

Supplementary figure legends:

Figure S1. Flow diagram for databases and registers identification and screening.

Figure S2. Comparison of the pooled risk ratio of treatment response with or without T-VEC.

Figure S3. Detailed frequency of all types of common adverse events.

Figure S4. Comparison of the pooled risk ratio of top six common adverse events in treatments with or without T-VEC.

Figure S5. Comparison of the pooled risk ratio of top six serious adverse events in treatments with or without T-VEC.

Figure S6. Detailed frequency of all types of serious adverse events.

Previous studies

Identification of new studies via databases and registers

Identification

Studies included in previous version of review, duplicates removed.
(n = 17)

Records identified from:
PubMed (n = 372)
EMBASE (n = 87)
Medline (n=195)
Web of Science (n = 207)
Cochrane Library (n = 16)
Clinicaltrials.gov (n = 37)

Records removed *before screening*:
Duplicate records (n = 416)
Clinical trials: recruiting, withdrawn, or terminated, etc. (n = 14)
Records removed for other reasons (n = 327)

Screening

Records screened
(n = 157)

Records excluded
Case reports(n = 32)
Meetings (n = 5)

Reports sought for retrieval
(n = 120)

Reports not retrieved (n = 9)
No results posted (n = 14)

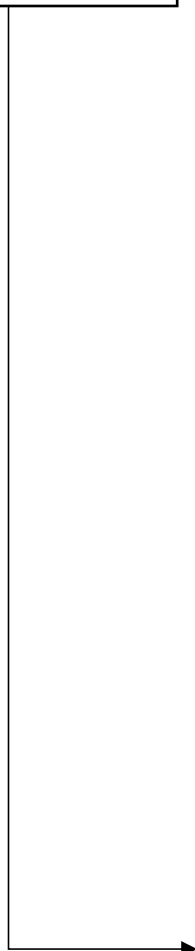
Reports assessed for eligibility
(n = 97)

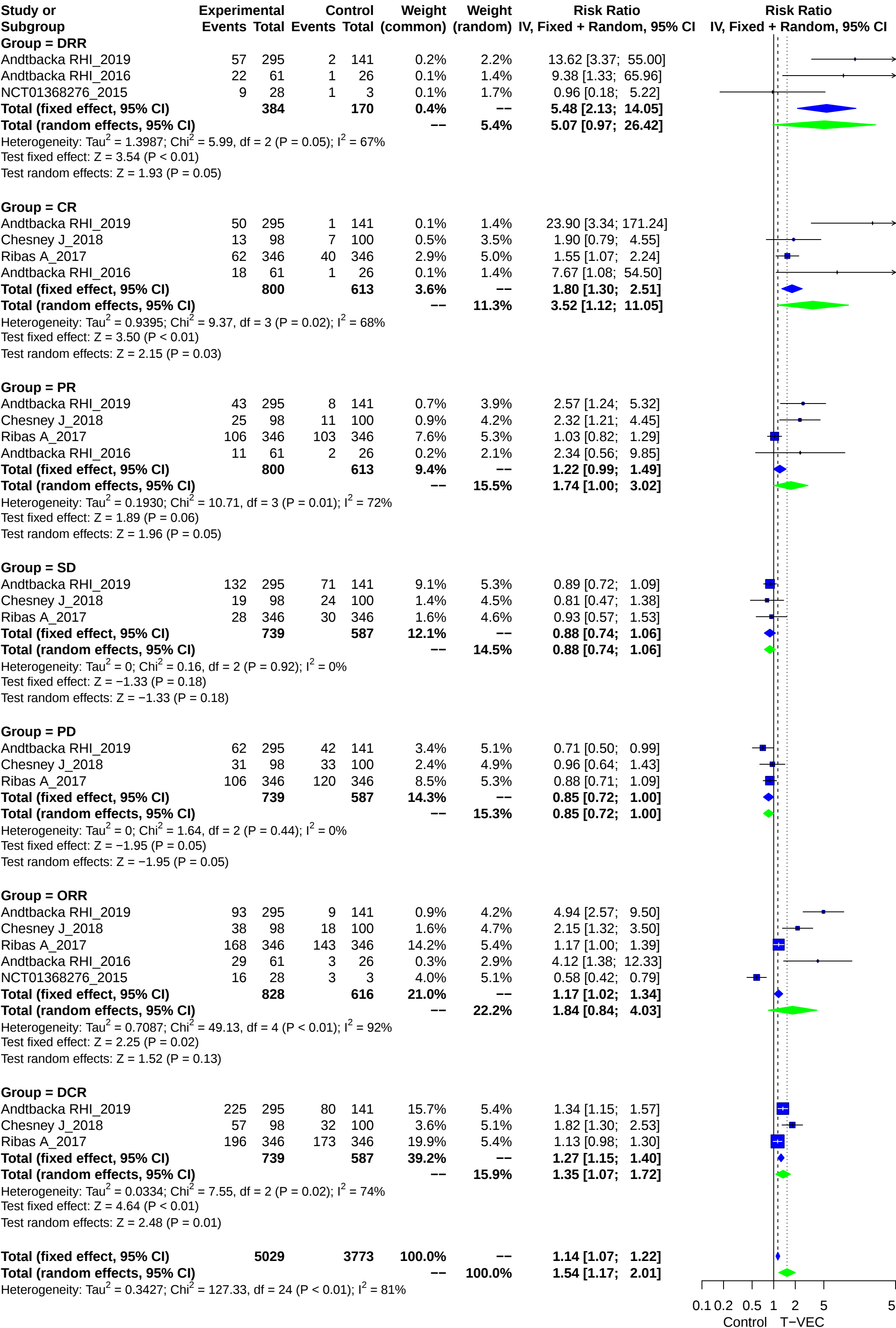
Reports excluded:
Non-human research (n = 15)
Systematic reviews (n = 10)
Assessment tools are not include in criteria (n = 23)
Reports with the same data (n = 8)
Without properly data record (n = 7)
Included in previous review (n = 17)

