

Supplementary Methods. Disproportionality analysis and ROR calculation.

In pharmacovigilance research, disproportionality analysis serves as a primary method for evaluating potential associations between specific adverse events (AEs) and pharmaceutical agents. In this study, we utilized the reporting odds ratio (ROR) to quantify the likelihood of target AEs occurring in suspected association with the drug of interest based on historical reporting data. To facilitate this analysis, we first constructed a 2×2 contingency table for adverse drug reactions (**Supplementary Table 3**), which formed the basis for the subsequent ROR calculations. Within this framework, a represents the number of cases of the target AE following BiTE treatment; b represents the number of cases of other AEs following BiTE treatment; c represents the number of cases of the target AE following non-BiTE treatments; and d represents the number of cases of other AEs following non-BiTE treatments.

Furthermore, to evaluate the fatality risk specifically associated with BiTEs, a separate contingency table was established (**Supplementary Table 4**). In this mortality analysis, a represents the number of fatal reports for the target AE following BiTE treatment; b represents the number of fatal reports for other AEs following BiTE treatment; c represents the number of non-fatal reports for the target AE following BiTE treatment; and d represents the number of non-fatal reports for other AEs following BiTE treatment.

The ROR and its 95% confidence interval (95% CI) were calculated using the following standard equations:

$$ROR = \frac{a * d}{c * b}$$

$$ROR_{0.025} = e^{Ln(ROR) - 1.96 \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}}$$

$$ROR_{0.075} = e^{Ln(ROR) + 1.96 \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}}$$

Supplementary Table 1. Search terms for hematological malignancies in MedDRA 25.1.

Acute erythroid leukaemia	High grade B-cell lymphoma Burkitt-like lymphoma stage III	Malignant lymphoma unclassifiable high grade
Acute myeloid leukaemia	High grade B-cell lymphoma Burkitt-like lymphoma stage IV	Malignant lymphoma unclassifiable low grade
Acute leukaemia	High grade B-cell lymphoma Burkitt-like lymphoma	Myelodysplastic syndrome
Acute lymphocytic leukaemia	Enteropathy-associated T-cell lymphoma	Mature B-cell type acute leukaemia
Acute megakaryocytic leukaemia	Intestinal T-cell lymphoma refractory	Myelodysplastic syndrome unclassifiable
Acute monocytic leukaemia	Intestinal T-cell lymphoma stage I	Natural killer-cell leukaemia
Acute myelomonocytic leukaemia	Intestinal T-cell lymphoma stage II	Plasmacytoma
Acute promyelocytic leukaemia	Intestinal T-cell lymphoma stage III	Follicular lymphoma
Adult T-cell lymphoma/leukaemia	Intestinal T-cell lymphoma stage IV	Non-Hodgkin's lymphoma refractory
Adult T-cell lymphoma/leukaemia refractory	Peripheral T-cell lymphoma unspecified	Non-Hodgkin's lymphoma unspecified histology aggressive refractory
Adult T-cell lymphoma/leukaemia stage I	Peripheral T-cell lymphoma unspecified stage I	Non-Hodgkin's lymphoma unspecified histology aggressive stage I
Adult T-cell lymphoma/leukaemia stage II	Peripheral T-cell lymphoma unspecified stage II	Non-Hodgkin's lymphoma unspecified histology aggressive stage II
Adult T-cell lymphoma/leukaemia stage III	Peripheral T-cell lymphoma unspecified stage III	Non-Hodgkin's lymphoma unspecified histology aggressive stage III
Adult T-cell lymphoma/leukaemia stage IV	Peripheral T-cell lymphoma unspecified stage IV	Non-Hodgkin's lymphoma unspecified histology aggressive stage IV
Lymphoma AIDS related	Peripheral T-cell lymphoma unspecified refractory	Non-Hodgkin's lymphoma unspecified histology indolent stage I
Aleukaemic leukaemia	Non-Hodgkin's lymphoma	Non-Hodgkin's lymphoma unspecified histology indolent stage II
Anaplastic large cell lymphoma T- and null-cell types	Lymphoplasmacytoid lymphoma/immunocytoma	Non-Hodgkin's lymphoma unspecified histology indolent stage III
Anaplastic large cell lymphoma T- and null-cell types refractory	Lymphoplasmacytoid lymphoma/immunocytoma refractory	Non-Hodgkin's lymphoma unspecified histology indolent stage IV
Anaplastic large cell lymphoma T- and null-cell types stage I	Lymphoplasmacytoid lymphoma/immunocytoma stage I	Prolymphocytic leukaemia
Anaplastic large cell lymphoma T- and null-cell types stage II	Lymphoplasmacytoid lymphoma/immunocytoma stage II	Refractory anaemia with an excess of blasts
Anaplastic large cell lymphoma T- and null-cell types stage III	Lymphoplasmacytoid lymphoma/immunocytoma stage III	Myelodysplastic syndrome transformation
Anaplastic large cell lymphoma T- and null-cell types stage IV	Lymphoplasmacytoid lymphoma/immunocytoma stage IV	Refractory anaemia with ringed sideroblasts
Refractory cytopenia with unilineage dysplasia	Nodal marginal zone B-cell lymphoma	Splenic marginal zone lymphoma
Angiocentric lymphoma	Nodal marginal zone B-cell lymphoma refractory	Splenic marginal zone lymphoma refractory

Angiocentric lymphoma refractory	Nodal marginal zone B-cell lymphoma stage I	Splenic marginal zone lymphoma stage I
Angiocentric lymphoma stage I	Nodal marginal zone B-cell lymphoma stage II	Splenic marginal zone lymphoma stage II
Angiocentric lymphoma stage II	Nodal marginal zone B-cell lymphoma stage III	Splenic marginal zone lymphoma stage III
Angiocentric lymphoma stage III	Nodal marginal zone B-cell lymphoma stage IV	Splenic marginal zone lymphoma stage IV
Angiocentric lymphoma stage IV	Light chain disease	T-cell chronic lymphocytic leukaemia
Angioimmunoblastic T-cell lymphoma	Eosinophilic leukaemia	T-cell lymphoma
Angioimmunoblastic T-cell lymphoma refractory	Extranodal marginal zone B-cell lymphoma (MALT type)	T-cell lymphoma refractory
Angioimmunoblastic T-cell lymphoma stage I	Extranodal marginal zone B-cell lymphoma (MALT type) refractory	T-cell lymphoma stage I
Angioimmunoblastic T-cell lymphoma stage II	Extranodal marginal zone B-cell lymphoma (MALT type) stage I	T-cell lymphoma stage II
Angioimmunoblastic T-cell lymphoma stage III	Extranodal marginal zone B-cell lymphoma (MALT type) stage II	T-cell lymphoma stage III
Angioimmunoblastic T-cell lymphoma stage IV	Extranodal marginal zone B-cell lymphoma (MALT type) stage III	T-cell lymphoma stage IV
T-cell type acute leukaemia	Extranodal marginal zone B-cell lymphoma (MALT type) stage IV	T-cell prolymphocytic leukaemia
B precursor type acute leukaemia	Follicle centre lymphoma diffuse small cell lymphoma	T-cell unclassifiable lymphoma high grade
B-cell small lymphocytic lymphoma	Follicle centre lymphoma diffuse small cell lymphoma refractory	T-cell unclassifiable lymphoma low grade
B-cell small lymphocytic lymphoma refractory	Follicle centre lymphoma diffuse small cell lymphoma stage I	Acute undifferentiated leukaemia
B-cell small lymphocytic lymphoma stage I	Follicle centre lymphoma diffuse small cell lymphoma stage II	Waldenstrom's macroglobulinaemia refractory
B-cell small lymphocytic lymphoma stage II	Follicle centre lymphoma diffuse small cell lymphoma stage III	Waldenstrom's macroglobulinaemia stage I
B-cell small lymphocytic lymphoma stage III	Follicle centre lymphoma diffuse small cell lymphoma stage IV	Waldenstrom's macroglobulinaemia stage II
B-cell small lymphocytic lymphoma stage IV	Hairy cell leukaemia	Waldenstrom's macroglobulinaemia stage III
B-cell lymphoma	Heavy chain disease	Waldenstrom's macroglobulinaemia stage IV
B-cell lymphoma refractory	Hodgkin's disease	Blast crisis in myelogenous leukaemia
B-cell lymphoma stage I	Hodgkin's disease stage IV	Cutaneous lymphoma
B-cell lymphoma stage II	Hodgkin's disease lymphocyte depletion stage I site unspecified	Lymphocytic lymphoma
B-cell lymphoma stage III	Hodgkin's disease lymphocyte depletion stage I subdiaphragm	Central nervous system leukaemia
B-cell lymphoma stage IV	Hodgkin's disease lymphocyte depletion stage I supradiaphragm	Leukaemia cutis

B-cell type acute leukaemia	Hodgkin's disease lymphocyte depletion stage II site unspecified	Immunoblastic lymphoma
B-cell unclassifiable lymphoma high grade	Hodgkin's disease lymphocyte depletion stage II subdiaphragm	Disseminated large cell lymphoma
B-cell unclassifiable lymphoma low grade	Hodgkin's disease lymphocyte depletion stage II supradiaphragm	Metastatic lymphoma
Diffuse large B-cell lymphoma	Hodgkin's disease lymphocyte depletion type refractory	Mastocytic leukaemia
Diffuse large B-cell lymphoma refractory	Hodgkin's disease lymphocyte depletion type stage III	Chronic lymphocytic leukaemia transformation
Diffuse large B-cell lymphoma stage I	Hodgkin's disease lymphocyte depletion type stage IV	Richter's syndrome
Diffuse large B-cell lymphoma stage II	Hodgkin's disease lymphocyte depletion type stage unspecified	Natural killer-cell lymphoblastic lymphoma
Diffuse large B-cell lymphoma stage III	Hodgkin's disease lymphocyte predominance stage I site unspec	Non-Hodgkin's lymphoma unspecified histology aggressive
Diffuse large B-cell lymphoma stage IV	Hodgkin's disease lymphocyte predominance stage I subdiaphragm	Lymphoma transformation
Precursor B-lymphoblastic lymphoma	Hodgkin's disease lymphocyte predominance stage I supradiaphragm	Plasmablastic lymphoma
Precursor B-lymphoblastic lymphoma refractory	Hodgkin's disease lymphocyte predominance stage II site unspec	Chronic eosinophilic leukaemia
Precursor B-lymphoblastic lymphoma stage I	Hodgkin's disease lymphocyte predominance stage II subdiaphragm	Non-Hodgkin's lymphoma unspecified histology indolent
Precursor B-lymphoblastic lymphoma stage II	Hodgkin's disease lymphocyte predominance stage II supradiaphragm	Primary effusion lymphoma
Precursor B-lymphoblastic lymphoma stage III	Hodgkin's disease lymphocyte predominance type refractory	Hepatosplenic T-cell lymphoma
Precursor B-lymphoblastic lymphoma stage IV	Hodgkin's disease lymphocyte predominance type stage III	Burkitt's leukaemia
B-cell prolymphocytic leukaemia	Hodgkin's disease lymphocyte predominance type stage IV	Acute biphenotypic leukaemia
Burkitt's lymphoma	Hodgkin's disease lymphocyte predominance type stage unspecified	Refractory cytopenia with multilineage dysplasia
Burkitt's lymphoma refractory	Hodgkin's disease mixed cellularity stage unspecified	Chronic myeloid leukaemia transformation
Burkitt's lymphoma stage I	Hodgkin's disease mixed cellularity refractory	Epstein-Barr virus associated lymphoma
Burkitt's lymphoma stage II	Hodgkin's disease mixed cellularity stage I site unspecified	Non-Hodgkin's lymphoma metastatic
Burkitt's lymphoma stage III	Hodgkin's disease mixed cellularity stage I subdiaphragmatic	Thyroid B-cell lymphoma
Burkitt's lymphoma stage IV	Hodgkin's disease mixed cellularity stage I supradiaphragmatic	Anaplastic large-cell lymphoma
Central nervous system lymphoma	Hodgkin's disease mixed cellularity stage II subdiaphragmatic	Composite lymphoma
Follicle centre lymphoma, follicular grade I, II, III refractory	Hodgkin's disease mixed cellularity stage II supradiaphragmatic	TEMPI syndrome
Follicle centre lymphoma, follicular grade I, II, III stage I	Hodgkin's disease mixed cellularity stage III	Ocular lymphoma

Follicle centre lymphoma, follicular grade I, II, III stage II	Hodgkin's disease mixed cellularity stage IV	Blastic plasmacytoid dendritic cell neoplasia
Follicle centre lymphoma, follicular grade I, II, III stage III	Hodgkin's disease nodular sclerosis	Marginal zone lymphoma
Follicle centre lymphoma, follicular grade I, II, III stage IV	Hodgkin's disease nodular sclerosis refractory	Acute lymphocytic leukaemia refractory
Follicle centre lymphoma, follicular grade I, II, III	Hodgkin's disease nodular sclerosis stage I	Marginal zone lymphoma stage I
Mantle cell lymphoma	Hodgkin's disease nodular sclerosis stage II	Marginal zone lymphoma stage II
Mantle cell lymphoma refractory	Hodgkin's disease nodular sclerosis stage III	Marginal zone lymphoma stage III
Mantle cell lymphoma stage I	Hodgkin's disease nodular sclerosis stage IV	Marginal zone lymphoma stage IV
Mantle cell lymphoma stage II	Hodgkin's disease refractory	Marginal zone lymphoma refractory
Mantle cell lymphoma stage III	Hodgkin's disease stage I	Leptomeningeal myelomatosis
Mantle cell lymphoma stage IV	Hodgkin's disease stage II	Primary gastrointestinal follicular lymphoma
Cutaneous T-cell lymphoma	Hodgkin's disease stage III	Transformation to acute myeloid leukaemia
Cutaneous T-cell lymphoma refractory	Hodgkin's disease unclassifiable	Chronic myelomonocytic leukaemia with N-ras gene mutation
Cutaneous T-cell lymphoma stage I	Plasma cell myeloma	Philadelphia positive acute lymphocytic leukaemia
Cutaneous T-cell lymphoma stage II	Juvenile chronic myelomonocytic leukaemia	Triple hit lymphoma
Cutaneous T-cell lymphoma stage III	Primary mediastinal large B-cell lymphoma	Nodular lymphocyte predominant Hodgkin lymphoma
Cutaneous T-cell lymphoma stage IV	Primary mediastinal large B-cell lymphoma refractory	Double hit lymphoma
Chloroma	Primary mediastinal large B-cell lymphoma stage I	High-grade B-cell lymphoma
Chronic myeloid leukaemia	Primary mediastinal large B-cell lymphoma stage II	Acute bilineal leukaemia
Chronic leukaemia	Primary mediastinal large B-cell lymphoma stage III	Primary breast lymphoma
Chronic lymphocytic leukaemia	Primary mediastinal large B-cell lymphoma stage IV	Extranodal marginal zone B-cell lymphoma (BALT type)
Chronic lymphocytic leukaemia refractory	Leukaemia	Acute myeloid leukaemia refractory
Chronic lymphocytic leukaemia stage 0	Leukaemia basophilic	Plasma cell myeloma refractory
Chronic lymphocytic leukaemia stage 1	Leukaemia granulocytic	Philadelphia positive chronic myeloid leukaemia
Chronic lymphocytic leukaemia stage 2	Lymphocytic leukaemia	Precursor T-lymphoblastic leukaemia acute
Chronic lymphocytic leukaemia stage 3	Leukaemia monocytic	Breast implant-associated anaplastic large cell lymphoma

Chronic lymphocytic leukaemia stage 4	Myeloid leukaemia	Grey zone lymphoma
Chronic myelomonocytic leukaemia	Neonatal leukaemia	Follicular lymphoma stage I
Precursor T-lymphoblastic lymphoma/leukaemia	Plasma cell leukaemia	Follicular lymphoma stage II
Precursor T-lymphoblastic lymphoma/leukaemia refractory	Leukaemic lymphoma	Follicular lymphoma stage IV
Precursor T-lymphoblastic lymphoma/leukaemia stage I	Lymphoma	Follicular lymphoma stage III
Precursor T-lymphoblastic lymphoma/leukaemia stage II	Non-Hodgkin's lymphoma stage I	Lineage switch leukaemia
Precursor T-lymphoblastic lymphoma/leukaemia stage III	Non-Hodgkin's lymphoma stage II	Cutaneous B-cell lymphoma
Precursor T-lymphoblastic lymphoma/leukaemia stage IV	Non-Hodgkin's lymphoma stage III	B-cell lymphoma unclassifiable
High grade B-cell lymphoma Burkitt-like lymphoma refractory	Non-Hodgkin's lymphoma stage IV	Malignant unclassifiable lymphoma
High grade B-cell lymphoma Burkitt-like lymphoma stage I	Waldenstrom's macroglobulinaemia	Malignant lymphoid neoplasm
High grade B-cell lymphoma Burkitt-like lymphoma stage II	T-cell lymphoma unclassifiable	

Supplementary Table 2. Examples of the inference of second primary malignancies (SPMs) using “acute myeloid leukemia” as an adverse reaction.

