

# Colony Stimulating Factors

Overrides	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Quantity Limit
Fulphila (pegfilgrastim-jmdb)	May be subject to quantity limit
Fylnetra (pegfilgrastim-pbbk)	May be subject to quantity limit
Granix (tbo-Filgrastim)	N/A
Leukine (sargramostim)	N/A
Neulasta/Neulasta Onpro (pegfilgrastim)	May be subject to quantity limit
Neupogen (filgrastim)	N/A
Nivestym (filgrastim-aafi)	N/A
Nyvepria (pegfilgrastim-apgf)	May be subject to quantity limit
Releuko (filgrastim-ayow)	N/A
Rolvedon (eflapegastim-xnst)	May be subject to quantity limit
Stimufend (pegfilgrastim-fpgk)	May be subject to quantity limit
Udenyca (pegfilgrastim-cbqv)	May be subject to quantity limit
Zarxio (filgrastim-sndz)	N/A
Ziextenzo (pegfilgrastim-bmez)	May be subject to quantity limit

## **APPROVAL CRITERIA**

- I. Requests for filgrastim (Neupogen), filgrastim-aafi (Nivestym), filgrastim-ayow (Releuko), or filgrastim-sndz (Zarxio) may be approved if the following criteria are met:
- A. Individual with nonmyeloid malignancy is using for primary prophylaxis of febrile neutropenia (FN); **AND**
  - B. Individual has a risk of FN of 20% or greater based on chemotherapy regimen (see Appendix, Table 1);

### **OR**

- C. Individual with nonmyeloid malignancy is using for primary prophylaxis of FN; **AND**
  - D. Individual's risk of developing FN is greater than or equal to 10% and less than 20% based on chemotherapy regimen (see Appendix, Table 1) and individual has any of the following risk factors for FN:
    1. Age greater than 65 years (Lyman 2014; Aagaard 2018); **OR**
    2. Poor performance status (Eastern Cooperative Oncology Group 3 or 4) or HIV infection (in particular, those with low CD4 counts ( $\leq 450/\mu\text{L}$ ) but chemotherapy still indicated (Lyman 2014); **OR**
    3. Prior radiation therapy (within the previous 1 year) (Terbuch 2018; Fujiwara 2017; Shigeta 2015); **OR**
    4. Bone marrow involvement by tumor producing cytopenias (Lyman 2014);
- OR**

5. Persistent neutropenia (absolute neutrophil count [ANC] less than 1500mm<sup>3</sup>) (Lyman 2014); **OR**
6. Poor renal function (glomerular filtration rate [GFR] less than 60mL/min) (Lyman 2014; Aagaard 2018); **OR**
7. Liver dysfunction (liver function tests at least 2X upper limit of normal or bilirubin > 2.0 mg/dL) (Lyman 2014; Aagaard 2018); **OR**
8. Recent surgery performed as part of cancer management within the previous 30 days (not to include a procedure such as port placement, drain placement, IVC filter, etc.) (Lyman 2014; Aagaard 2018); **OR**
9. History of active infection within the previous 60 days (Lyman 2014; Aagaard 2018); **OR**
10. Current open wound and chemotherapy cannot be delayed (Lyman 2014; Aagaard 2018);

**OR**

E. Individual with nonmyeloid malignancy is using for secondary prophylaxis of FN;  
**AND**

F. Individual has experienced a neutropenic complication from a prior cycle of chemotherapy (for which primary prophylaxis was not received), in which a reduced dose may compromise disease-free or overall survival or treatment outcome (NCCN 2A);

**OR**

G. Individual is using as adjunctive treatment for FN (NCCN 2A); **AND**

H. Individual has been on prophylactic therapy with filgrastim;

**OR**

I. Individual has not received prophylactic therapy with granulocyte colony stimulating factor (NCCN Guidelines Myeloid Growth Factors); **AND**

J. Individual has a high risk for infection-associated complications as demonstrated by any of the following (NCCN 2A):

1. Expected prolonged (greater than 10 days) and profound (less than 0.1 x 10<sup>9</sup>/L) neutropenia; **OR**
2. Age greater than 65 years; **OR**
3. Pneumonia or other clinically documented infections; **OR**
4. Hypotension and multi organ dysfunction (sepsis syndrome); **OR**
5. Invasive fungal infection; **OR**
6. Prior episode of febrile neutropenia; **OR**
7. Hospitalized at the time of the development of fever;

**OR**

K. Individual is 18 years of age or older and has a diagnosis of acute myeloid leukemia (AML); **AND**

L. Individual is using shortly after the completion of induction or repeat induction chemotherapy or after the completion of consolidation chemotherapy for AML;

**OR**

M. Individual has a diagnosis of hairy cell leukemia with severe neutropenia (AHFS, NCCN Guidelines Hairy Cell Leukemia);

**OR**

- N. Individual has a diagnosis of myelodysplastic syndromes (MDS) (NCCN 2A); **AND**  
O. Individual has severe neutropenia (ANC less than or equal to 500 mm<sup>3</sup>) or experiencing recurrent infection or resistant infections;

**OR**

- P. Individual is receiving dose dense therapy (treatment given more frequently, such as every 2 weeks instead of every 3 weeks) for adjuvant treatment of breast cancer (ASCO Smith 2015);

**OR**

- Q. Individual is using for chronic administration to reduce the incidence and duration of sequelae of neutropenia (for example, fever, infections, oropharyngeal ulcers) in symptomatic individuals with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia;

**OR**

- R. Individual is using for the treatment of (non-chemotherapy) drug-induced neutropenia (AHFS);

**OR**

- S. Individual is less than 21 years of age and has a diagnosis of glycogen storage disease type 1b; **AND**  
T. Individual is using for the treatment of low neutrophil counts (AHFS);

**OR**

- U. Individual is using for the treatment for neutropenia associated with human immunodeficiency virus infection and antiretroviral therapy (AHFS);

**OR**

- V. Individual is using after accidental or intentional total body radiation of myelosuppressive doses (greater than 2 Grays [Gy]) (such as Hematopoietic Syndrome of Acute Radiation Syndrome);

**OR**

- W. Individual is using after a hematopoietic progenitor stem cell transplant (HPCT/HSCT) to promote myeloid reconstitution or when engraftment is delayed or has failed;

**OR**

- X. Individual is using to mobilize progenitor cells into peripheral blood for collection by leukapheresis, as an adjunct to peripheral blood/hematopoietic stem cell transplantation (PBSCT/PHSCT);

**OR**

- Y. Individual is using as an alternate or adjunct to donor leukocyte infusions (DLI) in individuals with leukemic relapse after an allogeneic hematopoietic stem cell transplant (DrugPoints B IIa);

**OR**

- Z. Individual is using to reduce the duration of neutropenia and neutropenia related clinical sequelae in those with nonmyeloid malignancies undergoing myeloblastic chemotherapy followed by bone marrow transplant (BMT);

**OR**

- AA. Individual is using for treatment for hematopoietic cell mobilization for autologous donors in combination with plerixafor (NCCN 2A);

**OR**

- BB. Individual is using for Wilms Tumor (Nephroblastoma) (NCCN 2A); **AND**

- CC. Using with Regimen M and Regimen I for one of the following courses:

1. Cyclophosphamide and etoposide; **OR**
2. Cyclophosphamide, doxorubicin, and vincristine;

**OR**

- DD. Individual is using for autologous hematopoietic stem cell (HSC) mobilization as part of the development of an FDA-approved ex vivo gene therapy (e.g. Zynteglo (betibeglogene autotemcel)) (NCCN 2A).

