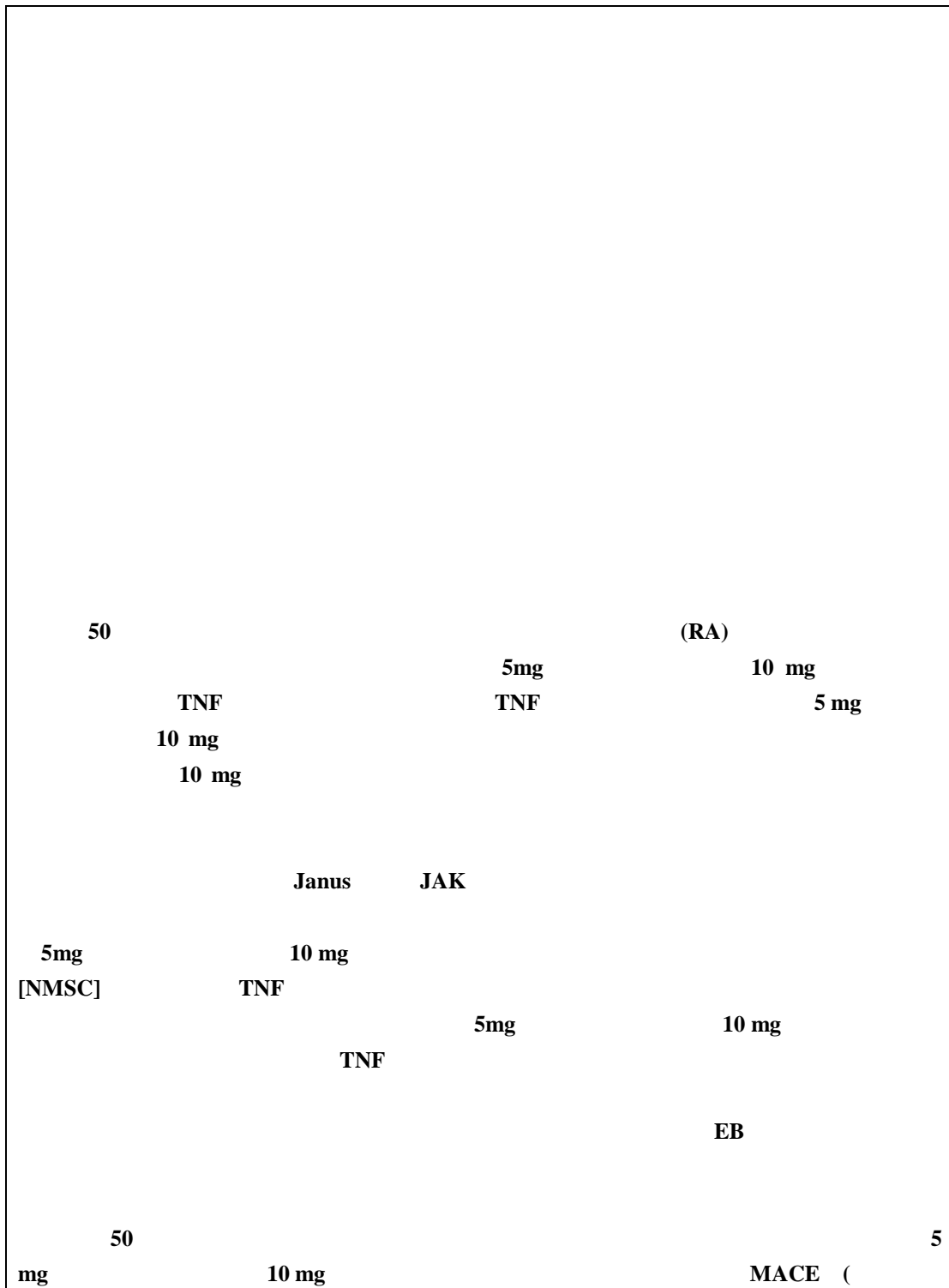
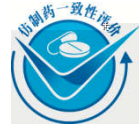
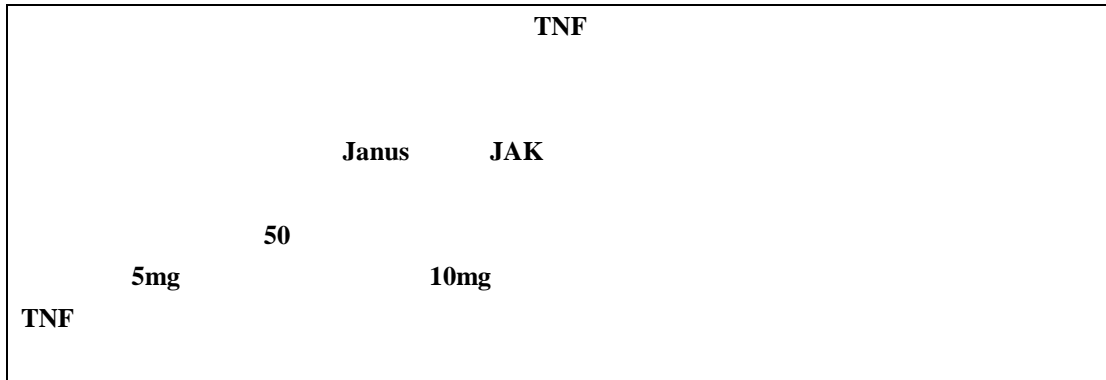


