

## THROMBOPENIE CHIMIO-INDUITE

La thrombopénie dont le score CTCAE est rappelé dans le tableau 15, peut être induite par de nombreuses molécules de chimiothérapie (**Tableau 17**). Cette thrombopénie peut être responsable d'hémorragie, individuellement évaluable dans la classification CTCAE ou bien par le score OMS du tableau 16.

Le délai avant cette myélo-suppression est souvent long (plusieurs semaines), correspondant au délai nécessaire pour détruire la population des mégacaryocytes (62).

Il s'agit donc d'une **thrombopénie centrale**. Dans ce cas précis, elle pose rarement de problème diagnostique car il s'agit d'un effet secondaire attendu.

Le romiplostim (protéine de fusion analogue de la thrombopoïétine, se fixant sur les récepteurs rTPO) et l'eltrombopag olamine (facteur de croissance plaquettaire oral) sont disponibles en France mais n'ont pas d'AMM en oncologie solide.

En 2018, l'ASCO a actualisé ses recommandations sur ce sujet (63).

Grade 1	75 000/mm <sup>3</sup> ≤ Plaquettes < 100 000/mm <sup>3</sup>
Grade 2	50 000/mm <sup>3</sup> ≤ Plaquettes < 75 000/mm <sup>3</sup>
Grade 3	25 000/mm <sup>3</sup> ≤ Plaquettes < 50 000/mm <sup>3</sup>
Grade 4	Plaquettes < 25 000/mm <sup>3</sup>
Grade 5	-

Tableau 15 – Scores OMS - Evaluation de la sévérité de la thrombopénie.

Grade 0	Pas de saignement
Grade 1	Saignement pétéchial
Grade 2	Perte de sang légère (cliniquement significatif)
Grade 3	Perte de sang importante, nécessité de transfusion (sévère)
Grade 4	Perte de sang invalidante, hémorragie rétinienne ou cérébrale, décès

Tableau 16 – Scores OMS - Evaluation de la sévérité des saignements

### 1. Indication des transfusions prophylactiques de plaquette

Chez un patient stable sur le plan hémodynamique (situation prophylactique), sans saignement actif, il est recommandé de prescrire une transfusion de plaquette aux seuils suivants (63–65) :

- **Thrombopénie < 10 000/mm<sup>3</sup>** en cas de thrombopénie chronique secondaire à une chimiothérapie, y compris pour les patients porteurs d'une tumeur solide en cours de chimiothérapie.
- **Thrombopénie < 20 000/mm<sup>3</sup>** pour les patients présentant au moins l'un des critères suivants :
  - Fièvre > 38,5°C
  - Tableau septique
  - Leucocytose > 75 000/mm<sup>3</sup>
  - Aspergillose invasive
  - Traitement par l'amphotéricine B

