

# Effects of Additional Sarpogrelate HCL (ANPLAG) on Platelet Inhibition in Patients Underwent Percutaneous Coronary Intervention

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# INTRODUCTION

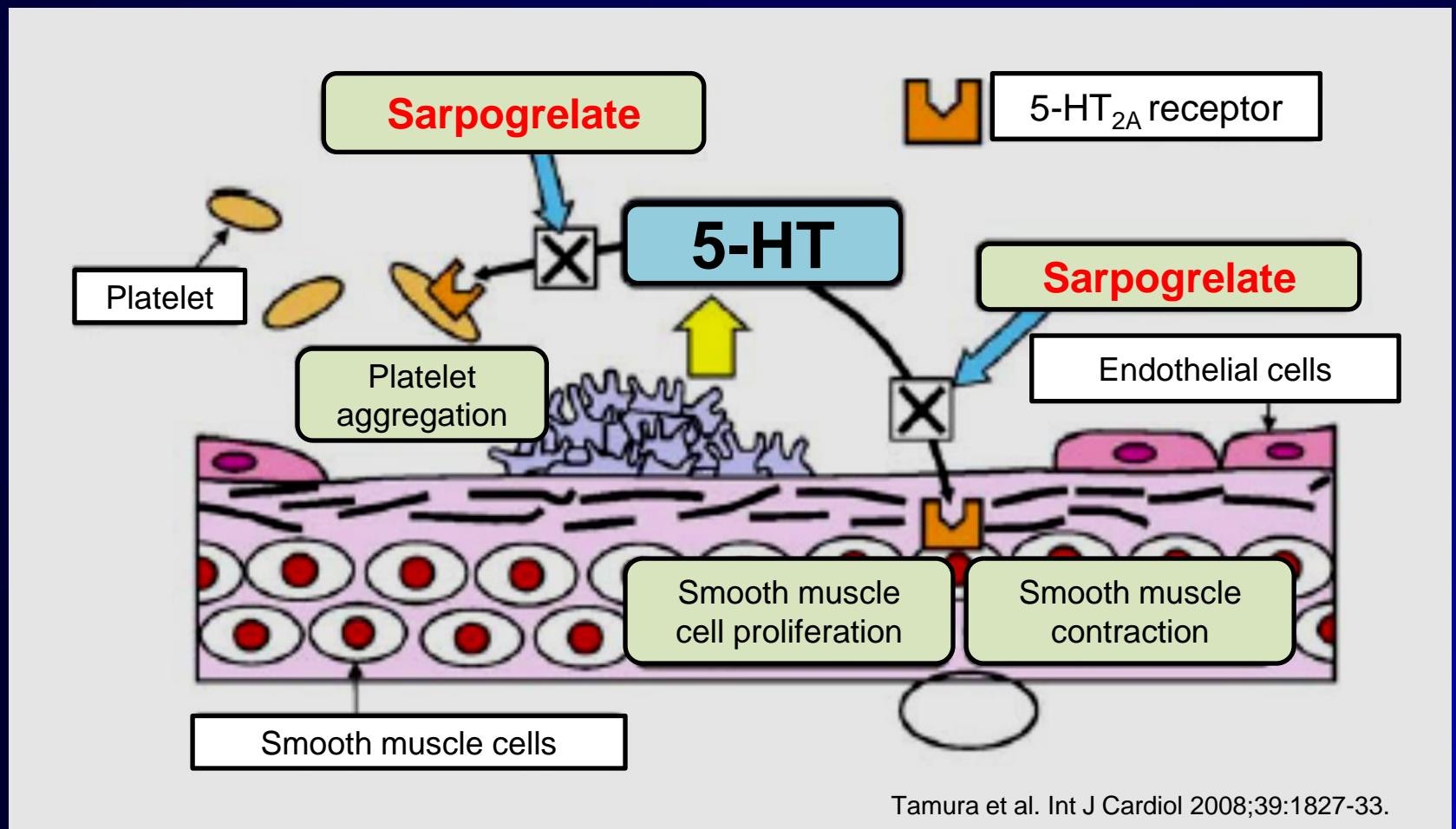


Fig. 1. A diagram of pharmacological actions of sarpogrelate (Anplag™) as a selective 5-hydroxytryptamine (HT) subtype 2A receptor antagonist.

# INTRODUCTION

## Previous studies and results

- Coronary stenting induces a greater release of 5-HT into the coronary circulation. It may contribute to subacute stent thrombosis and restenosis.
- High plasma 5-HT are associated with occurrence of cardiac events.
- Sarpogrelate in addition to aspirin and ticlopidine significantly decreased the restenosis rate.