Reported reaction	Corresponding indications
Acute myeloid leukaemia	Acute myeloid leukaemia
Acute myeloid leukaemia	Acute promyelocytic leukaemia
Acute myeloid leukaemia	Myeloid leukaemia
Acute myeloid leukaemia	Acute myelomonocytic leukaemia
Acute myeloid leukaemia	Acute myeloid leukaemia refractory
Acute myeloid leukaemia	Acute leukaemia

Supplementary Table 3. Contingency table for adverse drug reaction association risk.

2x2 contingency table for investigating associations between BiTEs and the target adverse events in patients with hematological malignancies.

Exposure	Adverse events	Target adverse events	Other adverse events
With BiTEs		a	b
Without BiTEs		c	d

a represents the number of cases of the target AE following BiTE treatment; b represents the number of cases of other AEs following BiTE treatment; c represents the number of cases of the target AE following non-BiTE treatments; and d represents the number of cases of other AEs following non-BiTE treatments.

Supplementary Table 4. Contingency table for fatality risk.

2x2 contingency table for investigating association between target adverse events and fatal outcomes in patients following BiTE treatment.

Outcome	Adverse events	Target adverse events	Other adverse events
Death outcome		a	b
Non-death outcome		c	d

a represents the number of fatal reports for the target AE following BiTE treatment; b represents the number of fatal reports for other AEs following BiTE treatment; c represents the number of non-fatal reports for the target AE following BiTE treatment; and d represents the number of non-fatal reports for other AEs following BiTE treatment.

Supplementary Table 5. The demographic characteristics and clinical information of the hematological malignancy patients with and without BiTE therapy in the FAERS database.

Clinical Characteristics	With BiTEs (N = 9350)	Without BiTEs (N = 773488)	Total (N = 782838)	P Value
Sex (%)				
Male	4188 (55.04)	378757 (54.17)	382945 (54.18)	<0.001
Female	3421 (44.96)	320456 (45.83)	323877 (45.82)	
Missing	1741	74275	76016	
Age (year)				
Mean (SD)	52.8 (23.16)	64.8 (17.29)	64.6 (17.43)	<0.001
Missing	3015	296101	299116	
Age Group (%)				
< 18	761 (12.01)	17372 (3.64)	18133 (3.75)	<0.001
18-44	1147 (18.11)	32414 (6.79)	33561 (6.94)	
45-64	1907 (30.10)	134271 (28.13)	136178 (28.15)	
>= 65	2520 (39.78)	293330 (61.44)	295850 (61.16)	
Missing	3015	296101	299116	
Country (%)				
United States	3741 (40.01)	507600 (65.62)	511341 (65.32)	<0.001
Japan	1087 (11.63)	30450 (3.94)	31537 (4.03)	
France	641 (6.86)	28530 (3.69)	29171 (3.73)	
Canada	135 (1.44)	24026 (3.11)	24161 (3.09)	
Germany	183 (1.96)	17637 (2.28)	17820 (2.28)	
China	703 (7.52)	17063 (2.21)	17766 (2.27)	
United Kingdom	210 (2.25)	15601 (2.02)	15811 (2.02)	
Italy	261 (2.79)	14825 (1.92)	15086 (1.93)	
Spain	224 (2.40)	10010 (1.29)	10234 (1.31)	
Australia	176 (1.88)	8643 (1.12)	8819 (1.13)	
Country Not Specified	0 (0.00)	15583 (2.01)	15583 (1.99)	
Others	1989 (21.27)	83519 (10.80)	85508 (10.92)	
Received Year (%)				
2015	181 (1.94)	58363 (7.55)	58544 (7.48)	<0.001
2016	301 (3.22)	51509 (6.66)	51810 (6.62)	
2017	399 (4.27)	59794 (7.73)	60193 (7.69)	
2018	336 (3.59)	64671 (8.36)	65007 (8.30)	
2019	338 (3.61)	72118 (9.32)	72456 (9.26)	
2020	463 (4.95)	81407 (10.53)	81870 (10.46)	
2021	601 (6.43)	100937 (13.05)	101538 (12.97)	
2022	621 (6.64)	87947 (11.37)	88568 (11.31)	
2023	1993 (21.32)	70713 (9.14)	72706 (9.29)	
2024	1995 (21.34)	74184 (9.59)	76179 (9.73)	
2025 Q1-Q3	2122 (22.69)	51845 (6.70)	53967 (6.89)	
Fatal Outcome (%)[†]				

Fatal	2180 (23.32)	124084 (16.04)	126264 (16.13)	<0.001
Non-fatal	7170 (76.68)	649404 (83.96)	656574 (83.87)	
Indication (%)				
Lymphoma	1832 (19.42)	134913 (17.67)	136745 (17.69)	<0.001
Leukemia	4582 (49.12)	228352 (29.91)	232934 (30.14)	
Myeloma	2935 (31.46)	400265 (52.42)	403200 (52.17)	
Unspecified ¹	1	9958	9959	

1. This category includes reports where the Indication cannot be clearly classified into lymphoma, leukemia, or myeloma.

Supplementary Table 6. The demographic characteristics and clinical information of the hematological malignancy patients with and without BiTE therapy in the VigiBase database.

Clinical Characteristics	With BiTEs (N = 9578)	Without BiTEs (N = 731870)	Total (N = 741448)	P Value
Sex (%)				
Male	4579 (54.86)	367186 (53.37)	371765 (53.38)	<0.001
Female	3767 (45.14)	320877 (46.63)	324644 (46.62)	
Missing	1232	43807	45039	
Age Group (%)				
< 18	400 (5.80)	12057 (2.55)	12457 (2.59)	<0.001
18-44	895 (12.99)	36773 (7.77)	37668 (7.84)	
45-64	2219 (32.20)	140823 (29.75)	143042 (29.78)	
>=65	3378 (49.01)	283707 (59.93)	287085 (59.78)	
Missing	2686	258510	261196	
Region (%)				
African region	11 (0.11)	975 (0.13)	986 (0.13)	<0.001
Eastern Mediterranean region	23 (0.24)	5115 (0.70)	5138 (0.69)	
European region	4169 (43.53)	88005 (12.03)	92174 (12.43)	
Region of the Americas	4466 (46.63)	526533 (71.94)	530999 (71.62)	
South-East Asia region	20 (0.21)	18565 (2.54)	18585 (2.51)	
Western Pacific region	889 (9.28)	92677 (12.66)	93566 (12.62)	
Received Year (%)				
2015	107 (7.55)	55870 (7.63)	55977 (7.55)	<0.001
2016	127 (6.41)	47365 (6.47)	47492 (6.41)	
2017	383 (8.30)	61122 (8.35)	61505 (8.30)	
2018	307 (8.33)	61472 (8.40)	61779 (8.33)	
2019	307 (10.55)	77911 (10.65)	78218 (10.55)	
2020	201 (8.37)	61874 (8.45)	62075 (8.37)	
2021	267 (12.31)	91036 (12.44)	91303 (12.31)	
2022	500 (9.94)	73210 (10.00)	73710 (9.94)	
2023	1556 (9.72)	70510 (9.63)	72066 (9.72)	
2024	2865 (12.34)	88631 (12.11)	91496 (12.34)	
2025 Jan-Oct	2958 (6.18)	42869 (5.86)	45827 (6.18)	
Fatal Outcome (%)				
Fatal	1086 (18.50)	69057 (17.68)	70143 (17.69)	0.106
Non-fatal	4783 (81.47)	321422 (82.30)	326205 (82.29)	
Died- Unrelated to Reaction	2 (0.03)	59 (0.02)	61 (0.02)	
Missing	3707	341332	345039	
Indication (%)				
Lymphoma	2433 (25.44)	136152 (18.85)	138585 (18.94)	<0.001
Leukemia	2920 (30.54)	198696 (27.51)	201616 (27.55)	
Myeloma	4210 (44.02)	387445 (53.64)	391655 (53.51)	
Unspecified ¹	15	9577	9592	

1. This category includes reports where the Indication cannot be clearly classified into lymphoma, leukemia, or myeloma.

Supplementary Table 7. Adjusted reporting odds ratios (aROR) for occurrence-based positive signals with limited cases (n ≤ 30) in FAERS and Vigibase.

PT	FAERS ¹		Vigibase ²	
	aROR (95% CI)	P value	aROR (95% CI)	P value
Injection Site Hypersensitivity	40.33 (8.14 - 199.71)	< 0.001	28.03 (5.62 - 139.71)	< 0.001
Xerosis ³	-	-	14.34 (5.13 - 40.08)	< 0.001
Injection Site Swelling	-	-	3.73 (1.59 - 8.74)	0.002
Hypothermia	4.43 (1.89 - 10.41)	< 0.001	-	-
Hyperthermia	2.35 (1.15 - 4.80)	0.019	4.53 (2.34 - 8.76)	< 0.001
Injection Site Rash	10.89 (4.77 - 24.87)	< 0.001	9.56 (5.37 - 17.04)	< 0.001
Injection Site Pruritus	4.32 (1.31 - 14.26)	0.016	7.07 (3.06 - 16.34)	< 0.001
Injection Site Pain	3.42 (1.58 - 7.40)	0.002	2.42 (1.43 - 4.10)	< 0.001
Injection Site Erythema	6.87 (3.90 - 12.11)	< 0.001	8.10 (5.63 - 11.66)	< 0.001
Injection Site Haemorrhage	31.67 (16.72 - 59.97)	< 0.001	9.43 (3.16 - 28.16)	< 0.001
Hyperpyrexia	4.03 (2.64 - 6.16)	< 0.001	8.80 (4.03 - 19.20)	< 0.001
Engraftment Syndrome	3.36 (1.00 - 11.23)	0.049	-	-
Cytokine Storm	3.08 (1.22 - 7.73)	0.017	5.36 (2.09 - 13.74)	< 0.001
Dysaesthesia	-	-	8.71 (3.91 - 19.40)	< 0.001
Hypotonia	2.66 (0.96 - 7.37)	0.061	5.58 (1.66 - 18.79)	0.006
Slow Response to Stimuli	20.11 (5.10 - 79.23)	< 0.001	22.74 (4.82 - 107.29)	< 0.001
Vlth Nerve Paralysis	5.50 (1.91 - 15.82)	0.002	9.00 (2.53 - 31.99)	< 0.001
Neurological Decompensation	1.07 (0.34 - 3.41)	0.905	6.43 (2.48 - 16.69)	< 0.001
Myoclonus	7.03 (2.94 - 16.81)	< 0.001	5.06 (1.78 - 14.39)	0.002
Anosmia	4.26 (1.95 - 9.29)	< 0.001	7.21 (3.90 - 13.31)	< 0.001
Apraxia	8.57 (3.71 - 19.80)	< 0.001	22.52 (8.23 - 61.67)	< 0.001
Motor Dysfunction	2.78 (1.40 - 5.52)	0.004	4.76 (2.16 - 10.52)	< 0.001
Hemiparesis	1.85 (1.05 - 3.24)	0.033	2.54 (1.24 - 5.20)	0.011
Unresponsive to Stimuli	3.81 (2.19 - 6.63)	< 0.001	4.17 (2.23 - 7.80)	< 0.001
Status Epilepticus	4.36 (2.60 - 7.31)	< 0.001	7.85 (4.19 - 14.69)	< 0.001
Haemorrhage Intracranial	1.99 (1.13 - 3.49)	0.017	3.35 (1.70 - 6.59)	< 0.001
Facial Paralysis	1.59 (0.89 - 2.85)	0.119	1.11 (0.46 - 2.71)	0.816
Ataxia	5.52 (3.46 - 8.79)	< 0.001	8.05 (4.69 - 13.81)	< 0.001
Dysgraphia	8.97 (5.35 - 15.05)	< 0.001	8.03 (4.62 - 13.95)	< 0.001
Speech Disorder	2.84 (1.84 - 4.38)	< 0.001	2.09 (1.19 - 3.67)	0.01
Encephalitis	1.48 (0.69 - 3.15)	0.315	2.75 (1.20 - 6.32)	0.017
Encephalitis Viral	-	-	6.14 (1.78 - 21.18)	0.004
Ophthalmic Herpes Zoster	4.73 (1.43 - 15.68)	0.011	9.34 (2.69 - 32.42)	< 0.001
Parvovirus Infection	9.70 (2.65 - 35.60)	< 0.001	24.97 (7.44 - 83.84)	< 0.001
Empyema	2.63 (0.81 - 8.50)	0.107	-	-
Toxoplasmosis	-	-	-	-
Gastroenteritis Salmonella	7.72 (2.95 - 20.16)	< 0.001	9.05 (3.30 - 24.85)	< 0.001
Enterococcal Bacteraemia	1.78 (0.72 - 4.40)	0.209	5.02 (2.29 - 11.04)	< 0.001