Included

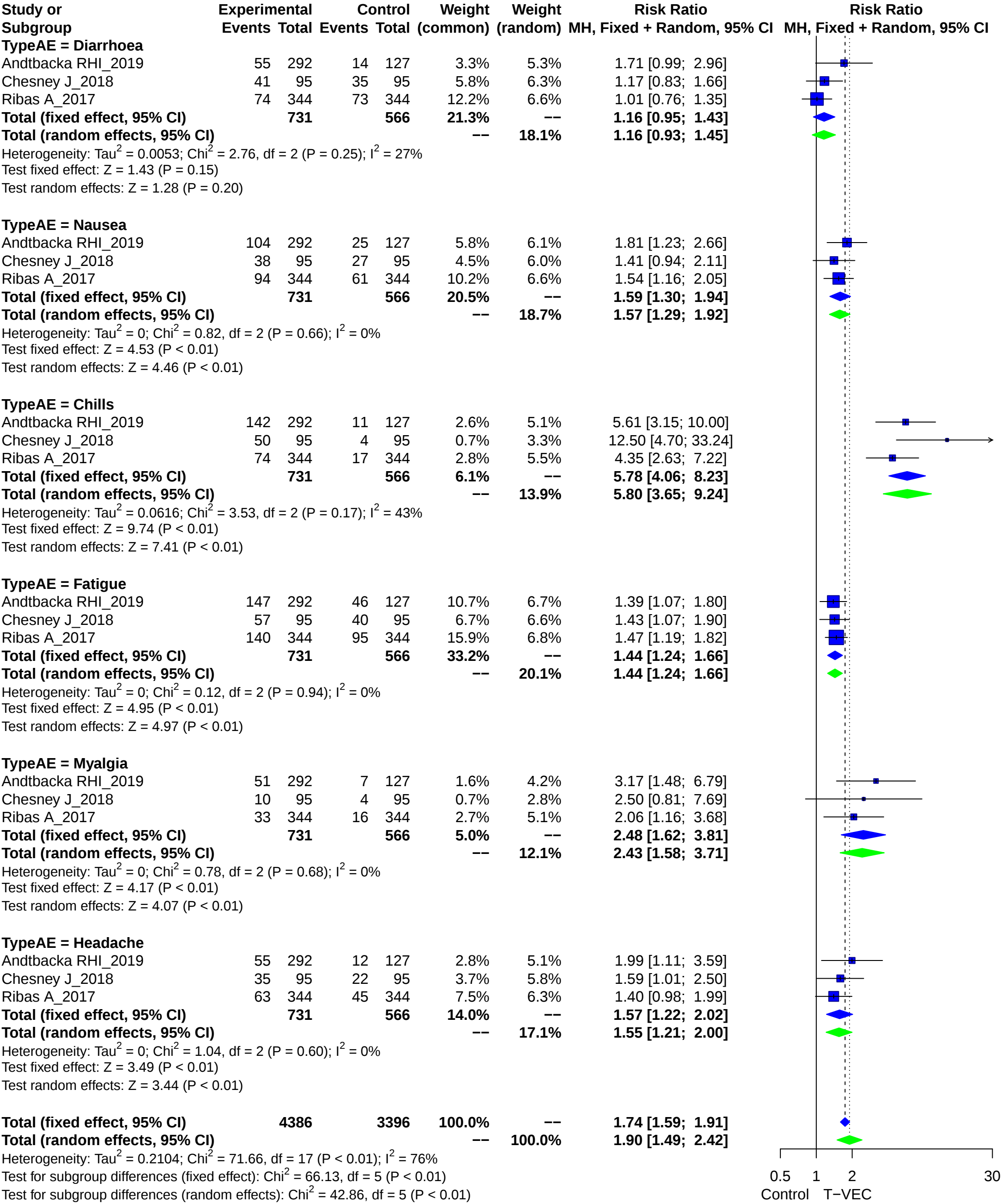
New studies/trials included in this study
(n = 17)

