DukeHeart *On The Go*

Bentracimab Immediately and Significantly Reverses the Antiplatelet Effects of Ticagrelor in Older People

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Disclosures

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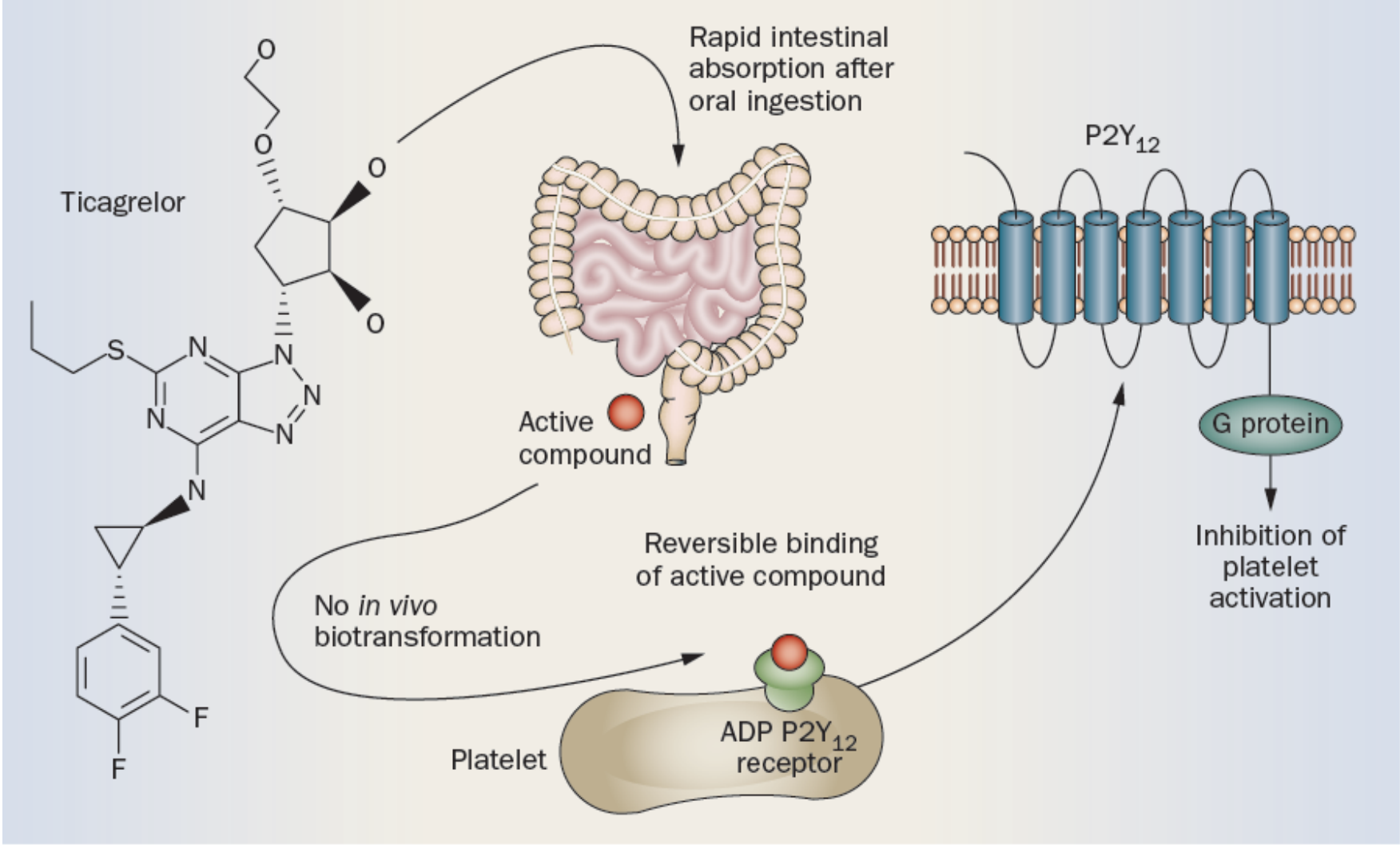
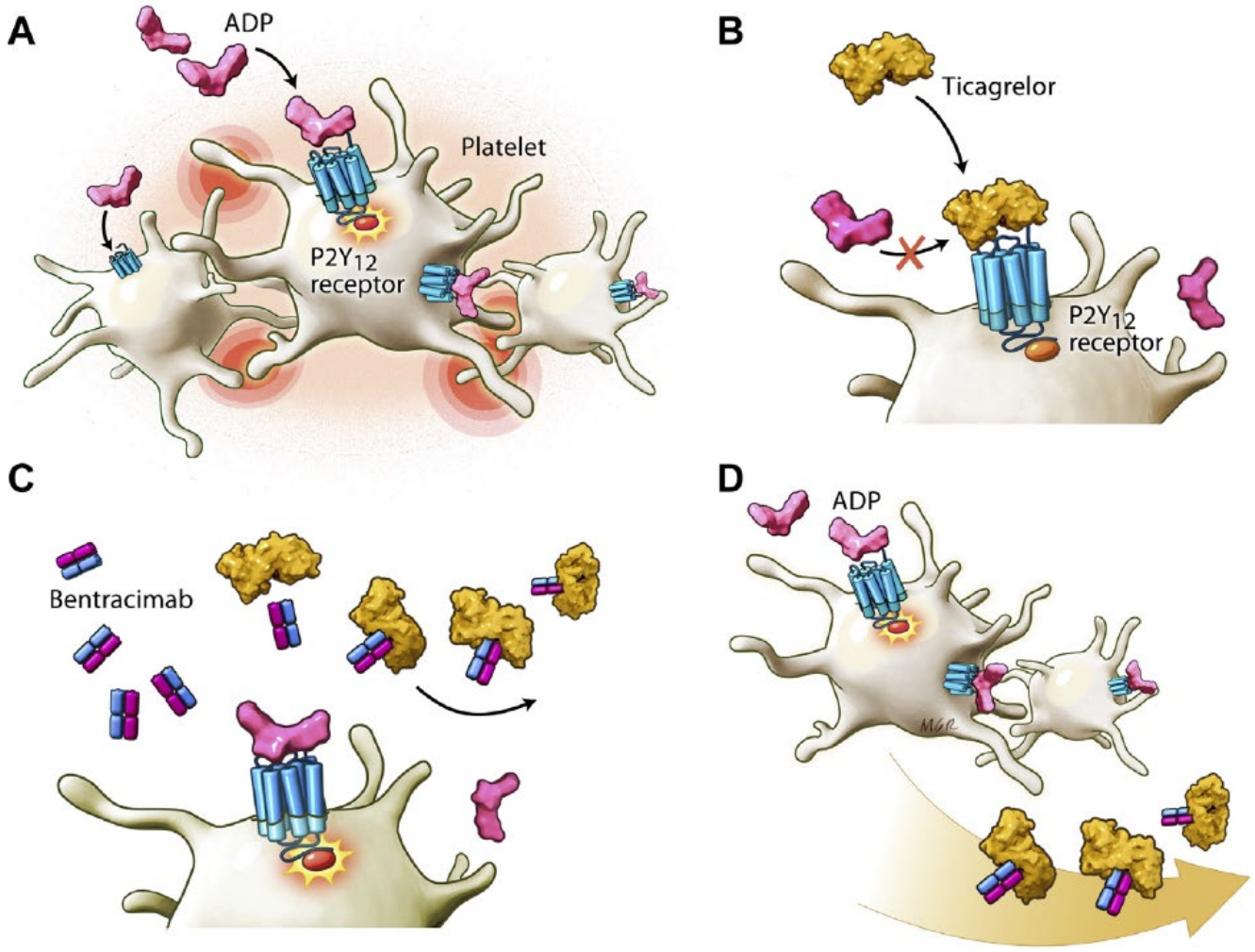
This presentation includes the off-label and investigational uses of drugs.

