Données cliniques
-
Intérêt du TDM en gastroentérologie/rhumatologie

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Club utilisateurs

-

Octobre 2023

Theradiag
INNOVATION FOR BIOTHERAPIES

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Sommaire

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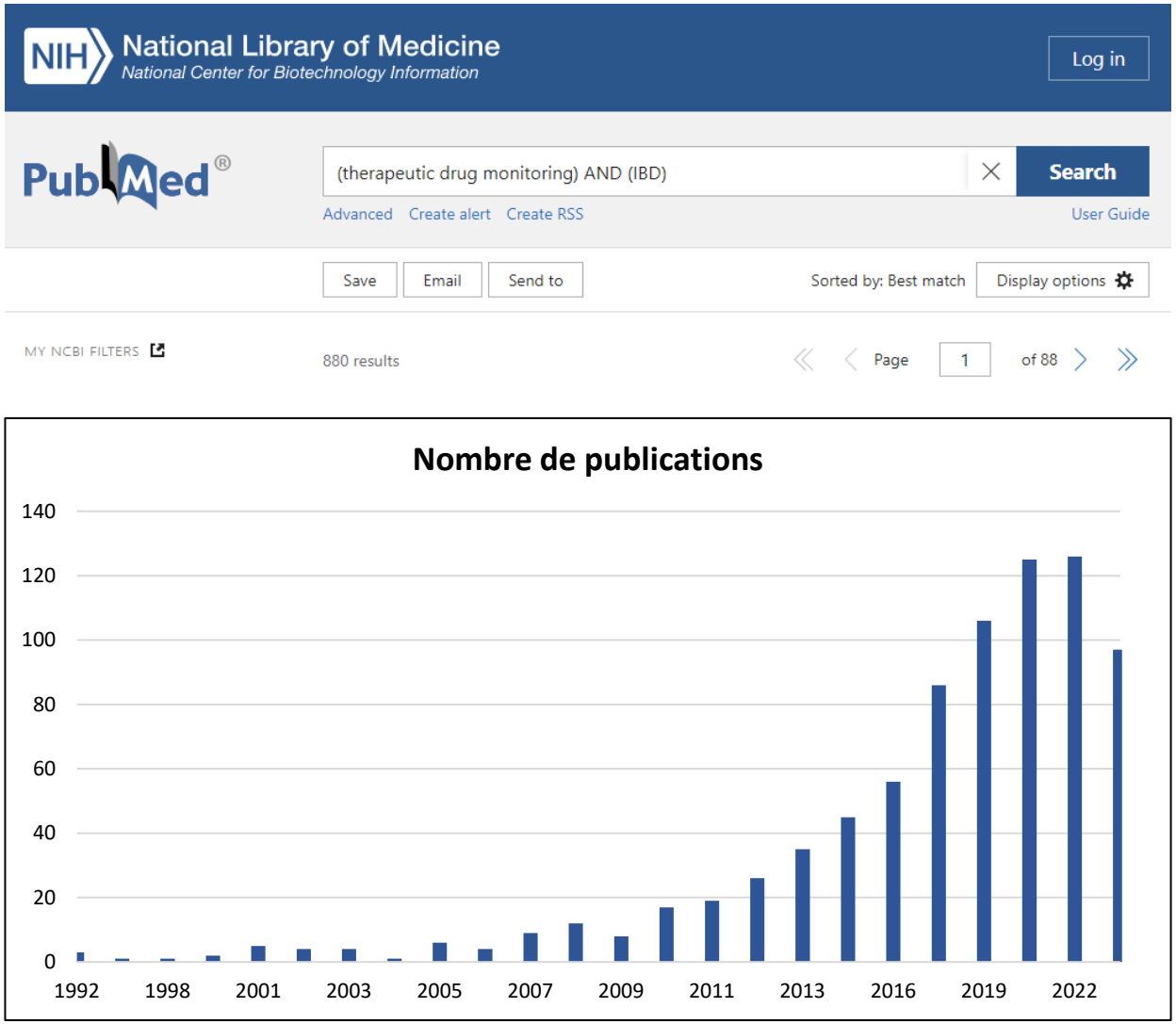
TDM dans les MICI - Où en sommes-nous en 2023 ?

TDM dans les MICI - Où en sommes-nous en 2023 ?



Pubmed

2

Nouvelles recommandations

Maladies Inflammatoires Chroniques de l’Intestin

Optimizing Therapies Using Therapeutic Drug Monitoring: Current Strategies and Future Perspectives

- **Objectifs :** Mise à jour sur le TDM des molécules biologiques, évaluer le rôle du TDM réactif par rapport au TDM proactif et identifier les lacunes dans les preuves actuelles.

Table 2. Pragmatic Recommendations Regarding the Use of TDM in IBD

		Induction		Post-induction		Maintenance	
Agent		Reactive	Proactive	Reactive	Proactive	Reactive	Proactive[a]
Infliximab[b]	Recommendation	Consider	Consider	Recommend	Consider	Recommend	Recommend
	Target	Week 2: 20–25 μg/mL Week 6: 15–20 μg/mL		Week 14: 7–10 μg/mL		5–10 μg/mL	
Adalimumab	Recommendation	Consider	Consider	Recommend	Consider	Recommend	Recommend
	Target	Week 4: 8–12 μg/mL		Week 12: 8–12 μg/mL		8–12 μg/mL	
Golimumab	Recommendation	N/A	N/A	Consider	Consider	Consider	Consider
	Target			3–7 μg/mL		1–3 μg/mL	
Certolizumab	Recommendation	N/A	N/A	Consider	Consider	Consider	Consider
	Target			32–36 μg/mL		13–15 μg/mL	
Vedolizumab[b]	Recommendation	Consider	Consider	Consider	Consider	Consider	Consider
	Target	Week 6: 33–37 μg/mL		Week 14: 15–20 μg/mL		15–20 μg/mL	
Ustekinumab	Recommendation	N/A	N/A	Consider	Consider	Consider	Consider
	Target			Week 8: 3–7 μg/mL		1–3 μg/mL	
Thiopurines	Recommendation	Not recommended[c]	Consider[d]	Recommended	Recommended	Recommended	Recommended
	Target	Week 4: 235 pmol/8 × 10^8 RBC		Week 12: 235 pmol/8 × 10^8 RBC		235 pmol/8 × 10^8 RBC	

Irving et al. 2022. Gastroenterology

Therapeutic Drug Monitoring of Biologics for Patients with Inflammatory Bowel Diseases: How, When, and for Whom?

- **Objectifs :** Résumer les données issues des essais et des recommandations sur l'application clinique du TDM proactif et réactif chez des patients atteints de MICI et traités par des produits biologiques.

Table 1. Therapeutic Outcomes by Biologic Trough Levels in Crohn's Disease and Ulcerative Colitis

Disease	Biologics	Week	Trough levels (μg/mL)	Therapeutic outcomes
Crohn's disease	Infliximab[21]	14	≥3.5	Clinical response (week 54)
	Infliximab[25]	2	>23.1	Endoscopic remission (week 12)
		6	>10.0	Endoscopic remission (week 12)
	Infliximab[26]	6	>13.9	Complete fistula response (week 14)
		14	>4.8	Complete fistula response (week 14)
	Infliximab[29]		>5	Mucosal healing
	Infliximab[13]	14	>7	Clinical remission (week 54)
	Adalimumab[13]	14	>12	Clinical remission (week 54)
	Adalimumab[28]		>4.9	Mucosal healing
	Adalimumab[29]		>7.1	Mucosal healing
	Certolizumab pegol[31]	6	>31.8	Clinical response (week 6)
		6	>36.1	Fecal calprotectin <250 mg/g and Crohn's Disease Activity Index ≤150 (week 26)
		12	>14.8	Clinical response (week 26)
	Vedolizumab[33]	6	>33.3	Clinical remission (week 6)
	Vedolizumab[35]	2	>35.2	Biomedical remission (week 6)
	Ustekinumab[39]	8	>3.3	Clinical remission (week 8)
	Ustekinumab[40]	8	>7.2	Biological remission (week 8)

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Therapeutic Drug Monitoring of Biologics for Patients with Inflammatory Bowel Diseases: How, When, and for Whom?

