JDP Journées dermatologiques de Paris

12-16 DÉCEMBRE 2017
PALAIS DES CONGRES / PORTE MAILLOT - PARIS

Psoriasis et traitements systémiques : présentation des premières recommandations françaises

Florent Amatore, Marie Tauber, Axel Villani, Bernard Guillot, Manuelle Viguier

Marseille, Toulouse, Lyon, Montpellier, Reims

GRPso
Groupe de Recherche sur le Psoriasis

Société Française de Dermatologie et de Pathologie Sexuellement Transmissible

CENTRE DE PREUVES
EN DERMATOLOGIE

Déclaration de lien d'intérêt

Je déclare avoir les liens d’intérêt suivants :

Pourquoi des recommandations françaises?

- Existence de recommandations américaines, allemandes, européennes mais
  - Déjà obsolètes compte tenu de la rapidité des progrès thérapeutiques
  - Pas toujours applicables à la situation française
  - Pas de hiérarchisation de la stratégie thérapeutique
- Souhait du Groupe Psoriasis de la SFD de se doter d'un outil pratique applicable à la pratique française

Méthodologie

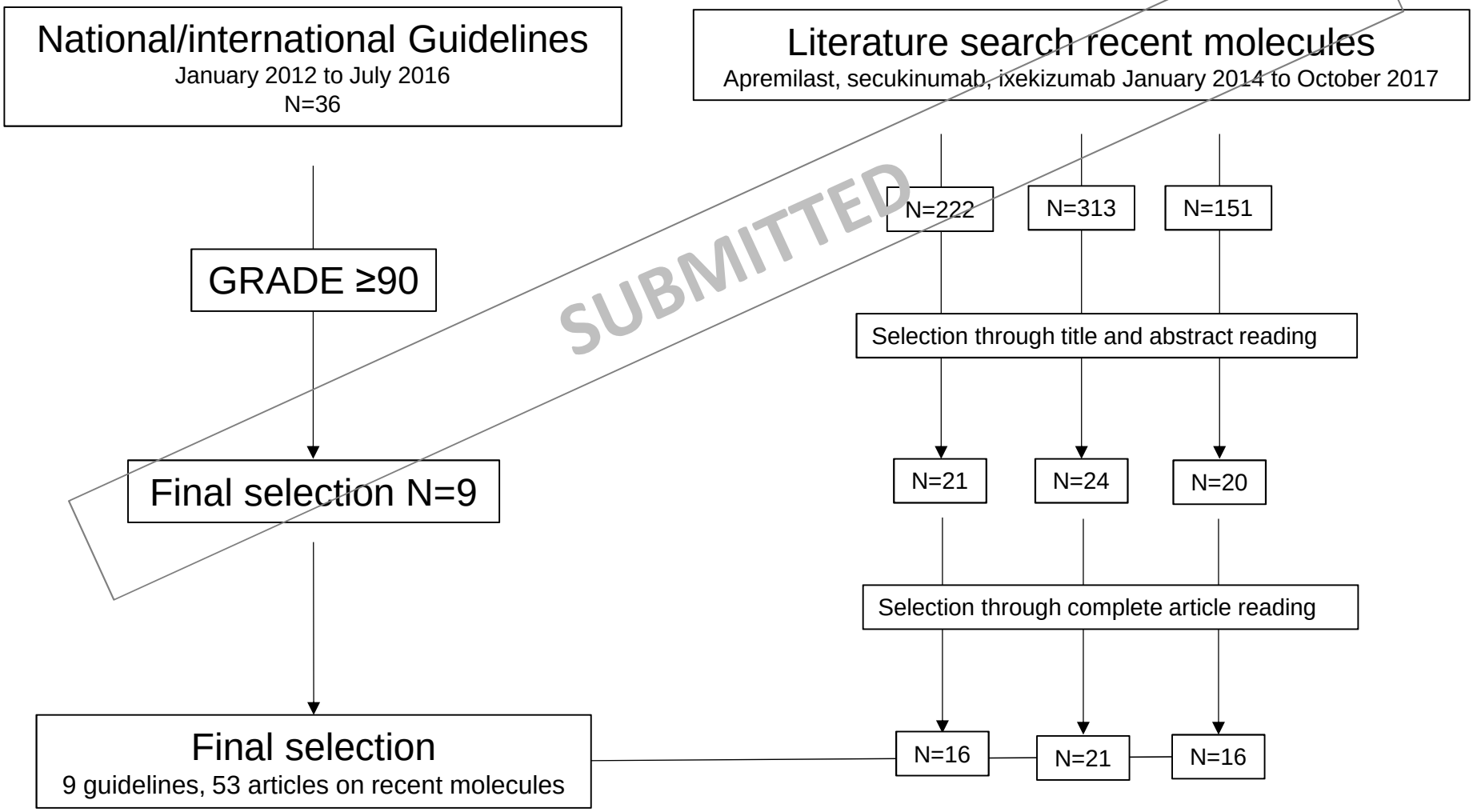
- Inspirée des préconisations de la HAS pour la rédaction de recommandations de pratique clinique
- Méthode ADAPTE
  - Analyse des recommandations publiées entre janvier 2012 et juillet 2016
  - Deux lecteurs indépendants à l'aide de l'échelle AGREE-2
  - Recommandation retenue si score ≥ à 90
- Revue systématique de la littérature pour les molécules non incluses dans les recommandations sélectionnées
  - Evaluation à l'aide de l'échelle GRADE

Méthodologie

- ADAPTE :
  - 36 Recommandations identifiées
  - 9 Recommandations retenues

- Revue de la littérature récente :
  - Article en anglais de janvier 2014 à octobre 2017
  - Résumés de congrès non retenus

Flowchart



Méthodologie

- Groupe de travail :
  - 3 dermatologues sans lien d'intér avec l'industrie
  - FA, MT, AV

- Associés à MV pour supervision et organisation et BG pour la méthodologie

- 1ère réunion juillet 2016 …

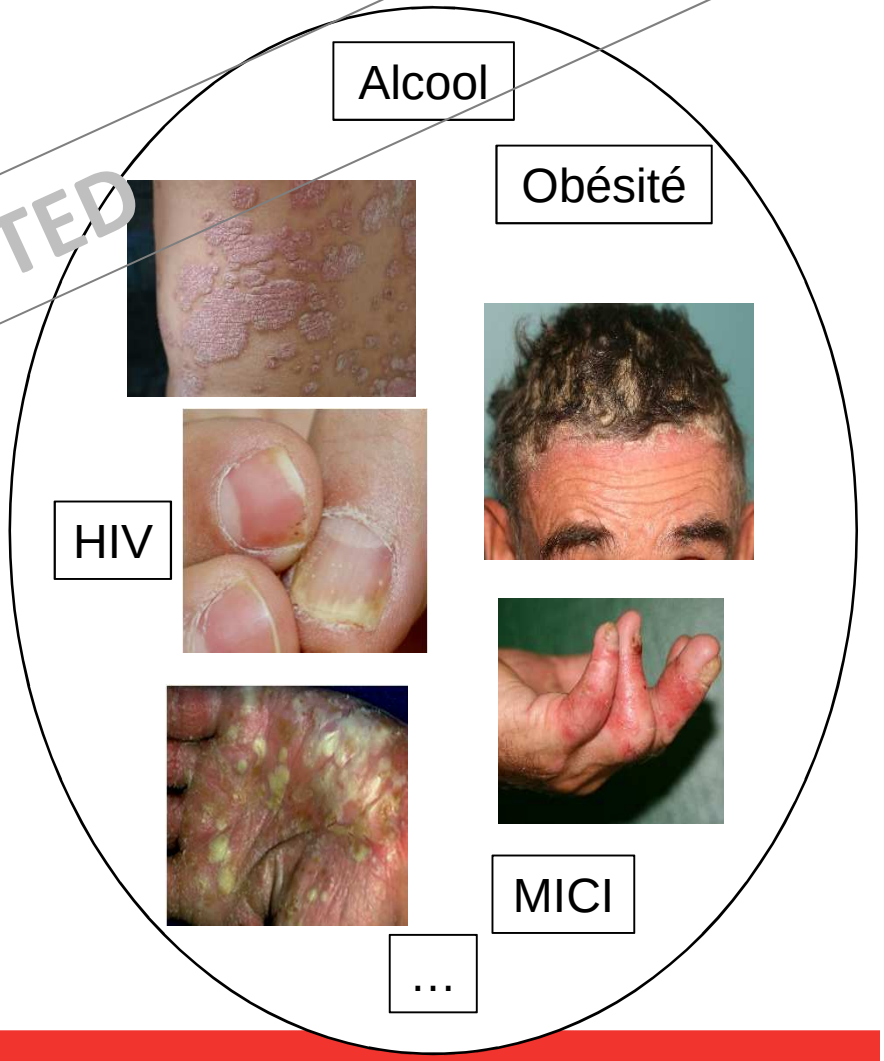
Méthodologie

- Interrogation d'experts (liens avec l'industrie identifiés) si absence de preuve dans la littérature et absence de consensus dans le groupe de travail

- Relecture par large panel de médecins impliqués dans le traitement du psoriasis : 32 réponses sur 36 sollicitations dont Association de patients (2)

Objectifs et champs des recommandations

- Traitement du psoriasis modéré à sévère de l'adulte
  - Non compliqué
  - Associé à des comorbidités
  - Formes particulières de psoriasis



Professionnels concernés

- Dermatologues libéraux et hospitaliers
- Rhumatologues
- Professionnels de santé prenant en charge des patients psoriasiques
  - Médecins généralistes
  - Infirmières
  - Autres spécialistes….
- Associations de patients concernés par le psoriasis

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LES RECOMMANDATIONS EN PRATIQUE

Axel Villani, Marie Tauber, Florent Amatore, Bernard Guillot, Manuelle Viguier

Lyon, Toulouse, Marseille, Montpellier, Reims

Quand initier un traitement systémique?

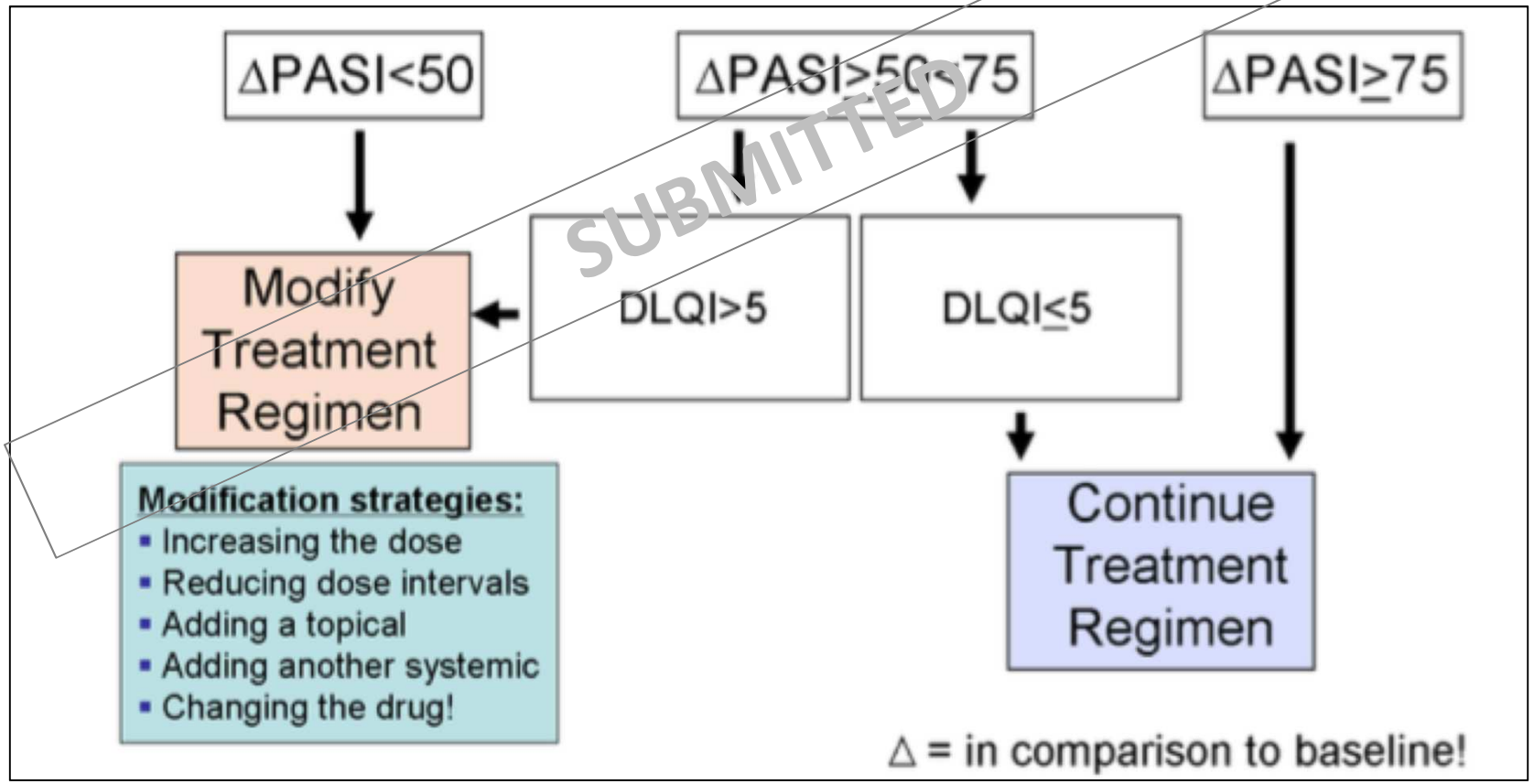
- Psoriasis modéré à sévère
  - ✓ SCA > 10%
  - ✓ PASI > 10
  - ✓ DLQI > 10
- Ou retentissement physique, psychologique ou social jugé significatif
- Ou psoriasis localisé mais non contrôlé par un traitement topique bien conduit et responsable d'un handicap fonctionnel, psychologique ou social jugé significatif
  - ✓ Penser aux sites spécifiques
  - ✓ Ongles, paumes et plantes, plis, organes génitaux, visage et cuir chevelu

Objectifs thérapeutiques (1)

- **Mettre le patient au cœur de la prise en charge :**
- **Sévérité** de la maladie
- **Retentissement** sur le bien-être physique, psychique et social du patient
- Existence de **comorbidités** et/ou d'un rhumatisme associé
- **Rapport bénéfice/risque** en faveur ou non de la poursuite du traitement
- **Point de vue du patient** (son degré de satisfaction)

Objectifs thérapeutiques (2)

