Hôpitaux Universitaires Genève

Groupe Médical d'Onex

MICI: bilan prétraitement et suivi, comment optimaliser

Dr Marc Girardin

Actualités et controverses en gastroentérologie – CHUV 02/2016

Plan

- Introduction
  - Quels sont les but thérapeutiques et de prise en charge?
- Bilan pré-traitement
  - Bilan de la maladie
  - Traitement
    - Immunomodulateurs
    - Biologiques
- Stratégies de suivi
  - Invasives ou non invasives
- Conclusion

Prise en charge de la maladie de Crohn

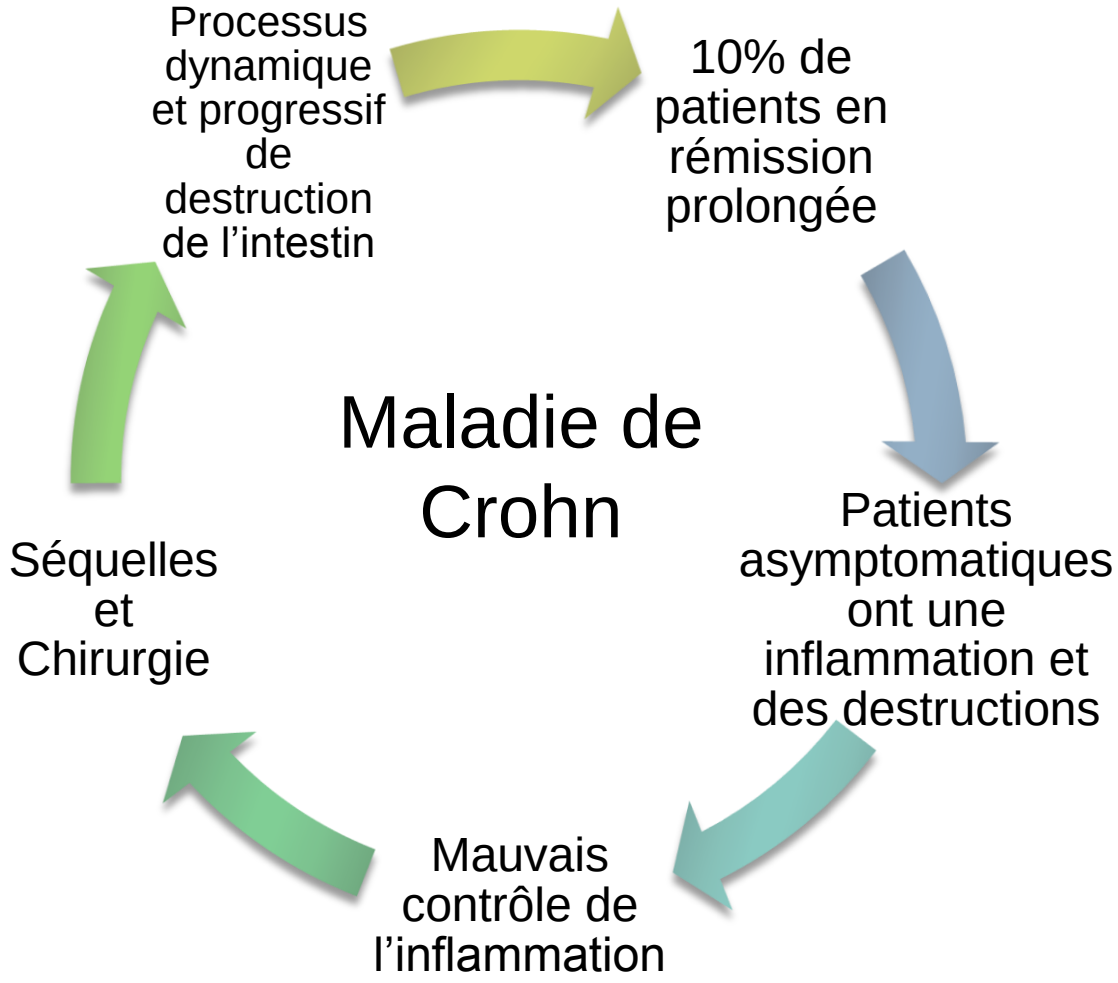
«Traditionnelle»

Intensification du traitement basée sur les symptômes

Mauvaise corrélation symptôme-lésion; délai avant traitement efficace; séquelles-destruction-invalidité

- Bouguen G et al. CGH 2015; 13: 1042-50

Processus des MICI



- Solberg IC et al. CGH 2007; Thia KT et al. Gastro 2010; Bouguen G et al. Gut 2011

Bilan des MICI

- Bilan de Base
  - Localisation de la maladie
  - Intensité de la maladie
  - Catégorie de risque de la maladie

Outils validés

- Traitement dédié précisément à ce patient-cette maladie

Outils validés

- 6 mois, Evaluation de l'efficacité
  - OUI
    - Poursuite
    - Évaluation périodique

Outils validés

  - NON
    - Ré-évaluation ➔ Bilan de Base

Bilan de base de la maladie

1. Iléo-coloscopie
2. Gastroscopie
3. Entéro-IRM
4. US

ECCO statement 2F

For suspected CD, ileocolonoscopy and biopsies from the terminal ileum as well as each colonic segment to look for microscopic evidence of CD are first line procedures to establish the diagnosis [EL1b, RG A]. Irrespective of the findings at ileocolonoscopy, further investigation is recommended to examine the location and extent of any CD in the upper gastrointestinal tract or small bowel [EL5, RG D].

ECCO statement 2G

MR and CT enterography or enteroclysis is an imaging technique with the highest diagnostic accuracy for the detection of intestinal involvement and penetrating lesions in CD [EL1b, RGB]. Radiation exposure should be considered when selecting techniques. Because of the lower sensitivity of barium studies, alternative techniques are preferred if available. Transabdominal ultrasonography is a useful additional technique for assessing bowel inflammation.

- Van Assche G et al. JCC 2010; 4: 7-27

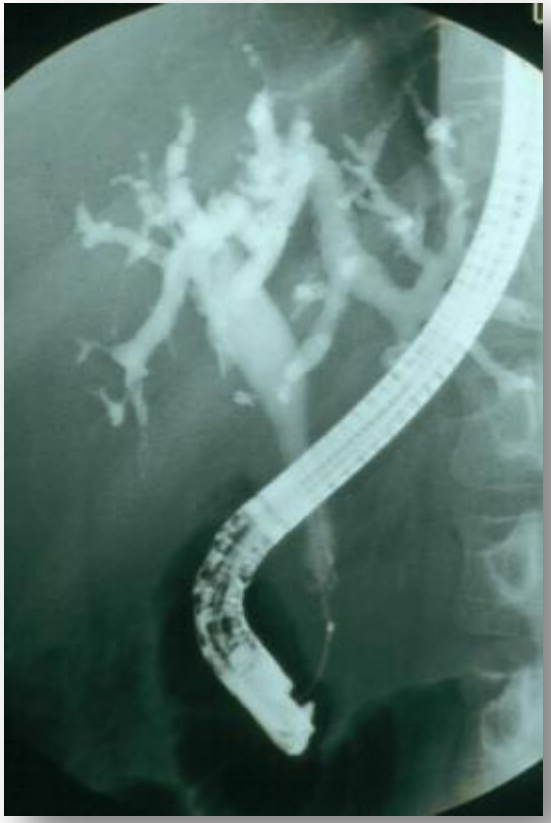
Classification de Montréal

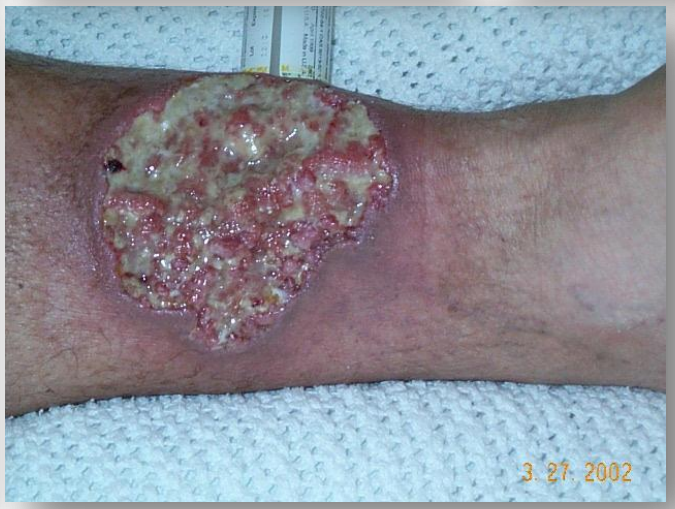
Age / Location / Behavior	
A1	< 16 years
A2	17 - 40 years
A3	> 40 years
B1	Non stricturing non penetrating
B2	Strituring
B3	Penetrating
P	Perianal disease