Ticagrelor: Reversible Mechanism of Action



Bhatt DL. *Nature Reviews Cardiology.* 2009;6:737-38.

Bentracimab: An Intravenous Monoclonal Antibody



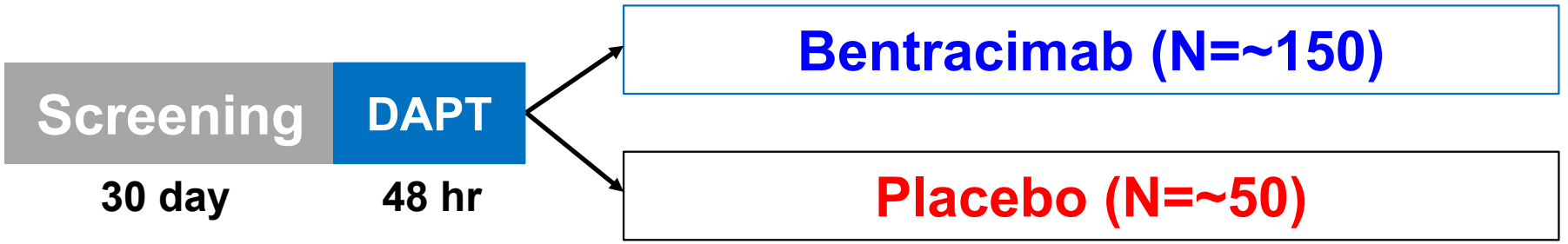
The P2Y12 receptor is activated by adenosine diphosphate (ADP) (**A)**

Ticagrelor reversibly binds to the P2Y12 receptor on platelets. This induces a conformational change that prevents ADP from signaling through to the P2Y12 receptor, inhibiting platelet activation (**B**)

Bentracimab is a recombinant human IgG1 monoclonal antibody fragment that binds to free ticagrelor with high affinity and specificity. This allows ADP to activate platelets while the bentracimab–ticagrelor complex is eliminated from the bloodstream (C&D)

Ha AC, et al. *J Am Coll Cardiol.* 2021;78(13):1372-1384.

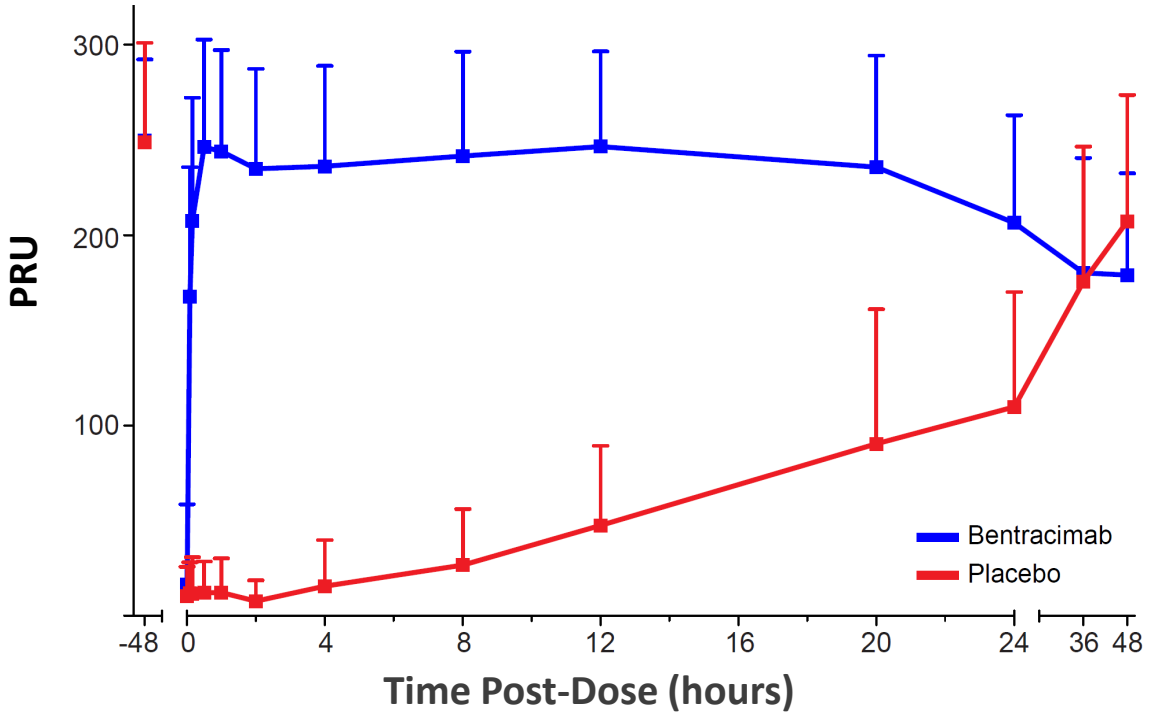
Phase 2B Study Design



- **Randomized, double-blind, placebo-controlled trial (3 active:1 placebo)**
  - 50–80-year-old volunteers pretreated with ticagrelor and aspirin for 48 hours
  - Primary endpoint – inhibition of PRU