2023 08 01
2024 02 19





Tofacitinib Citrate Tablets
 Juyuansuan Tuofatibu Pian



$C_{16}H_{20}N_6O \cdot C_6H_8O_7$
 504.5

PsA

MTX

TNF

(AS)

DMARD

5mg C₁₆H₂₀N₆O

重要用药说明

- 500 /mm³ ANC 1000
- /mm³ 9g/dL
-
-
-

针对类风湿关节炎、银屑病关节炎和强直性脊柱炎的推荐剂量

1 CYP2C19 / CYP3A4

1

1

1

	5mg
<ul style="list-style-type: none"> ● CYP3A4 ● CYP3A4 CYP2C19 <i>见药物相互作用</i>	5mg
<ul style="list-style-type: none"> ● ● *	5mg
500 /mm ³	
ANC 500 1000 /mm ³	

	ANC	1000	5mg
ANC	500	/mm ³	
	8g/dL	2g/dL	

1

DMARD

*

-
-
-
-
-
-
-
-

临床试验经验

				5mg			
10mg				RA	1	1455	
	5mg	1456		10mg		1451	
	TNF		4.0				
		2	3				
			5mg	292		10mg	
306		5mg	1044		10mg	1043	
	DMARD			809			
				3		6	

3 12

5mg 10mg

0 3

4% 3%

0 3 5mg 10mg

20% 22% 18%

4%

3% 2%

0 3 1

0.5 100 5mg 10mg 11

1.7 100 5mg 10mg

95% 1.1 -0.4

2.5 100

0 12 5mg

34 2.7 100 10mg 33

2.7 100 10mg 5mg

95% -0.1 -1.3 1.2 100

0 3 5mg

10mg

0

10mg

0 12

5mg

3

- 5mg LDL 15% 10mg
- 5mg LDL 19%
- 5mg HDL 10% 10mg
- HDL 12%
- LDL/HDL
- LDL ApoB

12

0.1mg/dL

2%

50%

DMARD

5mg

10mg

2%

1%

2

2

DMARD 0-3

*

	5mg	10mg	**
	N=1336	N=1349	N=809
	%	%	%
	4	4	3
	4	3	3
	4	3	2
	4	3	2
	2	2	1

N			
*		2%	
	1%		
**		5mg	(见用法用量)