Table 1. Therapeutic Outcomes by Biologic Trough Levels in Crohn's Disease and Ulcerative Colitis

Disease	Biologics	Week	Trough levels (μg/mL)	Therapeutic outcomes
Ulcerative colitis	Infliximab[20]	14	>5.1	Clinical response (week 30)
	Infliximab[24]	2	≥18.6	Mayo endoscope subscore ≤ 1 (week 8)
		6	≥10.6	Mayo endoscope subscore ≤ 1 (week 8)
		8	≥34.9	Mayo endoscope subscore ≤ 1 (week 8)
		14	≥5.1	Mayo endoscope subscore ≤ 1 (week 30)
		14	≥6.7	Mayo endoscope subscore = 0 (week 30)
		30	≥2.3	Mayo endoscope subscore ≤ 1 (week 30)
		30	≥3.8	Mayo endoscope subscore = 0 (week 30)
	Adalimumab[28]		>4.9	Mucosal healing
	Golimumab[32]	2	>8.9	Clinical response (week 6)
		6	>2.5	Clinical response (week 6)
	Vedolizumab[14]	6	>37.5	Clinical remission (week 6)
	Vedolizumab[34]	6	>16.55	Vedolizumab persistence (1 year)
	Vedozinumab[35]	2	>28.9	Clinical response (week 14)
		6	>20.8	Clinical response (week 14)
		14	>17.0	Mucosal healing (week 14)
		14	>12.6	Clinical response (week 14)

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Therapeutic Drug Monitoring of Biologics for Patients with Inflammatory Bowel Diseases: How, When, and for Whom?

Table 2. Trough Levels of Biologics Recommended by Current Clinical Practice Guidelines

Drugs	Phase	Trough level (μg/mL)	Reference
Infliximab	Post-induction phase (week 14)	≥7	Papamichael *et al.*[11]
	Maintenance phase	≥3	Papamichael *et al.*[11]
	Maintenance phase	≥5	Feuerstein *et al.*[10]
	Maintenance phase	≥5	Vande Casteele *et al.*[16]
	Induction phase (week 2)	≥25	van Rheenen *et al.*[40]
	Induction phase (week 6)	≥15	van Rheenen *et al.*[40]
	Post-induction phase (week 14)	≥5	van Rheenen *et al.*[40]
Adalimumab	Induction phase (week 4)	≥7	Papamichael *et al.*[11]
	Maintenance phase	≥7.5	Feuerstein *et al.*[10]
	Maintenance phase	≥5	Papamichael *et al.*[11]
	Maintenance phase	≥7.5	Vande Casteele *et al.*[16]
	Induction phase (week 4)	≥7.5	van Rheenen *et al.*[40]
	Maintenance phase (week 8)	≥7.5	van Rheenen *et al.*[40]
Certolizumab pegol	Induction phase (week 6)	≥32	Papamichael *et al.*[11]
	Maintenance phase	≥15	Papamichael *et al.*[11]
	Maintenance phase	≥20	Feuerstein *et al.*[10]
	Maintenance phase	≥20	Vande Casteele *et al.*[16]
Golimumab	Induction phase (week 6)	≥2.5	Papamichael *et al.*[11]
	Maintenance phase	≥1	Papamichael *et al.*[11]
Vedolizumab	Induction phase (week 6)	>20	Shukla *et al.*[12]
	Maintenance phase (week 14 and beyond)	>12	Shukla *et al.*[12]
Ustekinumab	Induction phase (week 8)	>4	Shukla *et al.*[12]
	Maintenance phase (week 16 and beyond)	>2	Shukla *et al.*[12]

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Therapeutic Drug Monitoring of Biologics for Patients with Inflammatory Bowel Diseases: How, When, and for Whom?

Table 3. Proposed Mechanisms of Biologic Treatment Failure in Inflammatory Bowel Disease[10,16]

	Drug trough level	Anti-drug antibody	Phase of treatment	Cause of failure
Non-immune mediated pharmacokinetic failure	Suboptimal	Undetectable	Primary non-responder at induction phase	Excessive inflammatory burden Low serum albumin level
			Secondary loss of response at maintenance phase	Rapid drug clearance Excessive drug wastage
Anti-drug antibodies mediated pharmacokinetic failure	Suboptimal	Detectable	Secondary loss of response at maintenance phase	Neutralizing anti-drug antibodies
Mechanistic failure	Optimal	Undetectable	Primary non-responder at induction phase	Inflammatory mechanisms not blocked by the applied biologics

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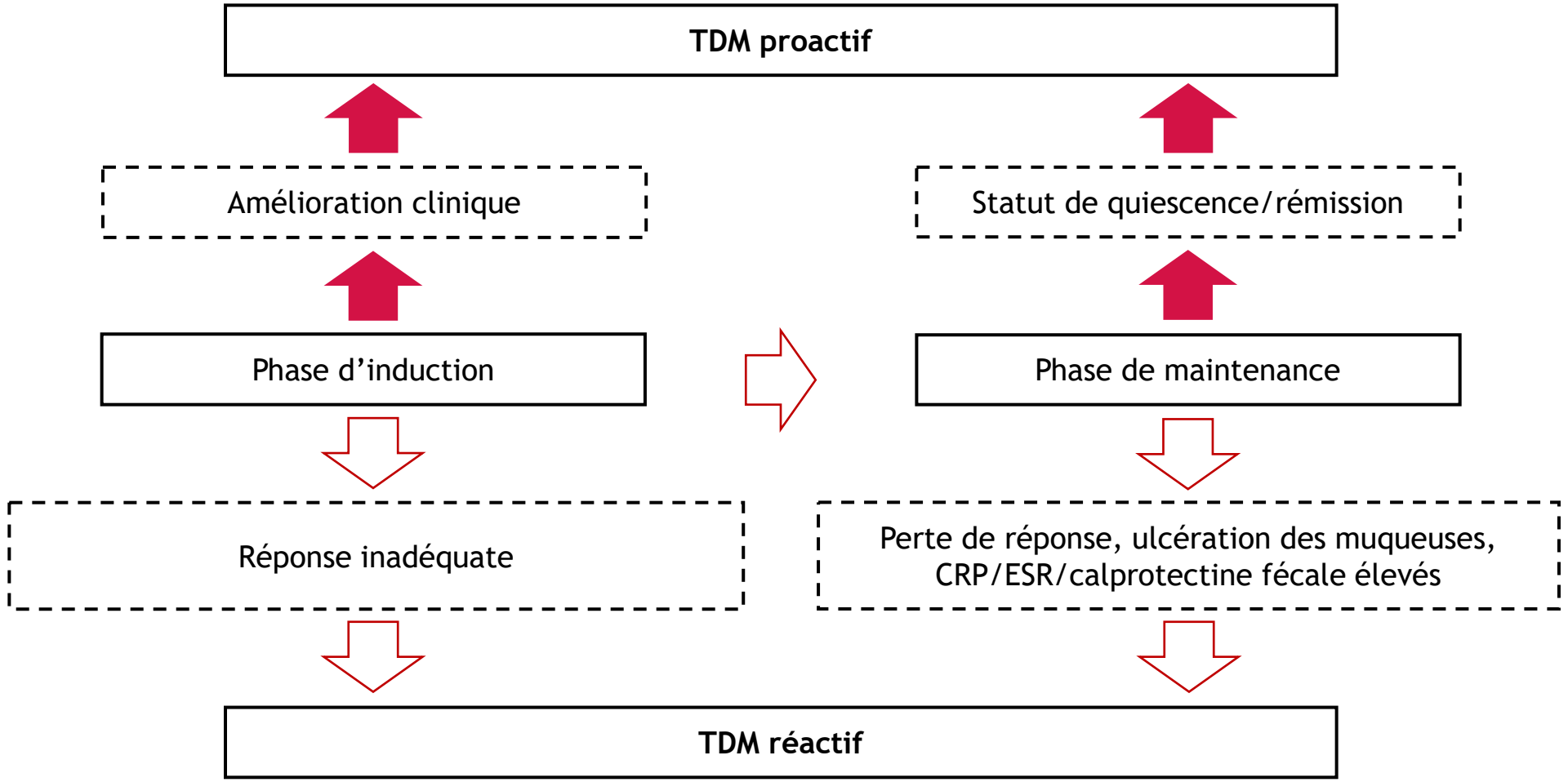
Therapeutic Drug Monitoring of Biologics for Patients with Inflammatory Bowel Diseases: How, When, and for Whom?



