

SUPPLEMENTAL TABLE: Immunotherapy ch14.18 + GM-CSF + IL-2+ Isotretinoin

ANBL0931 Reporting Period 1: Immunotherapy ch14.18 + GM-CSF + Isotretinoin

| Non-Targeted Toxicities              |  | Grade 1 or 2<br>(N = 104) |               |
|--------------------------------------|--|---------------------------|---------------|
|                                      |  | count                     | Incidence (%) |
| Primary Category                     |  |                           |               |
| Blood and lymphatic system disorders | 13200-Anemia   | 85                        | 81.7          |
|                                      | 17200-Blood and lymphatic system disorders - Other specify | 1                         | 1.0           |
|                                      | 25800-Disseminated intravascular coagulation               | 1                         | 1.0           |
| Cardiac disorders                    | 20100-Cardiac disorders - Other specify                    | 3                         | 2.9           |
|                                      | 21300-Chest pain - cardiac                                 | 2                         | 1.9           |
|                                      | 63100-Pericardial effusion                                 | 1                         | 1.0           |
|                                      | 74200-Sinus bradycardia                                    | 4                         | 3.8           |
|                                      | 74500-Sinus tachycardia                                    | 64                        | 61.5          |
|                                      | 78900-Supraventricular tachycardia                         | 1                         | 1.0           |
|                                      | 81400-Tricuspid valve disease                              | 1                         | 1.0           |
| Ear and labyrinth disorders          | 28000-Ear pain   | 1                         | 1.0           |
|                                      | 31600-External ear pain                                    | 1                         | 1.0           |
| Endocrine disorders                  | 41900-Hyperparathyroidism                                  | 1                         | 1.0           |
|                                      | 43800-Hypothyroidism                                       | 1                         | 1.0           |
| Eye disorders                        | 17800-Blurred vision                                       | 2                         | 1.9           |
|                                      | 26000-Dry eye  | 1                         | 1.0           |
|                                      | 31900-Eye disorders - Other specify                        | 6                         | 5.8           |
|                                      | 32100-Eye pain   | 1                         | 1.0           |
|                                      | 59300-Optic nerve disorder                                 | 1                         | 1.0           |

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| Non-Targeted Toxicities    |                             | Grade 1 or 2<br>(N = 104) |               |
|----------------------------|-----------------------------|---------------------------|---------------|
|                            |                             | count                     | Incidence (%) |
| Gastrointestinal disorders | 10100-Abdominal distension  | 3                         | 2.9           |
|                            | 10300-Abdominal pain        | 46                        | 44.2          |
|                            | 12800-Anal pain             | 1                         | 1.0           |
|                            | 21200-Cheilitis             | 7                         | 6.7           |
|                            | 23400-Constipation          | 14                        | 13.5          |
|                            | 25700-Diarrhea              | 28                        | 26.9          |
|                            | 29400-Enterocolitis         | 3                         | 2.9           |
|                            | 34400-Flatulence            | 2                         | 1.9           |
|                            | 36900-Gastrointestinal pain | 1                         | 1.0           |
|                            | 57600-Nausea                | 38                        | 36.5          |
|                            | 59700-Oral pain             | 1                         | 1.0           |
|                            | 77900-Stomach pain          | 2                         | 1.9           |
|                            | 87900-Vomiting              | 42                        | 40.4          |

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| Non-Targeted Toxicities                              |  | Grade 1 or 2<br>(N = 104) |               |
|--|--|---------------------------|---------------|
|  |  | count                     | Incidence (%) |
| General disorders and administration site conditions | 21500-Chills   | 11                        | 10.6          |
|  | 28200-Edema face   | 18                        | 17.3          |
|  | 28300-Edema limbs  | 11                        | 10.6          |
|  | 28400-Edema trunk  | 1                         | 1.0           |
|  | 32500-Facial pain  | 1                         | 1.0           |
|  | 33200-Fatigue  | 9                         | 8.7           |
|  | 33900-Fever  | 93                        | 89.4          |
|  | 34600-Flu like symptoms  | 1                         | 1.0           |
|  | 35000-Gait disturbance   | 1                         | 1.0           |
|  | 37200-General disorders and administration site conditions - Other specify | 1                         | 1.0           |
|  | 43700-Hypothermia  | 1                         | 1.0           |
|  | 45000-Infusion related reaction  | 2                         | 1.9           |
|  | 45200-Injection site reaction  | 2                         | 1.9           |
|  | 48700-Irritability   | 14                        | 13.5          |
|  | 52800-Localized edema  | 4                         | 3.8           |
|  | 54000-Malaise  | 1                         | 1.0           |
|  | 58600-Non-cardiac chest pain   | 2                         | 1.9           |
|  | 60600-Pain   | 55                        | 52.9          |
| Immune system disorders                              | 12000-Allergic reaction  | 19                        | 18.3          |
| Infections and infestations                          | 20500-Catheter related infection   | 1                         | 1.0           |
|  | 29500-Enterocolitis infectious   | 2                         | 1.9           |
|  | 30400-Esophageal infection   | 1                         | 1.0           |
|  | 44800-Infections and infestations - Other specify                          | 5                         | 4.8           |
|  | 57200-Nail infection   | 1                         | 1.0           |
|  | 60100-Otitis media   | 1                         | 1.0           |
|  | 72600-Rhinitis infective   | 2                         | 1.9           |
|  | 75200-Skin infection   | 1                         | 1.0           |
|  | 82300-Upper respiratory infection  | 1                         | 1.0           |
|  | 83100-Urinary tract infection  | 1                         | 1.0           |

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| Non-Targeted Toxicities                        |   | Grade 1 or 2<br>(N = 104) |               |
|--|---|---------------------------|---------------|
|  |   | count                     | Incidence (%) |
| Injury, poisoning and procedural complications | 19400-Bruising  | 4                         | 3.8           |
|  | 45700-Injury poisoning and procedural complications - Other specify | 1                         | 1.0           |
|  | 86400-Vascular access complication                                  | 4                         | 3.8           |
| Investigations                                 | 10900-Activated partial thromboplastin time prolonged               | 2                         | 1.9           |
|  | 11600-Alanine aminotransferase increased                            | 65                        | 62.5          |
|  | 11800-Alkaline phosphatase increased                                | 7                         | 6.7           |
|  | 15000-Aspartate aminotransferase increased                          | 54                        | 51.9          |
|  | 17400-Blood bilirubin increased                                     | 5                         | 4.8           |
|  | 21700-Cholesterol high  | 1                         | 1.0           |
|  | 24100-Creatinine increased  | 11                        | 10.6          |
|  | 37500-GGT increased   | 13                        | 12.5          |
|  | 39400-Hemoglobin increased  | 3                         | 2.9           |
|  | 53700-Lymphocyte count decreased                                    | 76                        | 73.1          |
|  | 58300-Neutrophil count decreased                                    | 22                        | 21.2          |
|  | 65800-Platelet count decreased                                      | 71                        | 68.3          |
|  | 88200-Weight gain   | 23                        | 22.1          |
|  | 88300-Weight loss   | 6                         | 5.8           |
|  | 88500-White blood cell decreased                                    | 68                        | 65.4          |

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| Non-Targeted Toxicities                         |  | Grade 1 or 2<br>(N = 104) |               |
|---|--|---------------------------|---------------|
|   |  | count                     | Incidence (%) |
| Metabolism and nutrition disorders              | 10700-Acidosis   | 2                         | 1.9           |
|   | 13500-Anorexia   | 17                        | 16.3          |
|   | 24700-Dehydration  | 2                         | 1.9           |
|   | 41300-Hypercalcemia  | 8                         | 7.7           |
|   | 41400-Hyperglycemia  | 27                        | 26.0          |
|   | 41600-Hyperkalemia   | 7                         | 6.7           |
|   | 41700-Hypermagnesemia                                      | 6                         | 5.8           |
|   | 41800-Hyponatremia   | 3                         | 2.9           |
|   | 42400-Hypertriglyceridemia                                 | 51                        | 49.0          |
|   | 42600-Hypoalbuminemia                                      | 92                        | 88.5          |
|   | 42700-Hypocalcemia   | 71                        | 68.3          |
|   | 42900-Hypoglycemia   | 14                        | 13.5          |
|   | 43100-Hypokalemia  | 55                        | 52.9          |
|   | 43200-Hypomagnesemia                                       | 22                        | 21.2          |
|   | 43300-Hyponatremia   | 71                        | 68.3          |
|   | 43500-Hypophosphatemia                                     | 26                        | 25.0          |
|   | 54900-Metabolism and nutrition disorders - Other   specify | 2                         | 1.9           |
| Musculoskeletal and connective tissue disorders | 14700-Arthralgia   | 2                         | 1.9           |
|   | 16200-Back pain  | 11                        | 10.6          |
|   | 18200-Bone pain  | 2                         | 1.9           |
|   | 19700-Buttock pain   | 1                         | 1.0           |
|   | 21400-Chest wall pain                                      | 3                         | 2.9           |
|   | 37300-Generalized muscle weakness                          | 1                         | 1.0           |
|   | 57800-Neck pain  | 4                         | 3.8           |
|   | 60700-Pain in extremity                                    | 22                        | 21.2          |