- II. Requests for pegfilgrastim (Neulasta/Neulasta Onpro), pegfilgrastim-jmdb (Fulphila), pegfilgrastim-pbbk (Fylmetra), pegfilgrastim-fpgk (Stimufend), pegfilgrastim-cbqv (Udenyca), pegfilgrastim-apgf (Nyvepria) or pegfilgrastim-bmez (Ziextenzo) may be approved if the following criteria are met:

- A. Individual with nonmyeloid malignancy is using for primary prophylaxis of FN; **AND**  
B. Individual has a risk of FN of 20% or greater based on chemotherapy regimen (see Appendix, Table 1);

**OR**

- C. Individual with nonmyeloid malignancy is using for primary prophylaxis of FN; **AND**  
D. Individual's risk of developing FN is greater than or equal to 10% and less than 20% based on chemotherapy regimen (see Appendix, Table 1) and individual has any of the following risk factors for FN:

1. Age greater than 65 years (Lyman 2014; Aagaard 2018); **OR**
2. Poor performance status (Eastern Cooperative Oncology Group 3 or 4) or HIV infection (in particular, those with low CD4 counts  $\leq 450/\mu\text{L}$ ) but chemotherapy still indicated (Lyman 2014); **OR**
3. Prior radiation therapy (within previous 1 year) (Terbuch 2018; Fujiwara 2017; Shigeta 2015); **OR**
4. Bone marrow involvement by tumor producing cytopenias (Lyman 2014); **OR**
5. Persistent neutropenia (absolute neutrophil count [ANC] less than  $1500\text{mm}^3$ ) (Lyman 2014); **OR**
6. Poor renal function (glomerular filtration rate [GFR] less than  $60\text{mL/min}$ ) (Lyman 2014; Aagaard 2018); **OR**
7. Liver dysfunction (liver function tests at least 2X upper limit of normal or bilirubin  $> 2.0\text{mg/dL}$ ) (Lyman 2014); **OR**
8. Recent surgery performed as part of cancer management within previous 30 days (not to include a procedure such as port placement, drain placement, IVC filter, etc.) (Lyman 2014; Aagaard 2018); **OR**

9. History of active infection within the previous 60 days (Lyman 2014; Aagaard 2018); **OR**
10. Current open wound and chemotherapy cannot be delayed (Lyman 2014; Aagaard 2018);

**OR**

- E. Individual with nonmyeloid malignancy is using for secondary prophylaxis of FN; **AND**
- F. Individual has experienced a neutropenic complication from a prior cycle of chemotherapy (for which prophylaxis was not received), in which a reduced dose may compromise disease-free or overall survival or treatment outcome (NCCN 2A);

**OR**

- G. Individual is using as adjunctive treatment for FN; **AND**
- H. Individual has not received prophylactic therapy with pegfilgrastim (NCCN 2A); **AND**
- I. Individual has a high risk for infection-associated complications as demonstrated by any of the following:
  1. Expected prolonged (greater than 10 days) and profound (less than  $0.1 \times 10^9/L$ ) neutropenia; **OR**
  2. Age greater than 65 years; **OR**
  3. Pneumonia or other clinically documented infections; **OR**
  4. Hypotension and multi organ dysfunction (sepsis syndrome); **OR**
  5. Invasive fungal infection; **OR**
  6. Prior episode of febrile neutropenia; **OR**
  7. Hospitalized at the time of the development of fever;

**OR**

- J. Individual is receiving dose dense therapy (treatment given more frequently, such as every 2 weeks instead of every 3 weeks) for adjuvant treatment of breast cancer (ASCO Smith 2015);

**OR**

- K. Individual is using after accidental or intentional total body radiation of myelosuppressive doses (greater than 2 Grays [Gy]) (such as Hematopoietic Syndrome of Acute Radiation Syndrome);

**OR**

- L. Individual is using after a hematopoietic progenitor stem cell transplant (HPCT/HSCT) to promote myeloid reconstitution or when engraftment is delayed or has failed (NCCN 2A);

**OR**

- M. Individual is using for treatment for hematopoietic cell mobilization for autologous donors in combination with plerixafor (NCCN 2A);

**OR**

- N. Individual is using for Wilms Tumor (Nephroblastoma) (NCCN 2A); **AND**
- O. Using with Regimen M and Regimen I for one of the following courses:

1. Cyclophosphamide and etoposide; **OR**
2. Cyclophosphamide, doxorubicin, and vincristine;

**OR**

- P. Individual is using for autologous hematopoietic stem cell (HSC) mobilization as part of the development of an FDA-approved ex vivo gene therapy (e.g. Zynteglo (betibeglogene autotemcel)).

III. Requests for sargramostim (Leukine) may be approved if the following criteria are met:

- A. Individual is using as adjunctive treatment for FN: **AND**
- B. Individual has not previously received prophylactic granulocyte colony-stimulating factors (NCCN 2A); **AND**
- C. Individual has a high risk for infection-associated complications as demonstrated by any of the following (NCCN 2A):
  1. Expected prolonged (greater than 10 days) and profound (less than  $0.1 \times 10^9/L$ ) neutropenia; **OR**
  2. Age greater than 65 years; **OR**
  3. Pneumonia or other clinically documented infections; **OR**
  4. Hypotension and multi organ dysfunction (sepsis syndrome); **OR**
  5. Invasive fungal infection; **OR**
  6. Prior episode of febrile neutropenia; **OR**
  7. Hospitalized at the time of the development of fever;

**OR**

- D. Individual is receiving dose dense therapy (treatment given more frequently, such as every 2 weeks instead of every 3 weeks) for adjuvant treatment of breast cancer (ASCO Smith 2015);

**OR**

- E. Individual has a diagnosis of acute myeloid leukemia (AML); **AND**
- F. Individual is 55 years and older **AND**
- G. Individual is using shortly after the completion of induction or repeat induction of chemotherapy of AML;

**OR**

- H. Individual has a diagnosis of myelodysplastic syndromes (MDS); **AND**
- I. Individual has severe neutropenia (ANC less than or equal to  $500 \text{ mm}^3$ ) or experiencing recurrent or resistant infections (NCCN Guidelines Myelodysplastic Syndromes; AHFS);

**OR**

- J. Individual is 18 years or older; **AND**
- K. Individual is using for the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis and autologous transplantation

**OR**

- L. Individual is 2 years of age and older; **AND**

M. Individual is using for the acceleration of myeloid reconstitution following autologous or allogenic bone marrow transplantation or peripheral blood progenitor cell transplantation;

**OR**

N. Individual is 2 years of age and older; **AND**

O. Individual is using for the treatment of delayed neutrophil recovery or graft failure after autologous or allogenic bone marrow transplantation;

**OR**

P. Individual is using to increase survival in adult and pediatric individuals (from birth to 17 years of age) acutely exposed to myelosuppressive doses of radiation (such as Hematopoietic Syndrome of Acute Radiation Syndrome (H-ARS);

**OR**

Q. Individual is 18 years of age or younger; **AND**

R. Individual is diagnosed with relapsed/refractory high-risk neuroblastoma; **AND**

S. Individual is using in combination with dinutuximab (Unituxin), 13-cis-retinoic acid (i.e. isotretinoin) and interleukin-2 (IL-2) (i.e. aldesleukin) (Ladensteinj); **AND**

T. Individual achieved a partial response to first-line multi-agent, multi-modality therapy (i.e. induction combination chemotherapy, or myeloablative consolidation chemotherapy followed by autologous stem cell transplant);

**OR**

U. Individual is diagnosed with relapsed/refractory high-risk neuroblastoma; **AND**

V. Individual is using in combination with Danyelza (naxitamab-gqgk).

IV. Requests for tbo-filgrastim (Granix) may be approved if the following criteria are met:

A. Individual with non-myeloid malignancy is using for primary prophylaxis of FN; **AND**

B. Individual has a risk of FN of 20% or greater based on chemotherapy regimen (see Appendix, Table 1);

**OR**

C. Individual with nonmyeloid malignancy is using for primary prophylaxis of FN; **AND**

D. Individual's risk of developing FN is greater than or equal to 10% and less than 20% based on chemotherapy regimen and individual has any risk factors for FN:

Patient risk factors for the development of febrile neutropenia include but are not limited to (NCCN Guidelines Version 1.2018):

1. Age greater than 65 years (Lyman 2014; Aagaard 2018); **OR**

2. Poor performance status (Eastern Cooperative Oncology Group 3 or 4) or HIV infection (in particular, those with low CD4 counts ( $\leq 450/\mu\text{L}$ )) but chemotherapy still indicated (Lyman 2014); **OR**

3. Prior radiation therapy (within previous 1 year) (Terbuch 2018) (Fujiwara 2017) (Shigeta 2015); **OR**

4. Bone marrow involvement by tumor producing cytopenias (Lyman 2014); **OR**

5. Persistent neutropenia (absolute neutrophil count [ANC] less than  $1500\text{mm}^3$ ) (Lyman 2014); **OR**

6. Poor renal function (glomerular filtration rate [GFR] less than  $60\text{mL/min}$ ) (Lyman 2014; Aagaard 2018); **OR**

