

# **Risk of Serious Infection Associated with Different Classes of Targeted Therapies Used in Psoriatic Arthritis:**

**A Nationwide Cohort Study from The French Health Insurance Database**

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# Disclosure

**I have no relevant financial relationship(s) with ineligible companies to disclose**

- ▶ Psoriatic arthritis (PsA) is an inflammatory disease associated with psoriasis and numerous comorbidities<sup>1</sup>
- ▶ Targeted therapies are recommended when standard treatments (csDMARDs, NSAIDs) fail to control the rheumatism or are not tolerated<sup>2</sup>
- ▶ Concerns regarding their potential infectious risk<sup>3,4,5</sup>
- ▶ Few is known in PsA with limits of existing randomized trials<sup>6,7</sup>

<sup>1</sup>Ritchlin *et al.* N Engl J Med 2017. <sup>2</sup>Gossec *et al.* Ann Rheum Dis 2023. <sup>3</sup>Winthrop *et al.* Ann Rheum Dis 2015. <sup>4</sup>Lortholary *et al.* Ann Rheum Dis 2020. <sup>5</sup>Christensen *et al.* Ann Rheum Dis 2021. <sup>6</sup>McInnes *et al.* Lancet Lond Engl 2020. <sup>7</sup>Mease *et al.* N Engl J Med 2017.

## Cohort study of new users of a targeted therapy for PsA

1

To assess the incidence rates of serious infections for each molecule and to describe the cases

2

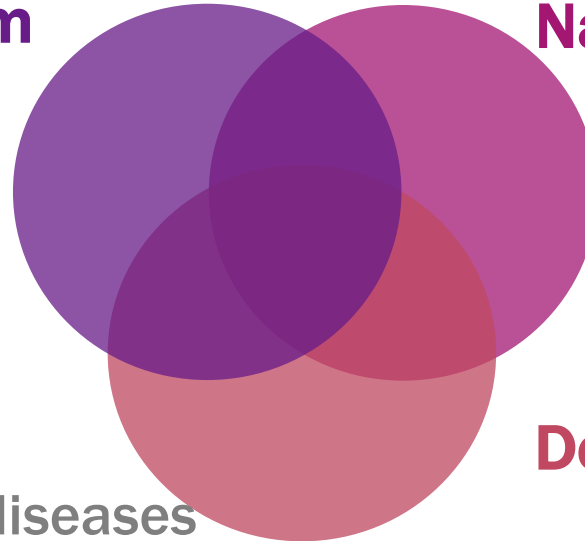
To estimate the risk of serious infections according to the molecule, taking into account confounding factors

## French National Health Insurance Database (SNDS)<sup>1</sup>

≈ 99% of the French population

### National Health Insurance System

- Age
- Sex
- Degree of social deprivation<sup>2</sup>
- Pharmacy-dispensed drugs
- Medical/paramedical acts
- Fully reimbursed care for costly diseases



### National Hospital Discharge System

- Admission/discharge dates
- Diagnosis ICD-10 codes

### Death Certificate Base

<sup>1</sup>Tupin *et al.* Rev Epidemiol Sante Publique 2017. <sup>2</sup>Temam *et al.* BMC Public Health 2017.

### ▶ All adults identified with PsA

ICD-10 codes: M07 except M07.4 and M07.5

- Inpatients with the ICD-10 diagnostic code for PsA
- Patients with fully reimbursed procedures related to PsA

### ▶ New users of a targeted therapy (“first line”)

- New users: no prescription for a targeted therapy the year before inclusion
- Targeted therapies: TNFi (adalimumab, certolizumab, etanercept, golimumab, infliximab); IL17i (ixekizumab, secukinumab); IL12/23i (ustekinumab); JAKi (tofacitinib)

### ▶ Exclusion of patients:

With HIV, cancer, transplant, or serious infection within 2 yrs. before inclusion

### Occurrence of a Serious Infection

- Defined by a hospital discharge diagnosis of an infection<sup>1</sup>
- Assessed according to the affected organ
- Only the first occurrence of a serious infection studied

<sup>1</sup>Sahli *et al.* Pharmacoepidemiol Drug Saf 2016.

- ▶ **Inclusion: from January 1, 2015 to June 30, 2021**
  
- ▶ **Study end point: on December 31, 2021**
  
- ▶ **Follow-up until:**
  - Main outcome
  - Death
  - End of treatment exposure
  - Lost to follow-up
  - Study end point



## ► Sociodemographic:

Age, sex, deprivation index<sup>1</sup>

## ► Associated inflammatory diseases:

Psoriasis, IBD, uveitis

## ► Comorbidities:

Diabetes, cardiovascular diseases, chronic respiratory diseases, chronic renal failure, chronic liver disease, obesity (proxy), tobacco use (proxy), alcohol use (proxy)

## ► Other treatments of interest:

csDMARDs, NSAIDs, prednisone

## ► Care consumption:

Hospitalization for PsA, specialist consultation, corticosteroids injections, opioids use, work stoppage

<sup>1</sup>Temam *et al.* BMC Public Health 2017.

- ▶ **Time-to-event analysis using a Cox model**
- ▶ **Weighted by the inverse of propensity score (IPTW)**  
Estimated with a multinomial logistic regression model
- ▶ **Adjusted for:**
  - Time-dependent covariates (csDMARDs, NSAIDs, prednisone during follow-up)
  - Calendar year
- ▶ **Use of the Sandwich estimator**

