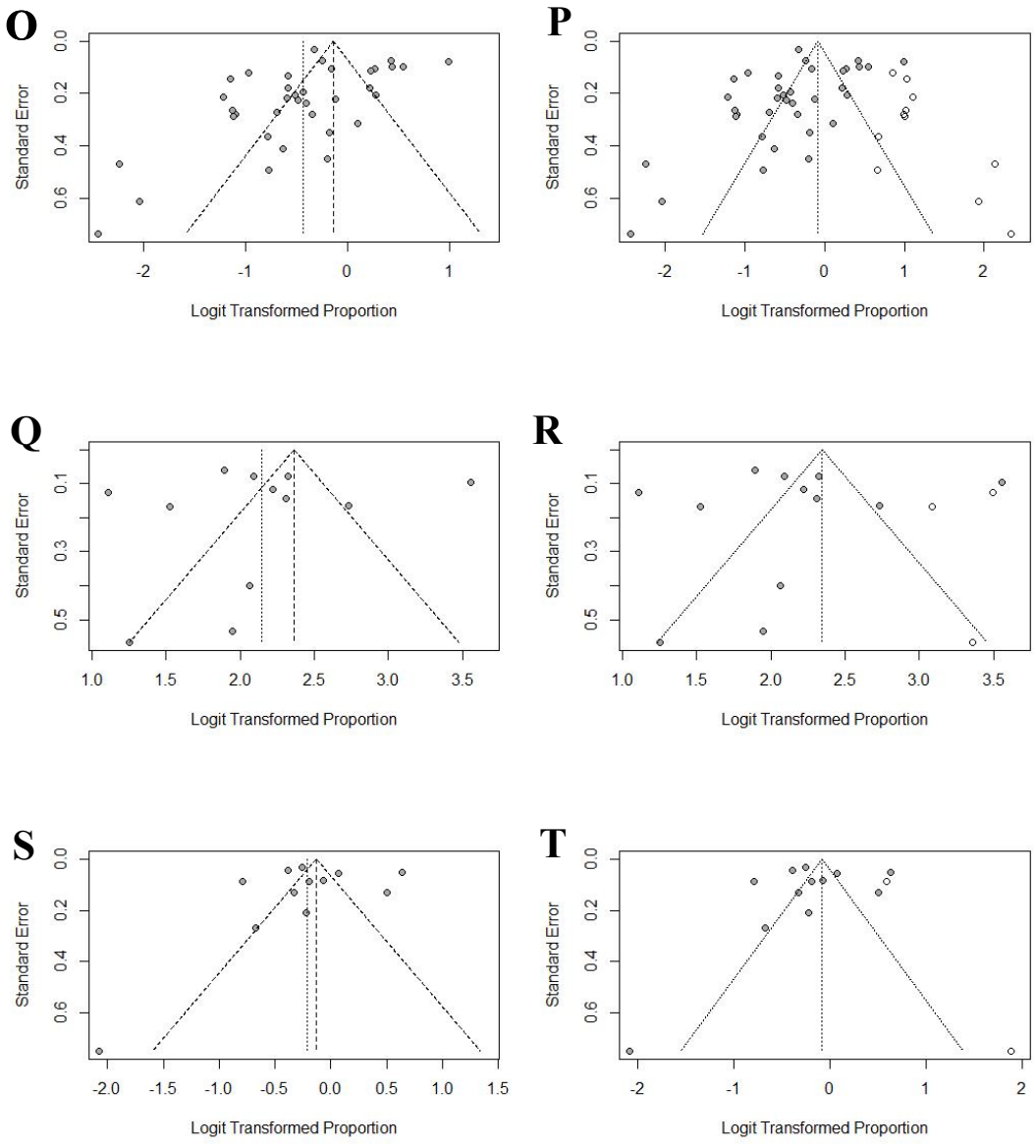


Abbreviation: MM, multiple myeloma.

A, All-grade adverse event. B, Grade 3 or higher adverse event.