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| Non-Targeted Toxicities                  |   | Grade 1 or 2<br>(N = 104) |               |
|--|---|---------------------------|---------------|
|  |   | count                     | Incidence (%) |
| Nervous system disorders                 | 11500-Akathisia                                   | 1                         | 1.0           |
|  | 22000-Cognitive disturbance                       | 1                         | 1.0           |
|  | 38800-Headache                                    | 9                         | 8.7           |
|  | 55400-Movements involuntary                       | 1                         | 1.0           |
|  | 58200-Neuralgia                                   | 3                         | 2.9           |
|  | 62100-Paresthesia                                 | 2                         | 1.9           |
|  | 64100-Peripheral sensory neuropathy               | 2                         | 1.9           |
|  | 76700-Somnolence                                  | 2                         | 1.9           |
|  | 81300-Tremor                                      | 1                         | 1.0           |
| Psychiatric disorders                    | 11400-Agitation                                   | 7                         | 6.7           |
|  | 13700-Anxiety                                     | 4                         | 3.8           |
|  | 23000-Confusion                                   | 1                         | 1.0           |
|  | 25400-Depression                                  | 2                         | 1.9           |
|  | 38500-Hallucinations                              | 3                         | 2.9           |
|  | 45900-Insomnia                                    | 3                         | 2.9           |
|  | 68500-Psychiatric disorders - Other specify       | 2                         | 1.9           |
| Renal and urinary disorders              | 39300-Hematuria                                   | 13                        | 12.5          |
|  | 68300-Proteinuria                                 | 19                        | 18.3          |
|  | 71000-Renal and urinary disorders - Other specify | 1                         | 1.0           |
|  | 83000-Urinary retention                           | 17                        | 16.3          |
|  | 83300-Urinary tract pain                          | 3                         | 2.9           |
|  | 83500-Urine discoloration                         | 2                         | 1.9           |
| Reproductive system and breast disorders | 62900-Penile pain                                 | 1                         | 1.0           |

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| Non-Targeted Toxicities                         |  | Grade 1 or 2<br>(N = 104) |               |
|---|--|---------------------------|---------------|
|   |  | count                     | Incidence (%) |
| Respiratory, thoracic and mediastinal disorders | 12100-Allergic rhinitis  | 6                         | 5.8           |
|   | 15400-Atelectasis  | 2                         | 1.9           |
|   | 19000-Bronchial stricture  | 1                         | 1.0           |
|   | 19300-Bronchospasm   | 5                         | 4.8           |
|   | 23800-Cough  | 30                        | 28.8          |
|   | 27800-Dyspnea  | 1                         | 1.0           |
|   | 29700-Epistaxis  | 2                         | 1.9           |
|   | 41000-Hoarseness   | 1                         | 1.0           |
|   | 43900-Hypoxia  | 12                        | 11.5          |
|   | 57500-Nasal congestion   | 5                         | 4.8           |
|   | 65900-Pleural effusion   | 1                         | 1.0           |
|   | 66300-Pneumonitis  | 1                         | 1.0           |
|   | 66700-Postnasal drip   | 1                         | 1.0           |
|   | 67600-Productive cough   | 1                         | 1.0           |
|   | 71600-Respiratory thoracic and mediastinal disorders - Other specify | 18                        | 17.3          |
|   | 76200-Sneezing   | 3                         | 2.9           |
|   | 76800-Sore throat  | 1                         | 1.0           |
|   | 88400-Wheezing   | 3                         | 2.9           |

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| Non-Targeted Toxicities                |  | Grade 1 or 2<br>(N = 104) |               |
|--|--|---------------------------|---------------|
|  |  | count                     | Incidence (%) |
| Skin and subcutaneous tissue disorders | 12200-Alopecia   | 10                        | 9.6           |
|  | 19500-Bullous dermatitis                                     | 1                         | 1.0           |
|  | 26200-Dry skin   | 27                        | 26.0          |
|  | 29900-Erythema multiforme                                    | 2                         | 1.9           |
|  | 42300-Hypertrichosis   | 1                         | 1.0           |
|  | 63600-Periorbital edema                                      | 4                         | 3.8           |
|  | 68400-Pruritus   | 38                        | 36.5          |
|  | 69600-Rash acneiform   | 2                         | 1.9           |
|  | 69700-Rash maculo-papular                                    | 21                        | 20.2          |
|  | 74700-Skin and subcutaneous tissue disorders - Other specify | 6                         | 5.8           |
|  | 74900-Skin hyperpigmentation                                 | 1                         | 1.0           |
|  | 75000-Skin hypopigmentation                                  | 2                         | 1.9           |
|  | 75100-Skin induration  | 1                         | 1.0           |
|  | 75300-Skin ulceration  | 1                         | 1.0           |
|  | 84100-Urticaria  | 17                        | 16.3          |
| Vascular disorders                     | 19800-Capillary leak syndrome                                | 24                        | 23.1          |
|  | 34700-Flushing   | 2                         | 1.9           |
|  | 41100-Hot flashes  | 2                         | 1.9           |
|  | 42100-Hypertension   | 29                        | 27.9          |
|  | 43600-Hypotension  | 58                        | 55.8          |
|  | 79600-Thromboembolic event                                   | 1                         | 1.0           |
|  | 86500-Vascular disorders - Other specify                     | 1                         | 1.0           |



## ANBL0931 Reporting Period 2: Immunotherapy ch14.18 + IL-2 + Isotretinoin

| Non-Targeted Toxicities              |   | Grade 1 or 2<br>(N = 100) |               |
|--------------------------------------|---|---------------------------|---------------|
|                                      |   | count                     | Incidence (%) |
| Primary Category                     |   |                           |               |
| Blood and lymphatic system disorders | 13200-Anemia                                      | 85                        | 85.0          |
| Cardiac disorders                    | 61000-Palpitations                                | 2                         | 2.0           |
|                                      | 74200-Sinus bradycardia                           | 2                         | 2.0           |
|                                      | 74500-Sinus tachycardia                           | 64                        | 64.0          |
|                                      | 78900-Supraventricular tachycardia                | 1                         | 1.0           |
| Ear and labyrinth disorders          | 27900-Ear and labyrinth disorders - Other specify | 1                         | 1.0           |
| Endocrine disorders                  | 42200-Hyperthyroidism                             | 1                         | 1.0           |
| Eye disorders                        | 17800-Blurred vision                              | 3                         | 3.0           |
|                                      | 31900-Eye disorders - Other specify               | 4                         | 4.0           |
|                                      | 32100-Eye pain                                    | 4                         | 4.0           |
| Gastrointestinal disorders           | 10100-Abdominal distension                        | 9                         | 9.0           |
|                                      | 10300-Abdominal pain                              | 32                        | 32.0          |
|                                      | 12800-Anal pain                                   | 1                         | 1.0           |
|                                      | 17100-Bloating                                    | 1                         | 1.0           |
|                                      | 21200-Cheilitis                                   | 4                         | 4.0           |
|                                      | 23400-Constipation                                | 14                        | 14.0          |
|                                      | 25700-Diarrhea                                    | 34                        | 34.0          |
|                                      | 27500-Dyspepsia                                   | 1                         | 1.0           |
|                                      | 27600-Dysphagia                                   | 2                         | 2.0           |
|                                      | 29400-Enterocolitis                               | 1                         | 1.0           |
|                                      | 36400-Gastritis                                   | 1                         | 1.0           |
|                                      | 36500-Gastroesophageal reflux disease             | 1                         | 1.0           |
|                                      | 36700-Gastrointestinal disorders - Other specify  | 2                         | 2.0           |
|                                      | 37600-Gingival pain                               | 1                         | 1.0           |
|                                      | 39800-Hemorrhoidal hemorrhage                     | 1                         | 1.0           |
|                                      | 57600-Nausea                                      | 33                        | 33.0          |
|                                      | 59700-Oral pain                                   | 3                         | 3.0           |
|                                      | 77900-Stomach pain                                | 2                         | 2.0           |
|                                      | 80200-Toothache                                   | 1                         | 1.0           |
|                                      | 87900-Vomiting                                    | 44                        | 44.0          |

## ANBL0931 Reporting Period 2: Immunotherapy ch14.18 + IL-2 + Isotretinoin

| Non-Targeted Toxicities                              |  | Grade 1 or 2<br>(N = 100) |               |
|--|--|---------------------------|---------------|
|  |  | count                     | Incidence (%) |
| General disorders and administration site conditions | 21500-Chills   | 8                         | 8.0           |
|  | 28200-Edema face   | 32                        | 32.0          |
|  | 28300-Edema limbs  | 21                        | 21.0          |
|  | 28400-Edema trunk  | 3                         | 3.0           |
|  | 33200-Fatigue  | 18                        | 18.0          |
|  | 33900-Fever  | 89                        | 89.0          |
|  | 34600-Flu like symptoms  | 2                         | 2.0           |
|  | 35000-Gait disturbance   | 2                         | 2.0           |
|  | 37200-General disorders and administration site conditions - Other specify | 1                         | 1.0           |
|  | 45000-Infusion related reaction  | 1                         | 1.0           |
|  | 48700-Irritability   | 16                        | 16.0          |
|  | 52800-Localized edema  | 2                         | 2.0           |
|  | 54000-Malaise  | 2                         | 2.0           |
|  | 60600-Pain   | 50                        | 50.0          |
| Immune system disorders                              | 12000-Allergic reaction  | 21                        | 21.0          |
| Infections and infestations                          | 20500-Catheter related infection   | 2                         | 2.0           |
|  | 29500-Enterocolitis infectious   | 2                         | 2.0           |
|  | 44800-Infections and infestations - Other specify                          | 3                         | 3.0           |
|  | 62200-Paronychia   | 1                         | 1.0           |
|  | 65200-Pharyngitis  | 1                         | 1.0           |
|  | 74600-Sinusitis  | 1                         | 1.0           |
|  | 75200-Skin infection   | 2                         | 2.0           |
|  | 76000-Small intestine infection  | 1                         | 1.0           |
|  | 82300-Upper respiratory infection  | 3                         | 3.0           |
|  | 83100-Urinary tract infection  | 2                         | 2.0           |
| Injury, poisoning and procedural complications       | 45700-Injury poisoning and procedural complications - Other specify        | 1                         | 1.0           |
|  | 86400-Vascular access complication   | 2                         | 2.0           |