### ▶ Subgroup analysis:

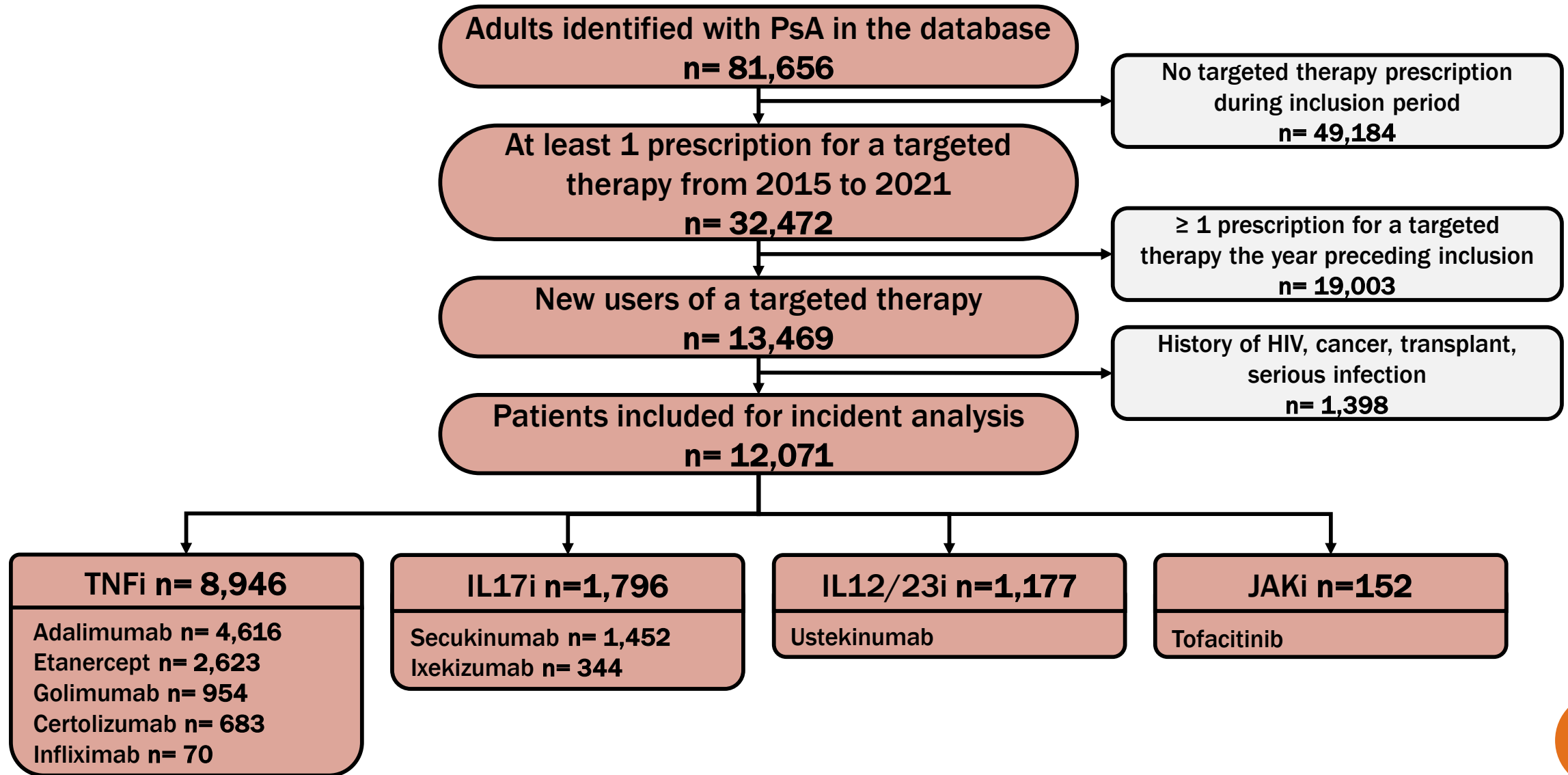
Patients without active skin psoriasis

### ▶ Sensitivity analyses:

- Modifying the treatment exposure
- Modifying the definition of new users
- Excluding the COVID pandemic period
- Fine & Gray model
- Conventional Cox model
- Weighted and trimmed propensity score
- 1:1 propensity score-matching

# Results

## Flow of Participants



# Results

## Patients Characteristics

Characteristics No. (%)	<b>TOTAL</b> n = 12071	ADALI n = 4616	ETANE n = 2623	GOLIM n = 954	CERTO n = 683	INFLIX n = 70	SECUK n = 1452	IXEKI n = 344	USTEK n = 1177	TOFAC n = 152
Follow-up, median (IQR)	<b>13 (6-32)</b>	13 (6-30)	13 (6-37)	14 (7-36)	11 (6-28)	11 (6-33)	15 (7-30)	13 (7-22)	17 (9-37)	9 (5-14)
Sociodemographics										
Age, mean (SD)	49 (13)	48 (13)	51 (13)	48 (12)	44 (13)	50 (15)	49 (12)	49 (12)	50 (13)	53 (13)
Female sex	6965 (58)	2538 (55)	1554 (59)	557 (58)	513 (75)	41 (59)	818 (56)	181 (53)	649 (55)	114 (75)
Associated inflammatory diseases										
Active psoriasis	3700 (31)	1382 (30)	645 (25)	163 (17)	139 (20)	12 (17)	556 (38)	174 (51)	601 (51)	28 (18)
IBD	569 (5)	378 (8)	14 (0.5)	46 (5)	21 (3)	21 (30)	11 (0.8)	2 (0.6)	69 (6)	7 (5)
Other treatments of interest at baseline										
csDMARDs	5207 (43)	2021 (44)	1282 (49)	478 (50)	306 (45)	23 (33)	520 (36)	124 (36)	373 (32)	80 (53)
NSAIDs	4297 (36)	1644 (36)	1129 (43)	405 (43)	264 (39)	23 (33)	504 (35)	82 (24)	322 (27)	33 (22)
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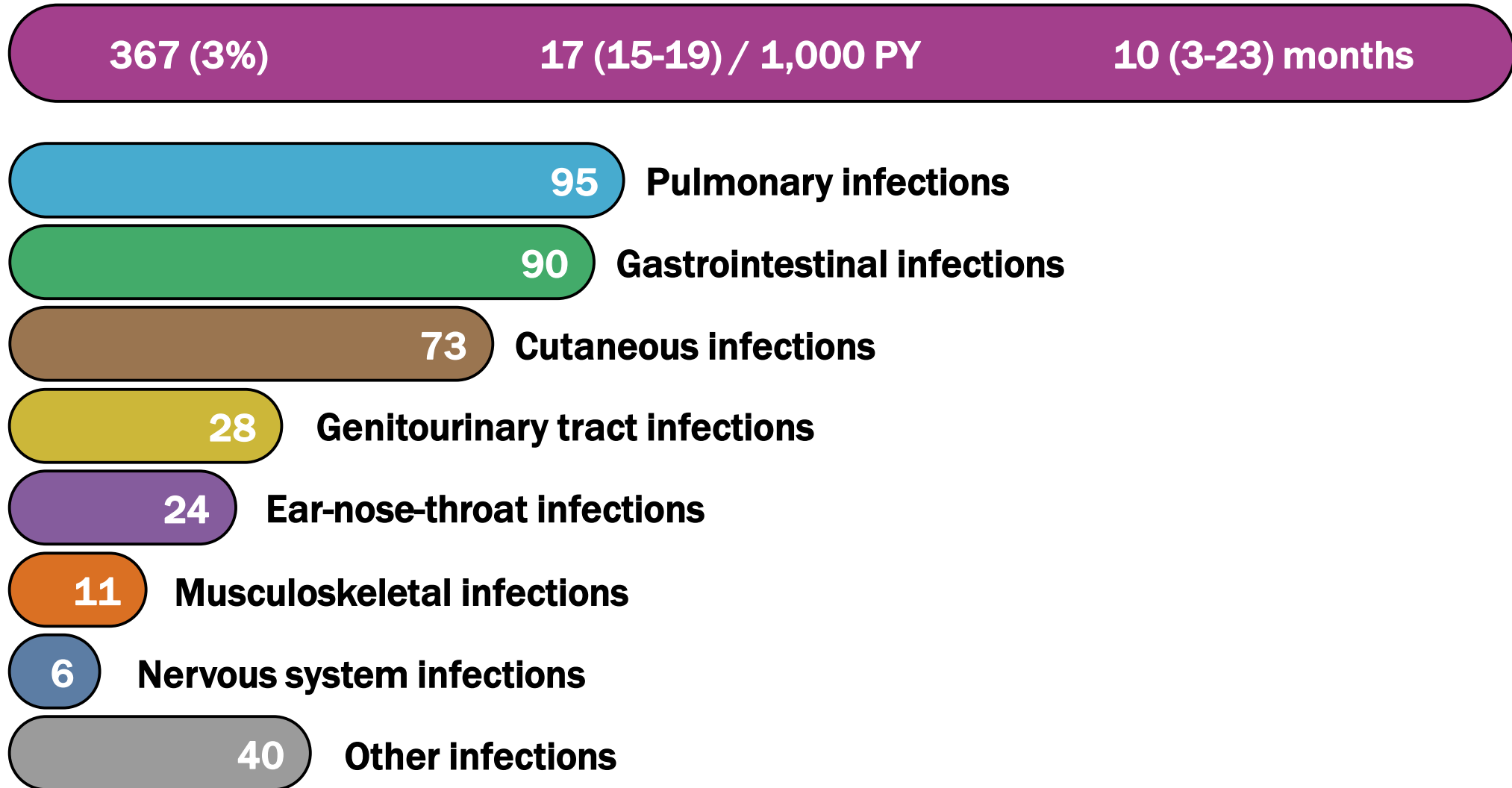
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Adalimumab	19 (16-22)	150 (3)
Etanercept	14 (11-18)	73 (3)
Golimumab	13 (8-18)	24 (3)
Certolizumab	15 (8-22)	17 (3)
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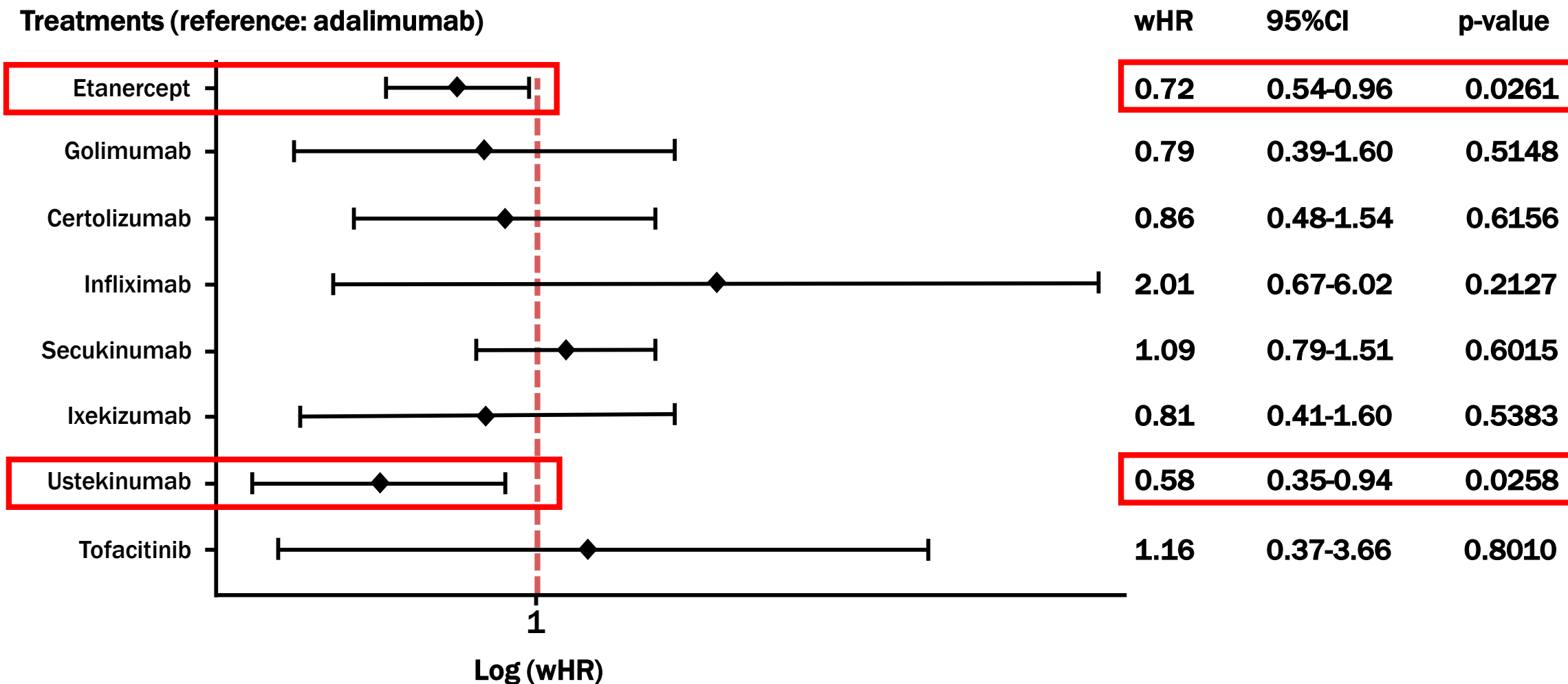
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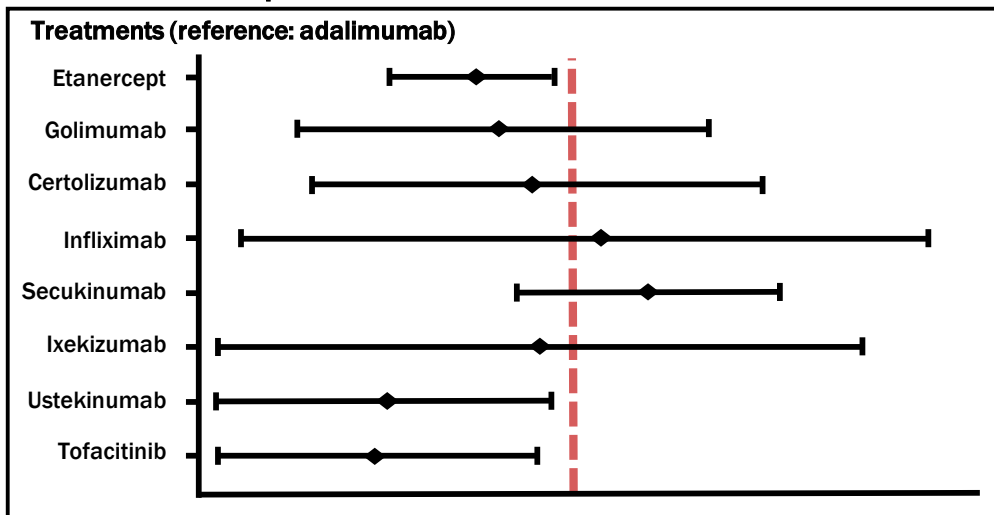
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## Adjusted IPTW Cox Model