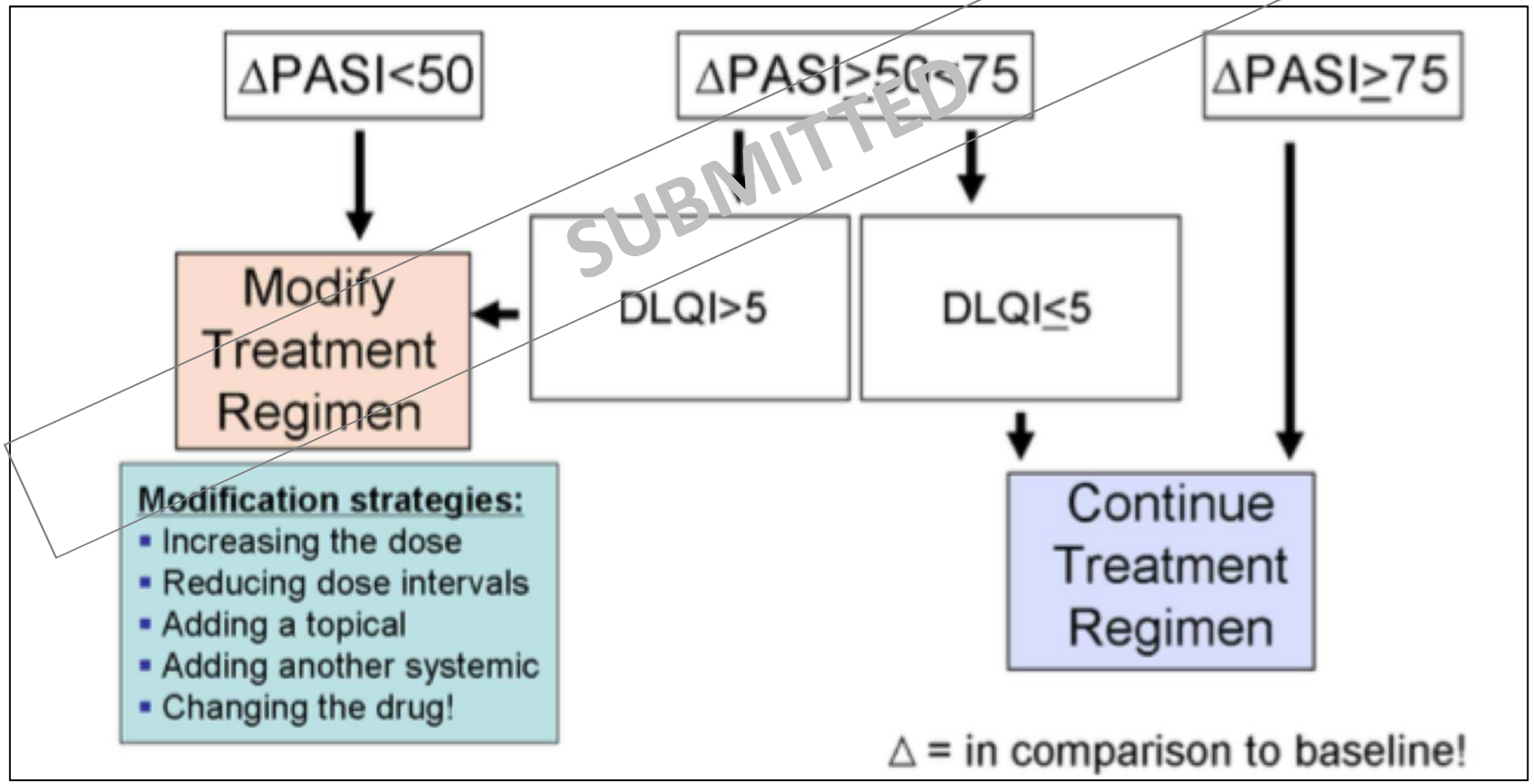
Algorithme adopté en 2011



Mrowietz et al. 2011

Objectifs thérapeutiques (2)

Algorithme **rejeté** par le groupe de travail et le groupe d'experts



Mrowietz et al. 2011

Objectifs thérapeutiques (2)

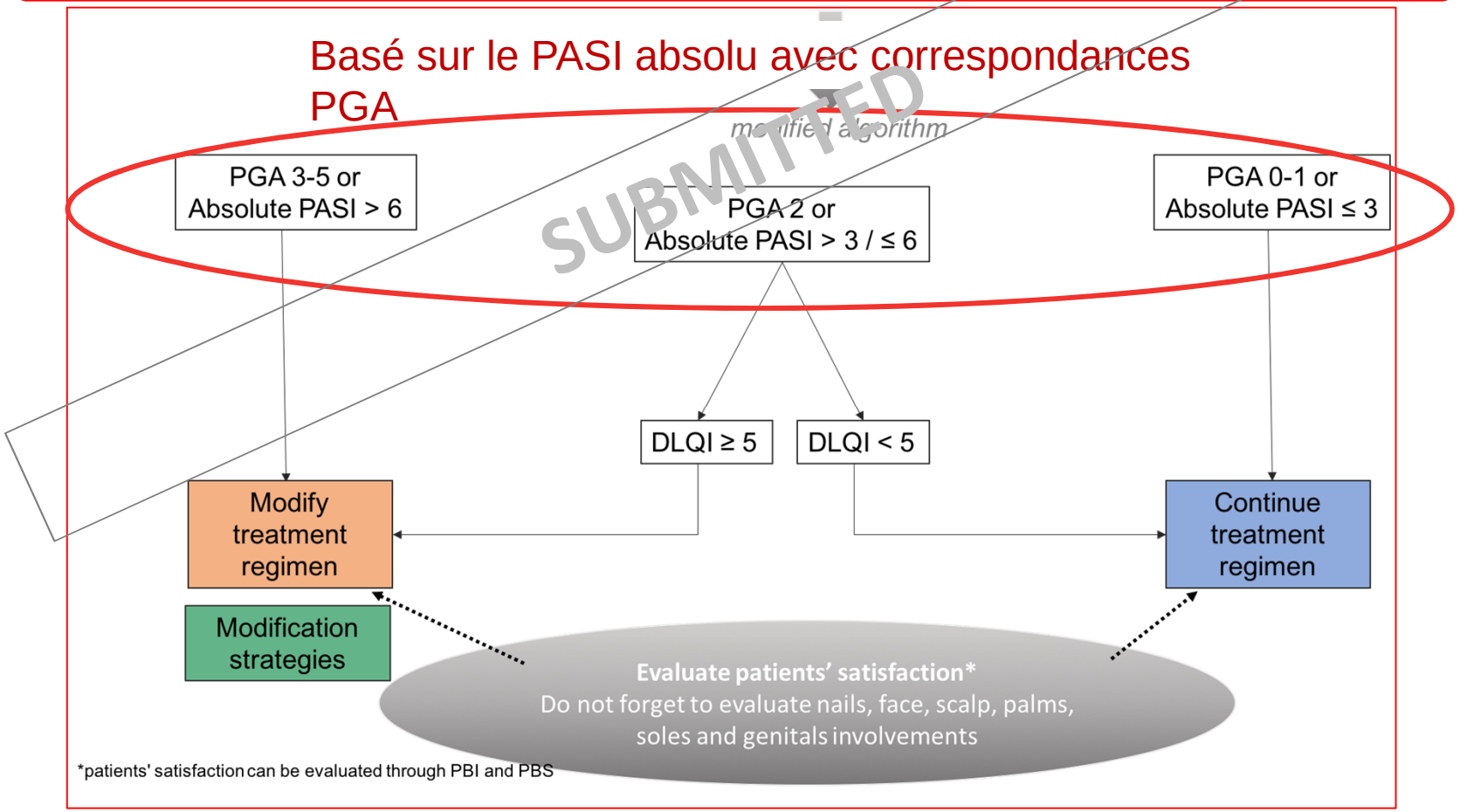
2 algorithmes finalement retenus sur les 4 proposés

- Propositions faites en raison de l'efficacité grandissante des nouvelles biothérapies
  - ✓Objectifs plus « ambitieux »
- Sur la base de critères discutés dans la littérature
  - ✓PASI absolu ≤ 3
  - ✓PASI 90
- Seuil de 5 pour le DLQI conservé

Objectifs thérapeutiques (2)

Premier algorithme retenu

Basé sur le PASI absolu avec correspondances PGA



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Premier algorithme retenu

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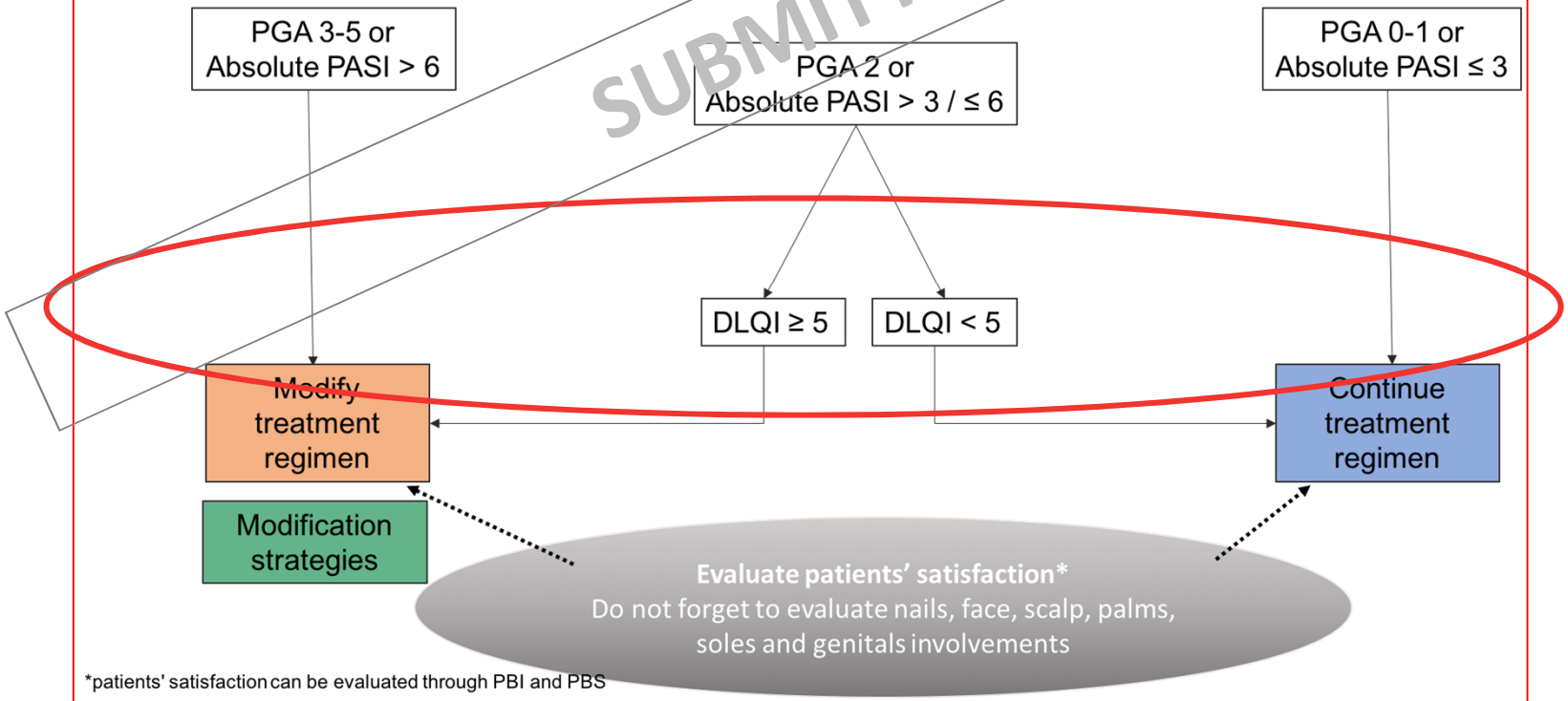
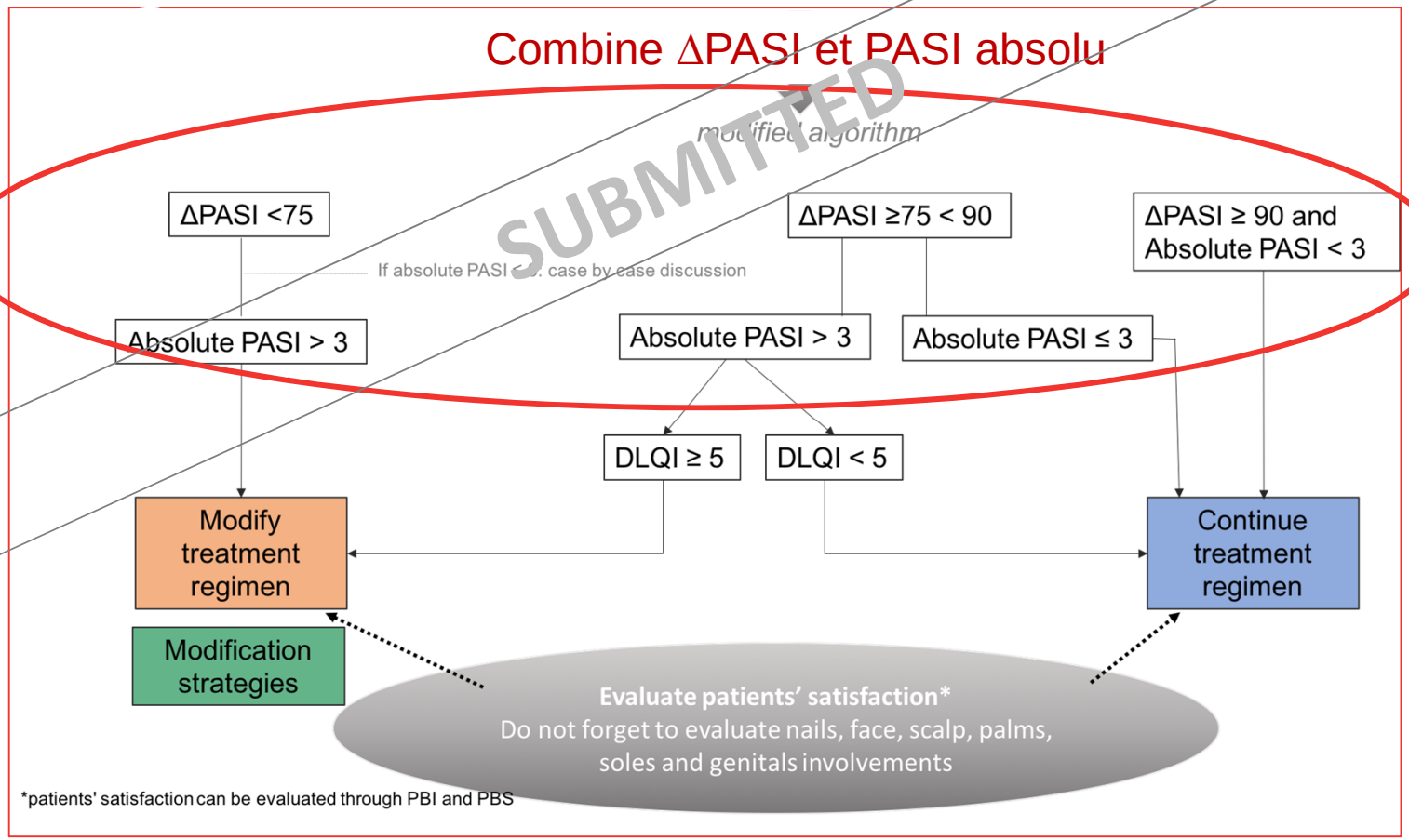


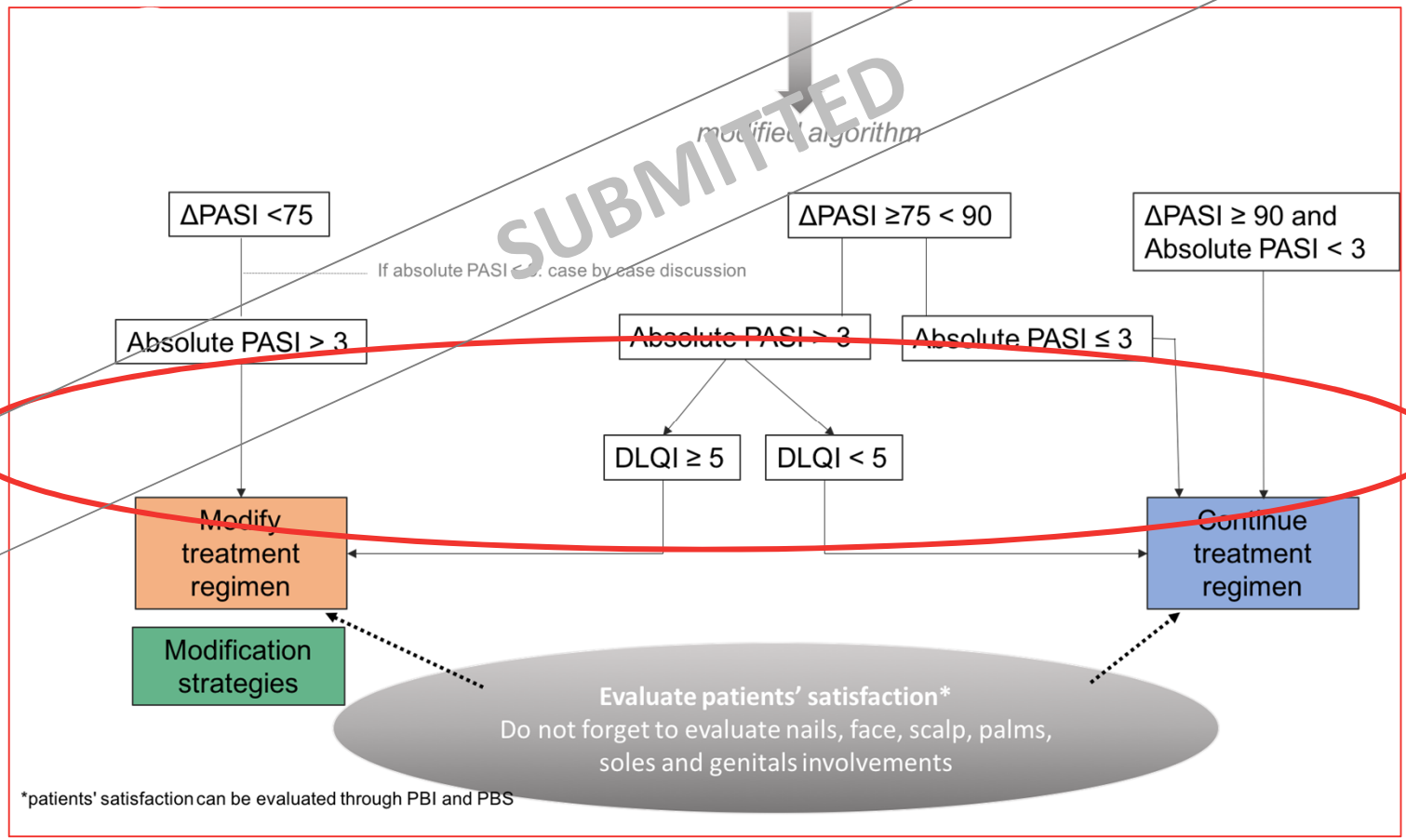
Objectifs thérapeutiques (2)

Deuxième algorithme retenu



Objectifs thérapeutiques (2)

Deuxième algorithme retenu



Quand évaluer la réponse thérapeutique?