**ANBL0931 Reporting Period 2: Immunotherapy ch14.18 + IL-2 + Isotretinoin**

| Non-Targeted Toxicities |   | Grade 1 or 2<br>(N = 100) |               |
|-------------------------|---|---------------------------|---------------|
|                         |   | count                     | Incidence (%) |
| Investigations          | 10900-Activated partial thromboplastin time prolonged | 1                         | 1.0           |
|                         | 11600-Alanine aminotransferase increased              | 64                        | 64.0          |
|                         | 11800-Alkaline phosphatase increased                  | 9                         | 9.0           |
|                         | 15000-Aspartate aminotransferase increased            | 72                        | 72.0          |
|                         | 17400-Blood bilirubin increased                       | 10                        | 10.0          |
|                         | 24100-Creatinine increased                            | 15                        | 15.0          |
|                         | 37500-GGT increased                                   | 8                         | 8.0           |
|                         | 39400-Hemoglobin increased                            | 5                         | 5.0           |
|                         | 45800-INR increased                                   | 2                         | 2.0           |
|                         | 48400-Investigations - Other specify                  | 1                         | 1.0           |
|                         | 53700-Lymphocyte count decreased                      | 80                        | 80.0          |
|                         | 53800-Lymphocyte count increased                      | 1                         | 1.0           |
|                         | 58300-Neutrophil count decreased                      | 60                        | 60.0          |
|                         | 65800-Platelet count decreased                        | 79                        | 79.0          |
|                         | 88200-Weight gain                                     | 34                        | 34.0          |
|                         | 88300-Weight loss                                     | 10                        | 10.0          |
|                         | 88500-White blood cell decreased                      | 74                        | 74.0          |

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| Non-Targeted Toxicities                         |  | Grade 1 or 2<br>(N = 100) |               |
|---|--|---------------------------|---------------|
|   |  | count                     | Incidence (%) |
| Metabolism and nutrition disorders              | 10700-Acidosis   | 1                         | 1.0           |
|   | 13500-Anorexia   | 17                        | 17.0          |
|   | 24700-Dehydration  | 3                         | 3.0           |
|   | 41300-Hypercalcemia  | 10                        | 10.0          |
|   | 41400-Hyperglycemia  | 36                        | 36.0          |
|   | 41600-Hyperkalemia   | 11                        | 11.0          |
|   | 41700-Hypermagnesemia  | 14                        | 14.0          |
|   | 41800-Hyponatremia   | 4                         | 4.0           |
|   | 42400-Hypertriglyceridemia   | 32                        | 32.0          |
|   | 42600-Hypoalbuminemia  | 89                        | 89.0          |
|   | 42700-Hypocalcemia   | 77                        | 77.0          |
|   | 42900-Hypoglycemia   | 21                        | 21.0          |
|   | 43100-Hypokalemia  | 66                        | 66.0          |
|   | 43200-Hypomagnesemia   | 20                        | 20.0          |
|   | 43300-Hyponatremia   | 78                        | 78.0          |
|   | 43500-Hypophosphatemia   | 52                        | 52.0          |
|   | 54900-Metabolism and nutrition disorders - Other specify             | 1                         | 1.0           |
| Musculoskeletal and connective tissue disorders | 16200-Back pain  | 11                        | 11.0          |
|   | 19700-Buttock pain   | 1                         | 1.0           |
|   | 21400-Chest wall pain  | 1                         | 1.0           |
|   | 55900-Muscle weakness lower limb                                     | 1                         | 1.0           |
|   | 56300-Musculoskeletal and connective tissue disorder - Other specify | 2                         | 2.0           |
|   | 56500-Myalgia  | 4                         | 4.0           |
|   | 57800-Neck pain  | 7                         | 7.0           |
|   | 60700-Pain in extremity  | 22                        | 22.0          |

**ANBL0931 Reporting Period 2: Immunotherapy ch14.18 + IL-2 + Isotretinoin**

| Non-Targeted Toxicities                  |   | Grade 1 or 2<br>(N = 100) |               |
|--|---|---------------------------|---------------|
|  |   | count                     | Incidence (%) |
| Nervous system disorders                 | 25300-Depressed level of consciousness      | 1                         | 1.0           |
|  | 25900-Dizziness                             | 2                         | 2.0           |
|  | 38800-Headache                              | 11                        | 11.0          |
|  | 51800-Lethargy                              | 2                         | 2.0           |
|  | 54400-Memory impairment                     | 1                         | 1.0           |
|  | 58200-Neuralgia                             | 2                         | 2.0           |
|  | 64100-Peripheral sensory neuropathy         | 2                         | 2.0           |
|  | 73600-Seizure                               | 2                         | 2.0           |
|  | 76700-Somnolence                            | 2                         | 2.0           |
| Psychiatric disorders                    | 11400-Agitation                             | 11                        | 11.0          |
|  | 13700-Anxiety                               | 3                         | 3.0           |
|  | 23000-Confusion                             | 5                         | 5.0           |
|  | 38500-Hallucinations                        | 8                         | 8.0           |
|  | 45900-Insomnia                              | 4                         | 4.0           |
|  | 68500-Psychiatric disorders - Other specify | 1                         | 1.0           |
|  | 71700-Restlessness                          | 2                         | 2.0           |
| Renal and urinary disorders              | 11100-Acute kidney injury                   | 1                         | 1.0           |
|  | 21800-Chronic kidney disease                | 1                         | 1.0           |
|  | 39300-Hematuria                             | 15                        | 15.0          |
|  | 68300-Proteinuria                           | 26                        | 26.0          |
|  | 82800-Urinary frequency                     | 1                         | 1.0           |
|  | 83000-Urinary retention                     | 10                        | 10.0          |
|  | 83300-Urinary tract pain                    | 1                         | 1.0           |
|  | 83500-Urine discoloration                   | 2                         | 2.0           |
| Reproductive system and breast disorders | 37400-Genital edema                         | 1                         | 1.0           |
|  | 62600-Pelvic pain                           | 1                         | 1.0           |

**ANBL0931 Reporting Period 2: Immunotherapy ch14.18 + IL-2 + Isotretinoin**

| Non-Targeted Toxicities                         |  | Grade 1 or 2<br>(N = 100) |               |
|---|--|---------------------------|---------------|
|   |  | count                     | Incidence (%) |
| Respiratory, thoracic and mediastinal disorders | 12100-Allergic rhinitis  | 3                         | 3.0           |
|   | 15400-Atelectasis  | 3                         | 3.0           |
|   | 19300-Bronchospasm   | 2                         | 2.0           |
|   | 23800-Cough  | 37                        | 37.0          |
|   | 27800-Dyspnea  | 3                         | 3.0           |
|   | 41000-Hoarseness   | 1                         | 1.0           |
|   | 43900-Hypoxia  | 21                        | 21.0          |
|   | 57500-Nasal congestion   | 5                         | 5.0           |
|   | 65300-Pharyngolaryngeal pain   | 1                         | 1.0           |
|   | 65900-Pleural effusion   | 1                         | 1.0           |
|   | 67600-Productive cough   | 1                         | 1.0           |
|   | 68700-Pulmonary edema  | 2                         | 2.0           |
|   | 71600-Respiratory thoracic and mediastinal disorders - Other specify | 19                        | 19.0          |
|   | 72200-Retinoic acid syndrome   | 1                         | 1.0           |
|   | 76800-Sore throat  | 2                         | 2.0           |
|   | 88400-Wheezing   | 5                         | 5.0           |
| Skin and subcutaneous tissue disorders          | 12200-Alopecia   | 3                         | 3.0           |
|   | 26200-Dry skin   | 46                        | 46.0          |
|   | 29900-Erythema multiforme  | 4                         | 4.0           |
|   | 57300-Nail loss  | 1                         | 1.0           |
|   | 63600-Periorbital edema  | 5                         | 5.0           |
|   | 68400-Pruritus   | 29                        | 29.0          |
|   | 69600-Rash acneiform   | 1                         | 1.0           |
|   | 69700-Rash maculo-papular  | 24                        | 24.0          |
|   | 74700-Skin and subcutaneous tissue disorders - Other specify         | 5                         | 5.0           |
|   | 74800-Skin atrophy   | 1                         | 1.0           |
|   | 75000-Skin hypopigmentation  | 1                         | 1.0           |
|   | 84100-Urticaria  | 25                        | 25.0          |