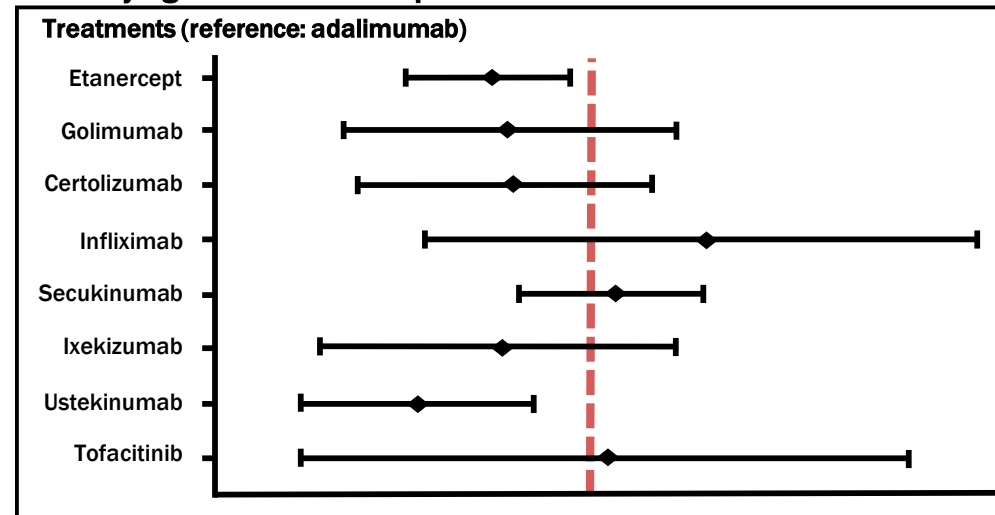
Treatments (reference: adalimumab)