# OBJECTIVES

- To assess effects of sarpogrelate in addition to aspirin and clopidogrel on post-treatment platelet reactivity in patients underwent DES implantation.
- To find clinical evidences for large scale trial of sarpogrelate.

# MATERIALS AND METHODS

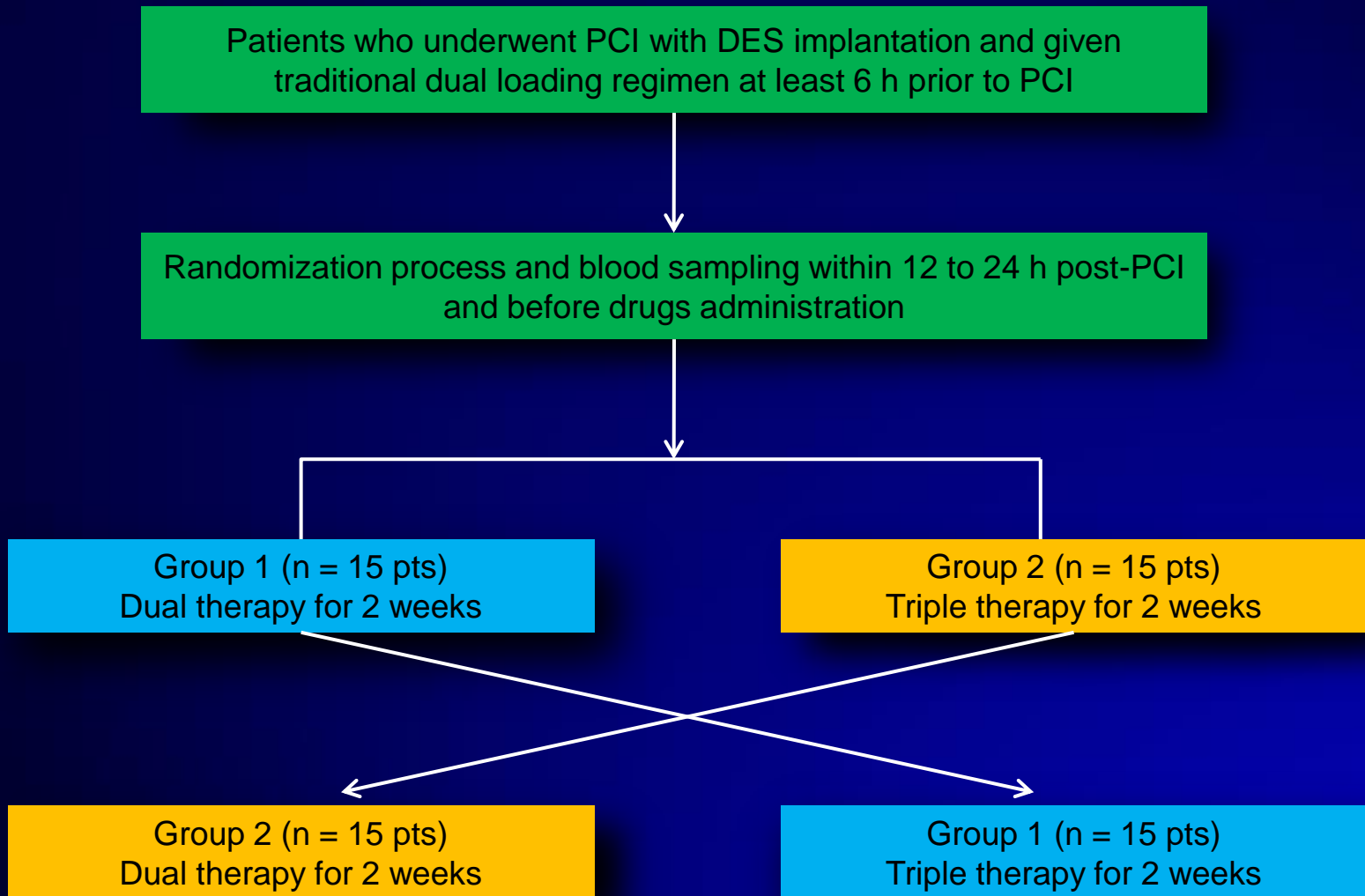


Fig. 1. Flow diagram of the study

# MATERIALS AND METHODS

## Inclusion Criteria

- ① Age of  $\geq 18$  years;
- ② Acute coronary syndrome or stable angina with  $\geq 3$  risk factors;
- ③ Underwent PCI with DES implantation after receiving dual loading therapy at least 6 h prior to PCI (300 mg aspirin and 300~600 mg clopidogrel).

