DYSTHYROÏDIE SOUS IMMUNOTHERAPIES

L'incidence des dysthyroïdies diffère en fonction du type d'immunothérapie utilisée, de la combinaison thérapeutique, de la séquence thérapeutique et de la prise en compte ou non des formes infra-cliniques. Ainsi, l'incidence varie de 1 à 9 % selon l'immunothérapie choisie.
En moyenne, la dysthyroïdie apparait entre le 2éme et 4éme cycle après le début de l'immunothérapie mais peut se développer jusqu'à 3 ans.

1. Classification de la toxicité

Grade 1	Asymptomatique. Ne nécessitant aucun traitement Diagnostic à l'examen clinique uniquement.
Grade 2	Symptomatique. Indication de traitement. Interférant avec les activités instrumentales de la vie quotidienne.
Grade 3	Symptômes sévères Nécessitant une hospitalisation. Interférant avec les activités élémentaires de la vie quotidienne.
Grade 4	Mise en jeu du pronostic vital. Nécessitant une prise en charge en urgence.
Grade 5	Décès

Tableau 32 – Classification des dysthyroïdies selon la classification CTCAEV5.0

Moins de 2 % des dysthyroïdies sont classées en grade 3 et plus.

2. Bilan pré-thérapeutique et surveillance

La société française d'endocrinologie a émis des recommandations sur le bilan pré-thérapeutique et le bilan biologique de surveillance à réaliser au cours d'un traitement par immunothérapie. Ils recommandent en pré-thérapeutique, un bilan thyroïdien (TSH, T4L). La surveillance biologique (TSH et T4L) est mensuelle pendant 6 mois puis uniquement en cas de signe clinique (134).
Bien que plus fréquent dans les 6 premiers mois, les événements indésirables immunologiques de l'immunothérapie peiuvent survenir à n'importe quel moment sous traitement, y compris tardivement (135). Par conséquent, il semble logique de poursuivre la surveillance biologique au-delà de 6 mois. Nous proposons qu'après 6 mois, le rythme de surveillance puisse être espacé à tous les 3 mois durant 6 mois puis tous les 6 mois durant 2 ans. Par contre une surveillance plus rapprochée peut être proposée en cas de double immunothérapie et surtout chez les patients sous une deuxième ligne d'immunothérapie, nous proposons alors un bilan thyroïdien (TSH, T4L) à chaque cycle durant les 3 premiers mois.

Recommandation

- **Il est recommandé de surveiller le bilan thyroïdien avant l'initiation et au cours du traitement par immunothérapie. La surveillance doit porter au minimum sur la TSH et la T4L.**
- **Il est recommandé d'intensifier la surveillance en cas de combinaison thérapeutique ou à partir de la seconde ligne d'immunothérapie.**

OPTION : Surveillance TSH et T4L tous les mois / 6 mois puis tous les 3 mois / 6 mois puis tous les 6 mois.

3. Prise en charge

Devant tout signe clinique en faveur d'une dysthyroïdie, on préconise la réalisation d'un bilan thyroïdien avec dosage TSH, T4L ± T3L.

L'arrêt de l'immunothérapie en lien avec une dysthyroïdie est exceptionnel (Figure 11). Le plus souvent, le traitement de l'épisode pouvant se faire sous immunothérapie ; soit par traitement symptomatique et surveillance en cas d'hyperthyroïdie (Figure 12) ; soit par hormonothérapie en cas d'hypothyroïdie (Figure 13).

La suspension de l'immunothérapie est a réservé aux hyperthyroïdies de grades 3 et plus jusqu'à résolution de l'épisode. L'hypothyroïdie étant définitive, l'arrêt de l'immunothérapie n'est pas recommandé.