ANBL0931 Reporting Period 2: Immunotherapy ch14.18 + IL-2 + Isotretinoin

| Non-Targeted Toxicities |  | Grade 1 or 2<br>(N = 100) |               |
|-------------------------|--|---------------------------|---------------|
|                         |  | count                     | Incidence (%) |
| Vascular disorders      | 19800-Capillary leak syndrome            | 36                        | 36.0          |
|                         | 34700-Flushing                           | 5                         | 5.0           |
|                         | 42100-Hypertension                       | 40                        | 40.0          |
|                         | 43600-Hypotension                        | 57                        | 57.0          |
|                         | 86500-Vascular disorders - Other specify | 1                         | 1.0           |

## ANBL0931 Reporting Period 3: Immunotherapy ch14.18 + GM-CSF + Isotretinoin

| Non-Targeted Toxicities              |  | Grade 1 or 2<br>(N = 98) |               |
|--------------------------------------|--|--------------------------|---------------|
|                                      |  | count                    | Incidence (%) |
| Primary Category                     |  |                          |               |
| Blood and lymphatic system disorders | 13200-Anemia   | 80                       | 81.6          |
|                                      | 17200-Blood and lymphatic system disorders - Other specify | 1                        | 1.0           |
| Cardiac disorders                    | 20100-Cardiac disorders - Other specify                    | 2                        | 2.0           |
|                                      | 63100-Pericardial effusion                                 | 1                        | 1.0           |
|                                      | 74200-Sinus bradycardia                                    | 1                        | 1.0           |
|                                      | 74500-Sinus tachycardia                                    | 56                       | 57.1          |
|                                      | 78900-Supraventricular tachycardia                         | 1                        | 1.0           |
| Eye disorders                        | 17800-Blurred vision                                       | 1                        | 1.0           |
|                                      | 31900-Eye disorders - Other specify                        | 1                        | 1.0           |
|                                      | 59300-Optic nerve disorder                                 | 1                        | 1.0           |
|                                      | 65600-Photophobia  | 2                        | 2.0           |
|                                      | 73200-Scleral disorder                                     | 1                        | 1.0           |
| Gastrointestinal disorders           | 10100-Abdominal distension                                 | 4                        | 4.1           |
|                                      | 10300-Abdominal pain                                       | 28                       | 28.6          |
|                                      | 21200-Cheilitis  | 2                        | 2.0           |
|                                      | 22100-Colitis  | 1                        | 1.0           |
|                                      | 23400-Constipation   | 12                       | 12.2          |
|                                      | 25700-Diarrhea   | 18                       | 18.4          |
|                                      | 26100-Dry mouth  | 1                        | 1.0           |
|                                      | 34400-Flatulence   | 1                        | 1.0           |
|                                      | 36500-Gastroesophageal reflux disease                      | 1                        | 1.0           |
|                                      | 36700-Gastrointestinal disorders - Other specify           | 1                        | 1.0           |
|                                      | 57600-Nausea   | 18                       | 18.4          |
|                                      | 70800-Rectal ulcer   | 1                        | 1.0           |
|                                      | 77900-Stomach pain   | 1                        | 1.0           |
|                                      | 87900-Vomiting   | 21                       | 21.4          |



**ANBL0931 Reporting Period 3: Immunotherapy ch14.18 + GM-CSF + Isotretinoin**

| Non-Targeted Toxicities                              |  | Grade 1 or 2<br>(N = 98) |               |
|--|--|--------------------------|---------------|
|  |  | count                    | Incidence (%) |
| General disorders and administration site conditions | 21500-Chills   | 2                        | 2.0           |
|  | 28200-Edema face   | 16                       | 16.3          |
|  | 28300-Edema limbs  | 7                        | 7.1           |
|  | 28400-Edema trunk  | 1                        | 1.0           |
|  | 32500-Facial pain  | 1                        | 1.0           |
|  | 33200-Fatigue  | 10                       | 10.2          |
|  | 33900-Fever  | 68                       | 69.4          |
|  | 34600-Flu like symptoms  | 1                        | 1.0           |
|  | 35000-Gait disturbance   | 1                        | 1.0           |
|  | 37200-General disorders and administration site conditions - Other specify | 1                        | 1.0           |
|  | 45000-Infusion related reaction  | 1                        | 1.0           |
|  | 45200-Injection site reaction  | 6                        | 6.1           |
|  | 48700-Irritability   | 8                        | 8.2           |
|  | 52800-Localized edema  | 2                        | 2.0           |
|  | 58600-Non-cardiac chest pain   | 2                        | 2.0           |
|  | 60600-Pain   | 48                       | 49.0          |
| Immune system disorders                              | 12000-Allergic reaction  | 10                       | 10.2          |
| Infections and infestations                          | 18800-Bronchial infection  | 1                        | 1.0           |
|  | 29500-Enterocolitis infectious   | 3                        | 3.1           |
|  | 44800-Infections and infestations - Other specify                          | 1                        | 1.0           |
|  | 53100-Lung infection   | 2                        | 2.0           |
|  | 65200-Pharyngitis  | 1                        | 1.0           |
|  | 72600-Rhinitis infective   | 1                        | 1.0           |
|  | 82300-Upper respiratory infection  | 1                        | 1.0           |
| Injury, poisoning and procedural complications       | 19400-Bruising   | 2                        | 2.0           |
|  | 86400-Vascular access complication   | 1                        | 1.0           |

**ANBL0931 Reporting Period 3: Immunotherapy ch14.18 + GM-CSF + Isotretinoin**

| Non-Targeted Toxicities |   | Grade 1 or 2<br>(N = 98) |               |
|-------------------------|---|--------------------------|---------------|
|                         |   | count                    | Incidence (%) |
| Investigations          | 10900-Activated partial thromboplastin time prolonged | 1                        | 1.0           |
|                         | 11600-Alanine aminotransferase increased              | 44                       | 44.9          |
|                         | 11800-Alkaline phosphatase increased                  | 6                        | 6.1           |
|                         | 15000-Aspartate aminotransferase increased            | 36                       | 36.7          |
|                         | 17400-Blood bilirubin increased                       | 3                        | 3.1           |
|                         | 21700-Cholesterol high                                | 1                        | 1.0           |
|                         | 24100-Creatinine increased                            | 11                       | 11.2          |
|                         | 37500-GGT increased                                   | 8                        | 8.2           |
|                         | 39400-Hemoglobin increased                            | 3                        | 3.1           |
|                         | 48400-Investigations - Other specify                  | 1                        | 1.0           |
|                         | 53700-Lymphocyte count decreased                      | 57                       | 58.2          |
|                         | 53800-Lymphocyte count increased                      | 1                        | 1.0           |
|                         | 58300-Neutrophil count decreased                      | 17                       | 17.3          |
|                         | 65800-Platelet count decreased                        | 55                       | 56.1          |
|                         | 88200-Weight gain                                     | 25                       | 25.5          |
|                         | 88300-Weight loss                                     | 8                        | 8.2           |
|                         | 88500-White blood cell decreased                      | 41                       | 41.8          |

## ANBL0931 Reporting Period 3: Immunotherapy ch14.18 + GM-CSF + Isotretinoin

| Non-Targeted Toxicities                         |  | Grade 1 or 2<br>(N = 98) |               |
|---|--|--------------------------|---------------|
|   |  | count                    | Incidence (%) |
| Metabolism and nutrition disorders              | 10700-Acidosis                                 | 1                        | 1.0           |
|   | 13500-Anorexia                                 | 7                        | 7.1           |
|   | 24700-Dehydration                              | 1                        | 1.0           |
|   | 41300-Hypercalcemia                            | 8                        | 8.2           |
|   | 41400-Hyperglycemia                            | 24                       | 24.5          |
|   | 41600-Hyperkalemia                             | 7                        | 7.1           |
|   | 41700-Hypermagnesemia                          | 5                        | 5.1           |
|   | 41800-Hybernatrium                             | 2                        | 2.0           |
|   | 42400-Hypertriglyceridemia                     | 30                       | 30.6          |
|   | 42600-Hypoalbuminemia                          | 73                       | 74.5          |
|   | 42700-Hypocalcemia                             | 52                       | 53.1          |
|   | 42900-Hypoglycemia                             | 9                        | 9.2           |
|   | 43100-Hypokalemia                              | 40                       | 40.8          |
|   | 43200-Hypomagnesemia                           | 12                       | 12.2          |
|   | 43300-Hyponatremia                             | 53                       | 54.1          |
|   | 43500-Hypophosphatemia                         | 13                       | 13.3          |
| Musculoskeletal and connective tissue disorders | 16200-Back pain                                | 4                        | 4.1           |
|   | 21400-Chest wall pain                          | 1                        | 1.0           |
|   | 56500-Myalgia                                  | 4                        | 4.1           |
|   | 57800-Neck pain                                | 6                        | 6.1           |
|   | 60700-Pain in extremity                        | 9                        | 9.2           |
| Nervous system disorders                        | 11500-Akathisia                                | 1                        | 1.0           |
|   | 25900-Dizziness                                | 1                        | 1.0           |
|   | 38800-Headache                                 | 8                        | 8.2           |
|   | 42000-Hypersomnia                              | 1                        | 1.0           |
|   | 55400-Movements involuntary                    | 1                        | 1.0           |
|   | 58100-Nervous system disorders - Other specify | 1                        | 1.0           |
|   | 58200-Neuralgia                                | 3                        | 3.1           |
|   | 64100-Peripheral sensory neuropathy            | 3                        | 3.1           |
|   | 76700-Somnolence                               | 1                        | 1.0           |