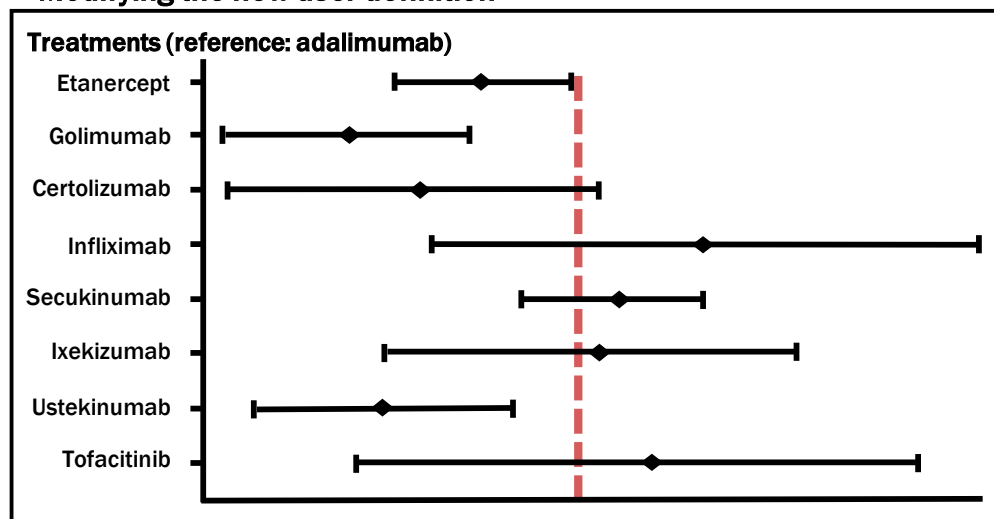
## Patients without psoriasis



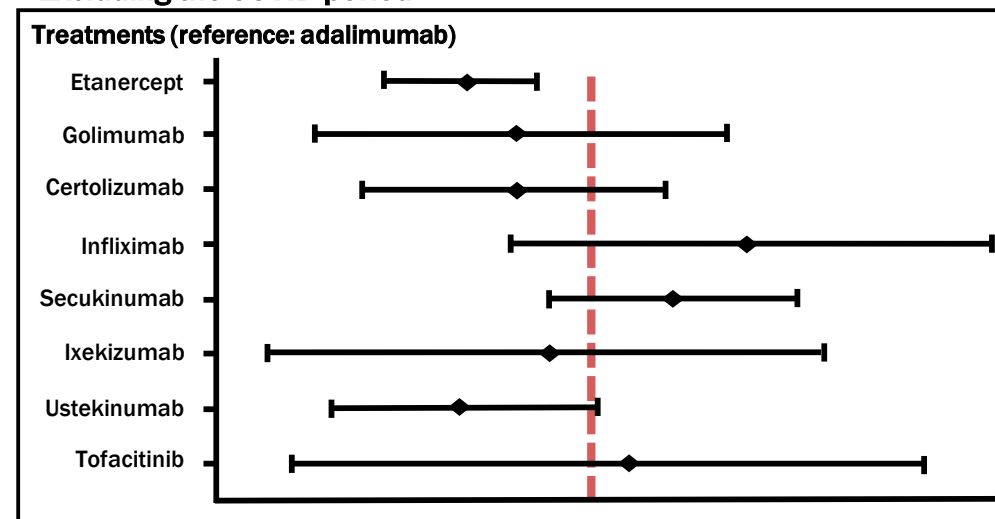
## Modifying the treatment exposure



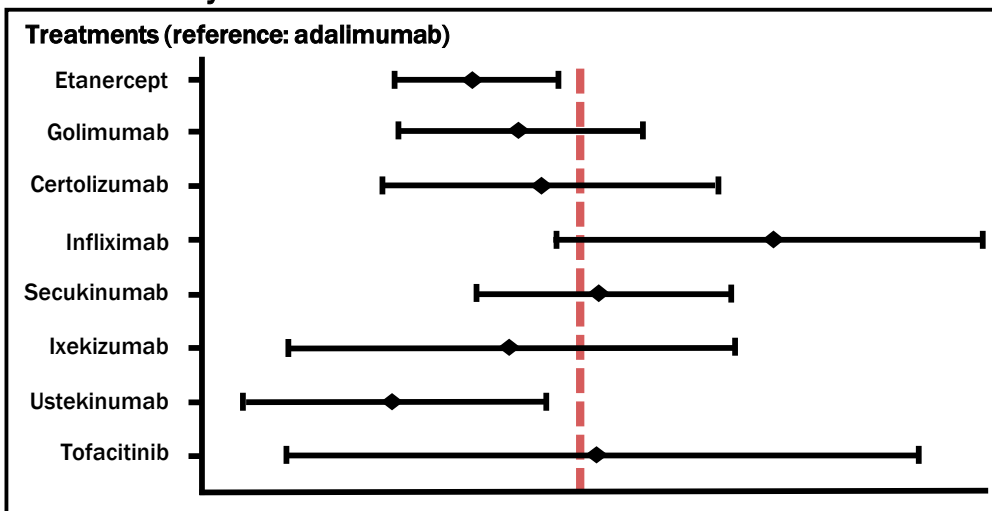
## Modifying the new user definition



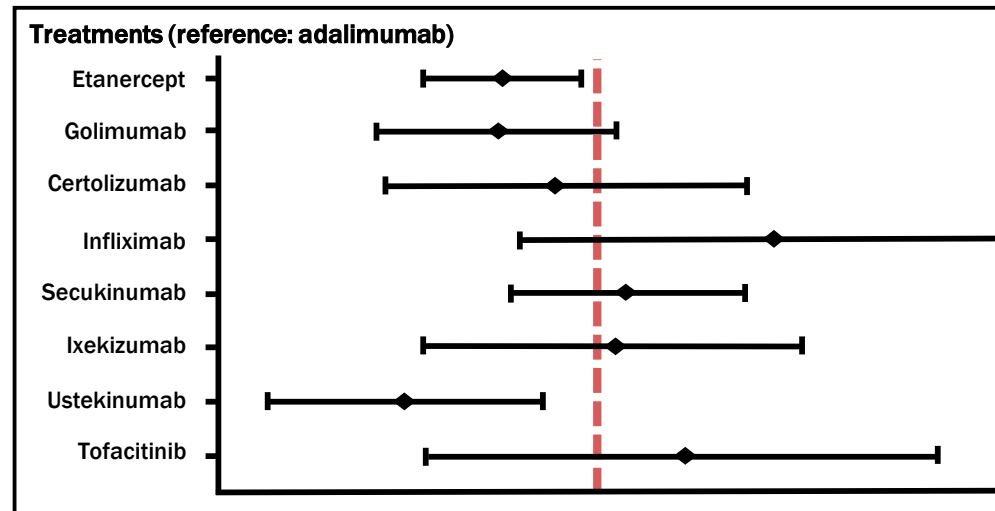
## Excluding the COVID period



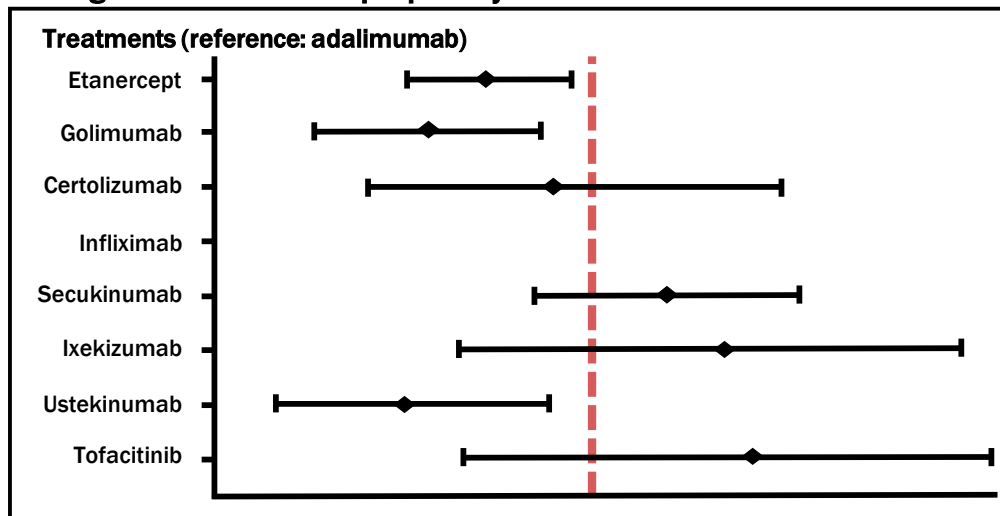
**Fine and Gray model**



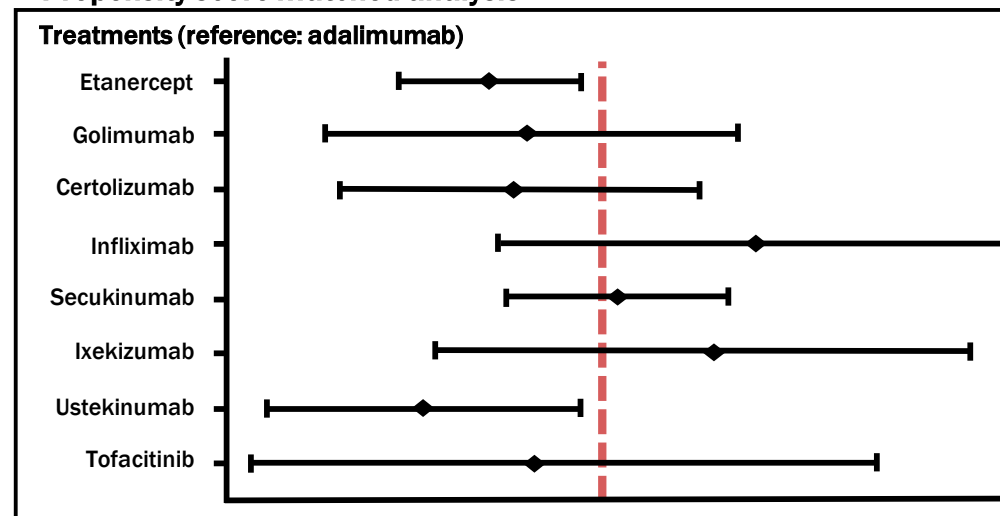
**Conventional Cox model**



**Weighted and trimmed propensity score**



**Propensity score matched analysis**



### ► Database:

- + Large sample size
- Treatment exposure based on fulfillment of a prescription
- Data availability for some covariates

### ► Statistical method:

- + Use of a propensity score with consistent results
- Unmeasured confounders