- Pour la **réponse primaire**, après initiation de la molécule :
  - **Délai précisé pour chaque molécule** → fiche médicament
- Réévaluation régulière **en cours de traitement**
  - Idéalement **2 fois par an** (avis d'experts)

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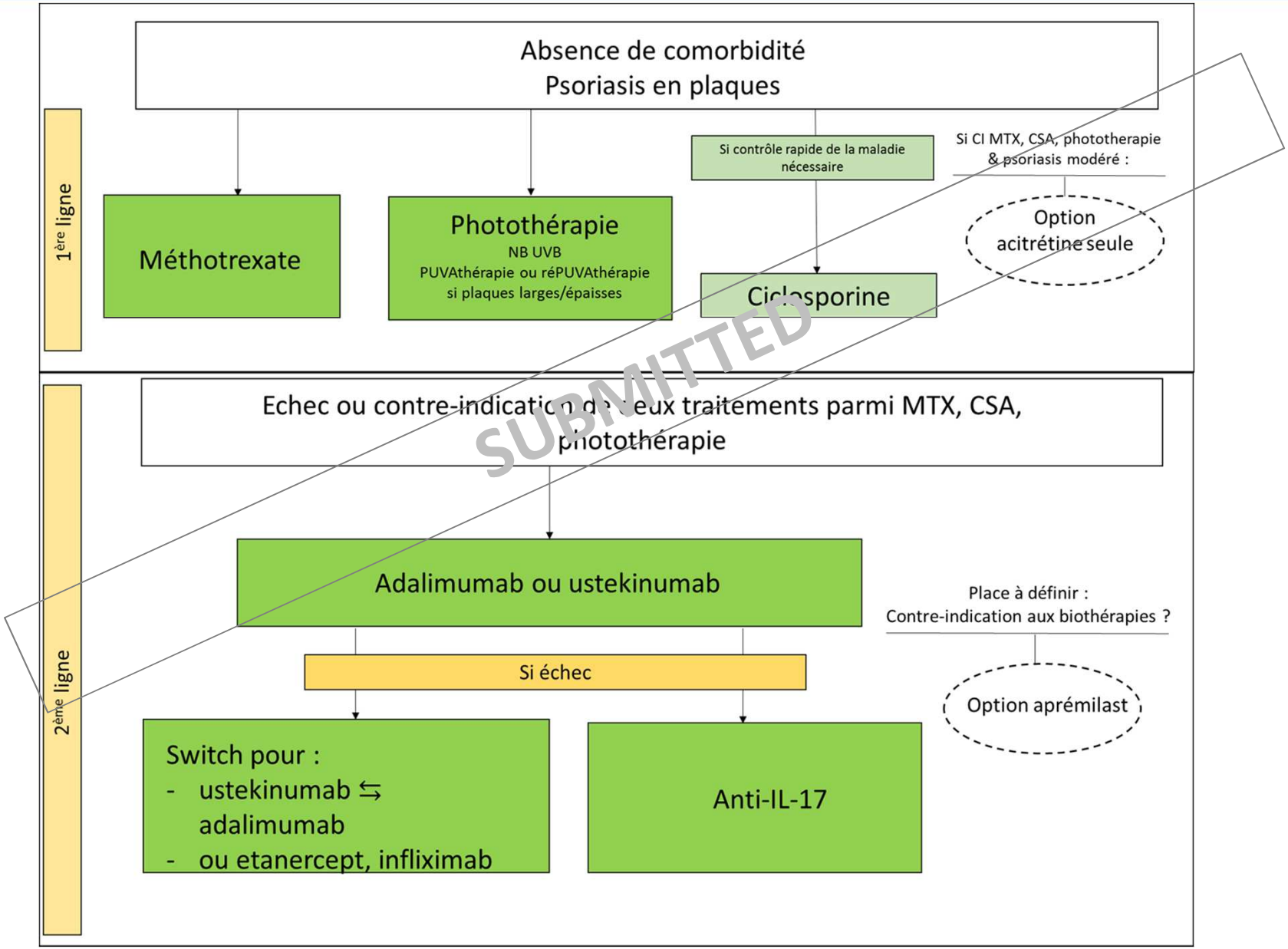
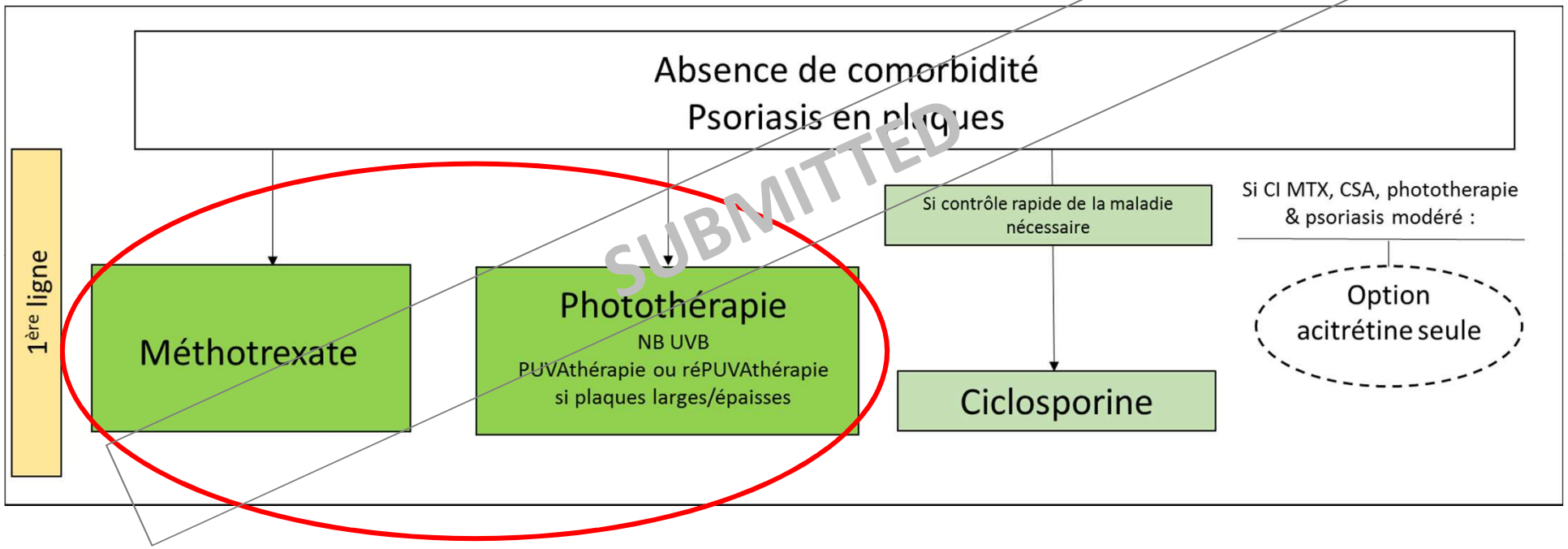
PRISE EN CHARGE DU PSORIASIS EN PLAQUES CHEZ LE PATIENT SANS COMORBIDITES

Florent Amatore, Marie Tauber, Axel Villani, Bernard Guillot, Manuelle Viguier

Marseille, Toulouse, Lyon, Montpellier, Reims

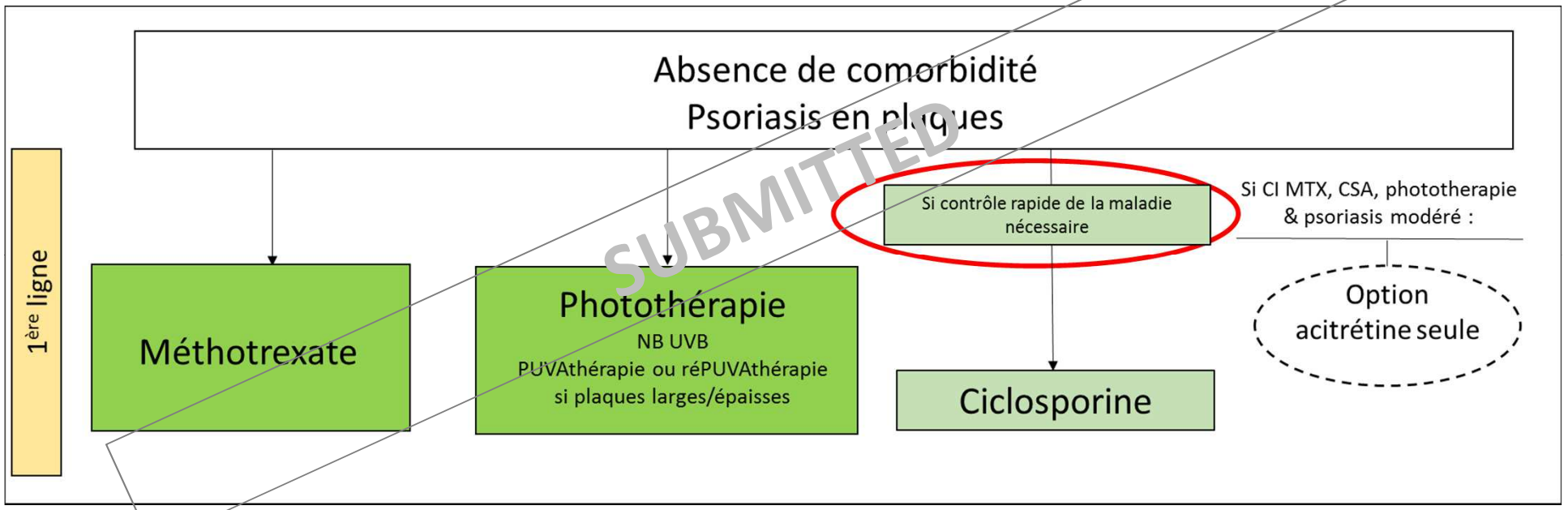

Absence de comorbidité
Psoriasis en plaques
1ère ligne
Méthotrexate
Photothérapie
NB UVB
PUVAthérapie ou réPUVAthérapie
si plaques larges/épaisses
Si contrôle rapide de la maladie nécessaire
Ciclosporine
Si CI MTX, CSA, photothérapie & psoriasis modéré :
Option acitrétine seule
Echec ou contre-indication de deux traitements parmi MTX, CSA, photothérapie
2ème ligne
Adalimumab ou ustekinumab
Si échec
Switch pour :
- ustekinumab ⇆ adalimumab
- ou etanercept, infliximab
Anti-IL-17
Place à définir :
Contre-indication aux biothérapies ?
Option aprémilast

PSORIASIS EN PLAQUES, PATIENT SANS COMORBIDITES :



En fonction de la préférence du patient, du médecin, de l'accès aux cabines…

PSORIASIS EN PLAQUES, PATIENT SANS COMORBIDITES :



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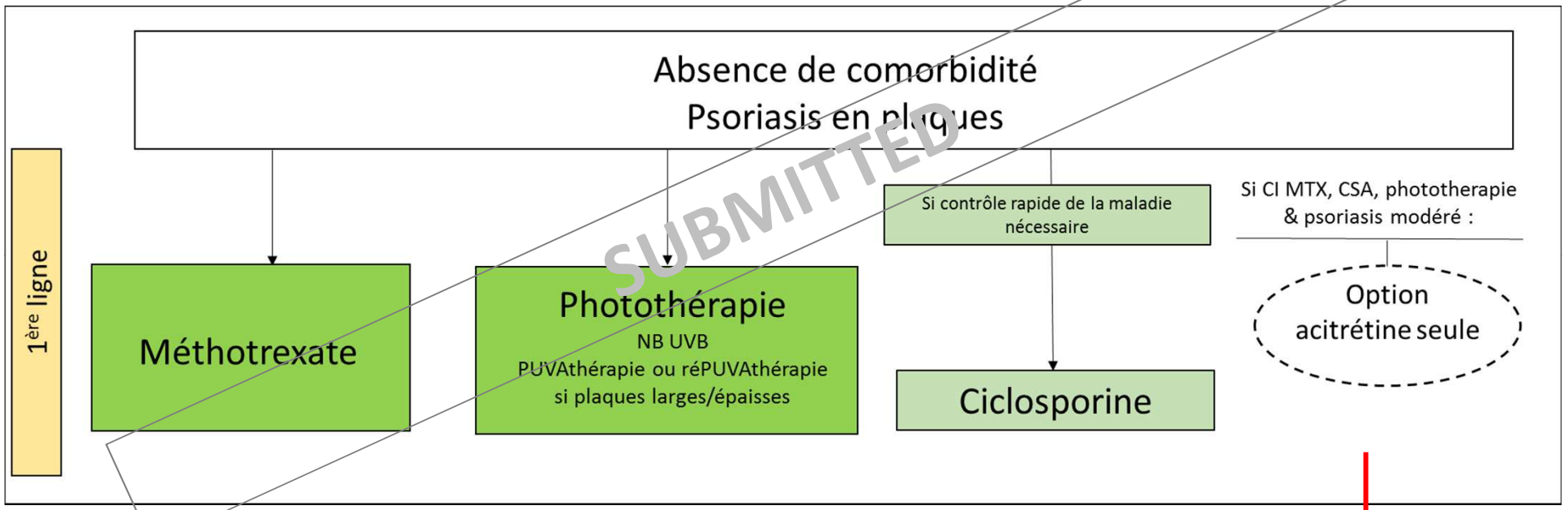
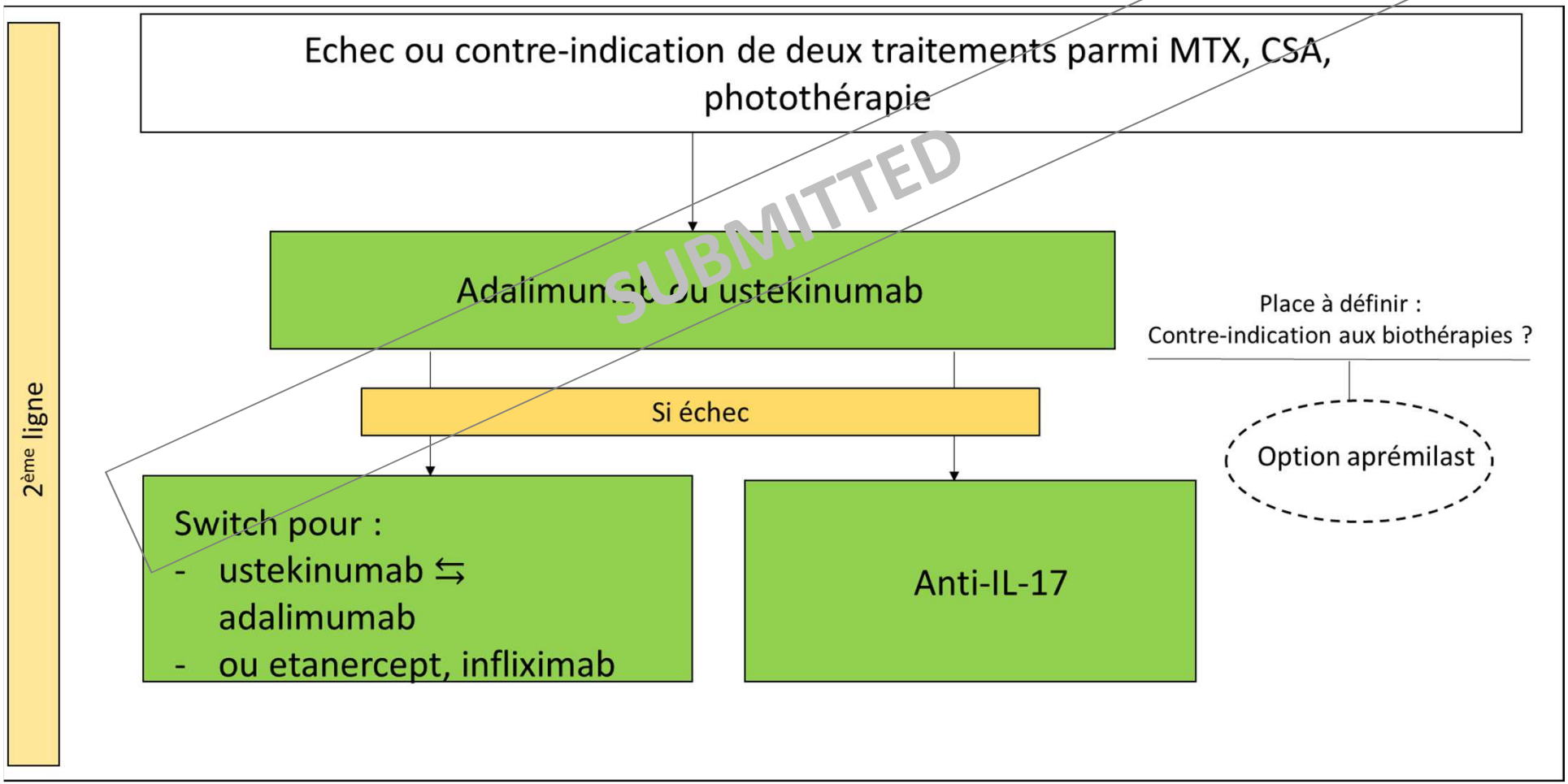


