Risk of Major Adverse Cardiovascular Events in Adults Treated with JAK inhibitors for Atopic Dermatitis: A nationwide population-based study using the French claims database

Madeleine NEILDEZ[1], Marion GUNDELWEIN[2], Sandrine KERBRAT[3], Emmanuel OGER[4], Lucie-Marie SCAILTEUX[4], Catherine DROITCOURT[1]

1. Department of Dermatology, CHU Rennes, Univ Rennes, Inserm, EHESP, Irset (Institut de recherche en santé, environnement et travail) - UMR_S 1085, Rennes, France,
2. Univ Rennes, Inserm, EHESP, Irset (Institut de recherche en santé, environnement et travail) - UMR_S 1085, Rennes, France,
3. Damad, Plouzané, France,
4. Department of Clinical Pharmacology, CHU Rennes, Univ Rennes, Inserm, EHESP, Irset (Institut de recherche en santé, environnement et travail) - UMR_S 1085, Rennes, France

Objective

Is there a higher risk of MACE in patients treated with JAKi for AD compared to the general population ?

Takeaway Message

No increased risk of CV events observed in AD patients on JAKi compared with the general population

Scan here to contact us

Catherine DROITCOURT served as a speaker for Sanofi, abbvie, almirall, ucb.
Madeleine NEILDEZ, Marion GUNDELWEIN, Sandrine KERBRAT, Emmanuel OGER and Lucie-Marie SCAILTEUX declare no conflicts of interest.

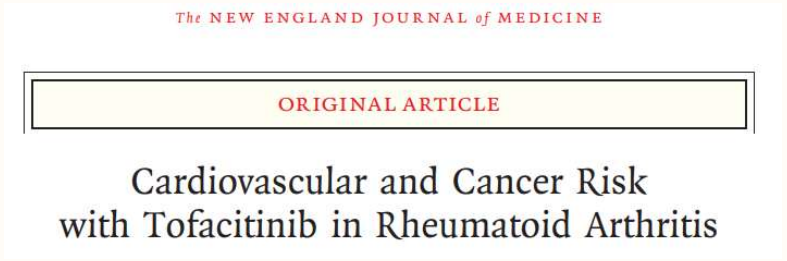
1 Context

Innovative systemic treatments in AD

Biologics since 2019 dupilumab, tralokinumab, lebrikizumab

JAK inhibitors since 2020 baricitinib, upadacitinib, abrocitinib

JAKi and potential risk of MACE*?



ORALSURV trial in 2021

A randomized open-label post authorization trial in rheumatoid arthritis:

No demonstration of the noninferiority of tofacitinib vs anti-TNFα regarding the risk of MACE*

Suggests an increased risk of MACE in people ≥50 with ≥ 1 cardiovascular risk factor

Recommendations of health authority agencies:

Limiting JAKi's use in cardiovascular risk patients§, regardless of the indication, including AD

*MACE: major adverse cardiovascular event

§≥1 cardiovascular risk factor (hypertension, diabetes, dyslipidemia, kidney failure) or ≥1 history of MACE (myocardial infarction, acute coronary syndrome including unstable angina, ischemic stroke or transient ischemic attack)

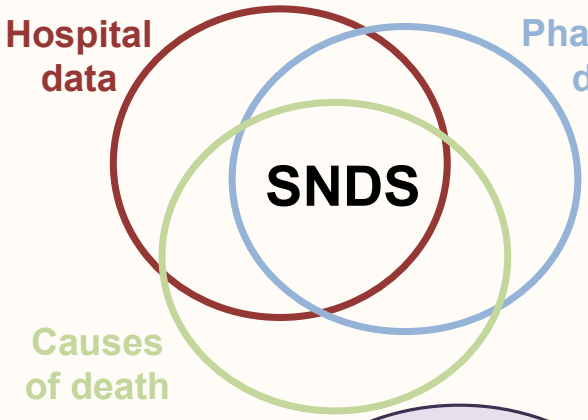
2 Method – cohort construction

Research question

Is there a higher risk of MACE in patients treated with JAKi for AD compared to the general population?