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Therapeutic Drug Monitoring of Biologics for Patients with Inflammatory Bowel Diseases: How, When, and for Whom?

Conclusions :

- Le TDM est un élément clé de la médecine de précision pour les patients atteints de MICI dans le contexte du traitement ciblé, étant donné la nécessité d'un contrôle étroit de l'activité de la maladie.

- Les stratégies de TDM proactives et réactives sont bien établies pour les produits biologiques anti-TNF-α, tandis que la stratégie de TDM réactive est généralement recommandée pour les produits biologiques non anti-TNF-α.

- La stratégie de TDM proactive pour les produits biologiques non anti-TNF-α dont l'immunogénicité est relativement faible présente également des avantages cliniques potentiels.

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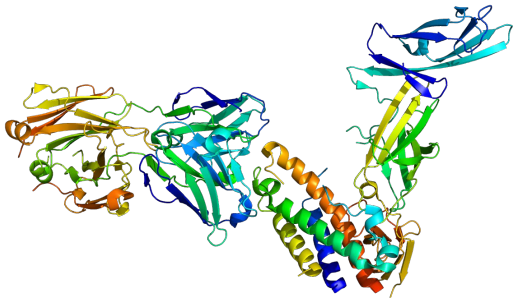
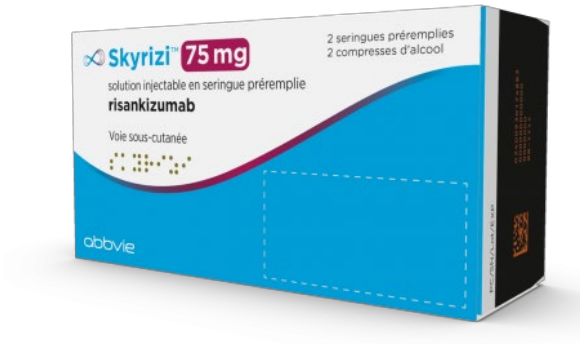
Risankizumab

Maladies Inflammatoires Chroniques de l’Intestin

RISANKIZUMAB – Informations générales





RISANKIZUMAB :

- Anticorps monoclonal humanisé IgG1
- **Cible :** sous-unité p19 de l'IL-23
- **Nom commercial :** Skyrizi®
- Commercialisé par abbvie
- **FDA 2019 / EMA 2019**
- **Expiration du brevet :** 2031 EU

RISANKIZUMAB – Indications & posologie

Skyrizi® (risankizumab) injection

•Psoriasis en plaques

- 150 mg SC à S0, S4, et toutes les 12 semaines après

•Arthrite psoriasique

- 150 mg SC à S0, S4, et toutes les 12 semaines après

•Maladie de Crohn

- Induction : 600 mg IV en perfusion d'au moins 1 heure à S0, à S4 et à S8
- Maintenance : 360 mg SC à S12, et toutes les 8 semaines après

•Rectocolite hémorragique *

* Le risankizumab (SKYRIZI®) atteint le critère d'évaluation primaire et tous les critères secondaires dans l'étude d'induction de phase 3 chez des patients atteints de rectocolite hémorragique.

RISANKIZUMAB – Immunogénicité

	Formation des Ac anti-médicament[1]	
Arthrite psoriasique	24% (52 semaines)	12.1% (28 semaines)
Maladie de Crohn	3.4%	

Table 3 Summary of ADAb formation rates for individual biologic/biosimilar by chronic inflammatory disease

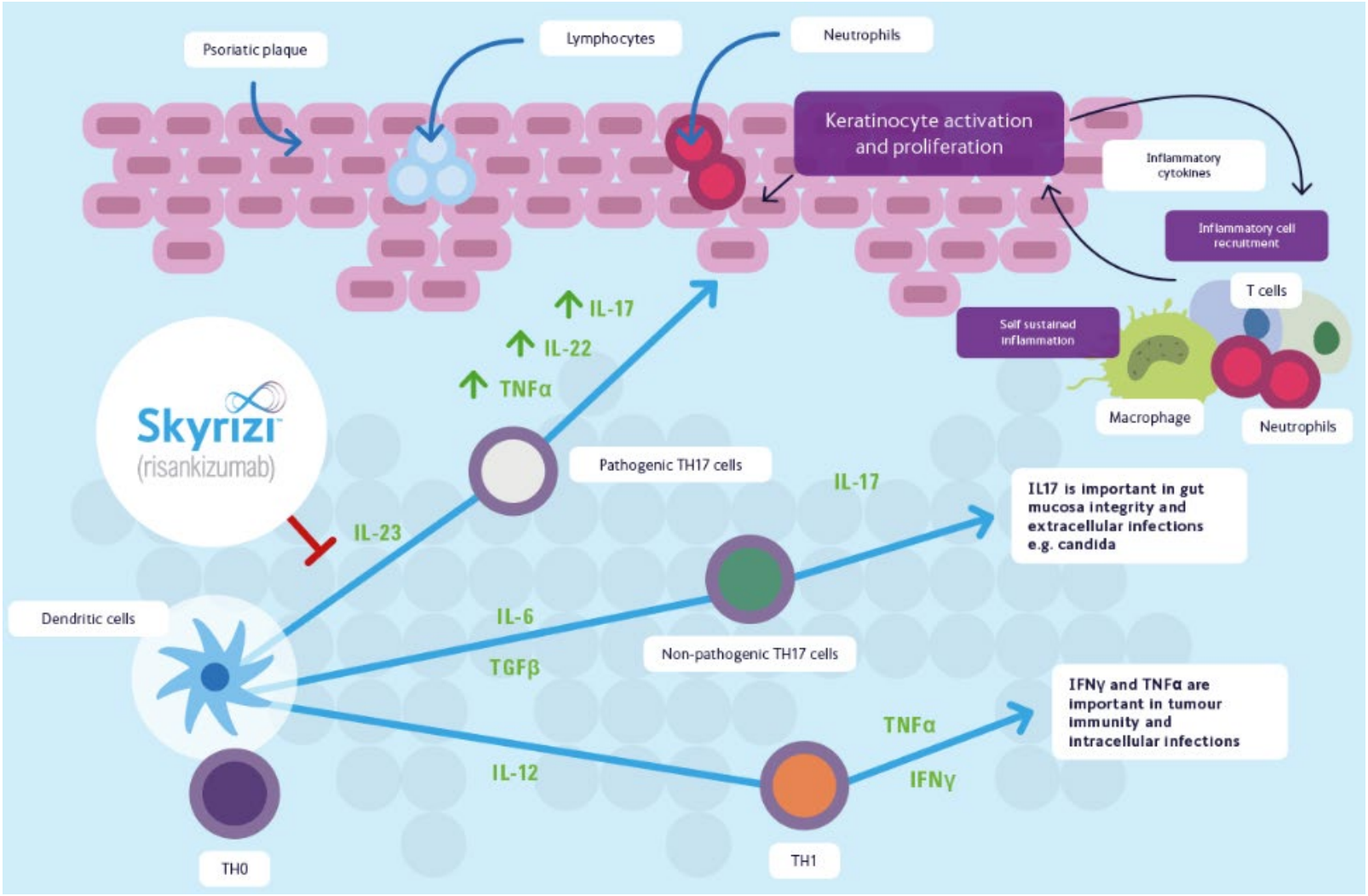
Biologic	Frequency of ADAb formation, % (no. of studies[a])							
	RA	PsA	JIA	AS	Ps	CD	UC	Range
ABA	2–20 (7)		2–11 (2)					2–20 (9)
ADA	0–51 (33)	0–54 (8)	6–33 (6)	8–39 (9)	0–51 (12)	0–35 (13)	3–5 (3)	0–54 (80)
CZP	2.8–37 (7)				21 (1)	3–25 (6)		3–37 (14)
ETN	0–13 (25)	0 (3)	0–6 (2)	0 (4)	2–5 (5)			0–13 (37)
GLM	2–10 (11)	6 (1)		0–6.4 (2)			0–19 (8)	0–19 (22)
INF	8–62 (48)	15–33 (3)	26–42 (2)	6.1–69 (10)	0–41 (12)	3–83 (29)	6–46 (10)	0–83 (110)
RTX	0–21 (8)							0–21 (8)
SEC		0–0.1 (3)		0–0.3 (3)	0–1 (8)			0–1 (14)
TCZ	0–16 (14)		1–8 (3)					0–16 (17)
UST		8–11 (3)			4–8.6 (10)	0–1 (2)		1–11 (15)
CT-P13	26–52 (2)			27 (1)		21 (1)	24 (1)	21–52 (5)

