Supplementary Table S3 The comprehensive detailed information of all AEs at the PTs level identified by PRR algorithms.

|  |  |  |  |
| --- | --- | --- | --- |
| Preferred Terms | SOC | Case Number | PRR (95% two side CI) |
| heterochromia iridis | Eye disorders | 7 | 2700.62 (1078.66-6761.47) |
| choroidal dystrophy | Eye disorders | 9 | 1612.1 (761.75-3411.73) |
| iris atrophy | Eye disorders | 15 | 817.73 (474.67-1408.73) |
| enophthalmos | Eye disorders | 8 | 771.61 (367.04-1622.09) |
| alveolar soft part sarcoma | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 4 | 743.03 (260.24-2121.45) |
| chorioretinal atrophy | Eye disorders | 15 | 518.84 (305.48-881.2) |
| brain stem glioma | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 5 | 385.8 (155.53-957.03) |
| arteriosclerotic retinopathy | Vascular disorders | 3 | 327.09 (101.82-1050.8) |
| proteus test positive | Investigations | 4 | 313.46 (114.27-859.92) |
| nephroblastoma | Renal and urinary disorders | 3 | 221.27 (69.68-702.61) |
| febrile bone marrow aplasia | General disorders and administration site conditions | 30 | 184.84 (128.76-265.36) |
| iris adhesions | Eye disorders | 7 | 170.43 (80.35-361.5) |
| lenticular opacities | Eye disorders | 6 | 168.12 (74.62-378.75) |
| chorioretinal disorder | Eye disorders | 3 | 131.99 (41.98-414.97) |
| cerebral cyst | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 8 | 116.64 (57.95-234.77) |
| ocular toxicity | Eye disorders | 7 | 102.66 (48.64-216.67) |
| cataract subcapsular | Eye disorders | 5 | 99.51 (41.11-240.89) |
| intracranial tumour haemorrhage | Nervous system disorders | 3 | 97.7 (31.19-306.01) |
| neuroblastoma | Endocrine disorders | 3 | 96.45 (30.8-302.05) |
| small cell lung cancer stage unspecified | Respiratory, thoracic and mediastinal disorders | 12 | 81.33 (46.06-143.61) |
| acute interstitial pneumonitis | Respiratory, thoracic and mediastinal disorders | 3 | 80.89 (25.88-252.89) |
| vitreous haemorrhage | Eye disorders | 18 | 73.04 (45.96-116.07) |
| monocyte count decreased | Investigations | 5 | 71.04 (29.42-171.54) |
| bone marrow depression | Blood and lymphatic system disorders | 8 | 70.89 (35.33-142.24) |
| scleritis | Immune system disorders | 7 | 65.26 (31-137.36) |
| acute febrile neutrophilic dermatosis | Skin and subcutaneous tissue disorders | 12 | 61.48 (34.85-108.43) |
| malignant ascites | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 3 | 53.93 (17.3-168.08) |
| subileus | Gastrointestinal disorders | 7 | 50.73 (24.13-106.67) |
| retinal ischaemia | Eye disorders | 3 | 47.47 (15.24-147.83) |
| conjunctival oedema | Eye disorders | 4 | 43.71 (16.35-116.83) |
| white blood cells urine positive | Investigations | 4 | 43.33 (16.21-115.82) |
| thrombocythaemia | Blood and lymphatic system disorders | 3 | 43.11 (13.85-134.21) |
| protein total decreased | Investigations | 10 | 41.21 (22.15-76.66) |
| autonomic neuropathy | Nervous system disorders | 3 | 41 (13.17-127.59) |
| neutrophil count decreased | Investigations | 103 | 39.21 (32.47-47.35) |
| platelet transfusion | Surgical and medical procedures | 3 | 39.08 (12.56-121.6) |
| ovarian cancer metastatic | Reproductive system and breast disorders | 3 | 37.43 (12.03-116.44) |
| haematotoxicity | Blood and lymphatic system disorders | 23 | 36.56 (24.32-54.97) |
| red blood cell count decreased | Investigations | 62 | 33.58 (26.26-42.93) |
| ocular vascular disorder | Eye disorders | 3 | 33.07 (10.64-102.83) |
| blood phosphorus increased | Investigations | 5 | 29.68 (12.33-71.4) |