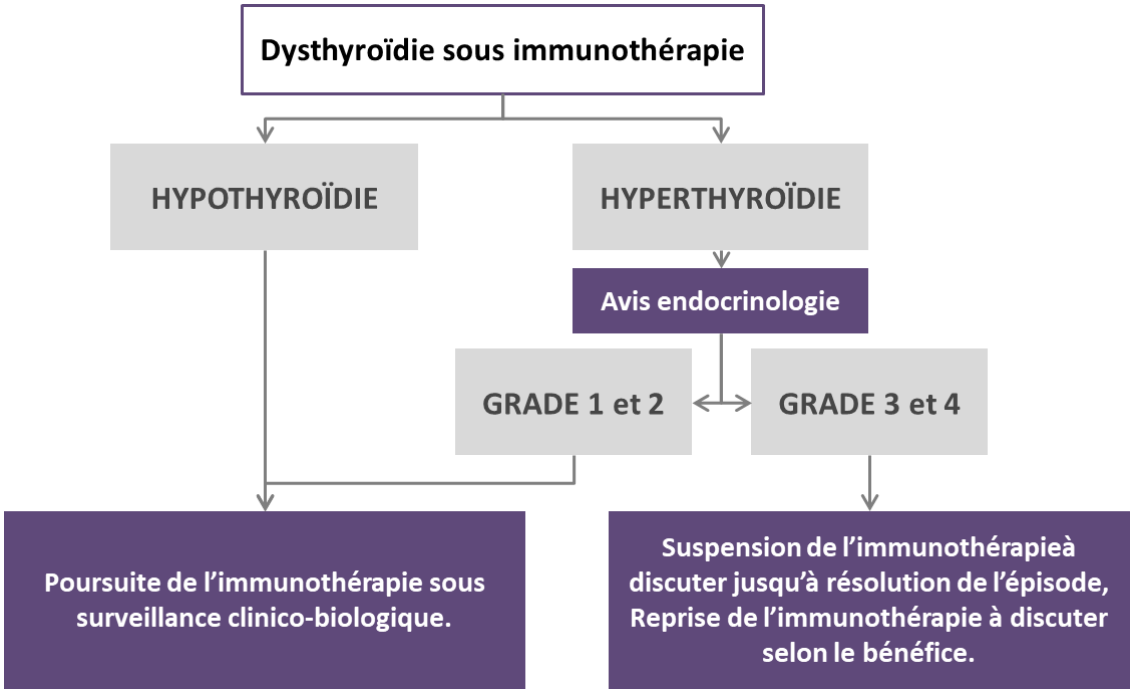

Figure 11 – Conduite à tenir pour la poursuite ou non de l'immunothérapie en cas de dysthyroïdie.