### ► Comparison of different molecules separately

- ▶ Overall low risk of serious infection with incidence rates similar to those found in other studies<sup>1,2</sup>
- ▶ Significantly lower risk among new users of etanercept and ustekinumab as compared to adalimumab new users<sup>3,4,5</sup>
- ▶ Other large-scale studies are needed to confirm the results and assess this risk with the newest molecules to optimize therapeutic choices

<sup>1</sup>Li *et al.* Ann Rheum Dis 2020. <sup>2</sup>Jin *et al.* Arthritis Care Res 2021. <sup>3</sup>Kalb *et al.* JAMA Dermatol. 2015. <sup>4</sup>Penso *et al.* JAMA Dermatol. 2021. <sup>5</sup>Gossec *et al.* Ann Rheum Dis 2023.

# Acknowledgements

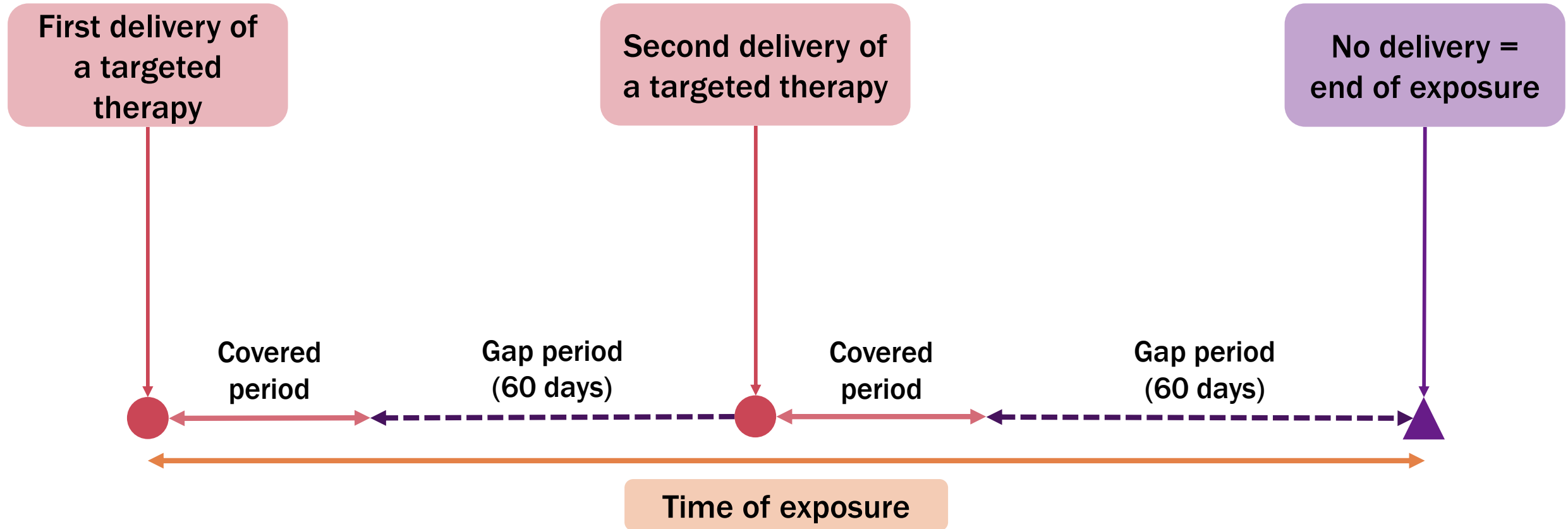
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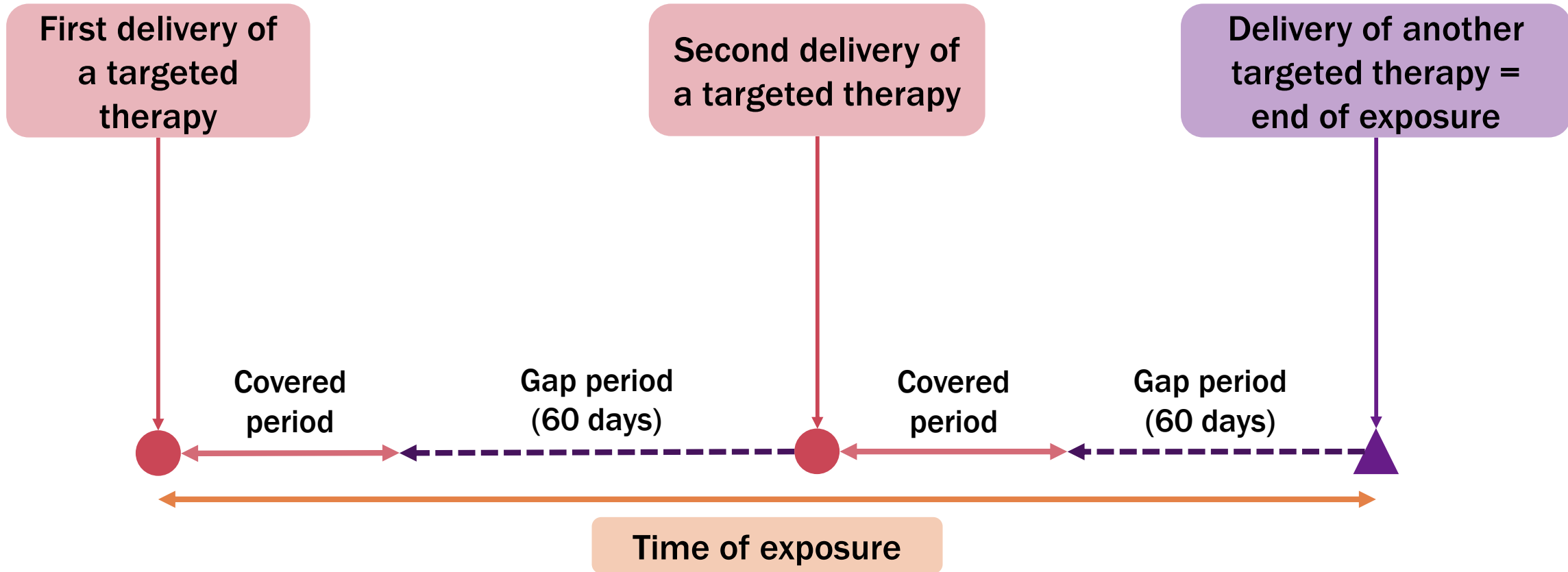
This work was supported by the French Society of Rheumatology