## REFERENCES

1. Temel JS, Greer JA, Muzikansky A, Gallagher ER, Admane S, Jackson VA, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med*. 2010 Aug 19;363(8):733–42.
2. Di Maio M, Basch E, Bryce J, Perrone F. Patient-reported outcomes in the evaluation of toxicity of anticancer treatments. *Nat Rev Clin Oncol*. 2016 May;13(5):319–25.
3. Basch E, Dueck AC, Rogak LJ, Mitchell SA, Minasian LM, Denicoff AM, et al. Feasibility of Implementing the Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events in a Multicenter Trial: NCCTG N1048. *JCO*. 2018 Nov;36(31):3120–5.
4. Lorusso D, Bria E, Costantini A, Di Maio M, Rosti G, Mancuso A. Patients' perception of chemotherapy side effects: Expectations, doctor-patient communication and impact on quality of life - An Italian survey. *Eur J Cancer Care (Engl)*. 2017 Mar;26(2).
5. Vidall C, Fernández-Ortega P, Cortinovis D, Jahn P, Amlani B, Scotté F. Impact and management of chemotherapy/radiotherapy-induced nausea and vomiting and the perceptual gap between oncologists/oncology nurses and patients: a cross-sectional multinational survey. *Support Care Cancer*. 2015 Nov;23(11):3297–305.
6. Durand J-P, Madelaine I, Scotté F. [Guidelines for prophylaxis and treatment of chemotherapy-induced nausea and vomiting]. *Bull Cancer*. 2009 Oct;96(10):951–60.
7. Feyer P, Jordan K. Update and new trends in antiemetic therapy: the continuing need for novel therapies. *Ann Oncol*. 2011 Jan;22(1):30–8.
8. Dranitsaris G, Molassiotis A, Clemons M, Roeland E, Schwartzberg L, Dielenseger P, et al. The development of a prediction tool to identify cancer patients at high risk for chemotherapy-induced nausea and vomiting. *Ann Oncol*. 2017 Jun 1;28(6):1260–7.
9. Ahrari S, Chow R, Goodall S, DeAngelis C. Anticipatory nausea: current landscape and future directions. *Ann Palliat Med*. 2017 Jan;6(1):1–2.
10. Karthaus M, Tibor C, Lorusso V, Singh-Arora R, Filippov A, Rizzi G, et al. Efficacy and safety of oral palonosetron compared with IV palonosetron administered with dexamethasone for the prevention of chemotherapy-induced nausea and vomiting (CINV) in patients with solid tumors receiving cisplatin-based highly emetogenic chemotherapy (HEC). *Support Care Cancer*. 2015 Oct;23(10):2917–23.
11. Raftopoulos H, Cooper W, O'Boyle E, Gabrail N, Boccia R, Gralla RJ. Comparison of an extended-release formulation of granisetron (APF530) versus palonosetron for the prevention of chemotherapy-induced nausea and vomiting associated with moderately or highly emetogenic chemotherapy: results of a prospective, randomized, double-blind, noninferiority phase 3 trial. *Support Care Cancer*. 2015 Mar;23(3):723–32.
12. VITAL-DURAND D. Guide pratique des médicaments Dorosz. 28th ed. 2009.
13. Saito H, Yoshizawa H, Yoshimori K, Katakami N, Katsumata N, Kawahara M, et al. Efficacy and safety of single-dose fosaprepitant in the prevention of chemotherapy-induced nausea and vomiting in patients receiving high-dose cisplatin: a multicentre, randomised, double-blind, placebo-controlled phase 3 trial. *Ann Oncol*. 2013 Apr;24(4):1067–73.
14. Aapro MS, Walko CM. Aprepitant: drug-drug interactions in perspective. *Ann Oncol*. 2010 Dec;21(12):2316–23.
15. Zhang L, Lu S, Feng J, Dechaphunkul A, Chang J, Wang D, et al. A Randomized Phase 3 Study Evaluating the Efficacy of Single-dose NEPA, a Fixed Antiemetic Combination of Netupitant and Palonosetron, Versus an Aprepitant Regimen for Prevention of Chemotherapy-induced Nausea and Vomiting (CINV) in Patients Receiving Highly Emetogenic Chemotherapy (HEC). *Ann Oncol*. 2017 Oct 28;
16. Ito Y, Tsuda T, Minatogawa H, Kano S, Sakamaki K, Ando M, et al. Placebo-Controlled, Double-Blinded Phase III Study Comparing Dexamethasone on Day 1 With Dexamethasone on Days 1 to 3 With Combined Neurokinin-1 Receptor Antagonist and Palonosetron in High-Emetogenic Chemotherapy. *Journal of Clinical Oncology*. 2018 Apr;36(10):1000–6.
17. Fonte C, Fatigoni S, Roila F. A review of olanzapine as an antiemetic in chemotherapy-induced nausea and vomiting and in palliative care patients. *Crit Rev Oncol Hematol*. 2015 Aug;95(2):214–21.
18. Navari RM, Qin R, Ruddy KJ, Liu H, Powell SF, Bajaj M, et al. Olanzapine for the Prevention of Chemotherapy-Induced Nausea and Vomiting. *N Engl J Med*. 2016 Jul 14;375(2):134–42.
19. Hesketh PJ, Kris MG, Basch E, Bohlke K, Barbour SY, Clark-Snow RA, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol*. 2017 Oct 1;35(28):3240–61.
20. Herrstedt J, Roila F, Warr D, Celio L, Navari RM, Hesketh PJ, et al. 2016 Updated MASCC/ESMO Consensus Recommendations: Prevention of Nausea and Vomiting Following High Emetic Risk Chemotherapy. *Support Care Cancer*. 2017 Jan;25(1):277–88.
21. Widgren Y, Enblom A. Emesis in patients receiving acupuncture, sham acupuncture or standard care during chemo-radiation: A randomized controlled study. *Complement Ther Med*. 2017 Oct;34:16–25.
22. Chen B, Guo Y, Zhao X, Gao L-L, Li B, Zhao T-Y, et al. Efficacy differences of electroacupuncture with single acupoint or matching acupoints for chemotherapy-induced nausea and vomiting: study protocol for a randomized controlled trial. *Trials*. 2017 Oct 13;18(1):477.
23. Gao L, Chen B, Zhang Q, Zhao T, Li B, Sha T, et al. Acupuncture with different acupoint combinations for chemotherapy-induced nausea and vomiting: study protocol for a randomized controlled trial. *BMC Complement Altern Med*. 2016 Nov 8;16(1):441.
24. Li Q-W, Yu M-W, Yang G-W, Wang X-M, Wang H, Zhang C-X, et al. Effect of acupuncture in prevention and treatment of chemotherapy-induced nausea and vomiting in patients with advanced cancer: study protocol for a randomized controlled trial. *Trials*. 2017 20;18(1):185.
25. Roila F, Molassiotis A, Herrstedt J, Aapro M, Gralla RJ, Bruera E, et al. 2016 MASCC and ESMO guideline update for the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting and of nausea and vomiting in advanced cancer patients. *Ann Oncol*. 2016 Sep;27(suppl 5):v119–33.
26. Hesketh PJ, Bohlke K, Lyman GH, Basch E, Chesney M, Clark-Snow RA, et al. Antiemetics: American Society of Clinical Oncology Focused Guideline Update. *J Clin Oncol*. 2016 Feb 1;34(4):381–6.
27. Grunberg SM, Warr D, Gralla RJ, Rapoport BL, Hesketh PJ, Jordan K, et al. Evaluation of new antiemetic agents and definition of antineoplastic agent emetogenicity--state of the art. *Support Care Cancer*. 2011 Mar;19 Suppl 1:S43-47.
28. Aapro MS, Bohlius J, Cameron DA, Dal Lago L, Donnelly JP, Kearney N, et al. 2010 update of EORTC guidelines for the use of granulocyte-colony stimulating factor to reduce the incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphoproliferative disorders and solid tumours. *Eur J Cancer*. 2011 Jan;47(1):8–32.

