Best of allergologie

Louise JAULENT

Interne en dermatologie à Lyon

Responsables d'enseignement

Dr Charles Dzviga

Dr Marion Braire

Nemolizumab : efficace dans la dermatite atopique

- Anti-récepteur A de l'IL 31
  - rôle dans prurit et inflammation
  - régulation de la barrière cutanée
- Essai de phase 3 en double aveugle sur 16 semaines
- DA et prurit modéré à sévère avec réponse insuffisante aux topiques
- Nemolizumab (60mg) vs placebo /4 semaines
- Critère Iaire : % moyen de changement de l'échelle de prurit (VAS score) entre S0 et S16
- Critères IIaires : diminution du VAS entre S0-S4, diminution de l'EASI, du DLQI, score ISI<7, sécurité

Table 2. Primary and Secondary Efficacy End Points (Modified Intention-to-Treat Population).*

End Point	Nemolizumab (N=143)	Placebo (N=72)	Difference (95% CI)
			percentage points
Primary end point: percent change in pruritus VAS score from baseline to wk 16	−42.8±2.6	−21.4±3.6	−21.5 (−30.2 to −12.7)†
Secondary end points‡			
Percent change in pruritus VAS score from baseline to day 29	−34.4±2.2	−15.3±3.0	−19.3 (−26.6 to −11.9)
Percent change in EASI score from baseline to wk 16	−45.9±3.3	−33.2±4.7	−12.6 (−24.0 to −1.3)
Percentage of patients with a DLQI score of ≤4 at wk 16 (no./total no.)§	40 (51/129)	22 (15/67)	17 (2 to 31)
Percentage of patients with a decrease of ≥4 points in the DLQI score from baseline to wk 16 (no./total no.)¶	67 (89/133)	50 (34/68)	17 (3 to 31)
Percentage of patients with an ISI score of ≤7 at wk 16 (no./total no.)‖	55 (59/108)	21 (12/56)	33 (17 to 48)

Conclusion

Nemolizumab efficace dans le prurit chez les patients atteints de dermatite atopique

Kabashima K, Matsumura T, Komazaki H, Kawashima M, for the Nemolizumab-JP01 Study Group. Trial of Nemolizumab and Topical Agents for Atopic Dermatitis with Pruritus. N Engl J Med 2020 July;383:141-150

Omalizumab et grossesse

- Etude EXPECT : observationnelle, prospective, évaluant critères périnataux chez femmes avec asthme modéré-sévère exposées au XOLAIR (max 375mg/2 semaines) pendant leur grossesse (2006)
- Obj : comparer résultats de l'étude EXPECT (n=250) à ceux d'un groupe contrôle (QECC : base de données québécoise, n=1153)

Conclusion :
Pas de preuve d'un risque augmenté de complication péri-natale chez les enfants de mères traitées par omalizumab pendant leur grossesse

TABLE IV. Pregnancy and infant outcomes (excluding congenital anomalies) in the EXPECT subcohort and the QECC

	EXPECT subcohort*	QECC†
Pregnancy outcomes	n = 230	n = 1153
Live births (% of pregnancies [95% CI])	99.1% (96.9% to 99.9%)	99.3% (92.9% to 100.0%)
Fetal death/stillbirths‡ (% of pregnancies [95% CI])	0.9% (0.1% to 3.1%)	0.9% (0.3% to 1.5%)†
Live-born infant outcomes§	n = 233	n = 1162
Birth weight (kg), mean ± SD‖		
All infants	3.2 ± 0.6	3.2 ± 0.6
Singletons	3.2 ± 0.6	3.2 ± 0.3
Twins	2.4 ± 0.4	2.0 ± 0.3
Low birth weight (% of infants [95% CI])‖¶		
All infants	13.7% (9.5% to 18.9%)	9.8% (7.9% to 11.8%)
All singletons, including premature births	11.6% (7.6% to 16.6%)	8.3% (6.5% to 10.2%)
All full-term infants	4.7% (2.2% to 8.8%)	2.9% (1.8% to 4.0%)
Full-term singletons	2.7% (0.9% to 6.1%)	2.9% (1.8% to 4.0%)
Oral corticosteroid use#		
Yes	18.2% (9.1% to 30.9%)	13.7% (8.8% to 18.6%)
No	12.3% (7.8% to 18.2%)	8.7% (6.6% to 10.8%)
SGA (% of infants [95% CI])**	9.7% (6.2% to 14.4%)	15.8% (13.3% to 18.4%)
Gestational age (wk), median (range)	39.0 (28.3 to 43.0)	39.0 (20.0 to 42.0)
Premature birth (% of infants [95% CI])††	15.0% (10.7% to 20.3%)	11.3% (9.2% to 13.5%)
Oral corticosteroid use		
Yes	32.7% (20.7% to 46.7%)	16.2% (10.9% to 21.4%)
No	9.6% (5.7% to 14.9%)	9.8% (7.5% to 12.1%)