Enterovirus Infection	1.02 (0.32 - 3.26)	0.968	3.40 (1.21 - 9.58)	0.02
Intervertebral Discitis	4.35 (1.73 - 10.93)	0.002	-	-
Pneumonia Klebsiella	1.48 (0.60 - 3.63)	0.393	4.54 (1.95 - 10.60)	< 0.001
Respiratory Tract Infection Viral	1.42 (0.52 - 3.88)	0.496	2.45 (0.75 - 8.03)	0.138
Campylobacter Gastroenteritis	6.65 (2.98 - 14.83)	< 0.001	16.79 (6.41 - 43.97)	< 0.001
Device Related Sepsis	3.06 (1.33 - 7.08)	0.009	7.54 (3.35 - 16.98)	< 0.001
Haemophilus Infection	4.91 (2.08 - 11.58)	< 0.001	14.05 (5.81 - 34.01)	< 0.001
Human Herpesvirus 6 Encephalitis	3.14 (0.96 - 10.32)	0.059	5.30 (1.58 - 17.80)	0.007
Pseudomonal Bacteraemia	-	-	-	-
Superinfection Bacterial	3.26 (0.99 - 10.74)	0.052	-	-
Klebsiella Sepsis	1.61 (0.71 - 3.67)	0.257	3.71 (1.48 - 9.32)	0.005
Viral Upper Respiratory Tract Infection	3.47 (1.67 - 7.23)	< 0.001	3.63 (1.73 - 7.62)	< 0.001
Escherichia Urinary Tract Infection	2.86 (1.45 - 5.64)	0.002	6.91 (3.70 - 12.88)	< 0.001
Meningitis Aseptic	3.74 (1.79 - 7.81)	< 0.001	8.77 (3.34 - 23.03)	< 0.001
Pneumonia Pseudomonal	2.51 (1.02 - 6.22)	0.046	4.36 (1.72 - 11.03)	0.002
Klebsiella Bacteraemia	2.66 (1.29 - 5.50)	0.008	4.62 (1.82 - 11.76)	0.001
Vascular Device Infection	2.31 (1.07 - 4.99)	0.032	1.78 (0.65 - 4.87)	0.262
Cytomegalovirus Colitis	2.40 (1.11 - 5.15)	0.025	8.22 (4.26 - 15.86)	< 0.001
Bacterial Sepsis	1.50 (0.77 - 2.94)	0.236	2.79 (1.29 - 6.02)	0.009
BK Virus Infection	1.55 (0.68 - 3.54)	0.302	-	-
Cytomegalovirus Chorioretinitis	1.65 (0.85 - 3.23)	0.142	2.51 (1.22 - 5.18)	0.013
Escherichia Bacteraemia	1.71 (0.96 - 3.06)	0.07	4.74 (2.66 - 8.47)	< 0.001
Parainfluenzae Virus Infection	2.13 (1.08 - 4.18)	0.029	4.33 (2.35 - 7.98)	< 0.001
Pneumonia Viral	3.68 (2.08 - 6.51)	< 0.001	6.77 (3.80 - 12.07)	< 0.001
Salmonellosis	7.52 (3.54 - 15.98)	< 0.001	4.58 (2.00 - 10.48)	< 0.001
Escherichia Infection	0.79 (0.37 - 1.68)	0.543	2.08 (1.09 - 3.95)	0.025
Adenovirus Infection	1.81 (0.91 - 3.58)	0.091	2.12 (0.85 - 5.25)	0.106
Pseudomonal Sepsis	2.96 (1.66 - 5.25)	< 0.001	7.71 (3.99 - 14.89)	< 0.001
Urosepsis	2.74 (1.52 - 4.93)	< 0.001	4.76 (2.44 - 9.27)	< 0.001
Respiratory Syncytial Virus Infection	0.74 (0.35 - 1.56)	0.422	1.16 (0.65 - 2.08)	0.614
Pneumonia Cytomegaloviral	4.90 (2.83 - 8.48)	< 0.001	1.79 (0.56 - 5.74)	0.325
Rhinovirus Infection	1.28 (0.72 - 2.30)	0.403	4.65 (2.93 - 7.39)	< 0.001
Bronchopulmonary Aspergillosis	0.96 (0.60 - 1.54)	0.875	2.59 (1.63 - 4.12)	< 0.001
Pneumonia Fungal	1.33 (0.83 - 2.14)	0.237	1.55 (0.82 - 2.91)	0.177
Uveitis	3.78 (1.91 - 7.50)	< 0.001	-	-
Muscle Twitching	3.93 (1.81 - 8.56)	< 0.001	4.02 (1.72 - 9.39)	0.001
Cardiogenic Shock	1.73 (0.88 - 3.40)	0.109	2.42 (1.06 - 5.53)	0.037
Myocarditis	1.03 (0.46 - 2.33)	0.941	0.99 (0.31 - 3.11)	0.983
Sinus Tachycardia	1.83 (1.00 - 3.37)	0.052	4.04 (2.32 - 7.01)	< 0.001
Tachycardia	1.54 (1.14 - 2.07)	0.005	1.63 (1.23 - 2.14)	< 0.001
Hepatobiliary Disease	7.66 (2.51 - 23.35)	< 0.001	19.33 (4.97 - 75.15)	< 0.001
Cholestasis	1.14 (0.62 - 2.08)	0.676	2.66 (1.29 - 5.45)	0.008
Hepatic Cytolysis	1.98 (1.21 - 3.24)	0.006	2.10 (1.17 - 3.77)	0.012

Hypertransaminasaemia	2.92 (1.86 - 4.59)	< 0.001	5.01 (3.22 - 7.78)	< 0.001
Mental Disorder	1.89 (1.00 - 3.58)	0.05	1.95 (0.96 - 3.99)	0.066
Shock Haemorrhagic	2.69 (1.31 - 5.55)	0.007	6.38 (2.86 - 14.22)	< 0.001
Capillary Leak Syndrome	2.62 (1.32 - 5.20)	0.006	2.66 (1.08 - 6.60)	0.034
Tumour Pain	-	-	-	-
Tumour Pseudoprogression	2.00 (0.62 - 6.48)	0.247	-	-
Bone Marrow Leukaemic Cell Infiltration	22.51 (8.30 - 61.06)	< 0.001	-	-
Onycholysis	24.06 (8.16 - 70.99)	< 0.001	52.95 (24.73 - 113.37)	< 0.001
Nail Discolouration	3.83 (1.53 - 9.57)	0.004	4.02 (2.24 - 7.22)	< 0.001
Nail Toxicity	-	-	48.87 (7.55 - 316.42)	< 0.001
Nail Dystrophy	50.76 (14.39 - 179.12)	< 0.001	66.19 (26.28 - 166.73)	< 0.001
Skin Toxicity	-	-	3.04 (1.47 - 6.29)	0.003
Onychomadesis	24.54 (13.14 - 45.80)	< 0.001	46.68 (27.45 - 79.37)	< 0.001
Acidosis	1.70 (0.62 - 4.70)	0.303	2.44 (0.88 - 6.72)	0.086
Hypovolaemia	3.17 (1.27 - 7.91)	0.013	5.16 (1.81 - 14.70)	0.002
Cachexia	3.15 (1.26 - 7.89)	0.014	2.59 (1.05 - 6.42)	0.039
Hyperphosphataemia	2.47 (1.25 - 4.87)	0.009	7.30 (3.70 - 14.42)	< 0.001
Hypomagnesaemia	2.52 (1.46 - 4.33)	< 0.001	3.92 (2.21 - 6.97)	< 0.001
Hypoalbuminaemia	1.02 (0.57 - 1.81)	0.957	2.78 (1.46 - 5.28)	0.002
Hypophosphataemia	2.35 (1.34 - 4.12)	0.003	7.30 (4.27 - 12.48)	< 0.001
Hypercalcaemia	2.17 (1.36 - 3.45)	0.001	3.60 (2.26 - 5.74)	< 0.001
Apnoea	2.13 (0.66 - 6.88)	0.208	6.88 (2.36 - 20.05)	< 0.001
Lung Opacity	1.93 (0.78 - 4.76)	0.154	2.75 (0.84 - 8.98)	0.093
Organising Pneumonia	1.90 (1.01 - 3.59)	0.047	2.73 (1.39 - 5.38)	0.004
Acute Respiratory Failure	1.31 (0.85 - 2.04)	0.222	1.46 (0.85 - 2.49)	0.171
Glossitis	-	-	-	-
Enterocolitis	1.14 (0.54 - 2.43)	0.729	2.25 (1.05 - 4.85)	0.037
Ascites	1.26 (0.77 - 2.08)	0.362	2.18 (1.25 - 3.81)	0.006
Monocytosis	16.75 (7.36 - 38.10)	< 0.001	17.97 (7.84 - 41.21)	< 0.001
Eosinophilia	2.36 (1.25 - 4.48)	0.008	3.07 (1.49 - 6.33)	0.002
Lymphopenia	1.18 (0.72 - 1.95)	0.512	4.66 (3.30 - 6.59)	< 0.001
Body Temperature Abnormal	5.40 (1.91 - 15.27)	0.001	4.22 (1.50 - 11.91)	0.007
Human Rhinovirus Test Positive	3.34 (1.00 - 11.17)	0.05	8.10 (2.22 - 29.49)	0.002
Staphylococcus Test Positive	-	-	4.24 (1.29 - 13.95)	0.018
Blood Fibrinogen Increased	11.79 (4.26 - 32.62)	< 0.001	13.09 (3.65 - 46.90)	< 0.001
Procalcitonin Increased	2.97 (1.28 - 6.86)	0.011	8.71 (3.30 - 22.99)	< 0.001
Blood Culture Positive	5.18 (2.33 - 11.53)	< 0.001	12.49 (5.37 - 29.04)	< 0.001
Blood Fibrinogen Decreased	1.05 (0.38 - 2.86)	0.927	5.01 (1.96 - 12.81)	< 0.001
Blood Lactic Acid Increased	3.50 (1.60 - 7.69)	0.002	3.10 (0.95 - 10.10)	0.06
Interleukin Level Increased	7.92 (3.62 - 17.34)	< 0.001	9.37 (3.35 - 26.21)	< 0.001
Blood Immunoglobulin G Decreased	2.07 (1.02 - 4.22)	0.045	5.65 (2.88 - 11.06)	< 0.001
Immunoglobulins Decreased	5.76 (3.05 - 10.91)	< 0.001	5.92 (3.05 - 11.49)	< 0.001
Body Temperature Increased	2.21 (1.29 - 3.79)	0.004	2.70 (1.62 - 4.51)	< 0.001

Blood Alkaline Phosphatase Increased	2.60 (1.63 - 4.14)	< 0.001	4.92 (3.19 - 7.59)	< 0.001
Serum Ferritin Increased	2.51 (1.48 - 4.26)	< 0.001	2.95 (1.60 - 5.44)	< 0.001
Liver Function Test Increased	2.45 (1.52 - 3.95)	< 0.001	2.30 (1.39 - 3.82)	0.001
Muscular Weakness	1.58 (1.15 - 2.17)	0.005	1.59 (1.12 - 2.26)	0.01
Minimal Residual Disease	4.87 (3.08 - 7.69)	< 0.001	3.72 (1.77 - 7.81)	< 0.001
Gamma-Glutamyltransferase Increased	1.43 (0.85 - 2.41)	0.174	3.25 (1.88 - 5.61)	< 0.001
Acute Respiratory Distress Syndrome	0.79 (0.45 - 1.38)	0.408	1.27 (0.65 - 2.46)	0.487
Gene Mutation	0.70 (0.22 - 2.19)	0.535	-	-
Generalised Tonic-Clonic Seizure	3.05 (1.84 - 5.06)	< 0.001	3.78 (1.82 - 7.84)	< 0.001
Guillain-Barre Syndrome	1.43 (0.63 - 3.23)	0.394	2.92 (1.26 - 6.78)	0.013
B-Cell Aplasia	3.37 (1.43 - 7.90)	0.005	-	-

1. In FAERS, aROR was adjusted for sex, age, reporting year, fatal outcome, and indication.
2. In Vigibase, aROR was adjusted for sex, age, reporting year, and indication.
3. The symbol “-” indicates that the number of cases was fewer than 3 after excluding reports with missing covariates.

Supplementary Table 8. BiTE-related adverse events with positive signals detected in a single database (FAERS or VigiBase).

PT	FAERS		VigiBase	
	ROR	95%CI	ROR	95%CI
Abdominal mass	3.52	1.56 - 7.97	3.06	0.96 - 9.70
Amylase increased	2.31	1.09 - 4.89	1.04	0.33 - 3.26
Bacterial infection	1.63	1.14 - 2.32	1.54	0.95 - 2.50
Blood pressure decreased	1.66	1.15 - 2.38	0.90	0.54 - 1.50
Bradyphrenia	3.31	1.22 - 8.99	2.73	0.86 - 8.64
Cardio-respiratory arrest	1.77	1.11 - 2.82	1.43	0.71 - 2.87
Cerebral haemorrhage	1.87	1.33 - 2.62	1.55	0.99 - 2.41
Chills	1.71	1.41 - 2.08	1.13	0.93 - 1.36
Coagulopathy	2.07	1.24 - 3.46	1.95	0.97 - 3.93
Cognitive disorder	1.94	1.36 - 2.75	1.32	0.84 - 2.08
Coordination abnormal	3.80	1.55 - 9.31	2.08	0.66 - 6.56
Coronavirus infection	2.06	1.27 - 3.33	0.72	0.30 - 1.74
Cytomegalovirus test positive	6.05	3.44 - 10.63	2.27	0.93 - 5.54
Cytomegalovirus viraemia	3.87	2.59 - 5.79	1.58	0.70 - 3.55
Dyskinesia	2.79	1.44 - 5.42	2.02	0.90 - 4.55
Epilepsy	3.19	1.99 - 5.10	1.63	0.61 - 4.40
Gastrointestinal infection	2.03	1.20 - 3.46	1.47	0.70 - 3.11
Hallucination	2.84	1.90 - 4.23	1.14	0.63 - 2.07
Hepatic function abnormal	2.83	2.14 - 3.74	0.66	0.33 - 1.32
Injection site bruising	4.36	1.77 - 10.71	2.18	0.69 - 6.88
Intracranial pressure increased	3.24	1.52 - 6.89	2.80	0.88 - 8.85
Leukoencephalopathy	2.25	1.35 - 3.77	1.59	0.71 - 3.57
Liver injury	2.28	1.41 - 3.70	1.18	0.44 - 3.17
Lymphocyte count decreased	1.57	1.11 - 2.23	1.38	0.92 - 2.07
Neutrophil count decreased	1.39	1.16 - 1.66	0.95	0.78 - 1.17
Oxygen saturation decreased	1.71	1.21 - 2.43	1.39	0.93 - 2.09
Papilloedema	4.39	2.15 - 8.93	2.49	0.79 - 7.87
Peroneal nerve palsy	2.94	1.30 - 6.63	2.68	0.99 - 7.27
Philadelphia chromosome positive	1.89	1.01 - 3.54	1.14	0.42 - 3.06
Pneumonia bacterial	2.77	1.89 - 4.07	1.71	0.96 - 3.02
Pneumonia influenzal	2.41	1.19 - 4.86	2.07	0.85 - 5.02
Post-acute COVID-19 syndrome	3.18	1.41 - 7.20	3.14	0.99 - 9.97
Pulmonary haemorrhage	2.05	1.12 - 3.72	1.24	0.46 - 3.32
Pyelonephritis	2.47	1.16 - 5.23	2.37	0.88 - 6.41
Soft tissue infection	2.55	1.20 - 5.42	1.85	0.59 - 5.81
Somnolence	1.37	1.06 - 1.78	0.80	0.58 - 1.09
Systemic mycosis	4.84	2.47 - 9.48	2.76	0.87 - 8.74
T-cell lymphoma	6.80	2.96 - 15.64	2.44	0.77 - 7.70
Abdominal infection	1.95	0.62 - 6.14	4.63	1.69 - 12.71