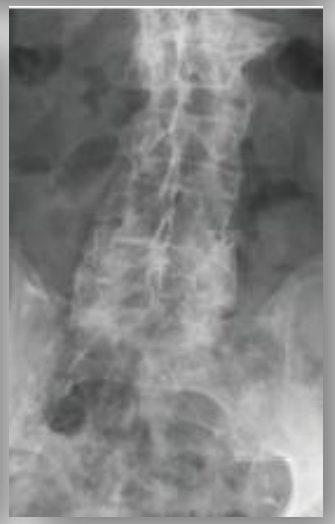
Extent	Anatomy
E1: Ulcerative proctitis	Limited to the rectum
E2: Left sided Ulcerative colitis	Distal to the splenic flexure
E3: Extensive Ulcerative colitis	Proximal to the splanic flexure

- Silverberg M S et al. Can J Gastroenterol 2005; 19: 5–36

Atteintes extra-intestinales







- Vavricka SR et al. Inflamm Bowel Dis. 2015; 21: 1982-92

Atteintes extra-intestinales

- 6% - 47%
- 25% ont plusieurs EIM
- Après 30 ans de maladie 50% des patients ont eu au moins un EIM

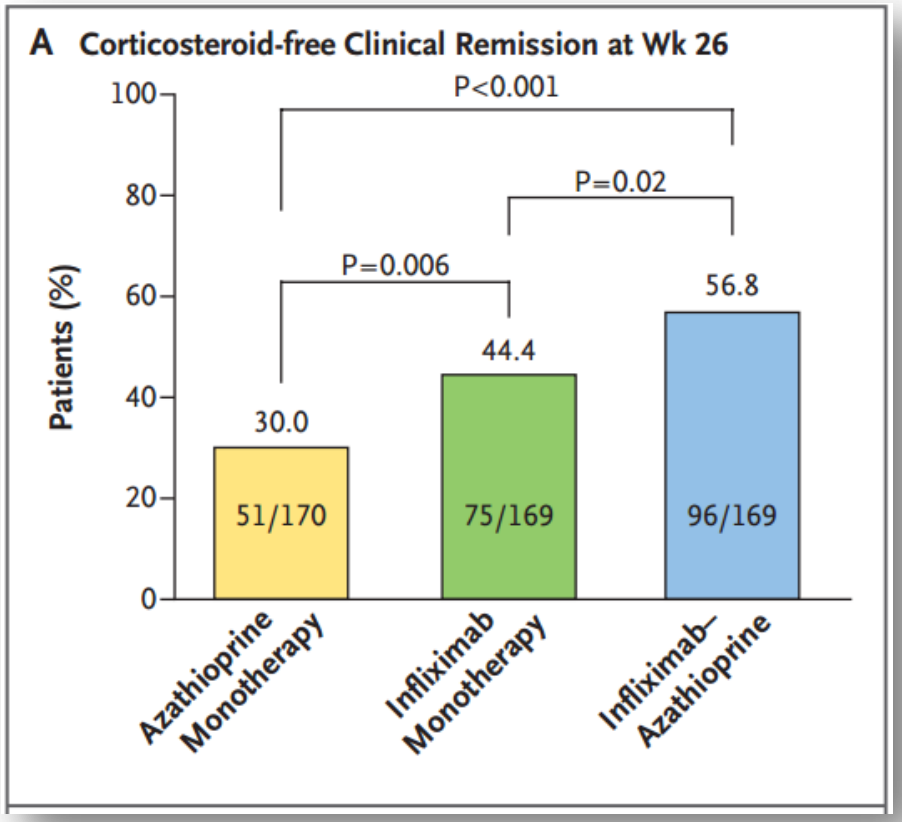
Type	Fréquence
Arthrite	40 %
Arthrite périphérique	5-20 %
Arthrite axiale	3-25 %
Erythème noueux	10-15 %
Pyoderma G.	0.4-2 %
Orales (Aphtes)	10 %
Oculaires	2-5 %

EIM	1ère ligne	2ème ligne
Arthrites périphérique	Stéroïdes, sulfasalazine, AINS, immunomodulateurs	Anti-TNF
Pyoderma gangrenosum	Stéroïdes, cyclosporine, immunomodulateurs	Anti-TNF
Uvéites	Stéroïdes, cyclosporine	Anti-TNF

- Vavricka SR et al. Inflamm Bowel Dis. 2015; 21: 1982-92

Critères de gravité – SONIC

- Maladie à évolution mutilante («disabling»)
  - CRP élevée
  - Ulcères creusants
  - Atteinte pancolique
  - Age jeune (< 40 ans)
  - Maladie diffuse grêle
  - Maladie périanale
  - Maladie perforante
  - Stéroïdes d'emblée

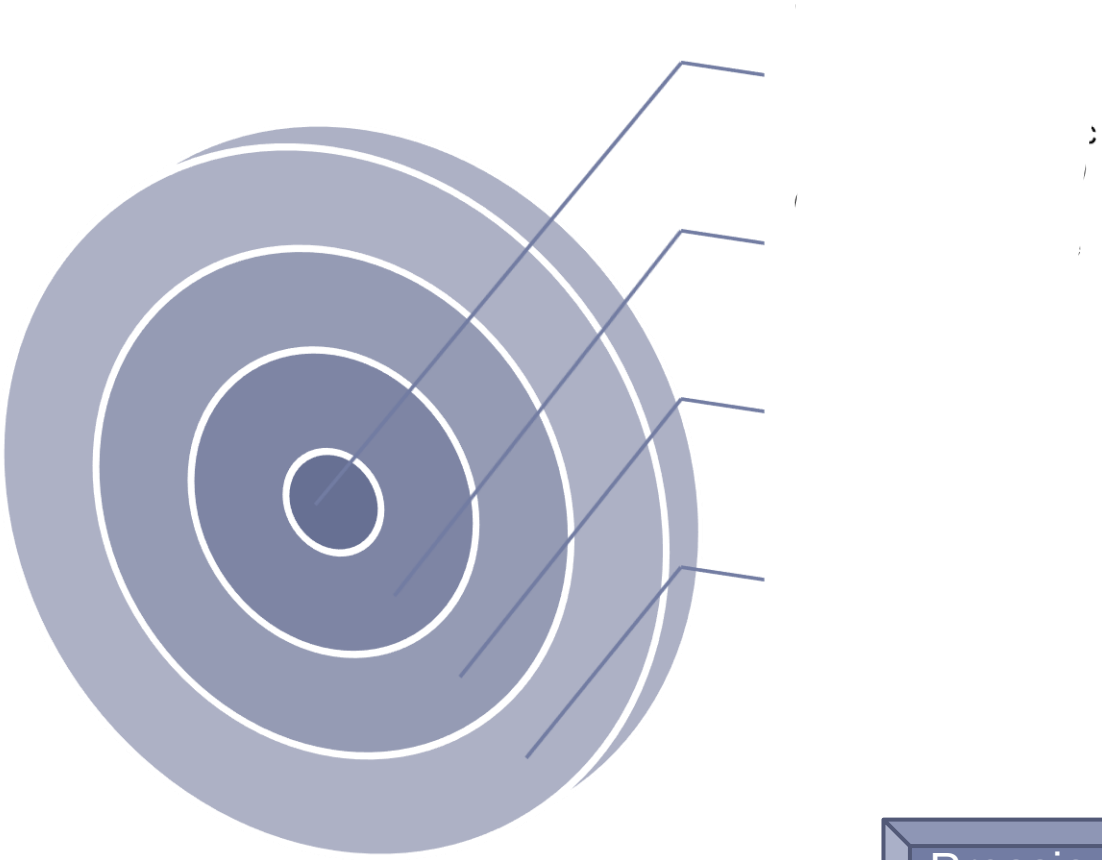


- Bilan approfondi
- Patients bénéficiant particulièrement d'une thérapie anti-inflammatoire agressive

Colombel JF et al. NEJM 2010; 362: 1383-95


Lausanne
Genève
Lyon F
Milano
Lugano
Locarno
Bellinzona Sud
Altstätten
Kriessern
St.Gallen
St.Margrethen
E 23 9
Lausanne 42 km
Orbe 12 km
E25 1
St.Gallen 250 km
Zürich 169 km
Basel 140 km
Meersburg
E 62 9
Genova I
Milano I
Domodossola I
Brig
Martigny
Z.I. Acacias

Cible – améliorer un résultat à long terme



Pression sanguine (HTA)
Hb glyquée (diabète)

Bilan des MICI

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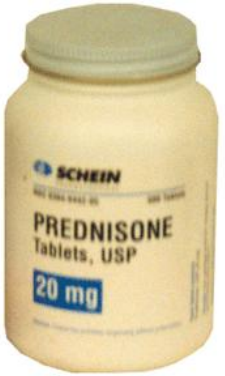
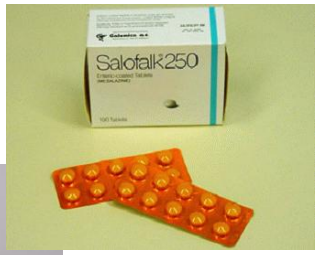
Traitement – Bilan
Outils validés – Suivi

Quel bilan pré-traitement?