(Grant Master 2<sup>nd</sup> year 2022)



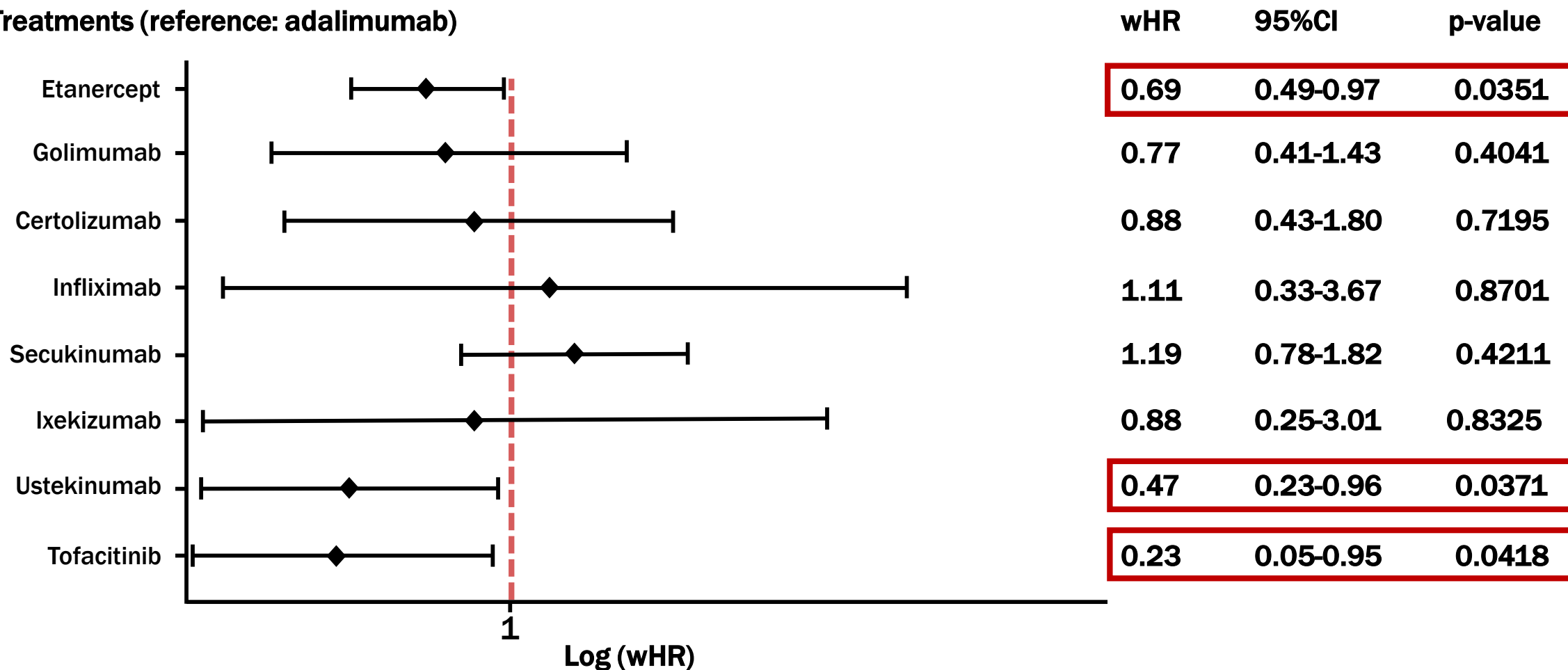






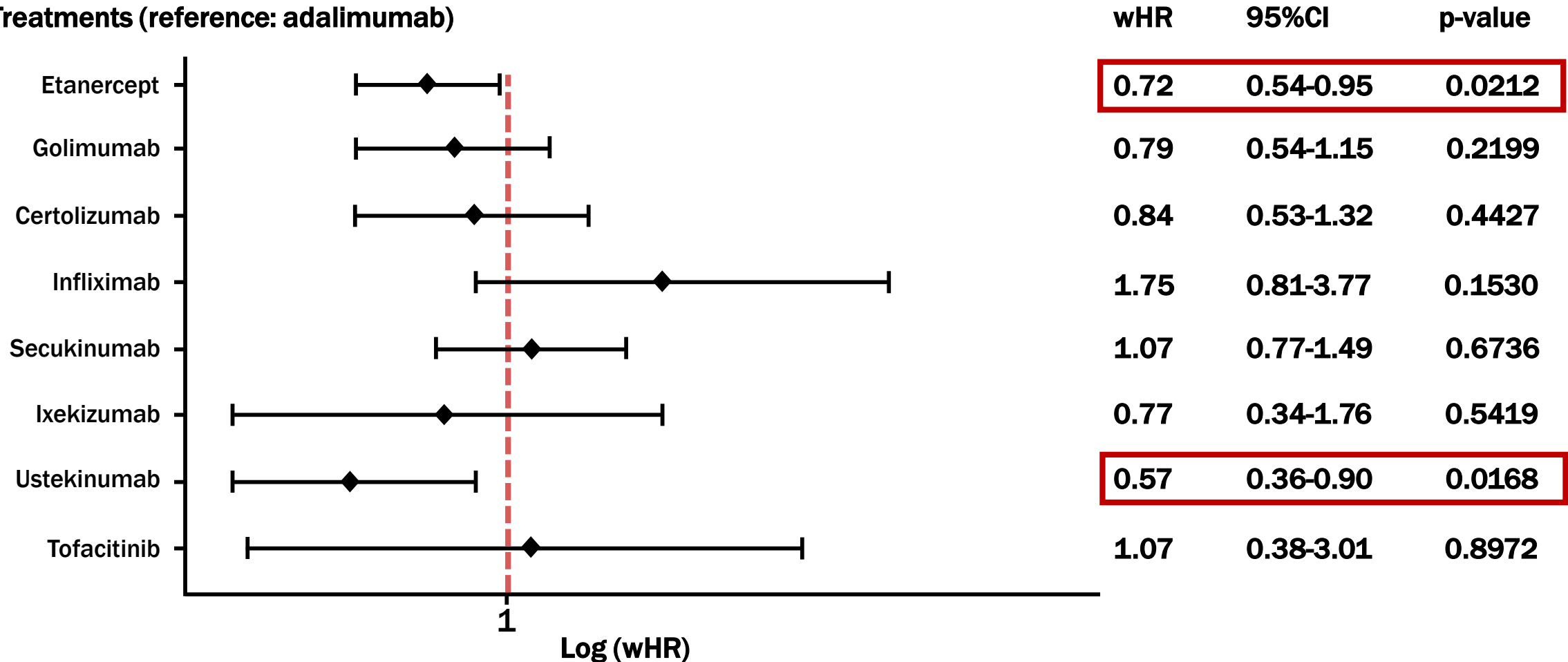
## Subgroup analysis: patients without psoriasis

Treatments (reference: adalimumab)