Sa place est limitée en première intention dans ce contexte

PSORIASIS EN PLAQUE, PATIENT SANS COMORBIDITES :



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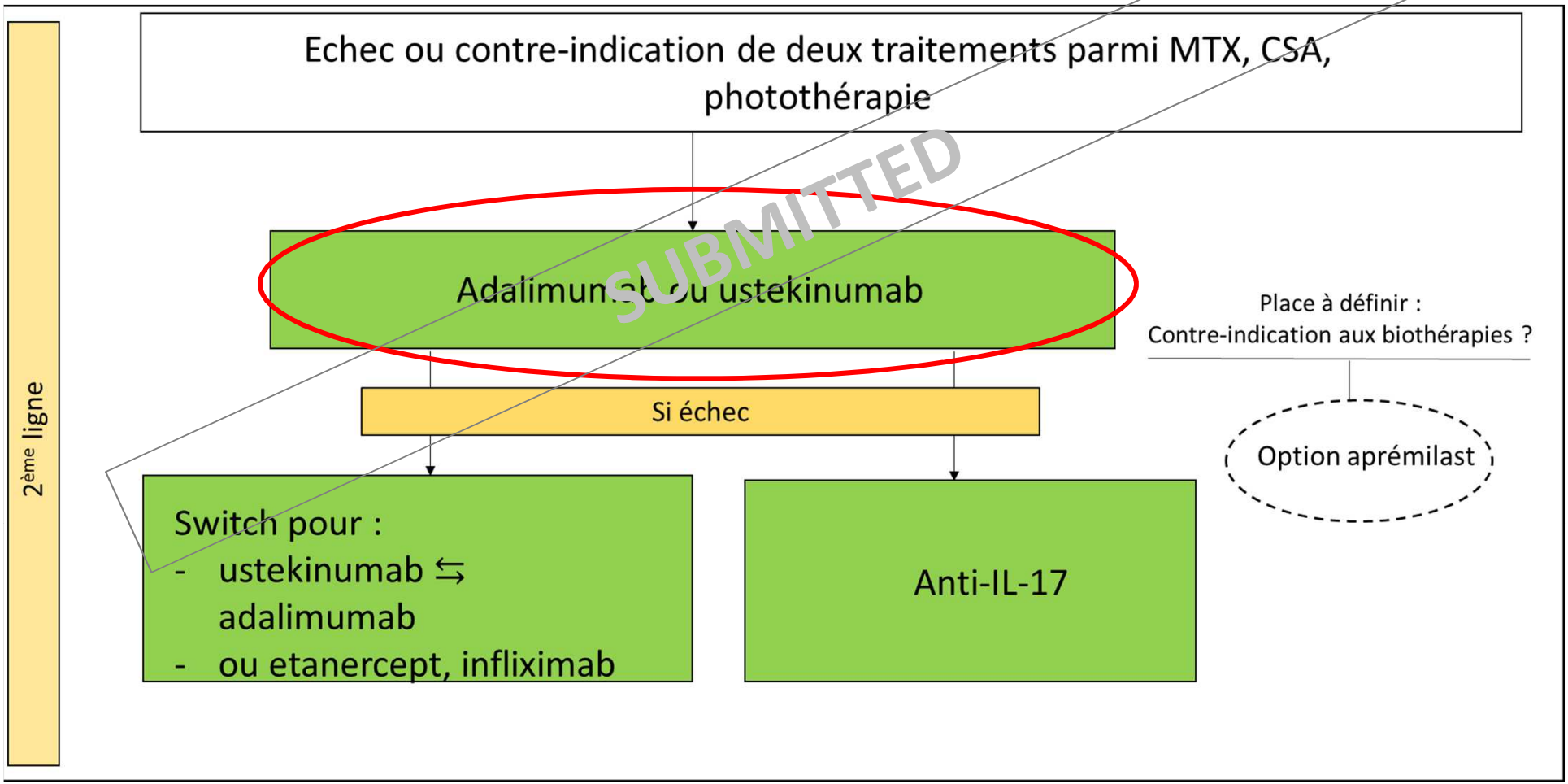

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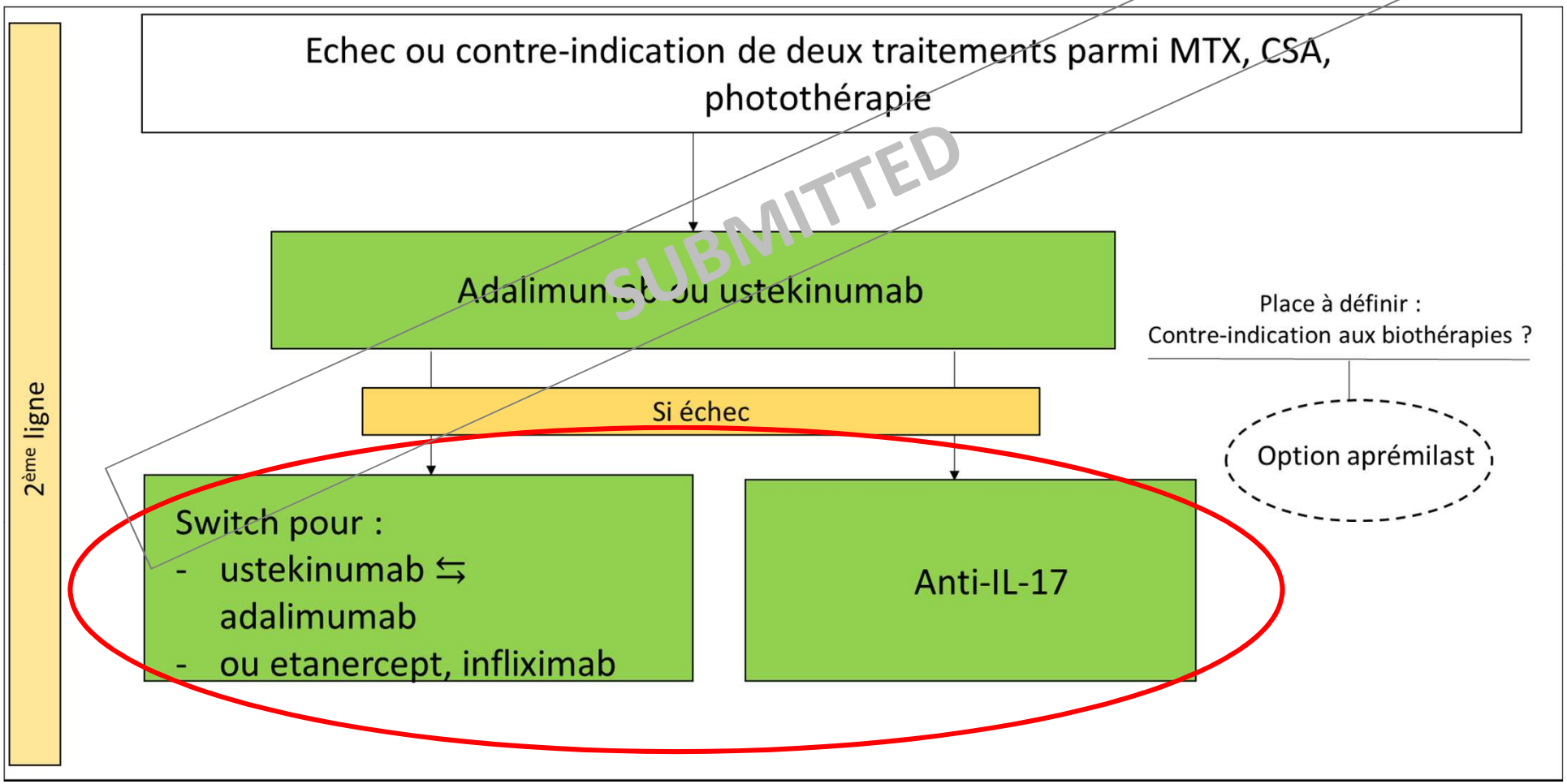

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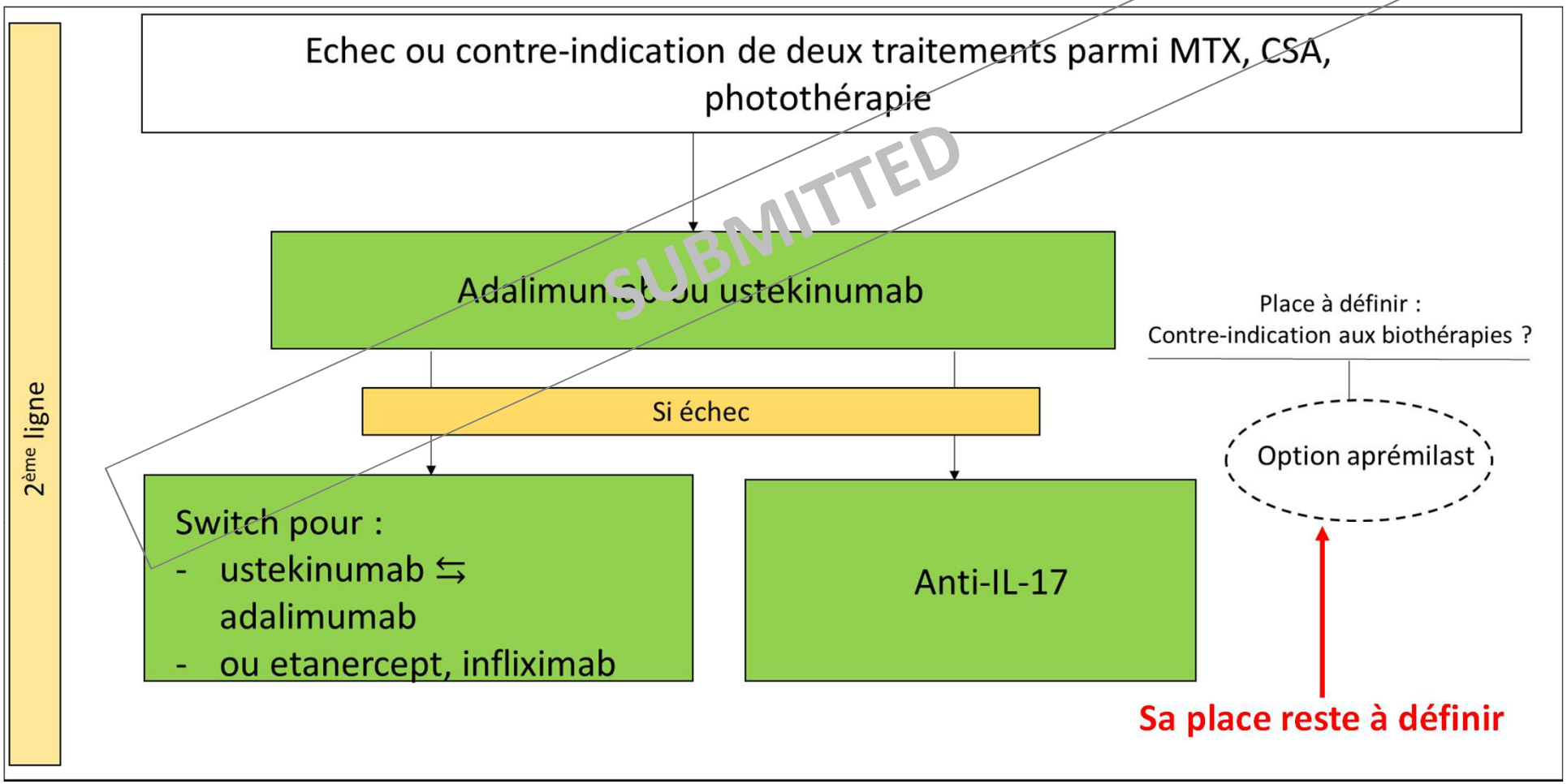

METHOTREXATE (MTX)	
Dosing scheme	Starting dose: in general, 7.5 - 15 mg/wk by oral or SC delivery (**Grade B**). One RCT suggests a starting dose of 17.5mg/wk SC with dose escalation to 22.5mg/wk after 8 weeks if patient has not achieved PASI50 (**Grade A**). No "low test dose" is mandatory (**Grade C**). No weight-based adaptation. Subcutaneous administration might reduce gastrointestinal AEs in patients treated orally (**Grade C**) but has not demonstrated superiority compared to the oral route. Maintenance dosage: 5 – 25 mg/week depending on efficacy and tolerability (**Grade B**). Use the lowest therapeutic dose. Folate supplementation: 5 mg/week of folic acid taken 24 hours after administration of MTX (**Grade B**). Interrupting treatment after a given cumulative dose is not recommended if MTX is well-tolerated and the follow-up required is completed **(Expert opinion)**.
Half-life	2 to 7 hours.
Efficacy (Monotherapy)	Onset of clinical effect: 4-8 weeks. Efficacy assessment: W12-16. Short-term efficacy (W16): PASI 75: 45% (W12-16) / PASI 90: 18% / DLQI: 9-point reduction. ACR20 (W12): 41%. Long-term efficacy (W52): PASI 75: 73%. Median drug survival: 30.1%, and 15.1% after 3 and 5 years.
Optional combination therapy	**Grade A** with etanercept, **Grade B** with NBUVB, **Grade B** with infliximab, **Grade C** with adalimumab.
Main adverse effects	Nausea, vomiting, moderate hair loss, fatigue, transaminase increase, bone marrow suppression, gastro-intestinal and mucosal ulcerations, infections, liver fibrosis, interstitial pneumonia.
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Surgery	No systematic interruption of MTX prior to minor surgery (**Grade B**). Discuss interruption of MTX (30 hours) prior to major surgery in patients with history of healing disorder or wound infections (**Grade C**).
Cost in France (2017)	For 20mg/week: between 84€ (oral form) and 1080€ (SC form) yearly.

FICHES MEDICAMENTS

Pour chaque fiche : 10 sous-chapitres pratiques

- Schéma(s) thérapeutique(s)
- Demi-vie
- Données d'efficacité
- Association thérapeutique possible
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Vaccination	French immunization schedule. Primary vaccination and/or boostering for HBV / Annual Influenza / Pneumococcal vaccination. Live-attenuated vaccines are contraindicated during treatment.
Surgery	No systematic interruption of MTX prior to minor surgery (**Grade B**). Discuss interruption of MTX (30 hours) prior to major surgery in patients with history of healing disorder or wound infections (**Grade C**).
Cost in France (2017)	For 20mg/week: between 84€ (oral form) and 1080€ (SC form) yearly.

