**Supplemental Table 1. Complete List of Cytotoxic Chemotherapy Regimens and Response Rate by Cancer Type**.a

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Cancer Type | Chemotherapy Regimen | Overall Response Rate (%) | Complete Response (%) | Partial Response (%) |
| Head and Neck Cancer (Squamous Cell Carcinoma) | Cisplatin or Carboplatin/Docetaxel | 20.0% | - | - |
|  | Cisplatin or Carboplatin/Docetaxel | 76.5% | 17.6% | 58.9% |
|  | Cisplatin or Carboplatin/Docetaxel | 25.0% | 7.0% | 18.0% |
|  | Cisplatin or Carboplatin/Paclitaxel | 26.0% | 7.0% | 19.0% |
|  | Cisplatin or Carboplatin/Paclitaxel | 61.7% | 4.2% | 57.5% |
|  | Cisplatin/Placebo | 9.8% | - | - |
|  | Cisplatin/Fluorouracil | 29.8% | 6.7% | 23.1% |
|  | Cisplatin/Fluorouracil | 32.0% | 6.0% | 26.0% |
|  | Cisplatin/Fluorouracil | 60.2% | 2.8% | 57.4% |
|  | Cisplatin/Fluorouracil | 42.0% | 2.8% | 39.2% |
|  | Cisplatin/Gemcitabine | 71.1% | 6.9% | 64.2% |
|  | Cisplatin/Gemcitabine | 64.1% | 8.3% | 55.8% |
| Esophageal and Esophagogastric Junction Cancer (Squamous Cell Carcinoma & Adenocarcinoma) | Fluorouracil/Cisplatin | 34.0% | 2.0% | 32.0% |
|  | Fluorouracil/Cisplatin | 30.0% | 3.0% | 27.0% |
|  | Fluorouracil/Cisplatin | 16.7% | - | - |
|  | Fluorouracil/Cisplatin | 27.0% | 0.0% | 27.0% |
|  | Capecitabine/Cisplatin | 46.0% | 2.0% | 44.0% |
|  | Fluorouracil/Oxaliplatin | 34.8% | 3.6% | 31.2% |
|  | Capecitabine/Oxaliplatin | 44.0% | 2.0% | 42.0% |
| Gastric Cancer | Fluorouracil/Cisplatin | 34.0% | 2.0% | 32.0% |
|  | Fluorouracil/Cisplatin | 30.0% | 3.0% | 27.0% |
|  | Fluorouracil/Cisplatin | 16.7% | - | - |
|  | Fluorouracil/Cisplatin | 27.0% | 0.0% | 27.0% |
|  | Capecitabine/Cisplatin | 46.0% | 2.0% | 44.0% |
|  | Fluorouracil/Oxaliplatin | 34.8% | 3.6% | 31.2% |
|  | Capecitabine/Oxaliplatin | 44.0% | 2.0% | 42.0% |
| Colorectal Cancer | FOLFOX | 50.7% | - | - |
|  | FOLFOX | 72.0% | 4.0% | 68.0% |
|  | FOLFOX | 39.0% | - | - |
|  | FOLFOX (RR for WT-KRAS) | 48.0% | - | - |
|  | FOLFOX (RR for MT-KRAS) | 40.0% | - | - |
|  | Capecitabine/Oxaliplatin | 38.0% | - | - |
|  | FOLFIRI | 47.2% | 5.3% | 41.9% |
|  | FOLFOXIRI | 66.0% | 8.0% | 58.0% |
|  | Capecitabine | 10.0% | 1.0% | 9.0% |
| Anal Carcinoma | Fluorouracil/Cisplatin | 63.0% | 9.0% | 54.0% |
|  | Fluorouracil/Cisplatin | 63.2% | 5.3% | 57.9% |
|  | Carboplatin/Paclitaxel | 37.0% | 4.0% | 33.0% |
| Biliary Tract Cancers (Gallbladder, Intrahepatic / Extrahepatic Cholangiocarcinoma) | Gemcitabine/Cisplatin | 26.1% | - | - |
| Pancreatic Adenocarcinoma | FOLFIRINOX | 31.6% | 0.6% | 31.0% |
|  | Gemcitabine/Albumin-Bound Paclitaxel | 22.9% | 0.2% | 22.7% |
|  | Gemcitabine | 8.0% | - | - |
|  | Gemcitabine/Cisplatin | 19.1% | 3.0% | 16.1% |
| Lung Cancer: SCLC | Carboplatin/Etoposide | 64.4% | 1.0% | 63.4% |
|  | Carboplatin/Etoposide | 75.0% | - | - |
|  | Carboplatin/Etoposide | 48.0% | 0.0% | 48.0% |
|  | Cisplatin/Etoposide | 86.0% | 43.0% | 43.0% |
|  | Cisplatin/Etoposide | 65.0% | 10.0% | 55.0% |
|  | Carboplatin/Irinotecan | 67.0% | 12.0% | 55.0% |
|  | Cisplatin / Irinotecan | 84.4% | 2.6% | 81.8% |
|  | Cisplatin / Irinotecan | 48.0% | - | - |