7. Liver dysfunction (liver function tests at least 2X upper limit of normal or bilirubin > 2.0 mg/dL) (Lyman 2014; Aagaard 2018); **OR**
8. Recent surgery performed as part of cancer management within previous 30 days (not to include a procedure such as port placement, drain placement, IVC filter, etc.) (Lyman 2014; Aagaard 2018); **OR**
9. History of active infection within previous 60 days (Lyman 2014; Aagaard 2018); **OR**
10. Current open wound and chemotherapy cannot be delayed (Lyman 2014; Aagaard 2018);

**OR**

- E. Individual with nonmyeloid malignancy is using for secondary prophylaxis of FN; **AND**
- F. Individual has experienced a neutropenic complication from a prior cycle of chemotherapy (for which prophylaxis was not received), in which a reduced dose may compromise disease-free or overall survival or treatment outcome (NCCN 2A);

**OR**

- G. Individual is using as an adjunctive treatment for FN;  
**AND**
- H. Individual was previously using Granix (tbo-filgrastim) prophylactically (NCCN 2A);  
**OR**
- I. Individual has not received prophylactic therapy with a granulocyte colony stimulating factor (NCCN Guidelines Myeloid Growth Factors);  
**AND**
- J. Individual has a high risk for infection-associated complications as demonstrated by any of the following:
  1. Expected prolonged (greater than 10 days) and profound (less than  $0.1 \times 10^9/L$ ) neutropenia (NCCN 2A); **OR**
  2. Age greater than 65 years; **OR**
  3. Pneumonia or other clinically documented infections; **OR**
  4. Hypotension and multi organ dysfunction (sepsis syndrome); **OR**
  5. Invasive fungal infection; **OR**
  6. Prior episode of febrile neutropenia; **OR**
  7. Hospitalized at the time of the development of fever;

**OR**

- K. Individual is using after a hematopoietic progenitor stem cell transplant (HPCT/HSCT) to promote myeloid reconstitution or when engraftment is delayed or has failed (NCCN 2A);

**OR**

- L. Individual has a diagnosis of myelodysplastic syndrome (MDS); **AND**
- M. Individual has severe neutropenia (ANC less than or equal to  $500\text{mm}^3$ ) or experiencing recurrent or resistant infections (NCCN 2A);

**OR**

- N. Individual is using to mobilize progenitor cells into peripheral blood for collection by leukapheresis, as an adjunct to peripheral blood/hematopoietic stem cell transplantation (PBSCT/PHSCT) (AHFS);



**OR**

O. Individual is using for treatment for hematopoietic cell mobilization for autologous donors in combination with plerixafor (NCCN 2A);

**OR**

P. Individual is using for autologous hematopoietic stem cell (HSC) mobilization as part of the development of an FDA-approved ex vivo gene therapy (e.g. Zynteglo (betibeglogene autotemcel)).

V. Requests for Rolvedon (eflapegastim-xnst) may be approved if the following criteria are met:

- A. Individual with nonmyeloid malignancy is using for primary prophylaxis of FN; **AND**
- B. Individual has a risk of FN of 20% or greater based on chemotherapy regimen (NCCN 2A) ([see Appendix](#), Table1);

**OR**

- C. Individual with nonmyeloid malignancy is using for primary prophylaxis of FN; **AND**
- D. Individual's risk of developing FN is greater than or equal to 10% and less than 20%

based on chemotherapy regimen ([see Appendix](#), Table 1) and individual has any of the following risk factors for FN:

1. Age greater than 65 years (Lyman 2014; Aagaard 2018); **OR**
2. Poor performance status (Eastern Cooperative Oncology Group 3 or 4) or HIV infection (in particular, those with low CD4 counts ( $\leq 450/\mu\text{L}$ ) but chemotherapy still indicated) (Lyman 2014); **OR**
3. Prior radiation therapy (within previous 1 year) (Terbuch 2018) (Fujiwara 2017) (Shigeta 2015); **OR**
4. Bone marrow involvement by tumor producing cytopenias (Lyman 2014); **OR**
5. Persistent neutropenia (absolute neutrophil count [ANC] less than  $1500\text{mm}^3$ ) (Lyman 2014); **OR**
6. Poor renal function (glomerular filtration rate [GFR] less than  $60\text{mL/min}$ ) (Lyman 2014; Aagaard 2018); **OR**
7. Liver dysfunction (liver function tests at least 2X upper limit of normal or bilirubin  $> 2.0\text{ mg/dL}$ ) (Lyman 2014; Aagaard 20218); **OR**
8. Recent surgery performed as part of cancer management within previous 30 days (not to include a procedure such as port placement, drain placement, IVC filter, etc.) (Lyman 2014; Aagaard 2018); **OR**
9. History of active infection within previous 60 days (Lyman 2014; Aagaard 2018); **OR**
10. Current open wound and chemotherapy cannot be delayed (Lyman 2014; Aagaard 2018);

**OR**

E. Individual with nonmyeloid malignancy is using for secondary prophylaxis of FN; **AND**

F. Individual has experienced a neutropenic complication from a prior cycle of chemotherapy (for which prophylaxis was not received), in which a reduced dose may compromise disease-free or overall survival or treatment outcome (NCCN

2A);

**OR**

G. Individual is using as adjunctive treatment for FN; **AND**

H. Individual has not received prophylactic therapy with pegfilgrastim (NCCN 2A);

**AND**

I. Individual has a high risk for infection-associated complications as demonstrated by any of the following:

1. Expected prolonged (greater than 10 days) and profound (less than  $0.1 \times 10^9/L$ ) neutropenia; **OR**
2. Age greater than 65 years; **OR**
3. Pneumonia or other clinically documented infections; **OR**
4. Hypotension and multi organ dysfunction (sepsis syndrome); **OR**
5. Invasive fungal infection; **OR**
6. Prior episode of febrile neutropenia; **OR**
7. Hospitalized at the time of the development of fever;

**OR**

J. Individual is using for autologous hematopoietic stem cell (HSC) mobilization as part of the development of an FDA-approved ex vivo gene therapy (e.g. Zynteglo (betibeglogene autotemcel)).

Colony Stimulating Factors (filgrastim and their biosimilars, pegfilgrastim and their biosimilars, sargramostim, and tbo-filgrastim) may not be approved for any of the following:

- I. Individual is using as prophylaxis for FN, except when criteria above are met; **OR**
- II. Individual is using as treatment in neutropenia in those who are afebrile, except when criteria above are met; **OR**
- III. Individual is using as adjunctive therapy in those with uncomplicated febrile neutropenia, defined as: fever less than 10 days duration, no evidence of pneumonia, cellulitis, abscess, sinusitis, hypotension, multi-organ dysfunction, or invasive fungal infection; and no uncontrolled malignancies; **OR**
- IV. Individual is using as chemo sensitization of myeloid leukemias; **OR**
- V. Individual is using as prophylaxis for FN during concomitant chemotherapy and radiation therapy; **OR**
- VI. Individual is continuing use if no response is seen within 28-42 days (individuals who have failed to respond within this time frame are considered non-responders); **OR**
- VII. Individual is using as a technique to increase the numbers of circulating hematopoietic stem cells as treatment of damaged myocardium.

#### **Key References:**

1. Aagaard T, Roen A, Reekie J., et.al. Development and Validation of a Risk Score for Febrile Neutropenia After Chemotherapy in Patients With Cancer: The FENCE Score. *JNCI Cancer Spectrum*. 2018; 2(4):1-8.
2. Abe T, Takeda K, Ohe Y, et al. Randomized phase III trial comparing weekly docetaxel plus cisplatin versus docetaxel monotherapy every 3 weeks in elderly patients with advanced non-small-cell lung cancer: the intergroup trial JCOG0803/WJOG4307L. *J Clin Oncol*. 2015;33(6):575-81.
3. Ajani JA, Baker J, Pisters PW, et al. CPT-11 plus cisplatin in patients with advanced, untreated gastric or gastroesophageal junction carcinoma: results of a phase II study. *Cancer*. 2002;94(3):641-6.

