Journeying Through Evidence: Scoping the Revival of Anti-TNF Alpha in **Psoriasis Treatment and Cardiovascular Risk Reduction**

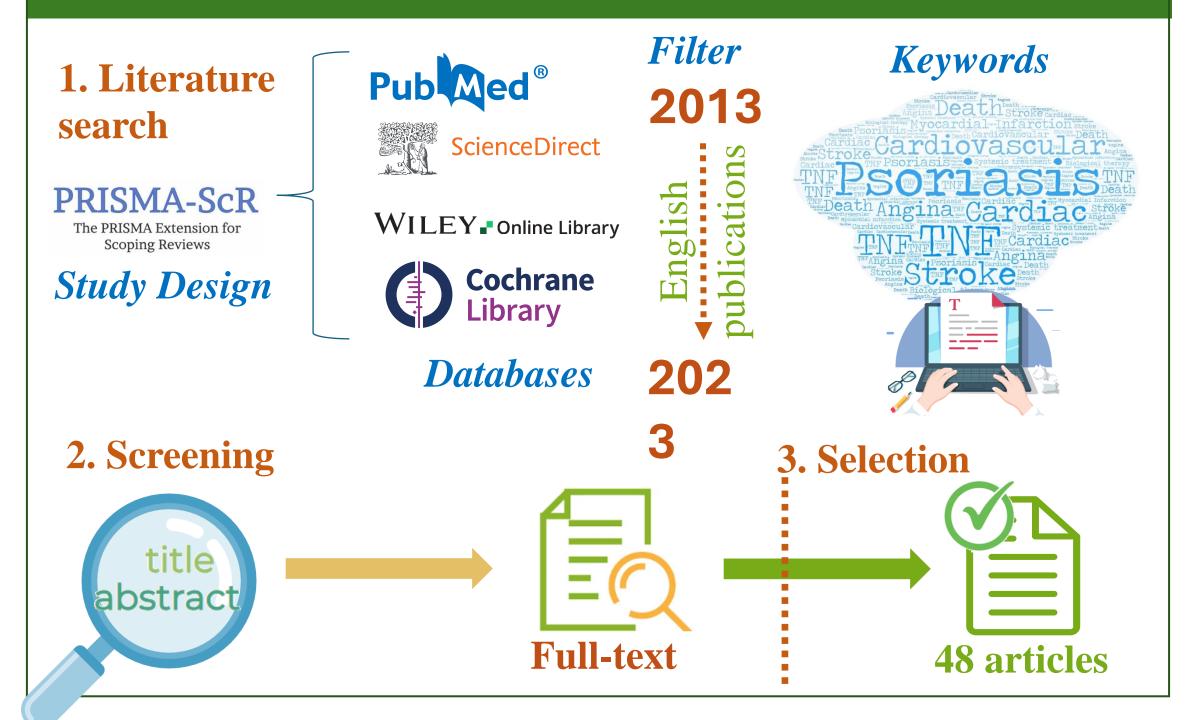
Son MAI^{1,2}, Thomas FRANCK³, Pauline GOUTTEFARDE^{3,4,5}, Yves MBAMA⁴, Gilles CIZERON¹, Mathieu ORIOL¹, François MACCARI⁶, Beatrice TROMBERT^{5,7}, Jean-Luc PERROT^{6,9,10}, Bienvenu BONGUE^{1,8}

¹Technical Support and Training Center for Health Examination Centers (CETAF); ²Science Engineering, Health, Jean Monnet University; ³Gérontopôle Auvergne Rhône Alpes (AURA); ⁴Institut PRESAGE, Jean Monnet University; ⁵SAINBIOSE Laboratory; ⁶RESO; ⁷CHU of Saint Etienne; ⁸Saint Etienne Dermatology University Hospital; ⁹Laboratory of Tribology of Systems UMR CNRS 5513; ¹⁰Elderly Health, Jean Monnet University.