FICHES MEDICAMENTS

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- Demi-vie
- Données d'efficacité
- Association thérapeutique possible
- Principaux effets secondaires
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METHOTREXATE (MTX)	
Dosing scheme	Starting dose: in general, 7.5 - 15 mg/wk by oral or SC delivery (**Grade B**). One RCT suggests a starting dose of 17.5mg/wk SC with dose escalation to 22.5mg/wk after 8 weeks if patient has not achieved PASI50 (**Grade A**). No "low test dose" is mandatory (**Grade C**). No weight-based adaptation. Subcutaneous administration might reduce gastrointestinal AEs in patients treated orally (**Grade C**) but has not demonstrated superiority compared to the oral route. Maintenance dosage: 5 – 25 mg/week depending on efficacy and tolerability (**Grade B**). Use the lowest therapeutic dose. Folate supplementation: 5 mg/week of folic acid taken 24 hours after administration of MTX (**Grade B**). Interrupting treatment after a given cumulative dose is not recommended if MTX is well-tolerated and the follow-up required is completed **(Expert opinion)**.
Half-life	2 to 7 hours.
Efficacy (Monotherapy)	Onset of clinical effect: 4-8 weeks. Efficacy assessment: W12-16. Short-term efficacy (W16): PASI 75: 45% (W12-16) / PASI 90: 18% / DLQI: 9-point reduction. ACR20 (W12): 41%. Long-term efficacy (W52): PASI 75: 73%. Median drug survival: 30.1%, and 15.1% after 3 and 5 years.
Optional combination therapy	**Grade A** with etanercept, **Grade B** with NBUVB, **Grade B** with infliximab, **Grade C** with adalimumab.
Main adverse effects	Nausea, vomiting, moderate hair loss, fatigue, transaminase increase, bone marrow suppression, gastro-intestinal and mucosal ulcerations, infections, liver fibrosis, interstitial pneumonia.
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BILAN PRE-THERAPEUTIQUE SURVEILLANCE

- 2 tableaux pour l'ensemble des molécules
- Regroupant :
  - ✓**Informations** à donner au patient avant et pendant le traitement
  - ✓Eléments **cliniques** à vérifier
  - ✓Bilan **paraclinique** recommandé

CLINIQUE

FIRST STEP SYSTEMIC TREATMENT				
	Phototherapy	**MTX**	**CSA**	**Acitretin**
Information to the patient	Long-term risk of skin cancer, synergistic effects of additional UV exposure during leisure time or self-treatment. Make sure that the patient wears goggles and protections of chronic sun exposed areas (face, neck) and genital regions during the session.	Adequate contraception for men and women. After the end of treatment, contraception for only 1 day is recommended in women (contraception should be continued until the end of treatment and conception is possible as soon as contraception is stopped) and 6 months in men. Inform the patient on how to take the drug (once a week), and about early symptoms of AE.	CSA is permitted during pregnancy, but may increase the probability of pregnancy-related complications. A reliable contraception is advised (note that efficacy of progesterone-containing contraceptives can be reduced). Avoidance of excessive sun exposure. Follow national cancer screening recommendations (breast, cervix, colon)	**Teratogenic risk and necessity of long-term effective contraception (at least 3 years after discontinuation).** Give a written information. Alcohol avoidance. Blood donation is forbidden during treatment and up to one year after. Start treatment on second or third day of the menstrual cycle, after satisfactory contraception for at least one month prior to treatment.
Clinical examination <u>before treatment</u>	Objective assessment of the disease (PASI/PGA/BSA/arthritis/DLQI)			
	- Preneoplastic skin lesions and malignant skin lesions - Dysplastic nevi. - Concomitant medication (phototoxic and immunosuppressive drugs).	- Past or active infection - Signs of liver cirrhosis and respiratory failure - Concomitant medication - Vaccination status	- Medical history of arterial hypertension, malignancies, renal and liver diseases - Past or active infection - Malignancies - Blood pressure measurement on two separate occasions - Concomitant medication - Vaccination status	- Concomitant medication - Signs of liver cirrhosis and metabolic syndrome
Clinical examination <u>during treatment</u>	Objective assessment of the disease (PASI/PGA/BSA/arthritis/DLQI) and evaluation of patient's satisfaction			
	- Control erythema before dosage increase and record UV dose. - Record the cumulative UV dosage and the number of sessions. - Lifelong screening of skin cancer is mandatory.	- AE : fatigue, nausea, vomiting, gastro-intestinal and mucosal ulcerations, signs of liver cirrhosis and respiratory failure, persistent cough	- AE : signs of renal impairment, nausea, diarrhea, hypertrichosis, gingival hyperplasia, paresthesia - Blood pressure measurement - Skin cancer screening - Regular gynecologic screening for papillomavirus infection	- AE : hypervitaminosis A (cheilitis, xerosis), headache, conjunctivitis (beware of contact lenses)

CLINIQUE

FIRST STEP SYSTEMIC TREATMENT				
	Phototherapy	**MTX**	**CSA**	**Acitretin**
Information to the patient	Long-term risk of skin cancer, synergistic effects of additional UV exposure during leisure time or self-treatment. Make sure that the patient wears goggles and protections of chronic sun exposed areas (face, neck) and genital regions during the session.	Adequate contraception for men and women. After the end of treatment, contraception for only 1 day is recommended in women (contraception should be continued until the end of treatment and conception is possible as soon as contraception is stopped) and 3 months in men. Inform the patient on how to take the drug (once a week), and about early symptoms of AE.	CSA is permitted during pregnancy, but may increase the probability of pregnancy-related complications. A reliable contraception is advised (note that efficacy of progesterone-containing contraceptives can be reduced). Avoidance of excessive sun exposure. Follow national cancer screening recommendations (breast, cervix, colon)	**Teratogenic risk and necessity of long-term effective contraception (at least 3 years after discontinuation).** Give a written information. Alcohol avoidance. Blood donation is forbidden during treatment and up to one year after. Start treatment on second or third day of the menstrual cycle, after satisfactory contraception for at least one month prior to treatment.
Clinical examination <u>before treatment</u>	Objective assessment of the disease (PASI/PGA/BSA/arthritis/DLQI)			
	- Preneoplastic skin lesions and malignant skin lesions - Dysplastic nevi. - Concomitant medication (phototoxic and immunosuppressive drugs).	- Past or active infection - Signs of liver cirrhosis and respiratory failure - Concomitant medication - Vaccination status	- Medical history of arterial hypertension, malignancies, renal and liver diseases - Past or active infection - Malignancies - Blood pressure measurement on two separate occasions - Concomitant medication - Vaccination status	- Concomitant medication - Signs of liver cirrhosis and metabolic syndrome
Clinical examination <u>during treatment</u>	Objective assessment of the disease (PASI/PGA/BSA/arthritis/DLQI) and evaluation of patient's satisfaction			
	- Control erythema before dosage increase and record UV dose. - Record the cumulative UV dosage and the number of sessions. - Lifelong screening of skin cancer is mandatory.	- AE : fatigue, nausea, vomiting, gastro-intestinal and mucosal ulcerations, signs of liver cirrhosis and respiratory failure, persistent cough	- AE : signs of renal impairment, nausea, diarrhea, hypertrichosis, gingival hyperplasia, paresthesia - Blood pressure measurement - Skin cancer screening - Regular gynecologic screening for papillomavirus infection	- AE : hypervitaminosis A (cheilitis, xerosis), headache, conjunctivitis (beware of contact lenses)

CLINIQUE

FIRST STEP SYSTEMIC TREATMENT				
	Phototherapy	**MTX**	**CSA**	**Acitretin**
Information to the patient	Long-term risk of skin cancer, synergistic effects of additional UV exposure during leisure time or self-treatment. Make sure that the patient wears goggles and protections of chronic sun exposed areas (face, neck) and genital regions during the session.	Adequate contraception for men and women. After the end of treatment, contraception for only 1 day is recommended in women (contraception should be continued until the end of treatment and conception is possible as soon as contraception is stopped) and 3 months in men. Inform the patient on how to take the drug (once a week), and about early symptoms of AE.	CSA is permitted during pregnancy, but may increase the probability of pregnancy-related complications. A reliable contraception is advised (note that efficacy of progesterone-containing contraceptives can be reduced). Avoidance of excessive sun exposure. Follow national cancer screening recommendations (breast, cervix, colon)	**Teratogenic risk and necessity of long-term effective contraception (at least 3 years after discontinuation).** Give a written information. Alcohol avoidance. Blood donation is forbidden during treatment and up to one year after. Start treatment on second or third day of the menstrual cycle, after satisfactory contraception for at least one month prior to treatment.
Clinical examination <u>before treatment</u>	Objective assessment of the disease (PASI/PGA/BSA/arthritis/DLQI)			
	- Preneoplastic skin lesions and malignant skin lesions - Dysplastic nevi. - Concomitant medication (phototoxic and immunosuppressive drugs).	- Past or active infection - Signs of liver cirrhosis and respiratory failure - Concomitant medication - Vaccination status	- Medical history of arterial hypertension, malignancies, renal and liver diseases - Past or active infection - Malignancies - Blood pressure measurement on two separate occasions - Concomitant medication - Vaccination status	- Concomitant medication - Signs of liver cirrhosis and metabolic syndrome
Clinical examination <u>during treatment</u>	Objective assessment of the disease (PASI/PGA/BSA/arthritis/DLQI) and evaluation of patient's satisfaction			
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CLINIQUE

FIRST STEP SYSTEMIC TREATMENT				
	Phototherapy	**MTX**	**CSA**	**Acitretin**
Information to the patient	Long-term risk of skin cancer, synergistic effects of additional UV exposure during leisure time or self-treatment. Make sure that the patient wears goggles and protections of chronic sun exposed areas (face, neck) and genital regions during the session.	Adequate contraception for men and women. After the end of treatment, contraception for only 1 day is recommended in women (contraception should be continued until the end of treatment and conception is possible as soon as contraception is stopped) and 3 months in men. Inform the patient on how to take the drug (once a week), and about early symptoms of AE.	CSA is permitted during pregnancy, but may increase the probability of pregnancy-related complications. A reliable contraception is advised (note that efficacy of progesterone-containing contraceptives can be reduced). Avoidance of excessive sun exposure. Follow national cancer screening recommendations (breast, cervix, colon)	**Teratogenic risk and necessity of long-term effective contraception (at least 3 years after discontinuation).** Give a written information. Alcohol avoidance. Blood donation is forbidden during treatment and up to one year after. Start treatment on second or third day of the menstrual cycle, after satisfactory contraception for at least one month prior to treatment.
Clinical examination <u>before treatment</u>	Objective assessment of the disease (PASI/PGA/BSA/arthritis/DLQI)			
	- Preneoplastic skin lesions and malignant skin lesions - Dysplastic nevi. - Concomitant medication (phototoxic and immunosuppressive drugs).	- Past or active infection - Signs of liver cirrhosis and respiratory failure - Concomitant medication - Vaccination status	- Medical history of arterial hypertension, malignancies, renal and liver diseases - Past or active infection - Malignancies - Blood pressure measurement on two separate occasions - Concomitant medication - Vaccination status	- Concomitant medication - Signs of liver cirrhosis and metabolic syndrome
Clinical examination <u>during treatment</u>	Objective assessment of the disease (PASI/PGA/BSA/arthritis/DLQI) and evaluation of patient's satisfaction			
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CLINIQUE

SECOND STEP SYSTEMIC TREATMENT				
	INFLI/ADA/ETA	**USTK**	**SECUKINUMAB/IXEKIZUMAB**	**APREMILAST**
Information to the patient	- Possible weight gain during treatment - Increased risk of infection - Need of contraception - Follow national cancer screening recommendations (breast, cervix, colon) - Rare cases of hypoglycaemia during treatment in diabetic patients	- Increased risk of infection - Need of contraception - Follow national cancer screening recommendations (breast, cervix, colon)	- Increased risk of infection, notably fungal infection - Need of contraception - Follow national cancer screening recommendations (breast, cervix, colon)	- Risk of diarrhea and nausea after treatment initiation - Increased risk of infection - Risk of depression - Need of contraception
Clinical examination <u>before treatment</u>	Objective assessment of the disease (PASI/PGA/BSA/arthritis/DLQI)			
	- Known chronic heart failure or heart failure symptoms - Adenopathy - Active/latent/exposure to tuberculosis - Active or chronic infection - Cancer - Multiple Sclerosis - Lupus erythematosus - Live vaccine: recent? in the future ?	- Cardiovascular risk factors - Adenopathy - Active/latent/exposure to tuberculosis - Active or chronic infection - Cancer - Live vaccine: recent? in the future ?	- Inflammatory Bowel Disease (personal or familial) - Candidosis - Cardiovascular risk factors - Adenopathy - Active/latent/exposure to tuberculosis - Active or chronic infection - Cancer - Live vaccine: recent? in the future ? - Psychiatric disorders - Suicide attempt	- Chronic infection - Adenopathy - Psychiatric disorder - Suicide attempt - Cancer
Clinical examination <u>during treatment</u>	Objective assessment of the disease (PASI/PGA/BSA/arthritis/DLQI) and evaluation of patient's satisfaction			
	- Weight gain - Site injection reactions - Infection - Cancer (particularly non-melanoma skin cancer)	- Cardiovascular risk factors and events (MACEs) - Site injection reactions - Infection - Cancer (particularly non-melanoma skin cancer)	- Cardiovascular risk factors and events (MACEs) - Site injection reactions - Infection (candidosis) - Diarrhea, weight loss - Psychiatric disorders - Suicide attempt - Cancer	- Diarrhea - Weight loss - Psychiatric disorder/depression - Suicide attempt - Infection - Cancer

PARACLINIQUE

	MTX	CSA	Acitretin	INFLI	ADA	ETA	USTK	SECU	IXE	APR
Blood count	X W1, W2, W4, *then every 2-3 months*	X W4		X			X	X		X
ASAT, ALAT, GGT, bilirubin	X W2, W4, *then every 2-3 months*	X W4, W12	X W4, W8, *then every 3 months*	X Only for INFLI: *before every infusion*			X	X		X
Creatinin	X W4, *then every 2-3 months*	X W2, W4, *then every month*	X	X			X	X		X
Electrolytes, Magnesium		X								
CRP				X			X	X		X
Fasting blood glucose (if elevated, add HbA1c dosage)		X *Then every 3 months*	X	X			X	X		
Albumin	X									
Plasma proteins electrophoresis				X						
Cholesterol, triglycerides		X W4, W12	X W4, *then every 3 months*							
Pregnancy test	X	X	X *Every month during treatment and after 1 and 2 months since discontinuation. Avoid pregnancy during 3 years*	X			X	X		X
HBV/HCV	X	X		X			X	X		X
HIV	X	X		X			X	X		X
TST or IGRA				X			X	X		
PIIIP or Fibroscan®	*Every 6-12 months for PIIIP or 1-2 years for Fibroscan®. Fibroscan® should be performed in pre-treatment in obese patients.*									
Chest X-Ray	X			X			X	X		
Liver ultrasound	X									

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PRISE EN CHARGE DU PSORIASIS AVEC SITUATIONS OU FORMES CLINIQUES PARTICULIERES

Florent Amatore, Marie Tauber, Axel Villani, Bernard Guillot, Manuelle Viguier

Marseille, Toulouse, Lyon, Montpellier, Reims

ALGORITHME DU CHOIX THERAPEUTIQUE EN CAS DE SITUATIONS PARTICULIERES

16 SITUATIONS PARTICULIERES / COMORBIDITES

PREFER > **CONSIDER** > **AVOID** > **ABSOLUTE CONTRAINDICATION**

OU

NO AVAILABLE DATA

DECISION A PRENDRE EN COLLABORATION
AVEC LE SPECIALISTE D'ORGANE CONCERNE

ALGORITHME DU CHOIX THERAPEUTIQUE EN CAS DE SITUATIONS PARTICULIERES

SPECIAL SITUATIONS		
A to Z	First step systemic treatments Phototherapy, MTX, CSA, acitretin	Second step systemic treatments TNFi (ETA, ADA or INFLI) , USTK, anti-IL17 (IXE or SECU), apremilast