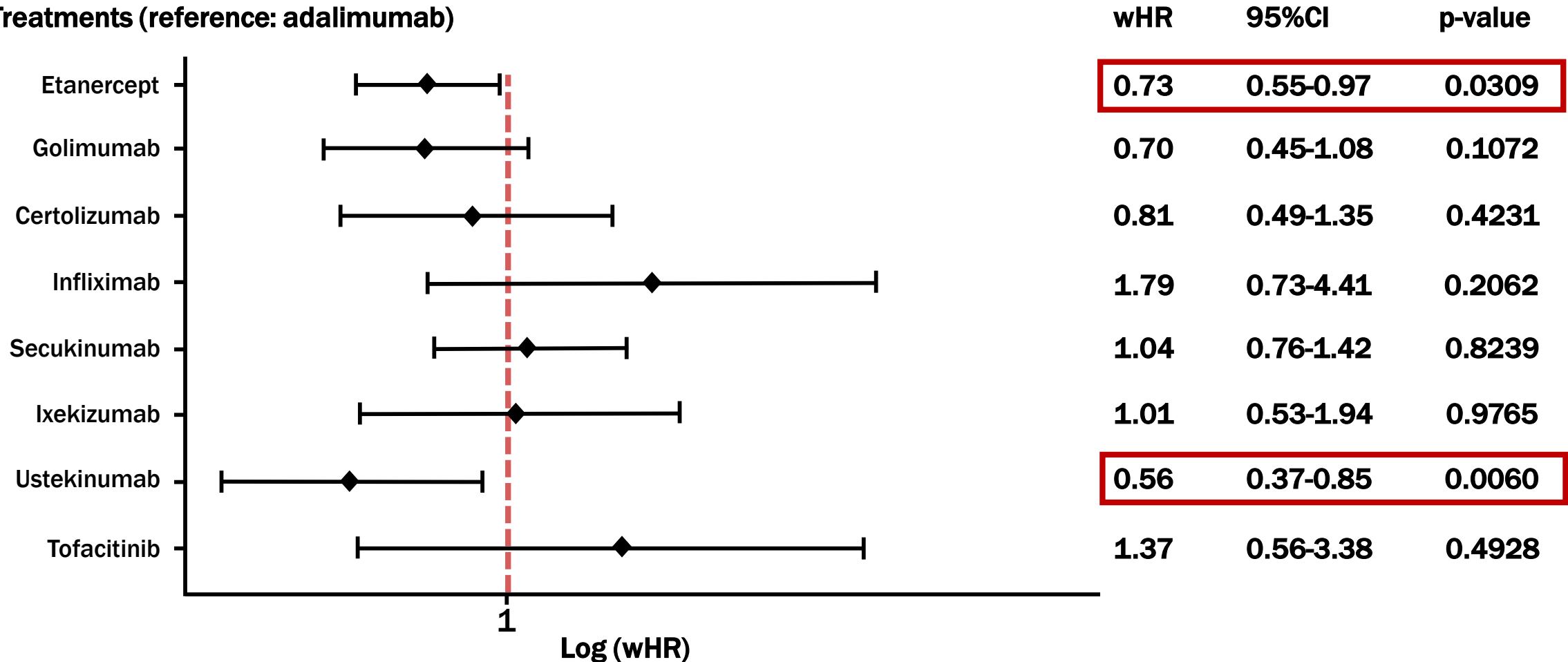
## Sensitivity analysis: Fine & Gray model

Treatments (reference: adalimumab)



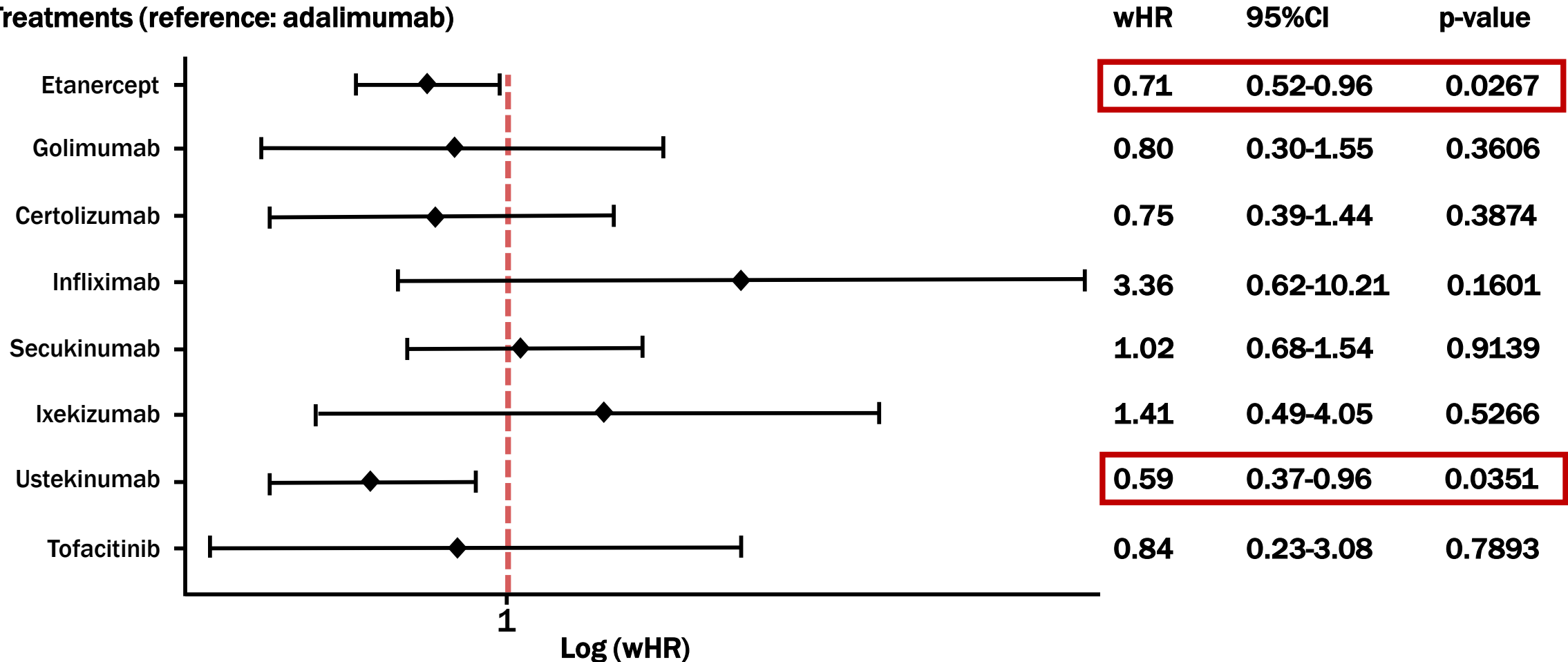
## Sensitivity analysis: Conventional Cox model

Treatments (reference: adalimumab)



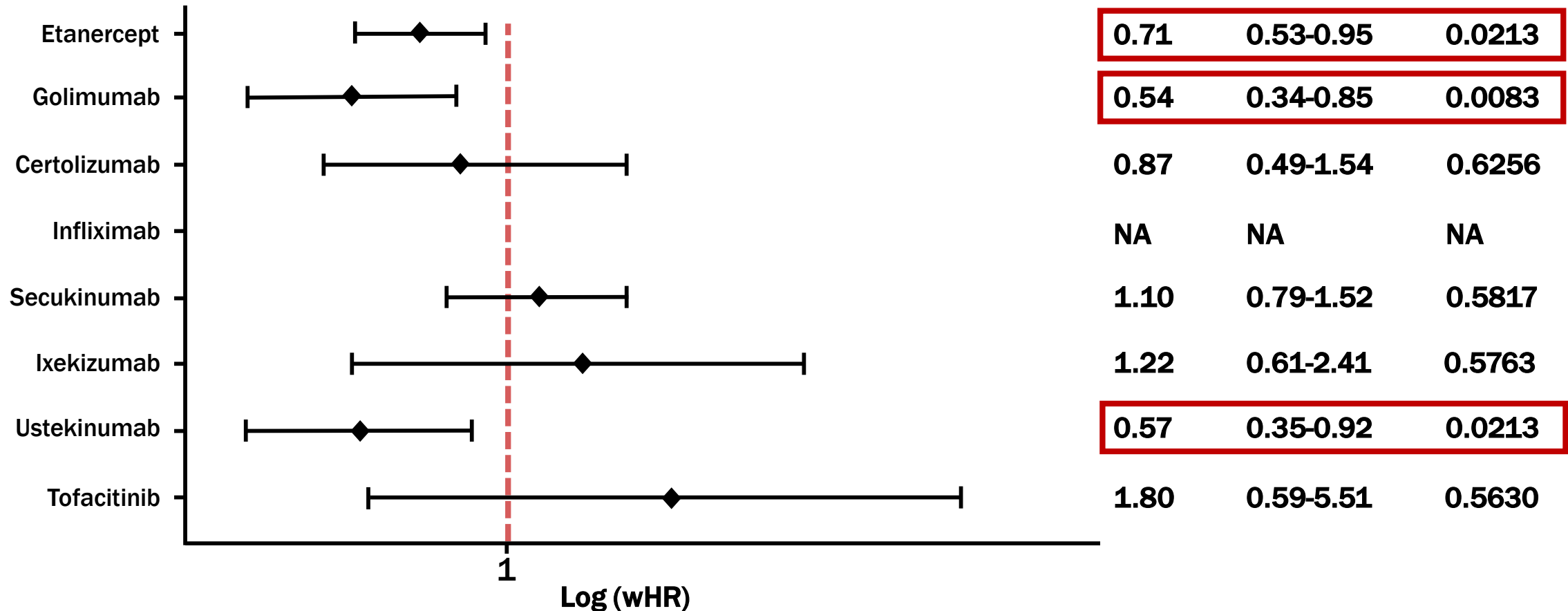
## Sensitivity analysis: Propensity score matching 1:1