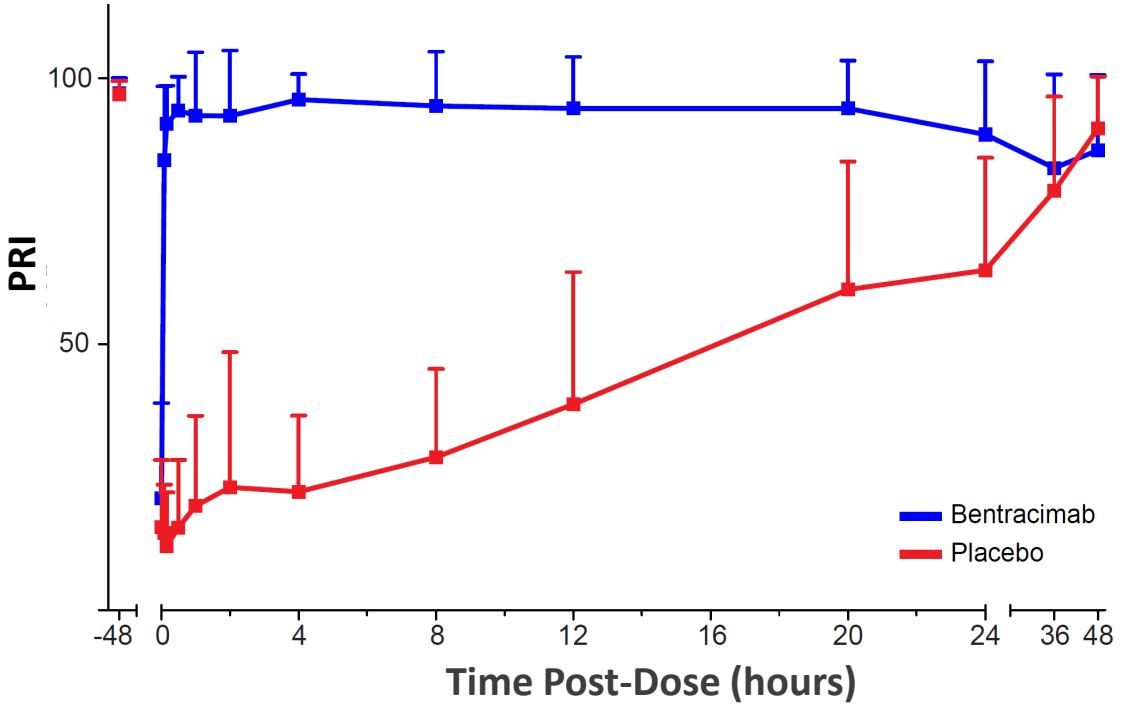
Immediate, Sustained Ticagrelor Reversal with Bentracimab (VerifyNow PRU and VASP PRI Assays)

PRU Analysis
(Bentracimab vs. Placebo 0–48 hours)



Timepoint	5 min	10 min	30 min	1 hr	4 hr	12 hr	20 hr	24 hr	36 hr	48 hr
P value	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.1102	0.0127

PRI Analysis
(Bentracimab vs. Placebo 0–48 hours)