| Lung Cancer: NSCLC | Carboplatin/Albumin-Bound Paclitaxel | 41.0% | - | - |
|  | Carboplatin/Albumin-Bound Paclitaxel | 33.0% | 0.0% | 33.0% |
|  | Carboplatin/Albumin-Bound Paclitaxel | 38.4% | 2.1% | 36.3% |
|  | Carboplatin/Docetaxel | 23.9% | 1.2% | 22.7% |
|  | Carboplatin/Etoposide | 16.0% | 1.0% | 15.0% |
|  | Carboplatin/Etoposide | 21.7% | - | - |
|  | Carboplatin/Gemcitabine | 30.0% | 1.0% | 29.0% |
|  | Carboplatin/Paclitaxel | 32.4% | - | - |
|  | Carboplatin/Paclitaxel | 38.4% | 2.1% | 36.3% |
|  | Carboplatin/Pemetrexed | 31.6% | 0.0% | 31.6% |
|  | Carboplatin/Pemetrexed | 29.0% | 0.0% | 29.0% |
|  | Carboplatin/Pemetrexed | 18.9% | - | - |
|  | Cisplatin/Docetaxel | 31.7% | 2.0% | 29.7% |
|  | Cisplatin/Etoposide | 21.9% | 0.0% | 21.9% |
|  | Cisplatin/Gemcitabine | 30.1% | - | - |
|  | Cisplatin/Gemcitabine | 28.2% | - | - |
|  | Cisplatin/Paclitaxel | 21.0% | 0.0% | 21.0% |
|  | Cisplatin/Pemetrexed | 30.6% | - | - |
|  | Cisplatin/Pemetrexed | 18.9% | - | - |
|  | Gemcitabine/Docetaxel | 31.0% | 0.0% | 31.0% |
|  | Gemcitabine/Vinorelbine | 28.0% | 1.9% | 26.1% |
| Osteosarcoma | Cisplatin/Doxorubicin | 41.0% | - | - |
|  | Cisplatin/Doxorubicin | 29.9% | - | - |
|  | Cisplatin/Doxorubicin | 50.0% | - | - |
|  | Methotrexate High Dose/Cisplatin/Doxorubicin | 71.0% | - | - |
|  | Methotrexate High Dose/Cisplatin/Doxorubicin | 60.0% | - | - |
| Soft Tissue Sarcomas | Doxorubicin/Dacarbazine | 17.0% | 5.0% | 12.0% |
|  | Doxorubicin/Dacarbazine | 17.0% | 2.0% | 15.0% |
|  | Doxorubicin/Ifosfamide/Mesna | 34.0% | - | - |
|  | Mesna/Doxorubicin/Ifosfamide/ Dacarbazine | 47.0% | 10.0% | 37.0% |
|  | Gemcitabine/Docetaxel | 52.9% | 8.8% | 44.1% |
|  | Gemcitabine/Docetaxel | 16.0% | - | - |
|  | Gemcitabine/Vinorelbine | 12.5% | 2.5% | 10.0% |
|  | Gemcitabine/Dacarbazine | 12.0% | - | - |
|  | Doxorubicin | 11.9% | - | - |
| Breast Cancer | Doxorubicin | 33.3% | 4.2% | 29.1% |
|  | Doxorubicin | 38.0% | - | - |
|  | Liposomal Doxorubicin | 33.0% | - | - |
|  | Paclitaxel | 32.0% | - | - |
|  | Paclitaxel | 21.5% | 2.3% | 19.2% |
|  | Capecitabine | 38.0% | - | - |
|  | Gemcitabine | 37.1% | - | - |
|  | Vinorelbine | 25.0% | - | - |
|  | Eribuline | 57.0% | 3.0% | 54.0% |
|  | Docetaxel | 34.0% | 2.0% | 32.0% |
|  | Doxorubicin or Epirubicin/Cyclophosphamide or Paclitaxel | 32.0% | - | - |
| Cervical Cancer | Cisplatin/Paclitaxel | 45.0% | - | - |
|  | Cisplatin/Paclitaxel | 29.1% | 2.9% | 26.2% |
|  | Cisplatin/Paclitaxel | 36.0% | 15.0% | 21.0% |
|  | Topotecan/Paclitaxel | 27.0% | - | - |
|  | Carboplatin/Paclitaxel | 53.3% | 26.7% | 26.7% |
|  | Carboplatin/Paclitaxel | 62.6% | 7.1% | 55.5% |
| Uterine Cancer | Carboplatin/Paclitaxel | 75.0% | 25.0% | 50.0% |
| Ovarian Cancer (Epithelial, Fallopian Tube, Peritoneal) | Carboplatin/Gemcitabine | 47.2% | 14.6% | 32.6% |
|  | Carboplatin/Gemcitabine | 57.4% | 9.1% | 48.3% |
|  | Carboplatin/Paclitaxel | 66.0% | - | - |
|  | Carboplatin/Paclitaxel | 59.0% | 18.0% | 41.0% |
| Vulvar Cancer (Squamous Cell Carcinoma) | Cisplatin/Fluorouracil | 60.0% | - | 60.0% |
| Prostate Cancer | Docetaxel | 17.0% | - | 17.0% |