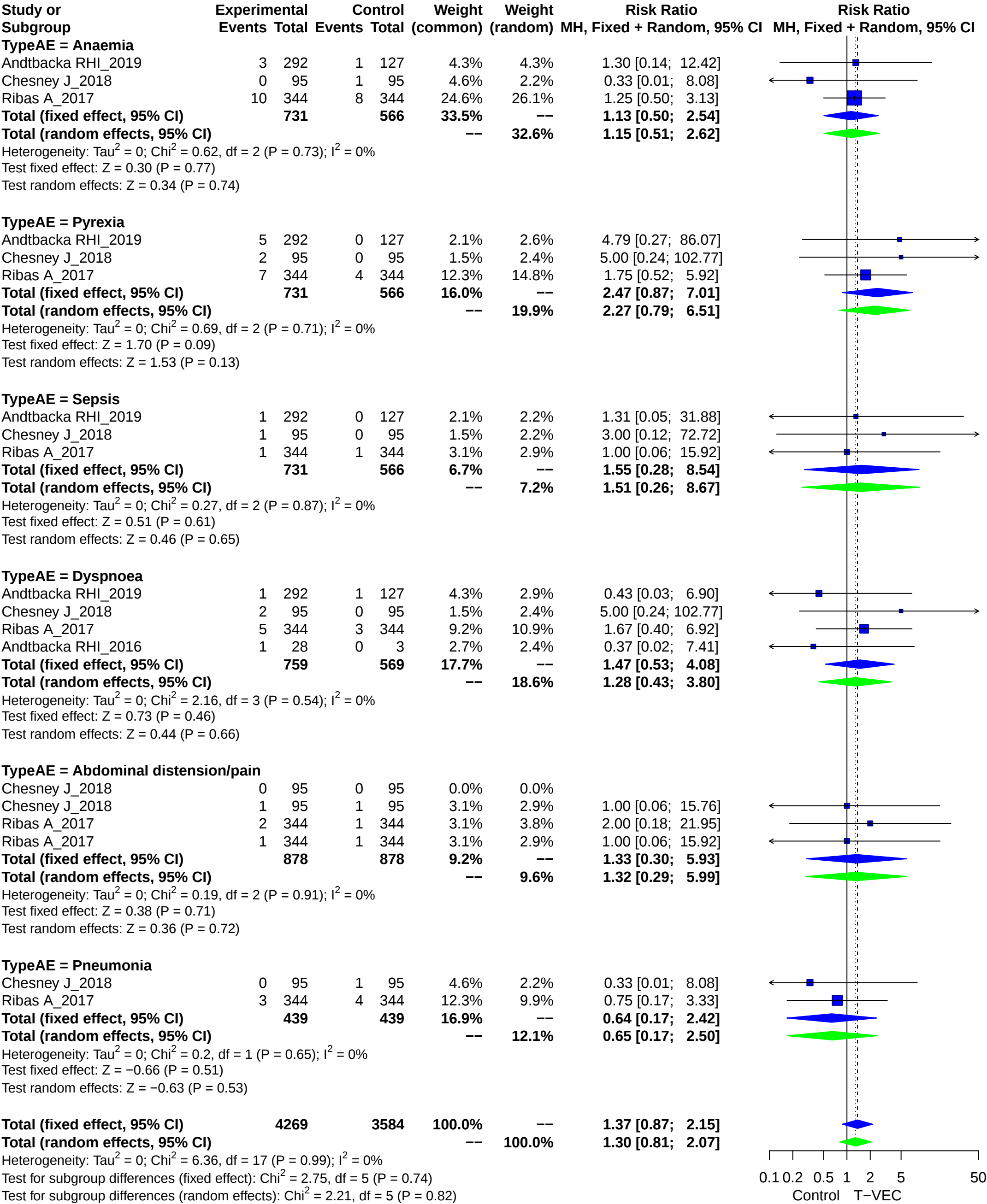
Total studies/trials included in this study
(n = 34)