-

	5mg		10mg	
			NMSC	

		PsA	2	III
5mg	10 mg			
		5mg	10mg	
PsA-I	NCT01877668	12		DMARD
TNF		PsA-I	3	
12		40mg		
PsA-II	NCT01882439	6	1	TNF

	III	238			5 mg
236		10 mg			
	DMARD	[79%]	
	474	45	9.5%	65	66 13.9%

	III	AS-I	II
AS-II	(AS)	5 mg	
AS-I (NCT03502616)	48	2 NSAID	
AS-I	16	5 mg	
	32	5 mg	
AS-II (NCT01786668)	16	2 NSAID	
	12	2 mg 5 mg 10 mg	
II III	420	2 mg 5 mg 10 mg	
	316	5 mg	48
	185	5 mg	187
16		DMARD NSAID	10
mg/		13 (3.1%)	65
18 (4.3%)	AS	RA	

上市后经验

严重感染

BK

结核病

病毒再激活

死亡

mg	10 mg	RA	1	5
		50		

10 mg

血栓形成

	Janus	JAK				
	PE		DVT			
RA	1	50				
	5mg		10mg			
TNF		100	DVT	0.22	5 mg	
0.28	10 mg		0.16 TNF	100	PE	
0.18	5 mg		0.49	10 mg	0.05 TNF	
	10mg					

胃肠道穿孔

JAK

NSAID

NSAID

超敏反应

实验室检查异常

淋巴细胞异常

12

10%

500

/mm³

500 /mm³

500 /mm³

3

中性粒细胞减少症

2000 /mm³

ANC 1000 /mm³

ANC 500-1000 /mm³

ANC 1000 /mm³

ANC 500 /mm³

4-8

3

ANC

贫血

9g/dL

8g/dL

2g/dL

4-8

3

肝酶升高

DMARD

血脂升高

HDL

6

LDL/HDL

LDL

4-8

疫苗接种

Zostavax 16

5mg

2

糖尿病患者用药

肾功能损害

肝功能损害

见药代动力学

2-4% 15-20%

疾病相关母体和/或胚胎/胎儿风险

37

2500g

18

6

3315

505

65

71 75

65

65

3

3

CYP3A4	
	(3)
CYP3A4	CYP2C19
	(3)
CYP3A4	
	(3)
	DMARD
	(3)

ESRD

/

[=-0.73 0.15]

Janus JAK JAK

-

JAK STAT

JAK

STAT JAK JAK JAK1/JAK3 JAK1/JAK2 JAK1/TyK2
JAK2/JAK2 JAK1/JAK2 JAK1/JAK3 JAK2/JAK2

IC₅₀ 406 56 1377nM JAK

	Ames		CHO-HGPRT	
DNA				
		5mg	17	10mg 2
8.3	10mg/kg/		AUC	
	5mg		10mg	0.5
	1mg/kg/		AUC	
5mg)	133		10mg	67
100mg/kg/	AUC			
-				
5mg	146		10mg 2	73
100mg/kg/	AUC			
			5mg	58
	10mg 2	29		30mg/kg/ AUC
-				
5mg	13		10mg 2	6.3 30mg/kg/
AUC		/		
			5mg	3
	10mg 2	1.5	10mg/kg/	AUC
			6	20
5mg	73		10mg 2	36
	50mg/kg/	AUC		
	5mg	17		10mg 2 8.3
	10mg/kg/	AUC	F1	
	F2			

RasH2 6 5mg 34
 10mg 2 17 200mg/kg/ AUC

SD 2 30mg/kg/
 5mg AUC 42 10mg 2 AUC 21

39 5mg 6
 10mg 3 5mg/kg AUC
 5mg 1 10mg 0.5
 1mg/kg AUC

0.5-1 3
 24-48

吸收

74% AUC
 C_{max} 32%

分布

87L 40%
 1

代谢和排泄

70% 30%
 CYP3A4 CYP2C19
 65% 35% 8 8%

患者人群中药代动力学特点

AUC % 22%
 34% 4

4	5 mg	5 mg
	^a	
	(CV%)	

