

3HP and 1HP

H: isoniazid; P: rifapentine

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LTBI regimen	Dose per kg body weight	Maximum dose
INH, daily, 6-9 months	Adult: 5 mg Children: 10 mg (7-15 mg)	300 mg
RMP, daily, 3-4 months	Adult: 10 mg Children: 15 mg (10-20 mg)	600 mg
INH + RMP, daily, 3-4 months	As above for individual drugs	INH: 300 mg; RMP: 600 mg
INH + RPT, weekly, 12 doses	INH: ≥12 years: 15 mg 2-11 years: 25 mg RPT: 10.0 – 14.0 kg → 300 mg 14.1 – 25.0 kg → 450 mg 25.1 – 32.0 kg → 600 mg 32.1 – 50.0 kg → 750 mg >50 kg → 900 mg	INH: 900 mg; RPT: 900 mg

Systemic Drug Reaction during 3HP

- 1. Hypotension, urticaria, angioedema, acute bronchospasm, or conjunctivitis that occurred in relation to study drug;**
- 2. >4 of the following (one had to be \geq Gr. 2): weakness, fatigue, nausea, vomiting, headache, fever, aches, sweats, dizziness, shortness of breath, flushing, or chills.**

Outcome of 3HP Tx in different Taiwan cohorts

	LTBI contacts (n=101)	LTBI contacts (n=132)	LTBI contacts ≥50Y (n=2348)	RA with LTBI (n=21)	Hemodialysis with LTBI (n=26)	LTBI contacts (n=306)
Reference	<i>Medicine</i> 2016;95:34	<i>Tuberculosis</i> 2018;111:121	<i>ERJ</i> 2019;53:18023 96	<i>ARD</i> 2018;77:1688	<i>JMII</i> 2019;52:158	<i>J Clin Med</i> 2019;8:812
Male	43.6%	61.4%	48.1%	6 (29%)	18 (69%)	51.0%
Age	34.9	31.7 ± 15.0	87.5% (age <75)	62.1 ± 14.9	63.8 ± 12.2	42.0 ± 18.5
Tx completed	97.0%	89.4%	83.9%	19 (90%)	17 (65%)	86.9%
Permanent stop						
Any AE	3.0%	9.1%	12.0%	2 (10%)	9 (35%)	
Hepatotoxicity	0%	1.5%	0.8%	0 (0%)	0 (0%)	

Safety Profile of 3HP in 579 Cases – Severe AE

Age Group	All (n=579)	< 35 (n=165)	35 ~ 65 (n=280)	≥ 65 (n=134)
Systemic drug reaction	65 (11.2%)	8 (4.8%)	48 (17.1%)	9 (6.7%)
Flu-like syndrome	47 (8.1%)	6 (3.6%)	34 (12.1%)	7 (5.2%)
Hypotension	10 (1.7%)	2 (1.2%)	7 (2.5%)	1 (0.7%)
Urticaria	6 (1.0%)	0 (0%)	6 (2.1%)	0 (0%)
Conjunctivitis	4 (0.7%)	0 (0%)	3 (1.1%)	1 (0.7%)
Severe hepatotoxicity	7 (1.2%)	0 (0%)	6 (2.1%)	1 (0.7%)