Aetiology	COVID	HSV	Poxvirus	Reovirus	Group
5	6	39	3	14	Anaemia
				18	Hemoglobin decreased
	5				Iron deficiency anaemia
		8		9	Leukopenia
		3			Lymphadenopathy
		10		6	Lymphocytopenia
		7		17	Neutrophil count decreased
		2		12	Thrombocytopenia
		2			Angina pectoris
				1	Atrial fibrillation
		2			Atrial flutter
		2			Atrioventricular block
	3	1			Cardiac arrest
		5			Cardiac failure
		6			Myocardial infarction
		4			Vertigo
		5			Adrenal insufficiency
		25			Hyperthyroidism
		62			Hypothyroidism
		7			Lymphocytic hypophysitis
		9			Vision blurred
		8			Visual impairment
6	2	109		2	Abdominal distension/pain
		18			Colitis
5	7	117		6	Constipation
7	10	256		15	Diarrhoea
		16			Dry mouth
	1	21	1	4	Dyspepsia
		1		1	Dysphagia
		2			Frequent bowel movements
		7			Gastroesophageal reflux
		4			Gastrointestinal AEs
		5			Gastrointestinal haemorrhage
		5			Intestinal obstruction
9	12	388	2	35	Nausea
		2			Pancreatitis
2		5			Stomatitis
	1	1			Toothache
5	10	213	1	22	Vomiting
7		74			Asthenia
	1	12			Chest pain
11	18	494	2	29	Chills
		2			Death
		16		1	Disease progression
		5			Face oedema
6	27	556	8	43	Fatigue
		20			Fatigue/malaise
9		56	4	23	Fever
		4			General physical health deterioration
		2			Inflammation
	7	362			Influenza like illness
7					Injection
	3				Injection site discharge
	9	58	1		Injection site erythema
	1	2			Injection site inflammation
	4	2			Injection site oedema
	19	220	3		Injection site pain
	4	29	1		Injection site pruritus
		3	1		Injection site rash
	3	76			Injection site reaction
		16			Injection site swelling
2	5	17			Malaise
5					Oedema
3	14	136	1	5	Pain
		2			Performance status decreased
	3	126			Peripheral edema
		4			Peripheral swelling
12	7	521	3	12	Pyrexia
		7	1		Tenderness
		2			Autoimmune hepatitis
		4			Cholecystitis
		2			Cytokine release syndrome
	1	2			Bronchitis
	1	39		2	Cellulitis
		2			Erysipelas
	1	2			Escherichia infection
		3			Eye infection
		2			Gastroenteritis
		3			Herpes zoster
		5			Infection
		2			Inflammatory syndrome
		14			Influenza
		2			Lower respiratory tract infection
		45			Nasopharyngitis
		33			Oral herpes
1		7			Pneumonia
		2			Postoperative wound infection
	5	10			Rhinitis
	1	5			Sepsis
		7			Sinusitis
		2			Skin infection
	5	56		5	Upper respiratory tract infection
9					Urinary
	1	33			Urinary tract infection
		2			Wound infection
		10			Contusion
		9			Fall
		3			Femur fracture
		2			Humerus fracture
		8			Infusion related reaction
		11			Procedural pain
		2			Spinal compression fracture
7		43			Alanine aminotransferase increased
		4			Amylase increased
5		32		1	Aspartate aminotransferase increased
9					Blood
3		22		1	Blood alkaline phosphatase increased
					Blood bilirubin increased
		2			Blood iron decreased
		5		1	Blood lactate dehydrogenase increased
		6			Blood urea increased
		6			Body temperature increased
		2		2	Creatinine increased
		3			Lipase increased
				9	Platelet count decreased
9					Transaminitis