29. Crawford J, Caserta C, Roila F, ESMO Guidelines Working Group. Hematopoietic growth factors: ESMO Clinical Practice Guidelines for the applications. *Ann Oncol*. 2010 May;21 Suppl 5:v248-251.
30. Smith TJ, Bohlke K, Lyman GH, Carson KR, Crawford J, Cross SJ, et al. Recommendations for the Use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update. *Journal of Clinical Oncology*. 2015 Oct 1;33(28):3199–212.
31. Xu H, Gong Q, Vogl FD, Reiner M, Page JH. Risk factors for bone pain among patients with cancer receiving myelosuppressive chemotherapy and pegfilgrastim. *Support Care Cancer*. 2016 Feb;24(2):723–30.
32. Lyman GH, Dale DC, Wolff DA, Culakova E, Poniewierski MS, Kuderer NM, et al. Acute myeloid leukemia or myelodysplastic syndrome in randomized controlled clinical trials of cancer chemotherapy with granulocyte colony-stimulating factor: a systematic review. *J Clin Oncol*. 2010 Jun 10;28(17):2914–24.
33. Klastersky J, de Naurois J, Rolston K, Rapoport B, Maschmeyer G, Aapro M, et al. Management of febrile neutropenia: ESMO Clinical Practice Guidelines. *Ann Oncol*. 2016 Sep;27(suppl 5):v111–8.
34. Crawford J, Becker PS, Armitage JO, Blayney DW, Chavez J, Curtin P, et al. Myeloid Growth Factors, Version 2.2017, NCCN Clinical Practice Guidelines in Oncology. *Journal of the National Comprehensive Cancer Network*. 2017 Dec;15(12):1520–41.
35. Crawford J, Armitage J, Balducci L, Becker PS, Blayney DW, Cataland SR, et al. Myeloid growth factors. *J Natl Compr Canc Netw*. 2013 Oct 1;11(10):1266–90.
36. Smith TJ, Khatcheressian J, Lyman GH, Ozer H, Armitage JO, Balducci L, et al. 2006 update of recommendations for the use of white blood cell growth factors: an evidence-based clinical practice guideline. *J Clin Oncol*. 2006 Jul 1;24(19):3187–205.
37. Rapoport BL, Aapro M, Paesmans M, van Eeden R, Smit T, Krendyukov A, et al. Febrile neutropenia (FN) occurrence outside of clinical trials: occurrence and predictive factors in adult patients treated with chemotherapy and an expected moderate FN risk. Rationale and design of a real-world prospective, observational, multinational study. *BMC Cancer* [Internet]. 2018 Dec [cited 2019 Jan 2];18(1). Available from: <https://bmccancer.biomedcentral.com/articles/10.1186/s12885-018-4838-z>
38. Crawford J, Dale DC, Kuderer NM, Culakova E, Poniewierski MS, Wolff D, et al. Risk and timing of neutropenic events in adult cancer patients receiving chemotherapy: the results of a prospective nationwide study of oncology practice. *J Natl Compr Canc Netw*. 2008 Feb;6(2):109–18.
39. Bennett CL, Djulbegovic B, Norris LB, Armitage JO. Colony-stimulating factors for febrile neutropenia during cancer therapy. *N Engl J Med*. 2013 Mar 21;368(12):1131–9.
40. Crawford J, Dale DC, Kuderer NM, Culakova E, Poniewierski MS, Wolff D, et al. Risk and timing of neutropenic events in adult cancer patients receiving chemotherapy: the results of a prospective nationwide study of oncology practice. *J Natl Compr Canc Netw*. 2008 Feb;6(2):109–18.
41. Sheikh H, Colaco R, Lorigan P, Blackhall F, Califano R, Ashcroft L, et al. Use of G-CSF during concurrent chemotherapy and thoracic radiotherapy in patients with limited-stage small-cell lung cancer safety data from a phase II trial. *Lung Cancer*. 2011 Oct;74(1):75–9.
42. Taplitz RA, Kennedy EB, Bow EJ, Crews J, Gleason C, Hawley DK, et al. Antimicrobial Prophylaxis for Adult Patients With Cancer-Related Immunosuppression: ASCO and IDSA Clinical Practice Guideline Update. *Journal of Clinical Oncology*. 2018 Oct 20;36(30):3043–54.
43. Skoetz N, Bohlius J, Engert A, Monsef I, Blank O, Vehreschild J-J. Prophylactic antibiotics or G(M)-CSF for the prevention of infections and improvement of survival in cancer patients receiving myelotoxic chemotherapy. *Cochrane Database Syst Rev*. 2015 Dec 21;(12):CD007107.
44. Réseau Régional de Cancérologie Rhône-Alpes Auvergne. Référentiel soins oncologiques de support. (consulté le 13/10/2011) [Internet]. 2010. Available from: <http://www.rrc-ra.fr/Ressources/referentiels/PRA-SOS-1012ANEMIE.pdf>
45. Campos MPO, Hassan BJ, Riechelmann R, Del Giglio A. Cancer-related fatigue: a practical review. *Ann Oncol*. 2011 Jun;22:1273–9.
46. Schrijvers D, De Samblanx H, Roila F, ESMO Guidelines Working Group. Erythropoiesis-stimulating agents in the treatment of anaemia in cancer patients: ESMO Clinical Practice Guidelines for use. *Ann Oncol*. 2010 May;21 Suppl 5:v244-247.
47. Watkins T, Surowiecka MK, McCullough J. Transfusion indications for patients with cancer. *Cancer Control*. 2015 Jan;22(1):38–46.
48. Aapro M, Beguin Y, Bokemeyer C, Dicato M, Gascón P, Glaspy J, et al. Management of anaemia and iron deficiency in patients with cancer: ESMO Clinical Practice Guidelines. *Ann Oncol*. 2018 Oct 1;29(Supplement\_4):iv271.
49. Rizzo JD, Brouwers M, Hurley P, Seidenfeld J, Arcasoy MO, Spivak JL, et al. American Society of Clinical Oncology/American Society of Hematology clinical practice guideline update on the use of epoetin and darbepoetin in adult patients with cancer. *J Clin Oncol*. 2010 Nov 20;28(33):4996–5010.
50. Tonia T, Mettler A, Robert N, Schwarzer G, Seidenfeld J, Weingart O, et al. Erythropoietin or darbepoetin for patients with cancer. *Cochrane Database Syst Rev*. 2012 Dec 12;12:CD003407.
51. Bennett CL, Djulbegovic B, Norris LB, Armitage JO. Colony-stimulating factors for febrile neutropenia during cancer therapy. *N Engl J Med*. 2013 Mar 21;368(12):1131–9.
52. Grant MD, Piper M, Bohlius J, Tonia T, Robert N, Vats V, et al. Epoetin and Darbepoetin for Managing Anemia in Patients Undergoing Cancer Treatment: Comparative Effectiveness Update [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 [cited 2016 Jan 28]. (AHRQ Comparative Effectiveness Reviews). Available from: <http://www.ncbi.nlm.nih.gov/books/NBK143013/>
53. Mhaskar R, Wao H, Miladinovic B, Kumar A, Djulbegovic B. The role of iron in the management of chemotherapy-induced anemia in cancer patients receiving erythropoiesis-stimulating agents. *Cochrane Database Syst Rev*. 2016 Feb 4;2:CD009624.
54. Pedrazzoli P, Farris A, Del Prete S, Del Gaizo F, Ferrari D, Bianchessi C, et al. Randomized trial of intravenous iron supplementation in patients with chemotherapy-related anemia without iron deficiency treated with darbepoetin alpha. *J Clin Oncol*. 2008 Apr 1;26(10):1619–25.
55. Steensma DP, Sloan JA, Dakhil SR, Dalton R, Kahanic SP, Prager DJ, et al. Phase III, randomized study of the effects of parenteral iron, oral iron, or no iron supplementation on the erythropoietic response to darbepoetin alfa for patients with chemotherapy-associated anemia. *J Clin Oncol*. 2011 Jan 1;29(1):97–105.
56. Petrelli F, Borgonovo K, Cabiddu M, Lonati V, Barni S. Addition of iron to erythropoiesis-stimulating agents in cancer patients: a meta-analysis of randomized trials. *J Cancer Res Clin Oncol*. 2012 Feb;138(2):179–87.
57. Lebrun F, Klastersky J, Levacq D, Wissam Y, Paesmans M. Intravenous iron therapy for anemic cancer patients: a review of recently published clinical studies. *Support Care Cancer*. 2017 Jul;25(7):2313–9.

