recommandations MASCC/ESMO, qui n'ont pas été actualisées depuis 2016, ainsi que dans celles de l'AFSOS actualisées en 2017[G], l'olanzapine reste une option (20).

- **Les autres anti-émétiques :**
  -Le niveau d'efficacité des cannabinoïdes (marijuana à usage médical) ne permet pas de les recommander dans le traitement préventif des nausées/vomissements. Leur intérêt est néanmoins croissant. On rappelle qu'ils ne sont pas autorisés en France dans cette indication.

  -Le Lorazepam est un adjuvant utile mais ne doit pas être utilisé seul.

- **Régles hygiéno-diététiques (cf. référentiel AFSOS[G]) :**
  -Favoriser l'hydratation
  -Fractionner l'alimentation : 6 à 8 petits repas/collations /jour
  -Privilégier des petits repas froids, éviter les aliments gras/frits/épicés
  -Manger lentement
  -Boissons selon les goûts du patient entre les repas (eau, infusion, jus de pomme, coca), si besoin avec une tasse fermée et une paille (limitation des odeurs)
  -Maintenir une position assise 30 minutes après les repas (à défaut, en décubitus latéral droit)

- **Médecines complémentaires :**
  Il n'y a pas d'évidence en faveur ou défaveur des traitements dits complémentaires.
  L'acupuncture, en complément d'une prophylaxie médicamenteuse bien conduite, pourrait être efficace sur les nausées aigues sur la base de quelques essais randomisés de petites tailles (21). D'autres essais de plus grande ampleur sont en cours (22–24).

3. Prévention et prise en charge des NVCI

La prévention et le traitement des NVCI sont repris dans les tableaux 5 (chimiothérapies cytotoxiques & immunothérapie) et 6 (thérapies ciblées orales), adaptés des recommandations 2016 du du MASCC/ESMO (20,25) et 2017 de l'ASCO (19,26).
Les différents types de chimiothérapies utilisées dans le traitement des CBNPC sont classés en quatre catégories en fonction de leur risque émétogène : hautement, moyennement, faiblement et minimal (27). Pour chacun de ces risques, un protocole de prévention et de traitement précis est recommandé. Dans les protocoles utilisant plusieurs drogues, il est nécessaire de tenir compte du niveau de la drogue la plus émétisante.
Il faut aussi adapter d'emblée le protocole en fonction des facteurs de risque éventuels du patient ; c'est la notion de « **prophylaxie surclassée** » si besoin dès la 1ère cure.

[G] AFSOS, Prise En Charge Des Nausées-Vomissements Chimio-Induits, MAJ 15/12/2017, disponible sur http://www.afsos.org/fiche-referentiel/nausees-vomissements-chimio-induits, accédé le 08/11/2019

Degré (fréquence)	Molécules	NVCI aiguës	NVCI retardées		
		J1	J2	J3	J4
Hautement émétisantes (>90%)	Cisplatine Cyclophosphamide $\geq$ 1500 mg/m^2	Aprépitant 125 Sétron[1] Corticoïde[2] (Olanzapine[4])	Aprépitant 80 Corticoïde[3] (Olanzapine[4])	Aprépitant 80 Corticoïde[3] (Olanzapine[4])	Corticoïde[3] (Olanzapine[4])
	Cisplatine	Nétupitant + palonosetron (NEPA) Corticoïde[2]	Corticoïde[3]	Corticoïde[3]	Corticoïde[3]
	Cyclophosphamide + Anthracycline	Aprépitant 125 Sétron[1] Corticoïde[2] (Olanzapine[4])	Aprépitant 80 (Olanzapine[4])	Aprépitant 80 (Olanzapine[4])	(Olanzapine[4])
Moyennement émétisantes (30-90%)	Carboplatine (AUC≥4)	Aprépitant 125 Sétron[1] Corticoïde[4]	Aprépitant 80	Aprépitant 80	
	Cyclophosphamide < 1500 mg/m^2 Carboplatine AUC<4 Doxorubicine Irinotecan Vinorelbine orale	Sétron[1] Corticoïde[5]	(Corticoïde[6#])	(Corticoïde[6#])	
Faiblement émétisante (10-30%)	Atezolizumab Cetuximab Docetaxel Etoposide IV et po Gemcitabine Ipilimumab (Nab-)Paclitaxel Pemetrexed Topotecan	Corticoïde[7]* OU Sétron[1] (OU Metoclopramide[8])			
Minimale (<10%)	Bevacizumab Bleomycine Nivolumab Pembrolizumab Vincristine Vinorelbine IV	Aucune en l'absence d'ATCD de NVCI			