INTRODUCTION

- 2%-3% of the world's population suffer from psoriasis, imposing significant physical and psychological burdens on patients¹. There is no cure for psoriasis, but it is **TREATABLE**².
- Mounting evidence suggests a potential revival of Anti-tumor necrosis factor alpha \bullet (anti-TNF- α) therapy, driven by insights into its efficacy, safety profile, and intriguing cardio-protective properties³.
- This review seeks to navigate the existing literature, mapping the landscape of **anti-**

METHODS



TNF-\alpha's resurgence in psoriasis treatment and its implications for cardiovascular risk reduction.

RESULTS

TNF-\alpha inhibitors, exhibit a low and stable rate of cardiac events (CEs) over the last 10 years. Studies from 2013 to 2023, including randomized controlled trials (RCTs) and cohorts involving 254,051 psoriasis patients, affirm the safety of adalimumab, etanercept, infliximab, certolizumab, and golimumab, suggesting their long-term use poses no significant CE risks.

Cardiac-related risk profiles in psoriasis-treated patients with TNF-α

Treatment	Time points	Cardiac Events (CEs)	Major CEs	Heart failure	Myocardial infarction	Stroke	Angina	CE deaths		Cardiac Risks	
Adalimumab	3 months - 12 months	0 (0.0) ⁽⁴⁾	0 (0.0) ⁽¹⁰⁾	0 (0.0) ⁽¹⁸⁾	2 (0.8) ⁽²³⁾		1 (0.3) (26)		6 months - 1 years		
		2 (1.9) ⁽⁵⁾	0 (0.0) ⁽¹¹⁾	1 (0.9) ⁽¹⁹⁾	1 (0.2) ⁽²⁴⁾				Composed TNF-α (vs baseline) ⁽⁴²⁾		
		1 (3.1) ⁽⁶⁾	0 (0.0) ⁽¹²⁾		2 (0.1) ⁽¹⁶⁾				Reduced risks ***		
			2 (0.7) ⁽¹³⁾						Adalimumab (vs baseline) ⁽⁴³⁾		
			IR=0.0 ⁽¹⁴⁾						Reduced risks ***		
			IR=1.6 ⁽¹⁵⁾						Adalimumab (vs Healthy subjects) ⁽⁴⁴⁾		
			IR=0.5 ⁽¹⁶⁾						Reduced risks ***		
	1-12 years	9 (2.9) ⁽⁷⁾	IR=0.5 ⁽¹⁷⁾	3 (IR=0.3) ⁽²⁰⁾	1 (1.3) ⁽²⁵⁾	ID-0 4 ⁽¹⁷⁾	3 (1.9) ⁽²⁵⁾	2 (0.06) ⁽²²⁾	Up to 15 years		
			IK-0.0		22 (IR<0.1) ⁽²¹⁾		5 (1.9)	2 (0.00)	Composed TNF-α (vs non-PsO) ⁽⁴⁵⁾ Reduced risks***		
		2 (0.4) ⁽⁸⁾		11 (IR<0.1) ⁽²¹⁾					Composed TNF-a (vs phototherapy) ⁽⁴⁶⁾		
	0	IR=0.5 ⁽⁹⁾		14 (0.3) ⁽²²⁾	IR=0.2 ⁽¹⁷⁾				Reduced risks		
Certolizumab Pegol	3 months - 12 months			0 (0.0) ⁽²⁹⁾					(HR= 0.9, 0.76-0.95)**		C
	>12 months		10 (2.5, IR=0.8) ⁽²⁷⁾	IR=0.1 ⁽³⁰⁾	IR=0.1 ⁽³⁰⁾	_	IR=0.1 ⁽³⁰⁾	2 (0.5, IR=0.2) ⁽²⁷⁾	Adalimumab (vs Methotrexate) ⁽⁴⁷⁾		
	-12 years		IR=0.4 ⁽²⁸⁾			_			Increased risk		
Etanercept	3 months - 12	0 (0.0) ⁽³¹⁾	IR=0.3 ⁽³²⁾	1 (1.2) ⁽³³⁾	1 (1.4) ⁽³⁵⁾		1 (4.3) ⁽³⁷⁾		(IRR=3.6, 1.3-9.7)**		
	months	0 (0.0) ⁽⁴⁾		- ()	1 (0.1) ⁽³⁶⁾		- ()			Maias Operation Diales	
	>12 months	3 (1.7) ⁽⁸⁾		14 (0.6) ⁽³⁴⁾	17 (0.7) ⁽³⁴⁾			1 (0.04) ⁽³⁴⁾		Major Cardiac Risks	
	-12 years	IR=0.4 ⁽⁹⁾		14 (0.0)	17 (0.77			1 (0.04)	I		
Golimumab	3 months - 12				(00)					Up to 15 years	
	months				1 (0.4) ⁽³⁹⁾				Myocardial infarction	Stroke	
	>12 months	a (a a) ⁽³⁸⁾				_			Composed TNF-a (vs Methotrexate) ⁽⁵¹⁾	Composed TNF-a (vs ⁽⁵¹⁾	¹⁾ C
	-12 years	0 (0.0) ⁽³⁸⁾							Reduced risks	Methotrexate	
Infliximab	3 months - 12				1 (6.3) ⁽⁴⁾				(HR= 0.5, 0.34-0.71)***	Reduced risks	
	months				1 (0.5)				Composed TNF-a (vs topical	(HR= 0.6, 0.42-0.71)***	1.
	>12 months	13 (IR=0.9) ⁽⁴⁰⁾		1 (0.5) ⁽⁴¹⁾	3 (0.6) ⁽⁴¹⁾				agents) ⁽⁴²⁾ Significantly lower ricks		
	-12 years			- (0.0)	- (0.0)				Significantly lower risks		