| vith nerve paralysis | Nervous system disorders | 3 | 27.76 (8.93-86.27) |
| hypoproteinaemia | Hepatobiliary disorders | 3 | 26.92 (8.66-83.64) |
| blood chloride decreased | Investigations | 5 | 26.01 (10.82-62.57) |
| ileus | Gastrointestinal disorders | 22 | 24.33 (16.04-36.9) |
| packed red blood cell transfusion | Surgical and medical procedures | 3 | 22.26 (7.17-69.13) |
| carbohydrate antigen 125 increased | Investigations | 6 | 21.37 (9.6-47.6) |
| blood culture positive | Investigations | 6 | 20.81 (9.35-46.34) |
| neutropenic sepsis | Blood and lymphatic system disorders | 12 | 20.6 (11.71-36.26) |
| radiation pneumonitis | Respiratory, thoracic and mediastinal disorders | 3 | 20.33 (6.55-63.13) |
| conjunctival hyperaemia | Eye disorders | 6 | 20.24 (9.09-45.06) |
| retinopathy | Vascular disorders | 7 | 20.23 (9.65-42.45) |
| metastases to meninges | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 3 | 20.11 (6.48-62.45) |
| hospice care | Surgical and medical procedures | 13 | 19.75 (11.47-33.98) |
| aspergillosis | Infections and infestations | 3 | 18 (5.8-55.87) |
| hydronephrosis | Renal and urinary disorders | 10 | 17.75 (9.55-32.97) |
| large intestine perforation | Injury, poisoning and procedural complications | 9 | 16.73 (8.71-32.14) |
| renal tubular disorder | Renal and urinary disorders | 4 | 16.43 (6.16-43.8) |
| pulmonary toxicity | Respiratory, thoracic and mediastinal disorders | 8 | 16.07 (8.04-32.12) |
| white blood cell count decreased | Investigations | 127 | 16.05 (13.56-18.99) |
| conjunctival haemorrhage | Eye disorders | 6 | 15.96 (7.17-35.53) |
| febrile neutropenia | General disorders and administration site conditions | 63 | 15.79 (12.38-20.13) |
| cardiac dysfunction | Cardiac disorders | 3 | 15.61 (5.03-48.44) |
| metastases to central nervous system | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 15 | 15.59 (9.41-25.83) |
| cerebellar syndrome | Nervous system disorders | 3 | 15.56 (5.01-48.29) |
| venous thrombosis | Vascular disorders | 5 | 14.95 (6.22-35.93) |
| rash vesicular | Skin and subcutaneous tissue disorders | 5 | 14.69 (6.11-35.3) |
| platelet count decreased | Investigations | 113 | 14.62 (12.23-17.49) |
| protein urine present | Investigations | 5 | 14.43 (6.01-34.67) |
| pyelonephritis | Renal and urinary disorders | 8 | 13.62 (6.81-27.21) |
| anaemia | Blood and lymphatic system disorders | 187 | 13.43 (11.72-15.39) |
| pulmonary haemorrhage | Vascular disorders | 9 | 13.19 (6.87-25.33) |
| disease progression | General disorders and administration site conditions | 123 | 12.9 (10.87-15.31) |
| pancytopenia | Blood and lymphatic system disorders | 50 | 12.45 (9.47-16.37) |
| performance status decreased | General disorders and administration site conditions | 5 | 12.45 (5.18-29.9) |
| blood test abnormal | Investigations | 12 | 12.44 (7.07-21.88) |
| thrombocytopenia | Blood and lymphatic system disorders | 101 | 12.36 (10.22-14.95) |
| blood lactic acid increased | Investigations | 5 | 12.21 (5.08-29.34) |
| orthopnoea | Respiratory, thoracic and mediastinal disorders | 3 | 12.2 (3.93-37.86) |
| hypomagnesaemia | Metabolism and nutrition disorders | 12 | 12.19 (6.93-21.43) |
| hyperammonaemia | Hepatobiliary disorders | 5 | 11.85 (4.93-28.46) |
| bone marrow disorder | Blood and lymphatic system disorders | 3 | 11.76 (3.79-36.46) |
| deafness neurosensory | Nervous system disorders | 3 | 11.57 (3.73-35.9) |
| optic ischaemic neuropathy | Eye disorders | 3 | 11.31 (3.65-35.09) |
| escherichia infection | Infections and infestations | 6 | 11.1 (4.99-24.69) |