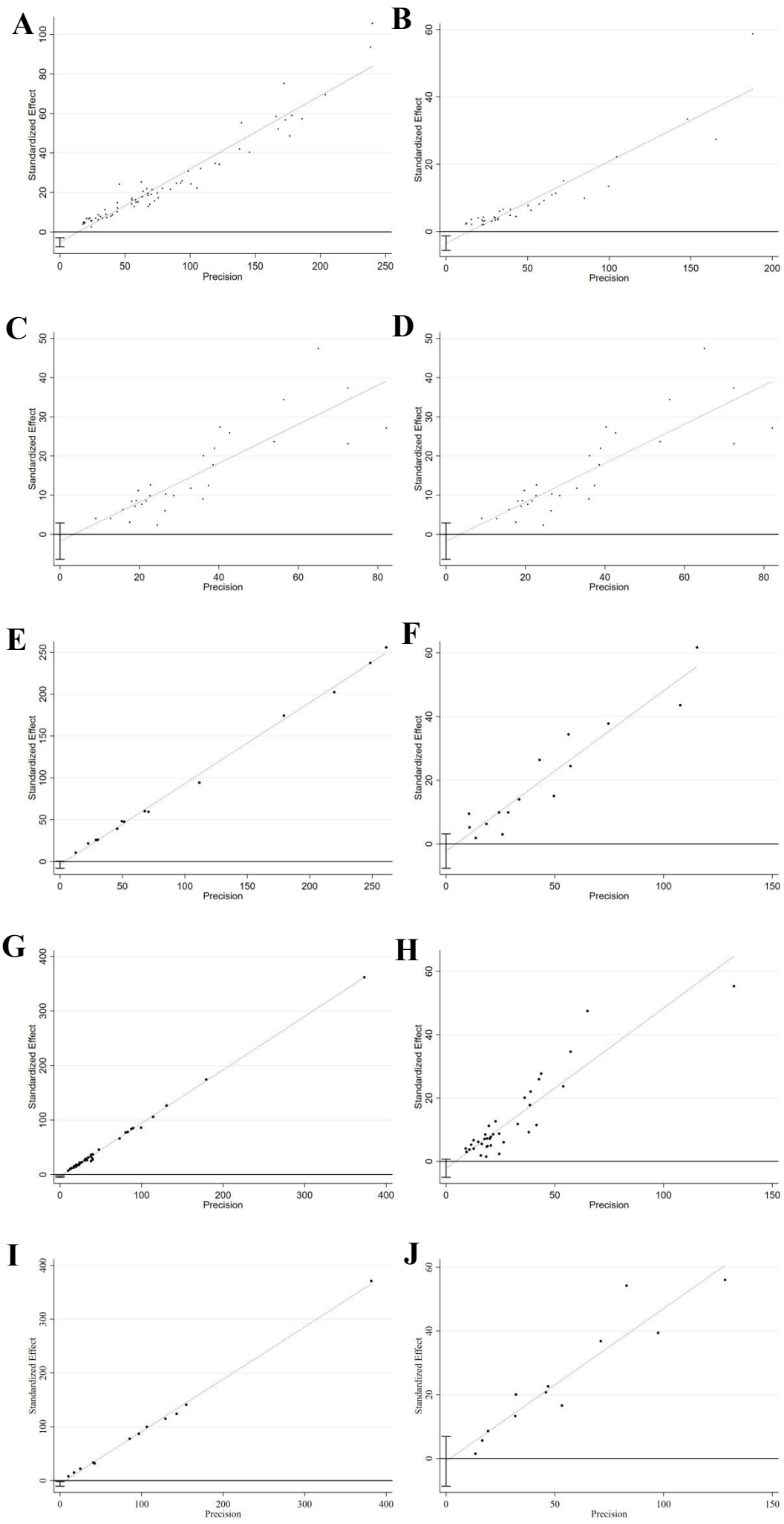
eFigure 9. Funnel plots of the incidence of adverse events.





A, Classic funnel plot of logit transformed against standard error in all-grade adverse events. B, Trim-and-fill method to adjusted funnel plot of logit transformed against standard error in all-grade adverse events. C, Classic funnel plot of logit transformed against standard error in grade 3 or higher adverse events. D, Trim-and-fill method to adjusted funnel plot of logit transformed against standard error in grade 3 or higher adverse events. E, Classic funnel plot of logit transformed against standard error in all-grade adverse events of ADCs. F, Trim-and-fill method to adjusted funnel plot of logit transformed against standard error in all-grade adverse events of ADCs. G, Classic funnel plot of logit transformed against standard error in grade 3 or higher adverse events of ADCs. H, Trim-and-fill method to adjusted funnel plot of logit transformed against standard error in grade 3 or higher adverse events of ADCs. I, Classic funnel plot of logit transformed against standard error in all-grade adverse events of payload-conjugates ADCs. J, Trim-and-fill method to adjusted funnel plot of logit transformed against standard error in all-grade adverse events of payload-conjugates ADCs. K, Classic funnel plot of logit transformed against standard error in grade 3 or higher adverse events of payload-conjugates ADCs. L,Trim-and-fill method to adjusted funnel plot of logit transformed against standard error in grade 3 or higher adverse events of payload-conjugates ADCs. M, Classic funnel plot of logit transformed against standard error in all-grade adverse events of anti-target monoclonal antibody ADCs. N, Trim-and-fill method to adjusted funnel plot of logit transformed against standard error in all-grade adverse events of anti-target monoclonal antibody ADCs. O, Classic funnel plot of logit transformed against standard error in grade 3 or higher adverse events of anti-target monoclonal antibody ADCs. P, Trim-and-fill method to adjusted funnel plot of logit transformed against standard error in grade 3 or higher adverse events anti-target monoclonal antibody ADCs. Q, Classic funnel plot of logit transformed against standard error in all-grade adverse events by cancer types. R, Trim-and-fill method to adjusted funnel plot of logit transformed against standard error in all-grade adverse events by cancer types. S Classic funnel plot of logit transformed against standard error in grade 3 or higher adverse events by cancer types. T, Trim-and-fill method to adjusted funnel plot of logit transformed against standard error in grade 3 or higher adverse events by cancer types.

eFigure 10. Egger's plot of the incidence of adverse events.



A, Egger's plot of precision against standard error in all-grade adverse events. B, Egger's plot of precision against standard error in grade 3 or higher adverse events. C, Egger's plot of precision against standard error in all-grade adverse events of ADCs. D, Egger's plot of precision against standard error in grade 3 or higher adverse events of ADCs. E, Egger's plot of precision against standard error in all-grade adverse events of payload-conjugates ADCs. F, Egger's plot of precision against standard error in grade 3 or higher adverse events of payload-conjugates ADCs. G, Egger's plot of precision against standard error in all-grade adverse events of anti-target monoclonal antibody ADCs. H, Egger's plot of precision against standard error in grade 3 or higher adverse events of anti-target monoclonal antibody ADCs. I, Egger's plot of precision against standard error in all-grade adverse events of by cancer types. J, Egger's plot of precision against standard error in grade 3 or higher adverse events by cancer types.

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