Data source

SNDS*: the French national health data system – **98% representation (68 millions)**



≥ 18 years old
≥ 1 dispensation for systemic treatment for AD between 2018 and 2024
Without reimbursement before 2018 (new initiators)

Exclusion of other indications than DA (*Rheumatoid arthritis, IBD§…)*

In the year before treatment initiation:
Consultation with a dermatologist or hospitalization with a diagnostic of AD or ≥ 2 dispensations of topical corticosteroids

ESND† = sample of 2% of the SNDS

Adults initiating JAKi and biologics for AD from 2018 to 2024

JAKi cohort

Biologic cohort

JAKi and biologic cohorts were not directly compared with each other due to indication bias

General population cohort

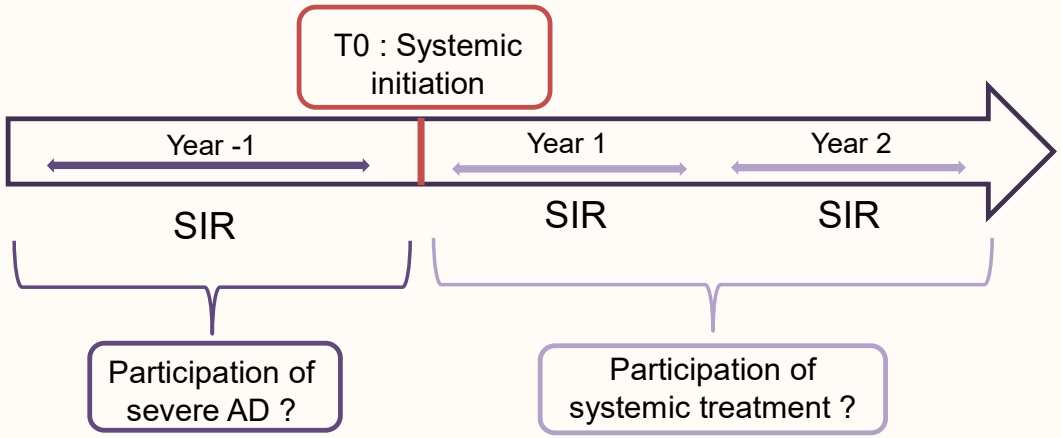
*SNDS (*Système National des Données de Santé)*
§Inflammatory bowel diseases
†*Echantillon du SNDS*

2 Method – Standardized Incidence Ratio

Analysis performed in the JAKi and biologic cohort versus general population cohort

$$SIR = \frac{\text{Number of MACE}_{observed} \text{ in AD cohort}}{\text{Number of MACE}_{expected}\ ^{*}}$$

*Application to the **AD cohort** the incidences obtained by sex and age in the **general population cohort**