| posterior reversible encephalopathy syndrome | Nervous system disorders | 8 | 10.7 (5.35-21.37) |
| blood urea increased | Investigations | 14 | 10.41 (6.18-17.56) |
| hepatic lesion | Hepatobiliary disorders | 3 | 9.86 (3.18-30.58) |
| papule | Skin and subcutaneous tissue disorders | 4 | 9.86 (3.7-26.26) |
| mucosal inflammation | General disorders and administration site conditions | 18 | 9.81 (6.19-15.54) |
| gastrointestinal toxicity | Gastrointestinal disorders | 3 | 9.7 (3.13-30.09) |
| neutropenia | Blood and lymphatic system disorders | 86 | 9.57 (7.78-11.77) |
| leukopenia | Blood and lymphatic system disorders | 34 | 9.24 (6.62-12.9) |
| recurrent cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 3 | 9.2 (2.97-28.54) |
| lymphopenia | Blood and lymphatic system disorders | 9 | 9.11 (4.75-17.5) |
| blood albumin decreased | Investigations | 5 | 8.99 (3.74-21.59) |
| ileus paralytic | Gastrointestinal disorders | 3 | 8.8 (2.84-27.29) |
| failure to thrive | Pregnancy, puerperium and perinatal conditions | 4 | 8.64 (3.24-23.03) |
| periorbital oedema | Immune system disorders | 4 | 8.48 (3.18-22.59) |
| oesophageal pain | Gastrointestinal disorders | 3 | 8.41 (2.71-26.07) |
| blood creatine increased | Investigations | 3 | 8.14 (2.63-25.25) |
| ascites | Cardiac disorders | 18 | 8.05 (5.08-12.75) |
| gastrointestinal perforation | Gastrointestinal disorders | 3 | 8.03 (2.59-24.9) |
| metastatic neoplasm | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 3 | 7.9 (2.55-24.49) |
| neoplasm progression | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 24 | 7.89 (5.3-11.75) |
| malignant neoplasm progression | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 57 | 7.67 (5.94-9.91) |
| blood lactate dehydrogenase increased | Investigations | 9 | 7.6 (3.96-14.59) |
| blood magnesium decreased | Investigations | 4 | 7.58 (2.85-20.19) |
| hypotonia | Nervous system disorders | 7 | 7.34 (3.5-15.38) |
| atelectasis | Respiratory, thoracic and mediastinal disorders | 5 | 7.27 (3.03-17.45) |
| haemodialysis | Surgical and medical procedures | 7 | 7.15 (3.41-14.99) |
| ovarian cancer | Reproductive system and breast disorders | 7 | 6.91 (3.3-14.49) |
| full blood count decreased | Investigations | 9 | 6.89 (3.59-13.23) |
| drug toxicity | Injury, poisoning and procedural complications | 13 | 6.88 (4-11.84) |
| haemoglobin decreased | Investigations | 50 | 6.66 (5.07-8.76) |
| interstitial lung disease | Immune system disorders | 22 | 6.47 (4.27-9.8) |
| metastases to bone | Musculoskeletal and connective tissue disorders | 7 | 6.43 (3.07-13.47) |
| haematocrit decreased | Investigations | 10 | 6.4 (3.45-11.88) |
| hypoalbuminaemia | Hepatobiliary disorders | 3 | 6.37 (2.05-19.75) |
| ischaemia | Vascular disorders | 3 | 6.35 (2.05-19.69) |
| blood sodium decreased | Investigations | 9 | 6.35 (3.31-12.19) |
| cholestasis | Hepatobiliary disorders | 8 | 6.34 (3.17-12.67) |
| septic shock | Vascular disorders | 18 | 6.31 (3.98-9.99) |
| pleural effusion | Respiratory, thoracic and mediastinal disorders | 29 | 6.17 (4.3-8.85) |
| platelet count increased | Investigations | 6 | 6.15 (2.77-13.69) |
| hydrocephalus | Nervous system disorders | 3 | 6.13 (1.98-19.02) |
| lipase increased | Investigations | 4 | 6.11 (2.29-16.26) |
| diarrhoea haemorrhagic | Gastrointestinal disorders | 4 | 6.05 (2.27-16.1) |
| hypoxia | Respiratory, thoracic and mediastinal disorders | 15 | 6.02 (3.63-9.97) |
| small intestinal obstruction | Gastrointestinal disorders | 5 | 6.01 (2.5-14.42) |