Safety Profile of 3HP in 579 Cases – Individual Symptoms

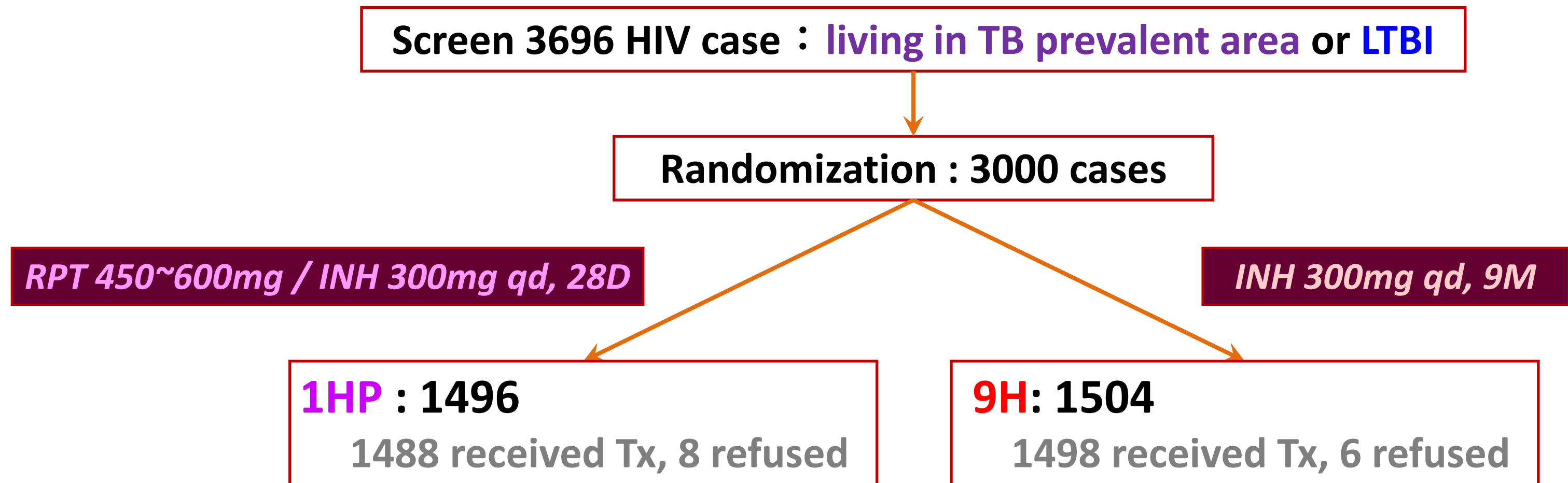
Age Group	All (n=579)	< 35 (n=165)	35 ~ 65 (n=280)	≥ 65 (n=134)
Flu-like symptoms				
Malaise	261 (45.1%)	60 (36.4%)	135 (48.2%)	66 (49.3%)
Febrile sensation	81 (14.0%)	15 (9.1%)	50 (17.9%)	16 (11.9%)
Fever	147 (25.4%)	26 (15.8%)	87 (31.1%)	34 (25.4%)
Dizziness	184 (31.8%)	31 (18.8%)	111 (39.6%)	42 (31.3%)
Headache	158 (27.3%)	33 (20.0%)	101 (36.1%)	24 (17.9%)
Chills	85 (14.7%)	10 (6.1%)	59 (21.1%)	16 (11.9%)
Myalgia	138 (23.8%)	23 (13.9%)	92 (32.9%)	23 (17.2%)
URI symptoms	87 (15.0%)	22 (13.3%)	51 (18.2%)	14 (10.4%)
Dyspnea	34 (5.9%)	6 (3.6%)	20 (7.1%)	8 (6.0%)
GI symptoms				
UGI symptoms	199 (34.4%)	42 (25.5%)	101 (36.1%)	56 (41.8%)
Diarrhea	28 (4.8%)	5 (3.0%)	17 (6.1%)	6 (4.5%)
Cutaneous reaction				
	101 (17.4%)	21 (12.7%)	60 (21.4%)	20 (14.9%)
Cardiovascular symptoms				
Palpitation	35 (6.0%)	7 (4.2%)	22 (7.9%)	6 (4.5%)
Hypertension	22 (3.8%)	0 (0%)	7 (2.5%)	15 (11.2%)

Safety Profile of 3HP in 579 Cases – Outcome

	Total (n=579)	Age < 35 (n=165)	Age 35 ~ 65 (n=280)	Age ≥ 65 (n=134)
Complete Tx	481 (83.1%)	156 (94.5%)	226 (80.7%)	99 (73.9%)
AE without interruption	226 (39.0%)	86 (52.1%)	106 (37.9%)	34 (25.4%)
AE with interruption	38 (6.6%)	12 (7.3%)	19 (6.8%)	7 (5.2%)
Incomplete Tx	98 (16.9%)	9 (5.5%)	54 (19.3%)	35 (26.1%)
No. of dose	4.3 ± 2.2	4.3 ± 2.3	4.4 ± 2.1	4.2 ± 2.4
Cause				
SDR	37 (6.3%)	4 (2.4%)	27 (9.6%)	6 (4.5%)
Hepatotoxicity	18 (3.1%)	0 (0%)	12 (4.3%)	6 (4.5%)
Other AEs	29 (5.0%)	5 (3%)	10 (3.6%)	14 (10.4%)
Refuse	9 (1.6%)	0 (0%)	5 (1.8%)	4 (3.0%)
Active TB	2 (0.3%)	0 (0%)	0 (0%)	2 (1.5%)
Others	3 (0.5%)	0 (0%)	1 (0.4%)	2 (1.5%)