Acute kidney injury	0.96	0.77 - 1.19	1.33	1.07 - 1.65
Acute lymphocytic leukaemia	0.57	0.21 - 1.51	3.45	2.33 - 5.11
Acute pulmonary oedema	1.70	0.80 - 3.59	3.34	1.57 - 7.13
Anaemia	0.98	0.85 - 1.14	1.31	1.15 - 1.49
Arthritis bacterial	1.62	0.60 - 4.37	3.24	1.32 - 7.93
Aspergillus infection	0.83	0.47 - 1.47	2.13	1.23 - 3.69
Blood creatinine increased	1.10	0.79 - 1.52	1.37	1.01 - 1.86
Bone pain	0.99	0.74 - 1.32	1.32	1.03 - 1.70
Campylobacter infection	2.32	0.74 - 7.31	9.80	3.86 - 24.87
Candida infection	0.94	0.53 - 1.66	1.90	1.19 - 3.04
Catheter site infection	1.59	0.51 - 4.99	3.03	1.11 - 8.22
Cerebellar syndrome	2.59	0.96 - 7.00	5.27	1.91 - 14.52
Clostridium difficile colitis	1.17	0.74 - 1.84	1.77	1.18 - 2.65
Colitis	1.15	0.81 - 1.64	1.75	1.27 - 2.42
Conjunctivitis	1.16	0.55 - 2.45	2.03	1.11 - 3.69
Decreased immune responsiveness	1.55	0.77 - 3.13	3.23	1.85 - 5.63
Dry skin	1.08	0.80 - 1.44	2.23	1.82 - 2.72
Dysphagia	1.26	0.90 - 1.76	1.83	1.37 - 2.46
Eczema	1.25	0.59 - 2.63	2.16	1.22 - 3.83
End stage renal disease	1.50	0.56 - 4.03	2.85	1.26 - 6.44
Enterococcal infection	1.63	0.84 - 3.16	2.26	1.06 - 4.79
Epstein-Barr virus infection	1.56	0.74 - 3.29	3.29	1.35 - 8.07
Escherichia sepsis	1.70	0.94 - 3.10	2.92	1.50 - 5.68
Febrile bone marrow aplasia	0.18	0.06 - 0.55	2.30	1.02 - 5.19
Febrile neutropenia	1.00	0.87 - 1.15	1.65	1.45 - 1.88
Fungaemia	2.18	0.90 - 5.29	3.61	1.59 - 8.19
Hepatic lesion	2.07	0.66 - 6.51	3.77	1.38 - 10.30
Hepatitis E	1.18	0.38 - 3.69	7.14	3.29 - 15.49
Hepatocellular injury	0.89	0.44 - 1.79	3.89	1.22 - 12.40
Human herpesvirus 6 infection	1.81	0.81 - 4.07	3.64	1.33 - 9.93
Hydronephrosis	1.42	0.53 - 3.82	3.64	1.48 - 8.93
Hyperbilirubinaemia	1.25	0.74 - 2.12	1.85	1.07 - 3.22
Hyperuricaemia	1.34	0.67 - 2.70	2.07	1.02 - 4.17
Hyponatraemia	1.23	0.84 - 1.80	1.75	1.21 - 2.52
Inflammation	1.23	0.74 - 2.05	1.85	1.16 - 2.96
Influenza like illness	0.73	0.39 - 1.37	1.62	1.07 - 2.45
Listeriosis	2.14	0.68 - 6.73	4.33	1.35 - 13.85
Liver function test abnormal	1.40	0.75 - 2.63	1.91	1.12 - 3.24
Lower gastrointestinal haemorrhage	1.22	0.39 - 3.80	2.96	1.21 - 7.24
Lower respiratory tract infection	0.89	0.53 - 1.47	2.61	1.81 - 3.79
Lung infiltration	1.54	0.79 - 2.97	3.01	1.69 - 5.36
Malnutrition	1.00	0.45 - 2.23	3.13	1.71 - 5.72
Mucosal inflammation	0.81	0.56 - 1.17	1.51	1.06 - 2.15

Neutropenic infection	1.44	0.54 - 3.87	5.10	2.23 - 11.65
Non-cardiac chest pain	1.92	0.79 - 4.65	3.34	1.65 - 6.79
Oesophageal candidiasis	2.01	0.95 - 4.26	4.54	1.99 - 10.35
Onychoclasia	1.16	0.62 - 2.17	2.75	1.85 - 4.11
Oral candidiasis	1.07	0.48 - 2.40	3.04	1.78 - 5.19
Palmar-plantar erythrodysaesthesia syndrome	1.01	0.45 - 2.25	3.66	2.36 - 5.67
Peripheral sensory neuropathy	1.31	0.77 - 2.22	2.80	1.93 - 4.06
Pneumocystis jirovecii infection	1.43	0.46 - 4.49	7.64	3.05 - 19.17
Pneumonia aspiration	1.22	0.67 - 2.20	1.90	1.07 - 3.37
Rash maculo-papular	1.52	0.95 - 2.42	1.84	1.27 - 2.68
Respiratory tract infection	1.24	0.86 - 1.80	3.67	2.82 - 4.78
Secondary immunodeficiency	1.52	0.72 - 3.22	6.55	2.85 - 15.09
Spinal cord compression	1.90	0.85 - 4.27	2.89	1.36 - 6.15
Staphylococcal bacteraemia	1.75	0.99 - 3.10	3.75	2.15 - 6.55
Staphylococcal sepsis	1.66	0.89 - 3.11	2.23	1.05 - 4.73
Subarachnoid haemorrhage	1.57	0.70 - 3.52	2.27	1.01 - 5.12
Systemic candida	1.72	0.85 - 3.46	3.39	1.59 - 7.22
Tachypnoea	1.68	0.90 - 3.15	3.16	1.78 - 5.64
Taste disorder	1.21	0.81 - 1.79	1.88	1.36 - 2.59
Thrombocytopenia	1.12	0.98 - 1.29	1.26	1.10 - 1.44
Thrombotic microangiopathy	1.67	0.96 - 2.89	2.10	1.19 - 3.74
Tonsillitis	2.51	0.93 - 6.78	3.18	1.17 - 8.66
Toxic skin eruption	1.14	0.51 - 2.55	2.72	1.34 - 5.50
Tubulointerstitial nephritis	1.35	0.50 - 3.63	2.85	1.26 - 6.44
Upper respiratory tract infection	1.10	0.79 - 1.52	2.15	1.69 - 2.73
Ventricular tachycardia	1.57	0.78 - 3.17	2.23	1.15 - 4.34
Weight decreased	0.92	0.76 - 1.12	1.23	1.03 - 1.46

Supplementary Table 9. BiTE-related adverse events showing no significant signals in either database (FAERS or VigiBase).

PT	FAERS		VigiBase	
	ROR	95% CI	ROR	95% CI
Abdominal discomfort	0.10	0.05 - 0.23	0.12	0.06 - 0.24
Abdominal distension	0.28	0.15 - 0.55	0.25	0.13 - 0.50
Abdominal pain	0.80	0.61 - 1.04	0.66	0.50 - 0.88
Abdominal pain upper	0.20	0.12 - 0.35	0.32	0.21 - 0.49
Acute hepatic failure	1.26	0.62 - 2.53	0.99	0.32 - 3.10
Acute myocardial infarction	0.60	0.31 - 1.16	1.25	0.71 - 2.22
Aggression	2.21	0.98 - 4.97	1.41	0.45 - 4.41
Agitation	1.43	0.83 - 2.48	1.18	0.67 - 2.09
Agranulocytosis	0.62	0.32 - 1.20	0.83	0.34 - 2.00
Alopecia	0.39	0.24 - 0.61	0.49	0.34 - 0.72
Amnesia	0.74	0.44 - 1.26	0.58	0.32 - 1.05
Anal incontinence	1.58	0.65 - 3.83	1.64	0.68 - 3.98
Angioedema	0.83	0.31 - 2.23	0.48	0.15 - 1.49
Anxiety	0.55	0.36 - 0.82	0.51	0.34 - 0.76
Apathy	2.39	0.98 - 5.82	1.76	0.56 - 5.54
Aphthous ulcer	1.06	0.34 - 3.31	1.29	0.48 - 3.47
Aplastic anaemia	0.65	0.21 - 2.02	1.54	0.49 - 4.83
Appendicitis	0.72	0.27 - 1.92	1.05	0.39 - 2.83
Arrhythmia	0.49	0.26 - 0.92	0.67	0.36 - 1.25
Arthralgia	0.56	0.43 - 0.72	0.80	0.64 - 0.98
Arthritis	0.15	0.05 - 0.47	0.32	0.14 - 0.71
Asthenia	0.53	0.45 - 0.64	0.64	0.55 - 0.76
Asthma	0.36	0.13 - 0.95	1.32	0.76 - 2.29
Atrial fibrillation	0.53	0.41 - 0.69	0.61	0.47 - 0.80
Atrial flutter	0.46	0.17 - 1.23	0.60	0.22 - 1.59
Atrioventricular block	1.08	0.35 - 3.37	1.90	0.70 - 5.12
Back pain	0.44	0.33 - 0.58	0.66	0.52 - 0.83
Balance disorder	0.91	0.63 - 1.31	0.82	0.55 - 1.20
Blister	0.38	0.17 - 0.85	0.23	0.09 - 0.61
Blood calcium decreased	0.45	0.17 - 1.21	0.48	0.18 - 1.29
Blood calcium increased	0.65	0.24 - 1.75	0.51	0.16 - 1.59
Blood disorder	0.35	0.11 - 1.09	0.42	0.13 - 1.29
Blood glucose decreased	0.60	0.22 - 1.59	0.60	0.22 - 1.61
Blood glucose increased	0.44	0.25 - 0.78	0.49	0.29 - 0.85
Blood magnesium decreased	0.96	0.48 - 1.93	0.73	0.33 - 1.64
Blood potassium decreased	0.31	0.17 - 0.58	0.28	0.14 - 0.53
Blood pressure abnormal	0.38	0.14 - 1.00	0.66	0.31 - 1.39
Blood pressure increased	0.49	0.30 - 0.79	0.26	0.14 - 0.51
Blood sodium decreased	0.43	0.16 - 1.15	0.34	0.11 - 1.04

Blood urea increased	0.85	0.32 - 2.28	0.90	0.34 - 2.41
Blood uric acid increased	1.19	0.56 - 2.51	0.79	0.29 - 2.12
Bone lesion	0.98	0.44 - 2.19	0.91	0.38 - 2.21
Bone marrow failure	0.67	0.45 - 0.98	1.06	0.65 - 1.71
Bradycardia	1.10	0.62 - 1.94	0.91	0.47 - 1.75
Brain oedema	1.91	0.95 - 3.86	1.92	0.79 - 4.67
Bronchitis	0.39	0.24 - 0.63	0.94	0.69 - 1.28
Cardiac arrest	1.03	0.70 - 1.50	1.29	0.86 - 1.93
Cardiac disorder	0.14	0.07 - 0.28	0.21	0.12 - 0.38
Cardiac failure	0.90	0.68 - 1.20	0.82	0.59 - 1.16
Cardiac failure congestive	0.14	0.06 - 0.33	0.11	0.04 - 0.29
Cardiac tamponade	1.33	0.50 - 3.58	1.51	0.48 - 4.73
Cardiotoxicity	0.95	0.55 - 1.63	1.18	0.59 - 2.37
Cellulitis	0.81	0.56 - 1.15	0.88	0.61 - 1.28
Cerebral infarction	0.82	0.39 - 1.73	0.39	0.12 - 1.20
Cerebral ischaemia	1.99	0.82 - 4.83	2.34	0.74 - 7.38
Cerebrovascular accident	0.32	0.21 - 0.51	0.30	0.18 - 0.49
Chest discomfort	0.19	0.08 - 0.47	0.23	0.12 - 0.47
Chest pain	0.38	0.25 - 0.58	0.33	0.21 - 0.51
Cholecystitis	0.49	0.16 - 1.52	1.09	0.41 - 2.93
Cholelithiasis	0.95	0.49 - 1.83	0.79	0.35 - 1.77
Chronic kidney disease	0.41	0.17 - 0.99	0.39	0.15 - 1.05
Chronic myeloid leukaemia	0.11	0.04 - 0.35	0.35	0.11 - 1.09
Chronic obstructive pulmonary disease	0.50	0.26 - 0.96	0.69	0.38 - 1.26
Circulatory collapse	1.45	0.65 - 3.25	2.15	0.80 - 5.82
Clostridium difficile infection	0.67	0.40 - 1.12	1.08	0.70 - 1.67
Coma	1.15	0.57 - 2.30	0.97	0.36 - 2.59
Conjunctival haemorrhage	1.65	0.61 - 4.45	1.57	0.58 - 4.22
Constipation	0.19	0.14 - 0.27	0.30	0.23 - 0.38
Coronary artery disease	0.31	0.10 - 0.97	0.39	0.12 - 1.20
Cough	0.48	0.36 - 0.63	0.97	0.80 - 1.17
Cystitis	0.32	0.13 - 0.77	0.42	0.19 - 0.94
Cytopenia	1.26	1.00 - 1.60	0.80	0.57 - 1.12
Deafness	0.74	0.37 - 1.48	0.69	0.33 - 1.45
Decreased appetite	0.57	0.46 - 0.71	0.77	0.64 - 0.92
Deep vein thrombosis	0.39	0.25 - 0.59	0.41	0.27 - 0.62
Dehydration	0.38	0.27 - 0.54	0.35	0.24 - 0.51
Dementia	0.64	0.33 - 1.23	1.01	0.57 - 1.79
Depressed mood	0.59	0.27 - 1.33	0.66	0.30 - 1.48
Depression	0.47	0.29 - 0.75	0.70	0.47 - 1.04
Dermatitis	1.24	0.55 - 2.77	1.50	0.74 - 3.01
Dermatitis exfoliative generalised	0.90	0.29 - 2.82	1.64	0.61 - 4.43
Diabetes mellitus	0.14	0.04 - 0.43	0.16	0.05 - 0.49

Diarrhoea	0.26	0.22 - 0.30	0.41	0.36 - 0.47
Diplopia	1.34	0.66 - 2.69	1.34	0.64 - 2.84
Disturbance in attention	0.94	0.45 - 1.98	0.69	0.28 - 1.65
Diverticulitis	0.35	0.16 - 0.79	0.52	0.26 - 1.04
Dizziness	0.45	0.36 - 0.57	0.38	0.30 - 0.48
Drug reaction with eosinophilia and systemic symptoms	0.67	0.25 - 1.79	0.71	0.23 - 2.20
Drug-induced liver injury	1.55	0.89 - 2.68	1.66	0.78 - 3.50
Dyspepsia	0.21	0.10 - 0.45	0.19	0.09 - 0.38
Dysphonia	0.30	0.13 - 0.67	0.48	0.26 - 0.90
Dyspnoea	0.50	0.41 - 0.61	0.47	0.39 - 0.58
Dyspnoea exertional	0.46	0.21 - 1.02	0.74	0.38 - 1.42
Ear infection	0.53	0.22 - 1.27	0.32	0.10 - 1.00
Ear pain	0.69	0.26 - 1.86	1.05	0.47 - 2.35
Eating disorder	0.67	0.28 - 1.61	0.72	0.30 - 1.75
Ejection fraction decreased	0.58	0.26 - 1.30	0.86	0.38 - 1.92
Electrocardiogram QT prolonged	0.53	0.24 - 1.18	0.35	0.13 - 0.92
Embolism	1.16	0.58 - 2.34	1.57	0.81 - 3.03
Endocarditis	1.00	0.32 - 3.12	1.75	0.56 - 5.50
Epistaxis	0.60	0.39 - 0.91	0.67	0.44 - 1.01
Erythema	0.57	0.38 - 0.86	0.81	0.60 - 1.08
Eye disorder	0.31	0.12 - 0.84	0.31	0.12 - 0.82
Eye pain	1.04	0.49 - 2.19	1.36	0.70 - 2.62
Eyelid ptosis	2.36	0.87 - 6.39	2.64	0.83 - 8.33
Face oedema	1.11	0.50 - 2.49	0.40	0.13 - 1.23
Failure to thrive	1.54	0.69 - 3.45	0.73	0.24 - 2.29
Fatigue	0.33	0.28 - 0.38	0.42	0.37 - 0.48
Feeding disorder	1.18	0.61 - 2.28	1.73	0.98 - 3.07
Feeling abnormal	0.16	0.08 - 0.31	0.18	0.09 - 0.33
Feeling cold	0.65	0.27 - 1.58	0.73	0.33 - 1.64
Feeling hot	0.37	0.14 - 1.00	0.22	0.07 - 0.68
Fluid retention	0.13	0.05 - 0.35	0.10	0.03 - 0.30
Flushing	1.15	0.69 - 1.92	0.63	0.36 - 1.11
Full blood count abnormal	0.64	0.35 - 1.15	0.21	0.10 - 0.42
Full blood count decreased	0.18	0.11 - 0.28	0.04	0.01 - 0.10
Gait disturbance	1.09	0.81 - 1.46	1.00	0.74 - 1.37
Gait inability	0.57	0.27 - 1.19	0.35	0.14 - 0.83
Gastroenteritis	1.30	0.67 - 2.52	1.58	0.78 - 3.17
Gastrointestinal disorder	0.58	0.38 - 0.86	0.61	0.40 - 0.94
Gastrointestinal haemorrhage	0.82	0.54 - 1.26	0.80	0.50 - 1.29
Gastrointestinal pain	1.27	0.47 - 3.42	1.19	0.44 - 3.21
Gastrointestinal toxicity	0.57	0.24 - 1.38	0.93	0.38 - 2.24
Gastrooesophageal reflux disease	0.19	0.07 - 0.49	0.41	0.21 - 0.78
Glomerular filtration rate decreased	1.54	0.64 - 3.74	1.47	0.55 - 3.95