Bilan en général

- Maladies infectieuses
  - Tuberculose latente
  - HBV
  - HPV
  - Varicelle
- Cancer
  - AP

Journal of Crohn's and Colitis (2014) 8, 443–468

Available online at www.sciencedirect.com

ScienceDirect

ELSEVIER

CONSENSUS/GUIDELINES

Second European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease

J.F. Rahier[a,*], F. Magro[b,c,d], C. Abreu[e], A. Armuzzi[f], S. Ben-Horin[g], Y. Chowers[h], M. Cottone[i], L. de Ridder[j], G. Doherty[k], R. Ehehalt[l], M. Esteve[m], K. Katsanos[n], C.W. Lees[o], E. MacMahon[p], T. Moreels[q], W. Reinisch[r,s], H. Tilg[t], L. Tremblay[u], G. Veereman-Wauters[v], N. Viget[w], Y. Yazdanpanah[x], R. Eliakim[y], J.F. Colombel[z], on behalf of the European Crohn's and Colitis Organisation (ECCO)

Patient identification

2. PHYSICAL EXAMINATION

Remember to look for and ask about s

3. TUBERCULOSIS SCREENI

Normal chest X-ray

Tuberculin skin test (TST) > 5mm

TST Booster

IFN-γ release assay
QuantiFERON, ELISPOT (best discussed
diseases specialist)

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acc
sho
It c

1.

Infection history

- **Bacterial**
- **Fungal**
- **Viral**
  - HSV (cold sores, genital)
  - VZV (chickenpox and/or shingles)
  - Other
- **Parasitic**
- **Treatment for latent or active tuberculosis**

Immunization status

- **BCG (live vaccine)**

Environmental risks

- **Tuberculosis**
  - Potential contact with TB patients
  - At-risk country of origin or prolong stay in an endemic area
  - Plans to travel to TB-endemic area
- **Other infections**
  - Prolonged stay or plans to travel to tropics or endemic areas

4. LABORATORY TESTS

	POS	NEG
Serology		
EBV	☐	☐
Hep. A V (physician discretion)	☐	☐
Hep. B V		
Ag Hbs	☐	☐
Ag Hbe	☐	☐
Ab anti-HBs	☐	☐
Ab anti-HBc	☐	☐
Hep. C V	☐	☐
HIV (after appropriate counselling)	☐	☐
Measles (physician discretion)	☐	☐
Strongyloidiasis (for travellers returning from highly endemic zones[3])	☐	☐
VZV (in patients without reliable history of varicella)	☐	☐
Urinalysis (for patients with history of urinary tract infection or urinary symptoms)		
Stool examination for ova, cysts, parasites (for returning travellers)		

5. VACCINATION[4]

	NO	YES	Date (mm/yyyy)
Routine vaccination[2]			
Diphtheria	☐	☐	__/__
Tetanus	☐	☐	__/__
Poliomyelitis	☐	☐	__/__
Pertussis	☐	☐	__/__
HPV vaccine	☐	☐	__/__
Ideally at IBD diagnosis			
HBV vaccine (seronegative patients)	☐	☐	__/__
VZV vaccine (live vaccine - seronegative patients without reliable history of chickenpox/shingles)	☐	☐	__/__
Prior to immunomodulation			
Inactivated trivalent influenza vaccine (to be administred once a year)	☐	☐	__/__
Pneumococcal vaccine (PCV13)	☐	☐	__/__
Pneumococcal polysaccharide vaccine (PPSV23)	☐	☐	__/__
Booster injection			
Pneumococcal polysaccharide vaccine (PPSV23) (single booster injection 5 years later)	☐	☐	__/__

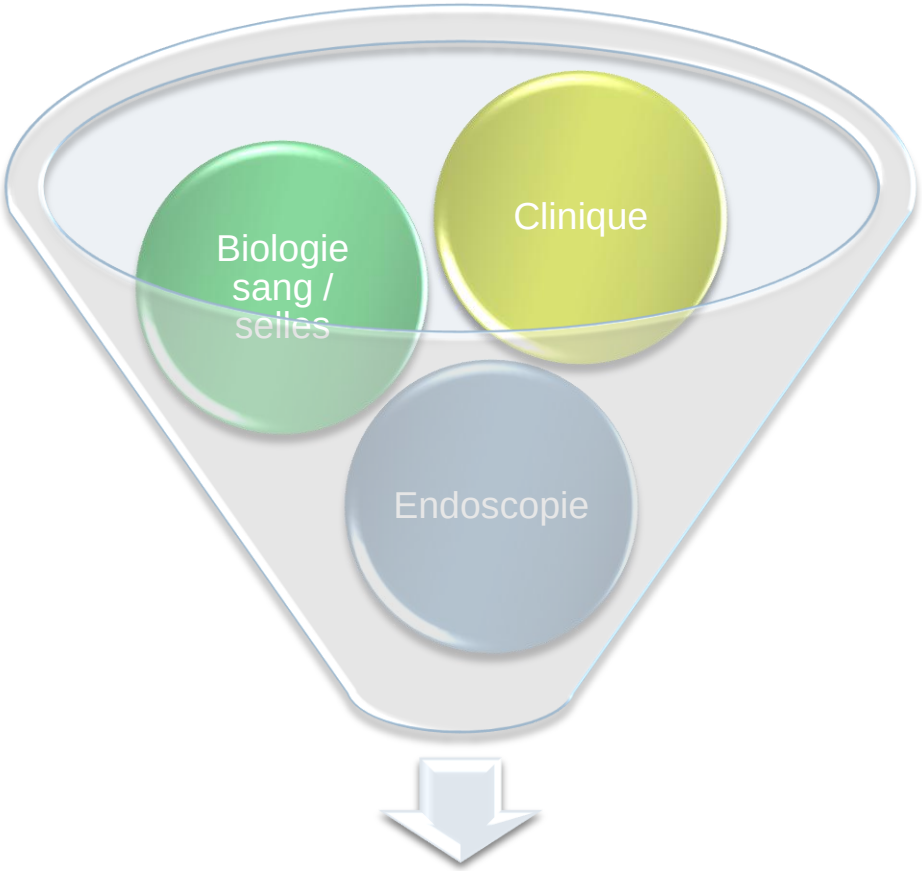
Bilan spécifique

- Azathioprine
  - TPMT
  - EBV
- Méthotrexate
  - Tests hépatiques
  - HCV
- Biologiques
  - Anti-TNF
    - Insuffisance cardiaque
    - AP ou AF de sclérose en plaque
  - Anti-intégrine
    - Atteintes neurologiques

Examens	Avant thérapie
Hémoglobine, MCV Leucocytes (< 3 x $10^3/\mu l$: Diff.), Thrombocytes	+
Créatinine, transaminases	+
Sérologie hépatite B, C. HIV	+
Albumine	+
Dosage d'acide folique	+
Radiographie du thorax	+
Fonction pulmonaire avec capacité de diffusion	facultatif

Société suisse de rhumatologie

Suivi



Buts du suivi

- Médical
  - Moins d’hospitalisation
  - Moins de chirurgie
  - Moins d'effets secondaires (infections et cancer)
- Qualité de vie
  - Moins de symptôme
  - Travail
  - Loisirs

Médicaments

- Methotrexate
  - Tests hépatiques
  - Pulmonaire
- Azathioprine
  - Tests sanguins