|  | Docetaxel | 12.0% | 12.0% | - |
| Testicular Cancer (Germ Cell Tumors) | Etoposide/Cisplatin | 99.0% | 91.0% | 8.0% |
|  | Bleomycin/Etoposide/Cisplatin | 62.0% | 31.0% | 31.0% |
|  | Etoposide/Ifosfamide/Cisplatin | 60.0% | 37.0% | 22.0% |
| Penile Cancer | Cisplatin/Ifosfamide/Paclitaxel | 50.0% | 10.0% | 40.0% |
| Bladder (Urothelial) Cancer | Gemcitabine/Cisplatin | 49.4% | 12.2% | 37.2% |
|  | Dose-Dense Methotrexate/Vinblastine/Doxorubicin/Cisplatin | 73.0% | 25.0% | 48.0% |
|  | Gemcitabine/Carboplatin | 41.2% | 3.4% | 37.8% |
| Central Nervous System Cancers | Temozolomide | 14.0% | 0.0% | 14.0% |
|  | Lomustine or Carmustine | 4.3% | - | - |
| Hodgkin Lymphoma | Doxorubicin/Bleomycin/Vinblastine/ Dacarbazine | 74.6% | 74.6% | - |
|  | Doxorubicin/Bleomycin/Vinblastine/ Dacarbazine | 73.0% | 73.0% | - |
|  | Doxorubicin/Bleomycin/Vinblastine/ Dacarbazine | 81.7% | 81.7% | - |
|  | Doxorubicin/Vinblastine/ Mechlorethamine/Etoposide/ Vincristine/Bleomycin/Prednisone | 69.0% | 69.0% | - |
| Non-Hodgkin Lymphoma | Cyclophosphamide / Doxorubicin / Vincristine / Prednisone | 68.0% | 68.0% | - |
|  | Cyclophosphamide / Doxorubicin / Vincristine / Prednisone | 44.0% | 44.0% | - |
|  | Cyclophosphamide / Doxorubicin / Vincristine / Prednisone | 63.0% | 63.0% | - |
|  | Cyclophosphamide / Doxorubicin / Vincristine / Prednisone | 76.0% | 76.0% | - |
|  | Cyclophosphamide / Doxorubicin / Vincristine / Prednisone | 82.2% | 82.2% | - |
|  | Cyclophosphamide / Doxorubicin / Vincristine / Prednisone | 76.1% | 76.1% | - |
|  | Cyclophosphamide / Doxorubicin / Vincristine / Prednisone | 68.0% | 68.0% | - |
|  | Cyclophosphamide / Doxorubicin / Vincristine / Prednisone | 62.3% | 62.3% | - |
|  | Cyclophosphamide / Doxorubicin / Vincristine / Intrathecal Methotrexate and Cytarabine / High Dose Systemic Methotrexate | 86.0% | 86.0% | - |
|  | Cyclophosphamide / Doxorubicin / Vincristine / Intrathecal Methotrexate and Cytarabine / High Dose Systemic Methotrexate | 85.0% | 85.0% | - |
|  | Cyclophosphamide / Doxorubicin / Vincristine / Intrathecal Methotrexate and Cytarabine / High Dose Systemic Methotrexate | 92.0% | 92.0% | - |
|  | Cyclophosphamide / Doxorubicin / Etoposide / Vincristine / Prednisone | 90.4% | 90.4% | - |
|  | Cyclophosphamide / Doxorubicin / Etoposide / Vincristine / Prednisone | 71.6% | 71.6% | - |
| Acute Lymphoblastic Leukemia | Daunorubicin / Vincristine / Prednisone / Pegaspargase / Cyclophosphamide | 93.5% | 93.5% | - |
|  | Daunorubicin / Vincristine / Prednisone / Pegaspargase | 93.0% | 93.0% | - |
|  | Daunorubicin / Vincristine / Prednisone / Pegaspargase / Cyclophosphamide | 85.0% | 85.0% | - |
|  | Daunorubicin / Vincristine / Prednisone / Pegaspargase (induction phase I); and Cyclophosphamide/ Cytarabine | 91.0% | 91.0% | - |
| Chronic Lymphocytic Leukemia / Small Lymphocytic Leukemia | Fludarabine / Cyclophosphamide | 58.0% | 13.0% | 44.9% |
| Acute Myeloid Leukemia | Daunorubicin / Cytarabine | 70.6% | 70.6% | - |
|  | Daunorubicin / Cytarabine | 71.0% | 71.0% | - |
|  | Daunorubicin (60 mg/m2)/ Cytarabine | 84.0% | 84.0% | - |