Haematemesis	1.47	0.76 - 2.85	1.11	0.46 - 2.68
Haematochezia	0.64	0.33 - 1.24	0.24	0.08 - 0.73
Haematoma	0.27	0.09 - 0.84	0.29	0.09 - 0.91
Haematotoxicity	0.89	0.58 - 1.37	1.13	0.67 - 1.92
Haematuria	0.70	0.36 - 1.34	1.01	0.56 - 1.84
Haemodynamic instability	1.31	0.42 - 4.11	2.47	0.78 - 7.79
Haemoglobin decreased	0.32	0.24 - 0.44	0.28	0.20 - 0.40
Haemorrhage	0.69	0.48 - 1.00	0.37	0.20 - 0.66
Haemorrhagic stroke	1.33	0.42 - 4.15	2.05	0.65 - 6.44
Heart rate increased	0.96	0.63 - 1.46	0.87	0.55 - 1.37
Hemiplegia	1.66	0.62 - 4.48	2.18	0.69 - 6.88
Hepatic cirrhosis	1.09	0.45 - 2.64	1.71	0.70 - 4.14
Hepatic failure	1.30	0.81 - 2.10	1.09	0.54 - 2.19
Hepatitis	0.91	0.45 - 1.82	0.68	0.22 - 2.11
Hepatitis acute	1.94	0.62 - 6.09	2.36	0.75 - 7.46
Hepatitis B	0.82	0.37 - 1.84	1.05	0.39 - 2.82
Hepatitis B reactivation	1.19	0.69 - 2.06	0.81	0.36 - 1.81
Hepatomegaly	1.44	0.64 - 3.23	1.84	0.76 - 4.46
Herpes simplex	1.75	0.90 - 3.38	2.00	0.82 - 4.86
Herpes virus infection	1.54	0.63 - 3.73	2.18	0.90 - 5.31
Herpes zoster	0.80	0.57 - 1.13	0.54	0.35 - 0.83
Hyperhidrosis	0.60	0.37 - 0.97	0.45	0.28 - 0.73
Hyperkalaemia	1.31	0.77 - 2.22	1.69	0.99 - 2.87
Hypersensitivity	0.21	0.11 - 0.39	0.21	0.12 - 0.38
Hypersomnia	0.68	0.32 - 1.43	0.56	0.25 - 1.24
Hypertension	0.74	0.56 - 0.97	0.82	0.63 - 1.07
Hypertriglyceridaemia	1.16	0.58 - 2.33	1.82	0.86 - 3.85
Hypervolaemia	1.51	0.62 - 3.66	1.53	0.82 - 2.86
Hypoacusis	0.46	0.24 - 0.88	0.57	0.33 - 0.99
Hypoaesthesia	0.61	0.44 - 0.83	0.39	0.27 - 0.58
Hypoaesthesia oral	1.63	0.81 - 3.28	1.69	0.84 - 3.40
Hypoglycaemia	1.40	0.72 - 2.71	1.17	0.52 - 2.62
Hypophagia	0.83	0.44 - 1.55	1.25	0.72 - 2.16
Ileus	1.39	0.74 - 2.59	1.21	0.54 - 2.70
Immunodeficiency	0.87	0.50 - 1.51	0.53	0.24 - 1.19
Immunosuppression	1.31	0.68 - 2.54	1.25	0.56 - 2.80
Inappropriate antidiuretic hormone secretion	0.74	0.24 - 2.31	1.25	0.40 - 3.92
Incoherent	1.77	0.56 - 5.56	2.08	0.66 - 6.56
Incontinence	1.26	0.52 - 3.04	1.05	0.39 - 2.82
Influenza	0.69	0.52 - 0.91	1.00	0.79 - 1.27
Insomnia	0.27	0.17 - 0.41	0.36	0.25 - 0.52
International normalised ratio increased	1.72	0.77 - 3.86	1.08	0.40 - 2.91
Interstitial lung disease	0.80	0.53 - 1.21	0.45	0.24 - 0.83

Intestinal obstruction	0.54	0.26 - 1.14	0.30	0.10 - 0.92
Intestinal perforation	1.02	0.46 - 2.28	1.54	0.69 - 3.47
Irritability	1.20	0.60 - 2.41	0.88	0.39 - 1.96
Jaundice	0.68	0.28 - 1.64	0.82	0.31 - 2.20
Joint swelling	0.13	0.06 - 0.29	0.22	0.12 - 0.40
Laboratory test abnormal	0.19	0.11 - 0.32	0.19	0.12 - 0.32
Large intestine perforation	0.94	0.35 - 2.53	1.51	0.62 - 3.66
Lethargy	1.16	0.74 - 1.82	1.09	0.67 - 1.76
Leukaemia	1.00	0.32 - 3.14	0.76	0.36 - 1.61
Leukocytosis	0.78	0.41 - 1.51	0.99	0.51 - 1.91
Leukopenia	1.04	0.79 - 1.37	0.66	0.51 - 0.87
Light chain analysis increased	0.87	0.39 - 1.94	1.63	0.89 - 2.96
Lipase increased	1.31	0.62 - 2.77	1.51	0.75 - 3.03
Liver disorder	1.18	0.78 - 1.78	0.70	0.39 - 1.27
Loss of consciousness	0.85	0.59 - 1.21	0.70	0.46 - 1.07
Lung disorder	1.02	0.68 - 1.52	1.50	0.99 - 2.26
Lung neoplasm malignant	0.46	0.17 - 1.22	0.63	0.24 - 1.70
Lymphadenopathy	0.54	0.34 - 0.86	0.76	0.48 - 1.21
Lymphoma	0.75	0.45 - 1.25	1.19	0.66 - 2.16
Malaise	0.67	0.54 - 0.83	0.48	0.37 - 0.62
Melaena	1.61	0.86 - 3.01	1.09	0.45 - 2.63
Memory impairment	0.62	0.43 - 0.89	0.67	0.47 - 0.94
Meningitis	1.03	0.38 - 2.76	1.48	0.55 - 3.97
Mental impairment	1.81	0.86 - 3.83	1.81	0.86 - 3.84
Metabolic acidosis	1.68	0.83 - 3.38	1.59	0.66 - 3.86
Metapneumovirus infection	2.00	0.64 - 6.29	2.52	0.80 - 7.96
Migraine	0.46	0.17 - 1.24	0.56	0.23 - 1.34
Mobility decreased	0.89	0.46 - 1.71	1.32	0.72 - 2.39
Mouth ulceration	0.58	0.24 - 1.40	0.52	0.21 - 1.24
Mucormycosis	1.13	0.47 - 2.73	1.95	0.80 - 4.74
Muscle atrophy	1.38	0.52 - 3.72	1.48	0.55 - 3.99
Muscle spasms	0.12	0.07 - 0.20	0.11	0.07 - 0.19
Musculoskeletal chest pain	0.74	0.35 - 1.55	0.76	0.36 - 1.60
Musculoskeletal disorder	0.53	0.20 - 1.42	0.43	0.14 - 1.33
Musculoskeletal pain	0.92	0.52 - 1.62	1.02	0.60 - 1.73
Musculoskeletal stiffness	0.34	0.14 - 0.81	0.39	0.18 - 0.88
Myalgia	0.81	0.60 - 1.10	0.54	0.38 - 0.75
Myelodysplastic syndrome	0.60	0.41 - 0.89	0.80	0.51 - 1.26
Myelosuppression	1.13	0.91 - 1.40	0.58	0.35 - 0.94
Myocardial infarction	0.24	0.13 - 0.42	0.22	0.11 - 0.41
Myocardial ischaemia	0.82	0.31 - 2.19	0.97	0.31 - 3.03
Nasal congestion	0.53	0.25 - 1.11	0.56	0.29 - 1.08
Nasopharyngitis	0.26	0.17 - 0.39	0.44	0.33 - 0.61

Nausea	0.40	0.33 - 0.47	0.44	0.38 - 0.52
Nephrolithiasis	0.46	0.22 - 0.96	0.29	0.11 - 0.78
Neuralgia	0.54	0.26 - 1.14	0.50	0.24 - 1.06
Neuropathy peripheral	0.54	0.44 - 0.65	0.35	0.28 - 0.44
Neutropenic colitis	0.83	0.34 - 2.00	1.21	0.45 - 3.26
Neutropenic sepsis	0.77	0.45 - 1.33	1.20	0.64 - 2.23
Neutrophil count abnormal	0.74	0.28 - 1.98	0.99	0.41 - 2.39
Night sweats	0.31	0.14 - 0.70	0.71	0.41 - 1.22
Ocular hyperaemia	0.52	0.20 - 1.39	0.75	0.35 - 1.57
Oedema	0.90	0.60 - 1.35	0.33	0.17 - 0.63
Oedema peripheral	0.41	0.27 - 0.61	0.57	0.41 - 0.80
Oral disorder	0.95	0.39 - 2.29	1.09	0.45 - 2.64
Oral herpes	0.73	0.30 - 1.77	0.63	0.20 - 1.96
Oral pain	0.51	0.23 - 1.14	0.91	0.50 - 1.64
Oropharyngeal pain	0.61	0.38 - 0.99	0.78	0.52 - 1.17
Osteomyelitis	1.02	0.51 - 2.05	0.72	0.30 - 1.75
Osteonecrosis	0.71	0.32 - 1.59	0.63	0.23 - 1.68
Pain	0.63	0.52 - 0.78	0.70	0.57 - 0.85
Pain in extremity	0.53	0.40 - 0.70	0.69	0.54 - 0.88
Pain in jaw	0.77	0.32 - 1.85	1.73	0.98 - 3.07
Pancreatitis	1.34	0.91 - 1.97	1.21	0.78 - 1.86
Pancreatitis acute	1.52	0.88 - 2.64	0.74	0.31 - 1.78
Pancytopenia	1.08	0.89 - 1.32	1.03	0.83 - 1.29
Paraesthesia	0.61	0.43 - 0.86	0.54	0.38 - 0.75
Pericardial effusion	0.78	0.49 - 1.27	0.64	0.36 - 1.12
Pericarditis	0.79	0.33 - 1.90	0.63	0.20 - 1.96
Peripheral swelling	0.09	0.05 - 0.17	0.16	0.10 - 0.24
Petechiae	0.41	0.15 - 1.09	0.34	0.11 - 1.06
Plasma cell myeloma	1.39	0.45 - 4.37	0.13	0.07 - 0.25
Platelet count abnormal	0.41	0.15 - 1.11	0.54	0.23 - 1.31
Platelet count decreased	0.62	0.53 - 0.73	0.42	0.34 - 0.51
Pleural effusion	0.97	0.77 - 1.23	0.72	0.54 - 0.95
Pleurisy	1.69	0.70 - 4.09	1.36	0.44 - 4.27
Pneumonia	0.78	0.70 - 0.88	1.02	0.92 - 1.13
Pneumothorax	0.57	0.18 - 1.78	1.69	0.80 - 3.57
Pollakiuria	0.30	0.11 - 0.81	0.29	0.11 - 0.77
Polyneuropathy	0.48	0.25 - 0.93	0.64	0.31 - 1.35
Post procedural infection	2.15	0.96 - 4.84	1.30	0.41 - 4.06
Posterior reversible encephalopathy syndrome	0.21	0.07 - 0.65	0.88	0.39 - 1.96
Presyncope	0.84	0.35 - 2.03	1.02	0.42 - 2.46
Proctalgia	1.53	0.49 - 4.80	1.75	0.65 - 4.71
Productive cough	0.68	0.38 - 1.23	1.24	0.79 - 1.96
Pruritus	0.39	0.30 - 0.52	0.29	0.23 - 0.37

Psychotic disorder	1.46	0.47 - 4.57	2.03	0.64 - 6.39
Pulmonary alveolar haemorrhage	2.04	0.96 - 4.32	2.09	0.86 - 5.08
Pulmonary embolism	0.46	0.31 - 0.68	0.49	0.33 - 0.74
Pulmonary mass	0.51	0.19 - 1.38	0.95	0.43 - 2.13
Pulmonary oedema	0.53	0.34 - 0.83	0.54	0.33 - 0.87
Pulmonary sepsis	2.15	0.96 - 4.84	2.25	0.71 - 7.09
Rash	0.48	0.41 - 0.57	0.38	0.32 - 0.45
Rash erythematous	0.86	0.50 - 1.48	1.13	0.72 - 1.78
Rash pruritic	0.31	0.18 - 0.55	0.41	0.25 - 0.65
Red blood cell count decreased	0.26	0.15 - 0.46	0.15	0.07 - 0.32
Renal disorder	0.08	0.02 - 0.24	0.11	0.04 - 0.29
Renal failure	0.52	0.37 - 0.72	0.53	0.37 - 0.74
Renal impairment	0.84	0.62 - 1.14	0.41	0.26 - 0.63
Respiratory disorder	0.74	0.40 - 1.38	1.13	0.65 - 1.95
Respiratory distress	1.35	0.82 - 2.21	1.36	0.75 - 2.47
Restless legs syndrome	1.48	0.61 - 3.58	1.39	0.57 - 3.37
Restlessness	1.67	0.79 - 3.54	0.96	0.36 - 2.56
Rhinorrhoea	0.41	0.22 - 0.77	0.38	0.21 - 0.71
SARS-CoV-2 test positive	0.67	0.34 - 1.35	0.69	0.33 - 1.46
Second primary malignancy	0.78	0.50 - 1.19	0.91	0.50 - 1.64
Sensitive skin	1.39	0.45 - 4.37	2.30	0.95 - 5.61
Sensory loss	1.53	0.49 - 4.80	1.74	0.55 - 5.46
Shock	1.69	0.93 - 3.08	1.95	0.97 - 3.93
Sinusitis	0.55	0.37 - 0.81	1.14	0.86 - 1.51
Skin disorder	0.88	0.53 - 1.46	1.36	0.89 - 2.07
Skin infection	1.54	0.89 - 2.67	0.71	0.30 - 1.72
Skin lesion	0.27	0.10 - 0.72	0.58	0.29 - 1.16
Skin reaction	0.65	0.21 - 2.02	0.84	0.35 - 2.03
Small intestinal obstruction	0.94	0.39 - 2.27	0.66	0.21 - 2.07
Spinal disorder	0.54	0.17 - 1.69	0.54	0.17 - 1.69
Splenomegaly	0.73	0.39 - 1.36	0.66	0.32 - 1.40
Squamous cell carcinoma	0.36	0.12 - 1.13	1.10	0.52 - 2.32
Staphylococcal infection	1.16	0.74 - 1.80	1.03	0.61 - 1.74
Stomatitis	0.88	0.64 - 1.20	0.86	0.62 - 1.19
Streptococcal bacteraemia	1.18	0.38 - 3.68	2.61	0.96 - 7.08
Streptococcal sepsis	2.38	0.88 - 6.44	2.61	0.82 - 8.24
Stress cardiomyopathy	2.18	0.90 - 5.29	2.51	0.93 - 6.79
Suicidal ideation	1.22	0.39 - 3.80	1.36	0.43 - 4.25
Supraventricular tachycardia	1.58	0.75 - 3.34	1.13	0.42 - 3.04
Swelling	0.25	0.12 - 0.50	0.38	0.22 - 0.66
Swelling face	0.21	0.09 - 0.51	0.24	0.11 - 0.55
Swollen tongue	1.01	0.38 - 2.70	1.17	0.48 - 2.84
Syncope	0.70	0.48 - 1.03	1.02	0.72 - 1.44

Thinking abnormal	1.49	0.55 - 4.01	1.04	0.33 - 3.26
Thrombosis	0.13	0.07 - 0.22	0.12	0.07 - 0.21
Tinnitus	0.36	0.14 - 0.97	0.67	0.33 - 1.34
Toothache	0.56	0.21 - 1.49	0.76	0.34 - 1.70
Transient ischaemic attack	0.55	0.29 - 1.06	0.60	0.31 - 1.16
Troponin increased	1.50	0.62 - 3.63	1.54	0.57 - 4.13
Upper gastrointestinal haemorrhage	0.80	0.30 - 2.14	1.50	0.62 - 3.65
Urinary incontinence	1.34	0.69 - 2.59	1.37	0.68 - 2.76
Urinary retention	1.21	0.70 - 2.09	1.40	0.79 - 2.48
Urinary tract infection	0.58	0.44 - 0.74	0.94	0.76 - 1.16
Urine output decreased	1.40	0.52 - 3.75	1.53	0.57 - 4.11
Urticaria	0.22	0.11 - 0.43	0.15	0.08 - 0.27
Vertigo	0.74	0.39 - 1.37	0.54	0.27 - 1.08
Viral infection	0.94	0.61 - 1.45	0.93	0.58 - 1.51
Vision blurred	0.43	0.26 - 0.70	0.40	0.24 - 0.65
Visual impairment	0.48	0.28 - 0.83	0.52	0.31 - 0.87
Vomiting	0.63	0.51 - 0.76	0.50	0.41 - 0.61
Weight increased	0.33	0.20 - 0.53	0.23	0.13 - 0.40
Wheezing	0.95	0.47 - 1.90	0.83	0.39 - 1.75
White blood cell count abnormal	0.69	0.38 - 1.26	0.46	0.22 - 0.97
White blood cell count decreased	0.45	0.37 - 0.54	0.28	0.22 - 0.36
White blood cell count increased	0.80	0.57 - 1.12	0.67	0.45 - 0.99

Supplementary Table 10. High-risk syndromes associated with BiTE-related adverse events.