58. Canon J-L, Vansteenkiste J, Hedenus M, Gascon P, Bokemeyer C, Ludwig H, et al. Transfusion risk in cancer patients with chemotherapy-induced anemia when initiating darbepoetin alfa therapy at a baseline hemoglobin level of <9 g/dL versus 9 to <10 g/dL versus ≥ 10 g/dL: an exploratory analysis of a phase 3 trial. *Med Oncol*. 2012 Sep;29(3):2291–9.
59. Pirker R, Hedenus M, Vansteenkiste J, Hernandez E, Belton L, Terwey J-H. Effectiveness of Darbepoetin Alfa for Chemotherapy-induced Anemia When Initiated at Hemoglobin ≤10 g/dL. *Clin Ther*. 2016 Jan 1;38(1):122-135.e6.
60. Barni S, Cabiddu M, Guarneri P, Lonati V, Petrelli F. The risk for anemia with targeted therapies for solid tumors. *Oncologist*. 2012;17(5):715–24.
61. Tiotiu A, Clément-Duchêne C, Martinet Y. [Management of chemotherapy-induced anemia in lung cancer]. *Rev Mal Respir*. 2015 Oct;32(8):809–21.
62. Kenney B, Stack G. Drug-induced thrombocytopenia. *Arch Pathol Lab Med*. 2009 Feb;133(2):309–14.
63. Schiffer CA, Bohlke K, Delaney M, Hume H, Magdalinski AJ, McCullough JJ, et al. Platelet Transfusion for Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol*. 2018 Jan 20;36(3):283–99.
64. Slichter SJ. Evidence-based platelet transfusion guidelines. *Hematology Am Soc Hematol Educ Program*. 2007;172–8.
65. Liumbruno G, Bennardello F, Lattanzio A, Piccoli P, Rossetti G, Italian Society of Transfusion Medicine and Immunohaematology (SIMTI) Work Group. Recommendations for the transfusion of plasma and platelets. *Blood Transfus*. 2009 Apr;7(2):132–50.
66. Trüeb RM. Chemotherapy-induced alopecia. *Semin Cutan Med Surg*. 2009 Mar;28(1):11–4.
67. Institut National du Cancer. Traitements du cancer et chute de cheveux [Internet]. Available from: <http://www.e-cancer.fr/content/download/63520/571469/file/Traitement-du-cancer-et-chute-des-cheveux.pdf>
68. Shin H, Jo SJ, Kim DH, Kwon O, Myung S-K. Efficacy of interventions for prevention of chemotherapy-induced alopecia: a systematic review and meta-analysis. *Int J Cancer*. 2015 Mar 1;136(5):E442-454.
69. Perez-Soler R, Cappuzzo F, Leon L, Wojtowicz-Prag S. Time course of skin toxicity (tox) secondary to erlotinib (E) therapy in patients (pts) with non-small cell lung cancer (NSCLC) enrolled in the SATURN study. *J Clin Oncol*. 29(15).
70. Joshi SS, Ortiz S, Witherspoon JN, Rademaker A, West DP, Anderson R, et al. Effects of epidermal growth factor receptor inhibitor-induced dermatologic toxicities on quality of life. *Cancer*. 2010 Aug 15;116(16):3916–23.
71. Bachet J-B, Peuvrel L, Bachmeyer C, Reguiat Z, Gourraud PA, Bouché O, et al. Folliculitis induced by EGFR inhibitors, preventive and curative efficacy of tetracyclines in the management and incidence rates according to the type of EGFR inhibitor administered: a systematic literature review. *Oncologist*. 2012;17(4):555–68.
72. Bouhassira D, Attal N, Alchaar H, Boureau F, Brochet B, Bruxelle J, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). *Pain*. 2005 Mar;114(1–2):29–36.
73. Kerckhove N, Collin A, Condé S, Chaleteix C, Pezet D, Balayssac D. Long-Term Effects, Pathophysiological Mechanisms, and Risk Factors of Chemotherapy-Induced Peripheral Neuropathies: A Comprehensive Literature Review. *Front Pharmacol*. 2017;8:86.
74. Cioroiu C, Weimer LH. Update on Chemotherapy-Induced Peripheral Neuropathy. *Curr Neurol Neurosci Rep*. 2017 Jun;17(6):47.
75. Hershman DL, Unger JM, Crew KD, Minasian LM, Awad D, Moynour CM, et al. Randomized double-blind placebo-controlled trial of acetyl-L-carnitine for the prevention of taxane-induced neuropathy in women undergoing adjuvant breast cancer therapy. *J Clin Oncol*. 2013 Jul 10;31(20):2627–33.