- TNF-α reduced hazard risks for cardiac events (CEs), major CEs. myocardial infarction (MI), stroke, and angina.
- Adalimumab lowered cardiovascular biomarkers, but a longterm study noted increased cardiac disorder risk.
- Other TNF- α individual drugs do not have an effect on CE risks. lacksquare

Association of TNF- α and CEs in patients with psoriasis

Treatment	Time points	Cardiac Events (CEs)	Major CEs	Heart failure	Myocardial infarction	Stroke	Angina	CE deaths		Cardiac Risks	
Adalimumab	3 months - 12 months	0 (0.0) ⁽⁴⁾	0 (0.0) ⁽¹⁰⁾	0 (0.0) ⁽¹⁸⁾	2 (0.8) ⁽²³⁾		1 (0.3) (26)		6 months - 1 years		
		2 (1.9) ⁽⁵⁾	0 (0.0) ⁽¹¹⁾	1 (0.9) (19)	1 (0.2) ⁽²⁴⁾				Composed TNF-α (vs baseline) ⁽⁴²⁾		6 months - 1 years
		1 (3.1) ⁽⁶⁾	0 (0.0) ⁽¹²⁾		2 (0.1) ⁽¹⁶⁾				Reduced risks ***		Composed TNF-α (vs topical
			2 (0.7) ⁽¹³⁾						Adalimumab (vs baseline) ⁽⁴³⁾		therapy) ⁽⁴⁸⁾
			IR=0.0 ⁽¹⁴⁾						Reduced risks ***		Reduced risks**
			IR=1.6 ⁽¹⁵⁾						Adalimumab (vs Healthy subjects) ⁽⁴⁴⁾		Up to 15 years
			IR=0.5 ⁽¹⁶⁾						Reduced risks ***		Composed TNF-α (vs other
		9 (2.9) ⁽⁷⁾	IR=0.5 ⁽¹⁷⁾	3 (IR=0.3) ⁽²⁰⁾	1 (1.3) ⁽²⁵⁾	ID=0 4 ⁽¹⁷⁾	3 (1.9) ⁽²⁵⁾	2 (0.06) ⁽²²⁾	Up to 15 years Composed TNF-α (vs non-PsO) ⁽⁴⁵⁾		Reduced risk (HR= 0.5, 0.22-0.98)*
	1-12 years	2 (0.4) ⁽⁸⁾	IN-0.0	11 (IR<0.1) ⁽²¹⁾	22 (IR<0.1) ⁽²¹⁾		5 (1.5)	2 (0.00)	Reduced risks***		Composed TNF-α (vs Bio-na
		2 (0.4) IR=0.5 ⁽⁹⁾		14 (0.3) ⁽²²⁾	IR=0.2 ⁽¹⁷⁾				Composed TNF-a (vs phototherapy) ⁽⁴⁶⁾		Reduced risks
Certolizumab Pegol	3 months - 12	IK=0.0			IK=U.Z [*]				Reduced risks		(H=0.8, 0.60-0.99)*
	months			0 (0.0) ⁽²⁹⁾					(HR= 0.9, 0.76-0.95)**		Composed TNF-α (vs Methotre