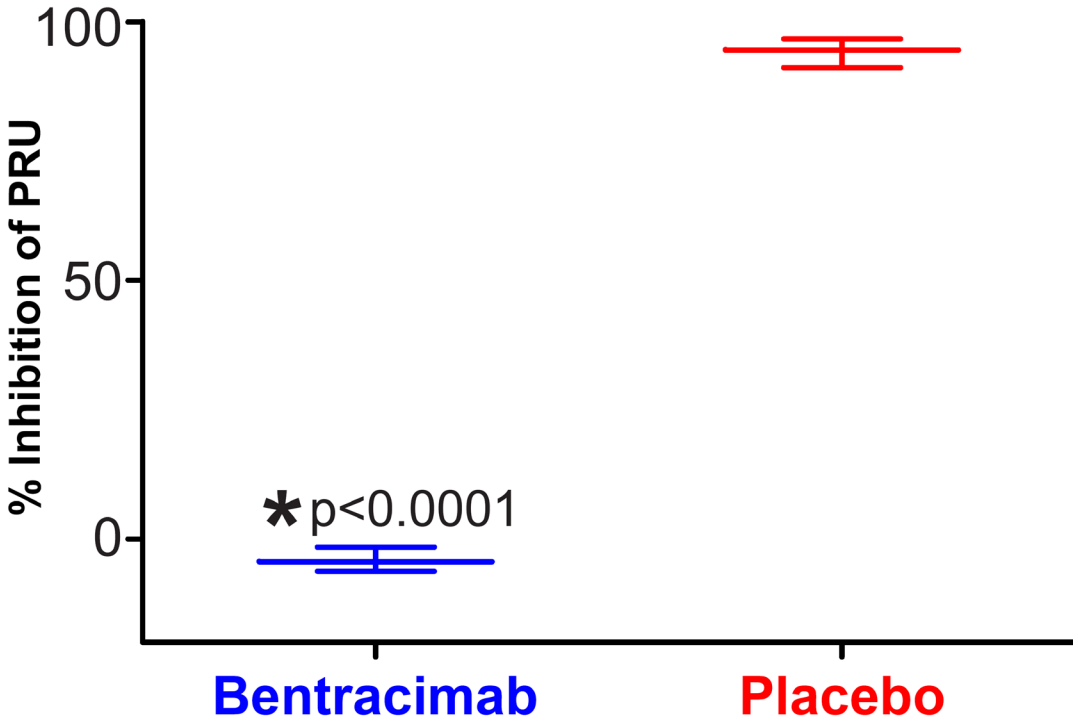
Timepoint	5 min	10 min	30 min	1 hr	4 hr	12 hr	20 hr	24 hr	36 hr	48 hr
P value	0.0572	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.2802	0.4562

Bentracimab achieved immediate and sustained reversal in 50–80 year olds pretreated with DAPT

Primary Endpoint and Subgroup Analysis

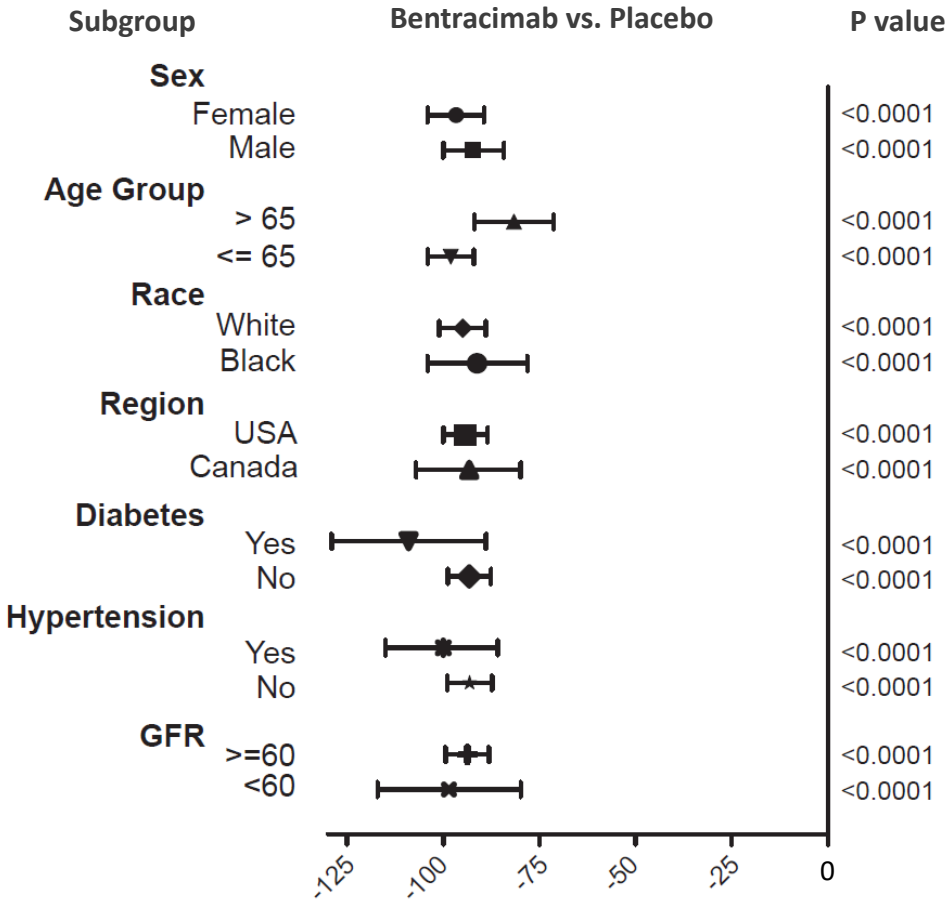
Primary Endpoint Analysis

(Minimum % inhibition of PRU within 4 hr)