# MATERIALS AND METHODS

## Exclusion Criteria

- ① Age of  $\geq 80$  years;
- ② Who implanted with bare metal stents (BMS);
- ③ Use of GP 2b/3a inhibitors during PCI procedure;
- ④ History of ISR or CABG or stroke within 6 months prior to screening;
- ⑤ Active internal bleeding;
- ⑥ Need for oral anticoagulation;
- ⑦ Intolerance to antiplatelet agents (aspirin, etc.)
- ⑧ AST and ALT levels more than 3 times upper normal limit;
- ⑨ Severe renal failure (serum creatinine  $>2.5$  mg/dl);
- ⑩ Thrombocytopenia (PLT count  $<80,000/L$ ) or anemia (Hb  $<8.0$  g/dL);
- ⑪ Left ejection fraction less than 40%;
- ⑫ Who has received any investigational drug within 2 months prior to screening.

# MATERIALS AND METHODS

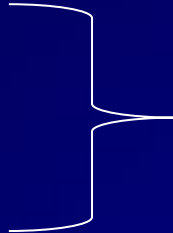
## Medication

- Dual maintenance dose therapy  
Aspirin 100 mg/d plus clopidogrel 75 mg/d
- Triple maintenance dose therapy  
Aspirin 100 mg/d plus clopidogrel 75 mg/d plus  
sarpogrelate 100 mg TID



# MATERIALS AND METHODS

## ❖ Light transmittance aggregometry (LTA)

- 0.5 mM arachidonic acid
  - 10  $\mu$ M adenosine diphosphate
  - 2  $\mu$ g/mL collagen
- Maximum platelet aggregation
- 

## ❖ Multiple electrode aggregometry (MEA)

- ADPtest
  - ASPtest
  - COLtest
- Area under the aggregation curve (U)
- 

# MATERIALS AND METHODS

## Statistical Analysis

- Two-way Repeated-Measures ANOVA => To assess effects of treatment, period and treatments\*period and calculate carryover effects.
- A p-value of  $<0.05$  was considered as statistical significance.
- SPSS version 14.0 (SPSS Inc. Chicago, USA)