4. Andersson M, Lidbrink E, Bjerre K, et al. Phase III randomized study comparing docetaxel plus trastuzumab with vinorelbine plus trastuzumab as first-line therapy of metastatic or locally advanced human epidermal growth factor receptor 2-positive breast cancer: the HERNATA study. *J Clin Oncol*. 2011;29(3):264-71.
5. Angioli R, Plotti F, Aloisi A, et al. A randomized controlled trial comparing four versus six courses of adjuvant platinum-based chemotherapy in locally advanced cervical cancer patients previously treated with neo-adjuvant chemotherapy plus radical surgery. *Gynecol Oncol*. 2015;139(3):433-8.
6. Aoki D, Katsumata N, Nakanishi T, et al. A phase II clinical trial of topotecan in Japanese patients with relapsed ovarian carcinoma. *Jpn J Clin Oncol*. 2011;41:320-7.
7. Arranz Arijá JA, García del Muro X, Gumà J, et al. E400P in advanced seminoma of good prognosis according to the international germ cell cancer collaborative group (IGCCCG) classification: the Spanish Germ Cell Cancer Group experience. *Ann Oncol*. 2001;12(4):487-91.
8. Baetz T, Belch A, Couban S, et al. Gemcitabine, dexamethasone and cisplatin is an active and non-toxic chemotherapy regimen in relapsed or refractory Hodgkin's disease: a phase II study by the National Cancer Institute of Canada Clinical Trials Group. *Ann Oncol*. 2003;14(12):1762-7.
9. Barlesi F, Vansteenkiste J, Spigel D, et al. Avelumab versus docetaxel in patients with platinum-treated advanced non-small-cell lung cancer (JAVELIN Lung 200): an open-label, randomised, phase 3 study. *Lancet Oncol*. 2018;19(11):1468-1479.
10. Baselga J, Cortés J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *N Engl J Med*. 2012;366(2):109-19.
11. Bookman MA, Blessing JA, Hanjani P, Herzog TJ, Andersen WA. Topotecan in squamous cell carcinoma of the cervix: A Phase II study of the Gynecologic Oncology Group. *Gynecol Oncol*. 2000;77(3):446.
12. Burris HA 3rd. Single-agent docetaxel (Taxotere) in randomized phase III trials. *Semin Oncol*. 1999;26(3 Suppl 9):1-6.
13. Burtneß B, Goldwasser MA, Flood W, et al. Eastern Cooperative Oncology Group. Phase III randomized trial of cisplatin plus placebo compared with cisplatin plus cetuximab in metastatic/recurrent head and neck cancer: an Eastern Cooperative Oncology Group study. *J Clin Oncol Off J Am Soc Clin Oncol*. 2005;23(34):8646-8654.
14. Burtneß B, Harrington KJ, Greil R, et al. Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. *Lancet*. 2019;394(10212):1915-1928.
15. Camps C, Massuti B, Jiménez A, et al. Randomized phase III study of 3-weekly versus weekly docetaxel in pretreated advanced non-small-cell lung cancer: a Spanish Lung Cancer Group trial. *Ann Oncol*. 2006;17(3):467-72.
16. Chiorean EG, Cheung WY, Giordano G, et al. Real-world comparative effectiveness of nab-paclitaxel plus gemcitabine versus FOLFIRINOX in advanced pancreatic cancer: a systematic review. *Therapeutic Advances in Medical Oncology*. 2019;11(eCollection 2019):1-17. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2022. URL: <http://www.clinicalpharmacology.com>. Updated periodically.
17. Clamp AR, James EC, McNeish IA, et al. Weekly dose-dense chemotherapy in first-line epithelial ovarian, fallopian tube, or primary peritoneal carcinoma treatment (ICON8): primary progression free survival analysis results from a GCIG phase 3 randomised controlled trial. *Lancet*. 2019;394:2084-2095.
18. Coleman RL, Brady MF, Herzog TJ, et al. Bevacizumab and paclitaxel-carboplatin chemotherapy and secondary cytoreduction in recurrent, platinum-sensitive ovarian cancer (NRG Oncology/Gynecologic Oncology Group study GOG-0213): a multicentre, open-label, randomised, phase 3 trial. *Lancet Oncol*. 2017;18:779-791.
19. Conroy T, Desseigne F, Ychou M, et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. *N Engl J Med*. 2011;364:1817-25.
20. Conroy T, Paillet B, François E, et al. Irinotecan plus oxaliplatin and leucovorin-modulated fluorouracil in advanced pancreatic cancer--a Groupe Tumeurs Digestives of the Federation Nationale des Centres de Lutte Contre le Cancer study. *J Clin Oncol*. 2005;23:1228-36.
21. Coronel J, Cetina L, Candelaria M, et al. Weekly topotecan as second- or third-line treatment in patients with recurrent or metastatic cervical cancer. *Med Oncol*. 2009;26(2):210-4.
22. Crump M, Baetz T, Couban S, et al. Gemcitabine, dexamethasone, and cisplatin in patients with recurrent or refractory aggressive histology B-cell non-Hodgkin lymphoma: a Phase II study by the National Cancer Institute of Canada Clinical Trials Group (NCIC-CTG). *Cancer*. 2004;101(8):1835-42.
23. Crump M, Kuruvilla J, Couban S, et al. Randomized comparison of gemcitabine, dexamethasone, and cisplatin versus dexamethasone, cytarabine, and cisplatin chemotherapy before autologous stem-cell transplantation for relapsed and refractory aggressive lymphomas: NCIC-CTG LY.12. *J Clin Oncol*. 2014;32(31):3490-6.
24. de Bono JS, Oudard S, Ozguroglu M, et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. *Lancet*. 2010;376(9747):1147-54.
25. de Wit R, Skoneczna I, Daugaard G, et al. Randomized phase III study comparing paclitaxel-bleomycin, etoposide, and cisplatin (BEP) to standard BEP in intermediate-prognosis germ-cell cancer: intergroup study EORTC 30983. *J Clin Oncol*. 2012;30(8):792-9.
26. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. <http://dailymed.nlm.nih.gov/dailymed/about.cfm>. Accessed: March 28, 2020.
27. Do T, Medhekar R, Bhat R, Chen H, Niravath P, Trivedi MV. The risk of febrile neutropenia and need for G-CSF primary prophylaxis with the docetaxel and cyclophosphamide regimen in early-stage breast cancer patients: a meta-analysis. *Breast Cancer Res Treat*. 2015;153:591-7.
28. Douillard JY, Rosell R, De Lena M, et al. Adjuvant vinorelbine plus cisplatin versus observation in patients with completely resected stage IB-IIIa non-small-cell lung cancer (Adjuvant Navelbine International Trialist Association [ANITA]): a randomised controlled trial. *Lancet Oncol*. 2006;7(9):719-27.

29. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
30. Eisenberger M, Hardy-Bessard AC, Kim CS, et al. Phase III study comparing a reduced dose of cabazitaxel (20 mg/m<sup>2</sup>) and the currently approved dose (25 mg/m<sup>2</sup>) in postdocetaxel patients with metastatic castration-resistant prostate cancer — PROSELICA. *J Clin Oncol*. 2017;35:3198-206. 21.
31. Enzinger PC, Burtness BA, Niedzwiecki D, et al. CALGB 80403 (Alliance)/E1206: a randomized phase II study of three chemotherapy regimens plus cetuximab in metastatic esophageal and gastroesophageal junction cancers. *J Clin Oncol*. 2016;34(23):2736-42.
32. Fizazi K, Pagliaro L, Laplanche A, et al. Personalised chemotherapy based on tumour marker decline in poor prognosis germ-cell tumours (GETUG 13): a phase 3, multicentre, randomised trial. *Lancet Oncol*. 2014;15(13):1442-1450.
33. Fossella F, Pereira JR, von Pawel J, et al. Randomized, multinational, phase III study of docetaxel plus platinum combinations versus vinorelbine plus cisplatin for advanced non-small-cell lung cancer: the TAX 326 study group. *J Clin Oncol*. 2003;21(16):3016-24.
34. Fujiwara T, Kenmotsu H, Naito T, et al. The incidence and risk factors of febrile neutropenia in chemotherapy-naïve lung cancer patients receiving etoposide plus platinum. *Cancer Chemother Pharmacol*. 2017; 79 (6):1229–1237
35. Gadgeel SM, Stevenson JP, Langer CJ, et al. Pembrolizumab and platinum-based chemotherapy as first-line therapy for advanced non-small-cell lung cancer: Phase 1 cohorts from the KEYNOTE-021 study. *Lung Cancer*. 2018;125:273-281.
36. Gandhi L, Rodriguez-Abreu D, Gadgeel S, et al. Pembrolizumab plus chemotherapy in metastatic non-small-cell lung cancer. *N Engl J Med*. 2018;378(22):2078-92.
37. Garcia-del-Muro X, Maroto P, Gumà J, et al. Chemotherapy as an alternative to radiotherapy in the treatment of stage IIA and IIB testicular seminoma: a Spanish Germ Cell Cancer Group Study. *J Clin Oncol*. 2008;26(33):5416-21.
38. Garon EB, Ciuleanu TE, Arrieta O, et al. Ramucirumab plus docetaxel versus placebo plus docetaxel for second-line treatment of stage IV non-small-cell lung cancer after disease progression on platinum-based therapy (REVEL): a multicentre, double-blind, randomised phase 3 trial. *Lancet*. 2014;384(9944):665-73.
39. Gaut D, Tang K, Sim M, et al. Granulocyte Colony-Stimulating Factor (G-CSF) Interactions with Chimeric Antigen Receptor (CAR) T-Cell Therapy for Diffuse Large B-Cell Lymphoma. *Blood*. 2019;Supp(1): 4109.
40. Gebbia V, Galetta D, Lorusso V, et al. Cisplatin plus weekly vinorelbine versus cisplatin plus vinorelbine on days 1 and 8 in advanced non-small cell lung cancer: a prospective randomized phase III trial of the G.O.I.M. (Gruppo Oncologico Italia Meridionale). *Lung Cancer*. 2008;61(3):369-77.
41. Georgoulas V, Ardavanis A, Agelidou A, et al. Docetaxel versus docetaxel plus cisplatin as front-line treatment of patients with advanced non-small-cell lung cancer: a randomized, multicenter phase III trial. *J Clin Oncol*. 2004;22(13):2602-9.
42. Georgoulas V, Ardavanis A, Tsiafaki X, et al. Vinorelbine plus cisplatin versus docetaxel plus gemcitabine in advanced non-small-cell lung cancer: a phase III randomized trial. *J Clin Oncol*. 2005;23(13):2937-45.
43. Gilbar P, McPherson I, Sorour N, Sanmugarajah J. High incidence of febrile neutropenia following adjuvant breast chemotherapy with docetaxel, carboplatin and trastuzumab. *Breast Cancer Manage*. 2014;3:327-333.
44. Gordon AN, Fleagle JT, Guthrie D, et al. Recurrent epithelial ovarian carcinoma: a randomized phase III study of pegylated liposomal doxorubicin versus topotecan. *J Clin Oncol*. 2001;19:3312-22.
45. Gordon AN, Tonda M, Sun S, et al. Long-term survival advantage for women treated with pegylated liposomal doxorubicin compared with topotecan in a phase 3 randomized study of recurrent and refractory epithelial ovarian cancer. *Gynecol Oncol*. 2004;95:1-8.
46. Gore M, Oza A, Rustin G, et al. A randomised trial of oral versus intravenous topotecan in patients with relapsed epithelial ovarian cancer. *Eur J Cancer*. 2002;38:57-63.
47. Gridelli C, Gallo C, Di Maio M, et al. A randomised clinical trial of two docetaxel regimens (weekly vs 3 week) in the second-line treatment of non-small-cell lung cancer. The DISTAL 01 study. *Br J Cancer*. 2004;91(12):1996-2004.
48. Hanna N, Shepherd FA, Fossella FV, et al. Randomized phase III trial of pemetrexed versus docetaxel in patients with non-small-cell lung cancer previously treated with chemotherapy. *J Clin Oncol*. 2004;22(9):1589-97.
49. Harvey V, Mouridsen H, Semiglazov V, et al. Phase III trial comparing three doses of docetaxel for second-line treatment of advanced breast cancer. *J Clin Oncol*. 2006;24(31):4963-70.
50. Herbst RS, Sun Y, Eberhardt WE, et al. Vandetanib plus docetaxel versus docetaxel as second-line treatment for patients with advanced non-small-cell lung cancer (ZODIAC): a double-blind, randomised, phase 3 trial. *Lancet Oncol*. 2010;11(7):619-26.
51. Horn L, Mansfield AS, Szczesna A, et al. First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. *N Engl J Med*. 2018;379:2220-9.
52. Horwich A, Oliver RT, Wilkinson PM, et al. A medical research council randomized trial of single agent carboplatin versus etoposide and cisplatin for advanced metastatic seminoma. MRC Testicular Tumour Working Party. *Br J Cancer*. 2000;83(12):1623-9.
53. Hosein PJ, Macintyre J, Kawamura C, et al. A retrospective study of neoadjuvant FOLFIRINOX in unresectable or borderline-resectable locally advanced pancreatic adenocarcinoma. *BMC Cancer*. 2012;12 (Article No. 199):17.
54. Hurvitz SA, Martin M, Symmans WF, et al. Neoadjuvant trastuzumab, pertuzumab, and chemotherapy versus trastuzumab emtansine plus pertuzumab in patients with HER2-positive breast cancer (KRISTINE): a randomised, open-label, multicentre, phase 3 trial. *Lancet Oncol*. 2018;19(1):115-126.
55. Ilson DH. Phase II trial of weekly irinotecan/cisplatin in advanced esophageal cancer. *Oncology (Williston Park)*. 2004;18(14 Suppl 14):22-5.
56. Ilson DH(1), Minsky BD, Ku GY, et al. Phase 2 trial of induction and concurrent chemoradiotherapy with weekly irinotecan and cisplatin followed by surgery for esophageal cancer. *Cancer*. 2012;118(11):2820-7.
57. Jones SE, Erban J, Overmoyer B, et al. Randomized phase III study of docetaxel compared with paclitaxel in metastatic breast cancer. *J Clin Oncol*. 2005;23(24):5542–5551.