76. Leal AD, Qin R, Atherton PJ, Haluska P, Behrens RJ, Tiber CH, et al. North Central Cancer Treatment Group/Alliance trial N08CA-the use of glutathione for prevention of paclitaxel/carboplatin-induced peripheral neuropathy: a phase 3 randomized, double-blind, placebo-controlled study. *Cancer*. 2014 Jun 15;120(12):1890–7.
77. Seretny M, Colvin L, Fallon M. Therapy for chemotherapy-induced peripheral neuropathy. *JAMA*. 2013 Aug 7;310(5):537–8.
78. Smith EML, Pang H. Therapy for chemotherapy-induced peripheral neuropathy--in reply. *JAMA*. 2013 Aug 7;310(5):538.
79. Smith EML, Pang H, Cirrincione C, Fleishman S, Paskett ED, Ahles T, et al. Effect of duloxetine on pain, function, and quality of life among patients with chemotherapy-induced painful peripheral neuropathy: a randomized clinical trial. *JAMA*. 2013 Apr 3;309(13):1359–67.
80. Mendoza TR, Wang XS, Cleeland CS, Morrissey M, Johnson BA, Wendt JK, et al. The rapid assessment of fatigue severity in cancer patients: use of the Brief Fatigue Inventory. *Cancer*. 1999 Mar 1;85(5):1186–96.
81. Montgomery GH, David D, Kangas M, Green S, Sucala M, Bovbjerg DH, et al. Randomized controlled trial of a cognitive-behavioral therapy plus hypnosis intervention to control fatigue in patients undergoing radiotherapy for breast cancer. *J Clin Oncol*. 2014 Feb 20;32(6):557–63.
82. Posadzki P, Moon T-W, Choi T-Y, Park T-Y, Lee MS, Ernst E. Acupuncture for cancer-related fatigue: a systematic review of randomized clinical trials. *Support Care Cancer*. 2013 Jul;21(7):2067–73.
83. Ling W-M, Lui LYY, So WKW, Chan K. Effects of acupuncture and acupressure on cancer-related fatigue: a systematic review. *Oncol Nurs Forum*. 2014 Nov 1;41(6):581–92.
84. Oldervoll LM, Loge JH, Lydersen S, Paltiel H, Asp MB, Nygaard UV, et al. Physical exercise for cancer patients with advanced disease: a randomized controlled trial. *Oncologist*. 2011;16(11):1649–57.
85. Steindorf K, Schmidt ME, Klassen O, Ulrich CM, Oelmann J, Habermann N, et al. Randomized, controlled trial of resistance training in breast cancer patients receiving adjuvant radiotherapy: results on cancer-related fatigue and quality of life. *Ann Oncol*. 2014 Nov;25(11):2237–43.
86. Tomlinson D, Diorio C, Beyene J, Sung L. Effect of exercise on cancer-related fatigue: a meta-analysis. *Am J Phys Med Rehabil*. 2014 Aug;93(8):675–86.
87. Kuehr L, Wiskemann J, Abel U, Ulrich CM, Hummler S, Thomas M. Exercise in patients with non-small cell lung cancer. *Med Sci Sports Exerc*. 2014 Apr;46(4):656–63.
88. Cavalheri V, Tahirah F, Nonoyama M, Jenkins S, Hill K. Exercise training for people following lung resection for non-small cell lung cancer - a Cochrane systematic review. *Cancer Treat Rev*. 2014 May;40(4):585–94.
89. Granger CL, McDonald CF, Berney S, Chao C, Denehy L. Exercise intervention to improve exercise capacity and health related quality of life for patients with Non-small cell lung cancer: a systematic review. *Lung Cancer*. 2011 May;72(2):139–53.
90. Jones LW, Hornsby WE, Goetzinger A, Forbes LM, Sherrard EL, Quist M, et al. Prognostic significance of functional capacity and exercise behavior in patients with metastatic non-small cell lung cancer. *Lung Cancer*. 2012 May;76(2):248–52.
91. Salakari MRJ, Surakka T, Nurminen R, Pylkkänen L. Effects of rehabilitation among patients with advanced cancer: a systematic review. *Acta Oncol*. 2015 May;54(5):618–28.