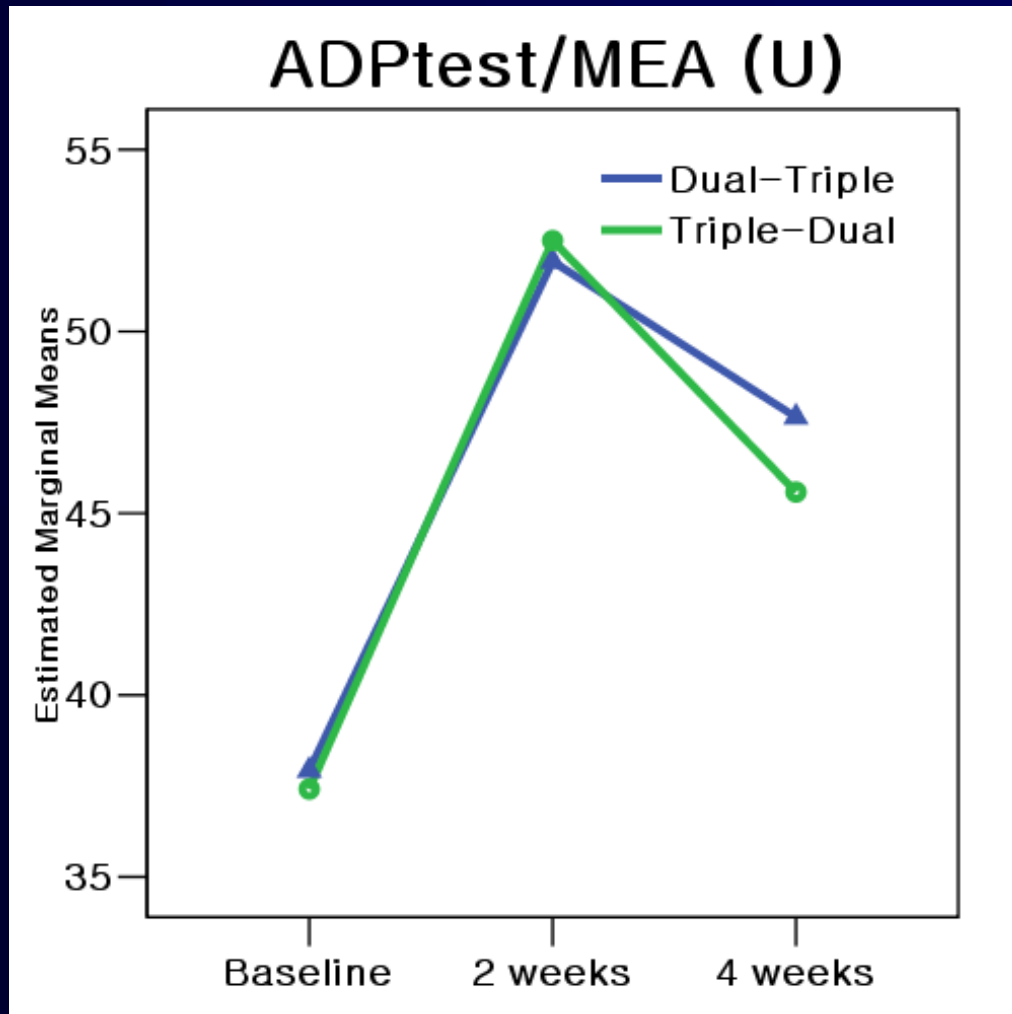
# RESULTS

Variables	Group 1 (n=14) (From dual to triple)	Group 2 (n =12) (From Triple to dual)	p-value
Age (years)	67.2 ± 8.0	62.1 ± 10.4	0.168
Gender (Male/Female)	8/6	8/4	0.701
Diagnosis, n (%)			0.952
Stable angina (SA)	1/14 (7.1%)	1/12 (8.3%)	
Unstable angina (UA)	10/14 (71.4%)	9/12 (75.0%)	
NSTEMI	3/14 (21.4%)	2/12 (16.7%)	
STEMI	0	0	
Risk factor, n (%)			
Diabetes Mellitus	4/14 (28.6%)	4/12 (33.3%)	0.793
Hypertension	9/14 (64.3%)	5/12 (41.7%)	0.249
Active Smoker	0/14	1/12 (8.3%)	0.462
Hyperlipidemia	1/14 (7.1%)	1/12 (8.3%)	0.910
Pre-PCI, n (%)	2/14 (14.3%)	5/12 (41.7%)	0.190
Pre-MI, n (%)	3/14 (21.4%)	3/12 (25.0%)	0.829
Pre-stroke, n (%)	0	0	NS
Hemoglobin (g/dL)	13.0 ± 2.0	12.7 ± 1.6	0.742
WBC count (10 <sup>3</sup> /μL)	7.20 ± 1.91	7.00 ± 2.13	0.806
Platelet count (10 <sup>3</sup> /μL)	207.7 ± 47.6	227.7 ± 45.9	0.289

# RESULTS

Variables	Group 1 (n=14) (From dual to triple)	Group 2 (n =12) (From Triple to dual)	p-value
Angiographic diagnosis			0.763
1-VD, n (%)	5/14 (35.7%)	6/12 (50.0%)	
2-VD, n (%)	6/14 (42.9%)	4/12 (33.3%)	
3-VD, n (%)	3/14 (21.4%)	2/12 (16.7%)	
Target lesion			0.420
LAD, n (%)	6/14 (42.9%)	5/12 (41.7%)	
LCx, n (%)	5/14 (35.7%)	2/12 (16.7%)	
RCA, n (%)	3/14 (21.4%)	5/12 (41.7%)	

# RESULTS



## 1. Two-way ANOVA

- Multivariate Tests:  
Period:  $p = 0.007$ ;  
Treatment\*period:  $p = 0.926$ .
- Mauchly's Test of Sphericity:  $P = 0.333$ .  
Period:  $p = 0.002$ ;  
Treatment\*period:  $p = 0.944$ .
- Tests of between subjects effects:  
 $p = 0.902$ .