Principal outcome

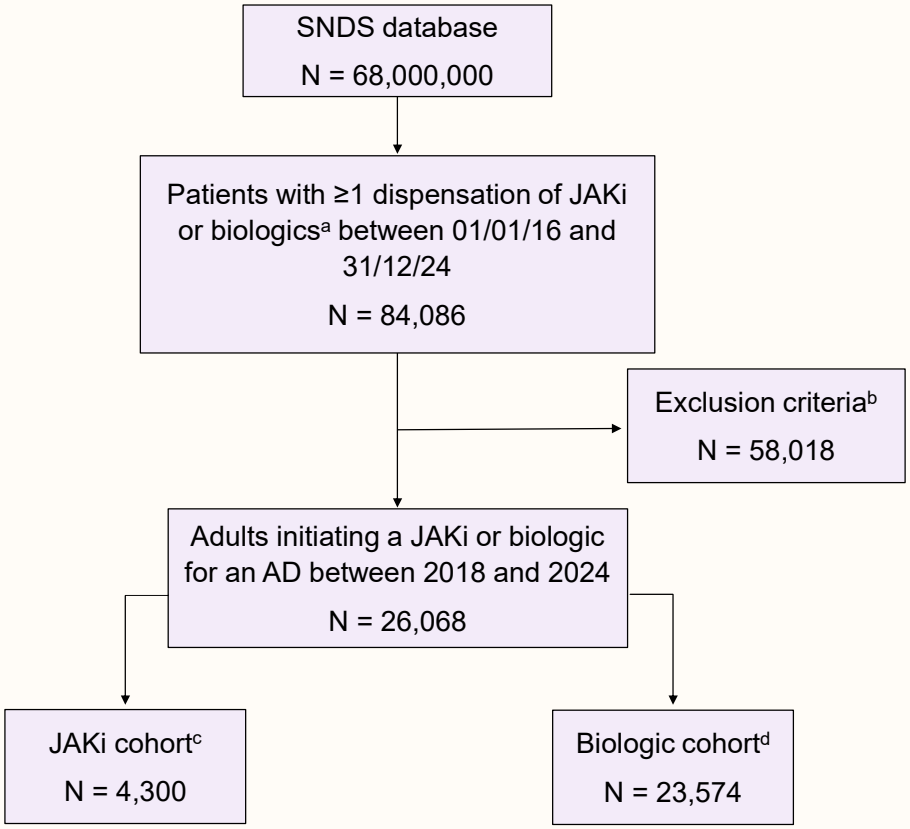
Myocardial infarction

Ischemic stroke

Sensitivity analyses

- 2 analyses with expanded outcomes :
  - ❖ myocardial infarction, ischemic stroke, unstable angina
  - ❖ myocardial infarction, ischemic stroke, unstable angina, transient ischemic attack, unspecified stroke
- 1 analysis with standardization for CV risk

3 Results – Study population



[a]JAKi: abrocitinib, baricitinib, upadacitinib; biologics: dupilumab, tralokinumab

[b]Excluded indications : asthma stage 5, ankylosing spondylitis, bone marrow transplant, bullous pemphigoid, dermatomyositis and myositis, giant cell arthritis, inflammatory bowel diseases, juvenile arthritis, lupus, psoriatic arthritis, rheumatoid arthritis, scleroderma, Takayasu's disease, other systemic connective tissue disorders; prescription by other specialists than dermatologist, general medicine, and not specified.

[c]Could have been treated with other systemic treatments, including biologics, before JAKi initiation.

[d]Could not have been treated with JAKi before biologic initiation.

Baseline characteristics at T0 (initiation of treatment)

	JAKi cohort (N=4,300)	Biologic cohort (N=23,574)	SMD
Age Median [Q1, Q3]	36.0 [26, 48]	44.0 [29, 64]	0.44
Female	2,257 (52.5%)	11,430 (48.5%)	0.08
Asthma	652 (15.2%)	5,389 (22.9%)	0.19
PRAC+	735 (17.1%)	9,000 (38.2%)	0.45
Detailed PRAC criteria			
Age≥65 years old	230 (5.3%)	5,723 (24.3%)	0.47
CV risk factor[a]	512 (11.9%)	6,973 (29.6%)	0.40
History of MACE[b]	13 (0.3%)	457 (1.9%)	0.13
Smoking	155 (3.6%)	1,569 (6.7%)	0.13
History of tumor	57 (1.3%)	1,362 (5.8%)	0.20
Time of exposure (days) Median [Q1-Q3]	224 [95.75-442.25]	307 [127-679.0]	0.34

PRAC: Pharmacovigilance Risk Assessment Commitee; SMD: Standardized Mean Difference