**ANBL0931 Reporting Period 3: Immunotherapy ch14.18 + GM-CSF + Isotretinoin**

| Non-Targeted Toxicities                         |  | Grade 1 or 2<br>(N = 98) |               |
|---|--|--------------------------|---------------|
|   |  | count                    | Incidence (%) |
| Psychiatric disorders                           | 11400-Agitation  | 9                        | 9.2           |
|   | 13700-Anxiety  | 5                        | 5.1           |
|   | 23000-Confusion  | 1                        | 1.0           |
|   | 25400-Depression   | 2                        | 2.0           |
|   | 38500-Hallucinations   | 1                        | 1.0           |
|   | 54100-Mania  | 1                        | 1.0           |
|   | 71700-Restlessness   | 2                        | 2.0           |
| Renal and urinary disorders                     | 39300-Hematuria  | 12                       | 12.2          |
|   | 68300-Proteinuria  | 14                       | 14.3          |
|   | 82900-Urinary incontinence   | 1                        | 1.0           |
|   | 83000-Urinary retention  | 13                       | 13.3          |
|   | 83300-Urinary tract pain   | 2                        | 2.0           |
|   | 83400-Urinary urgency  | 1                        | 1.0           |
|   | 83500-Urine discoloration  | 2                        | 2.0           |
| Reproductive system and breast disorders        | 37400-Genital edema  | 1                        | 1.0           |
| Respiratory, thoracic and mediastinal disorders | 19300-Bronchospasm   | 3                        | 3.1           |
|   | 23800-Cough  | 30                       | 30.6          |
|   | 27800-Dyspnea  | 2                        | 2.0           |
|   | 43900-Hypoxia  | 8                        | 8.2           |
|   | 57500-Nasal congestion   | 7                        | 7.1           |
|   | 65900-Pleural effusion   | 1                        | 1.0           |
|   | 66200-Pleuritic pain   | 1                        | 1.0           |
|   | 68700-Pulmonary edema  | 1                        | 1.0           |
|   | 71600-Respiratory thoracic and mediastinal disorders - Other specify | 17                       | 17.3          |
|   | 76200-Sneezing   | 1                        | 1.0           |
|   | 88400-Wheezing   | 8                        | 8.2           |

**ANBL0931 Reporting Period 3: Immunotherapy ch14.18 + GM-CSF + Isotretinoin**

| Non-Targeted Toxicities                |  | Grade 1 or 2<br>(N = 98) |               |
|--|--|--------------------------|---------------|
|  |  | count                    | Incidence (%) |
| Skin and subcutaneous tissue disorders | 12200-Alopecia   | 1                        | 1.0           |
|  | 26200-Dry skin   | 26                       | 26.5          |
|  | 29900-Erythema multiforme                                    | 2                        | 2.0           |
|  | 63600-Periorbital edema                                      | 4                        | 4.1           |
|  | 65700-Photosensitivity                                       | 1                        | 1.0           |
|  | 68400-Pruritus   | 34                       | 34.7          |
|  | 69700-Rash maculo-papular                                    | 13                       | 13.3          |
|  | 74700-Skin and subcutaneous tissue disorders - Other specify | 8                        | 8.2           |
|  | 75000-Skin hypopigmentation                                  | 1                        | 1.0           |
|  | 75300-Skin ulceration  | 2                        | 2.0           |
|  | 84100-Urticaria  | 11                       | 11.2          |
| Vascular disorders                     | 19800-Capillary leak syndrome                                | 14                       | 14.3          |
|  | 42100-Hypertension   | 29                       | 29.6          |
|  | 43600-Hypotension  | 54                       | 55.1          |
|  | 86500-Vascular disorders - Other specify                     | 1                        | 1.0           |

**ANBL0931 Reporting Period 4: Immunotherapy ch14.18 + IL-2 + Isotretinoin**

| Non-Targeted Toxicities              |   | Grade 1 or 2<br>(N = 90) |               |
|--------------------------------------|---|--------------------------|---------------|
|                                      |   | count                    | Incidence (%) |
| Primary Category                     |   |                          |               |
| Blood and lymphatic system disorders | 13200-Anemia                                      | 79                       | 87.8          |
| Cardiac disorders                    | 20100-Cardiac disorders - Other specify           | 3                        | 3.3           |
|                                      | 21300-Chest pain - cardiac                        | 1                        | 1.1           |
|                                      | 74200-Sinus bradycardia                           | 4                        | 4.4           |
|                                      | 74500-Sinus tachycardia                           | 56                       | 62.2          |
|                                      | 78900-Supraventricular tachycardia                | 1                        | 1.1           |
| Ear and labyrinth disorders          | 27900-Ear and labyrinth disorders - Other specify | 1                        | 1.1           |
|                                      | 28000-Ear pain                                    | 1                        | 1.1           |
| Endocrine disorders                  | 43400-Hypoparathyroidism                          | 1                        | 1.1           |
| Eye disorders                        | 17800-Blurred vision                              | 1                        | 1.1           |
|                                      | 31900-Eye disorders - Other specify               | 1                        | 1.1           |
| Gastrointestinal disorders           | 10100-Abdominal distension                        | 5                        | 5.6           |
|                                      | 10300-Abdominal pain                              | 21                       | 23.3          |
|                                      | 21200-Cheilitis                                   | 2                        | 2.2           |
|                                      | 23400-Constipation                                | 12                       | 13.3          |
|                                      | 25700-Diarrhea                                    | 26                       | 28.9          |
|                                      | 26100-Dry mouth                                   | 1                        | 1.1           |
|                                      | 27600-Dysphagia                                   | 1                        | 1.1           |
|                                      | 34400-Flatulence                                  | 1                        | 1.1           |
|                                      | 36700-Gastrointestinal disorders - Other specify  | 1                        | 1.1           |
|                                      | 55600-Mucositis oral                              | 1                        | 1.1           |
|                                      | 57600-Nausea                                      | 19                       | 21.1          |
|                                      | 77900-Stomach pain                                | 2                        | 2.2           |
|                                      | 87900-Vomiting                                    | 30                       | 33.3          |

**ANBL0931 Reporting Period 4: Immunotherapy ch14.18 + IL-2 + Isotretinoin**

| Non-Targeted Toxicities                              |  | Grade 1 or 2<br>(N = 90) |               |
|--|--|--------------------------|---------------|
|  |  | count                    | Incidence (%) |
| General disorders and administration site conditions | 21500-Chills   | 6                        | 6.7           |
|  | 28200-Edema face   | 23                       | 25.6          |
|  | 28300-Edema limbs  | 11                       | 12.2          |
|  | 28400-Edema trunk  | 1                        | 1.1           |
|  | 33200-Fatigue  | 11                       | 12.2          |
|  | 33900-Fever  | 77                       | 85.6          |
|  | 34600-Flu like symptoms  | 1                        | 1.1           |
|  | 37200-General disorders and administration site conditions - Other specify | 1                        | 1.1           |
|  | 45000-Infusion related reaction  | 2                        | 2.2           |
|  | 45200-Injection site reaction  | 1                        | 1.1           |
|  | 48700-Irritability   | 8                        | 8.9           |
|  | 52800-Localized edema  | 4                        | 4.4           |
|  | 54000-Malaise  | 1                        | 1.1           |
|  | 60600-Pain   | 44                       | 48.9          |
| Immune system disorders                              | 12000-Allergic reaction  | 13                       | 14.4          |
|  | 24400-Cytokine release syndrome  | 2                        | 2.2           |
| Infections and infestations                          | 20500-Catheter related infection   | 2                        | 2.2           |
|  | 23300-Conjunctivitis infective   | 1                        | 1.1           |
|  | 44800-Infections and infestations - Other specify                          | 5                        | 5.6           |
|  | 65200-Pharyngitis  | 2                        | 2.2           |
|  | 75200-Skin infection   | 1                        | 1.1           |
|  | 82300-Upper respiratory infection  | 2                        | 2.2           |
|  | 83100-Urinary tract infection  | 2                        | 2.2           |
| Injury, poisoning and procedural complications       | 45700-Injury poisoning and procedural complications - Other specify        | 1                        | 1.1           |
|  | 66800-Postoperative hemorrhage   | 1                        | 1.1           |
|  | 86400-Vascular access complication   | 5                        | 5.6           |