|  | Daunorubicin (90 mg/m2)/ Cytarabine | 81.0% | 81.0% | - |
|  | Daunorubicin or Idarubicin | 77.0% | 77.0% | - |

a. Refer to references 1-135 for corresponding primary clinical trial from which the response rates were obtained.

**Supplemental Table 2. List of Cancer Types Deemed Ineligible to Achieve Response from Cytotoxic Chemotherapy**.

|  |  |
| --- | --- |
| **Cancer Site** | **Rationale for Exclusion** |
| "Other" Digestive Organs | Mortality data did not specify what types of cancers were included in this category. |
| "Other" Female Genital | Mortality data did not specify what types of cancers were included in this category |
| "Other" Respiratory Organs | Mortality data did not specify what types of cancers were included in this category. |
| Adult Intracranial and Spinal Ependymoma (excluding Subependymoma) | Mainstay of therapy includes surgery. |
| Adult Low-Grade Infiltrative Supratentorial Astrocytoma/Oligodendroglioma | Mainstay of therapy includes surgery; systemic chemotherapy often in adjuvant setting. |
| Adult Medulloblastoma | Mainstay of therapy includes surgery; systemic chemotherapy often concurrently with radiation. |
| AIDS-Related Kaposi Sarcoma | Uncommon malignancy. |
| Alveolar Soft Part Sarcoma | Uncommon malignancy; mainstay of therapy is sunitinib. |
| Anaplastic Glioma | Mainstay of therapy includes surgery; systemic chemotherapy often in adjuvant setting. |
| Angiosarcoma | Uncommon malignancy; mainstay of therapy includes platinum-based therapies, vinorelbine, sorafenib, sunitinib, or bevacizumab. |
| Cancers of the Eye/Orbit (Uveal Melanoma) | Mainstay of therapy includes immunotherapy or targeted therapy (although clinical trial preferred). |
| Chondrosarcoma | Chemotherapy regimens were not NCCN "preferred" regimens (i.e. category 1 or 2A). |
| Chordoma | Mainstay of therapy includes imatinib, erlotinib, sunitinib, lapatinib, sorafenib, or dasatinib. |
| Chronic Myeloid Leukemia | Preferred regimen includes tyrosine kinase inhibitors. |
| Cutaneous Basal Cell or Squamous Cell Carcinoma | No corresponding mortality data for analysis. |
| Cutaneous Melanoma | Mainstay of therapy includes anti-PD1 monotherapy (i.e., pembrolizumab) or targeted therapy (BRAF V600 mutation) |
| Dermatofibrosarcoma Protuberans | Mainstay of therapy includes surgical excision. |
| Desmoid Tumors (Aggressive Fibromatosis) | Uncommon malignancy; mainly endocrinologic agents, tyrosine kinase inhibitors, or other chemotherapy. |
| Ewing Sarcoma | Mainly affecting children, thus unlikely to cause significant mortality. |
| Extranodal NK/T-Cell Lymphoma, Nasal Type | Uncommon malignancy. |
| Follicular Lymphoma | Preferred regimen includes rituximab or obinutuzumab. |
| Gastrointestinal Stromal Tumors (GIST) | Mainstay of treatment is imatinib, which is not a cytotoxic chemotherapy agent |
| Gestational Trophoblastic Neoplasia | Uncommon malignancy. |
| Giant Cell Tumor of Bone | Mainstay of therapy includes denosumab or interferon alfa-2b. |
| Hairy Cell Leukemia | Uncommon malignancy. |
| Hepatocellular Carcinoma | Mainstay of therapy often includes surgery and/or radiation/ablative procedures. |