One month of Rifapentine plus Isoniazid to Prevent HIV-related Tuberculosis

Swindells S. *NEJM*. 2019;380:1001-11.



	Gr. 3	Gr. 4	Gr. 5	Gr. 3~5	Gr. 3	Gr. 4	Gr. 5	Gr. 3~5
Targeted AE	34	9	1	44 (3.0)	32	20	0	52 (3.5)
SAE	41	22	12	75 (5.0)	49	25	19	93 (6.2)
Any systemic event	101	9	1	111 (7.5)	123	12	0	135 (9.0)
Any AE	198	47	5	250 (16.8)	213	59	2	274 (18.3)

Characteristics	1HP	3HP
Age (yr)	54.8 ± 19.1	54.7 ± 16.8
>65	33.5%	30.5%
Male sex	49.5%	47.7%
BMI	24.5 ± 4.1	24.1 ± 4.2
<18.5	5.0%	6.2%
Smoking		
Current smoker	12.4%	18.8%
Ex-Smoker	13.9%	7.8%
Never smoker	74.3%	74.1%
Abnormal CxR	18.0%	18.8%

Comorbidity

1HP

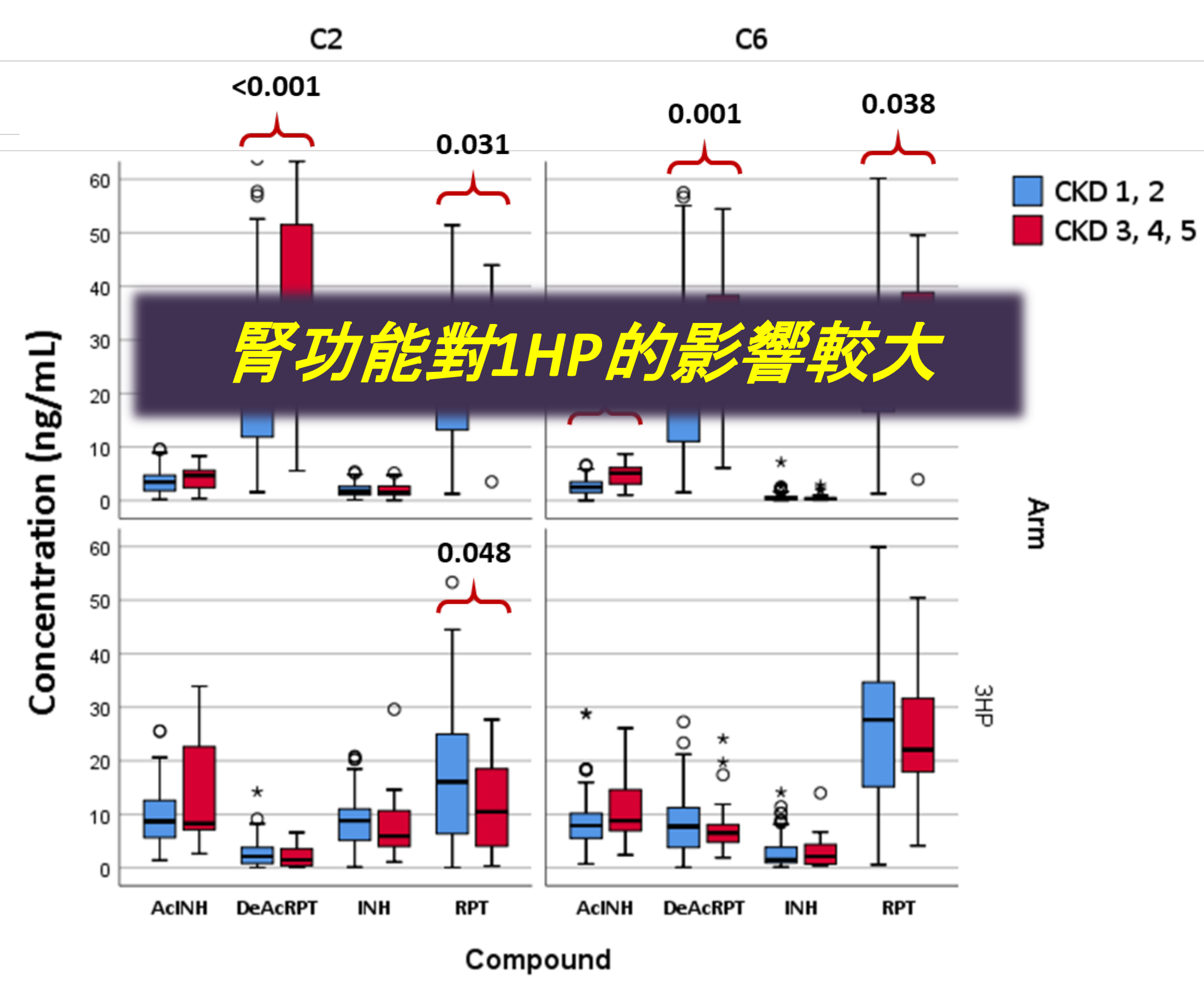
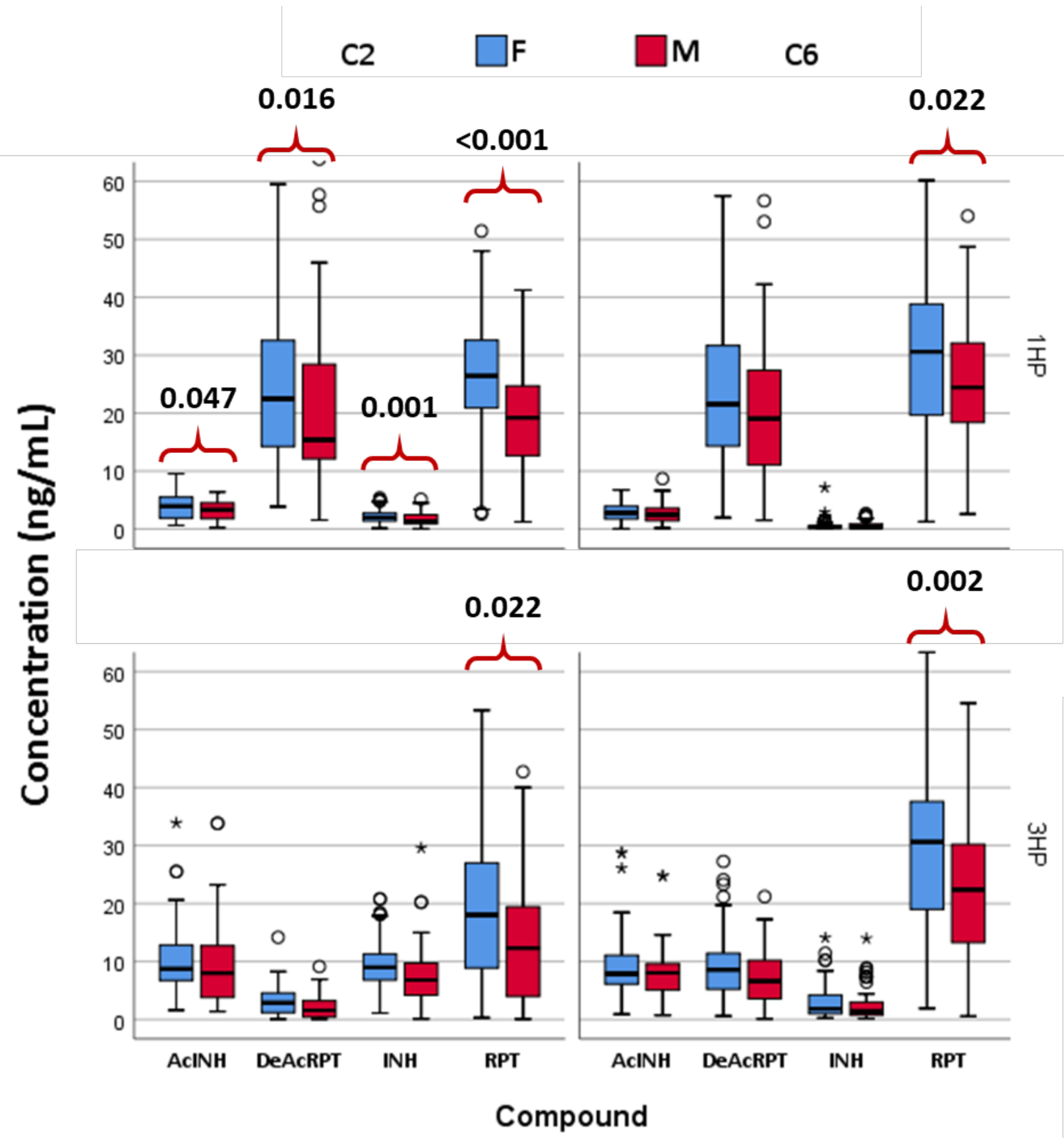
3HP