PREFER > CONSIDER > AVOID > ABSOLUTE CONTRAINDICATION

OU

NO AVAILABLE DATA

ALGORITHME DU CHOIX THERAPEUTIQUE EN CAS DE SITUATIONS PARTICULIERES

SPECIAL SITUATIONS		
A to Z	First step systemic treatments Phototherapy, MTX, CSA, acitretin	Second step systemic treatments TNFi (ETA, ADA or INFLI) , USTK, anti-IL17 (IXE or SECU), apremilast
k) Major cardiovascular risk	Involve a consultant cardiologist • Prefer MTX (Grade B) • Consider phototherapy or acitretin (Expert opinion) • *Avoid* CSA because of increased blood pressure (**Grade A**)	• Prefer TNFi (grade A) • Consider USTK (**Grade A**) or anti-IL17 (**Grade B**) in case of TNFi failure and control of risk factors • No data are available for apremilast

PREFER > CONSIDER > AVOID > ABSOLUTE CONTRAINDICATION

OU

NO AVAILABLE DATA

ALGORITHME DU CHOIX THERAPEUTIQUE EN CAS DE SITUATIONS PARTICULIERES

SPECIAL SITUATIONS		
A to Z	First step systemic treatments Phototherapy, MTX, CSA, acitretin	Second step systemic treatments TNFi (ETA, ADA or INFLI) , USTK, anti-IL17 (IXE or SECU), apremilast
h) HIV infection	Involve relevant specialist. Optimize effective antiretroviral treatment (**Grade C**). Close monitoring of bacterial and mycobacterial infections. • Prefer NBUVB (**Grade C**) rather than PUVA • Consider acitretin or MTX (**Grade C**) • Consider CSA only if NBUVB, acitretin or MTX are contraindicated (**Grade C**)	• Consider ETA (before ADA, UST, INFLI) if no alternative and viral load persistently undetectable (**Grade B**) • No sufficient data available for anti-IL17 or apremilast

PREFER > **CONSIDER** > **AVOID** > **ABSOLUTE CONTRAINDICATION**

OU

NO AVAILABLE DATA

ALGORITHME DU CHOIX THERAPEUTIQUE EN CAS DE SITUATIONS PARTICULIERES

SPECIAL SITUATIONS		
A to Z	First step systemic treatments Phototherapy, MTX, CSA, acitretin	Second step systemic treatments TNFi (ETA, ADA or INFLI) , USTK, anti-IL17 (IXE or SECU), apremilast
o) Psychiatric disorders (Depression)	Involve a consultant psychiatrist • Prefer phototherapy or CSA (**Grade B**) • Consider MTX (**Expert opinion**) • No sufficient data available for acitretin	• Prefer TNFi or USTK (**Grade B**) • *Avoid* apremilast (**Grade B**) and anti-IL17 (**Expert opinion**, possible class-effect)

PREFER > **CONSIDER** > **AVOID** > **ABSOLUTE CONTRAINDICATION**

OU

NO AVAILABLE DATA

ALGORITHME DU CHOIX THERAPEUTIQUE EN CAS DE SITUATIONS PARTICULIERES

SPECIAL SITUATIONS		
A to Z	First step systemic treatments Phototherapy, MTX, CSA, acitretin	Second step systemic treatments TNFi (ETA, ADA or INFLI) , USTK, anti-IL17 (IXE or SECU), apremilast
o) Psychiatric disorders (Depression)	Involve a consultant psychiatrist • Prefer phototherapy or CSA (**Grade B**) • Consider MTX (**Expert opinion**) • No sufficient data available for acitretin	• Prefer TNFi or USTK (**Grade B**) • *Avoid* apremilast (**Grade B**) and anti-IL17 (**Expert opinion**, possible class-effect)

Idem pour :

- Alcoolisme chronique
- MICI
- Cirrhose / fibrose hépatique
- Hépatites virales

ALGORITHME DU CHOIX THERAPEUTIQUE EN CAS DE SITUATIONS PARTICULIERES

SPECIAL SITUATIONS		
A to Z	First step systemic treatments Phototherapy, MTX, CSA, acitretin	Second step systemic treatments TNFi (ETA, ADA or INFLI) , USTK, anti-IL17 (IXE or SECU), apremilast
o) Psychiatric disorders (Depression)	Involve a consultant psychiatrist • Prefer phototherapy > CSA (**Grade B**) • Consider MTX (**Expert opinion**) • No sufficient data available for acitretin	• Prefer TNFi or USTK (**Grade B**) • *Avoid* apremilast (**Grade B**) and anti-IL17 (**Expert opinion**, possible class-effect)

Idem pour :

Grossesse

Allaitement

Désir de grossesse

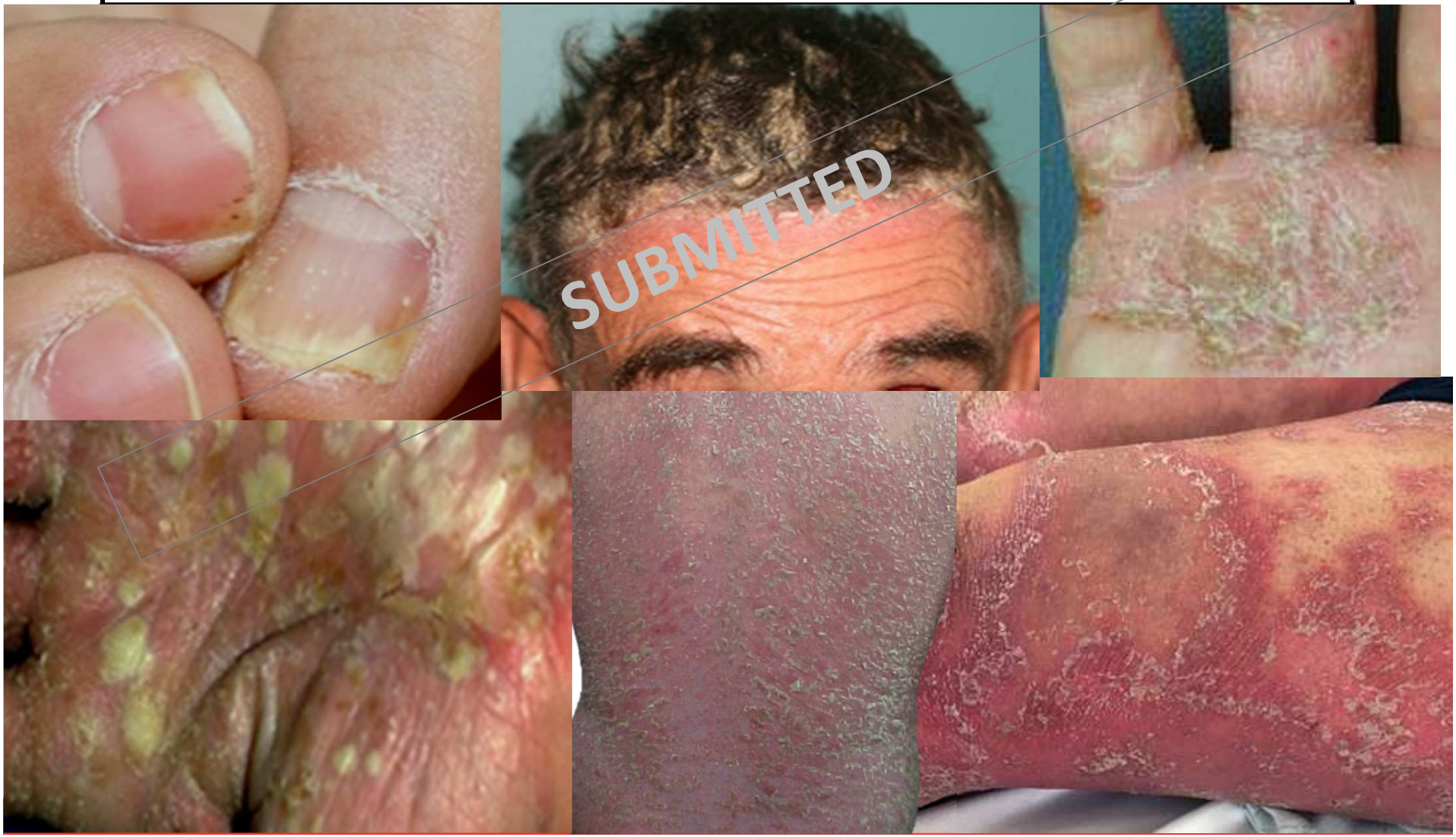
ALGORITHME DU CHOIX THERAPEUTIQUE EN CAS DE SITUATIONS PARTICULIERES

SPECIAL SITUATIONS		
A to Z	First step systemic treatments Phototherapy, MTX, CSA, acitretin	Second step systemic treatments TNFi (ETA, ADA or INFLI) , USTK, anti-IL17 (IXE or SECU), apremilast
o) Psychiatric disorders (Depression)	Involve a consultant psychiatrist • Prefer phototherapy or CSA (**Grade B**) • Consider MTX (**Expert opinion**) • No sufficient data available for acitretin	• Prefer TNFi or USTK (**Grade B**) • *Avoid* apremilast (**Grade B**) and anti-IL17 (**Expert opinion**, possible class-effect)

Idem pour :

- Maladies démyélinisantes
- Insuffisance cardiaque
- Obésité
- Diabète
- Insuffisance rénale

ALGORITHME DU CHOIX THERAPEUTIQUE EN FONCTION DE LA FORME CLINIQUE



ALGORITHME DU CHOIX THERAPEUTIQUE EN FONCTION DE LA FORME CLINIQUE

c) Generalized pustular Psoriasis	• Prefer CSA (**Grade C**) or acitretin (**Grade C**) • Consider MTX (**Grade C**) • Phototherapy not recommended (**Expert opinion**)	• Prefer INFLI (**Grade B**, rapidity of action) • Consider USTK (**Grade B**) • Consider anti-IL17 (**Grade C**) • No data available for apremilast
d) Erythrodermic Psoriasis	• Prefer CSA (**Grade B**) • Consider acitretin (**Grade C**) or MTX (**Grade C**) • Phototherapy not recommended (**Expert opinion**)	• Consider TNFi (Prefer INFLI for speed of action), or USTK or anti-IL17 (**Grade D**) • No available data for aprmilast
e) Nail Psoriasis	• Prefer MTX (**Grade B**) • Consider CSA (**Grade B**) or acitretin (**Grade C**)	• Prefer USTK or TNFi (Prefer ADA or INFLI) or apremilast (**Grade B**) • In case of failure, consider switching from USTK to TNFi and vice versa (**Grade B**) or consider anti-IL17 (**Grade C**)

ALGORITHME DU CHOIX THERAPEUTIQUE EN FONCTION DE LA FORME CLINIQUE

MANAGEMENT OF PARTICULAR FORMS OF PSORIASIS

	First step systemic treatments (Phototherapy, MTX, CSA, acitretin)	Second step systemic treatments (TNFi, USTK, anti-IL17, apremilast)
a) Palmoplantar non pustular Psoriasis	• Idem plaque psoriasis	• Idem plaque psoriasis
f) Scalp Psoriasis	• Idem Plaque psoriasis	• Idem Plaque psoriasis

Pas assez de données robustes dans la littérature pour émettre des recommandations spécifiques à ces deux formes

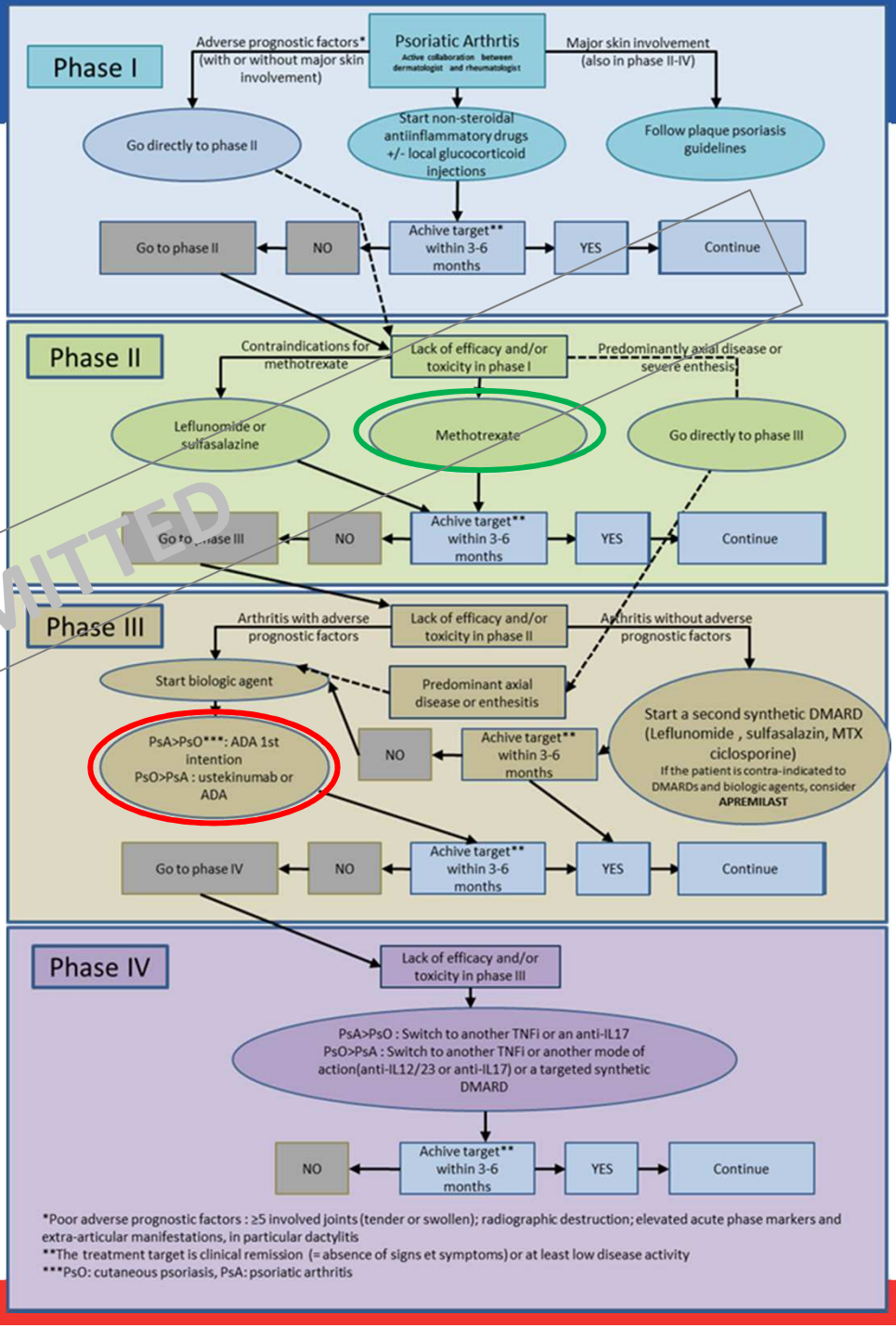
RHUMATISME PSORIASIQUE

Modification et actualisation de l'algorithme de l'EULAR

Inclusion de l'ixekizumab et de l'apremilast

Introduction d'une biothérapie : choix différent si PsA > PsO ou PsO > PsA

Place de l'apremilast : peu de données ! Uniquement si CI aux biothérapies, et forme mineure de la maladie



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Cas clinique illustratif 1

Florent Amatore, Marie Tauber, Axel Villani, Bernard Guillot, Manuelle Viguier

Marseille, Toulouse, Lyon, Montpellier, Reims

Cas clinique (1)

- Patiente de 32 ans
- Pas d'antécédent particulier
- G1P0, **grossesse en cours 28SA**
- Psoriasis en plaques sévère en poussée depuis le 1er trimestre de grossesse
- Sous traitement topique seul actuellement


SUBMITTED

Cas clinique (1)

SPECIAL SITUATIONS		
A to Z	First step systemic treatments Phototherapy, MTX, CSA, acitretin	Second step systemic treatments TNFi (ETA, ADA or INFLI) , USTK, anti-IL17 (IXE or SECU), apremilast
m) Pregnancy	Close collaboration with an obstetrician-gynaecologist and paediatrician if CSA or TNFi are maintained during pregnancy	
	• Prefer NBUVB (**Grade B**) • Consider CSA (**Grade B**) • Avoid PUVA (no sufficient data) (Expert opinion) • *Absolute contraindication*: acitretin, MTX, (**Grade A**)	• Consider start or maintenance of ETA if there is no alternative (**Grade C**). ADA or INLI can be maintained until the 3rd trimester if there is no alternative (**Expert opinion**). • *Avoid* USTK and anti-IL17 and apremilast (**Expert opinion**): not enough available data