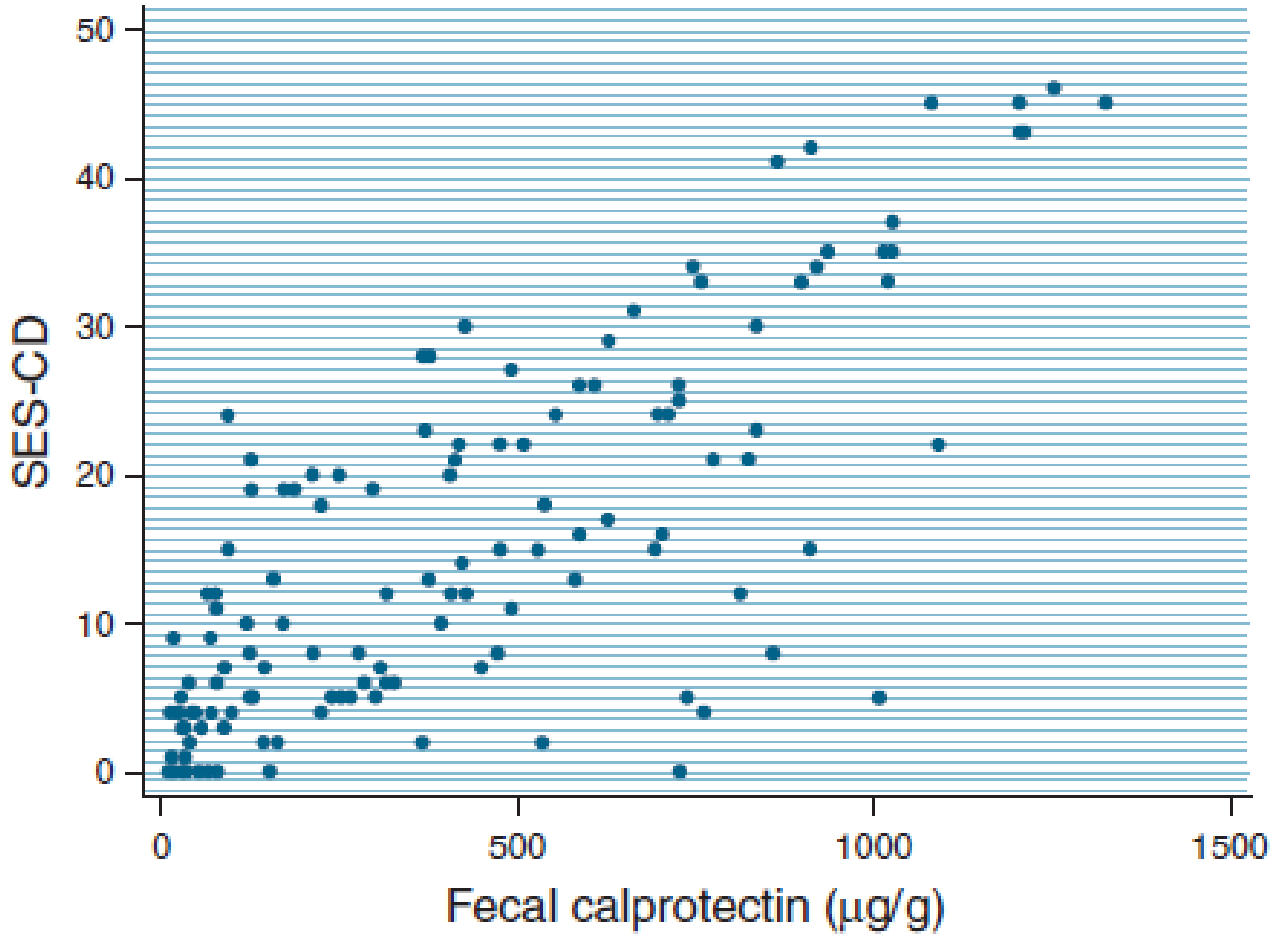
Examens	1er mois	2ème mois	A partir du 3ème mois
Hémoglobine, MCV Leucocytes (< 3 x 10^3/µl: Diff.), Thrombocytes	Chaque semaine	chaque 2 semaines	chaque 1 à 2 mois
Créatinine, transaminases	Chaque semaine	chaque 2 semaines	chaque 2 mois
Sérologie hépatite B, C. HIV			
Albumine			chaque 3 à 6 mois

- Société suisse de rhumatologie

Monitoring

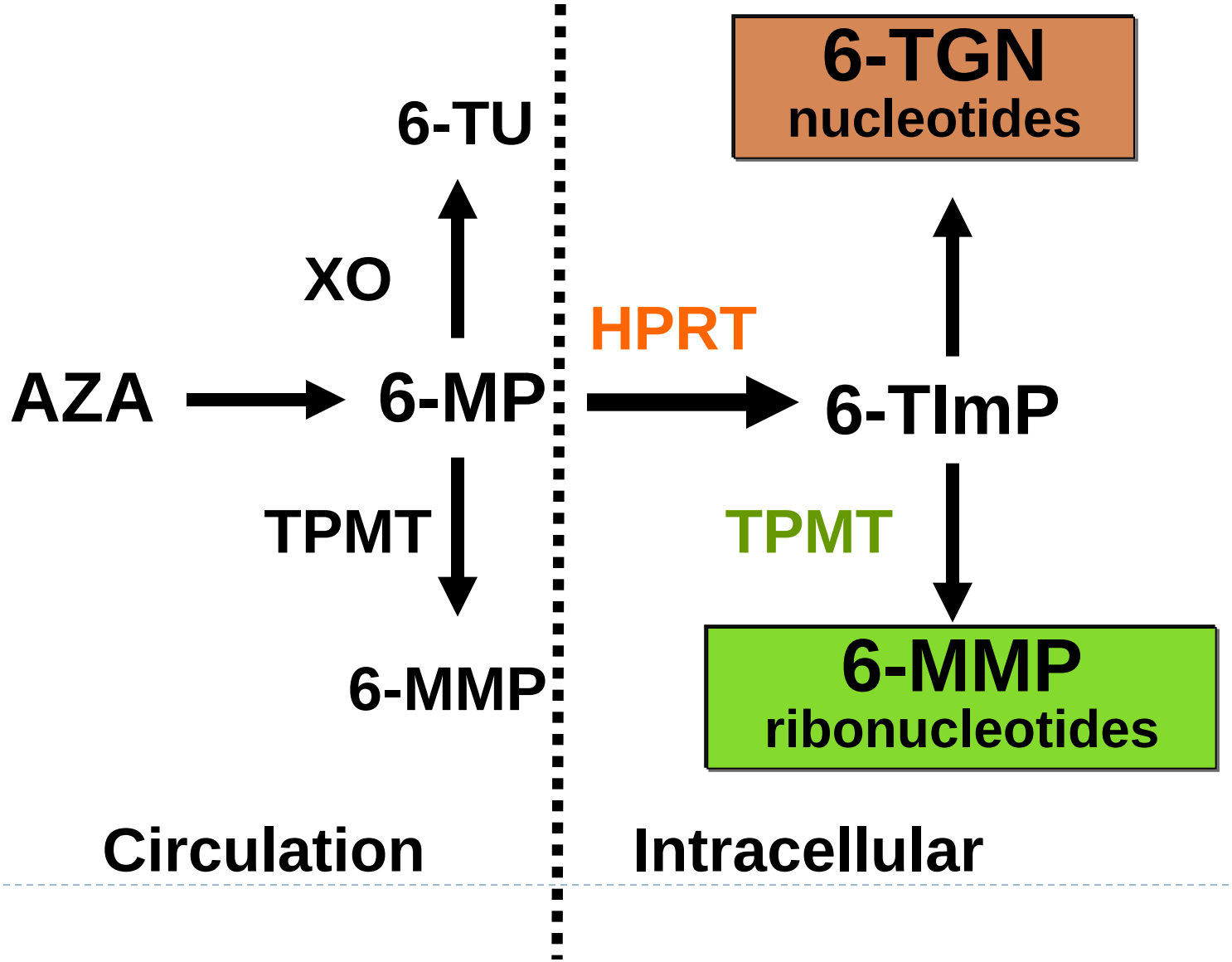
- Vérifier la compliance
- Optimiser la prise d'un traitement
  - Couts
- Optimiser l'effet du traitement
  - Clinique
  - Le dosage ou l'intervalle
  - Eviter les effets secondaires
  - Endoscopique: «mucosal healing»
  - Immunogénéicité: combothérapie
- Aider à la prise de décision

Calprotectine

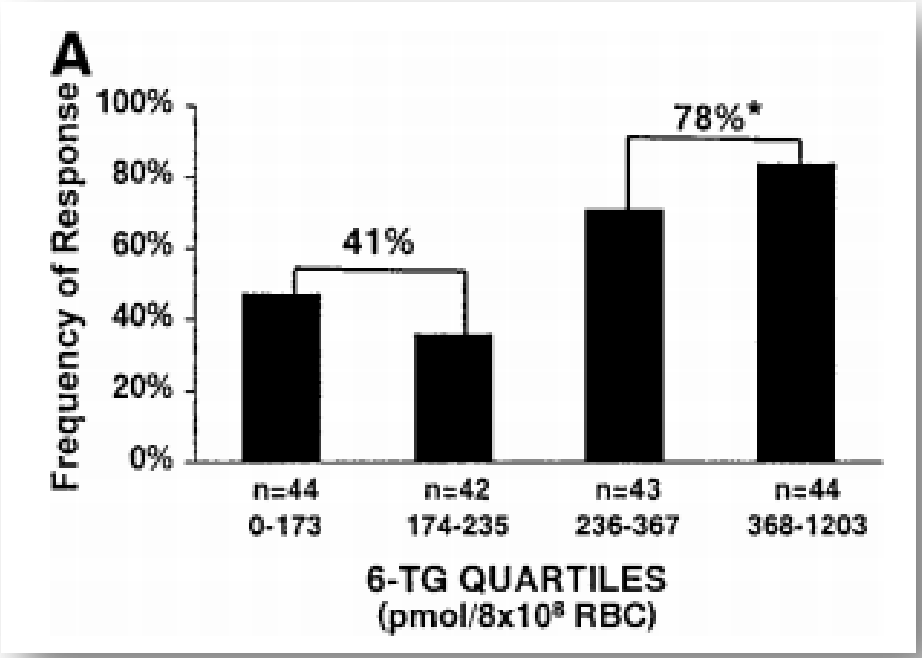


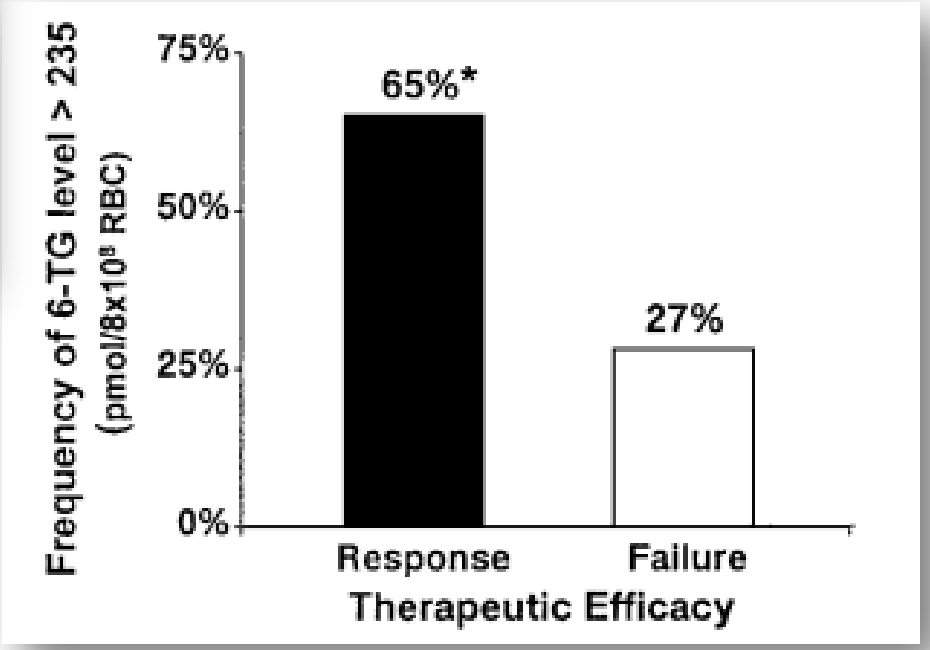
- Schoepfer AM et al. Am J Gastroenterol. 2010; 105: 162-9