[a] Studies of patients with multiple chronic inflammatory diseases are included for each disease state

Importance de la mesure du taux d'anticorps anti-médicament

1. Skyrizi, INN-Risankizumab (europa.eu)
2. Strand et al. 2017. BioDrugs.

RISANKIZUMAB – Mécanisme d'action



SKYRIZI - Product Information
Adapted from Kofoed K et al. 2015.

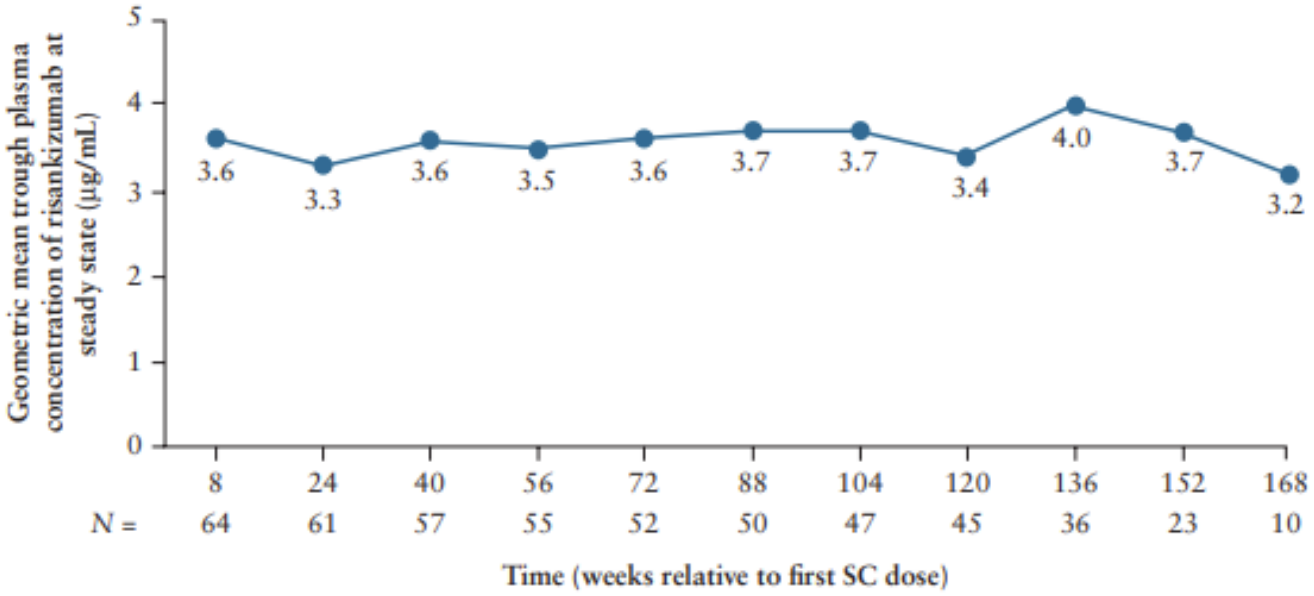
Etudes cliniques

RISANKIZUMAB

Long-Term Safety and Efficacy of Risankizumab Treatment in Patients with Crohn's Disease: Results from the Phase 2 Open-Label Extension Study

- **Buts :** Étudier la tolérance, la pharmacocinétique, l'immunogénicité et l'efficacité à long terme du risankizumab chez les patients ayant répondu au risankizumab dans l'étude mère de phase 2.

- **Resultats :**



- **Conclusion :** Le traitement de maintenance à long terme par risankizumab sous-cutané 180 mg toutes les 8 semaines a été bien toléré par les patients atteints de la maladie de Crohn, sans nouveaux signaux de toxicité.

Ferrante et al. 2021. J Crohns Colitis.

Risankizumab levels are significantly correlated and predictive of biomarker remission in Crohn's disease

Tracker

- **Objectifs :** Étudier si les niveaux de risankizumab sont en corrélation avec la rémission basée sur les biomarqueurs.

- **Méthodes :**

  - Tous les patients sous RZB étaient éligibles pour l'étude.
  - Tous les patients ont été traités avec un schéma de dosage du RZB (600mg S0, S4 et S8) suivi de 360mg par voie SC toutes les 8 semaines à partir de S12.
  - 25 patients avec 72 échantillons de RZB en phase de maintenance étaient éligibles.
  - Avant chaque perfusion ou injection SC, les taux de calprotectine fécale, de CRP et de RZB ont été mesurés.
  - Les dosages ont été effectués en aveugle par rapport aux données cliniques et aux biomarqueurs.
  - La rémission des biomarqueurs a été définie par des taux de calprotectine fécale inférieurs à 250 µg/ml et une CRP <5 mg/l.

Roblin et al. 2023

Risankizumab levels are significantly correlated and predictive of biomarker remission in Crohn's disease

Tracker

➢ **Résultats :**

Figure 1: Average RZB rates in the case of biomarker remission (R) and in their absence (NR).