**ANBL0931 Reporting Period 4: Immunotherapy ch14.18 + IL-2 + Isotretinoin**

| Non-Targeted Toxicities |   | Grade 1 or 2<br>(N = 90) |               |
|-------------------------|---|--------------------------|---------------|
|                         |   | count                    | Incidence (%) |
| Investigations          | 10900-Activated partial thromboplastin time prolonged | 2                        | 2.2           |
|                         | 11600-Alanine aminotransferase increased              | 60                       | 66.7          |
|                         | 11800-Alkaline phosphatase increased                  | 12                       | 13.3          |
|                         | 15000-Aspartate aminotransferase increased            | 53                       | 58.9          |
|                         | 17400-Blood bilirubin increased                       | 6                        | 6.7           |
|                         | 24100-Creatinine increased                            | 23                       | 25.6          |
|                         | 37500-GGT increased                                   | 10                       | 11.1          |
|                         | 39400-Hemoglobin increased                            | 7                        | 7.8           |
|                         | 45800-INR increased                                   | 1                        | 1.1           |
|                         | 48400-Investigations - Other specify                  | 1                        | 1.1           |
|                         | 53700-Lymphocyte count decreased                      | 71                       | 78.9          |
|                         | 53800-Lymphocyte count increased                      | 1                        | 1.1           |
|                         | 58300-Neutrophil count decreased                      | 45                       | 50.0          |
|                         | 65800-Platelet count decreased                        | 60                       | 66.7          |
|                         | 88200-Weight gain                                     | 32                       | 35.6          |
|                         | 88300-Weight loss                                     | 7                        | 7.8           |
|                         | 88500-White blood cell decreased                      | 58                       | 64.4          |



## ANBL0931 Reporting Period 4: Immunotherapy ch14.18 + IL-2 + Isotretinoin

| Non-Targeted Toxicities                         |                                     | Grade 1 or 2<br>(N = 90) |               |
|---|-------------------------------------|--------------------------|---------------|
|   |                                     | count                    | Incidence (%) |
| Metabolism and nutrition disorders              | 10700-Acidosis                      | 2                        | 2.2           |
|   | 13500-Anorexia                      | 11                       | 12.2          |
|   | 24700-Dehydration                   | 4                        | 4.4           |
|   | 41300-Hypercalcemia                 | 6                        | 6.7           |
|   | 41400-Hyperglycemia                 | 23                       | 25.6          |
|   | 41600-Hyperkalemia                  | 13                       | 14.4          |
|   | 41700-Hypermagnesemia               | 5                        | 5.6           |
|   | 41800-Hybernatriemia                | 1                        | 1.1           |
|   | 42400-Hypertriglyceridemia          | 34                       | 37.8          |
|   | 42600-Hypoalbuminemia               | 79                       | 87.8          |
|   | 42700-Hypocalcemia                  | 67                       | 74.4          |
|   | 42900-Hypoglycemia                  | 13                       | 14.4          |
|   | 43100-Hypokalemia                   | 54                       | 60.0          |
|   | 43200-Hypomagnesemia                | 19                       | 21.1          |
|   | 43300-Hyponatremia                  | 68                       | 75.6          |
|   | 43500-Hypophosphatemia              | 36                       | 40.0          |
| Musculoskeletal and connective tissue disorders | 16200-Back pain                     | 9                        | 10.0          |
|   | 19700-Buttock pain                  | 1                        | 1.1           |
|   | 21400-Chest wall pain               | 2                        | 2.2           |
|   | 37300-Generalized muscle weakness   | 1                        | 1.1           |
|   | 56500-Myalgia                       | 1                        | 1.1           |
|   | 57800-Neck pain                     | 5                        | 5.6           |
|   | 60700-Pain in extremity             | 21                       | 23.3          |
| Nervous system disorders                        | 25900-Dizziness                     | 1                        | 1.1           |
|   | 38800-Headache                      | 9                        | 10.0          |
|   | 58200-Neuralgia                     | 3                        | 3.3           |
|   | 64100-Peripheral sensory neuropathy | 3                        | 3.3           |
|   | 76700-Somnolence                    | 1                        | 1.1           |
|   | 81300-Tremor                        | 1                        | 1.1           |
| Psychiatric disorders                           | 11400-Agitation                     | 4                        | 4.4           |
|   | 13700-Anxiety                       | 2                        | 2.2           |
|   | 23000-Confusion                     | 1                        | 1.1           |

**ANBL0931 Reporting Period 4: Immunotherapy ch14.18 + IL-2 + Isotretinoin**

| Non-Targeted Toxicities                         |  | Grade 1 or 2<br>(N = 90) |               |
|---|--|--------------------------|---------------|
|   |  | count                    | Incidence (%) |
| Renal and urinary disorders                     | 11100-Acute kidney injury  | 1                        | 1.1           |
|   | 39300-Hematuria  | 14                       | 15.6          |
|   | 68300-Proteinuria  | 21                       | 23.3          |
|   | 71000-Renal and urinary disorders - Other specify                    | 1                        | 1.1           |
|   | 83000-Urinary retention  | 9                        | 10.0          |
|   | 83300-Urinary tract pain   | 1                        | 1.1           |
|   | 83500-Urine discoloration  | 2                        | 2.2           |
| Reproductive system and breast disorders        | 37400-Genital edema  | 1                        | 1.1           |
|   | 62900-Penile pain  | 1                        | 1.1           |
|   | 71400-Reproductive system and breast disorders - Other specify       | 1                        | 1.1           |
| Respiratory, thoracic and mediastinal disorders | 12100-Allergic rhinitis  | 2                        | 2.2           |
|   | 15400-Atelectasis  | 1                        | 1.1           |
|   | 19300-Bronchospasm   | 2                        | 2.2           |
|   | 23800-Cough  | 33                       | 36.7          |
|   | 27800-Dyspnea  | 2                        | 2.2           |
|   | 29700-Epistaxis  | 3                        | 3.3           |
|   | 40700-Hiccups  | 1                        | 1.1           |
|   | 43900-Hypoxia  | 12                       | 13.3          |
|   | 51500-Laryngopharyngeal dysesthesia                                  | 1                        | 1.1           |
|   | 57500-Nasal congestion   | 9                        | 10.0          |
|   | 65900-Pleural effusion   | 2                        | 2.2           |
|   | 71600-Respiratory thoracic and mediastinal disorders - Other specify | 15                       | 16.7          |
|   | 76800-Sore throat  | 2                        | 2.2           |
|   | 88400-Wheezing   | 6                        | 6.7           |

ANBL0931 Reporting Period 4: Immunotherapy ch14.18 + IL-2 + Isotretinoin

| Non-Targeted Toxicities                |  | Grade 1 or 2<br>(N = 90) |               |
|--|--|--------------------------|---------------|
|  |  | count                    | Incidence (%) |
| Skin and subcutaneous tissue disorders | 12200-Alopecia   | 2                        | 2.2           |
|  | 26200-Dry skin   | 21                       | 23.3          |
|  | 29900-Erythema multiforme                                    | 1                        | 1.1           |
|  | 63600-Periorbital edema                                      | 8                        | 8.9           |
|  | 68400-Pruritus   | 33                       | 36.7          |
|  | 69700-Rash maculo-papular                                    | 23                       | 25.6          |
|  | 74700-Skin and subcutaneous tissue disorders - Other specify | 11                       | 12.2          |
|  | 84100-Urticaria  | 19                       | 21.1          |
| Vascular disorders                     | 19800-Capillary leak syndrome                                | 29                       | 32.2          |
|  | 34700-Flushing   | 2                        | 2.2           |
|  | 42100-Hypertension   | 29                       | 32.2          |
|  | 43600-Hypotension  | 56                       | 62.2          |
|  | 86500-Vascular disorders - Other specify                     | 2                        | 2.2           |

**ANBL0931 Reporting Period 5: Immunotherapy ch14.18 + GM-CSF + Isotretinoin**

| Non-Targeted Toxicities              |  | Grade 1 or 2<br>(N = 88) |               |
|--------------------------------------|--|--------------------------|---------------|
|                                      |  | count                    | Incidence (%) |
| Primary Category                     |  |                          |               |
| Blood and lymphatic system disorders | 13200-Anemia                                     | 64                       | 72.7          |
| Cardiac disorders                    | 20100-Cardiac disorders - Other specify          | 1                        | 1.1           |
|                                      | 74200-Sinus bradycardia                          | 1                        | 1.1           |
|                                      | 74500-Sinus tachycardia                          | 51                       | 58.0          |
|                                      | 78900-Supraventricular tachycardia               | 1                        | 1.1           |
| Ear and labyrinth disorders          | 28000-Ear pain                                   | 1                        | 1.1           |
| Endocrine disorders                  | 43800-Hypothyroidism                             | 1                        | 1.1           |
| Eye disorders                        | 31900-Eye disorders - Other specify              | 1                        | 1.1           |
|                                      | 61900-Papilledema                                | 1                        | 1.1           |
|                                      | 65600-Photophobia                                | 1                        | 1.1           |
| Gastrointestinal disorders           | 10100-Abdominal distension                       | 3                        | 3.4           |
|                                      | 10300-Abdominal pain                             | 25                       | 28.4          |
|                                      | 23400-Constipation                               | 7                        | 8.0           |
|                                      | 25700-Diarrhea                                   | 14                       | 15.9          |
|                                      | 27500-Dyspepsia                                  | 1                        | 1.1           |
|                                      | 27600-Dysphagia                                  | 1                        | 1.1           |
|                                      | 34400-Flatulence                                 | 2                        | 2.3           |
|                                      | 36400-Gastritis                                  | 1                        | 1.1           |
|                                      | 36700-Gastrointestinal disorders - Other specify | 1                        | 1.1           |
|                                      | 55600-Mucositis oral                             | 1                        | 1.1           |
|                                      | 57600-Nausea                                     | 16                       | 18.2          |
|                                      | 77900-Stomach pain                               | 1                        | 1.1           |
|                                      | 80200-Toothache                                  | 1                        | 1.1           |
|                                      | 87900-Vomiting                                   | 24                       | 27.3          |