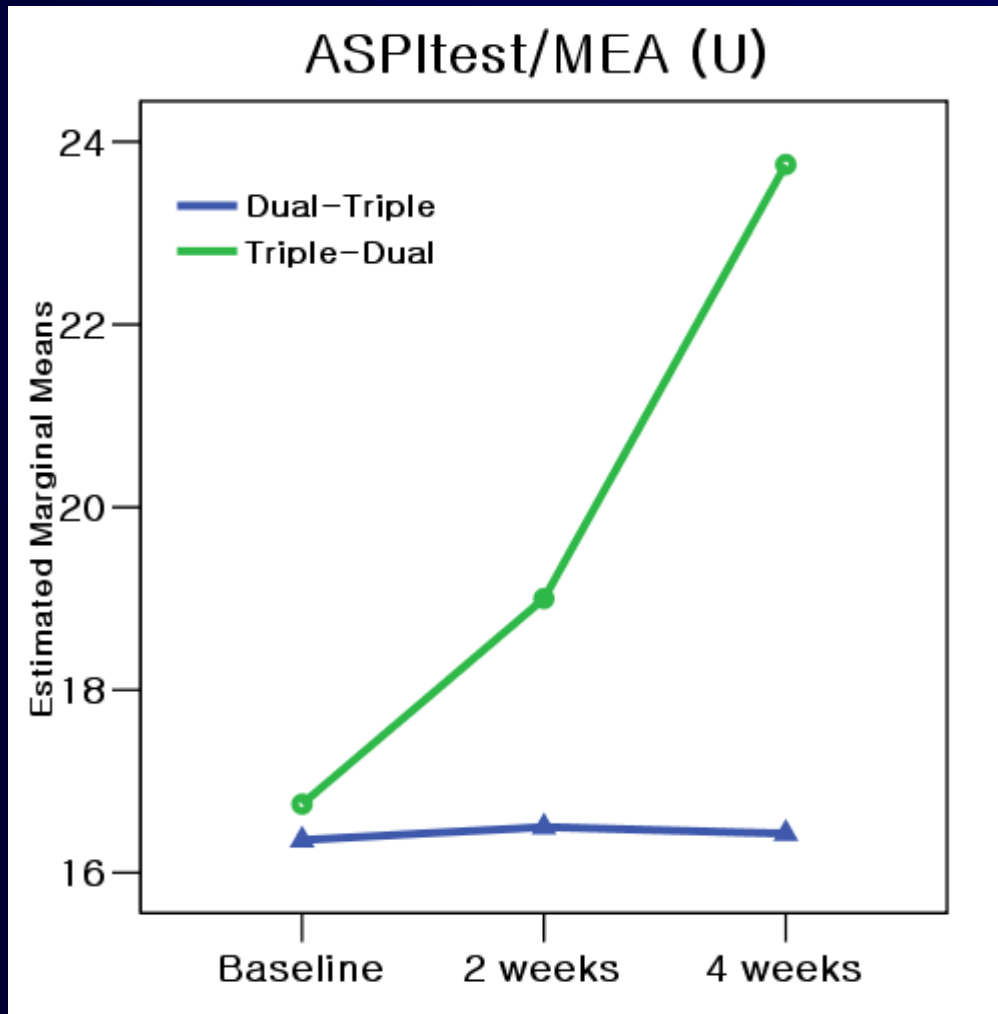
## 2. One-way ANOVA

- Dual-Triple group:  $p = 0.034$ ;
- Triple-Dual group:  $p = 0.057$ .

## 3. Paired Samples test

- Baseline & 2 weeks:  $p = 0.050$ ,  
in the triple-dual group.

# RESULTS



## 1. Two-way ANOVA

- Multivariate Tests:  
Period:  $p = 0.445$ ;  
Treatment\*period:  $p = 0.441$ .
- Mauchly's Test of Sphericity:  $P = 0.074$ .  
Period:  $p = 0.404$ ;  
Treatment\*period:  $p = 0.413$ .
- Tests of between subjects effects:  
 $p = 0.362$ .

