

TRAITEMENT DE L'ANEMIE CHIMIO-INDUITE

1. Généralités

L'anémie est un événement fréquent au cours des chimiothérapies anti cancéreuses, particulièrement en cancérologie pulmonaire (près de 75 % des patients sous CT). Les causes en sont multiples :

- Causes périphériques : hémorragie, hémolyse, carence nutritionnelle, insuffisance rénale
- Insuffisance médullaire
- Effets toxiques directs des traitements anticancéreux (chimiothérapie, radiothérapie)
- Inflammation responsable d'une diminution de la survie des hématies et de l'utilisation du fer (38)

L'incidence de l'anémie augmente avec le nombre de cycles de chimiothérapie. L'anémie est la cause réversible la plus importante d'asthénie liée au cancer (39). Par ailleurs, elle est associée à une mauvaise qualité de vie et il s'agit d'un facteur pronostic péjoratif (40).

Grade 1	10 g/dL < Hb < Normale
Grade 2	8 g/dL < Hb < 10 g/dL
Grade 3	Hb < 8 g/dL (Projet CTC v5 : indication de transfusion)
Grade 4	Conséquences vitales ; nécessité de mesures de réanimation
Grade 5	Décès

Tableau 12 – Cotation de l'anémie chimio-induite selon la classification CTCAE v4.03

Le diagnostic positif repose sur la mesure du taux d'hémoglobine (< 12 g/dL chez la femme et à 13 g/dL chez l'homme). Il est ensuite recommandé de réaliser un bilan à la recherche d'autres causes d'anémie.

La ferritine sérique est le marqueur à doser pour faire le diagnostic d'une carence en fer. La recommandation française de l'ANDEM, publiée en 1995, proposait de doser la ferritine ou le coefficient de saturation de la transferrine.

En plus de la ferritine, le couple fer sérique et transferrine [permettant le calcul du coefficient de saturation de la transferrine (CSTRF)] est recommandé dans les situations inflammatoires (en particulier lors des cancers, des maladies intestinales chroniques inflammatoires), les cas d'insuffisance rénale chronique ou quand le résultat de la ferritine sérique n'est pas contributif (valeur normale ou élevée alors que la suspicion de carence en fer est forte). En outre, dans ces situations, les seuils de ferritine exigés pour poser le diagnostic de carence en fer sont plus élevés.

- Le fer sérique seul et le couple fer sérique + ferritine (sans la transferrine) ne sont jamais recommandés.
- Les récepteurs solubles de la transferrine ne sont mentionnés que dans les deux recommandations de l'OMS, en association avec la ferritine sérique.

Pour mémoire, les valeurs du bilan ferrique en fonction des principales causes d'anémie sont rappelées dans le tableau 13.

Le traitement des anémies chimio-induites repose sur les transfusions sanguines et les agents stimulant l'érythropoïèse (ASE).



	Anémie par carence martiale vraie	Anémie inflammatoire pure	Anémie inflammatoire + carence martiale fonctionnelle
Fer sérique	N à ↘↘	N à ↘↘	N à ↘↘
Transferrine	↗↗	↘↘	N à ↘
CsTRF	↘↘	N à ↘	N à ↘
Ferritine	↘↘	↗↗	↗↗

Tableau 13 – Valeurs du bilan ferrique selon les principales causes de celle-ci

2. Transfusion sanguine

Le seuil transfusionnel (taux seuil d'hémoglobine en deçà duquel il est recommandé de proposer une transfusion sanguine au patient) est variable en fonction des facteurs de fragilité du patient, de la chronicité de l'anémie, ainsi que des symptômes liés à l'anémie et à leur tolérance. La commission d'évaluation du collège français d'hématologie a fixé le seuil critique à 8 g/dL. Ce seuil doit être plus élevé chez les patients à risque et notamment, les personnes âgées de plus de 65 ans, les patients coronariens ou présentant une maladie cardio-pulmonaire. Inversement, ce seuil peut être abaissé à 7 g/dL chez les patients sans comorbidités cardiovasculaires (41).

3. Les Agents Stimulant l'Erythropoïèse

L'utilisation de ces molécules en cancérologie fait l'objet de recommandations de l'ESMO et de l'ASCO/ASH (42). Les différents produits commercialisés en France sont présentés dans le Tableau 14. La forme pegylée de l'epoétine bêta n'a pas l'AMM dans le domaine de l'oncologie.

DCI	Nom Commercial	Dose initiale	Augmentation de dose si pas d'augmentation de l'Hb (1 g/dL à 4 sem)
Epoétine alfa	EPREX®	150 UI/kg x3/sem ou	300 UI/kg x2/sem
	BINOCRIT®*	450 UI/kg x1/sem.	
Epoétine bêta	NEORECORMON®	30000 UI /sem	60000 UI/sem
	MIRCERA®*	Pas d'AMM dans cette indication	
Epoétine zêta	RETACRIT®*	150 UI/kg x3/sem ou 450 UI/kg 1 fois/sem	300 UI/kg x3/sem
Epoétine thêta	EPORATIO®* ^{§H}	20000 UI x1/sem	40000 UI x1/sem
			A 8 sem : 60000 UI x1/sem
Darbepoétine alfa	ARANESP®	2,25 µg/kg x1/sem ou 500 µg (6,75 µg/kg) x1/3 sem	Non recommandée

Tableau 14 – Différents ASE disponibles en France et posologies recommandées

Les * indiquent un produit biosimilaire

^H Site de l'EMA, Résumé des Caractéristiques du Produit, http://www.ema.europa.eu/docs/fr_FR/document_library/EPAR_Product_Information/human/001033/WC500043300.pdf



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