**ANBL0931 Reporting Period 5: Immunotherapy ch14.18 + GM-CSF + Isotretinoin**

| Non-Targeted Toxicities                              |   | Grade 1 or 2<br>(N = 88) |               |
|--|---|--------------------------|---------------|
|  |   | count                    | Incidence (%) |
| General disorders and administration site conditions | 28200-Edema face                                  | 7                        | 8.0           |
|  | 28300-Edema limbs                                 | 7                        | 8.0           |
|  | 33200-Fatigue                                     | 8                        | 9.1           |
|  | 33900-Fever                                       | 59                       | 67.0          |
|  | 45200-Injection site reaction                     | 10                       | 11.4          |
|  | 48700-Irritability                                | 8                        | 9.1           |
|  | 52800-Localized edema                             | 1                        | 1.1           |
|  | 60600-Pain  | 39                       | 44.3          |
| Immune system disorders                              | 12000-Allergic reaction                           | 9                        | 10.2          |
| Infections and infestations                          | 20500-Catheter related infection                  | 1                        | 1.1           |
|  | 29500-Enterocolitis infectious                    | 2                        | 2.3           |
|  | 44800-Infections and infestations - Other specify | 2                        | 2.3           |
|  | 55500-Mucosal infection                           | 1                        | 1.1           |
|  | 60100-Otitis media                                | 1                        | 1.1           |
|  | 65200-Pharyngitis                                 | 1                        | 1.1           |
|  | 72600-Rhinitis infective                          | 1                        | 1.1           |
|  | 75200-Skin infection                              | 2                        | 2.3           |
|  | 82300-Upper respiratory infection                 | 1                        | 1.1           |
|  | 83100-Urinary tract infection                     | 2                        | 2.3           |
| Injury, poisoning and procedural complications       | 19400-Bruising                                    | 1                        | 1.1           |

## ANBL0931 Reporting Period 5: Immunotherapy ch14.18 + GM-CSF + Isotretinoin

| Non-Targeted Toxicities |   | Grade 1 or 2<br>(N = 88) |               |
|-------------------------|---|--------------------------|---------------|
|                         |   | count                    | Incidence (%) |
| Investigations          | 10900-Activated partial thromboplastin time prolonged | 1                        | 1.1           |
|                         | 11600-Alanine aminotransferase increased              | 32                       | 36.4          |
|                         | 11800-Alkaline phosphatase increased                  | 5                        | 5.7           |
|                         | 15000-Aspartate aminotransferase increased            | 15                       | 17.0          |
|                         | 17400-Blood bilirubin increased                       | 2                        | 2.3           |
|                         | 24100-Creatinine increased                            | 15                       | 17.0          |
|                         | 37500-GGT increased                                   | 6                        | 6.8           |
|                         | 39400-Hemoglobin increased                            | 5                        | 5.7           |
|                         | 45800-INR increased                                   | 1                        | 1.1           |
|                         | 53700-Lymphocyte count decreased                      | 41                       | 46.6          |
|                         | 53800-Lymphocyte count increased                      | 1                        | 1.1           |
|                         | 58300-Neutrophil count decreased                      | 15                       | 17.0          |
|                         | 65800-Platelet count decreased                        | 44                       | 50.0          |
|                         | 88200-Weight gain                                     | 29                       | 33.0          |
|                         | 88300-Weight loss                                     | 3                        | 3.4           |
|                         | 88500-White blood cell decreased                      | 21                       | 23.9          |

## ANBL0931 Reporting Period 5: Immunotherapy ch14.18 + GM-CSF + Isotretinoin

| Non-Targeted Toxicities                         |  | Grade 1 or 2<br>(N = 88) |               |
|---|--|--------------------------|---------------|
|   |  | count                    | Incidence (%) |
| Metabolism and nutrition disorders              | 10700-Acidosis   | 1                        | 1.1           |
|   | 13500-Anorexia   | 7                        | 8.0           |
|   | 24700-Dehydration  | 3                        | 3.4           |
|   | 41300-Hypercalcemia  | 3                        | 3.4           |
|   | 41400-Hyperglycemia  | 17                       | 19.3          |
|   | 41600-Hyperkalemia   | 5                        | 5.7           |
|   | 41700-Hypermagnesemia  | 6                        | 6.8           |
|   | 41800-Hybernatriemia   | 3                        | 3.4           |
|   | 42400-Hypertriglyceridemia   | 19                       | 21.6          |
|   | 42500-Hyperuricemia  | 2                        | 2.3           |
|   | 42600-Hypoalbuminemia  | 65                       | 73.9          |
|   | 42700-Hypocalcemia   | 37                       | 42.0          |
|   | 42900-Hypoglycemia   | 11                       | 12.5          |
|   | 43100-Hypokalemia  | 26                       | 29.5          |
|   | 43200-Hypomagnesemia   | 11                       | 12.5          |
|   | 43300-Hyponatremia   | 46                       | 52.3          |
|   | 43500-Hypophosphatemia   | 9                        | 10.2          |
| Musculoskeletal and connective tissue disorders | 16200-Back pain  | 9                        | 10.2          |
|   | 18200-Bone pain  | 1                        | 1.1           |
|   | 21400-Chest wall pain  | 2                        | 2.3           |
|   | 56300-Musculoskeletal and connective tissue disorder - Other specify | 1                        | 1.1           |
|   | 57800-Neck pain  | 4                        | 4.5           |
|   | 60700-Pain in extremity  | 9                        | 10.2          |
| Nervous system disorders                        | 38800-Headache   | 7                        | 8.0           |
|   | 51800-Lethargy   | 2                        | 2.3           |
|   | 54500-Meningismus  | 1                        | 1.1           |
|   | 55400-Movements involuntary  | 2                        | 2.3           |
|   | 58200-Neuralgia  | 1                        | 1.1           |
|   | 58700-Nystagmus  | 1                        | 1.1           |
|   | 59000-Oculomotor nerve disorder                                      | 1                        | 1.1           |
|   | 81300-Tremor   | 1                        | 1.1           |

**ANBL0931 Reporting Period 5: Immunotherapy ch14.18 + GM-CSF + Isotretinoin**

| Non-Targeted Toxicities                         |  | Grade 1 or 2<br>(N = 88) |               |
|---|--|--------------------------|---------------|
|   |  | count                    | Incidence (%) |
| Psychiatric disorders                           | 11400-Agitation  | 4                        | 4.5           |
|   | 13700-Anxiety  | 1                        | 1.1           |
|   | 23000-Confusion  | 1                        | 1.1           |
|   | 25400-Depression   | 1                        | 1.1           |
|   | 38500-Hallucinations   | 1                        | 1.1           |
|   | 45900-Insomnia   | 1                        | 1.1           |
|   | 71700-Restlessness   | 1                        | 1.1           |
| Renal and urinary disorders                     | 39300-Hematuria  | 8                        | 9.1           |
|   | 68300-Proteinuria  | 12                       | 13.6          |
|   | 71000-Renal and urinary disorders - Other specify                    | 1                        | 1.1           |
|   | 83000-Urinary retention  | 6                        | 6.8           |
|   | 83300-Urinary tract pain   | 1                        | 1.1           |
|   | 83500-Urine discoloration  | 1                        | 1.1           |
| Reproductive system and breast disorders        | 37400-Genital edema  | 1                        | 1.1           |
|   | 71400-Reproductive system and breast disorders - Other specify       | 1                        | 1.1           |
| Respiratory, thoracic and mediastinal disorders | 12100-Allergic rhinitis  | 1                        | 1.1           |
|   | 23800-Cough  | 21                       | 23.9          |
|   | 27800-Dyspnea  | 1                        | 1.1           |
|   | 43900-Hypoxia  | 14                       | 15.9          |
|   | 57500-Nasal congestion   | 3                        | 3.4           |
|   | 66300-Pneumonitis  | 2                        | 2.3           |
|   | 67600-Productive cough   | 1                        | 1.1           |
|   | 71600-Respiratory thoracic and mediastinal disorders - Other specify | 11                       | 12.5          |
|   | 76200-Sneezing   | 2                        | 2.3           |
|   | 88400-Wheezing   | 2                        | 2.3           |