Thiopurines – 6-TGN / 6-MMP



Metabolite Measurement for thiopurine



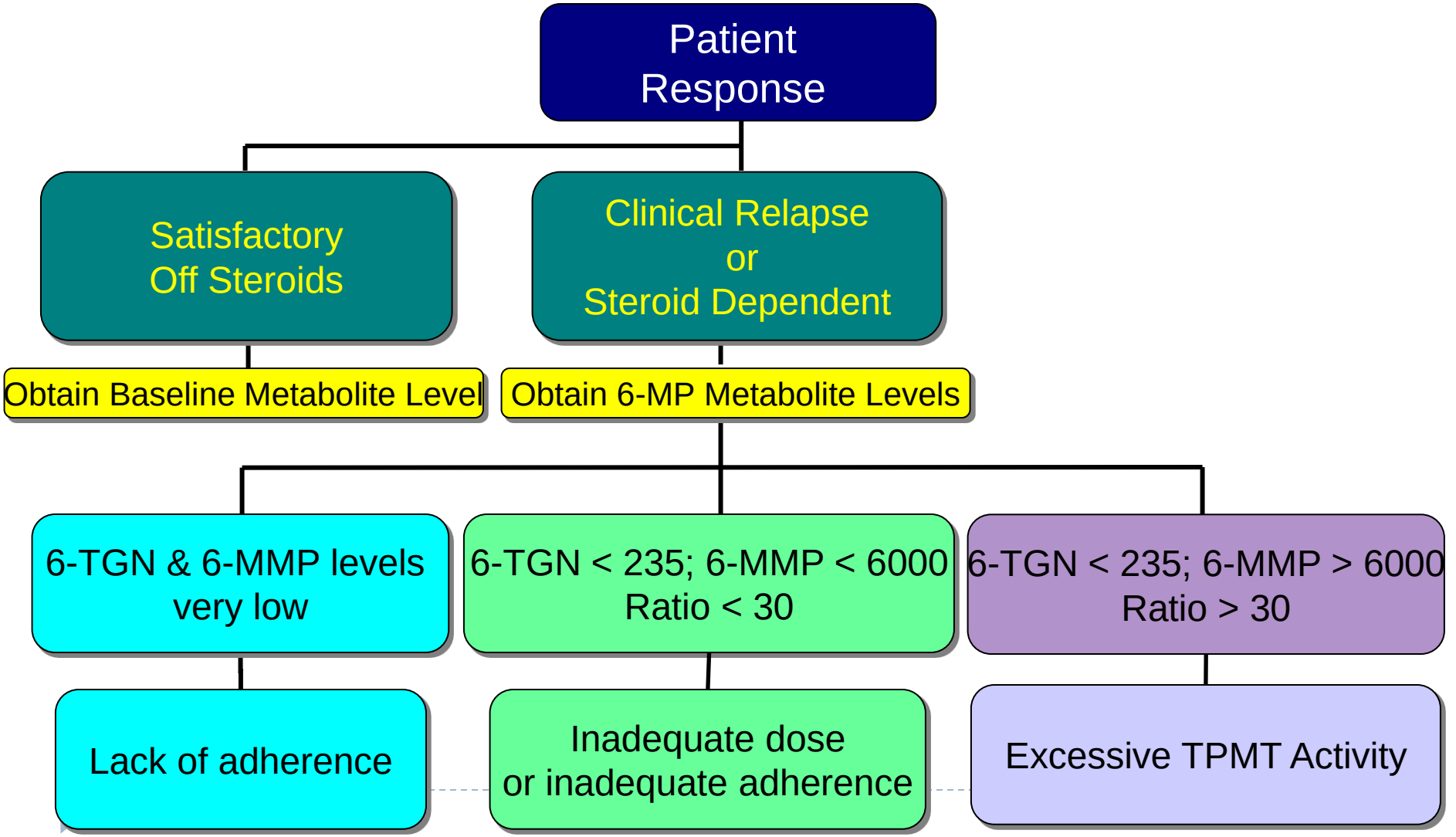


- Dubinsky MC et al. Gastroenterology 2000; 118: 705-13

6-MMP/6-TG Ratio Reflects TPMT Activity & Therapeutic Outcomes

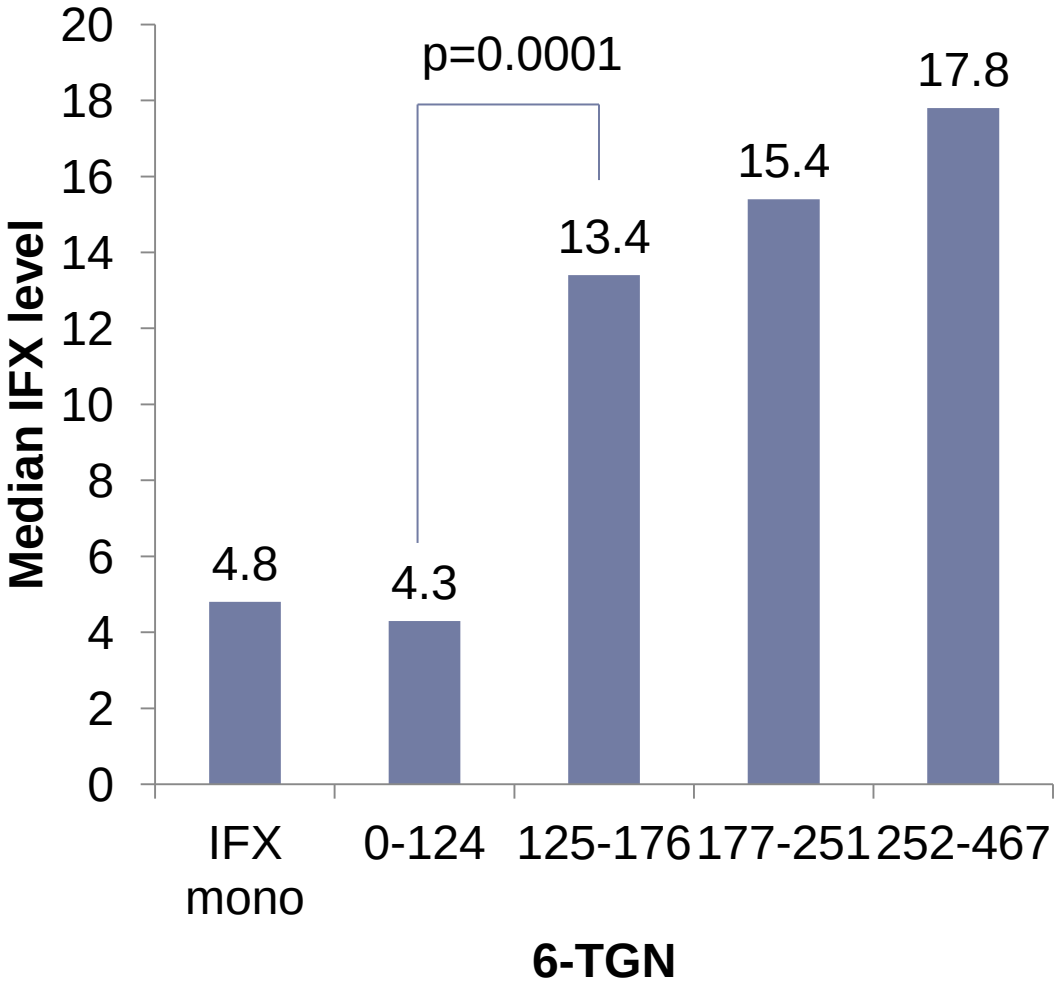
6-MMP / 6-TGN	TPMT genotype	Likelihood of Clinical Response (potential toxicity)
<3	Deficient (heterozygote)	High (myelotoxicity)
3-30	Normal (wild type)	Very good
30 to >100	Excessive (wild type)	Low to Very low (hepatotoxicity)