Treatments (reference: adalimumab)



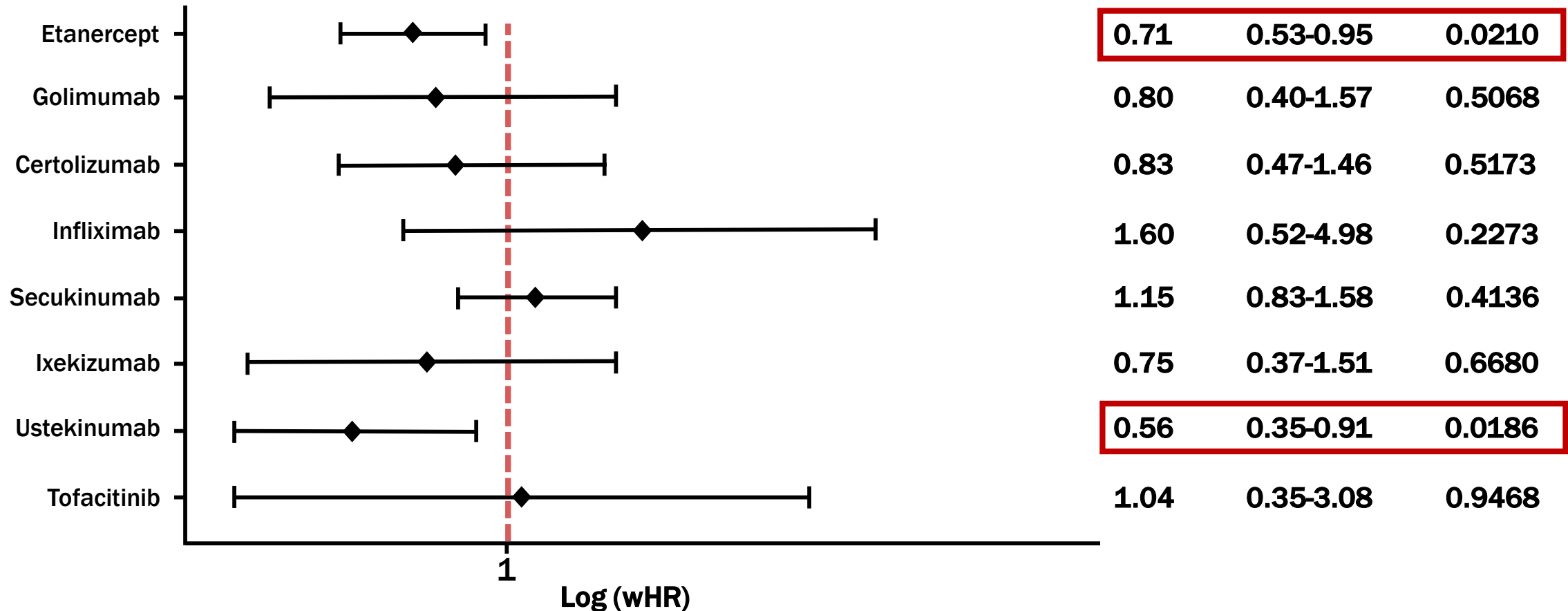
## Sensitivity analysis: Weighted & trimmed propensity score

Treatments (reference: adalimumab)



## Sensitivity analysis: Modifying the gap period

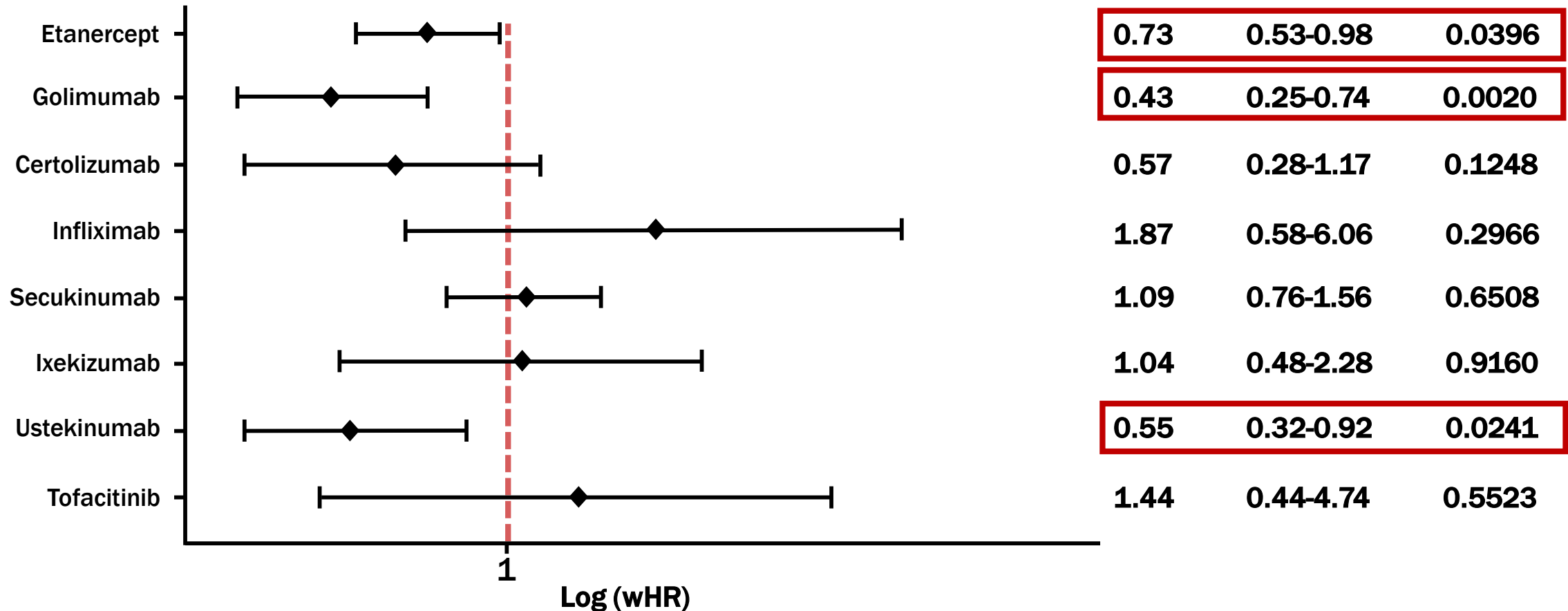
Treatments (reference: adalimumab)





## Sensitivity analysis: Modifying the definition of new users

Treatments (reference: adalimumab)



## Sensitivity analysis: Excluding the COVID period

Treatments (reference: adalimumab)