## 2. One-way ANOVA

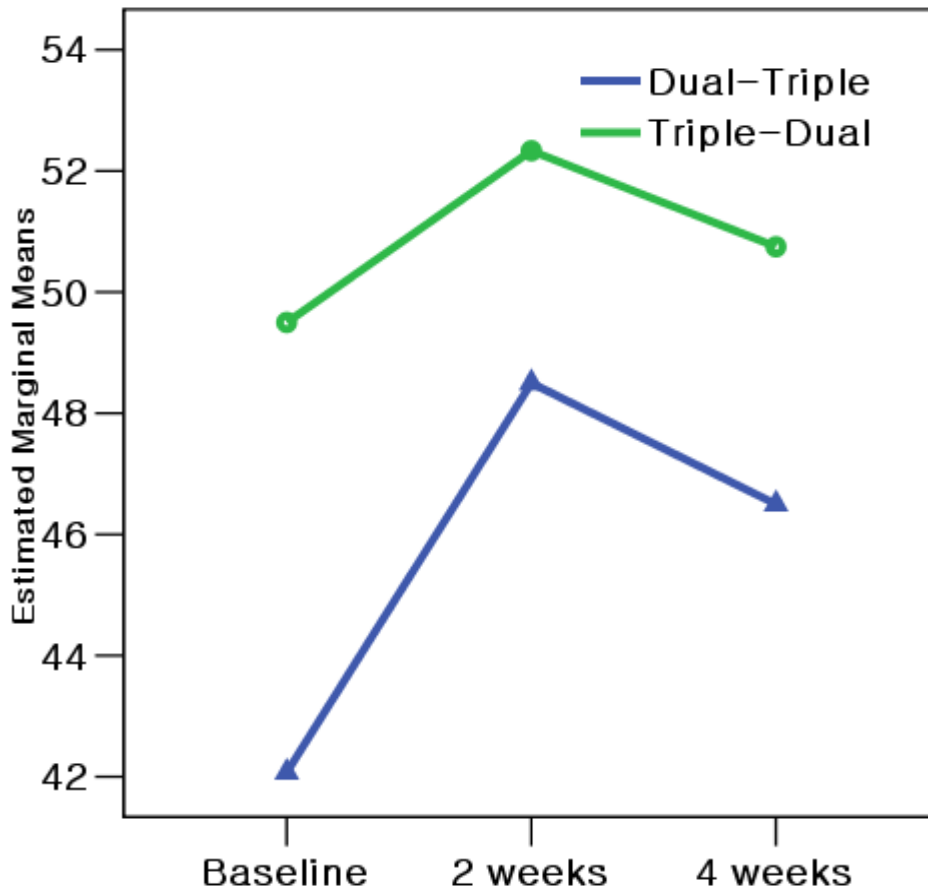
- Dual-Triple group:  $p = 0.999$ ;
- Triple-Dual group:  $p = 0.327$ .

## 3. Paired Samples test

There was no significant difference in both groups.

# RESULTS

## COLtest/MEA (U)



### 1. Two-way ANOVA

- Multivariate Tests:  
Period:  $p = 0.341$ ;  
Treatment\*period:  $p = 0.872$ .
- Mauchly's Test of Sphericity:  $P = 0.016$ .  
Period:  $p = 0.377$ ; (Greenhouse-Geisser)  
Treatment\*period:  $p = 0.790$ .
- Tests of between subjects effects:  
 $p = 0.301$ .