Cas clinique (1)

SPECIAL SITUATIONS		
A to Z	First step systemic treatments Phototherapy, MTX, CSA, acitretin	Second step systemic treatments TNFi (ETA, ADA or INFLI) , USTK, anti-IL17 (IXE or SECU), apremilast
m) Pregnancy	Close collaboration with an obstetrician-gynaecologist and paediatrician if CSA or TNFi are maintained during pregnancy • Prefer NBUVB (**Grade B**) • Consider CSA (**Grade B**) • Avoid PUVA (no sufficient data) (Expert opinion) • *Absolute contraindication*: acitretin, MTX, (**Grade A**)	• Consider start or maintenance of ETA if there is no alternative (**Grade C**). ADA or INLI can be maintained until the 3rd trimester if there is no alternative (**Expert opinion**). • *Avoid* USTK and anti-IL17 and apremilast (**Expert opinion**): not enough available data

Cas clinique (1)

SPECIAL SITUATIONS		
A to Z	First step systemic treatments Phototherapy, MTX, CSA, acitretin	Second step systemic treatments TNFi (ETA, ADA or INFLI) , USTK, anti-IL17 (IXE or SECU), apremilast
m) Pregnancy	Close (cian-gynaecologist and paediatrician if CSA or TNFi are maintained during pregnancy • Prefer NBUVB (Grade B) • Consider CSA (Grade B) • Avoid PUVA (no sufficient data) (Expert opinion) • *Absolute contraindication*: acitretin, MTX, (Grade A)	• Consider start or maintenance of ETA if there is no alternative (Grade C). ADA or INLI can be maintained until the 3rd trimester if there is no alternative (Expert opinion). • *Avoid* USTK and anti-IL17 and apremilast (Expert opinion): not enough available data

1er scénario : patiente naïve de systémique

Si cabine disponible, acceptation de la contrainte organisationnelle

Cas clinique (1)

SPECIAL SITUATIONS		
A to Z	First step systemic treatments Phototherapy, MTX, CSA, acitretin	Second step systemic treatments TNFi (ETA, ADA or INFLI) , USTK, anti-IL17 (IXE or SECU), apremilast
m) Pregnancy	Close (cian-gynaecologist and paediatrician if CSA or TNFi are maintained during pregnancy • Prefer NBUVB (Grade B) • Consider CSA (Grade B) • Avoid PUVA (no sufficient data) (Expert opinion) • *Absolute contraindication*: acitretin, MTX, (Grade A)	• Consider start or maintenance of ETA if there is no alternative (Grade C). ADA or INLI can be maintained until the 3rd trimester if there is no alternative (Expert opinion). • *Avoid* USTK and anti-IL17 and apremilast (Expert opinion): not enough available data

1er scénario : patiente naïve de systémique

Informer du risque modéré de pré-eclampsie, RCIU…

Cas clinique (1)

SPECIAL SITUATIONS		
A to Z	First step systemic treatments Phototherapy, MTX, CSA, acitretin	Second step systemic treatments TNFi (ETA, ADA or INFLI) , USTK, anti-IL17 (IXE or SECU), apremilast
m) Pregnancy	Close collaboration with an obstetrician-gynaecologis… maintained during preg…	…NFi are
	• Prefer NBUVB (Grade B) • Consider CSA (Grade B) • Avoid PUVA (no sufficient data) (Expert opinion) • *Absolute contraindication*: acitretin, MTX, (Grade A)	• Consider start or maintenance of ETA if there is no alternative (Grade C). ADA or INLI can be maintained until the 3rd trimester if there is no alternative (Expert opinion). • Avoid USTK and anti-IL17 and apremilast

2ème scenario : patiente en échec de 2 systémiques

eta > ada ou infli
Demi-vie plus courte
Théoriquement moins d'infections materno-foetales
Vaccins vivants > 15 jours de vie

Cas clinique (1)

Et après l'accouchement, pendant l'allaitement ?

b) Breastfeeding	• Prefer NBUVB **(Expert opinion)** or CSA **(Grade A).** • Consider MTX **(Grade C)** (wait 24 hours after the administration of MTX to breastfeed a child) • Avoid PUVA (no sufficient data) **(Expert opinion)**. • Absolute contraindication: Acitretin **(Grade A)**	• Consider start or maintenance of TNFi if there is no alternative **(Expert Opinion)**. • *Avoid* USTK, anti-IL17 and apremilast **(Expert opinion)**: not enough available data

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Cas clinique illustratif 2

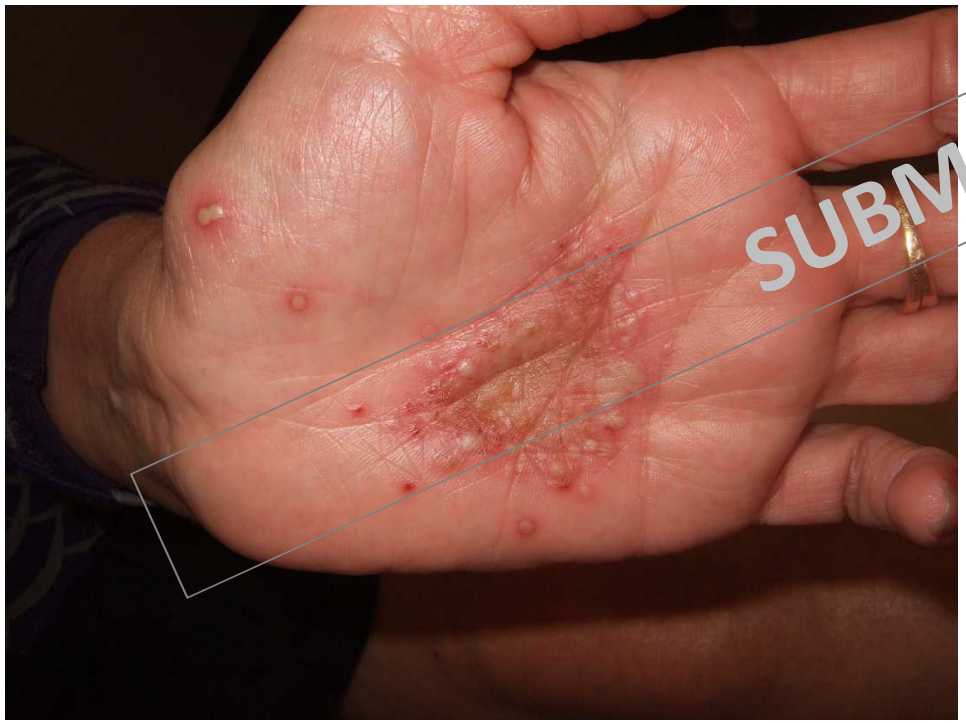
Florent Amatore, Marie Tauber, Axel Villani, Bernard Guillot, Manuelle Viguier

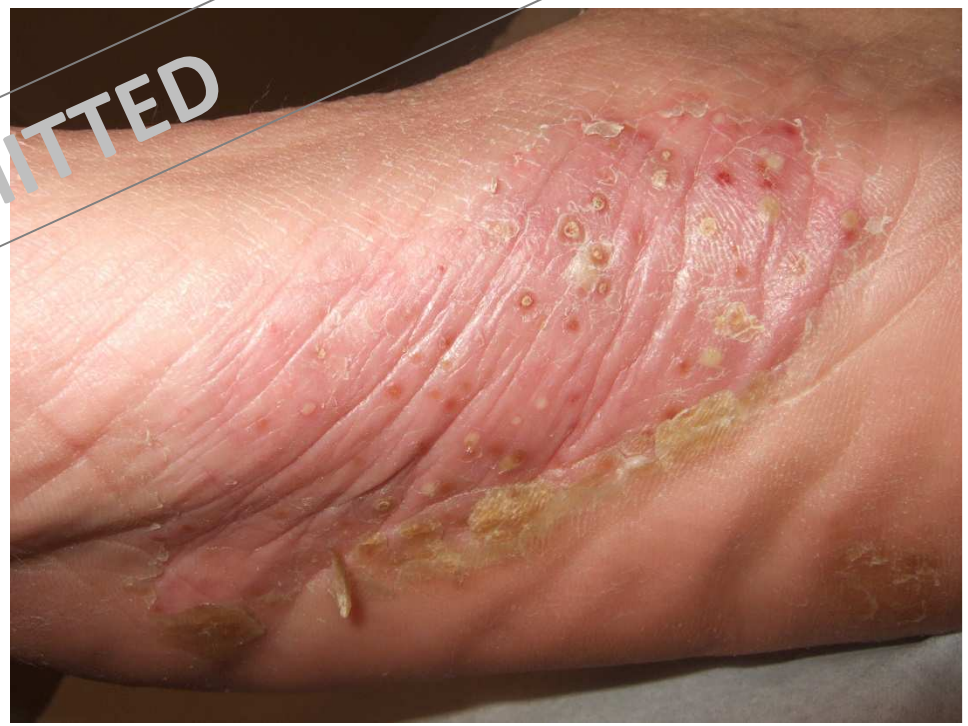
Marseille, Toulouse, Lyon, Montpellier, Reims

Cas clinique (2)

- Patiente de 51 ans
- Antécédent de cancer de vessie traité par chirurgie puis RT-CT il y a 2 ans, en rémission
- Tabagisme sevré depuis 10 ans
- Psoriasis pustuleux palmo-plantaire en poussée depuis 3 mois, résistant aux traitements locaux, impact majeur sur la qualité de vie

Cas clinique (2)





Cas clinique (2)

MANAGEMENT OF PARTICULAR FORMS OF PSORIASIS

	First step systemic treatments (Phototherapy, MTX, CSA, acitretin)	Second step systemic treatments (TNFi, USTK, anti-IL17, apremilast)
b) **Palmoplantar Pustular Psoriasis**	• Prefer CSA (**Grade B**) • Consider local PUVAtherapy (**Grade B**) or acitretin (Grade B) or acitretin and local PUVA therapy in combination (**Grade B**) • Consider MTX (**Grade C**)	• Prefer ETA or UTSK (**Grade B**): more available data for both molecules • In case of failure, consider other TNFi or anti-IL17 (**Grade B**)

1er scénario : patient naïf de systémique

Cas clinique (2)

Mais …

SPECIAL SITUATIONS		
A to Z	First step systemic treatments Phototherapy, MTX, CSA, acitretin	Second step systemic treatments TNFi (ETA, ADA or INFLI) , USTK, anti-IL17 (IXE or SECU), apremilast
c) Cancer (cured)	Close collaboration with oncologist and/or multidisciplinary cancer care	
	• Prefer MTX or phototherapy (except if skin cancer) or acitretin (**Grade C**) • *Avoid* CSA (**Grade A**)	• Case-by-case decision (**Grade C**) • The initiation of a biological agent has to be discussed with the oncologist depending of the stage and prognosis of the tumour (**Grade C**) • Consider USTK or TNFi (Prefer ETA or ADA) (**Grade C**) • Not enough follow up for apremilast and anti-il17

Cas clinique (2)

MANAGEMENT OF PARTICULAR FORMS OF PSORIASIS

	First step systemic treatments (Phototherapy, MTX, CSA, acitretin)	Second step systemic treatments (TNFi, USTK, anti-IL17, apremilast)
b) Palmoplantar Pustular Psoriasis	• Prefer CSA (Grade B) • Consider local PUVAtherapy (Grade B) or acitretin (Grade B) or acitretin and local PUVA therapy in combination (Grade B) • Consider MTX (Grade C)	• Prefer ETA or UTSK (Grade B): more available data for both molecules • In case of failure, consider other TNFi or anti-IL17 (Grade B)

1er scenario : patient naïf de systémique

Cas clinique (2)

MANAGEMENT OF PARTICULAR FORMS OF PSORIASIS

	First step systemic treatments (Phototherapy, MTX, CSA, acitretin)	Second step systemic treatments (TNFi, USTK, anti-IL17, apremilast)
b) Palmoplantar Pustular Psoriasis	• Prefer CSA (**Grade B**) • Consider local PUVAtherapy (**Grade B**) or acitretin (Grade B) or acitretin and local PUVA therapy in combination (**Grade B**) • Consider MTX (**Grade C**)	• Prefer ETA or UTSK (**Grade B**): more available data for both molecules • In case of failure, consider other TNFi or anti-IL17 (**Grade B**)

2ème scenario : patient en échec de 2 systémiques

Cas clinique (2)

Mais …

SPECIAL SITUATIONS		
A to Z	First step systemic treatments Phototherapy, MTX, CSA, acitretin	Second step systemic treatments TNFi (ETA, ADA or INFLI) , USTK, anti-IL17 (IXE or SECU), apremilast
c) **Cancer (cured)**	Close collaboration with oncologist and/or multidisciplinary cancer care • Prefer MTX or phototherapy (except if skin cancer) or acitretin (**Grade C**) • *Avoid* CSA (**Grade A**)	• Case-by-case decision (**Grade C**) • The initiation of a biological agent has to be discussed with the oncologist depending of the stage and prognosis of the tumour (**Grade C**) • Consider USTK or TNFi (Prefer ETA or ADA) (**Grade C**) • Not enough follow up for apremilast and anti-il17

Cas clinique (2)

MANAGEMENT OF PARTICULAR FORMS OF PSORIASIS

	First step systemic treatments (Phototherapy, MTX, CSA, acitretin)	Second step systemic treatments (TNFi, USTK, anti-IL17, apremilast)
b) Palmoplantar Pustular Psoriasis	• Prefer CSA (**Grade B**) • Consider local PUVAtherapy (**Grade B**) or acitretin (Grade B) or acitretin and local PUVA therapy in combination (**Grade B**) • Consider MTX (**Grade C**)	• Prefer ETA or UTSK (**Grade B**): more available data for both molecules • In case of failure, consider other TNFi or anti-IL17 (**Grade B**)

2ème scenario : patient en échec de 2 systémiques

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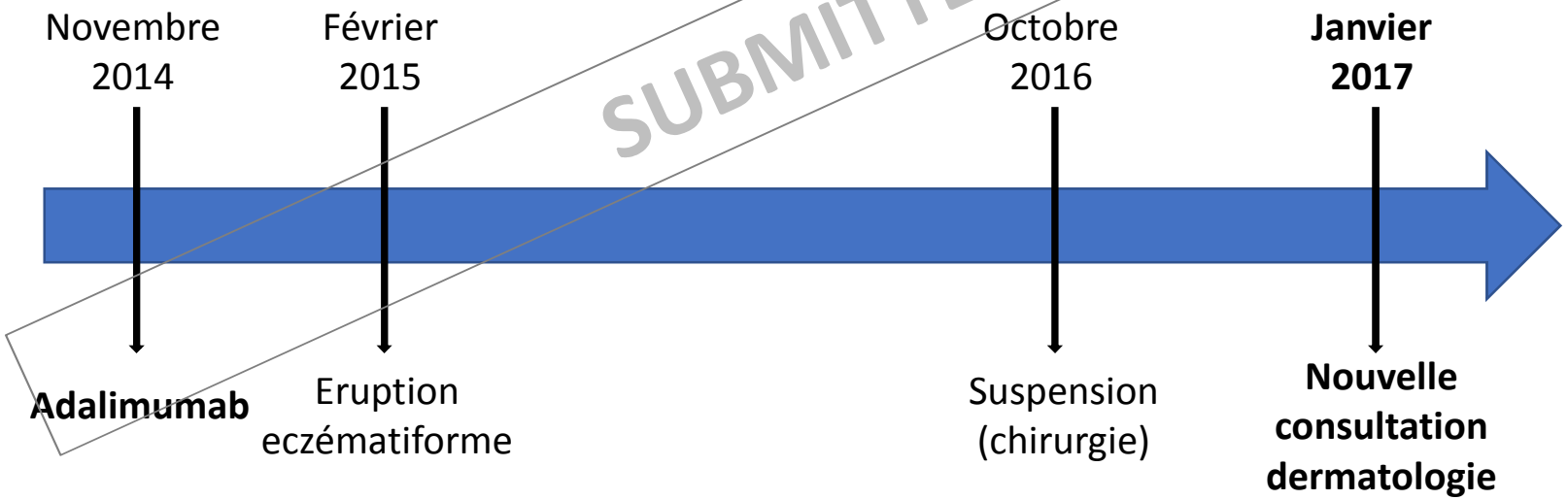
Cas clinique illustratif 3