58. Jones S, Holmes FA, O'Shaughnessy J, et al. Docetaxel With Cyclophosphamide Is Associated With an Overall Survival Benefit Compared With Doxorubicin and Cyclophosphamide: 7-Year Follow-Up of US Oncology Research Trial 9735. *J Clin Oncol*. 2009;27:1177-83.
59. Jones SE, Savin MA, Holmes FA, et al. Phase III trial comparing doxorubicin plus cyclophosphamide with docetaxel plus cyclophosphamide as adjuvant therapy for operable breast cancer. *J Clin Oncol*. 2006;24:5381-7.
60. Judson I, Verweij J, Gelderblom H, et al. Doxorubicin alone versus intensified doxorubicin plus ifosfamide for first-line treatment of advanced or metastatic soft-tissue sarcoma: a randomised controlled phase 3 trial. *Lancet Oncol*. 2014;15(4):415-23.
61. Karampeazis A, Vamvakas L, Agelidou A, et al. Docetaxel vs. vinorelbine in elderly patients with advanced non--small-cell lung cancer: a hellenic oncology research group randomized phase III study. *Clin Lung Cancer*. 2011;12(3):155-60.
62. Katsumata N, Yasuda M, Isonishi S, et al. Long-term results of dose-dense paclitaxel and carboplatin versus conventional paclitaxel and carboplatin for treatment of advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer (JGOG 3016): a randomised, controlled, open-label trial. *Lancet Oncol*. 2013;14:1020-6.
63. Katsumata N, Yasuda M, Takahashi F, et al. Dose-dense paclitaxel once a week in combination with carboplatin every 3 weeks for advanced ovarian cancer: a phase 3, open-label, randomised controlled trial. *Lancet*. 2009;374:1331-8.
64. Kenmotsu H, Yamamoto N, Yamanaka T, et al. Randomized phase III study of pemetrexed plus cisplatin versus vinorelbine plus cisplatin for completely resected stage II to IIIA nonsquamous non-small-cell lung cancer. *J Clin Oncol*. 2020;38(19):2187-2196.
65. Knox JJ, Wong R, Visbal AL, et al. Phase 2 trial of preoperative irinotecan plus cisplatin and conformal radiotherapy, followed by surgery for esophageal cancer. *Cancer*. 2010;116(17):4023-32.
66. Kosaka Y, Rai Y, Masuda N, et al. Phase III placebo-controlled, double-blind, randomized trial of pegfilgrastim to reduce the risk of febrile neutropenia in breast cancer patients receiving docetaxel/cyclophosphamide chemotherapy. *Support Care Cancer*. 2015;23:1137-43.
67. Kosmidis PA, Samantas E, Fountzillas G, et al. Cisplatin/etoposide versus carboplatin/etoposide chemotherapy and irradiation in small cell lung cancer randomized phase II study. Hellenic Cooperative Oncology Group for Lung Cancer Trials. *Semin Oncol* 1994;21(3 Suppl 6):23-30.
68. Kubota K, Sakai H, Katakami N, et al. A randomized phase III trial of oral S-1 plus cisplatin versus docetaxel plus cisplatin in Japanese patients with advanced non-small-cell lung cancer: TCOG0701 CATS trial. *Ann Oncol*. 2015;26(7):1401-8.
69. Kudoh S, Takeda K, Nakagawa K, et al. Phase III study of docetaxel compared with vinorelbine in elderly patients with advanced non-small-cell lung cancer: results of the West Japan Thoracic Oncology Group Trial (WJTOG 9904). *J Clin Oncol*. 2006 Aug 1;24(22):3657-63.
70. Ladenstein R, Potschger U, Valteau-Couanet D, et al. Interleukin 2 with anti-GD2 antibody ch14.18/CHO (dinutuximab beta) in patients with high-risk neuroblastoma (HR-NBL1/SIOPEN): a multicentre, randomized, phase 3 trial. *Lancet Oncol*. 2018;19:1617-1629.
71. Langer CJ, Gadgeel SM, Borghaei H, et al. Carboplatin and pemetrexed with or without pembrolizumab for advanced, non-squamous non-small-cell lung cancer: a randomised, phase 2 cohort of the open-label KEYNOTE-021 study. *Lancet Oncol*. 2016;17:1497-508.
72. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2020; Updated periodically.
73. Lhomme C, Joly F, Walker JL, et al. Phase III study of valspodar (PSC 833) combined with paclitaxel and carboplatin compared with paclitaxel and carboplatin alone in patients with stage IV or suboptimally debulked stage III epithelial ovarian cancer or primary peritoneal cancer. *J Clin Oncol*. 2008;26:2674-82.
74. Lilenbaum RC(1), Herndon JE 2nd, List MA, et al. Single-agent versus combination chemotherapy in advanced non-small-cell lung cancer: the cancer and leukemia group B (study 9730). *J Clin Oncol*. 2005;23:190-6.
75. Lissoni AA, Colombo N, Pellegrino A, et al. A phase II, randomized trial of neo-adjuvant chemotherapy comparing a three-drug combination of paclitaxel, ifosfamide, and cisplatin (TIP) versus paclitaxel and cisplatin (TP) followed by radical surgery in patients with locally advanced squamous cell cervical carcinoma: the Snap-02 Italian Collaborative Study. *Ann Oncol*. 2009;20(4):660-5.
76. Lorigan P, Verweij J, Papai Z, R et al. Phase III trial of two investigational schedules of ifosfamide compared with standard-dose doxorubicin in advanced or metastatic soft tissue sarcoma: a European Organisation for Research and Treatment of Cancer Soft Tissue and Bone Sarcoma Group Study. *J Clin Oncol*. 2007;25(21):3144-50.
77. Lorusso D, Mainenti S, Pietragalla A, et al. Phase II study on weekly bolus topotecan in advanced or recurrent cervical cancer. *Oncology*. 2011;80(5-6):390-4.
78. Lorusso D, Petrelli F, Coinu A, Raspagliesi F, Barni S. A systematic review comparing cisplatin and carboplatin plus paclitaxel-based chemotherapy for recurrent or metastatic cervical cancer. *Gynecol Oncol*. 2014;133(1):117-23.
79. Lyman G, Abella E, and Pettengell R. Risk Factors for Febrile Neutropenia Among Patients With Cancer Receiving Chemotherapy: A Systematic Review. *Crit Rev Oncol Hematol*. 2014; 90 (3), 190-9.
80. Marty M, Cognetti F, Maraninchi D, et al. Randomized phase II trial of the efficacy and safety of trastuzumab combined with docetaxel in patients with human epidermal growth factor receptor 2-positive metastatic breast cancer administered as first-line treatment: the M77001 study group. *J Clin Oncol*. 2005;23(19):4265-74.
81. Mauri D, Kamposioras K, Tsali L, et al. Overall survival benefit for weekly vs. three-weekly taxanes regimens in advanced breast cancer: A meta-analysis. *Cancer Treat Rev*. 2010;36(1):69.
82. McGonigle KF, Muntz HG, Vuky J, et al. Combined weekly topotecan and biweekly bevacizumab in women with platinum-resistant ovarian, peritoneal, or fallopian tube cancer: results of a phase 2 study. *Cancer*. 2011;117:3731-40.
83. Meier W, du Bois A, Reuss A, et al. Topotecan versus treosulfan, an alkylating agent, in patients with epithelial ovarian cancer and relapse within 12 months following 1st-line platinum/paclitaxel chemotherapy. A prospectively randomized phase III trial by the Arbeitsgemeinschaft Gynaekologische Onkologie Ovarian C/ancer Study Group (AGO-OVAR). *Gynecol Oncol*. 2009;114:199-205.