		3			Transpiration
2		19		2	Weight decreased
2		1			White blood cell count decreased
		11	1	32	Anorexia
	7	130			Decreased appetite
	1	14			Dehydration
1		4			Diabetes mellitus
1		3			Diabetic ketoacidosis
		5		2	Hypercalcemia
		35		2	Hyperglycaemia
		6			Hyperkalaemia
		2		1	Hyperuricaemia
4				8	Hypoalbuminemia
1				2	Hypocalcemia
		1	1		Hypoglycaemia
1		8		9	Hypokalaemia
1		4		7	Hypomagnesaemia
4		9		4	Hyponatraemia
1		16		4	Hypophosphatemia
	7	226	1	4	Arthralgia
3	3	113		4	Back pain
		2		1	Bone pain
		2			Generalized muscle weakness
		2			Intervertebral disc protrusion
		35			Muscle spasms
2					Muscular
1		6		3	Muscular weakness
		5			Musculoskeletal chest pain
		24			Musculoskeletal pain
6	9	160	6	29	Myalgia
	4	18			Neck pain
	5	145	1	6	Pain in extremity
		2			Pathological fracture
		2			Bladder transitional cell carcinoma
		3			Infected neoplasm
		29			Malignant melanoma
		3			Malignant neoplasm progression
		2			Malignant pleural effusion
		10			Metastases to central nervous system
	1	13			Metastatic malignant melanoma
		2			Neoplasms benign, malignant and unspecified (incl cysts and polyps) – Other, specify
	2	6			Squamous cell carcinoma
	1	4			Tumour haemorrhage
		39	1		Tumour pain
		2			Brain oedema
		2			Central nervous system lesion/necrosis
		3			Cerebral haemorrhage
		2			Convulsion
2	12	74		4	Dizziness
			1	4	Dysgeusia
		2			Encephalopathy
	1	1			Haemorrhage intracranial
4	12	282	3	13	Headache
		3			Hypoaesthesia
	3				Motor dysfunction
		2			Nervous system disorder
		19			Paresthesia
				5	Paresthesia
		9		7	Peripheral neuropathy
		2			Seizure
		5			Somnolence
1		3			Syncope
		3			Transient ischaemic attack
	5	55			Anxiety
		1		4	Confusion
		4			Delirium
		40			Depression
		65		1	Insomnia
		4			Mental status changes
		6			Acute kidney injury
		1		2	Dysuria
		3			Haematuria
2		4			Pollakiuria
		6			Proteinuria
1		1			Renal failure
		1		1	Ureteric obstruction
		4			Chronic obstructive pulmonary disease
4	9	156	1	18	Cough
5	3	80	1	12	Dyspnoea
		5		2	Flu-like illness
2		4			Hiccups
		3			Hypoxia
3		3			Nasal congestion
2					Oropharyngeal
	7	29			Oropharyngeal pain
		13			Pleural effusion
		29			Pneumonitis
1		1			Pneumothorax
		3			Productive cough
	1	5		2	Pulmonary embolism
		5			Respiratory failure
	7				Sinus congestion
		8			Actinic keratosis
		13		9	Alopecia
2		2			Dermatitis
2		6			Dry skin
		58	1		Erythema
				3	Flushing
	6	32			Hyperhidrosis
5			1	3	Maculopapular rash
		10			Night sweats
7	7	160		2	Pruritus
5	3	168			Rash
				3	Rash desquamating
		11			Rash erythematous
		8			Rash macular
		34			Rash maculo-papular
		4			Skin and subcutaneous tissue disorders – Other, specify
		2			Skin hypopigmentation
		2			Skin lesion
		2			Skin mass
		3			Skin reaction
		2			Skin ulcer
		5	1		Urticaria
		72	1		Vitiligo
		5		2	Deep vein thrombosis
2		1			Embolism
		3		1	Haemorrhage
		6			Hot flush
11		31			Hypertension
2		12		4	Hypotension