| bone marrow failure | Blood and lymphatic system disorders | 12 | 6 (3.42-10.56) |
| tachypnoea | Respiratory, thoracic and mediastinal disorders | 6 | 5.83 (2.62-12.97) |
| necrosis | General disorders and administration site conditions | 3 | 5.82 (1.88-18.05) |
| general physical health deterioration | General disorders and administration site conditions | 43 | 5.75 (4.28-7.73) |
| flank pain | General disorders and administration site conditions | 4 | 5.7 (2.14-15.19) |
| encephalitis | Infections and infestations | 3 | 5.61 (1.81-17.38) |
| acute respiratory distress syndrome | Immune system disorders | 8 | 5.59 (2.8-11.16) |
| dehydration | Metabolism and nutrition disorders | 54 | 5.56 (4.28-7.24) |
| hyponatraemia | Metabolism and nutrition disorders | 24 | 5.5 (3.69-8.18) |
| cyst | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 5 | 5.46 (2.27-13.11) |
| acute myeloid leukaemia | Blood and lymphatic system disorders | 7 | 5.43 (2.59-11.38) |
| eyelid oedema | Immune system disorders | 6 | 5.39 (2.42-11.98) |
| retinal detachment | Injury, poisoning and procedural complications | 4 | 5.31 (2-14.15) |
| agranulocytosis | Blood and lymphatic system disorders | 6 | 5.22 (2.35-11.61) |
| conjunctivitis | Eye disorders | 6 | 5.14 (2.31-11.44) |
| petechiae | Blood and lymphatic system disorders | 4 | 5.03 (1.89-13.39) |
| electrolyte imbalance | Metabolism and nutrition disorders | 4 | 4.98 (1.87-13.25) |
| transfusion | Surgical and medical procedures | 4 | 4.82 (1.81-12.84) |
| inappropriate antidiuretic hormone secretion | Metabolism and nutrition disorders | 4 | 4.75 (1.78-12.66) |
| diplopia | Nervous system disorders | 10 | 4.75 (2.56-8.81) |
| rash pustular | Skin and subcutaneous tissue disorders | 3 | 4.74 (1.53-14.7) |
| blood bilirubin increased | Investigations | 11 | 4.73 (2.62-8.52) |
| lymphocyte count decreased | Investigations | 6 | 4.71 (2.12-10.47) |
| blood potassium increased | Investigations | 6 | 4.7 (2.12-10.46) |
| dermatitis | Skin and subcutaneous tissue disorders | 6 | 4.7 (2.11-10.45) |
| anorexia | Metabolism and nutrition disorders | 82 | 4.68 (3.79-5.79) |
| metastases to liver | Hepatobiliary disorders | 6 | 4.67 (2.1-10.38) |
| blood calcium decreased | Investigations | 4 | 4.63 (1.74-12.33) |
| hiccups | Respiratory, thoracic and mediastinal disorders | 3 | 4.59 (1.48-14.21) |
| retinal haemorrhage | Eye disorders | 3 | 4.49 (1.45-13.91) |
| fistula | Musculoskeletal and connective tissue disorders | 3 | 4.43 (1.43-13.72) |
| malnutrition | Metabolism and nutrition disorders | 3 | 4.41 (1.42-13.67) |
| intestinal perforation | Gastrointestinal disorders | 4 | 4.4 (1.65-11.73) |
| c-reactive protein increased | Investigations | 9 | 4.4 (2.29-8.45) |
| second primary malignancy | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 3 | 4.37 (1.41-13.55) |
| urine output decreased | Investigations | 3 | 4.36 (1.41-13.52) |
| multi-organ failure | General disorders and administration site conditions | 9 | 4.35 (2.27-8.36) |
| pneumothorax | Respiratory, thoracic and mediastinal disorders | 5 | 4.34 (1.81-10.43) |
| mental status changes | Psychiatric disorders | 11 | 4.18 (2.32-7.54) |
| aspartate aminotransferase increased | Investigations | 18 | 4.17 (2.63-6.61) |
| sinus tachycardia | Cardiac disorders | 5 | 4.09 (1.7-9.82) |
| peritonitis | Infections and infestations | 5 | 4.05 (1.69-9.73) |
| polyneuropathy | Nervous system disorders | 3 | 4.02 (1.3-12.47) |
| myelodysplastic syndrome | Blood and lymphatic system disorders | 5 | 3.96 (1.65-9.49) |
| circulatory collapse | Vascular disorders | 6 | 3.87 (1.74-8.61) |