Frequency ¹	PTs					
93.0	Bacteraemia	CRS	ICANS			
92.3	CRS	Haemophagocytic lymphohistiocytosis	ICANS			
74.4	CRS	Fungal infection	ICANS	Infection	Neutropenia	
73.8	CRS	ICANS	Infection	Lymphopenia	Neutropenia	
67.3	CRS	Infection	Tumour lysis syndrome			
61.8	CRS	Hypocalcaemia	Infection	Neutropenia		
54.5	CRS	Dysgeusia	ICANS	Infection	Lymphopenia	
53.2	CRS	Dysgeusia	ICANS	Nail toxicity		
39.0	Hypocalcaemia	Hypotension	Pyrexia			
31.7	Aphasia	Confusional state	Headache	Pyrexia	Tremor	
31.0	Confusional state	Headache	Pyrexia	Tachycardia	Tremor	
31.0	CRS	Disseminated intravascular coagulation	Tumour lysis syndrome			
30.9	Confusional state	Hypotension	Pyrexia	Tachycardia	Tremor	
30.5	CRS	Hypocalcaemia	Hypophosphataemia	Neutropenia		
30.0	Hepatotoxicity	Infection	Neutropenia			
27.7	Alanine aminotransferase increased	Aspartate aminotransferase increased	Sinus tachycardia			
27.1	Cytomegalovirus infection reactivation	Hypogammaglobulinaemia	ICANS	Infection	Neutropenia	
26.4	Confusional state	Hypotension	Hypoxia	Pyrexia	Tachycardia	
25.7	Cytomegalovirus infection reactivation	Graft versus host disease	Infection	Neutropenia		
25.5	Blood lactate dehydrogenase increased	C-reactive protein increased	Hypotension	Pyrexia		
25.3	Aphasia	Headache	Muscular weakness	Pyrexia	Tremor	
24.2	Cytomegalovirus infection	Hypogammaglobulinaemia	Infection	Neutropenia		
24.0	Altered state of consciousness	Pyrexia	Tremor			

22.5	COVID-19	Fungal infection	Infection	Neutropenia		
22.5	COVID-19	Infection	Lymphopenia	Neutropenia		
22.3	Aphasia	Confusional state	Headache	Neurotoxicity	Tremor	
21.3	Alanine aminotransferase increased	Aspartate aminotransferase increased	Blood bilirubin increased	Neutropenia		
21.2	Dysgeusia	Hypogammaglobulinaemia	ICANS	Infection		
19.9	COVID-19	Cytomegalovirus infection reactivation	Hypogammaglobulinaemia	Infection	Neutropenia	
19.8	Alanine aminotransferase increased	Aspartate aminotransferase increased	Hypocalcaemia	Neutropenia		
19.1	Cytomegalovirus infection	Fungal infection	Graft versus host disease	Infection	Neutropenia	
18.7	Confusional state	Headache	Neurotoxicity	Speech disorder	Tremor	
18.0	Graft versus host disease	Infection	Venoocclusive disease			
17.7	Alanine aminotransferase increased	Aspartate aminotransferase increased	Blood alkaline phosphatase increased	Gamma-glutamyltransferase increased		
16.3	Ataxia	Confusional state	Headache	Tremor		
16.1	Aphasia	Encephalopathy	Headache	Neurotoxicity	Seizure	Tremor
15.7	C-reactive protein increased	Pyrexia	Serum ferritin increased			
14.3	Aphasia	Confusional state	Disorientation	Tremor		
14.3	Confusional state	Dysgraphia	Neurotoxicity			
14.3	Alanine aminotransferase increased	Hypocalcaemia	Pyrexia			
13.3	Dry mouth	Dysgeusia	Nail disorder	Skin exfoliation		
12.7	Aphasia	Depressed level of consciousness	Neurotoxicity	Seizure	Tremor	
12.7	Aphasia	Nervous system disorder	Tremor			
12.7	Hepatotoxicity	Neurotoxicity	Seizure			
12.3	Ageusia	Onychomadesis	Skin exfoliation			
12.3	Cytomegalovirus infection reactivation	Infection	Sepsis			
12.3	COVID-19	Neutropenia	Pseudomonas infection			
12.0	Dysgeusia	ICANS	Nail disorder			

11.7	Ageusia	Dry mouth	Nail disorder	Skin exfoliation		
11.7	Ataxia	Confusional state	Dysarthria	Tremor		
11.2	Confusional state	Disorientation	Speech disorder	Tremor		
11.0	Infection	Pneumocystis jirovecii pneumonia	Sepsis			
10.8	BK virus infection	Cytomegalovirus infection reactivation	Graft versus host disease	Neutropenia		
10.7	Hypocalcaemia	Hypokalaemia	Hypotension			
10.3	Blast cell count increased	Blood lactate dehydrogenase increased	Pyrexia			
10.3	COVID-19	Infection	Pneumocystis jirovecii pneumonia			
10.2	Alanine aminotransferase increased	Hypocalcaemia	Hypokalaemia	Neutropenia		
9.3	Hypocalcaemia	Hypokalaemia	Hypomagnesaemia			
9.3	Altered state of consciousness	Seizure	Tremor			
9.0	Adenovirus infection	Cytomegalovirus infection	Graft versus host disease			
8.5	Hypocalcaemia	Hypokalaemia	Hypophosphataemia	Neutropenia		
7.0	Hyperglycaemia	Hypoalbuminaemia	Hypocalcaemia	Hypotension		
6.3	COVID-19	Pseudomonas infection	Rhinovirus infection			
6.0	COVID-19	Respiratory syncytial virus infection	Rhinovirus infection			
5.3	Hyperglycaemia	Hypocalcaemia	Hypophosphataemia			

1. Frequency represents the mean pairwise co-occurrence count, calculated as the average number of cases sharing any two PTs within the identified syndrome.

Note: Yellow highlighting indicates BRAF-AEs; gray highlighting indicates PTs with positive fatal signals detected in a single database only.

Supplementary Table 11. BiTE-related adverse events with positive fatality signals detected in a single database (FAERS or Vigibase).

PT	FAERS		Vigibase	
	ROR	95% CI	ROR	95% CI
Altered state of consciousness	2.04	1.02 - 4.09	0.80	0.18 - 3.62
Ascites	2.59	1.18 - 5.72	2.21	0.66 - 7.34
Bacteraemia	1.92	1.07 - 3.43	1.77	0.78 - 4.02
COVID-19	1.84	1.40 - 2.42	1.24	0.90 - 1.71
Cytomegalovirus colitis	3.95	1.21 - 12.97	1.10	0.23 - 5.19
Disseminated intravascular coagulation	3.32	1.92 - 5.72	2.41	0.89 - 6.53
Hepatotoxicity	1.87	1.15 - 3.03	2.21	0.83 - 5.90
Hyperkalaemia	3.30	1.15 - 9.41	3.16	1.00 - 9.96
Leukopenia	2.13	1.21 - 3.75	0.94	0.39 - 2.28
Lower respiratory tract infection	3.77	1.37 - 10.41	0.84	0.29 - 2.45
Parainfluenzae virus infection	2.88	1.04 - 7.96	2.21	0.66 - 7.34
Pneumonia fungal	2.83	1.31 - 6.13	1.96	0.60 - 6.38
Pneumonia viral	9.09	2.89 - 28.56	1.20	0.33 - 4.31
Pseudomonas infection	3.30	1.61 - 6.77	2.01	0.70 - 5.79
Respiratory tract infection	3.54	1.71 - 7.35	1.10	0.53 - 2.29
Thrombotic microangiopathy	5.28	1.72 - 16.15	3.16	1.00 - 9.96
Blood bilirubin increased	0.89	0.44 - 1.79	3.07	1.31 - 7.19
Blood lactate dehydrogenase increased	1.65	0.85 - 3.21	2.34	1.04 - 5.27
Bone marrow failure	2.06	0.93 - 4.55	7.09	2.32 - 21.72
Cytopenia	1.48	0.89 - 2.46	3.54	1.39 - 9.00
Escherichia bacteraemia	1.83	0.61 - 5.46	3.68	1.12 - 12.09
Heart rate increased	1.54	0.63 - 3.77	10.34	2.67 - 40.04
Hypercalcaemia	1.23	0.48 - 3.16	2.58	1.01 - 6.57
Hypoalbuminaemia	1.10	0.35 - 3.40	4.42	1.42 - 13.74
Pulmonary embolism	2.06	0.93 - 4.55	3.10	1.18 - 8.15
Pulmonary oedema	1.92	0.76 - 4.89	3.68	1.12 - 12.09
Respiratory disorder	2.19	0.62 - 7.79	6.64	1.87 - 23.56
Urosepsis	1.37	0.48 - 3.90	3.68	1.12 - 12.09

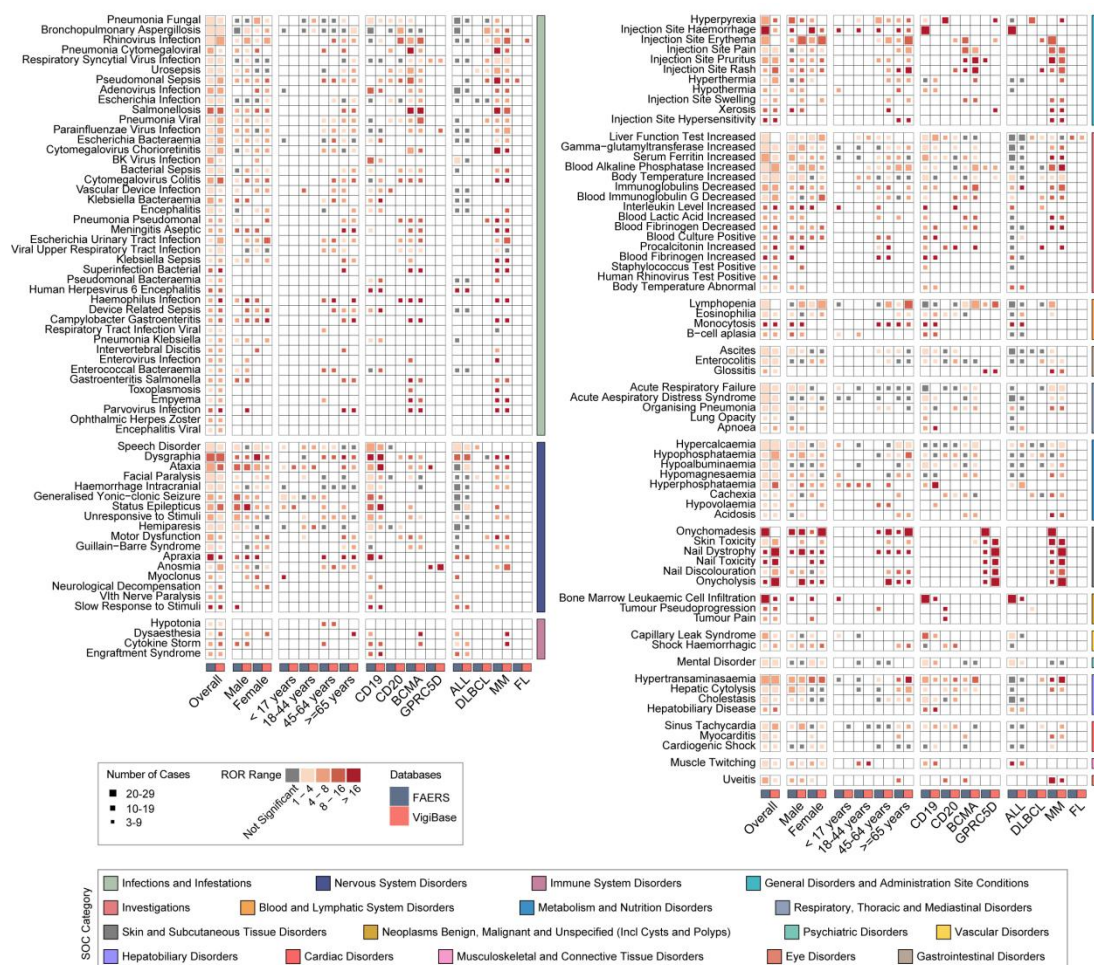
Supplementary Table 12. BiTES-related adverse events with no significant fatality signals detected in either database (FAERS or Vigibase).