| Inflammatory Myofibroblastic Tumor with ALK Translocation | Uncommon malignancy; mainstay of therapy includes crizotinib, ceritinib. |
| Kidney and Renal Pelvis (Clear Cell and Non-Clear Cell Carcinoma) | Mainstay of therapy includes surgery. |
| Lymphangioleiomyomatosis | Uncommon malignancy; mainstay of therapy includes sirolimus, everolimus, temsirolimus. |
| Mantle Cell Lymphoma | Preferred regimens include rituximab. |
| Marginal Zone Lymphoma | Preferred regimens include rituximab. |
| Meningioma | Mainstay of therapy includes surgery and radiation therapy; no "preferred" systemic therapies. |
| Merkel Cell Carcinoma | Uncommon malignancy; mainstay of therapy includes avelumab, pembrolizumab, or nivolumab. |
| Multiple Myeloma | Mainstay of therapy includes bortezomib. |
| Mycosis Fungoides / Sezary Syndrome | Uncommon malignancy. |
| Myelodysplastic Syndromes | Mainstay of therapy includes immunosuppressive therapy, but have chemotherapy (azacytidine, decitabine, or lenalidomide) if no good response. |
| Myeloproliferative Syndromes | Mainstay of therapy includes ruxolitinib or clinical trial. |
| Neuroendocrine/Adrenal Neoplasms | Preferred regimens include somatostatin analogues or peptide receptor radionuclide therapy (PRRT). |
| Non-Pleomorphic Rhabdomyosarcoma | Uncommon malignancy. |
| Perivascular Epitheloid Cell Neoplasm (PEComa) | Uncommon malignancy; mainstay of therapy includes sirolimus, everolimus, temsirolimus. |
| Ph-Positive Acute Lymphoblastic Leukemia | Preferred regimen includes tyrosine kinase inhibitors. |
| Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor | Uncommon Malignancy; mainstay of therapy is imatinib. |
| Primary CNS Lymphoma | Preferred regimen includes rituximab or radiation therapy. |
| Recurrent Angiomyolipoma | Uncommon malignancy; mainstay of therapy includes sirolimus, everolimus, temsirolimus. |
| Small Intestine | No corresponding NCCN Guideline for small intestinal malignancies. |
| Solitary Fibrous Tumor/Hemangiopericytoma | Uncommon malignancy; mainstay of therapy is bevacizumab + temozolomide, sunitinib, or sorafenib. |
| Systemic Light Chain Amyloidosis | Mainstay of therapy includes bortezomib. |
| Systemic Mastocytosis | Uncommon malignancy; but advanced disease can undergo clinical trial, midostaurin, cladribine, imatinib, or interferons. |
| Thymoma and Thymic Malignancies | Uncommon malignancy. |
| Thyroid Cancer (Papillary, Follicular, Hurthle Cell, Medullary, Anaplastic) | Mainstay of therapy includes surgery, radioactive iodine ablation, endocrinologic agents, or specific antibodies. |
| Ureter and "Other" Urinary Organs | No corresponding NCCN guideline for ureter malignancies; Mortality data did not specify what types of cancers were included in this category. |
| Uterine (Endometrial) Cancer | Mainstay of therapy includes surgery, with only adjuvant chemotherapy preferred. |
| Vagina | No corresponding NCCN Guideline for vaginal malignancies. |
| Waldenstrom Macroglobulinemia / Lymphoplasmacytic Lymphoma | Mainstay of therapy includes rituximab, bortezomib. |

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