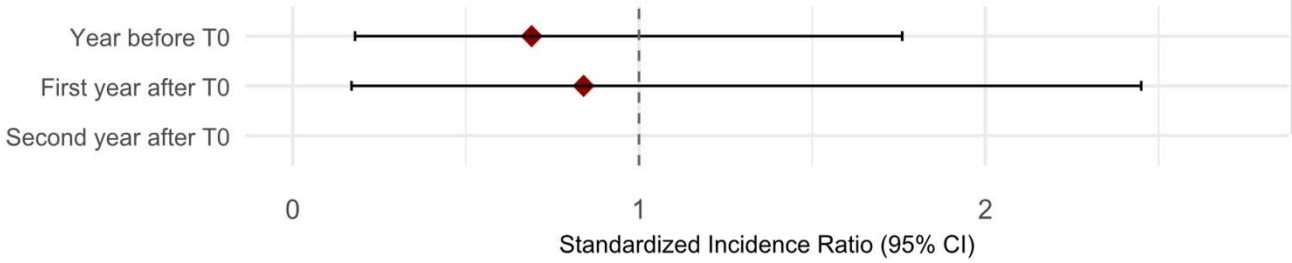
[a]≥1 CV risk factor among hypertension, diabetes, dyslipidemia, kidney failure

[b]Myocardial infarction, acute coronary syndrome including unstable angina, ischemic stroke or transient ischemic attack

3 Results – Standardized incidence ratios

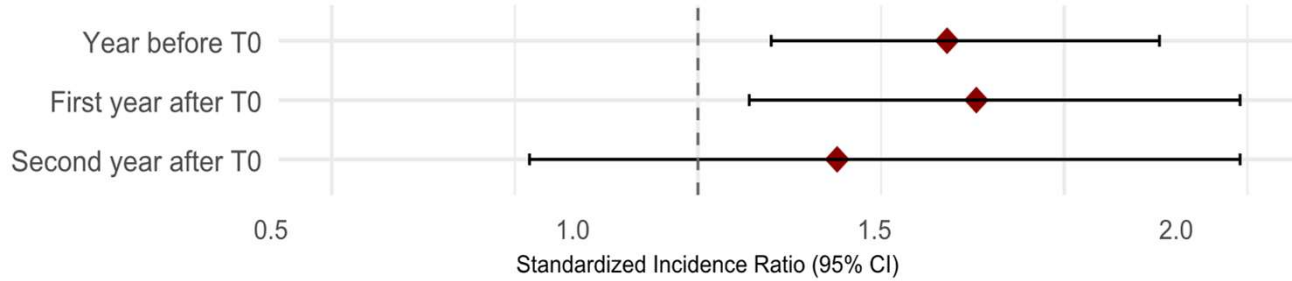
Primary analysis

JAKi cohort



SIR	Person-years (PY)	Number of events	Incidence per 1,000 PY
0.69 [0.18 ; 1.76]	4,237	<11*	<2.60*
0.84 [0.17 ; 2.45]	2,627	<11*	<2.60*
	872	0	

Biologic cohort



SIR	Person-years (PY)	Number of events	Incidence per 1,000 PY
1.34 [1.10 ; 1.63]	23,187	104	4.49
1.38 [1.07 ; 1.74]	16,085	70	4.35
1.19 [0.77 ; 1.74]	7,647	26	3.40

Sensitivity analyses:

Expanded outcomes: similar results in the JAKi and biologic cohorts

Standardization for CV risk: similar results in the JAKi cohort; **significance lost in the biologic cohort**

* According to SNDS rules, exact counts are not provided when the number of events is <11, to avoid the risk of re-identification.

4 Discussion – Main results

JAKi cohort

No increased risk of MACE observed in AD patients treated with JAKi compared with the general population

Biologic cohort

Year before T0
1st year after T0
→ Risk of MACE

2nd year after T0
Standardization for CV risk
→ Not significant

Application of health authorities' recommendations

Limiting JAKi's use in cardiovascular risk patients

PRAC+ : 17% in JAKi cohort vs 38% in biologic cohort

In line with previous large-scale studies

2 recent studies[1,2] using the TriNetX database: no evidence of increased risk of MACE in AD patients treated with JAKi versus dupilumab

[1]*Tsai et al. J Allergy Clin Immunol 2024*
[2]*Kridin et al. J Eur Acad Dermatol Venereol 2025*

AD an independent CV risk factor ?

Inconsistent results in literature

Increased risk of unstable angina in previous large-scale studies (*Silverwood et al. BMJ 2018*)

Role of AD's induced systemic inflammation ?