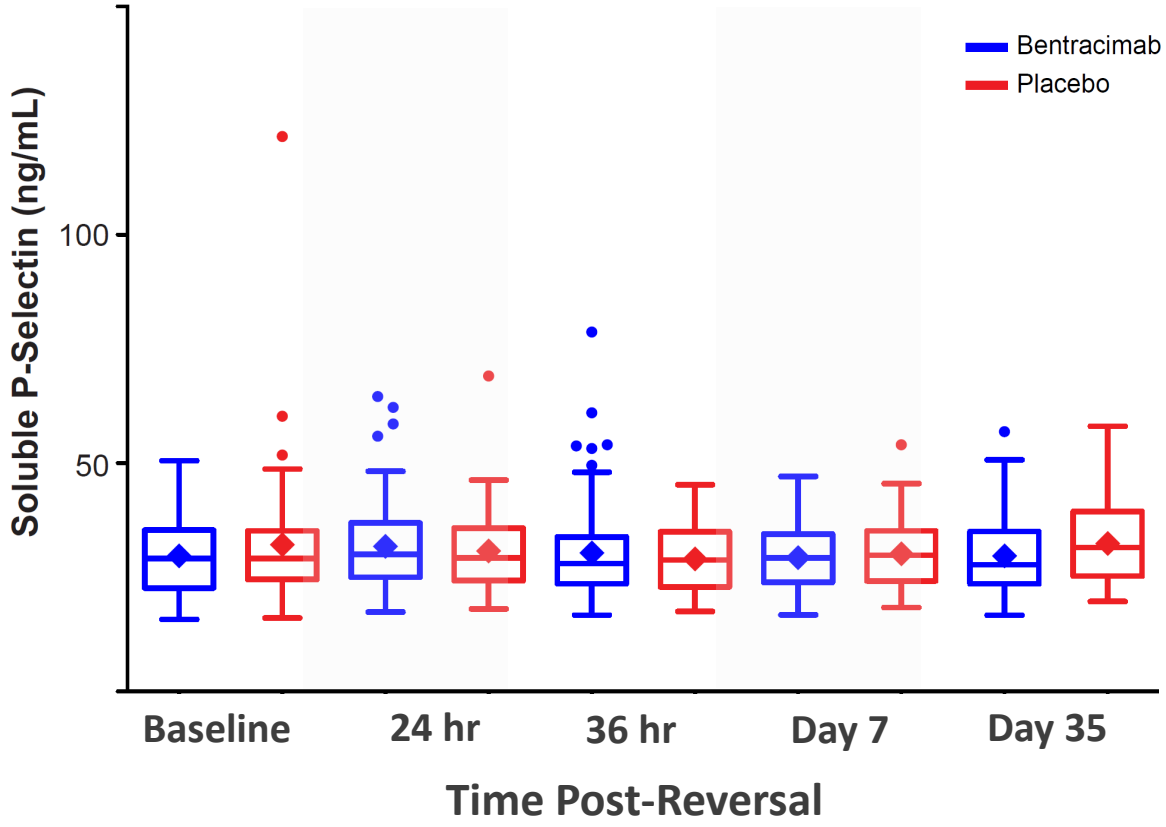
Forest Plot of Treatment Difference

(Mean change in minimum % inhibition of PRU)