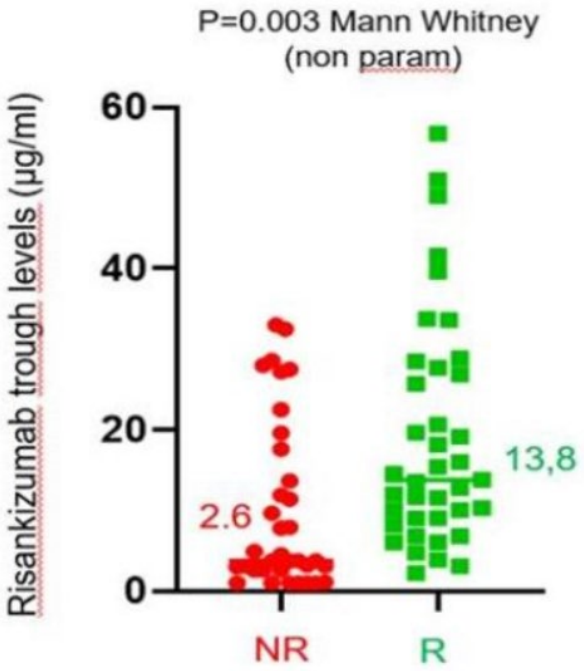
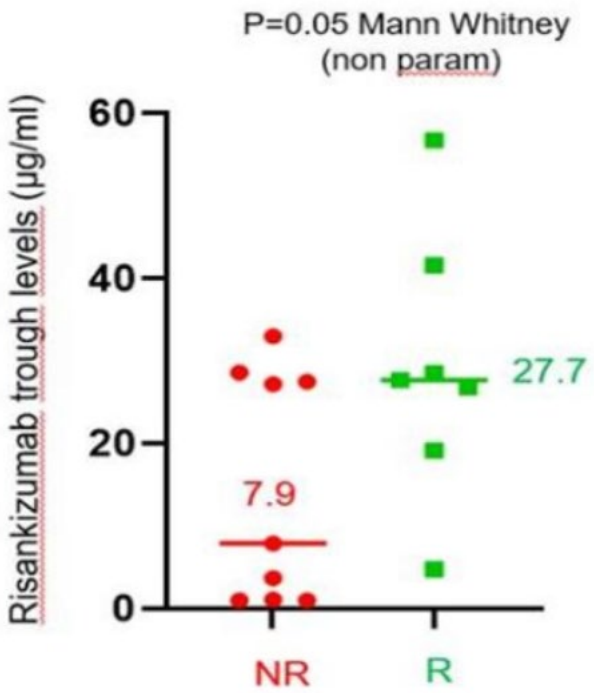


Figure 2: RZB level at S4 in case of biomarker remission (R) and in their absence (NR) in the follow-up.



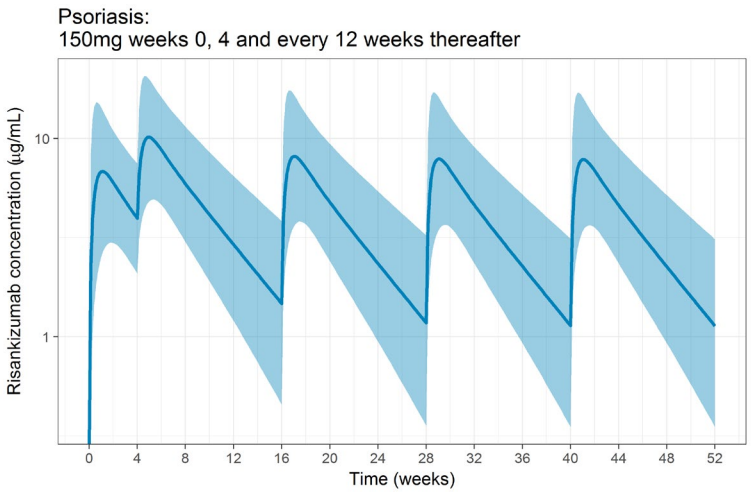
➢ **Conclusion :** Les taux moyens de RZB sont significativement plus élevés en cas de rémission due aux biomarqueurs dans la maladie de Crohn. Dès S4, ces taux sont significativement plus élevés chez les patients en rémission pendant le traitement de maintenance.

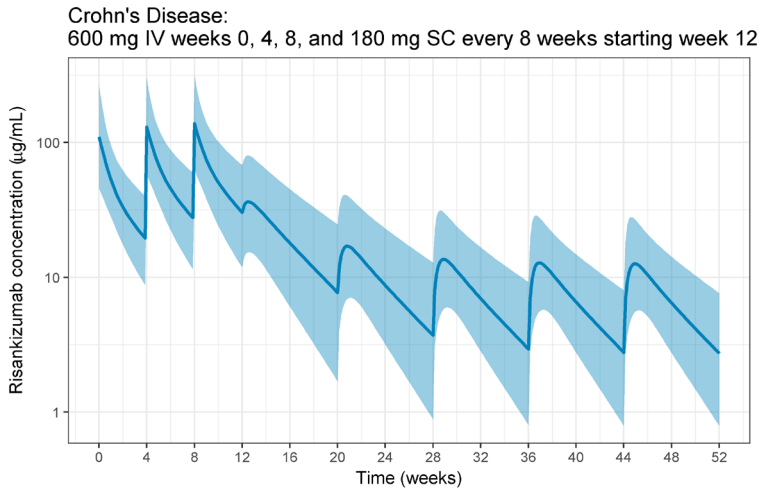
Roblin et al. 2023

Population Pharmacokinetics of the Interleukin-23 Inhibitor Risankizumab in Subjects with Psoriasis and Crohn's Disease: Analyses of Phase I and II Trials

- **Objectifs :** Caractériser la pharmacocinétique du risankizumab et évaluer les covariables susceptibles d'affecter son exposition en utilisant les données des essais de phase I et II chez des sujets atteints de psoriasis et de la maladie de Crohn.

- **Résultats :**





- **Conclusion :** Chez les sujets atteints de psoriasis, les concentrations plasmatiques minimales de risankizumab étaient de **1,72±1,11 et de 1,36±0,923 µg/mL** aux semaines 16 et 52, respectivement. De même, chez les sujets atteints de la maladie de Crohn, les concentrations plasmatiques minimales de risankizumab étaient de **33,9±18,1 et 3,29±2,32 µg/ml** aux semaines 12 (phase d'induction) et 52 (phase de maintenance), respectivement.

Suleiman et al. 2019. Clin Pharmacokinet.

TDM dans les MICI - Conclusion

Nouvelles recommandations dans les MICI

- De nombreuses données sont déjà disponibles, mais il est important de les mettre à jour afin d'optimiser le traitement et le suivi des patients.

Risankizumab

- Nouvelle indication dans la maladie de Crohn
- Essais de phase III pour la RC (en cours)
- Theradiag, leader sur le TDM dans les MICI
- Complète la gamme
- Demandé par les cliniciens

Nouveaux développements ?

- Guselkumab
- Mirikizumab

4

TDM en rhumatologie - Que pouvons-nous apprendre des MICI ?