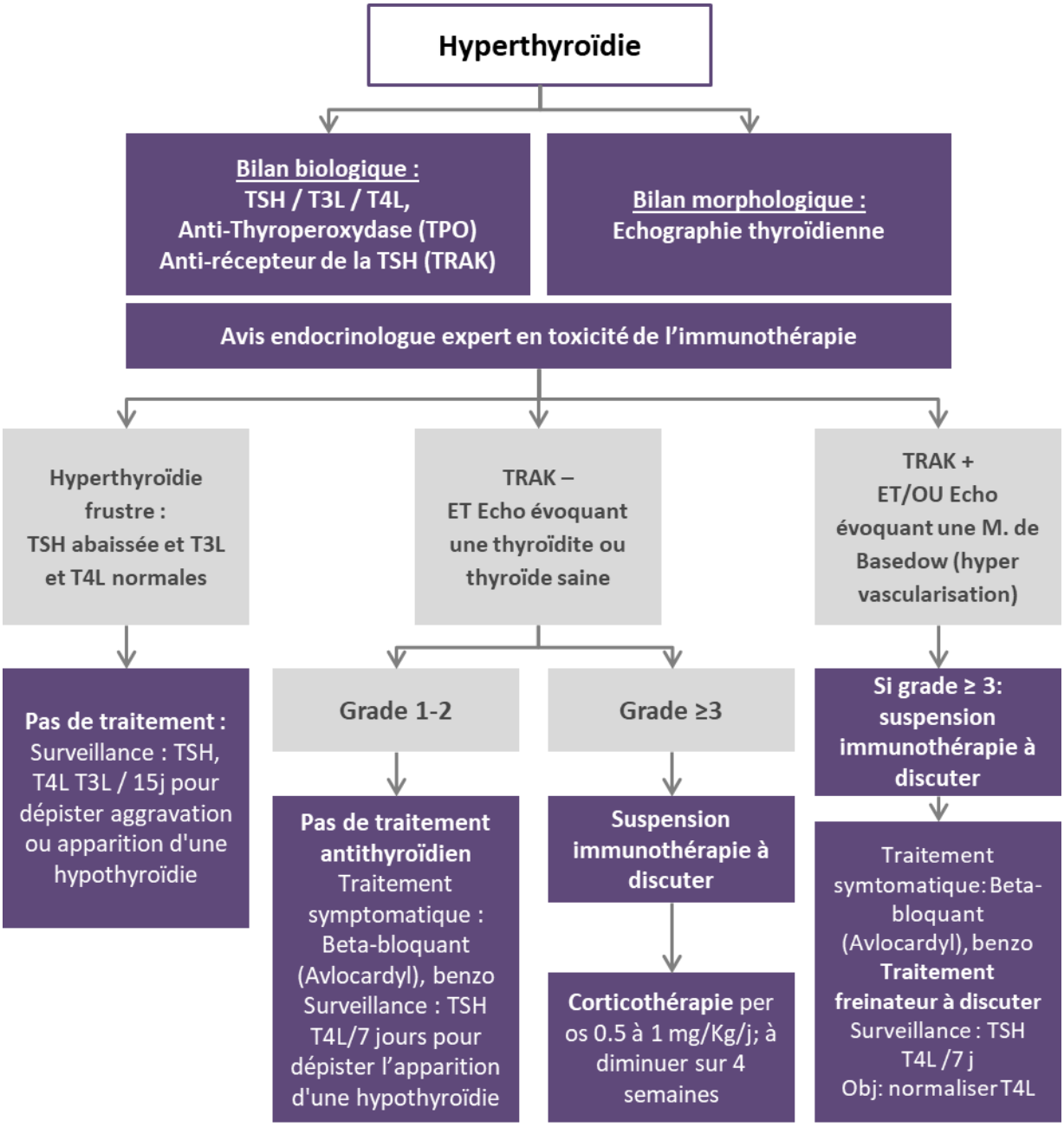

Figure 12 – **Prise en charge d'une hyperthyroïdie sous immunothérapie**

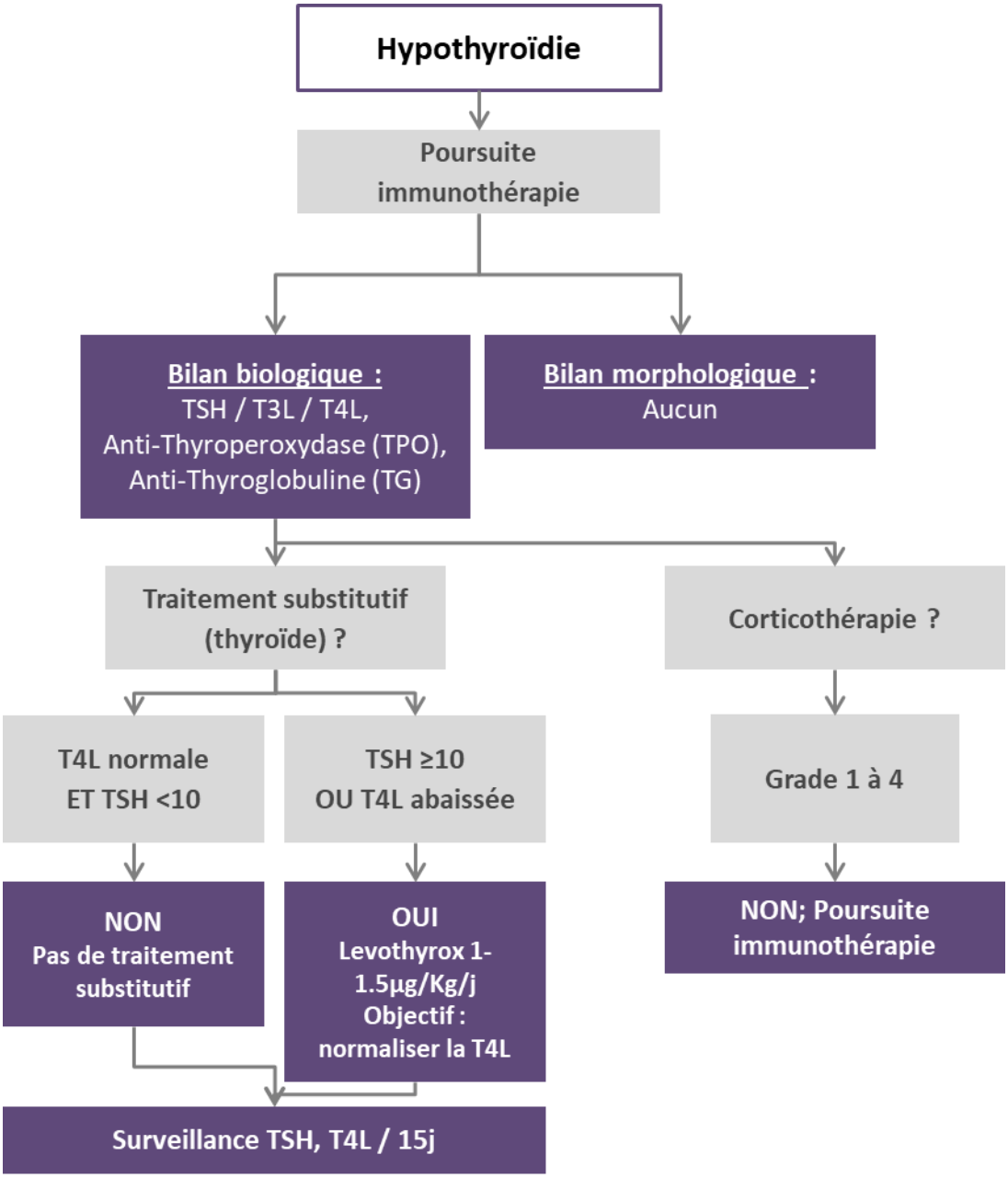

Figure 13 – **Prise en charge d'une hypothyroïdie sous immunothérapie**

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DECLARATION DES LIENS D'INTERETS