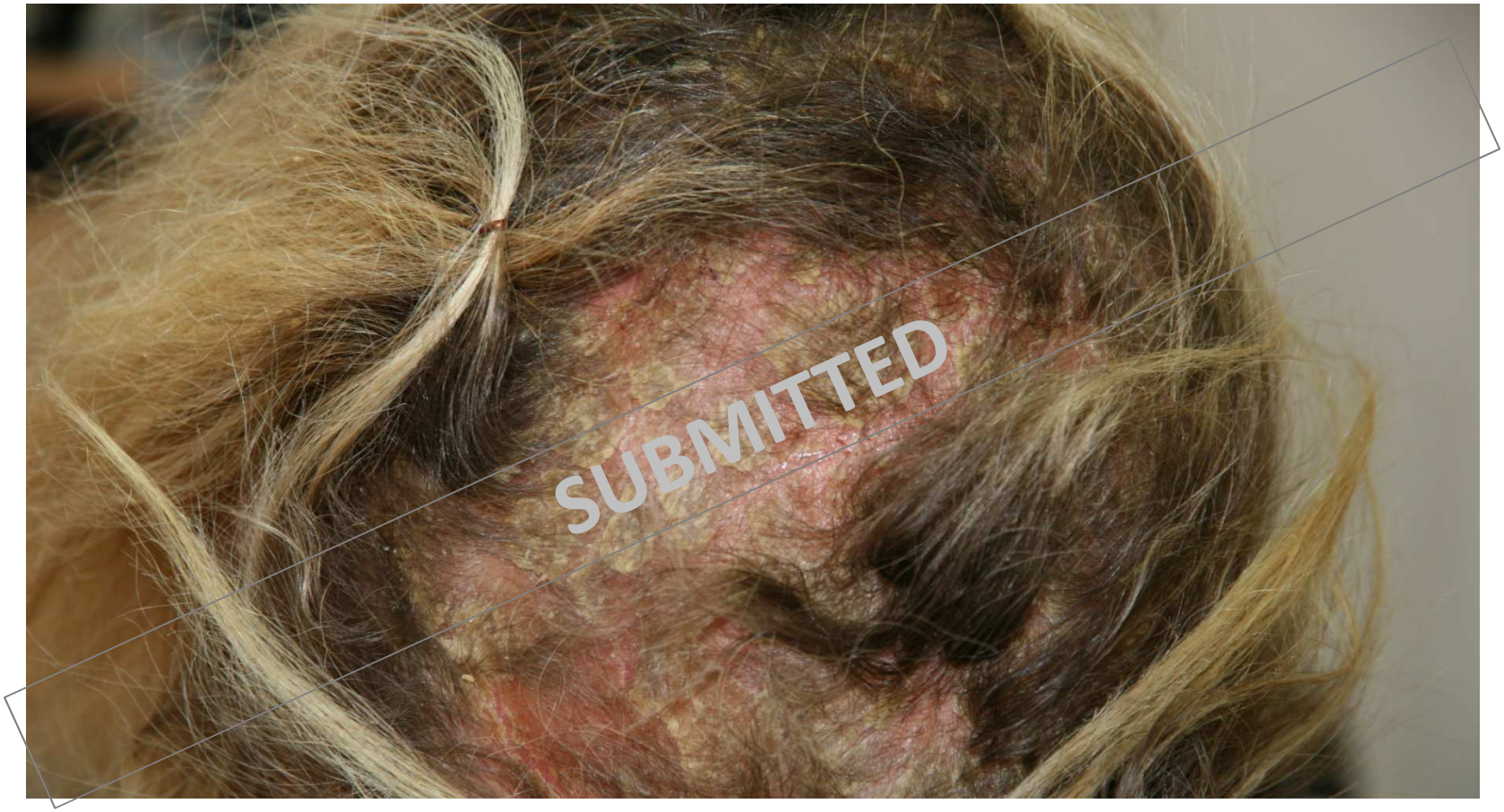
Axel Villani, Marie Tauber, Florent Amatore, Bernard Guillot, Manuelle Viguier

Lyon, Toulouse, Marseille, Montpellier, Reims

Mlle C. 24 ans

- Spondylarthrite ankylosante HLA B27 + (Juin 2013), pancolite attribuée aux AINS
- Pas d'autre ATCD personnel
- ATCD familiaux : maladie de Crohn (père)



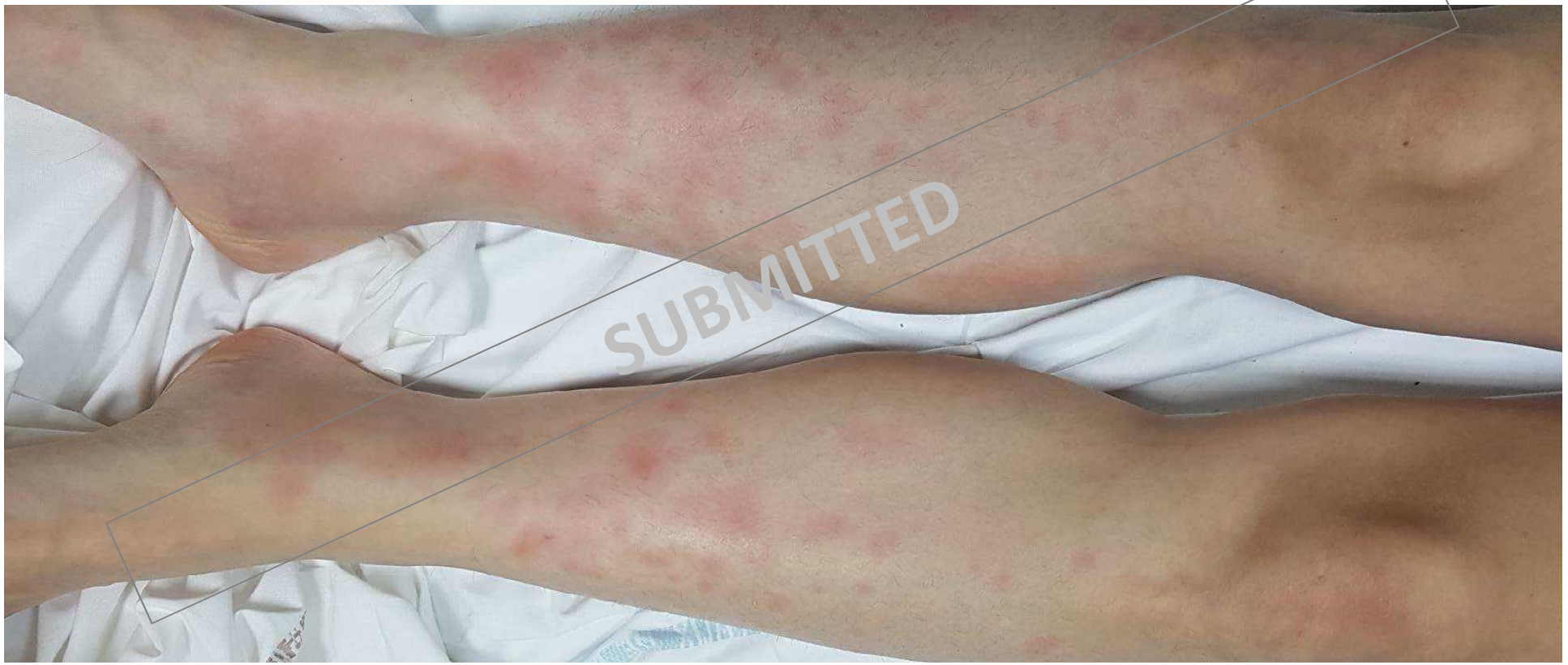


Psoriasis paradoxal sévère alopéciant lié à l'adalimumab

⇒ **Pas de reprise de l'adalimumab**

⇒ **Récidive SpA en février 2017 > Mise sous secukinumab**

5 injections de secukinumab plus tard…



+ diarrhées glairo-sanglantes avec -8kg en 4 semaines

Maladie de Crohn iléo-colique non sténosante non fistulisante révélée sous anti IL-17

- Arrêt Cosentyx => Switch INFLIXIMAB + METHOTREXATE après corticothérapie initiale

Maladies inflammatoires de l'intestin et anti IL17

	Secukinumab	Ixekizumab	Brodalumab
Nouveaux cas de MICI	7	15	1
Exacerbations de MICI	10	4	0
Total/patients traités	17/5004	19/4209	1/3275

Cosentyx (secukinumab) [prescribing information]. East Hanover: Novartis Pharmaceuticals Corporation. 2016; *Reich K et al. J Am Acad Dermatol. 2017 Mar;76(3):441-448.e2. doi: 10.1016/j.jaad.2016.10.027*

Au total

- 1 patient sur 4 ayant une MICI connue décompense sous anti-IL17A (4/16)

- **Dans un contexte de MICI (patient à risque ou MICI établie)**

  ⇒ **Eviter les anti-IL17**

- Pas d'efficacité sur la maladie de Crohn (arrêt prématuré des études Brodalumab (anti-IL17RA) et Secukinumab (anti-IL17A))

RECOMMENDATIONS 2017

Close collaboration with a gastroenterologist	
• Prefer MTX (**Grade A**)	• Prefer ADA, INFLI or USTK (**Grade A**)
• Consider CSA (**Grade B**) or NBUVB (**Grade C**)	• *Avoid* Anti-IL17 (**Grade C**)
• No data available for acitretin	• No data available for apremilast

Reich K et al. J Am Acad Dermatol. 2017 Mar;76(3):441-448.e2. doi: 10.1016/j.jaad.2016.10.027; Hueber W et al. Gut. 2012 Dec;61(12):1693-700. doi: 10.1136/gutjnl-2011-301668; Stephan R. Targan et al. Am J Gastroenterol. 2016 Nov;111(11):1599-1607. doi: 10.1038/ajg.2016.298

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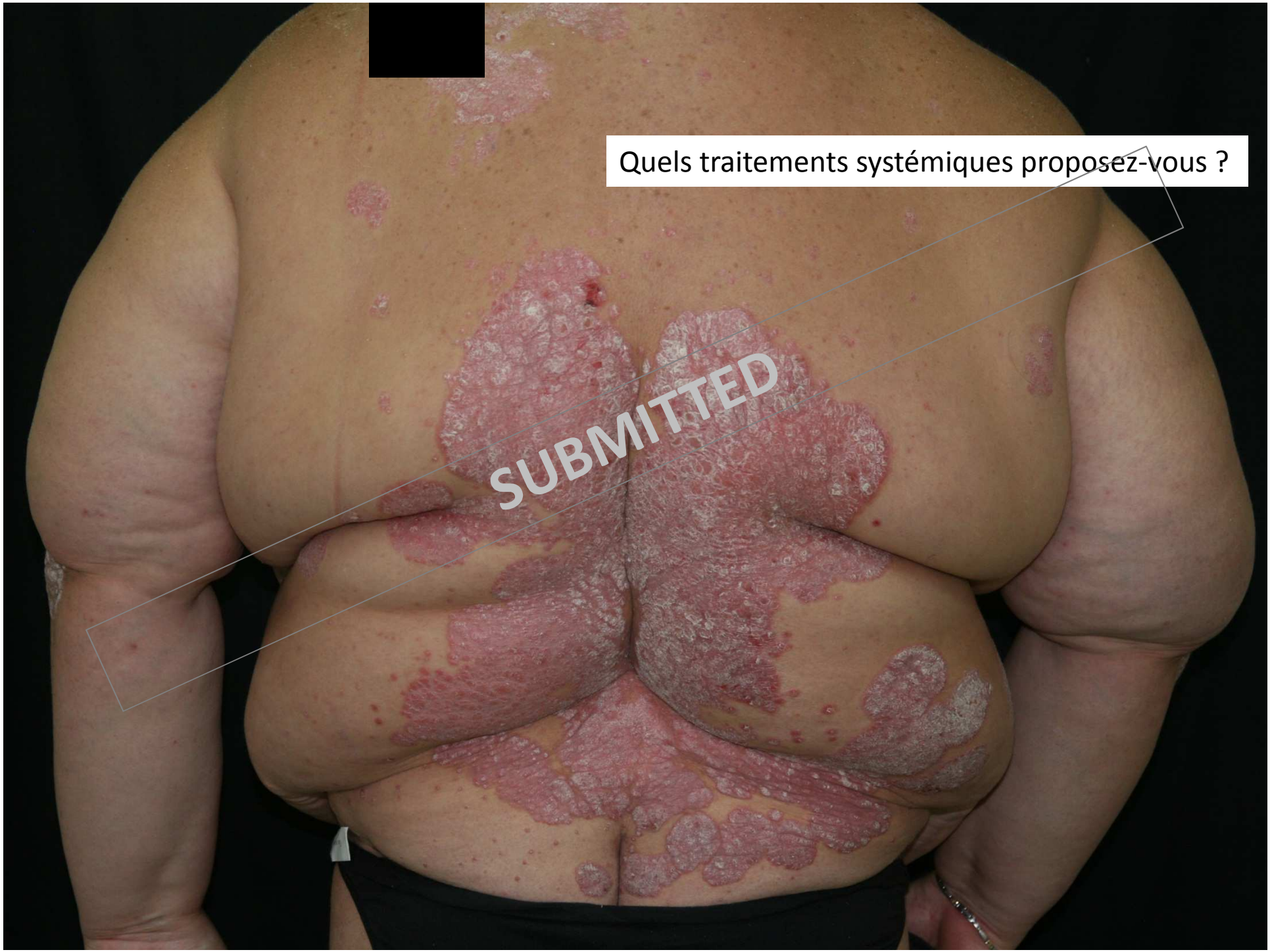
Cas clinique illustratif 4

Axel Villani, Marie Tauber, Florent Amatore, Bernard Guillot, Manuelle Viguier

Lyon, Toulouse, Marseille, Montpellier, Reims

M. P. 45 ans

- Obésité, IMC=36 – Poids= 130 kg
- Pas d'autre comoridités, pas d'antécédents familiaux notables
- Psoriasis en plaques évolutif depuis 10 ans, avec aggravation depuis plusieurs mois.
- PASI=15 – DLQI=25/30
- Photothérapie inefficace – méthotrexate inefficace


Quels traitements systémiques proposez-vous ?
SUBMITTED

Cas clinique (4)

SPECIAL SITUATIONS		
A to Z	First step systemic treatments Phototherapy, MTX, CSA, acitretin	Second step systemic treatments TNFi (ETA, ADA or INFLI) , USTK, anti-IL17 (IXE or SECU), apremilast
j) Obesity	Dietary intervention: encourage weight loss (Grade B) • Prefer phototherapy with prudent gradual increase of UV doses (**Grade C**) or MTX with close hepatic monitoring (**Grade C**) • Consider CSA (**Grade C**) or acitretin (**Grade C**)	• Prefer USTK (**Grade C**- weight based dosage and no association with weight gain) In case of USTK failure, consider IXE (**Grade C**) before TNFi, SECU and apremilast (**Expert opinion**)

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1er scenario : patient naïf de systémique

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2ème scenario : patient en échec de 2 systémiques

j) Obesity	Dietary intervention: encourage weight loss (Grade B)	
	• Prefer phototherapy with prudent gradual increase of UV doses (**Grade C**) or MTX with close hepatic monitoring (**Grade C**) • Consider CSA (**Grade C**) or acitretin (**Grade C**)	• Prefer USTK (**Grade C**- weight based dosage and no association with weight gain) In case of USTK failure, consider IXE (**Grade C**) before TNFi, SECU and apremilast (**Expert opinion**)

Au total

- Toujours encourager la perte de poids
- **1ère intention :**
  - Précautions MTX (syndrome métabolique, stéatose hépatique ?)
  - Précautions cyclosporine
- **2ème intention :**
  - Ustekinumab – posologie adaptée au poids – pas de prise de poids potentielle rapportée contraitement aux anti-TNFalpha
  - 2ème ligne de biothérapie : ixekizumab en priorité – Reich *et al. JEADV 2017* : peu d'effets du poids sur l'efficacité de cette molécule.

Pour conclure

- Recommandations = outil d'aide à la décision
- Outil qui se veut pratique et facilement consultable
- Pour en savoir plus : se référer aux 260 pages du texte long (analyse des données bibliographiques)

Recommandations seront disponibles sur :

Site du groupe Psoriasis : http://grpso.org/

GRPso
Groupe de Recherche sur le Psoriasis

Site de la SFD

Société Française de Dermatologie et de Pathologie Sexuellement Transmissible