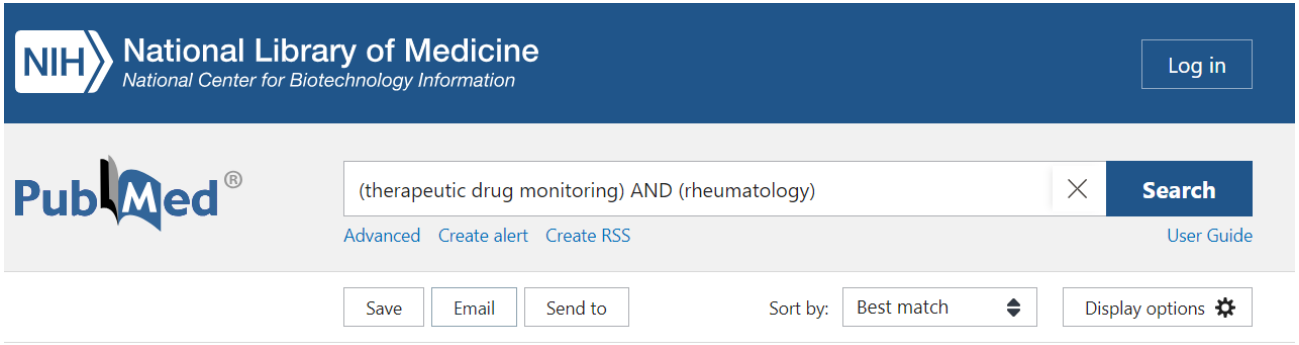
TDM en rhumatologie

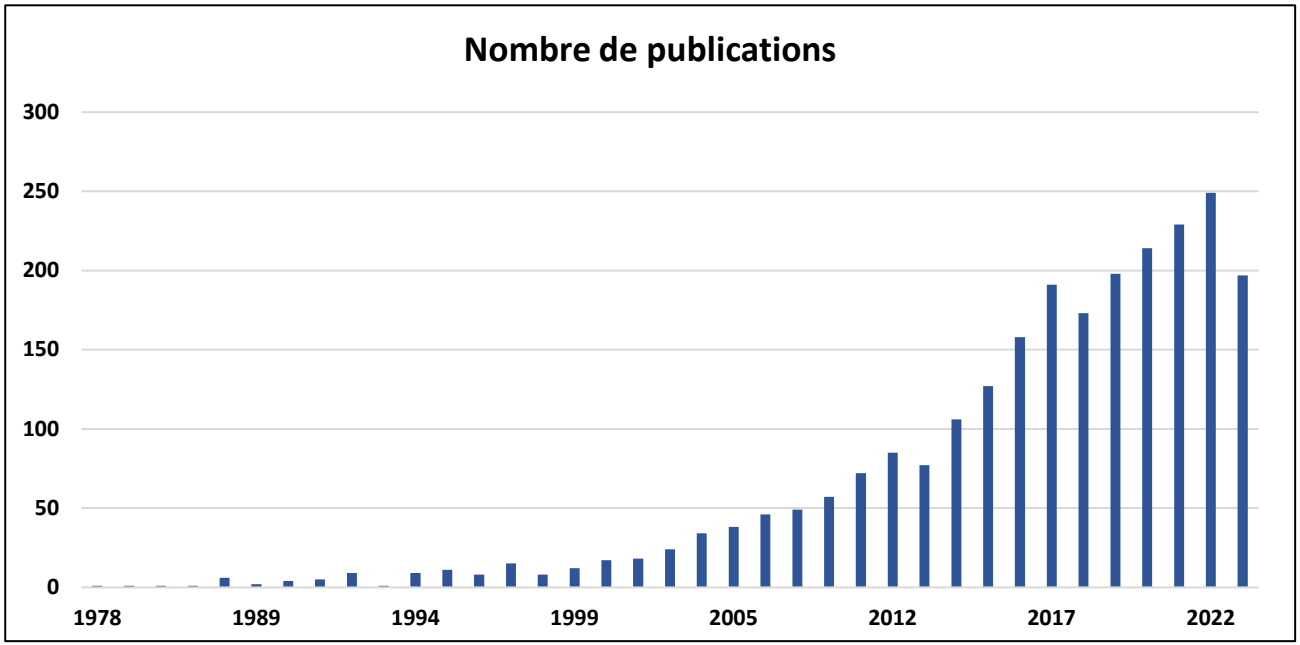
La plupart des cliniciens n'ont pas fait la promotion du TDM

Beaucoup de molécules sont disponibles

Peu de recommandations / données sur le TDM

TDM en rhumatologie - Où en sommes-nous en 2023 ?





Pubmed

5

Nouvelles recommandations

Rhumatologie

EULAR points to consider for therapeutic drug monitoring of biopharmaceuticals in inflammatory rheumatic and musculoskeletal diseases

- **Objectif :** Développer les recommandations de l'EULAR pour le suivi thérapeutique (TDM) des produits biopharmaceutiques dans les maladies rhumatismales et musculo-squelettiques inflammatoires (RMD).

- **Recommandations :**
  - Il s'agit de la première série de principes généraux et d'éléments à prendre en compte approuvés par l'EULAR pour savoir si, quand, chez qui et comment effectuer et interpréter le TDM des produits biopharmaceutiques dans les maladies rhumatismales en pratique clinique
  - Souligner l'utilité clinique potentielle de la mesure et de l'interprétation des concentrations sanguines de médicament et d'anticorps anti-médicament

7	Reactive TDM could be considered in the management of inflammatory RMDs	B	2b	9.5 (1.0)	84
8	Measurement of biopharmaceutical blood concentrations could be considered to identify those with high biopharmaceutical blood concentrations in whom tapering may be indicated	B	2b	9.3 (1.2)	88
9	Measurement of biopharmaceutical blood concentrations should be considered to understand clinical non-response	B	2b	9.5 (1.0)	96
10	Measurement of ADAb should be considered in the case of immunogenic biopharmaceuticals, alongside biopharmaceutical blood concentrations, at the time of clinical non-response	B	2b	9.4 (1.0)	96
11	Measurement of ADAb should be considered in the case of a hypersensitivity reaction, mainly related to infusions	B	2b	9.4 (1.4)	96
12	Measurement of ADAb is not recommended in the case of an injection-site reaction	D	5	8.8 (2.0)	84
13	Cost-effectiveness of TDM should be considered according to local context and standard of care	D	2c	8.8 (2.4)	80

Krieckaert et al. 2022. Ann Rheum Dis.

Therapeutic drug monitoring of biopharmaceuticals in inflammatory rheumatic and musculoskeletal disease: a systematic literature review informing EULAR points to consider

Table 1 Population-based blood concentration ranges that are associated with clinical response, per biopharmaceutical and disease

Drug	Rheumatoid arthritis	Axial spondyloarthritis	Psoriatic arthritis
ADA	~>8 µg/mL: remission (DAS-28 <2.6) ~>2 µg/mL: LDA (DAS-28 <3.2) <1 µg/mL: no response Range: 2–8 µg/mL[11 52–56 66 77 87 88 93]	~8 µg/mL: major improvement (ΔASDAS ≥2.0) ~5 µg/mL: low disease activity ~2.5 µg/mL: clinical improvement (ΔASDAS ≥1.1) Range: 2.5–8.0 µg/mL[9 63–65 95]	>1 µg/mL: clinical efficacy* >4 µg/mL: optimal efficacy* Range: 1–8 µg/mL[75 96]
ETN	Range: inconclusive[53 54 56 82 89 93]	Range: inconclusive[67]	Range: inconclusive[75]
IFX	Induction phase (week 6): ≥2.5 µg/mL: response Maintenance phase: >1 µg/mL: LDA (DAS-28 <3.2) Range: inconclusive [47 56 68 75 84 90 93]	No data	No data
GLM	Range: >1 µg/mL[80]	0.7–1.4 µg/mL: clinical improvement (ΔASDAS ≥1.1) Range: >1 µg/mL[12 80]	Range: >1 µg/mL[80]
CZP	23–28 µg/mL: remission (DAS-28 <2.3) Range: 20–39.9 µg/mL (largest improvement in DAS-28)[76 91 92]	Range: 20–39.9 µg/mL (largest improvement in ASDAS)[76]	Range: 20–39.9 µg/mL (largest improvement in DAS-28)[76]
TCZ	Intravenous: >1 µg/mL: DAS-28 ≥1.2 improvement Range: >1 µg/mL[6] Subcutaneous: range: inconclusive[94]	NA	NA

Krieckaert et al. 2022. RMD Open

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Comité scientifique

Rhumatologie

Table 1 Population-based blood concentration ranges that are associated with clinical response, per biopharmaceutical and disease

Drug	Rheumatoid arthritis	Axial spondyloarthritis	Psoriatic arthritis
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Peu de données

Seuils faibles, données à mettre à jour

Peu de données

Krieckaert et al. 2022. RMD Open

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Etudes cliniques

Rhumatologie

Effect of Therapeutic Drug Monitoring vs Standard Therapy During Maintenance Infliximab Therapy on Disease Control in Patients With Immune-Mediated Inflammatory Diseases A Randomized Clinical Trial (NOR-DRUM study)

- **Objectif :** Évaluer si un TDM proactif pendant le traitement de maintenance à l'infliximab améliore l'efficacité du traitement en prévenant l'aggravation de la maladie par rapport au traitement standard à l'infliximab sans TDM.