92. Hwang C-L, Yu C-J, Shih J-Y, Yang P-C, Wu Y-T. Effects of exercise training on exercise capacity in patients with non-small cell lung cancer receiving targeted therapy. *Support Care Cancer*. 2012 Dec;20(12):3169–77.
93. Taso C-J, Lin H-S, Lin W-L, Chen S-M, Huang W-T, Chen S-W. The effect of yoga exercise on improving depression, anxiety, and fatigue in women with breast cancer: a randomized controlled trial. *J Nurs Res*. 2014 Sep;22(3):155–64.
94. Larkey LK, Roe DJ, Weihs KL, Jahnke R, Lopez AM, Rogers CE, et al. Randomized controlled trial of Qigong/Tai Chi Easy on cancer-related fatigue in breast cancer survivors. *Ann Behav Med*. 2015 Apr;49(2):165–76.
95. Minton O, Richardson A, Sharpe M, Hotopf M, Stone P. A systematic review and meta-analysis of the pharmacological treatment of cancer-related fatigue. *J Natl Cancer Inst*. 2008 Aug 20;100(16):1155–66.
96. Moraska AR, Sood A, Dakhil SR, Sloan JA, Barton D, Atherton PJ, et al. Phase III, randomized, double-blind, placebo-controlled study of long-acting methylphenidate for cancer-related fatigue: North Central Cancer Treatment Group NCCTG-N05C7 trial. *J Clin Oncol*. 2010 Aug 10;28(23):3673–9.
97. Escalante CP, Meyers C, Reuben JM, Wang X, Qiao W, Manzullo E, et al. A randomized, double-blind, 2-period, placebo-controlled crossover trial of a sustained-release methylphenidate in the treatment of fatigue in cancer patients. *Cancer J*. 2014 Feb;20(1):8–14.
98. Cruciani RA, Zhang JJ, Manola J, Cella D, Ansari B, Fisch MJ. L-carnitine supplementation for the management of fatigue in patients with cancer: an eastern cooperative oncology group phase III, randomized, double-blind, placebo-controlled trial. *J Clin Oncol*. 2012 Nov 1;30(31):3864–9.
99. Jean-Pierre P, Morrow GR, Roscoe JA, Heckler C, Mohile S, Janelins M, et al. A phase 3 randomized, placebo-controlled, double-blind, clinical trial of the effect of modafinil on cancer-related fatigue among 631 patients receiving chemotherapy: a University of Rochester Cancer Center Community Clinical Oncology Program Research base study. *Cancer*. 2010 Jul 15;116(14):3513–20.
100. Spathis A, Fife K, Blackhall F, Dutton S, Bahadori R, Wharton R, et al. Modafinil for the treatment of fatigue in lung cancer: results of a placebo-controlled, double-blind, randomized trial. *J Clin Oncol*. 2014 Jun 20;32(18):1882–8.
101. Berenson JR, Yellin O, Shamasunder HK, Chen C-S, Charu V, Woliver TB, et al. A phase 3 trial of armodafinil for the treatment of cancer-related fatigue for patients with multiple myeloma. *Support Care Cancer*. 2015 Nov;23(6).
102. Yennurajalingam S, Frisbee-Hume S, Palmer JL, Delgado-Guay MO, Bull J, Phan AT, et al. Reduction of cancer-related fatigue with dexamethasone: a double-blind, randomized, placebo-controlled trial in patients with advanced cancer. *J Clin Oncol*. 2013 Sep 1;31(25):3076–82.
103. Paulsen O, Klepstad P, Rosland JH, Aass N, Albert E, Fayers P, et al. Efficacy of methylprednisolone on pain, fatigue, and appetite loss in patients with advanced cancer using opioids: a randomized, placebo-controlled, double-blind trial. *J Clin Oncol*. 2014 Oct 10;32(29):3221–8.
104. Xará S, Amaral TF, Parente B. [Undernutrition and quality of life in non small cell lung cancer patients]. *Rev Port Pneumol*. 2011 Aug;17(4):153–8.
105. Barret M, Malka D, Aparicio T, Dalban C, Locher C, Sabate J-M, et al. Nutritional status affects treatment tolerability and survival in metastatic colorectal cancer patients: results of an AGEO prospective multicenter study. *Oncology*. 2011;81(5–6):395–402.