Les personnes ci-dessous ont déclaré des liens d'intérêt en oncologie thoracique pour des participations à des congrès, séminaires ou formations ; des bourses ou autre financement ; des rémunérations personnelles ; des intéressements ; ou tout autre lien pertinent dans les 3 dernières années :

ARPIN D : Takeda, Roche
AUDIGIER-VALETTE C : Roche, Abbvie, BMS, MSD, Takeda, Boehringer, AstraZeneca, Pfizer, Novartis, Fabre, Amgen, Lilly
AVRILLON V : BMS, Abbvie.
BARANZELLI A. : Roche, Takeda, BMS, MSD
BAUD M. : Boehringer
BAYCE BLEUEZ S. : Roche, BMS, AMGEN
BERARD H : Roche, Pfizer, Boehringer
BERNARDI M. : BMS, Sandoz, Roche
BOMBARON P : Roche, AstraZeneca, BMS, Boehringer.
COURAUD S. : AstraZeneca, Boehringer Ingelheim, Lilly, Merck, MSD, Novartis, Pfizer, Roche, Sysmex Innostics, Chugai, Laidet.
DELCLAUX B : BMS, Boehringer, AstraZeneca, Novartis, Roche.
DEMIR S : Pfizer, BMS
FALCHERO L. : Roche, Boehringer, AstraZeneca, BMS, Pfizer, Amgen.
FOUCHER P : AstraZeneca, Roche, BMS, MSD, Chugai, Vifor, IFCT, PFIZER
FOURNEL P. : Lilly, Amgen, BMS, MSD, Roche, Pfizer, Astelas, Boehringer, AstraZeneca, Takeda, Novartis, PFO
GERINIERE L : Lilly
GIAJ LEVRA M. : MSD, BMS, Roche, AstraZeneca, Novartis, Pfizer, Boehringer
GONZALEZ G. : Roche, Novartis, Pharmadom
GOUNANT V : Takeda, Lilly, Roche, AstraZeneca, BMS, Boehringer, Pfizer, Novartis.
GROUET A. : Boehringer, Novartis
HAMMOU Y : Chiesi, ISIS, Elia
JACOULET P : Boehringer
JANICOT H. Boehringer
LARIVE S. : TEVA Santé, Pfizer, Boehringer, BMS, MSD, AstraZeneca.
LE TREUT J. : AstraZeneca, Boehringer, Roche, BMS, MSD
LOCATELLI SANCHEZ M. : Boehringer, BMS, AstraZeneca, LFB
LUCIANI S : Pfizer
MARTIN E. : Astra Zeneca
MASTROIANNI B : Amgen
MERLE P : MSD, AstraZeneca, BMS, Pfizer
MORO-SIBILOT D : Roche, Pfizer, Lilly, Boehringer, MSD, BMS, Takeda, AstraZeneca, Novartis, Amgen, Abbvie
NAKAD A : BMS
ODIER L. : Lilly, Amgen, Pfizer
PAULUS V : MSD, Roche
PEROL M. : Roche, AstraZeneca, Boehringer, Lilly, Takeda, BMS, MSD, Pfizer, Novartis, Chugai
PERROT E. : AstraZeneca
PINSOLLE J. : Takeda, MSD, Roche, Pfizer, Agiradom.
RANCHON F : CELGENE, JAZZPHORNA
SAKHRI L : Pfizer, BMS.
SOUQUET P.-J. : Amgen, AstraZeneca, BI, CHUGAI, P FABRE, LILLY, MSD, BMS, Pfizer, Novartis, Sandoz, Roche, Takeda, Bayer, Merrimack, Merck, Astellas,
TAVIOT B : Chiesi
TISSOT C : Amgen, Sandoz, BMS
WATKIN E. : MSD, AstraZeneca, Boehringer, Pfizer, Roche, BMS
ZALCMAN G. : Roche, AstraZeneca, BMS, Pfizer, Novartis, Abbvie, MSD, Boehringer, GSK, Inventiva

Les autres participants et membres des groupes de travail n'ont déclaré aucun lien d'intérêt en oncologie thoracique.
Aucun participant ou membre d'un groupe de travail n'a rapporté de lien d'intérêt avec l'industrie du tabac.

MENTIONS LEGALES

La réunion de mise à jour des référentiels (édition 2019) a été organisée par l'Association de Recherche d'Information Scientifique et Thérapeutique en Oncologie Thoracique (ARISTOT).
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