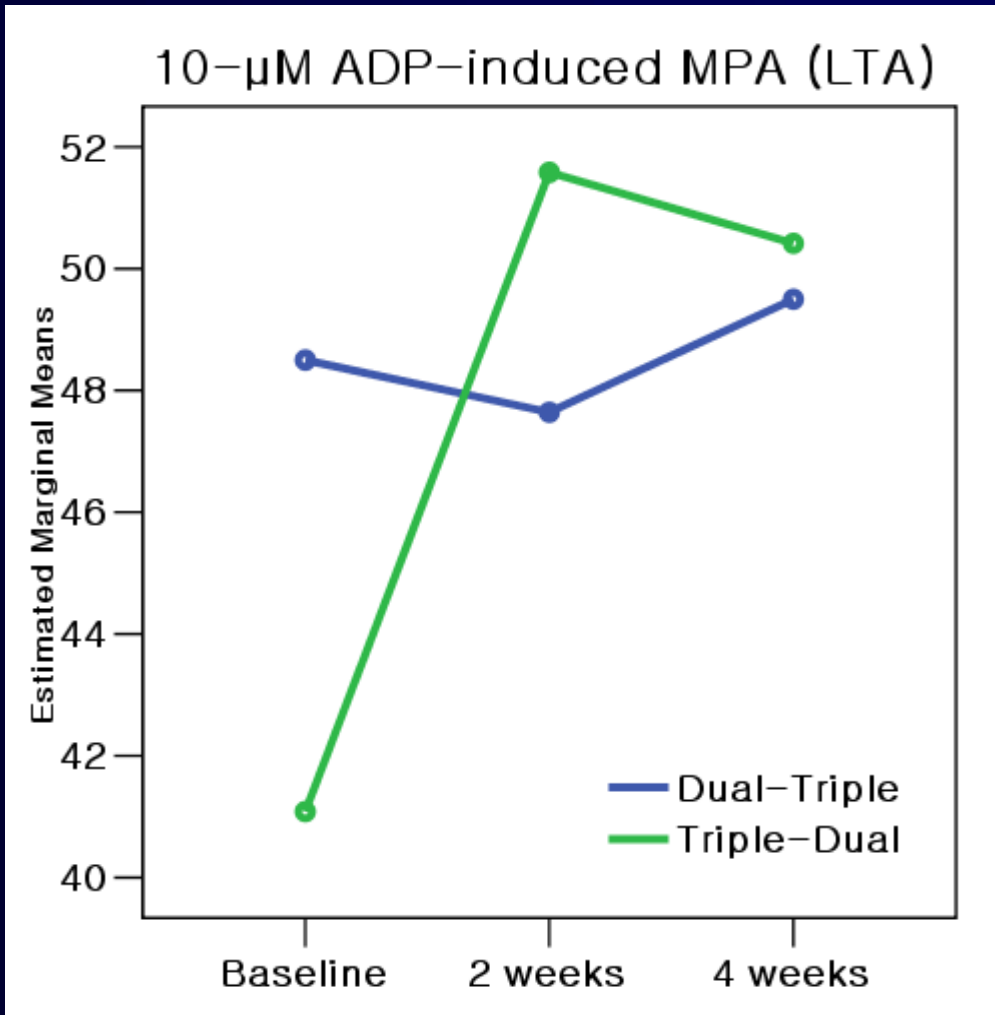
### 2. One-way ANOVA

- Dual-Triple group:  $p = 0.464$ ;
- Triple-Dual group:  $p = 0.365$ .

### 3. Paired Samples test

There was no significant difference in both groups.

# RESULTS



## 1. Two-way ANOVA

- Multivariate Tests:  
Period:  $p = 0.106$ ;  
Treatment\*period:  $p = 0.062$ .
- Mauchly's Test of Sphericity:  $P = 0.163$ .  
Period:  $p = 0.123$ ;  
Treatment\*period:  $p = 0.114$ .
- Tests of between subjects effects:  
 $p = 0.851$ .

## 2. One-way ANOVA

- Dual-Triple group:  $p = 0.866$ ;
- Triple-Dual group:  $p = 0.051$ .

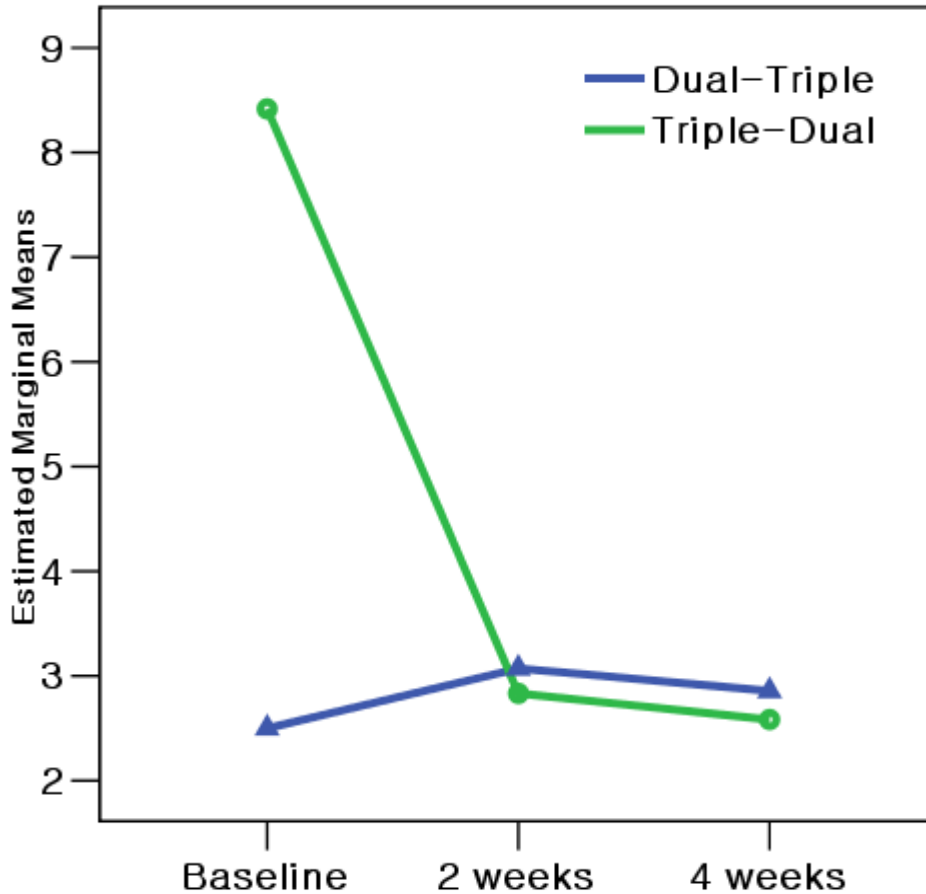
## 3. Paired Samples test

- Baseline & 2 weeks:  $p = 0.050$ ,  
in the triple-dual group.