106. Ross PJ, Ashley S, Norton A, Priest K, Waters JS, Eisen T, et al. Do patients with weight loss have a worse outcome when undergoing chemotherapy for lung cancers? *Br J Cancer*. 2004 May 17;90(10):1905–11.
107. Senesse P, Bachmann P, Bensadoun RJ, Besnard I, Bourdel-Marchasson I, Bouteloup C, et al. Nutrition chez le patient adulte atteint de cancer : textes courts. *Nutrition Clinique et Métabolisme*. 2012 Dec;26(4):151–8.
108. Arends J, Baracos V, Bertz H, Bozzetti F, Calder PC, Deutz NEP, et al. ESPEN expert group recommendations for action against cancer-related malnutrition. *Clin Nutr*. 2017 Oct;36(5):1187–96.
109. Detsky AS, McLaughlin JR, Baker JP, Johnston N, Whittaker S, Mendelson RA, et al. What is subjective global assessment of nutritional status? *JPEN J Parenter Enteral Nutr*. 1987 Feb;11(1):8–13.
110. Bauer J, Capra S, Ferguson M. Use of the scored Patient-Generated Subjective Global Assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. *Eur J Clin Nutr*. 2002 Aug;56(8):779–85.
111. Chambrier C, Sztark F, Société Francophone de nutrition clinique et métabolisme (SFNEP), Société française d'anesthésie et réanimation (SFAR). French clinical guidelines on perioperative nutrition. Update of the 1994 consensus conference on perioperative artificial nutrition for elective surgery in adults. *J Visc Surg*. 2012 Oct;149(5):e325-336.
112. Chambrier C, Sztark F. Recommandations de bonnes pratiques cliniques sur la nutrition périopératoire. Actualisation 2010 de la conférence de consensus de 1994 sur la « Nutrition artificielle périopératoire en chirurgie programmée de l'adulte ». *Nutrition Clinique et Métabolisme*. 2010 Dec;24(4):145–56.
113. Arends J, Bodoky G, Bozzetti F, Fearon K, Muscaritoli M, Selga G, et al. ESPEN Guidelines on Enteral Nutrition: Non-surgical oncology. *Clin Nutr*. 2006 Apr;25(2):245–59.
114. Sullivan RJ. Accepting death without artificial nutrition or hydration. *J Gen Intern Med*. 1993 Apr;8:220–3.
115. Burge FI. Dehydration symptoms of palliative care cancer patients. *J Pain Symptom Manage*. 1993 Oct;8(7):454–64.
116. McCann RM, Hall WJ, Groth-Juncker A. Comfort care for terminally ill patients. The appropriate use of nutrition and hydration. *JAMA*. 1994 Oct 26;272(16):1263–6.
117. Bruera E, Hui D, Dalal S, Torres-Vigil I, Trumble J, Roosth J, et al. Parenteral hydration in patients with advanced cancer: a multicenter, double-blind, placebo-controlled randomized trial. *J Clin Oncol*. 2013 Jan 1;31(1):111–8.
118. Baldwin C, Spiro A, McGough C, Norman AR, Gillbanks A, Thomas K, et al. Simple nutritional intervention in patients with advanced cancers of the gastrointestinal tract, non-small cell lung cancers or mesothelioma and weight loss receiving chemotherapy: a randomised controlled trial. *J Hum Nutr Diet*. 2011 Oct;24(5):431–40.
119. Murphy RA, Mourtzakis M, Chu QSC, Baracos VE, Reiman T, Mazurak VC. Nutritional intervention with fish oil provides a benefit over standard of care for weight and skeletal muscle mass in patients with nonsmall cell lung cancer receiving chemotherapy. *Cancer*. 2011 Apr 15;117(8):1775–82.
120. Murphy RA, Mourtzakis M, Chu QSC, Baracos VE, Reiman T, Mazurak VC. Supplementation with fish oil increases first-line chemotherapy efficacy in patients with advanced nonsmall cell lung cancer. *Cancer*. 2011 Aug 15;117(16):3774–80.
121. van der Meij BS, Langius JAE, Smit EF, Spreeuwenberg MD, von Blomberg BME, Heijboer AC, et al. Oral nutritional supplements containing (n-3) polyunsaturated fatty acids affect the nutritional status of patients with stage III non-small cell lung cancer during multimodality treatment. *J Nutr*. 2010 Oct;140(10):1774–80.