AUC _{0-24,ss} (ng·h/mL)	504	419	382
	22.0%	34.1%	25.4%

AUC_{0-24,SS} = 24

CV=

a

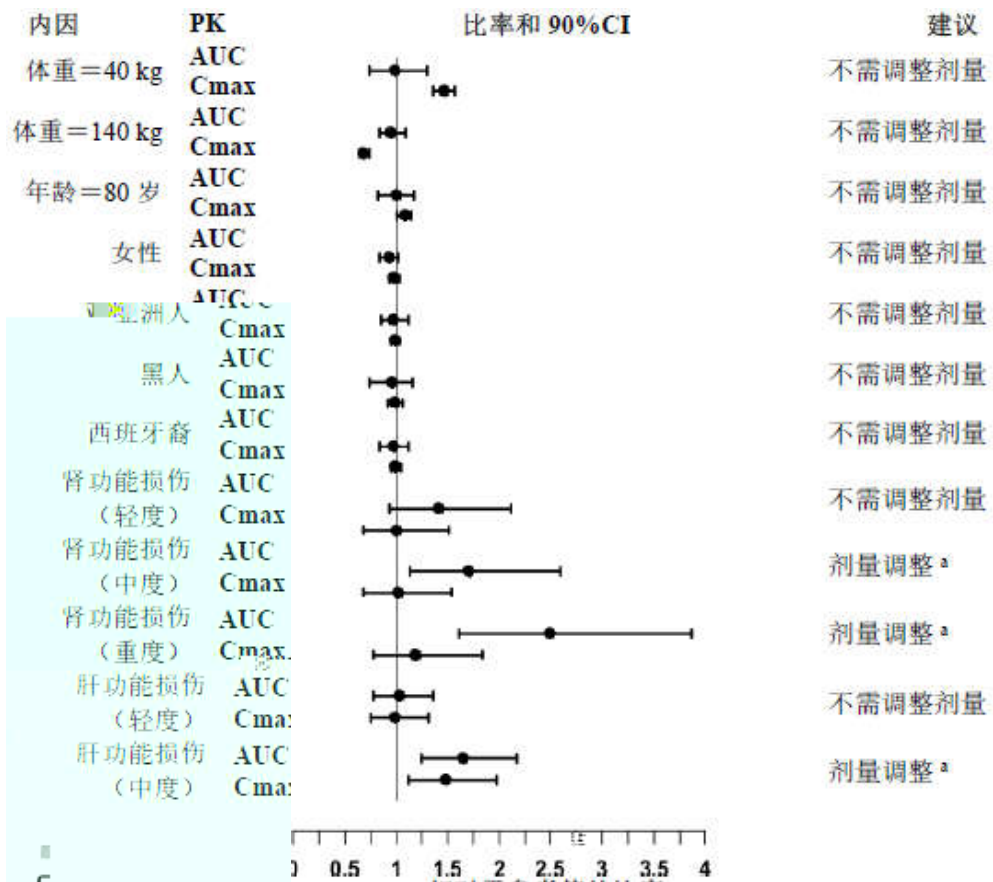
1

C_{max}

C_{min}

1

1



70kg 55

^a RA PsA AS ()