# RESULTS

0.5 mM AA-induced MPA (LTA)



## 1. Two-way ANOVA

- Multivariate Tests:  
Period:  $p = 0.556$ ;  
Treatment\*period:  $p = 0.561$ .
- Mauchly's Test of Sphericity:  $P = 0.000$ .  
Period:  $p = 0.358$ ; (Greenhouse-Geisser)  
Treatment\*period:  $p = 0.281$ .
- Tests of between subjects effects:  
 $p = 0.341$ .

## 2. One-way ANOVA

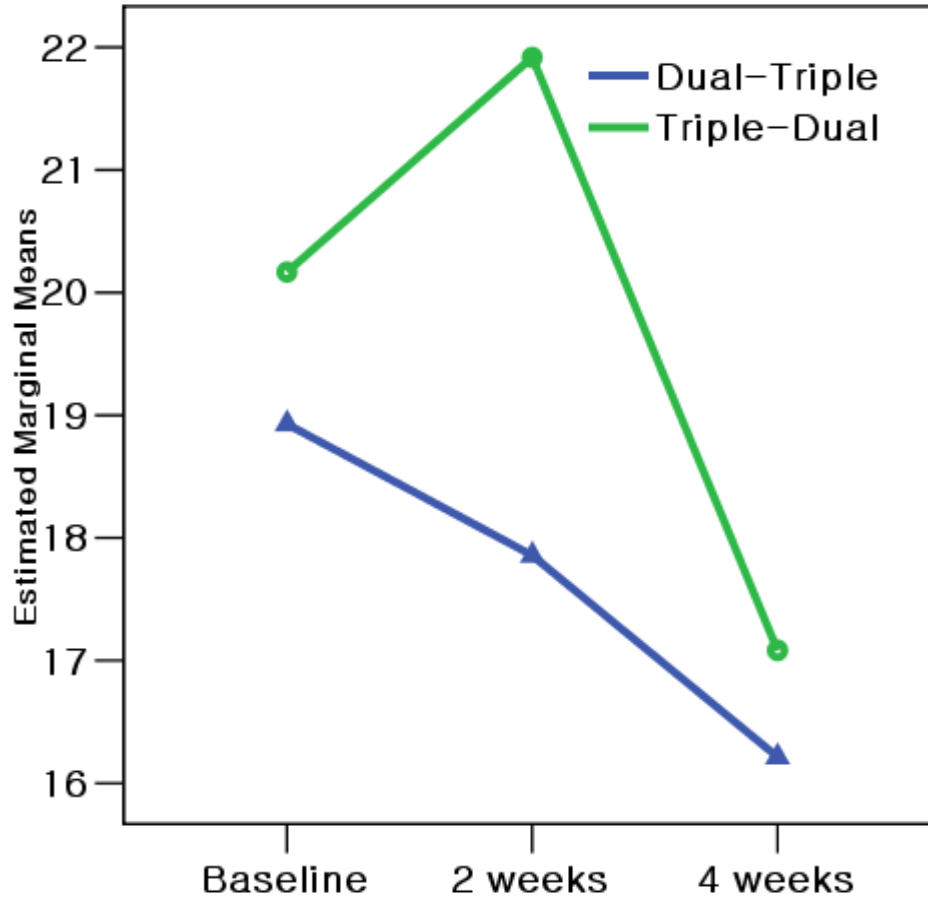
- Dual-Triple group:  $p = 0.866$ ;
- Triple-Dual group:  $p = 0.051$ .

## 3. Paired Samples test

There was no significant difference in both groups.

# RESULTS

2 µg/mL collagen-induced MPA (LTA)



## 1. Two-way ANOVA

- Multivariate Tests:  
Period:  $p = 0.518$ ;  
Treatment\*period:  $p = 0.880$ .
- Mauchly's Test of Sphericity:  $P = 0.464$ .  
Period:  $p = 0.594$ ;  
Treatment\*period:  $p = 0.881$ .
- Tests of between subjects effects:  
 $p = 0.612$ .

## 2. One-way ANOVA

- Dual-Triple group:  $p = 0.853$ ;
- Triple-Dual group:  $p = 0.618$ .

## 3. Paired Samples test

There was no significant difference in both groups.

# LIMITATION

- Total number of eligible patients: small (26 patients).
- Insensitive of LTA and MEA to detect small platelet aggregates by 5-HT.
- Negative Lab results did not absolutely concern with clinical effects of sarpogrelate.

# CONCLUSION

The adjunctive sarpogrelate to aspirin and clopidogrel did not benefit in reduction of post-treatment platelet reactivity in patients with DES implantation based on this study.