Algorithm to Interpret 6-MP Metabolite Levels



Taux de 6-TGN – TL IFX

- 72 patients
- Maintien sous combothérapie
- Groupe contrôle avec IFX seul
- ATI ➔ 6-TGN plus bas
- 6-TGN < 125 ➔ ATI
- TL> 8 ➔ mucosal healing



Andres JY et al. CGH 2015; 13: 1118-24

TL pour prédire la rémission (SONIC)

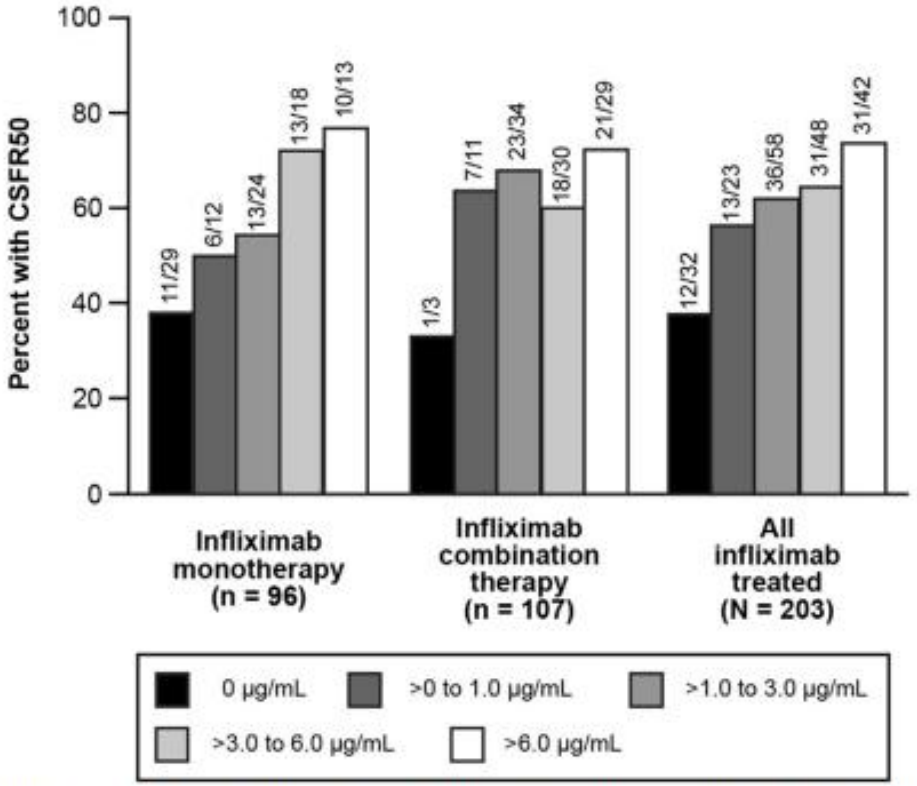
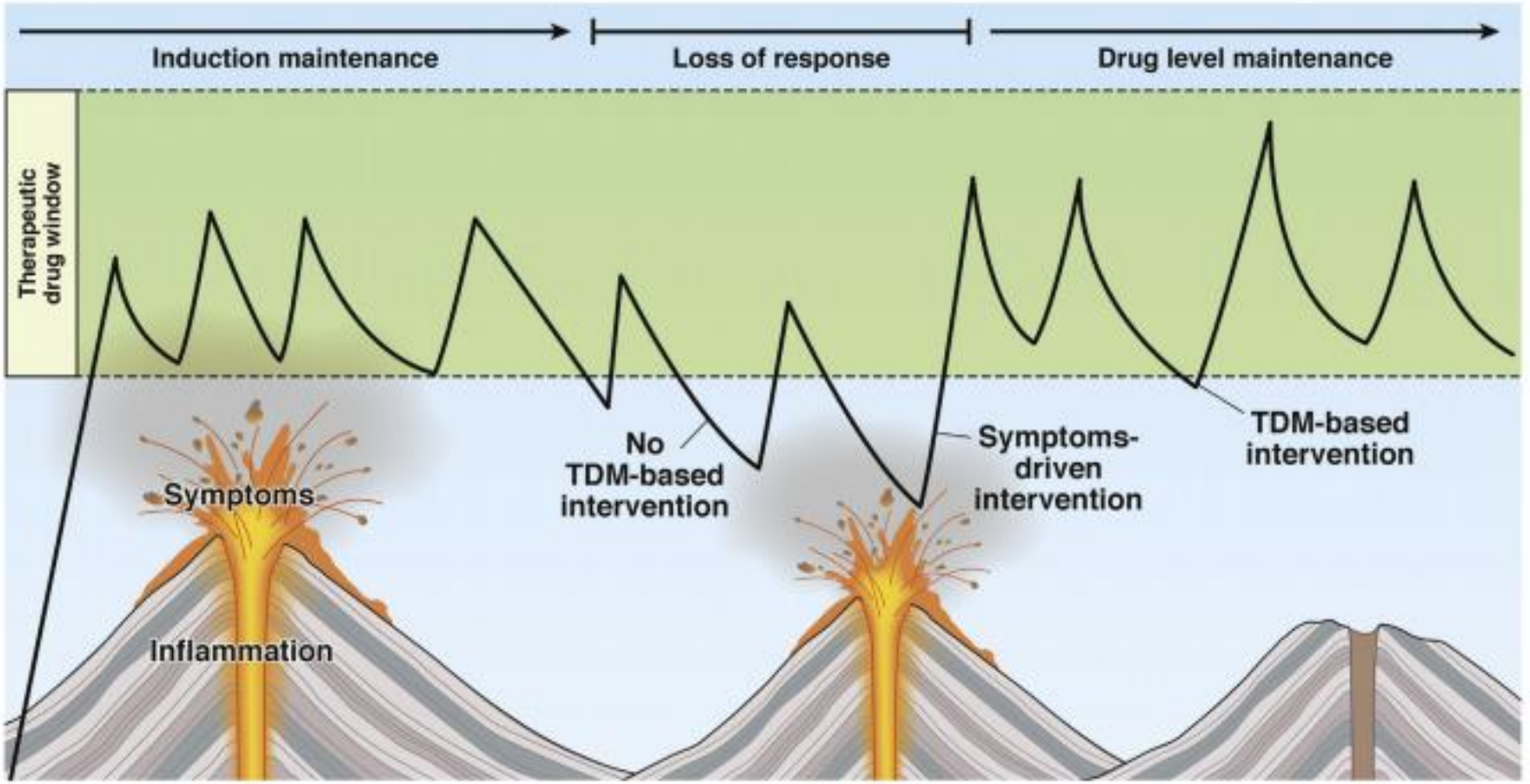


Figure 3. Association of CSFR50 using selected SIC30 ranges. Note: Patients with infliximab concentrations less than .1 µg/mL, are classified as zero. SIC30, serum infliximab concentration at week 30; CSFR50, corticosteroid-free remission at week 50.

- Reinisch W et al. Clinical Gastroenterology and Hepatology 2015; 13: 539–47

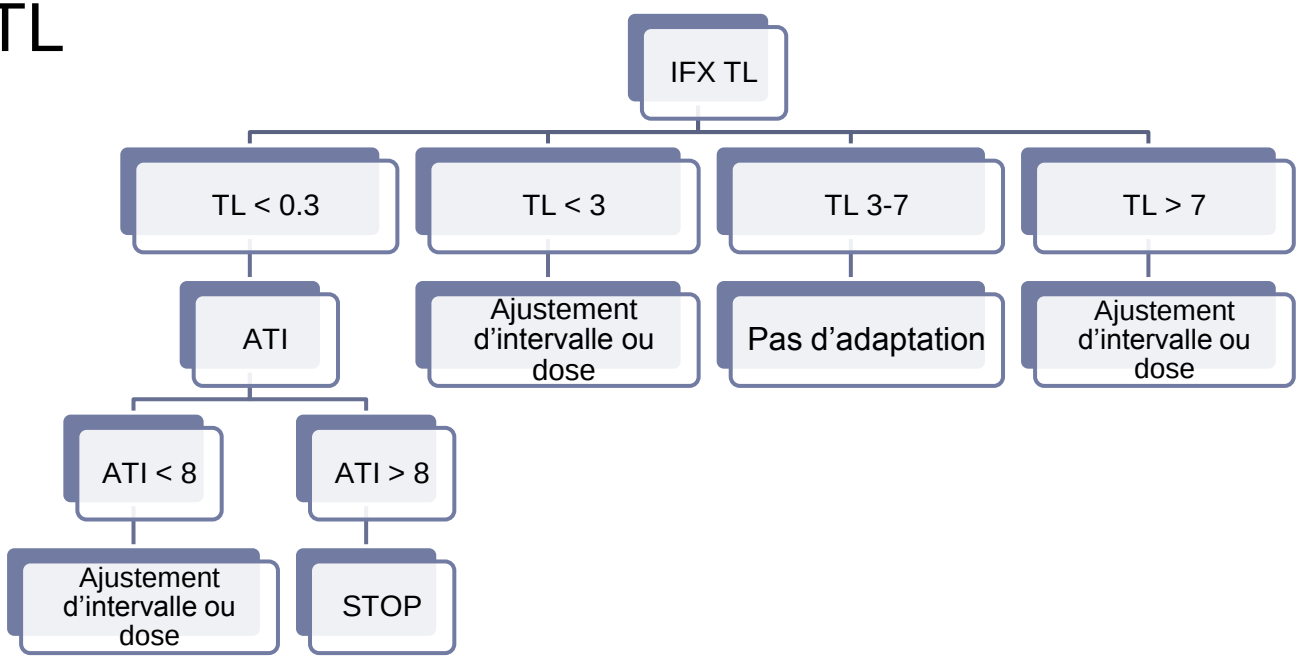
Suivi: TL ou clinique?