PT	FAERS		Vigibase	
	ROR	95%CI	ROR	95%CI
Abdominal pain	0.84	0.43 - 1.63	1.47	0.72 - 3.02
Abdominal pain upper	0.27	0.04 - 2.11	0.49	0.11 - 2.11
Agitation	0.60	0.13 - 2.70	1.47	0.40 - 5.44
Alanine aminotransferase increased	0.99	0.63 - 1.55	1.54	0.85 - 2.79
Anaemia	1.15	0.83 - 1.60	0.82	0.55 - 1.22
Anxiety	0.91	0.34 - 2.46	1.18	0.39 - 3.55
Aphasia	0.68	0.38 - 1.20	0.19	0.05 - 0.80
Arthralgia	0.75	0.39 - 1.45	0.26	0.10 - 0.73
Aspartate aminotransferase increased	1.08	0.65 - 1.79	1.07	0.52 - 2.23
Aspergillus infection	2.35	0.75 - 7.42	2.76	0.90 - 8.46
Asthenia	0.68	0.42 - 1.09	0.55	0.30 - 1.01
Ataxia	0.30	0.07 - 1.27	0.26	0.03 - 1.94
Atrial fibrillation	1.32	0.74 - 2.36	1.64	0.87 - 3.12
Back pain	0.38	0.15 - 0.96	0.44	0.19 - 1.01
Blast cell count increased	0.57	0.28 - 1.15	0.49	0.06 - 3.86
Blood alkaline phosphatase increased	0.58	0.17 - 1.98	1.10	0.37 - 3.30
Blood creatinine increased	0.40	0.14 - 1.12	0.63	0.22 - 1.79
Blood glucose increased	1.65	0.50 - 5.47	0.98	0.21 - 4.54
Bone pain	1.03	0.52 - 2.04	0.61	0.26 - 1.44
Bronchitis	1.01	0.33 - 3.11	0.27	0.06 - 1.11
Bronchopulmonary aspergillosis	1.28	0.53 - 3.07	1.47	0.53 - 4.05
C-reactive protein increased	0.61	0.31 - 1.19	0.63	0.27 - 1.48
Candida infection	2.35	0.75 - 7.42	1.10	0.31 - 3.91
Cellulitis	0.82	0.34 - 2.01	0.46	0.11 - 1.99
Cerebrovascular accident	1.18	0.42 - 3.27	2.21	0.66 - 7.34
Chest pain	0.97	0.36 - 2.62	1.47	0.47 - 4.57
Chills	0.43	0.24 - 0.79	0.29	0.12 - 0.72
Clostridium difficile colitis	0.62	0.18 - 2.12	0.29	0.04 - 2.22
Clostridium difficile infection	2.20	0.78 - 6.18	1.76	0.55 - 5.64
Cognitive disorder	1.10	0.49 - 2.44	1.65	0.44 - 6.24
Colitis	0.22	0.05 - 0.92	0.94	0.39 - 2.28
Confusional state	0.88	0.60 - 1.30	0.76	0.46 - 1.26
Constipation	1.34	0.66 - 2.71	0.97	0.47 - 1.99
Cough	0.44	0.19 - 1.03	0.43	0.21 - 0.89
Cytokine release syndrome	0.82	0.72 - 0.93	0.51	0.43 - 0.60
Cytomegalovirus infection	1.11	0.69 - 1.81	1.47	0.76 - 2.84
Cytomegalovirus infection reactivation	1.00	0.60 - 1.65	1.28	0.61 - 2.70
Decreased appetite	0.81	0.47 - 1.40	0.80	0.46 - 1.40
Deep vein thrombosis	0.33	0.08 - 1.41	1.20	0.33 - 4.31

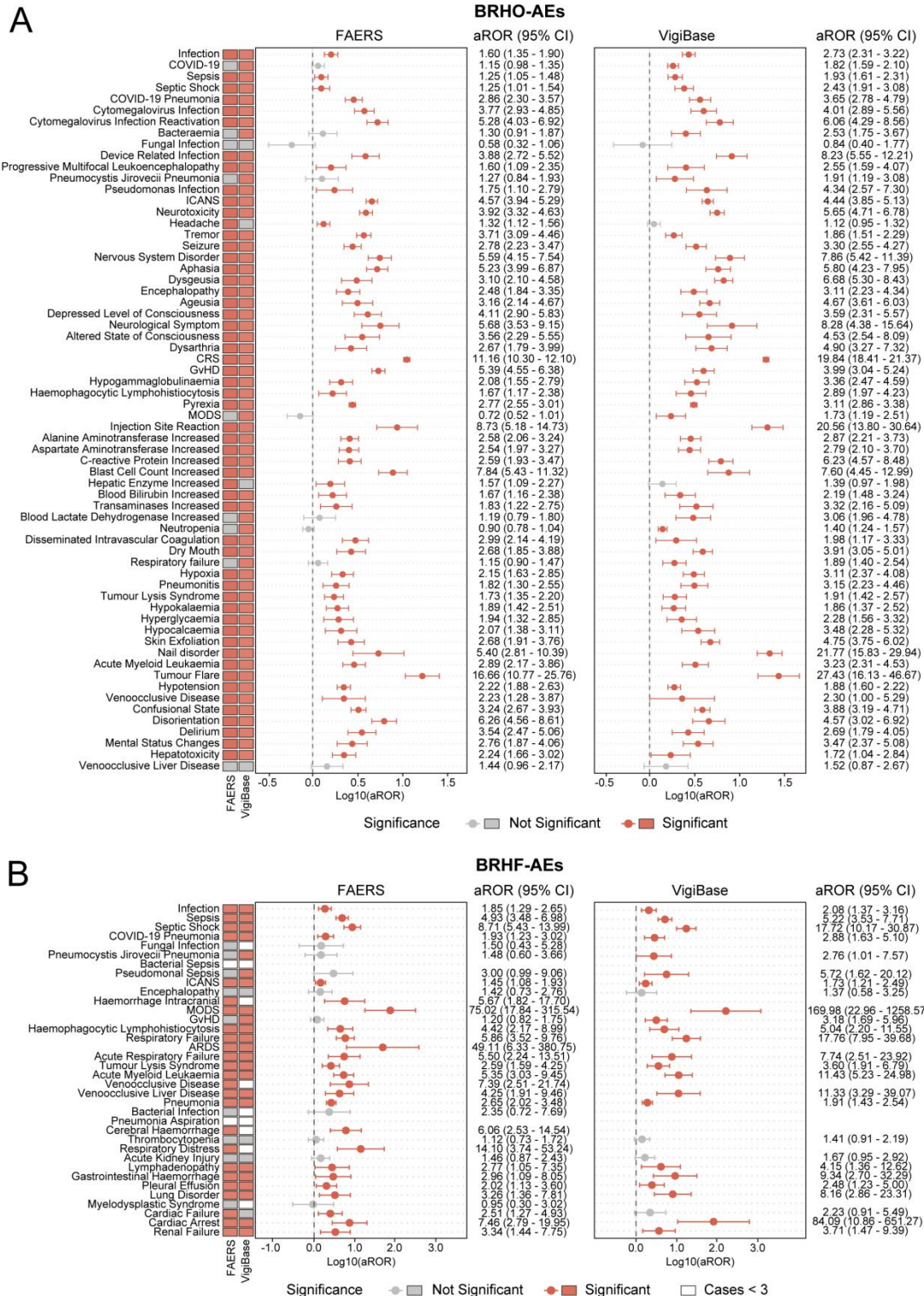
Dehydration	0.35	0.11 - 1.16	0.49	0.11 - 2.11
Delirium	0.88	0.40 - 1.91	1.22	0.45 - 3.31
Depressed level of consciousness	0.90	0.43 - 1.88	0.88	0.30 - 2.58
Depression	0.44	0.10 - 1.92	0.55	0.13 - 2.39
Device related infection	0.37	0.13 - 1.06	1.05	0.39 - 2.79
Diarrhoea	0.60	0.38 - 0.95	0.54	0.34 - 0.85
Disorientation	0.43	0.18 - 1.00	0.84	0.29 - 2.45
Dizziness	0.25	0.10 - 0.62	0.19	0.05 - 0.80
Dry skin	0.31	0.11 - 0.87	0.16	0.05 - 0.51
Dysarthria	0.59	0.23 - 1.52	0.84	0.29 - 2.45
Dysgeusia	0.28	0.12 - 0.64	0.08	0.02 - 0.34
Dysgraphia	0.29	0.07 - 1.21	0.49	0.06 - 3.86
Dysphagia	1.32	0.63 - 2.75	0.42	0.13 - 1.39
Dyspnoea	1.44	0.94 - 2.21	1.50	0.90 - 2.51
Epistaxis	2.28	0.97 - 5.35	1.70	0.60 - 4.77
Erythema	0.30	0.07 - 1.27	0.24	0.06 - 0.98
Escherichia infection	2.56	0.95 - 6.89	2.94	0.83 - 10.45
Facial paralysis	0.77	0.26 - 2.30	0.49	0.06 - 3.86
Fatigue	0.54	0.36 - 0.82	0.50	0.30 - 0.83
Febrile neutropenia	0.86	0.62 - 1.21	0.62	0.41 - 0.93
Gait disturbance	0.23	0.07 - 0.74	0.17	0.02 - 1.24
Gamma-glutamyltransferase increased	1.65	0.66 - 4.08	0.29	0.04 - 2.22
Gastrointestinal disorder	1.65	0.70 - 3.85	1.60	0.51 - 5.05
Haemoglobin decreased	1.59	0.82 - 3.08	1.47	0.53 - 4.05
Headache	0.52	0.36 - 0.76	0.41	0.23 - 0.74
Hepatic cytolysis	0.44	0.10 - 1.92	1.20	0.33 - 4.31
Hepatic enzyme increased	0.46	0.19 - 1.08	0.40	0.09 - 1.70
Herpes zoster	0.73	0.30 - 1.77	0.26	0.03 - 1.94
Hyperbilirubinaemia	1.83	0.61 - 5.46	1.65	0.44 - 6.24
Hyperglycaemia	0.55	0.21 - 1.41	0.92	0.35 - 2.41
Hyperhidrosis	0.21	0.03 - 1.55	0.37	0.05 - 2.82
Hyperphosphataemia	0.37	0.05 - 2.88	0.44	0.06 - 3.44
Hypertension	1.75	0.98 - 3.10	1.04	0.48 - 2.25
Hypertransaminaemia	0.94	0.38 - 2.33	1.26	0.41 - 3.83
Hypocalcaemia	0.66	0.25 - 1.72	1.30	0.48 - 3.52
Hypogammaglobulinaemia	0.91	0.54 - 1.54	0.20	0.05 - 0.84
Hypokalaemia	0.68	0.36 - 1.31	0.63	0.25 - 1.61
Hypomagnesaemia	0.51	0.11 - 2.24	0.37	0.05 - 2.82
Hyponatraemia	1.39	0.61 - 3.17	1.38	0.50 - 3.77
Hypophosphataemia	0.66	0.19 - 2.27	0.94	0.27 - 3.29
Hypotension	0.84	0.59 - 1.19	0.78	0.49 - 1.23
Hypoxia	0.78	0.42 - 1.42	1.55	0.84 - 2.86
Inflammation	1.20	0.38 - 3.76	0.98	0.21 - 4.54

Influenza	1.60	0.88 - 2.91	1.01	0.52 - 1.95
Injection site erythema	0.52	0.15 - 1.75	0.23	0.06 - 0.96
Injection site pain	1.10	0.30 - 4.05	0.34	0.04 - 2.59
Injection site reaction	0.23	0.06 - 0.98	0.25	0.06 - 1.04
Insomnia	0.17	0.02 - 1.29	0.66	0.20 - 2.22
Lethargy	0.62	0.18 - 2.12	0.98	0.21 - 4.54
Liver function test abnormal	0.82	0.17 - 3.87	1.89	0.49 - 7.32
Liver function test increased	0.12	0.02 - 0.89	0.29	0.04 - 2.22
Loss of consciousness	0.96	0.41 - 2.23	1.02	0.29 - 3.57
Lymphocyte count decreased	0.61	0.23 - 1.58	0.55	0.13 - 2.39
Lymphopenia	1.32	0.58 - 2.99	0.33	0.10 - 1.06
Malaise	0.95	0.57 - 1.58	1.80	0.89 - 3.64
Memory impairment	0.12	0.02 - 0.86	0.21	0.03 - 1.56
Mental status changes	0.73	0.30 - 1.77	1.10	0.37 - 3.30
Mucosal inflammation	0.53	0.18 - 1.51	0.55	0.13 - 2.39
Muscle spasms	0.23	0.03 - 1.78	0.40	0.05 - 3.10
Muscular weakness	0.88	0.45 - 1.72	0.63	0.22 - 1.79
Myalgia	1.00	0.49 - 2.03	0.55	0.17 - 1.83
Myelosuppression	0.66	0.37 - 1.17	1.47	0.40 - 5.44
Nail disorder	0.29	0.09 - 0.94	0.18	0.06 - 0.58
Nausea	0.55	0.34 - 0.92	0.57	0.33 - 0.98
Nervous system disorder	0.69	0.41 - 1.16	1.36	0.61 - 3.01
Neurological symptom	1.27	0.61 - 2.63	2.21	0.66 - 7.34
Neuropathy peripheral	0.40	0.22 - 0.74	0.26	0.08 - 0.84
Neurotoxicity	0.81	0.61 - 1.08	0.89	0.58 - 1.38
Neutropenia	1.17	0.92 - 1.50	0.70	0.51 - 0.95
Neutrophil count decreased	0.85	0.55 - 1.33	0.41	0.19 - 0.90
Oedema peripheral	0.87	0.32 - 2.32	0.70	0.24 - 2.03
Organising pneumonia	1.32	0.41 - 4.20	0.98	0.21 - 4.54
Oxygen saturation decreased	0.76	0.31 - 1.84	1.20	0.33 - 4.31
Pain	0.32	0.15 - 0.66	0.78	0.40 - 1.54
Pain in extremity	0.74	0.36 - 1.53	0.64	0.27 - 1.52
Pancreatitis	0.99	0.40 - 2.46	1.10	0.31 - 3.91
Pancytopenia	1.20	0.78 - 1.85	1.69	0.95 - 3.01
Paraesthesia	0.61	0.23 - 1.58	0.20	0.03 - 1.48
Pericardial effusion	2.31	0.88 - 6.07	1.65	0.44 - 6.24
Peripheral swelling	0.30	0.04 - 2.31	0.68	0.15 - 3.00
Platelet count decreased	1.10	0.75 - 1.61	0.64	0.32 - 1.28
Pneumonitis	1.34	0.70 - 2.55	2.01	0.95 - 4.26
Progressive multifocal leukoencephalopathy	1.72	0.85 - 3.46	1.20	0.33 - 4.31
Pruritus	0.28	0.10 - 0.79	0.27	0.08 - 0.86
Pyrexia	0.68	0.57 - 0.82	0.41	0.31 - 0.55
Rash	0.63	0.40 - 0.99	0.32	0.15 - 0.70

Rash erythematous	0.60	0.13 - 2.70	0.29	0.04 - 2.22
Rash maculo-papular	0.41	0.09 - 1.79	0.18	0.02 - 1.35
Renal impairment	0.77	0.36 - 1.67	1.10	0.31 - 3.91
Respiratory syncytial virus infection	2.10	0.81 - 5.41	0.98	0.21 - 4.54
Rhinovirus infection	1.65	0.66 - 4.08	1.10	0.37 - 3.30
Second primary malignancy	2.03	0.84 - 4.90	1.89	0.49 - 7.32
Seizure	0.89	0.59 - 1.33	0.47	0.20 - 1.09
Sinus tachycardia	0.66	0.14 - 3.00	1.10	0.31 - 3.91
Sinusitis	0.45	0.13 - 1.50	0.12	0.02 - 0.84
Skin disorder	0.51	0.11 - 2.24	0.88	0.19 - 4.02
Skin exfoliation	0.09	0.02 - 0.39	0.15	0.05 - 0.47
Somnolence	1.33	0.76 - 2.35	0.73	0.25 - 2.12
Speech disorder	1.10	0.47 - 2.58	0.40	0.05 - 3.10
Staphylococcal bacteraemia	1.65	0.50 - 5.47	1.65	0.44 - 6.24
Staphylococcal infection	1.77	0.71 - 4.45	0.80	0.18 - 3.62
Status epilepticus	1.27	0.45 - 3.55	0.98	0.21 - 4.54
Stomatitis	0.58	0.24 - 1.38	0.47	0.14 - 1.55
Syncope	0.13	0.02 - 0.93	0.16	0.02 - 1.20
Tachycardia	0.52	0.25 - 1.11	0.63	0.25 - 1.61
Transaminases increased	1.29	0.64 - 2.60	0.78	0.23 - 2.65
Tremor	0.63	0.42 - 0.95	0.36	0.17 - 0.79
Tumour flare	0.44	0.17 - 1.13	0.52	0.12 - 2.24
Upper respiratory tract infection	1.27	0.61 - 2.63	0.34	0.12 - 0.95
Urinary tract infection	1.12	0.62 - 2.02	0.89	0.49 - 1.63
Viral infection	1.65	0.66 - 4.08	2.45	0.82 - 7.34
Vision blurred	0.76	0.22 - 2.66	0.37	0.05 - 2.82
Visual impairment	0.27	0.04 - 2.11	0.44	0.06 - 3.44
Vomiting	0.56	0.33 - 0.98	0.51	0.25 - 1.07
Weight decreased	0.31	0.16 - 0.62	0.32	0.15 - 0.70
White blood cell count decreased	0.72	0.43 - 1.18	0.51	0.20 - 1.29
White blood cell count increased	0.33	0.10 - 1.08	0.37	0.05 - 2.82