84. Monk BJ, Sill MW, McMeekin DS, et al. Phase III trial of four cisplatin-containing doublet combinations in stage IVB, recurrent, or persistent cervical carcinoma: a Gynecologic Oncology Group study. *J Clin Oncol*. 2009;27(28):4649-55.
85. Moore DH, Blessing JA, McQuellon RP, et al. Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: a gynecologic oncology group study. *J Clin Oncol*. 2004;22(15):3113-9.
86. Motzer RJ, Sheinfeld J, Mazumdar M, et al. Etoposide and cisplatin adjuvant therapy for patients with pathologic stage II germ cell tumors. *J Clin Oncol*. 1995 Nov;13(11):2700-4.
87. Muderspach LI, Blessing JA, Levenback C, Moore JL Jr. A Phase II study of topotecan in patients with squamous cell carcinoma of the cervix: a gynecologic oncology group study. *Gynecol Oncol*. 2001;81(2):213-5.
88. Newman E, Potmesil M, Ryan T, et al. Neoadjuvant chemotherapy, surgery, and adjuvant intraperitoneal chemotherapy in patients with locally advanced gastric or gastroesophageal junction carcinoma: a phase II study. *Semin Oncol*. 2005;32(6 Suppl 9):S97-100.
89. Nichols CR, Williams SD, Loehrer PJ, et al. Randomized study of cisplatin dose intensity in poor-risk germ cell tumors: a Southeastern Cancer Study Group and Southwest Oncology Group protocol. *J Clin Oncol*. 1991;9(7):1163-72.
90. Nielsen OS, Dombrowsky P, Mouridsen H, et al. High-dose epirubicin is not an alternative to standard-dose doxorubicin in the treatment of advanced soft tissue sarcomas. A study of the EORTC soft tissue and bone sarcoma group. *Br J Cancer*. 1998;78(12):1634-1639.
91. NCCN Clinical Practice Guidelines in Oncology™. © 2020 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: <http://www.nccn.org/index.asp>. Updated periodically. Accessed on March 22, 2022.
  - a. Acute Myeloid Leukemia. V1.2022. Revised December 2, 2021.
  - b. Hematopoietic Growth Factors. V1.2022. Revised December 22, 2021.
  - c. Management of Immunotherapy-Related Toxicities. V1.2022. Revised February 28, 2022.
  - d. Myelodysplastic Syndromes. V3.2022. Revised January 13, 2022.
  - e. Wilms Tumor (Nephroblastoma). V2.2021. Revised June 17, 2021.
92. Ohe Y, Ohashi Y, Kubota K, et al. Randomized phase III study of cisplatin plus irinotecan versus carboplatin plus paclitaxel, cisplatin plus gemcitabine, and cisplatin plus vinorelbine for advanced non-small-cell lung cancer: Four-Arm Cooperative Study in Japan. *Ann Oncol*. 2007;18(2):317-23.
93. Okamoto I, Nokihara H, Nomura S, et al. Comparison of carboplatin plus Pemetrexed followed by maintenance pemetrexed with docetaxel monotherapy in elderly patients with advanced nonsquamous non-small cell lung cancer: a phase 3 randomized clinical trial. *JAMA Oncol*. 2020:e196828.
94. Okusaka T, Ikeda M, Fukutomi A, et al. Phase II study of FOLFIRINOX for chemotherapy-naïve Japanese patients with metastatic pancreatic cancer. *Cancer Sci*. 2014;105:1321-6.
95. Oudard S, Fizazi K, Sengeløv L, et al. Cabazitaxel versus docetaxel as first-line therapy for patients with metastatic castration-resistant prostate cancer: a randomized phase III trial — FIRSTANA. *J Clin Oncol* 2017; 35: 3189-97.
96. Paz-Ares L, Luft A, Vicente D, et al. Pembrolizumab plus chemotherapy for squamous non-small-cell lung cancer. *N Engl J Med*. 2018;379:2040-2051.
97. Paz-Ares L, Ross H, O'Brien M, et al. Phase III trial comparing paclitaxel poliglumex vs docetaxel in the second-line treatment of non-small-cell lung cancer. *Br J Cancer*. 2008;98(10):1608-13.
98. Peddi PF, Lubner S, McWilliams R, et al. Multi-institutional experience with FOLFIRINOX in pancreatic adenocarcinoma. *JOP*. 2012;13:497-501.
99. Pignata S, Scambia G, Katsaros D, et al. Carboplatin plus paclitaxel once a week versus every 3 weeks in patients with advanced ovarian cancer (MITO-7): a randomised, multicentre, open-label, phase 3 trial. *Lancet Oncol*. 2014;15:396-405.
100. Pujol JL, Breton JL, Gervais R, et al. Gemcitabine-docetaxel versus cisplatin-vinorelbine in advanced or metastatic non-small-cell lung cancer: a phase III study addressing the case for cisplatin. *Ann Oncol*. 2005;16(4):602-10.
101. Rivera E, Mejia JA, Arun BK, et al. Phase 3 study comparing the use of docetaxel on an every-3-week versus weekly schedule in the treatment of metastatic breast cancer. *Cancer*. 2008;112(7):1455-61.
102. Rodrigues-Pereira J(1), Kim JH, Magallanes M, et al. A randomized phase 3 trial comparing pemetrexed/carboplatin and docetaxel/carboplatin as first-line treatment for advanced, nonsquamous non-small cell lung cancer. *J Thorac Oncol*. 2011;6:1907-14.
103. Sasse EC, Sasse AD, Brandalise SR, et al. Colony stimulating factors for prevention of myelosuppressive therapy induced febrile neutropenia in children with acute lymphoblastic leukaemia. *Cochrane Database Syst Rev*. 2005; (3):CD004139.
104. Scagliotti GV, Parikh P, von Pawel J, et al. Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naïve patients with advanced-stage non-small-cell lung cancer. *J Clin Oncol*. 2008;26:3543-51.
105. Schiller JH, Harrington D, Belani CP, et al. Comparison of four chemotherapy regimens for advanced non-small-cell lung cancer. *N Engl J Med*. 2002;346(2):92-8.
106. Seddon B, Strauss SJ, Whelan J, et al. Gemcitabine and docetaxel versus doxorubicin as first-line treatment in previously untreated advanced unresectable or metastatic soft-tissue sarcomas (GeDDiS): a randomised controlled phase 3 trial. *Lancet Oncol*. 2017;18(10):1397-1410.
107. Sehouli J, Stengel D, Oskay-Oezcelik G, et al. Nonplatinum topotecan combinations versus topotecan alone for recurrent ovarian cancer: results of a phase III study of the North-Eastern German Society of Gynecological Oncology Ovarian Cancer Study Group. *J Clin Oncol*. 2008;26:3176-82.
108. Shigeta K, Kosaka T, Yazawa S, et al. Predictive factors for severe and febrile neutropenia during docetaxel chemotherapy for castration-resistant prostate cancer. *Int J Clin Oncol*. 2015; 20(3):605-612.

109. Smith TJ, Bohlke K, Lyman GH, et al. Recommendations for the Use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol.* 2015;33(28):3199-212.
110. Socinski MA, Jotte RM, Cappuzzo F, et al. Atezolizumab for first-line treatment of metastatic nonsquamous NSCLC. *N Engl J Med.* 2018;378:2288-301.
111. Socinski MA, Smit EF, Lorigan P, et al. Phase III study of pemetrexed plus carboplatin compared with etoposide plus carboplatin in chemotherapy-naïve patients with extensive-stage small-cell lung cancer. *J Clin Oncol.* 2009;27:4787-92.
112. Spannuth WA, Leath CA, Huh WK, et al. A phase II trial of weekly topotecan for patients with secondary platinum-resistant recurrent epithelial ovarian carcinoma following the failure of second-line therapy. *Gynecol Oncol.* 2007;104:591-5.
113. Sparano JA, Wang M, Martino S, et al. Weekly paclitaxel in the adjuvant treatment of breast cancer. *N Engl J Med.* 2008;358(16):1663.
114. Sugiyama T, Okamoto A, Enomoto T, et al. Randomized phase III trial of irinotecan plus cisplatin compared with paclitaxel plus carboplatin as first-line chemotherapy for ovarian clear cell carcinoma: JGOG3017/GCIG Trial. *J Clin Oncol.* 2016;34:2881-7.
115. Suker M, Beumer BR, Sadot E, et al. FOLFIRINOX for locally advanced pancreatic cancer: a systematic review and patient-level meta-analysis. *Lancet Oncol.* 2016;17:801-10.
116. Swisher EM, Mutch DG, Rader JS, et al. Topotecan in platinum- and paclitaxel-resistant ovarian cancer. *Gynecol Oncol.* 1997;66:480-6.
117. Tabernero J, Climent MA, Lluch A, et al. A multicentre, randomised phase II study of weekly or 3-weekly docetaxel in patients with metastatic breast cancer. *Ann Oncol.* 2004;15(9):1358-65.
118. Tap WD, Papai Z, Van Tine BA, et al. Doxorubicin plus evofosfamide versus doxorubicin alone in locally advanced, unresectable or metastatic soft-tissue sarcoma (TH CR-406/SARC021): an international, multicentre, open-label, randomised phase 3 trial. *Lancet Oncol.* 2017;18(8):1089-1103.
119. Tap WD, Wagner AJ, Schöffski P, et al. Effect of doxorubicin plus olaratumab vs doxorubicin plus placebo on survival in patients with advanced soft tissue sarcomas: the ANNOUNCE randomized clinical trial. *JAMA.* 2020;323(13):1266-1276.
120. Terbuch A, Posch F, Partl R, et al. Risk stratification for febrile neutropenia in patients with testicular germ cell tumors. *Cancer Medicine.* 2018; 7(2):508-514.
121. Tewari KS, Sill MW, Long HJ 3rd, et al. Improved survival with bevacizumab in advanced cervical cancer. *N Engl J Med.* 2014;370(8):734-43.
122. Tewari KS, Sill MW, Penson RT, et al. Bevacizumab for advanced cervical cancer: final overall survival and adverse event analysis of a randomised, controlled, open-label, phase 3 trial (Gynecologic Oncology Group 240). *Lancet.* 2017;390(10103):1654-1663.
123. Thibodeau S, Voutsadakis IA. FOLFIRINOX chemotherapy in metastatic pancreatic cancer: a systematic review and meta-analysis of retrospective and phase II studies. *J Clin Med.* 2018;7:1-11.
124. Tong H, Fan Z, Liu B, Lu T. The benefits of modified FOLFIRINOX for advanced pancreatic cancer and its induced adverse events: a systematic review and meta-analysis. *Sci Rep.* 2018;8:8666.
125. Vasey PA, Jayson GC, Gordon A, et al. Phase III randomized trial of docetaxel-carboplatin versus paclitaxel-carboplatin as first-line chemotherapy for ovarian carcinoma. *J Natl Cancer Inst.* 2004;96:1682-91.
126. Vermorken JB, Stöhlmacher-Williams J, Davidenko I, et al. Cisplatin and fluorouracil with or without panitumumab in patients with recurrent or metastatic squamous-cell carcinoma of the head and neck (SPECTRUM): an open-label phase 3 randomised trial. *Lancet Oncol.* 2013;14(8):697.
127. Vermorken JB, Mesia R, Rivera F, et al. Platinum-based chemotherapy plus cetuximab in head and neck cancer. *N Engl J Med.* 2008;359(11):1116-27.
128. Vorobiof DA, Rapoport BL, Chasen MR, Cohen GL, Mahomed R, Karime M. Phase II clinical trial of carboplatin and docetaxel in patients with metastatic ovarian cancer: active combination with low incidence of peripheral neuropathy. *Int J Gynecol Cancer.* 2003;13(3):287-91.
129. Wang Y, Herrstedt J, Havsteen H, et al. A multicenter, non-randomized, phase II study of docetaxel and carboplatin administered every 3 weeks as second line chemotherapy in patients with first relapse of platinum sensitive epithelial ovarian, peritoneal or fallopian tube cancer. *BMC Cancer.* 2014;14:937. Williamson SK, Crowley JJ, Lara PN Jr, et al. Phase III trial of paclitaxel plus carboplatin with or without tirapazamine in advanced non-small-cell lung cancer: Southwest Oncology Group Trial S0003. *J Clin Oncol.* 2005;23:9097-104.
130. Winton T, Livingston R, Johnson D, et al. Vinorelbine plus cisplatin vs. observation in resected non-small-cell lung cancer. *N Engl J Med.* 2005;352(25):2589-97.
131. Yang Z, Chen D, Zhang J, et al. The efficacy and safety of neoadjuvant chemotherapy in the treatment of locally advanced cervical cancer: A randomized multicenter study. *Gynecol Oncol.* 2016;141(2):231-239.
132. Yoh K, Hosomi Y, Kasahara K, et al. A randomized, double-blind, phase II study of ramucirumab plus docetaxel vs placebo plus docetaxel in Japanese patients with stage IV non-small cell lung cancer after disease progression on platinum-based therapy. *Lung Cancer.* 2016;99:186-93.
133. Younis T, Rayson D, Thompson K. Primary G-CSF prophylaxis for adjuvant TC or FEC-D chemotherapy outside of clinical trial settings: a systematic review and meta-analysis. *Support Care Cancer.* 2012;20:2523-30.