- Ben-Horin S. Gastroenterology 2015; 148: 1268-81

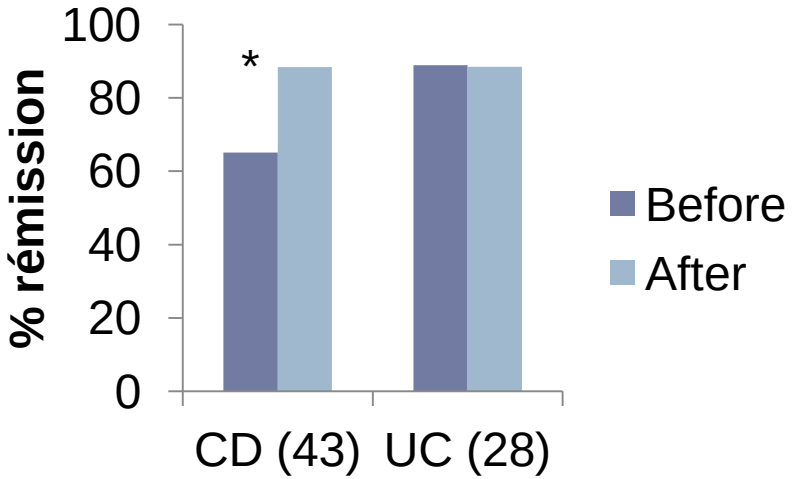
Suivi basé sur les TL – TAXIT

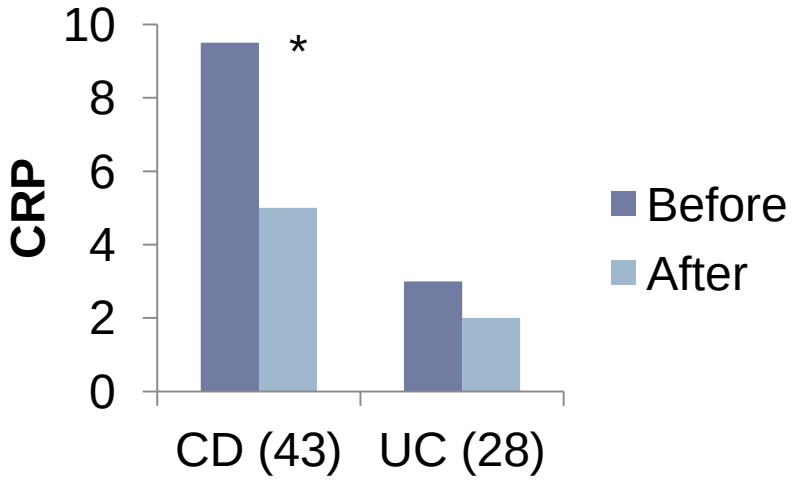
- RCT, 1 an de suivi
- 263 patients avec maladie stable sous IFX
- Modification des doses pour atteindre 3-7 ug/ml
- Randomisation entre adaptation clinique ou basée sur TL

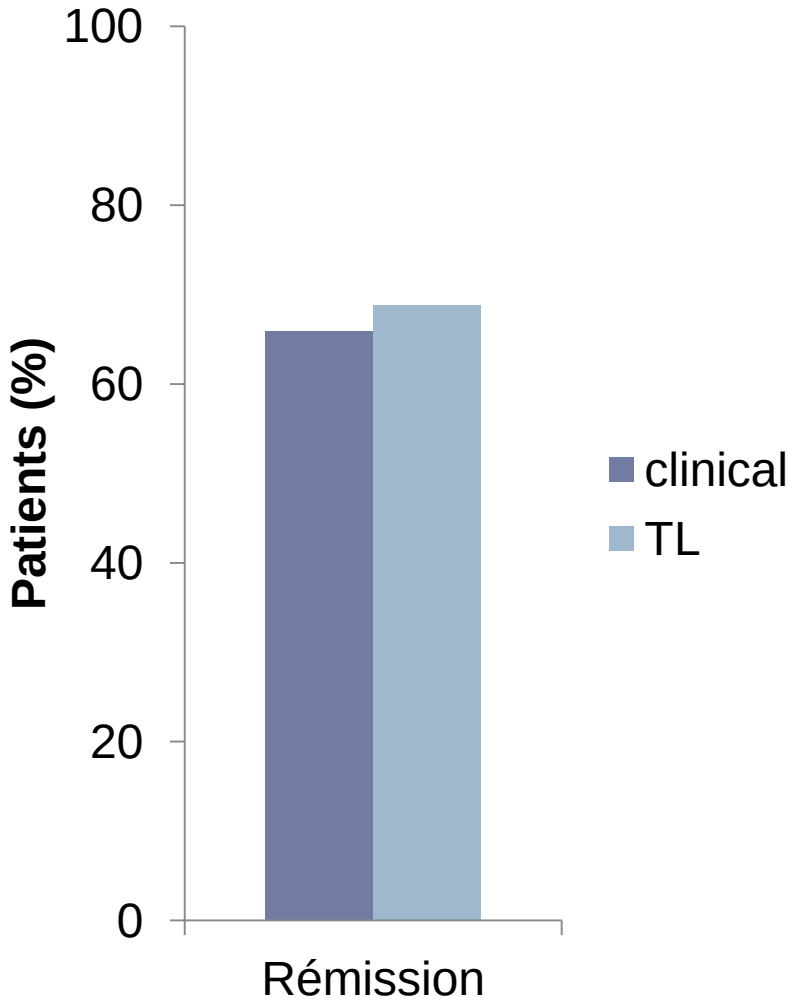


- Vande Casteele N et al. Gastroenterology 2015; 148: 1320-29

Suivi basé sur les TL – TAXIT







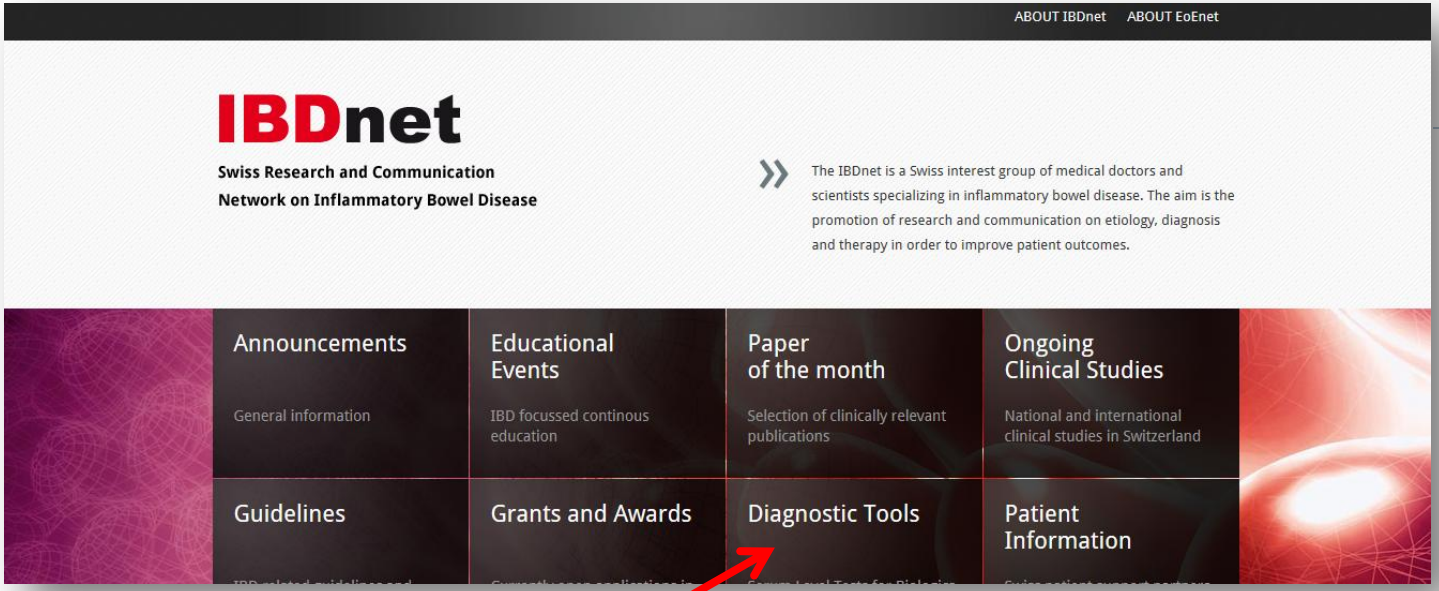
- Vande Casteele N et al. Gastroenterology 2015; 148: 1320-29