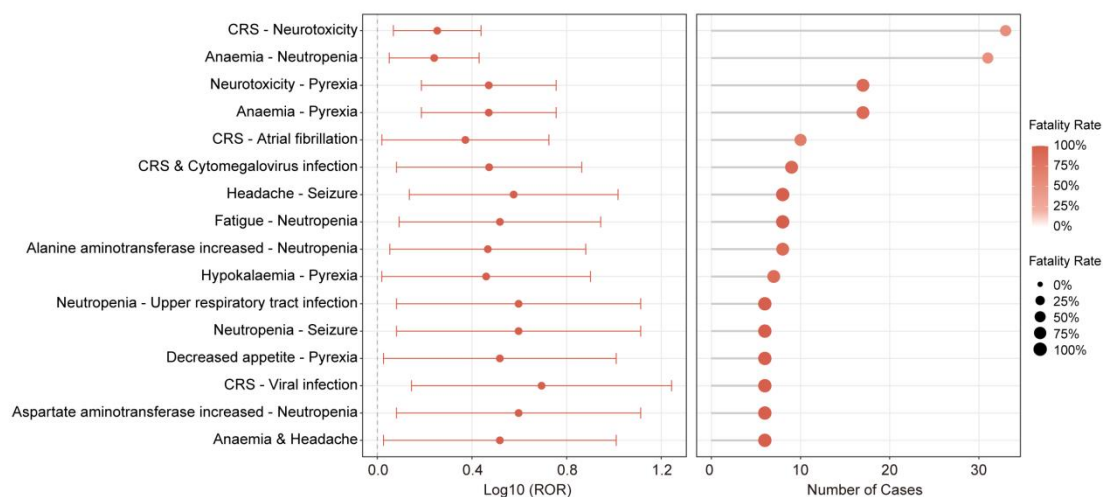


Supplementary Figure 1. Identification of BAHO-AEs. The heatmap displays the ROR for BAHO-AEs (case count < 30). Grouped by SOC, the left and right squares in each cell represent data from FAERS and VigiBase, respectively. The size of the square corresponds to the number of cases, while the color intensity (red) indicates the magnitude of the occurrence ROR. Gray indicates non-significant associations, and blank spaces indicate a case count of fewer than 3. Abbreviations: ALL, Acute Lymphoblastic Leukemia; DLBCL, Diffuse Large B-Cell Lymphoma; MM, Multiple Myeloma; FL, Follicular Lymphoma.

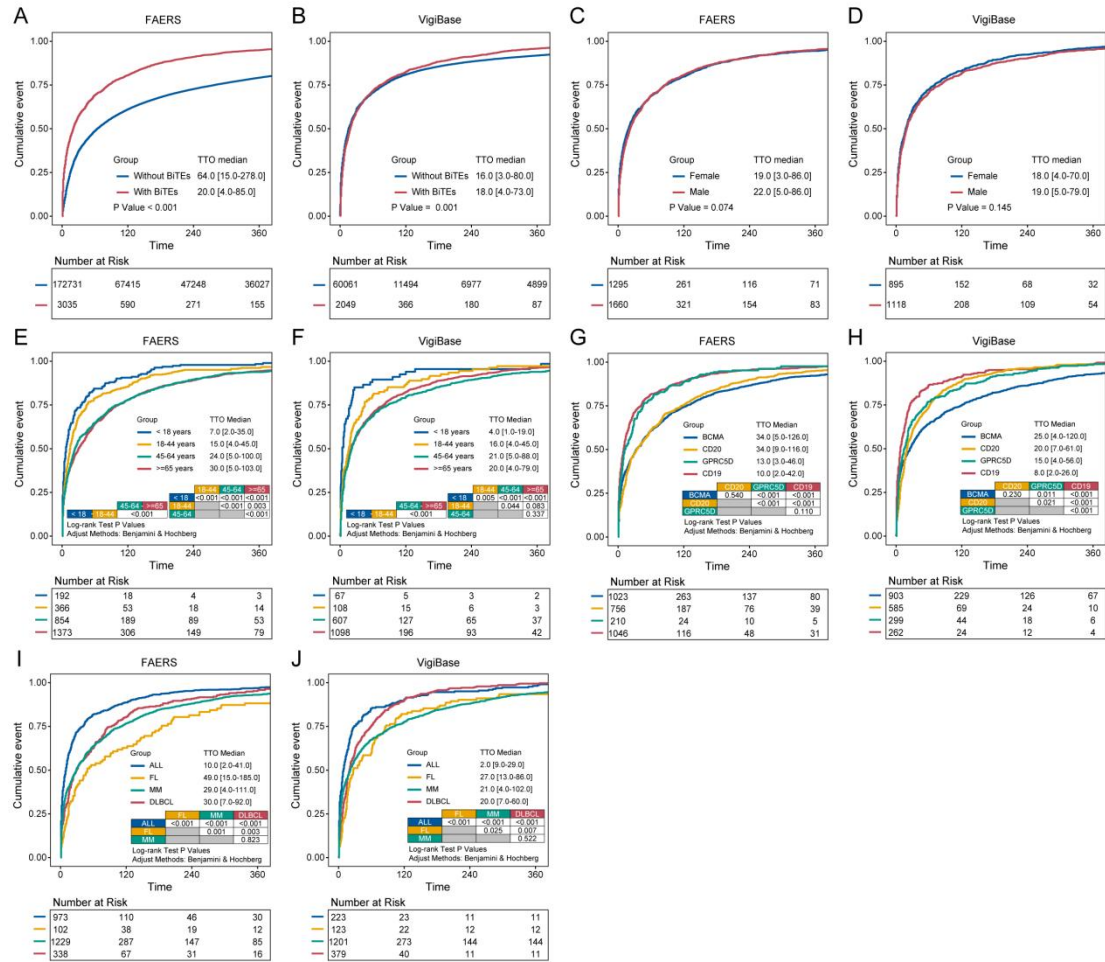


Supplementary Figure 2. Multivariate sensitivity analysis of BAHO-AEs and BAHF-AEs. (A) Adjusted ROR (aROR) and 95% CI for BAHO-AEs. Only PTs with a remaining case count of ≥ 30 after excluding reports with missing covariates are displayed. **(B)** The aROR and 95% CI for BAHF-AEs. Red markers indicate significant signals, gray markers indicate non-significant signals, and white markers indicate a case count fewer than 3 after filtering for missing covariates. Abbreviations: CRS, Cytokine Release Syndrome; ICANS, Immune Effector Cell-Associated

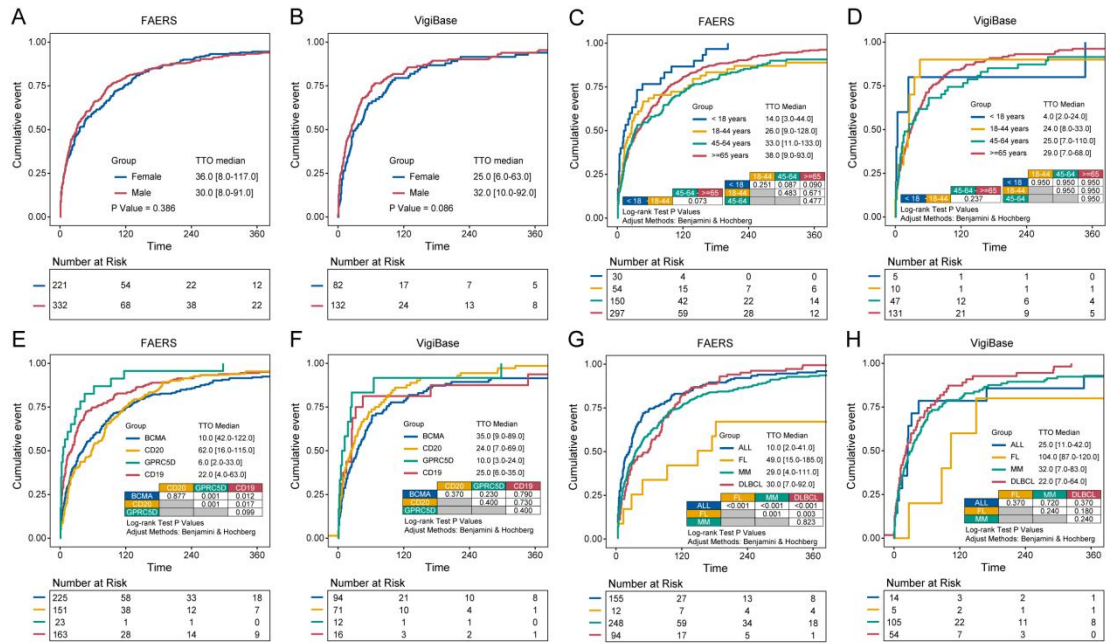
Neurotoxicity Syndrome; GvHD, Graft-versus-Host Disease; MODS, Multiple Organ Dysfunction Syndrome; ARDS, Acute Respiratory Distress Syndrome.



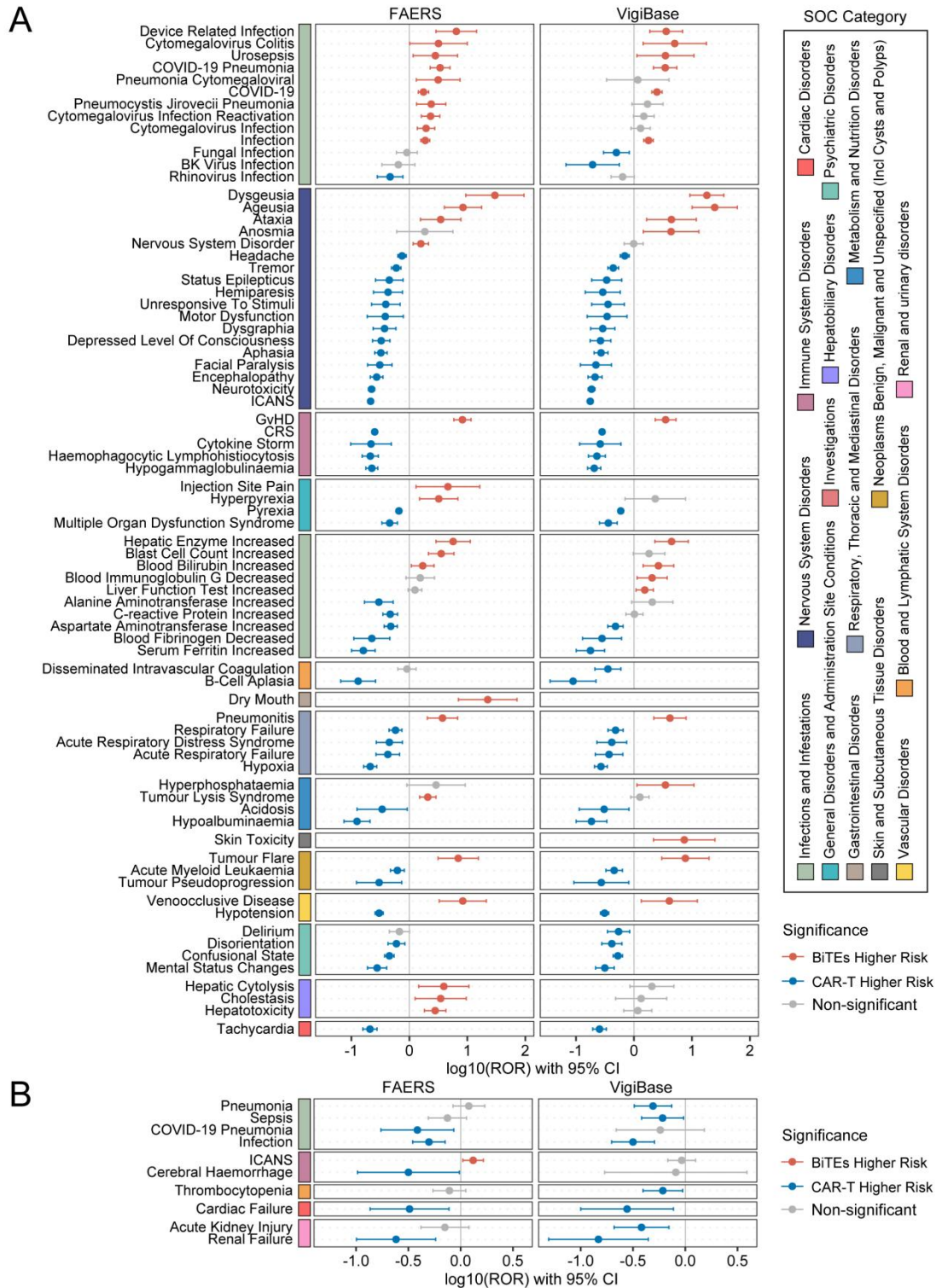
Supplementary Figure 3. Synergistic fatality risk of concurrent adverse events. Left panel: Forest plot displaying the fatality risk (Log10 ROR) for pairs of adverse events that individually lacked significant fatality signals in FAERS. Error bars represent 95% confidence intervals. Right panel: Distribution of case frequency and fatality rates. The x-axis represents the number of co-occurring cases. Both the bubble size and color intensity represent the fatality rate (%), with larger and darker bubbles indicating higher mortality. Abbreviations: CRS, cytokine release syndrome; ROR, reporting odds ratio.



Supplementary Figure 4. TTO kinetics of BiTE-associated AEs. Kaplan-Meier cumulative event curve analyses were performed using data from FAERS and Vigibase. (A–B) Comparisons between BiTEs and non-BiTEs groups within the overall hematologic malignancy population. (C–D) Stratification by sex restricted to the BiTEs-treated population. (E–F) Stratification by age groups restricted to the BiTEs-treated population. (G–H) Stratification by therapeutic targets restricted to the BiTEs-treated population. (I–J) Stratification by indication (tumor types) restricted to the BiTEs-treated population. Abbreviations: ALL, Acute Lymphoblastic Leukemia; DLBCL, Diffuse Large B-Cell Lymphoma; MM, Multiple Myeloma; FL, Follicular Lymphoma.



Supplementary Figure 5. TTO kinetics of BiTE-associated AEs in fatal cases. Kaplan-Meier cumulative event curve analyses were performed using data from FAERS and Vigibase. (A–B) Stratification by sex restricted to the fatal cases population. (C–D) Stratification by age groups restricted to the fatal cases population. (E–F) Stratification by therapeutic targets restricted to the fatal cases population. (G–H) Stratification by indication (cancer types) restricted to the fatal cases population. Abbreviations: ALL, Acute Lymphoblastic Leukemia; DLBCL, Diffuse Large B-Cell Lymphoma; MM, Multiple Myeloma; FL, Follicular Lymphoma.



Supplementary Figure 6. Comparative safety analysis between BiTEs and CAR-T therapies. (A) Comparative overview of AE risks. The ROR and 95% CI of BiTEs relative to CAR-T were calculated for the BAHO-AEs (case count ≥ 30); the PTs shown in the figure had significant results in at least one database. (B) Comparative overview of fatal risks. The ROR and 95% CI of BiTEs relative to CAR-T were calculated for the BAHF-AEs. In panels A and B, red dots indicate a significantly higher risk associated with BiTEs, blue dots indicate a significantly higher risk associated with CAR-T, and

gray dots indicate no significant difference. Abbreviations: ICANS, Immune Effector Cell-Associated Neurotoxicity Syndrome; GvHD, Graft-versus-Host Disease; CRS, Cytokine Release Syndrome.