	>12 months	_	10 (2.5, IR=0.8) ⁽²⁷⁾	IR=0.1 ⁽³⁰⁾	IR=0.1 ⁽³⁰⁾	_	IB=0 1 ⁽³⁰⁾	2 (0.5, IR=0.2) ⁽²⁷⁾	Adalimumab (vs Methotrexate) ⁽⁴⁷⁾		Reduced risks
	-12 years		IR=0.4 ⁽²⁸⁾	111 0.1		-		2 (0.0, 11 0.2)	Increased risk		(HR= 0.6, 0.45-0.67)***
	3 months - 12	0 (0.0) ⁽³¹⁾	IR=0.3 ⁽³²⁾	1 (1.2) ⁽³³⁾	1 (1.4) ⁽³⁵⁾		1 (4.3) ⁽³⁷⁾		(IRR=3.6, 1.3-9.7)**		Ī
Etanercept	months	0 (0.0) ⁽⁴⁾	IN 0.0	1 (1.2)	1 (0.1) ⁽³⁶⁾		1 (4.0)				
	>12 months	3 (1.7) ⁽⁸⁾		14 (0.6) ⁽³⁴⁾	17 (0.7) ⁽³⁴⁾			1 (0.04) ⁽³⁴⁾		Major Cardiac Risks	
	-12 years	IR=0.4 ⁽⁹⁾		14 (0.0)	17 (0.7)			1 (0.04)			
Golimumab	3 months - 12	IK-0.4							▼	Up to 15 years	*
	months				1 (0.4) ⁽³⁹⁾				Myocardial infarction	Stroke	Angina
	>12 months	(20)				_			Composed TNF-α (vs Methotrexate) ⁽⁵¹⁾	Composed TNF-a (vs ⁽⁵¹⁾	Composed TNF-a (vs Methotre
	-12 years	0 (0.0) ⁽³⁸⁾							Reduced risks	Methotrexate	Reduced risks
Infliximab	3 months - 12				1 (C 2)(4)				(HR= 0.5, 0.34-0.71)***	Reduced risks	(HR=0.6, 0.41-0.82)**
	months				1 (6.3) ⁽⁴⁾				Composed TNF-a (vs topical	(HR= 0.6, 0.42-0.71)***	
	>12 months	13 (IR=0.9) ⁽⁴⁰⁾		1 (0.5) ⁽⁴¹⁾	3 (0.6) ⁽⁴¹⁾				agents) ⁽⁴²⁾		
	-12 years	10 (11 0.0)		1 (0.0)	0 (0.0)				Significantly lower risks		

CONCLUSIONS

• TNF-α inhibitors are better than non-biologic psoriasis meds and even no systemic therapy, as they lower the risk of stroke and heart problems

• TNF-α inhibitors could be considered earlier in the treatment algorithm, before anti-IL17 or IL23 agents, thank to their potential cardiovascular

benefits and the chance of reaching PASI 90.

Further long-term studies are warranted to delineate their precise cardiovascular effects and optimize treatment strategies in psoriasis management.

References

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