**ANBL0931 Reporting Period 5: Immunotherapy ch14.18 + GM-CSF + Isotretinoin**

| Non-Targeted Toxicities                |  | Grade 1 or 2<br>(N = 88) |               |
|--|--|--------------------------|---------------|
|  |  | count                    | Incidence (%) |
| Skin and subcutaneous tissue disorders | 26200-Dry skin   | 11                       | 12.5          |
|  | 60900-Palmar-plantar erythrodysesthesia syndrome             | 1                        | 1.1           |
|  | 63600-Periorbital edema                                      | 4                        | 4.5           |
|  | 65700-Photosensitivity                                       | 1                        | 1.1           |
|  | 68400-Pruritus   | 28                       | 31.8          |
|  | 69600-Rash acneiform   | 1                        | 1.1           |
|  | 69700-Rash maculo-papular                                    | 13                       | 14.8          |
|  | 74700-Skin and subcutaneous tissue disorders - Other specify | 2                        | 2.3           |
|  | 75100-Skin induration  | 2                        | 2.3           |
|  | 75300-Skin ulceration  | 1                        | 1.1           |
|  | 84100-Urticaria  | 8                        | 9.1           |
| Vascular disorders                     | 19800-Capillary leak syndrome                                | 15                       | 17.0          |
|  | 42100-Hypertension   | 25                       | 28.4          |
|  | 43600-Hypotension  | 42                       | 47.7          |
|  | 86500-Vascular disorders - Other specify                     | 1                        | 1.1           |

## ANBL0931 Reporting Period 6: Isotretinoin (ISOT) only

| Non-Targeted Toxicities                              |   | Grade 1 or 2<br>(N = 81) |               |
|--|---|--------------------------|---------------|
|  |   | count                    | Incidence (%) |
| Primary Category                                     |   |                          |               |
| Blood and lymphatic system disorders                 | 13200-Anemia                                      | 39                       | 48.1          |
| Cardiac disorders                                    | 74500-Sinus tachycardia                           | 9                        | 11.1          |
| Ear and labyrinth disorders                          | 28000-Ear pain                                    | 1                        | 1.2           |
| Endocrine disorders                                  | 42200-Hyperthyroidism                             | 3                        | 3.7           |
| Eye disorders  | 23200-Conjunctivitis                              | 1                        | 1.2           |
|  | 26000-Dry eye                                     | 2                        | 2.5           |
|  | 31900-Eye disorders - Other specify               | 1                        | 1.2           |
|  | 32200-Eyelid function disorder                    | 1                        | 1.2           |
| Gastrointestinal disorders                           | 10300-Abdominal pain                              | 5                        | 6.2           |
|  | 23400-Constipation                                | 1                        | 1.2           |
|  | 25700-Diarrhea                                    | 5                        | 6.2           |
|  | 57600-Nausea                                      | 2                        | 2.5           |
|  | 77900-Stomach pain                                | 1                        | 1.2           |
|  | 87900-Vomiting                                    | 4                        | 4.9           |
| General disorders and administration site conditions | 21500-Chills                                      | 2                        | 2.5           |
|  | 33200-Fatigue                                     | 7                        | 8.6           |
|  | 33900-Fever                                       | 15                       | 18.5          |
|  | 35000-Gait disturbance                            | 1                        | 1.2           |
|  | 48700-Irritability                                | 2                        | 2.5           |
|  | 58600-Non-cardiac chest pain                      | 2                        | 2.5           |
|  | 60600-Pain  | 5                        | 6.2           |
| Infections and infestations                          | 29500-Enterocolitis infectious                    | 1                        | 1.2           |
|  | 44800-Infections and infestations - Other specify | 7                        | 8.6           |
|  | 60100-Otitis media                                | 3                        | 3.7           |
|  | 62000-Papulopustular rash                         | 1                        | 1.2           |
|  | 74600-Sinusitis                                   | 1                        | 1.2           |
|  | 75200-Skin infection                              | 1                        | 1.2           |
|  | 82300-Upper respiratory infection                 | 1                        | 1.2           |
| Injury, poisoning and procedural complications       | 19400-Bruising                                    | 1                        | 1.2           |
|  | 86400-Vascular access complication                | 1                        | 1.2           |

## ANBL0931 Reporting Period 6: Isotretinoin (ISOT) only

| Non-Targeted Toxicities                         |   | Grade 1 or 2<br>(N = 81) |               |
|---|---|--------------------------|---------------|
|   |   | count                    | Incidence (%) |
| Investigations                                  | 10900-Activated partial thromboplastin time prolonged | 2                        | 2.5           |
|   | 11600-Alanine aminotransferase increased              | 24                       | 29.6          |
|   | 11800-Alkaline phosphatase increased                  | 3                        | 3.7           |
|   | 15000-Aspartate aminotransferase increased            | 23                       | 28.4          |
|   | 24100-Creatinine increased                            | 11                       | 13.6          |
|   | 37500-GGT increased                                   | 5                        | 6.2           |
|   | 45800-INR increased                                   | 1                        | 1.2           |
|   | 53700-Lymphocyte count decreased                      | 16                       | 19.8          |
|   | 58300-Neutrophil count decreased                      | 24                       | 29.6          |
|   | 65800-Platelet count decreased                        | 18                       | 22.2          |
|   | 88200-Weight gain                                     | 4                        | 4.9           |
|   | 88300-Weight loss                                     | 2                        | 2.5           |
|   | 88500-White blood cell decreased                      | 35                       | 43.2          |
| Metabolism and nutrition disorders              | 10700-Acidosis  | 1                        | 1.2           |
|   | 13500-Anorexia  | 6                        | 7.4           |
|   | 24700-Dehydration                                     | 1                        | 1.2           |
|   | 41300-Hypercalcemia                                   | 4                        | 4.9           |
|   | 41400-Hyperglycemia                                   | 5                        | 6.2           |
|   | 41600-Hyperkalemia                                    | 8                        | 9.9           |
|   | 41700-Hypermagnesemia                                 | 1                        | 1.2           |
|   | 41800-Hybernatriem                                    | 2                        | 2.5           |
|   | 42400-Hypertriglyceridemia                            | 15                       | 18.5          |
|   | 42600-Hypoalbuminemia                                 | 3                        | 3.7           |
|   | 42700-Hypocalcemia                                    | 2                        | 2.5           |
|   | 42900-Hypoglycemia                                    | 5                        | 6.2           |
|   | 43100-Hypokalemia                                     | 1                        | 1.2           |
|   | 43200-Hypomagnesemia                                  | 3                        | 3.7           |
|   | 43300-Hyponatremia                                    | 10                       | 12.3          |
|   | 43500-Hypophosphatemia                                | 2                        | 2.5           |
| Musculoskeletal and connective tissue disorders | 18200-Bone pain                                       | 1                        | 1.2           |
|   | 56500-Myalgia   | 2                        | 2.5           |
|   | 60700-Pain in extremity                               | 3                        | 3.7           |

**ANBL0931 Reporting Period 6: Isotretinoin (ISOT) only**

| Non-Targeted Toxicities                         |  | Grade 1 or 2<br>(N = 81) |               |
|---|--|--------------------------|---------------|
|   |  | count                    | Incidence (%) |
| Nervous system disorders                        | 38800-Headache   | 4                        | 4.9           |
|   | 51800-Lethargy   | 1                        | 1.2           |
|   | 64100-Peripheral sensory neuropathy                                  | 1                        | 1.2           |
| Psychiatric disorders                           | 13700-Anxiety  | 1                        | 1.2           |
| Renal and urinary disorders                     | 39300-Hematuria  | 5                        | 6.2           |
|   | 68300-Proteinuria  | 7                        | 8.6           |
|   | 71000-Renal and urinary disorders - Other specify                    | 1                        | 1.2           |
| Reproductive system and breast disorders        | 85600-Vaginal inflammation   | 1                        | 1.2           |
| Respiratory, thoracic and mediastinal disorders | 12100-Allergic rhinitis  | 3                        | 3.7           |
|   | 15400-Atelectasis  | 2                        | 2.5           |
|   | 23800-Cough  | 9                        | 11.1          |
|   | 29700-Epistaxis  | 1                        | 1.2           |
|   | 43900-Hypoxia  | 1                        | 1.2           |
|   | 51600-Laryngospasm   | 1                        | 1.2           |
|   | 57500-Nasal congestion   | 5                        | 6.2           |
|   | 65300-Pharyngolaryngeal pain   | 1                        | 1.2           |
|   | 67600-Productive cough   | 1                        | 1.2           |
|   | 71600-Respiratory thoracic and mediastinal disorders - Other specify | 7                        | 8.6           |
|   | 76800-Sore throat  | 5                        | 6.2           |
|   | 88400-Wheezing   | 1                        | 1.2           |
| Skin and subcutaneous tissue disorders          | 26200-Dry skin   | 18                       | 22.2          |
|   | 29900-Erythema multiforme  | 1                        | 1.2           |
|   | 68400-Pruritus   | 4                        | 4.9           |
|   | 69600-Rash acneiform   | 1                        | 1.2           |
|   | 69700-Rash maculo-papular  | 3                        | 3.7           |
|   | 74700-Skin and subcutaneous tissue disorders - Other specify         | 1                        | 1.2           |
| Vascular disorders                              | 42100-Hypertension   | 4                        | 4.9           |
|   | 43600-Hypotension  | 11                       | 13.6          |

## Unacceptable toxicity grading according to the Common Terminology Criteria for Adverse Events (version 4.0):

Neuropathic pain codes: 58200-Neuralgia, 60700-Pain in extremity, 16200-Back pain ,60600-Pain, 10300-Abdominal pain  
Anatomical pain codes: listed in separate attachment

19800-Capillary leak syndrome,

12000-Allergic reaction, 13100- Anaphylaxis,

42100-hypertension,

33900-Fever

Ocular tox codes: 65600-Photophobia, 31900-Eye disorders - Other, specify, 17800-Blurred vision