Hypertension	26.2%	26.4%
DM	16.0%	21.3%
CKD III~V	11.7%	10.7%
Hyperlipidemia	10.2%	8.6%
Cerebral vascular attack	5.8%	3.6%
Dementia	4.4%	4.1%
Coronary artery disease	3.9%	3.0%
Cancer	2.9%	3.0%
GERD	2.9%	1.5%
Obstructive lung disease	1.9%	2.0%
Arrhythmia	2.4%	0.5%
Hyperuricemia	1.9%	0.5%
Autoimmune	1.0%	2.0%
Hyperthyroidism	1.9%	0
History of seizure	1.5%	0
Liver cirrhosis	1.0%	0
HBV infection	7.3%	10.7%
HCV infection	2.4%	3.6%
HIV infection	0	0.5%

Exposure	1HP	3HP
Male index sex	56.8%	62.9%
Sputum smear positivity*	57.3%	67.5%
Pulmonary cavity*	10.2%	17.8%
Exposure intensity		
Same room	30.1%	27.9%
Same house, different room	43.7%	40.6%
Household	44.2%	39.1%
Healthcare-associated	13.1%	16.8%
School	11.7%	6.1%
High-risk group	3.4%	4.6%
Occupational	27.7%	33.5%

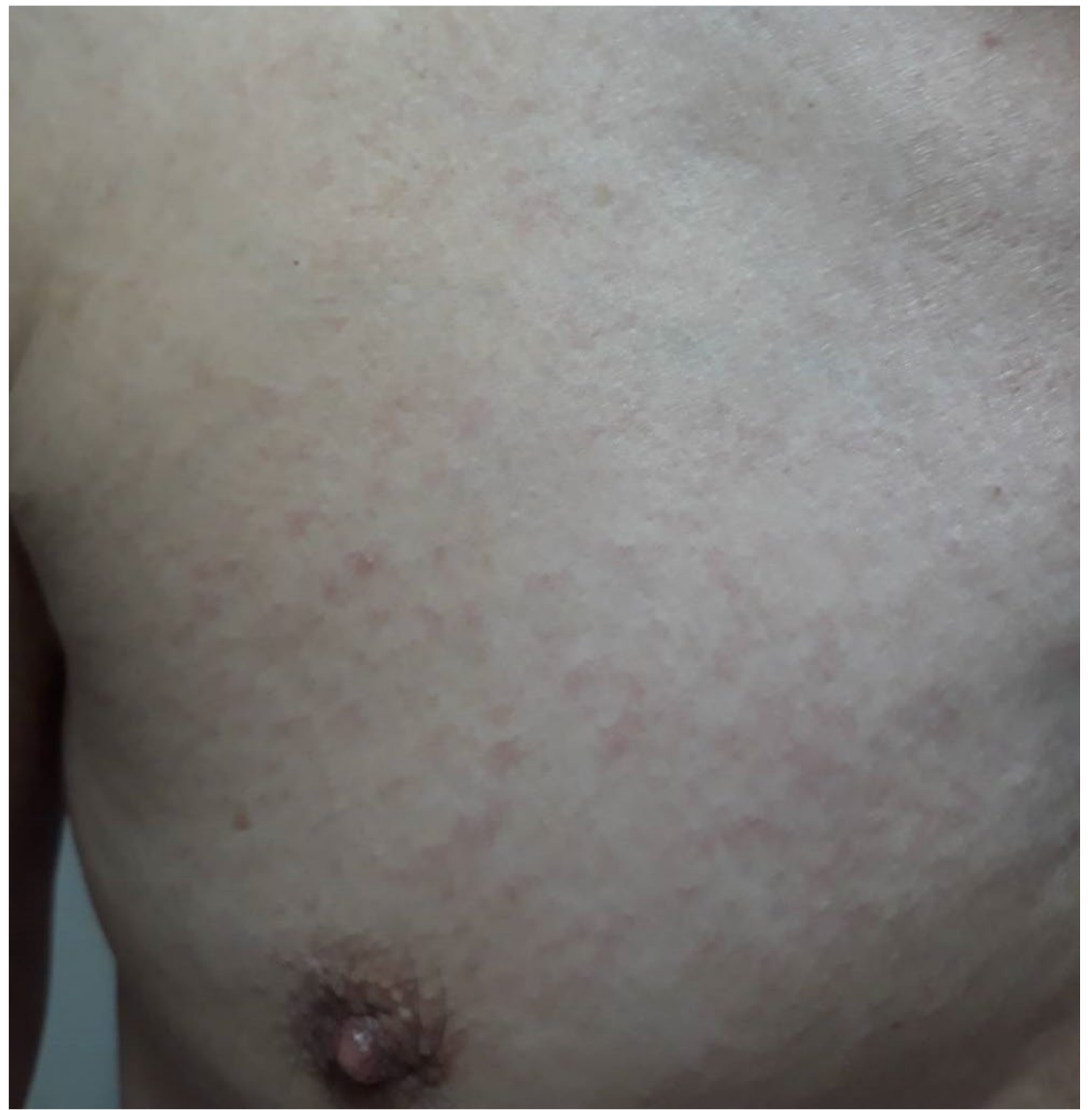
Lab - Baseline	1HP (n=206)	3HP (n=197)	P-value
Hemoglobin (g/dL)	14.0 ± 1.9	13.8 ± 1.7	0.668
Leukocyte (/uL)	6904 ± 1888	7051 ± 1861	0.458