| sepsis | Infections and infestations | 32 | 3.87 (2.74-5.45) |
| respiratory failure | Metabolism and nutrition disorders | 23 | 3.83 (2.55-5.75) |
| blood alkaline phosphatase increased | Investigations | 8 | 3.77 (1.89-7.53) |
| hypokalaemia | Metabolism and nutrition disorders | 12 | 3.74 (2.13-6.57) |
| haematuria | Renal and urinary disorders | 11 | 3.7 (2.05-6.67) |
| sudden death | General disorders and administration site conditions | 4 | 3.7 (1.39-9.85) |
| intestinal obstruction | Gastrointestinal disorders | 9 | 3.66 (1.91-7.02) |
| hepatic failure | Hepatobiliary disorders | 10 | 3.64 (1.96-6.76) |
| blood creatinine increased | Investigations | 19 | 3.61 (2.31-5.65) |
| hypophagia | Metabolism and nutrition disorders | 6 | 3.59 (1.62-7.99) |
| respiratory distress | Respiratory, thoracic and mediastinal disorders | 8 | 3.53 (1.77-7.06) |
| pyrexia | General disorders and administration site conditions | 89 | 3.53 (2.88-4.33) |
| eating disorder | Metabolism and nutrition disorders | 6 | 3.49 (1.57-7.77) |
| alanine aminotransferase increased | Investigations | 17 | 3.36 (2.09-5.4) |
| blood potassium decreased | Investigations | 7 | 3.34 (1.59-6.99) |
| bacterial infection | Infections and infestations | 4 | 3.29 (1.23-8.75) |
| hemiparesis | Nervous system disorders | 5 | 3.28 (1.37-7.88) |
| haematemesis | Gastrointestinal disorders | 7 | 3.26 (1.56-6.84) |
| body temperature increased | Investigations | 5 | 3.21 (1.34-7.7) |
| blood count abnormal | Investigations | 6 | 3.15 (1.42-7.01) |
| renal failure acute | Renal and urinary disorders | 14 | 3.15 (1.87-5.3) |
| product use in unapproved indication | Injury, poisoning and procedural complications | 47 | 3.06 (2.31-4.06) |
| vomiting | Gastrointestinal disorders | 115 | 3.04 (2.55-3.64) |
| cellulitis | Infections and infestations | 11 | 2.92 (1.62-5.27) |
| pneumonitis | Respiratory, thoracic and mediastinal disorders | 5 | 2.83 (1.18-6.8) |
| disorientation | Psychiatric disorders | 10 | 2.78 (1.5-5.17) |
| death | General disorders and administration site conditions | 247 | 2.77 (2.47-3.12) |
| abdominal pain | Gastrointestinal disorders | 47 | 2.71 (2.04-3.6) |
| pneumonia | Respiratory, thoracic and mediastinal disorders | 63 | 2.61 (2.04-3.32) |
| nausea | Gastrointestinal disorders | 169 | 2.6 (2.25-3.01) |
| lethargy | General disorders and administration site conditions | 13 | 2.51 (1.46-4.32) |
| ill-defined disorder | General disorders and administration site conditions | 10 | 2.49 (1.34-4.63) |
| confusional state | Psychiatric disorders | 34 | 2.44 (1.75-3.41) |
| white blood cell count increased | Investigations | 7 | 2.37 (1.13-4.96) |
| pulmonary embolism | Vascular disorders | 22 | 2.35 (1.55-3.56) |
| epistaxis | Vascular disorders | 14 | 2.3 (1.37-3.88) |
| tachycardia | Cardiac disorders | 16 | 2.22 (1.36-3.61) |
| dyspnoea | Respiratory, thoracic and mediastinal disorders | 97 | 2.19 (1.80-2.65) |
| abdominal distension | Gastrointestinal disorders | 17 | 2.19 (1.36-3.52) |
| lung neoplasm malignant | Respiratory, thoracic and mediastinal disorders | 10 | 2.19 (1.18-4.05) |
| asthenia | General disorders and administration site conditions | 61 | 2.15 (1.68-2.75) |
| constipation | Gastrointestinal disorders | 32 | 2.12 (1.5-2.99) |
| therapeutic response decreased | General disorders and administration site conditions | 11 | 2.03 (1.13-3.66) |
| fatigue | General disorders and administration site conditions | 117 | 2 (1.68-2.39) |
| renal failure | Renal and urinary disorders | 27 | 2 (1.38-2.91) |