% d'enfants avec anomalie congénitale majeure : 8.1% (EXPECT) vs 8.9% (QECC)

Namazy JA, Blais L, Andrews EB, Scheuerle AE, Cabana MD, Thorp JM, et al, Pregnancy outcomes in the omalizumab pregnancy registry and a disease-matched comparator cohort. J Allergy Clin Immunol, 2020 Feb;145(2):528-536.e1.

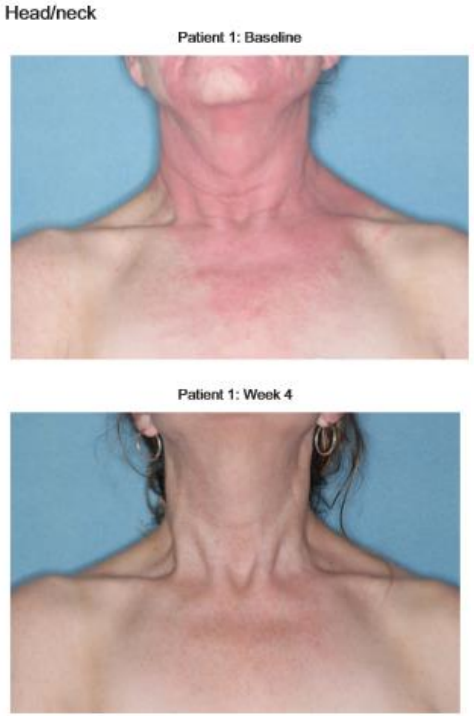
Topique au ruxolitinib dans la dermatite atopique

- Ruxolitinib : inhibiteur de JAK 1 et 2
- Essai de phase 2, randomisé, en double aveugle, sur 8 semaines
- 307 patients atteints de DA avec IGA 2-3 (léger à modéré) et surface atteinte 3-20%
- Ruxolitinib topique vs placebo
- Critère laire : amélioration du score EASI à S4

Résultats :

Ruxolitinib 1.5% 2 applications/J : effet bénéfique à S4

- Amélioration du score EASI à S4 (71.6% vs 15.5%; P < .0001)
- Amélioration de l'IGA à S4 (38.0% vs 7.7%; P < .001)
- vs triamcinolone acetonide à S4 : EASI score 71.6% vs 59.8%; IGA response 38.0% vs 25.5%
- Amélioration du prurit (EN) après 36h et jusqu'à 12 semaines (–1.8 vs –0.2; P < .0001)
- Bonne tolérance



Conclusion

Topique au ruxolitinib permet une réduction rapide et durable des symptômes de dermatite atopique

Kim BS, Howell MD, Sun K, Papp K, Nasir A, Kuligowski ME, for the INCB 18424-206 Study Investigators. Treatment of atopic dermatitis with ruxolitinib cream (JAK1/JAK2 inhibitor) or triamcinolone cream. J Allergy Clin Immunol, 2020 Feb;145(2):572-582