ESRD

AUC

40%

30%

ESRD

RA PsA AS

托法替布影响其他药物药代的可能性

10mg C_{max}

CYP CYP1A2 CYP2B6 CYP2C8 CYP2C9

CYP2C19 CYP2D6 CYP3A4 CYP3A4

10mg 250 C_{max}

5'- UGT [UGT1A1

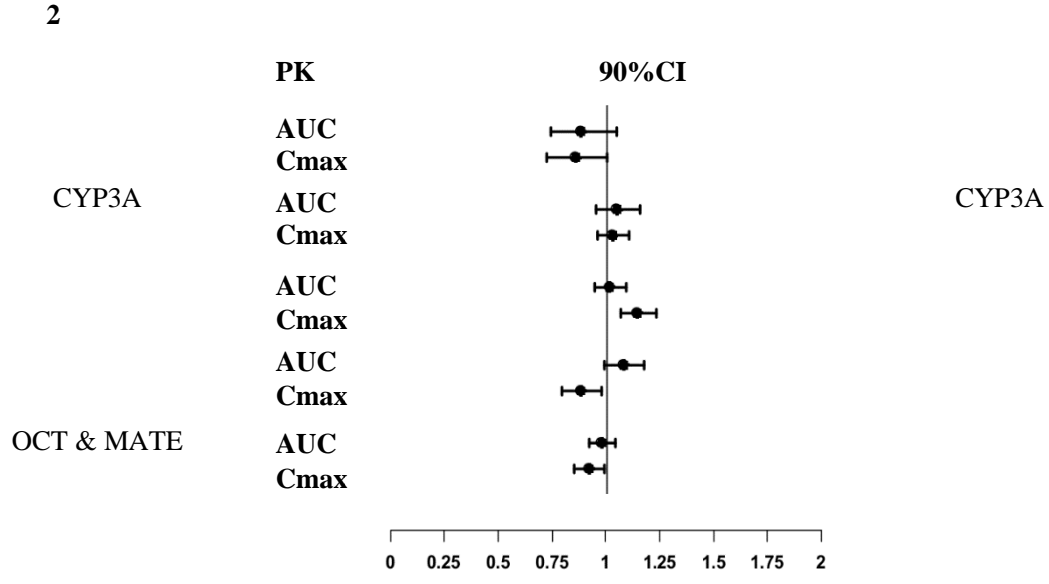
UGT1A4 UGT1A6 UGT1A9 UGT2B7]

CYP

CYP

P-

2



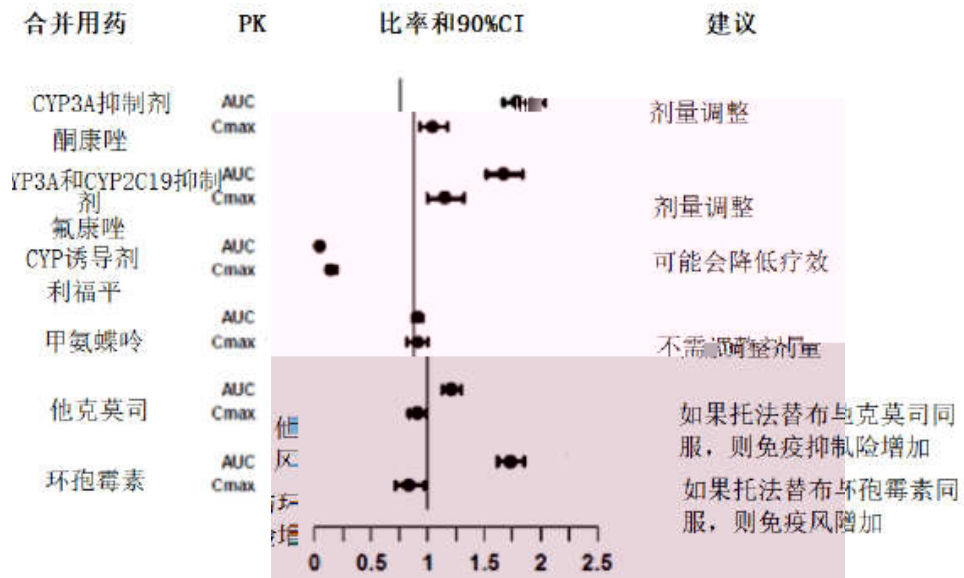
OCT
MATE

其他药物影响托法替布药代动力学的可能性

CYP3A4 CYP3A4

CYP2C19 P-

3



a

30°C

28 / 60 /

24

YBH10542023

H20233995

:

: 88

:

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