- **Conception, conditions et participants :** Essai clinique randomisé, en groupes parallèles, en ouvert, incluant 458 adultes atteints de **polyarthrite rhumatoïde, spondylarthrite, rhumatisme psoriasique, rectocolite hémorragique, maladie de Crohn ou psoriasis** sous traitement de maintenance par infliximab dans 20 hôpitaux norvégiens. Les patients ont été recrutés du 7 juin 2017 au 12 décembre 2019. Le suivi final a eu lieu le 14 décembre 2020.

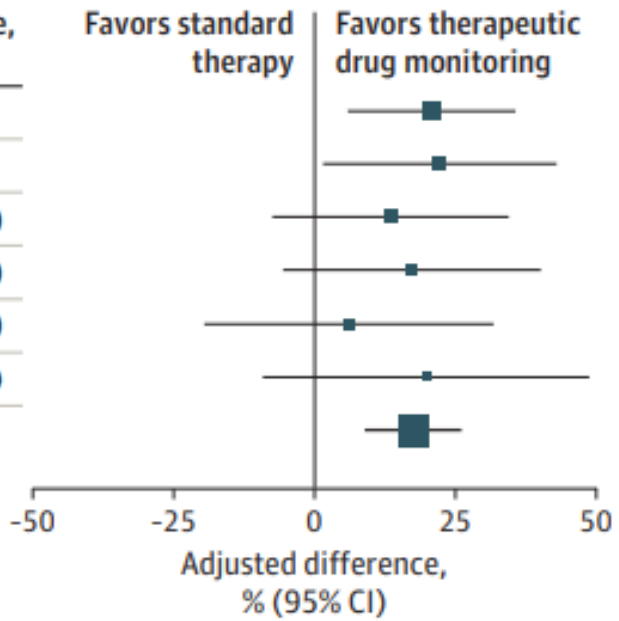
- **Interventions :** Les patients ont été randomisés 1:1 pour recevoir un TDM proactif avec des ajustements de dose et d'intervalle basés sur la surveillance programmée des taux sériques de médicaments et d'anticorps anti-médicaments (groupe TDM ; n = 228) ou pour recevoir un traitement standard par infliximab sans surveillance des taux de médicaments et d'anticorps (groupe traitement standard ; n = 230).

Watterdal et al. JAMA. 2021.

Effect of Therapeutic Drug Monitoring vs Standard Therapy During Maintenance Infliximab Therapy on Disease Control in Patients With Immune-Mediated Inflammatory Diseases A Randomized Clinical Trial (NOR-DRUM study)

- **Résultats :** Sur les 458 patients randomisés, 454 ont reçu l'intervention qui leur avait été attribuée et ont été inclus dans l'ensemble de l'analyse. **Le résultat principal, à savoir un contrôle durable de la maladie sans aggravation, a été observé chez 167 patients (73,6 %) dans le groupe TDM et chez 127 patients (55,9 %) dans le groupe de traitement standard.**

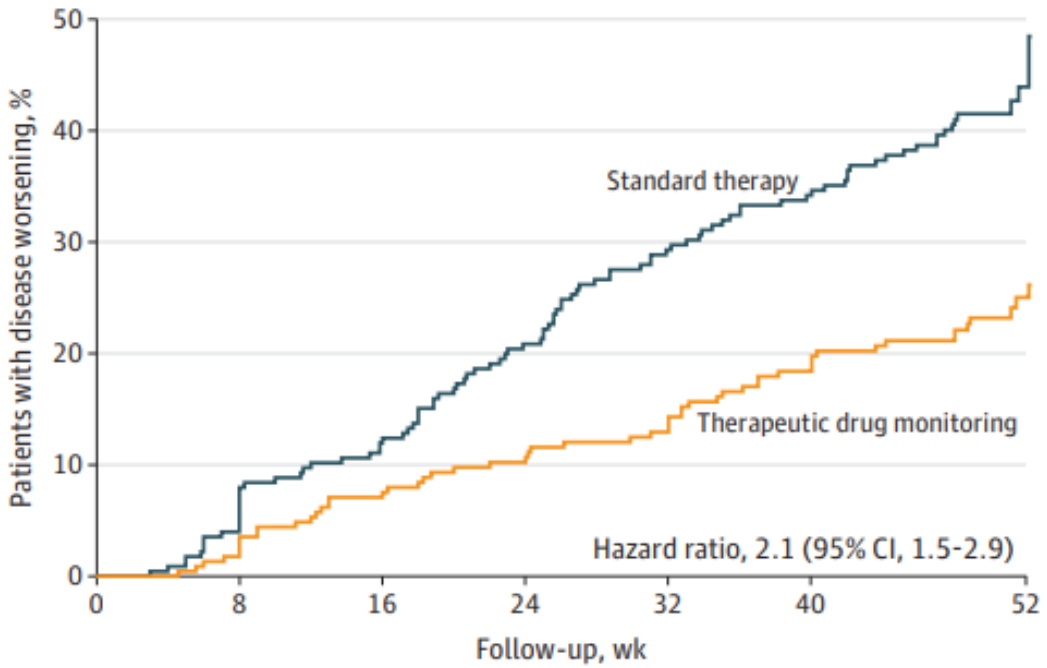
	Sustained disease control, No./total (%)		
	Therapeutic drug monitoring	Standard therapy	Adjusted difference, % (95% CI)
Spondyloarthritis	54/68 (79.4)	41/70 (58.6)	20.9 (6.0 to 35.8)
Ulcerative colitis	27/38 (71.1)	21/43 (48.8)	22.3 (1.6 to 43.1)
Rheumatoid arthritis	27/39 (69.2)	22/40 (55.0)	13.6 (-7.4 to 34.6)
Crohn disease	24/34 (70.6)	17/32 (53.1)	17.4 (-5.5 to 40.3)
Psoriatic arthritis	19/28 (67.9)	16/25 (64.0)	6.2 (-19.5 to 31.9)
Psoriasis	16/20 (80.0)	10/17 (58.8)	19.9 (-9.1 to 48.9)
Overall	167/227 (73.6)	127/227 (55.9)	17.6 (9.0 to 26.2)



Watterdal et al. JAMA. 2021.

Effect of Therapeutic Drug Monitoring vs Standard Therapy During Maintenance Infliximab Therapy on Disease Control in Patients With Immune-Mediated Inflammatory Diseases A Randomized Clinical Trial (NOR-DRUM study)