Anti IL 13 et œsophagite à éosinophile

- Oesophagite à éosinophile : Peu de traitement, aucun traitement ciblé
- IL13 (TH2) : rôle dans activation fibroblastes et PNE
- Fibrosténose : 1ère complication, médiée par la transition épithélio-mésenchymateuse (EMT)
- Sous-étude d'un essai de phase 2, randomisé, en double aveugle, contre placebo
- N=69
- Ttt hebdomadaire par anti IL13 à 180mg (n=19) ou 360mg (n=26) vs placebo (n=24)
- Critère Iaire : % de modification de l'expression en IF de vimentine sur les cell épithéliales entre S0 et S16

<u>Conclusion</u> :

Les Ac anti IL13 diminuent les marqueurs de l'EMT et peuvent ainsi améliorer la fibrose chez les patients atteints d'oesophagite à éosinophiles

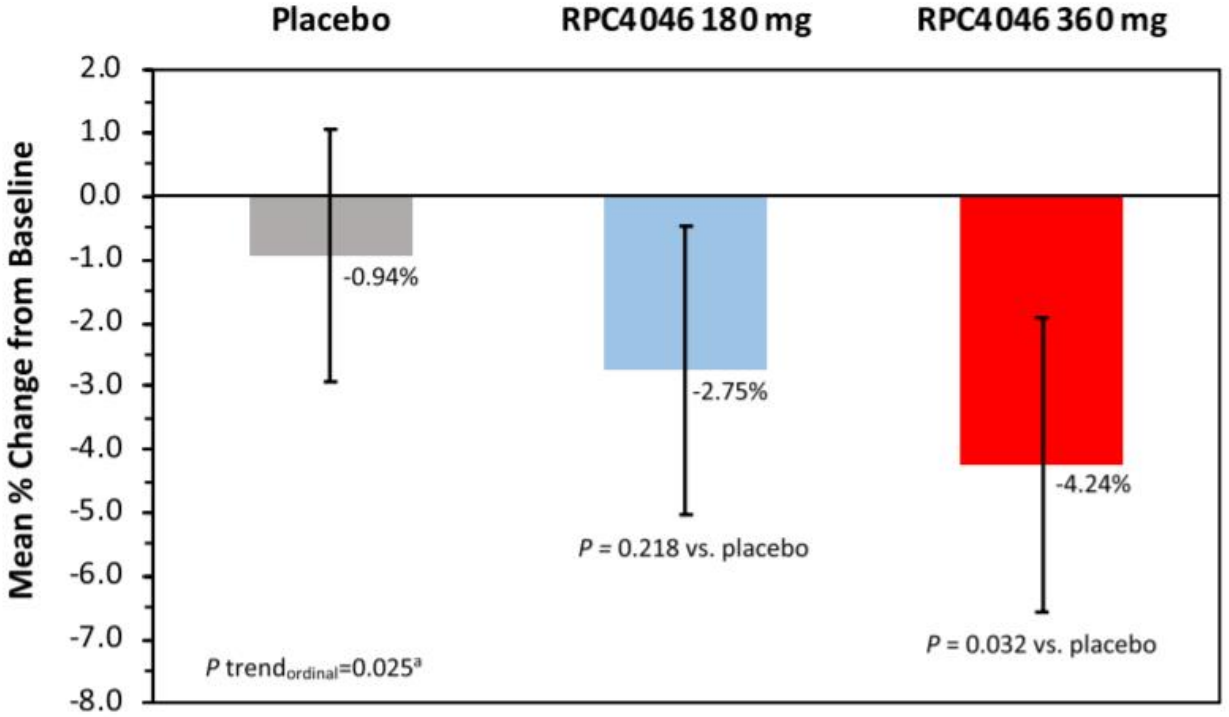


FIG 2. Mean change (95% CI) in the percentage of vimentin-positive epithelial cells from baseline to follow-up biopsy sample by treatment group. [a]*P* trend$_{ordinal}$ is a test for linear trend in the regression model with dose level coded as (1,2,3). All *P* values are 2 sided.