Platelet (K/uL)	253 ± 70	258 ± 73	0.575
Aspartate transaminase (U/L)	26.0 ± 17.6	25.0 ± 18.8	0.599
Alanine transaminase (U/L)	24.3 ± 16.6	24.3 ± 17.0	0.987
Total bilirubin (mg/dL)	0.7 ± 0.3	0.7 ± 1.0	0.754
eGFR (mL/min/1.73m²)	91.9 ± 32.3	89.0 ± 28.9	0.093

Plasma drug concentration : sex & kidney function



Outcome	1HP	3HP
Complete treatment	82.4%	85.0%
Incomplete treatment	17.6%	15.0%
Adverse drug reaction	17.0%	11.1%
Mortality	0	0.6%
Active TB	0	0.6%
Others	0.5%	2.8%

	1HP	3HP
Systemic drug reaction	9.2%	9.1%
Flu-like syndrome	3.4%	7.6%
Urticaria*	6.3%	1.5%
Complete treatment	74%	56%



Maculopapular eruption, not very itching

→ Education & Anti-histamine

Conclusion

- 1HP或3HP的完成率都很高，分別是82.4%和85.0%，沒有差別
- SDR的發生率，1HP組和3HP組分別是9.2%和9.1%
- 1HP組所產生的SDR，三分之二是urticaria
- 3HP組所產生的SDR，超過八成是flu-like syndrome
- 即使發生SDR，1HP組中仍有74%的機會完成治療（開立抗組織胺）
- 即使發生SDR，3HP組也仍有56%的機會完成治療（開立退燒止痛藥）
- 類流感症狀通常在3HP的第三、四劑最嚴重，中年人風險比較高