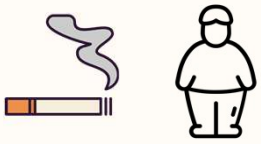
4 Discussion – Strengths and limits

Strengths

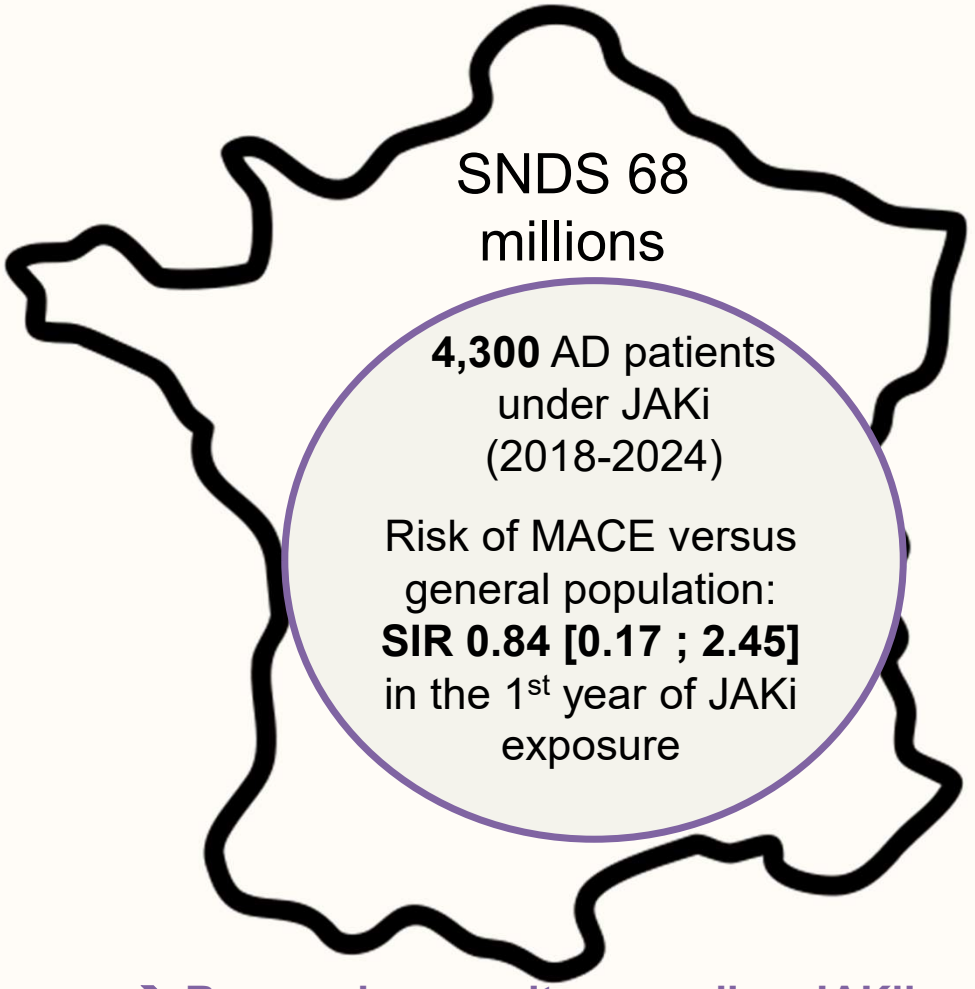
1. Database = 98% of the French population
No attrition bias
2. Real world data in an unselected AD population versus selected patients in randomized control trials
3. General population as comparator to assess the cardiovascular risk of each treatment
4. Strict algorithm to identify AD, limiting indication bias

Limitations

1. Lack of power: low number of events
➔ but a significant number of JAKi exposed patients (4,300)
2. Principal outcome not including cardiovascular death ➔ identification of limited reliability in the SNDS
3. Some data are complex to identify in the SNDS
➔ non-differential between cohorts



Conclusion



➔ **Reassuring results regarding JAKi's cardiovascular safety in AD patients in the context of current recommendations**