Tableau 5 – Recommandations concernant le traitement et la prévention des NVCI en fonction du type de chimiothérapie ou immunothérapie administrée (hors thérapies ciblées orales).

1. Ondansetron 8mg (0.15mg/kg) IV une fois ou 16mg per os en deux fois ; Granisetron 1mg (0.01mg/kg) IV ou 2mg (option : 1mg) per os en une fois ; Palonosetron 0.25mg IV ou 0.5mg per os une fois.
2. 12 mg de dexamethazone une fois (soit 80mg de Predniso(lo)ne) en cas d'administration concomitante d'aprépitant ; 20 mg une fois (130mg de Predniso(lo)ne) sinon.
3. 8mg de dexamethasone une fois (soit 50mg de Predniso(lo)ne) en cas d'utilisation associée à l'aprépitant ; 8mg de dexamethasone **deux fois par jour** (soit 50mg x 2/j de de Predniso(lo)ne) sinon.
4. 5mg/j - Recommandation ASCO - Option MASCC/ESMO et AFSOS
5. 8mg de dexamethasone une fois (soit 50mg de Predniso(lo)ne)
6. 8mg de dexamethasone une fois (soit 50mg de Predniso(lo)ne) bien que 4mg (25mg EP) soit une option.
7. 4 à 8mg de dexamethasone une fois (25 à 50mg de Predniso(lo)ne).
8. Recommandation MASCC/ESMO - Non figuré dans les recommandations ASCO

Recommandé en cas de chimiothérapie à risque de NVCI retardées; en option sinon (MASCC/ESMO et ASCO).
* Option non privilégiée en cas d'immunothérapie

Recommandation

Le choix de la prévention des NVCI repose sur le type de molécules utilisées pour la chimiothérapie et associe les Anti NK1 et/ou les Anti 5HT3 et/ou les corticoïdes et/ou l'olanzapine (hors AMM) et/ou les Anti D2.

Degré (fréquence)	Molécules	Prévention des NVCI
Moyennement émétisantes (30-90%)	Brigatinib# Dabrafenib# + Trametinib Ceritinib* Crizotinib*	AntiD2 systématiquement associés sur l'ordonnance ; à prendre en cas de besoin.
Faiblement émétisante (10-30%)	Afatinib Alectinib Dabrafenib# Trametinib Osimertinib*	
Minimale (< 10%)	Gefitinib Erlotinib	

*Les sétrons sont déconseillés en association au crizotinib et au ceritinib (allongement du QT).
#L'association aux sétrons peut réduire les concentrations plasmatiques du principe actif.

Tableau 6 – Recommandations concernant le traitement et la prévention des NVCI pour les thérapies ciblées orales (d'après (25)).

4. Prise en charge des NVCI anticipées

Les benzodiazépines ont montré un intérêt pour la prévention et le traitement des NVCI anticipées. Toutefois, les traitements comportementaux, et la prévention des NVCI aiguës ou retardées sont également essentiels dans cette indication.

5. Prise en charge des NVCI réfractaires

La définition des NVCI réfractaires n'est pas consensuelle, tout comme leur prise en charge (**Tableau 7**).
Avant de parler de NVCI réfractaires, il est recommandé de s'assurer que la prophylaxie adaptée au risque de chimiothérapie a bien été precrite et observée.
L'ASCO et l'ESMO/MASCC considèrent l'olanzapine comme l'option thérapeutique de choix pour les patients qui n'en ont pas reçu en prophylaxie. L'olanzapine peut donc être proposée comme un traitement de secours, d'autant plus que sa bonne tolérance et sa simplicité d'administration (1 cp par jour) facilitent la compliance. Une forme lyophilisée a été développée afin d'améliorer la prise (17).

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