						Group
		10	1		2	Anaemia
		3				Hemoglobin decreased
		2				Lymphadenopathy
		2				Angina pectoris
		5		1		Atrial fibrillation
		2				Atrial flutter
		2				Atrioventricular block
	1	3				Cardiac arrest
		6				Cardiac failure
		6				Myocardial infarction
		3				Vertigo
		5				Hypophysitis
1	1	5				Abdominal distension/pain
		3				Autoimmune colitis
		11				Colitis
		4				Constipation
1		5				Diarrhoea
		1			1	Dysphagia
		5				Gastrointestinal haemorrhage
		3				Intestinal obstruction
	1	5			1	Nausea
		2				Pancreatitis
	1	3			1	Vomiting
		4				Asthenia
		3				Chest pain
		2				Chills
		3				Death
		17			1	Disease progression
	1	5			2	Fatigue
		1	1		1	Fever
		4				General physical health deterioration
		2				Inflammation
		8				Influenza like illness
		2				Oedema peripheral
4		21				Pyrexia
		2				Autoimmune hepatitis
		3				Cholecystitis
		2				Bronchitis
	1	15				Cellulitis
		2				Erysipelas
		2				Gastroenteritis
		2				Influenza
		2				Lower respiratory tract infection
	1	5				Postoperative wound infection
		2				Sepsis
		8				Upper respiratory tract infection
		2				Urinary tract infection
		2				Wound infection
		3				Fall
		3				Femur fracture
		2				Humerus fracture
		2				Rib fracture
		2				Spinal compression fracture
		1			1	Aspartate aminotransferase increased
					2	Leukocyte count decreased
		1			2	Neutrophil count decreased
		5				Dehydration
		3				Diabetes mellitus
		3				Diabetic ketoacidosis
		2				Hypercalcaemia
		2				Hyperglycaemia
		1	1			Hypoglycaemia
1		4				Hyponatraemia
					4	Serum albumin decreased
					2	Serum calcium decreased
					2	Serum phosphate decreased
		2				Arthralgia
		7				Back pain
		1			1	Bone pain
		2				Intervertebral disc protrusion
		2				Pain in extremity
		2				Pathological fracture
		2				Bladder transitional cell carcinoma
		3				Infected neoplasm
		28				Malignant melanoma
		2				Malignant neoplasm progression
		3				Malignant pleural effusion
		9				Metastases to central nervous system
	1	14				Metastatic malignant melanoma
	2	2				Squamous cell carcinoma
		4				Tumour haemorrhage
		6				Tumour pain
		3				Cerebral haemorrhage
		2				Convulsion
		3				Dizziness
	1	1				Haemorrhage intracranial
		2				Seizure
2		2				Syncope
		3				Transient ischaemic attack
		3				Anxiety
		1			2	Confusion
		4				Delirium
		3				Mental status changes
		3				Acute kidney injury
		3				Haematuria
		2				Renal failure
		1			1	Ureteric obstruction
		3				Chronic obstructive pulmonary disease
1					1	Cough
1		12			1	Dyspnoea
		8				Pleural effusion
1		6				Pneumonia
	1	5				Pulmonary embolism
		6				Respiratory failure
		3				Dermatitis
		2				Skin ulcer
		5				Deep vein thrombosis
		4				Hypotension
Adenovirus	CVA21	HSV	Poxvirus	Reovirus		