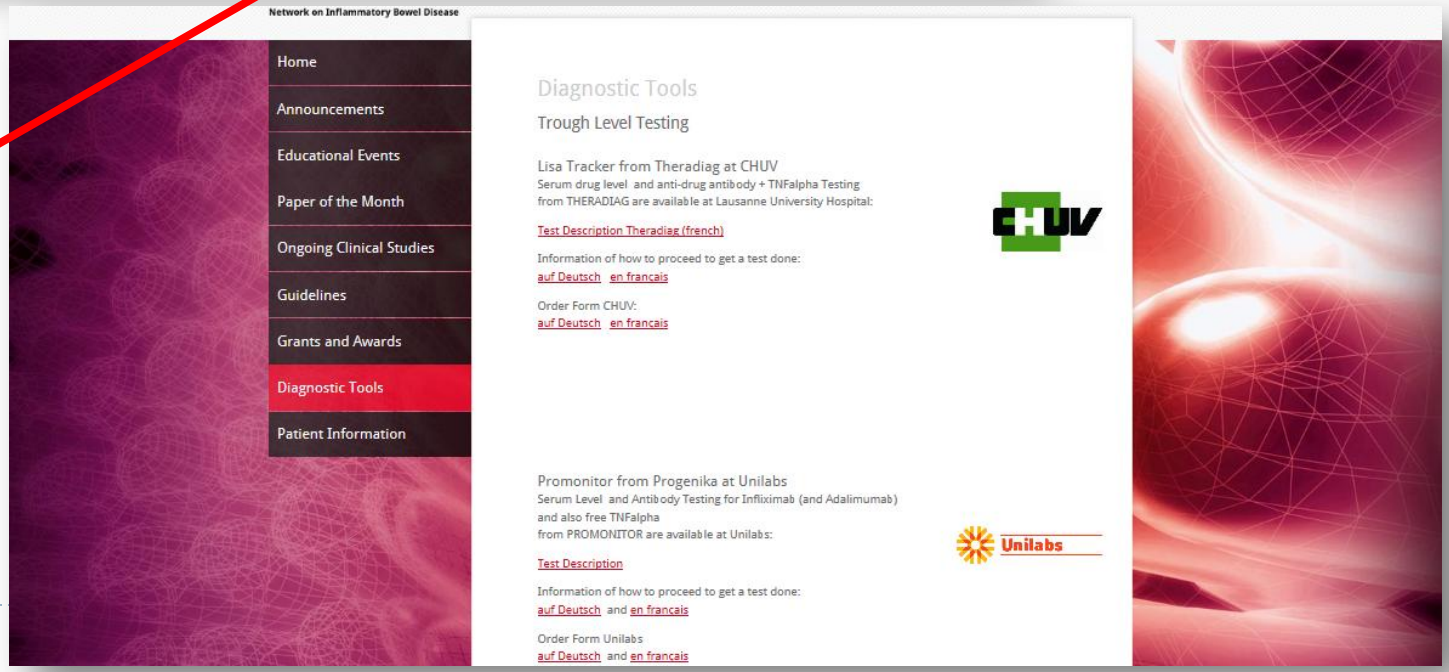
TL

- Adaptation du traitement à la hausse
  - Meilleur efficacité du traitement
- Adaptation du traitement à la baisse
  - Baisse des couts

- Pas d'effet sur le long terme (suivi plus long)

- Dans la vraie vie, utilisation du dosage pour optimiser le traitement lorsque la clinique le nécessite


ABOUT IBDnet
ABOUT EoEnet
IBDnet
Swiss Research and Communication
Network on Inflammatory Bowel Disease
The IBDnet is a Swiss interest group of medical doctors and scientists specializing in inflammatory bowel disease. The aim is the promotion of research and communication on etiology, diagnosis and therapy in order to improve patient outcomes.
Announcements
General information
Educational Events
IBD focussed continous education
Paper of the month
Selection of clinically relevant publications
Ongoing Clinical Studies
National and international clinical studies in Switzerland
Guidelines
Grants and Awards
Diagnostic Tools
Patient Information


Network on Inflammatory Bowel Disease
Home
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Diagnostic Tools
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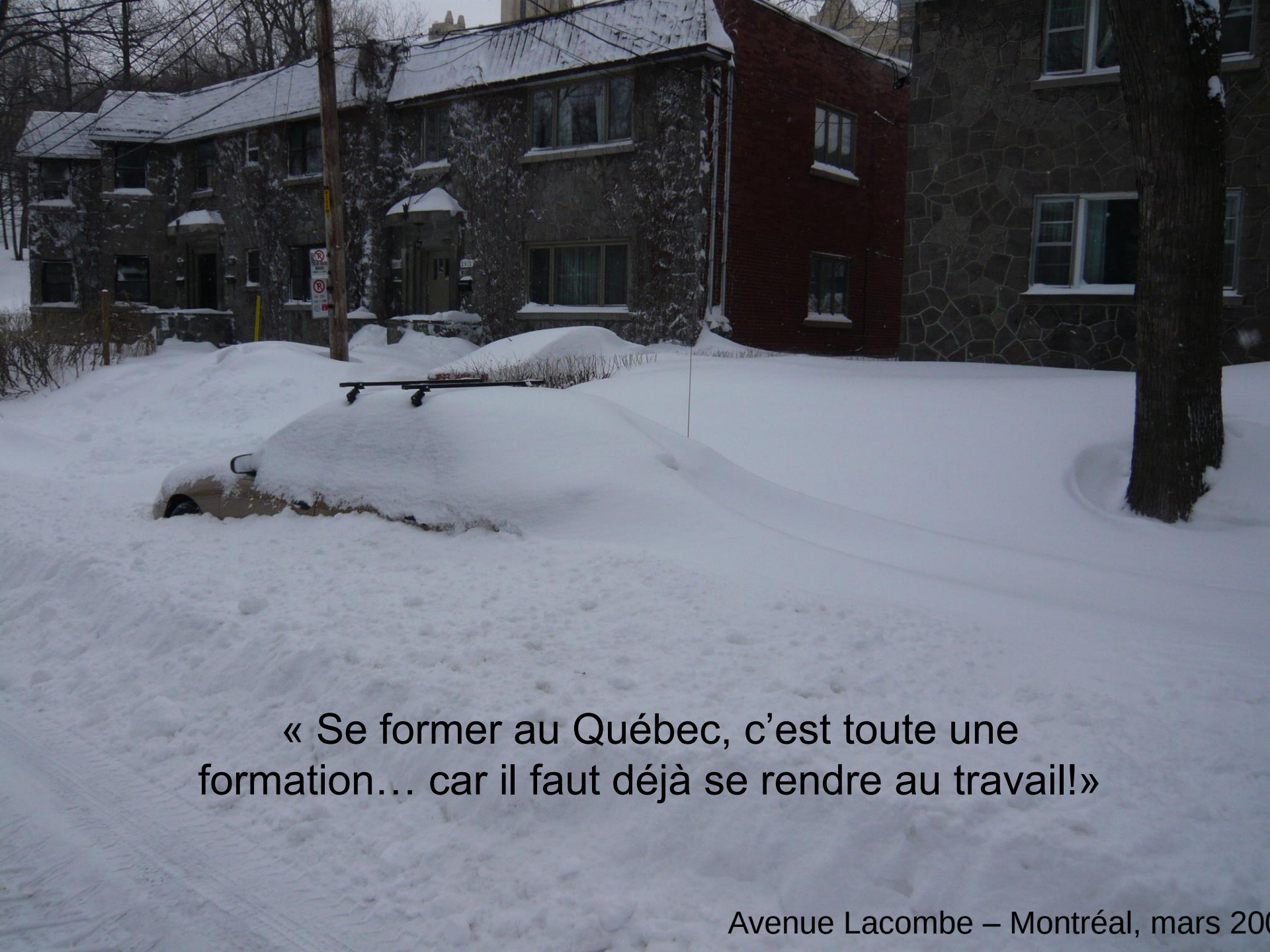
Diagnostic Tools
Trough Level Testing
Lisa Tracker from Theradiag at CHUV
Serum drug level and anti-drug antibody + TNFalpha Testing from THERADIAG are available at Lausanne University Hospital:
Test Description Theradiag (french)
Information of how to proceed to get a test done:
auf Deutsch en français
Order Form CHUV:
auf Deutsch en français
CHUV
Promonitor from Progenika at Unilabs
Serum Level and Antibody Testing for Infliximab (and Adalimumab) and also free TNFalpha from PROMONITOR are available at Unilabs:
Test Description
Information of how to proceed to get a test done:
auf Deutsch and en français
Order Form Unilabs
auf Deutsch and en français
Unilabs

Conclusion

- Approche traditionnelle ➔ «Treat to Target»
- Maladie et patient doivent être bien bilanté avant de choisir la bonne option de traitement
- Plan de suivi doit être établi
  - Calprotectine
  - Endoscopie
  - Métabolites ou taux de médicament



« Se former au Québec, c’est toute une formation… car il faut déjà se rendre au travail!»

Avenue Lacombe – Montréal, mars 20