Gann PH, Deaton RJ, McMahon N, Collins MH, Dellon ES, Hirano I, et al. An anti–IL-13 antibody reverses epithelialmesenchymal transition biomarkers in eosinophilic esophagitis: Phase 2 trial results. J Allergy Clinical Immunol. 2020 Aug;146(2):367-376.e3

Perioperative antibiotic prophylaxis and penicillin allergy

- Penicillin allergy label restricts perioperative use of beta-lactams
- Use of second-line antibiotics is associated with increased risk of surgical site infection
- Objective : to develop a streamlined approach to perioperative antibiotic selection for surgical patients with penicllin allergy label, to reduce the use of second-line antibiotics
- N=2296
- 22% received a cephalosporin before algorithm implementation, 80% after
- Results : Safe approach ++ : no serious adverse event

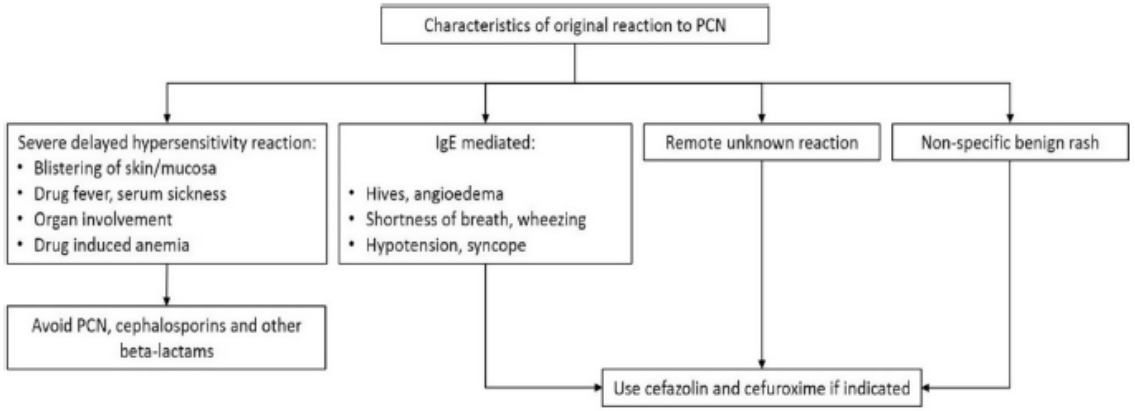


FIGURE 1. Perioperative penicillin allergy algorithm. Institutional algorithm for cefazolin/cefuroxime use in patients with reported allergy to penicillin. In the absence of a severe, delayed reaction, patients with a penicillin allergy can receive cefazolin and cefuroxime. *PCN*, Penicillin.

Penicillin Allergy Assessment

- Did you have a severe skin reaction involving blisters on your skin and shedding or detachment of your skin? (SJS/TEN)
- Were you told you had Stevens -Johnson Syndrome (SJS) or Toxic Epidermal Necrolysis (TEN)?
- Did you have liver injury or hepatitis caused by the medication?
- Did you have kidney injury, nephritis or acute renal failure caused by the medication (acute interstitial nephritis)?
- Were you told you had hemol ytic anemia caused by the medication? (Low hemoglobin or hematocrit or "blood counts" counts caused by penicillin)
- Did you have painful swollen joints caused by the medication (serum sickness)?
- Were you diagnosed with "drug fever"? (A fever caused by the antibiotic that developed about a week after starting the medication and then went away when you stopped the antibiotic?)
- Did you have a severe reaction involving the inside of your mouth, eye, or genital ulcers?

Conclusion :

The use of cefuroxime / cefazoline is possible in some patients labeled "allergic to penicillins“ without skin testing

Kuruvilla M, Sexton M, Wiley Z, Langfitt T, Lynde GC, Francis Wolf F. A Streamlined Approach to Optimize Perioperative Antibiotic Prophylaxis in the Setting of Penicillin Allergy Labels. J Allergy Clin Immunol Pract. 2020 Apr;8(4):1316-1322

Merci pour votre attention