## Appendix

### Febrile Neutropenia Risk of Selected Chemotherapy Regimens



The following table represents selected chemotherapy regimens requiring further examination in their disease setting and the associated risk for development of febrile neutropenia. This is not a comprehensive list, as there are other regimens that are associated with risk for the development of FN. The FN risk of these other regimens will follow the guidance within the NCCN Guidelines Management of Neutropenia. A high-risk chemotherapy regimen is defined as a  $\geq 20\%$  probability of developing febrile neutropenia, an intermediate-risk chemotherapy regimen is associated with  $\geq 10$  to  $\leq 20\%$  incidence of developing FN, and a low-risk chemotherapy regimen is associated with  $<10\%$  incidence of developing FN.

**Table 1**

<b>Disease State</b>	<b>Chemotherapy regimen</b>	<b>Risk of developing FN</b>	<b>References</b>
Breast Cancer	Adjuvant TC	Intermediate	Do 2015; Jones 2009; Jones 2006; Kosaka 2015; Younis 2012
Breast Cancer (Advanced)	Docetaxel (dosing of less than 75 mg/m <sup>2</sup> )	Low	Harvey V 2006; Mauri D 2010; Rivera E 2008; Sparano JA 2008; Tabernero J 2004
Breast Cancer (Advanced)	Docetaxel (dosing of 100 mg/m <sup>2</sup> every 3 weeks or less)	Intermediate	Andersson M 2011; Baselga J 2012; Burris HA 1999; Harvey V 2006; Jones SE 2005; Marty M 2005;
Castrate-Resistant Prostate Cancer (CRPC) (Advanced)	Cabazitaxel	Intermediate	De Bono JS. 2010; Eisenberger M 2017; Oudard S 2017
Cervical Cancer (Advanced)	Cisplatin and paclitaxel $\pm$ bevacizumab	Intermediate	Angioli R 2015; Lissoni AA 2009; Lorusso D 2014; Monk BJ 2009; Moore DH 2004; Tewari KS 2014, 2017; Yang Z 2016
	Topotecan	Intermediate	Bookman MA 2000; Coronel J 2009; Lorusso D 2011; Muderspach LI 2001;
Gastroesophageal Cancer	Cisplatin and irinotecan	Intermediate	Ajani JA 2002; Enzinger PC 2016; Ilson DH 2004, 2012; Knox JJ 2010; Newman E 2005
Germ Cell Tumors (Advanced)	Bleomycin, etoposide, and cisplatin	Intermediate	de Wit R 2012; Fizazi K 2014; Garcia del Muro X 2008; Nichols CR 1991
	Etoposide and cisplatin	Intermediate	Arranz A 2001; Horwich A 2000; Motzer RJ 1995
Head and Neck Cancer (Recurrent/Metastatic)	EGFR-inhibitor (cetuximab or panitumumab) and platinum-based chemotherapy	Low	Burtneess B 2005; Vermorken JB 2008; Vermorken JB 2013;
	Pembrolizumab plus platinum-based chemotherapy	Low	Burtneess B 2019;
Lymphoma	Gemcitabine, dexamethasone, and cisplatin $\pm$ rituximab	Intermediate	Baetz T 2003; Crump M 2004, 2014
Non-Small Cell Lung Cancer	Cisplatin and vinorelbine	Intermediate	Douillard JY 2006; Fossella F 2003; Gebbia V 2008; Georgoulas V 2005; Kenmotsu H 2020; Pujol JL 2005; Winton T 2005
Non-Small Cell Lung Cancer (Advanced)	Docetaxel	Intermediate	Abe T 2015; Barlesi F 2018; Camps C 2006; Georgoulas V 2004; Gridelli C 2004; Hanna N 2004; Herbst RS 2010; Karampeazis A 2011; Kudoh S 2006; Okamoto I 2020; Paz-Ares L 2008



Non-Small Cell Lung Cancer (Advanced)	Docetaxel and cisplatin	Low	Abe T 2015; Fossella F 2003; Kubota K 2015; Schiller JH 2002
Non-Small Cell Lung Cancer (Metastatic)	Carboplatin/cisplatin, pemetrexed, and pembrolizumab	Low	Gandhi 2018; Langer 2016; Rodrigues-Pereira 2011; Scagliotti 2008
Non-Small Cell Lung Cancer (Metastatic, non-squamous)	Carboplatin, paclitaxel, and atezolizumab ± bevacizumab	Low	Lilenbaum 2005; Ohe 2007; Socinski 2018; Williamson 2005
Non-Small Cell Lung Cancer (Metastatic, squamous)	Carboplatin, paclitaxel/nab-paclitaxel, and pembrolizumab	Low	Gadgeel 2018; Lilenbaum 2005; Ohe 2007; Paz-Ares 2018; Williamson 2005
Ovarian Cancer	Carboplatin and paclitaxel	Low	Clamp 2019; Coleman 2017; Katsumata 2009, 2013; Lhomme 2008; Pignata 2014; Sugiyama 2016; Vasey 2004
Ovarian Cancer (Advanced)	Topotecan	Intermediate	Aoki 2011; Gordon 2001, 2004; Gore 2002; McGonigle 2011; Meier 2009; Sehouli J 2008; Spannuth WA 2007; Swisher 1997
Pancreatic Cancer	FOLFIRINOX	Intermediate	Chloreaan 2019; Conroy 2011; Conroy 2005; Hosein 2012; Okusaka 2014; Peddi 2012; Suker 2016; Thibodeau 2018; Tong 2018
Small Cell Lung Cancer (Extensive Stage)	Carboplatin, etoposide, and atezolizumab	Low	Horn 2018; Kosmidis 1994; Socinski 2009
Soft Tissue Sarcoma (Advanced)	Doxorubicin	High	Judson I 2014; Lorigan P 2007; Nielsen OS 1998; Seddon B 2017; Tap WD 2017; Tap WD 2020

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