122. Spasovski G, Vanholder R, Allolio B, Annane D, Ball S, Bichet D, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. *Nephrol Dial Transplant*. 2014 Apr;29 Suppl 2:i1–39.
123. Gralla RJ, Ahmad F, Blais JD, Chiodo J, Zhou W, Glaser LA, et al. Tolvaptan use in cancer patients with hyponatremia due to the syndrome of inappropriate antidiuretic hormone: a post hoc analysis of the SALT-1 and SALT-2 trials. *Cancer Med*. 2017 Apr;6(4):723–9.
124. Verbalis JG, Goldsmith SR, Greenberg A, Korzelius C, Schrier RW, Sterns RH, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. *Am J Med*. 2013 Oct;126(10 Suppl 1):S1–42.
125. Mackall CL. T-cell immunodeficiency following cytotoxic antineoplastic therapy: a review. *Stem Cells*. 2000;18(1):10–8.
126. Wijn DH, Groeneveld GH, Vollaard AM, Muller M, Wallinga J, Gelderblom H, et al. Influenza vaccination in patients with lung cancer receiving anti-programmed death receptor 1 immunotherapy does not induce immune-related adverse events. *Eur J Cancer*. 2018 Nov;104:182–7.
127. Haanen JBAG, Carbone F, Robert C, Kerr KM, Peters S, Larkin J, et al. Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†. *Annals of Oncology*. 2017 Jul;28(suppl\_4):iv119–42.
128. Champiat S, Lambotte O, Barreau E, Belkhir R, Berdelou A, Carbone F, et al. Management of immune checkpoint blockade dysimmune toxicities: a collaborative position paper. *Annals of Oncology*. 2016 Apr;27(4):559–74.
129. Sgambato A, Casaluce F, Sacco PC, Palazzolo G, Maione P, Rossi A, et al. Anti PD-1 and PDL-1 Immunotherapy in the Treatment of Advanced Non- Small Cell Lung Cancer (NSCLC): A Review on Toxicity Profile and its Management. *Curr Drug Saf*. 2016;11(1):62–8.
130. Naidoo J, Wang X, Woo KM, Iyriboz T, Halpenny D, Cunningham J, et al. Pneumonitis in Patients Treated With Anti-Programmed Death-1/Programmed Death Ligand 1 Therapy. *J Clin Oncol*. 2017 Mar;35(7):709–17.
131. Delaunay M, Cadranet J, Lusque A, Meyer N, Gouyant V, Moro-Sibilot D, et al. Immune-checkpoint inhibitors associated with interstitial lung disease in cancer patients. *Eur Respir J*. 2017;50(2).
132. Brahmer JR, Lacchetti C, Schneider BJ, Atkins MB, Brassil KJ, Caterino JM, et al. Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol*. 2018 10;36(17):1714–68.
133. Castinetti F, Albarel F, Archambeaud F, Bertherat J, Bouillet B, Buffier P, et al. Endocrine side-effects of new anticancer therapies: Overall monitoring and conclusions. *Ann Endocrinol (Paris)*. 2018 Oct;79(5):591–5.
134. Horn L, Spigel DR, Vokes EE, Holgado E, Ready N, Steins M, et al. Nivolumab Versus Docetaxel in Previously Treated Patients With Advanced Non-Small-Cell Lung Cancer: Two-Year Outcomes From Two Randomized, Open-Label, Phase III Trials (CheckMate 017 and CheckMate 057). *J Clin Oncol*. 2017 Dec 10;35(35):3924–33.
135. Haanen JB a. G, Carbone F, Robert C, Kerr KM, Peters S, Larkin J, et al. Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2018 01;29(Suppl 4):iv264–6.
136. World Health Organization. WHO global report on traditional and complementary medicine 2019 [Internet]. WHO; 2019 [cited 2019 Jun 11]. Available from: <https://www.who.int/traditional-complementary-integrative-medicine/en/>
137. Johnson SB, Park HS, Gross CP, Yu JB. Use of Alternative Medicine for Cancer and Its Impact on Survival. *J Natl Cancer Inst*. 2018 01;110(1).
138. Johnson SB, Park HS, Gross CP, Yu JB. Complementary Medicine, Refusal of Conventional Cancer Therapy, and Survival Among Patients With Curable Cancers. *JAMA Oncol*. 2018 01;4(10):1375–81.
139. Witt CM, Balneaves LG, Cardoso MJ, Cohen L, Greenlee H, Johnstone P, et al. A Comprehensive Definition for Integrative Oncology. *J Natl Cancer Inst Monographs*. 2017 01;2017(52).
140. Le Rhun E, Devos P, Bourg V, Darlix A, Lorgis V, Ahle G, et al. Complementary and alternative medicine use in glioma patients in France. *J Neurooncol*. 2019 Oct 21;
141. Gras M, Vallard A, Brosse C, Beneton A, Sotton S, Guyotat D, et al. Use of Complementary and Alternative Medicines among Cancer Patients: A Single-Center Study. *Oncology*. 2019;97(1):18–25.
142. Rossanaly Vasram R, Zysman M, Ribeiro Baptista B, Ederle C, Nguyen-Thi PL, Clement-Duchene C, et al. [Complementary and alternative medicine use by lung cancer patients]. *Rev Pneumol Clin*. 2017 Sep;73(4):172–9.
143. Saghatchian M, Bihan C, Chenailler C, Mazouni C, Dauchy S, Delalogue S. Exploring frontiers: use of complementary and alternative medicine among patients with early-stage breast cancer. *Breast*. 2014 Jun;23(3):279–85.
144. Simon L, Prebay D, Beretz A, Bagot J-L, Lobstein A, Rubinstein I, et al. [Complementary and alternative medicines taken by cancer patients]. *Bull Cancer*. 2007 May;94(5):483–8.
145. Ninot G, Boulze-Launay I, Bourrel G, Gérazime A, Guerdoux-Ninot E, Lognos B, et al. De la définition des interventions non médicamenteuses à leur ontologie. HEGEL [Internet]. 2018 [cited 2019 Nov 8];(1). Available from: <http://hdl.handle.net/2042/65114>
146. Bontoux D, Couturier D, Menkès C-J, au nom d'un groupe de travail de la commission XV. THÉRAPIES COMPLÉMENTAIRES - acupuncture, hypnose, ostéopathie, tai-chi - leur place parmi les ressources de soins [Internet]. Académie Nationale de médecine; 2013 Mar [cited 2019 Nov 8]. Available from: <http://www.academie-medicine.fr/wp-content/uploads/2013/07/4.rapport-Th%C3%A9rapies-compl%C3%A9mentaires1.pdf>
147. Greenlee H, DuPont-Reyes MJ, Balneaves LG, Carlson LE, Cohen MR, Deng G, et al. Clinical practice guidelines on the evidence-based use of integrative therapies during and after breast cancer treatment. *CA Cancer J Clin*. 2017 06;67(3):194–232.
148. Staun M, Pironi L, Bozzetti F, Baxter J, Forbes A, Joly F, et al. ESPEN Guidelines on Parenteral Nutrition: home parenteral nutrition (HPN) in adult patients. *Clin Nutr*. 2009 Aug;28(4):467–79.
149. Bozzetti F, Arends J, Lundholm K, Micklewright A, Zurcher G, Muscaritoli M, et al. ESPEN Guidelines on Parenteral Nutrition: non-surgical oncology. *Clin Nutr*. 2009 Aug;28(4):445–54.
150. Cozzaglio L, Balzola F, Cosentino F, DeCicco M, Fellagara P, Gaggiotti G, et al. Outcome of cancer patients receiving home parenteral nutrition. Italian Society of Parenteral and Enteral Nutrition (S.I.N.P.E.). *JPEN J Parenter Enteral Nutr*. 1997 Dec;21(6):339–42.