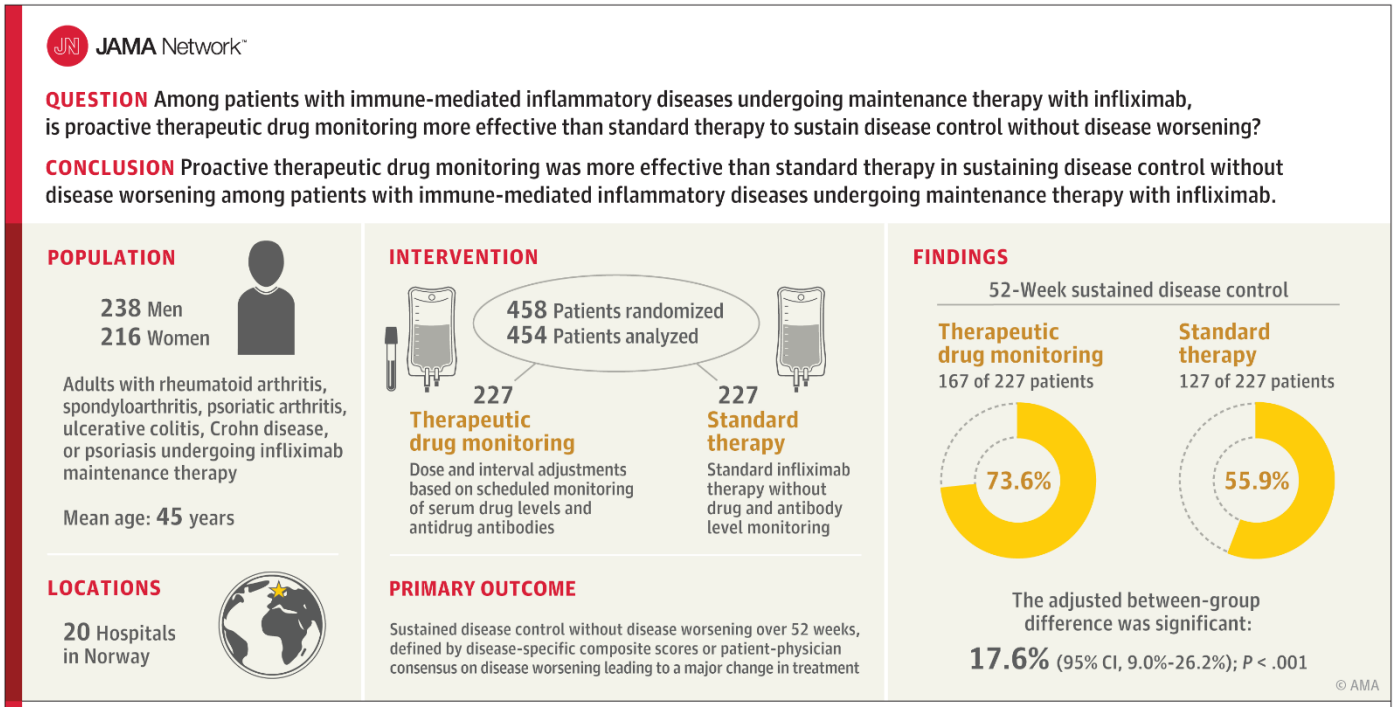
- **Résultats :** La différence ajustée estimée était de **17,6 % en faveur du TDM.** Des événements indésirables ont été signalés chez 137 patients (60 %) et 142 patients (63 %) dans les groupes TDM et traitement standard, respectivement.



No. at risk							
Standard therapy	227	224	203	187	165	150	136
Therapeutic drug monitoring	227	226	214	201	194	184	170

Watterdal et al. JAMA. 2021.

Effect of Therapeutic Drug Monitoring vs Standard Therapy During Maintenance Infliximab Therapy on Disease Control in Patients With Immune-Mediated Inflammatory Diseases A Randomized Clinical Trial (NOR-DRUM study)

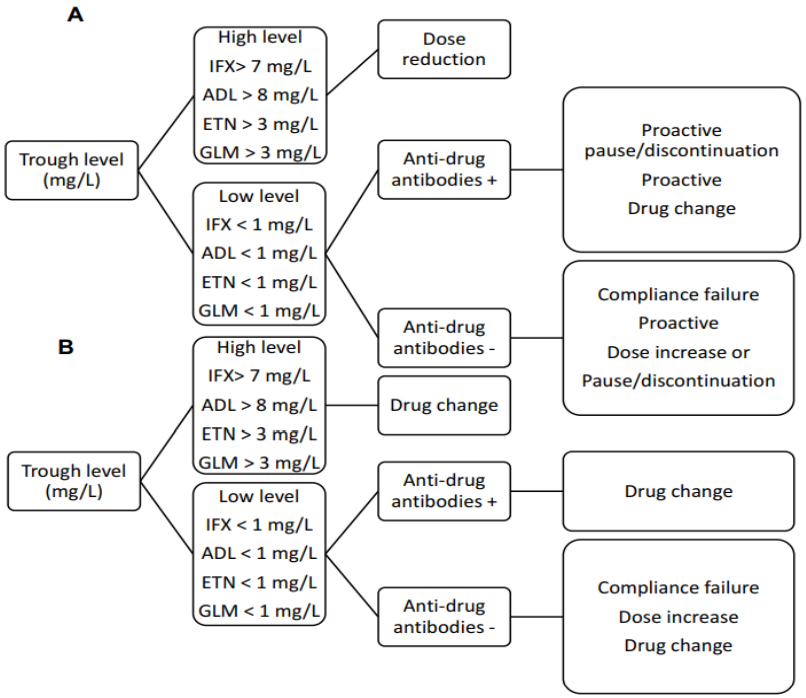


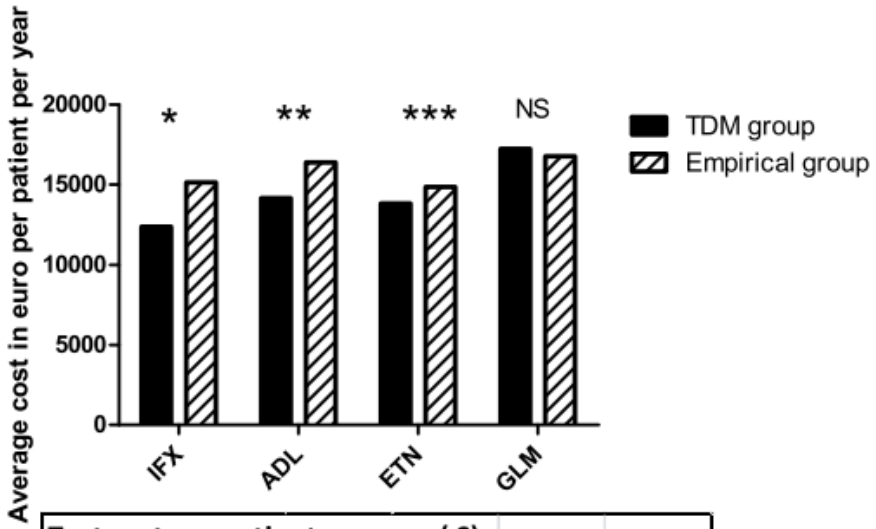
- **Conclusion :** Chez les patients souffrant de maladies inflammatoires et recevant un traitement de maintenance à l'infliximab, **le TDM proactif s'est avéré plus efficace que le traitement sans TDM** pour maintenir le contrôle de la maladie sans aggravation de celle-ci. Des recherches supplémentaires sont nécessaires pour comparer le TDM proactif au TDM réactif, pour évaluer les effets sur les complications à long terme de la maladie et pour évaluer le rapport coût-efficacité de cette approche.

Watterdal et al. JAMA. 2021.

Evaluation of Therapeutic Drug Monitoring in the Clinical Management of Patients with Rheumatic Diseases: Data from a Retrospective Single-Center Cohort Study

- **Objectif :** Étudier l'impact du TDM sur les résultats cliniques, la prise de décision et les dépenses liées aux médicaments biologiques.





Test cost per patient per year (€)	IFX	ADL	ETN	GLM
TDM group	106	92	123	142
Emperical group	88	97	90	159

- **Conclusion :** La prise de décision guidée par le TDM est utile chez les patients atteints de rhumatismes recevant des anti-TNF et peut **optimiser les décisions thérapeutiques, conduisant à un meilleur contrôle de l'activité de la maladie.** Le TDM proactif peut aider à prendre des décisions sur la réduction de la dose, ce qui permet de réduire la consommation de médicaments et les dépenses liées aux produits biologiques.

Pedersen et al. 2020. Biologics.

TDM en rhumatologie - Conclusion

Nouvelles recommandations en rhumatologie

- De plus en plus de données sont disponibles (fenêtres thérapeutiques, concentrations seuils...)
- De plus en plus de publications concernant l'utilisation du TDM

Intérêt/besoin des cliniciens

- Retours d'expérience des experts français lors du comité scientifique
- Présentations mentionnant l'utilisation du TDM lors de nombreuses conférences (EULAR...)

Nouveaux développements ?

- Guselkumab
- Mirikizumab