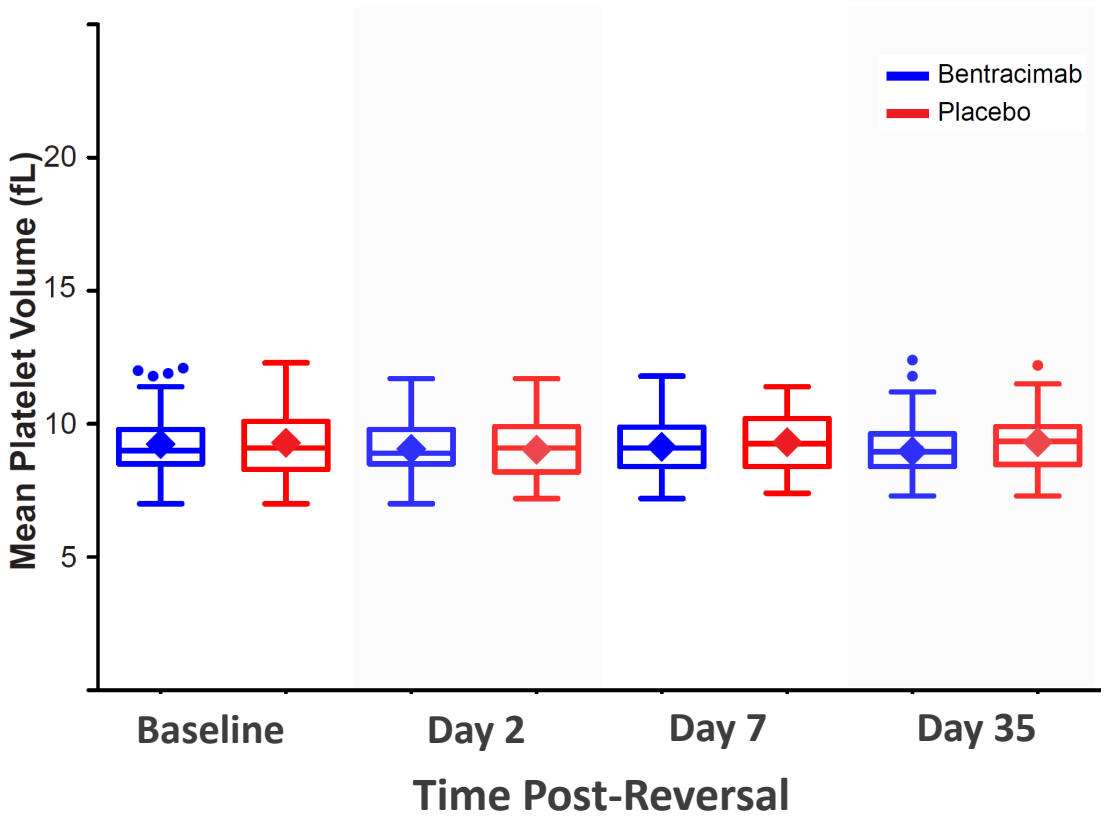


Markers of Platelet Activation

P-Selectin Analysis



Mean Platelet Volume Analysis



No evidence of elevated platelet activation post-reversal in Bentracimab or Placebo groups

Bentracimab Safety Profile

Treatment Emergent Adverse Events in >1 Subject

TEAEs	Placebo N=51 n (%)	Bentracimab* N=154 n (%)
Headache	4 (7.84)	6 (3.90)
Ecchymosis	2 (3.92)	6 (3.90)
Contusion	2 (3.92)	5 (3.25)
Vessel puncture bruise	1 (1.96)	4 (2.60)
Nausea	2 (3.92)	3 (1.95)
Diarrhea	1 (1.96)	3 (1.95)
Edema	1 (1.96)	2 (1.30)
Dizziness	1 (1.96)	2 (1.30)
Infusion site extravasation	0	2 (1.30)
Pain in extremity	0	2 (1.30)
Asymptomatic COVID-19	0	2 (1.30)
Catheter site bruise	1 (1.96)	1 (0.65)
Constipation	1 (1.96)	1 (0.65)
Occult blood	1 (1.96)	1 (0.65)
Hematochezia	2 (3.92)	0
Hyperglycemia	2 (3.92)	0

All Serious Adverse Events

Preferred Term	Placebo (N=51) n (%)	Bentracimab (N=153) n (%)
Total SAEs	1	0
Drug-related SAEs	0	0
Unrelated SAEs	1	0
Car accident	1	0

- **No drug-related SAEs**
- **No thrombotic events**

*There was no significant difference between Bentracimab and Placebo for any TEAE, P=0.52

Conclusions

- Compared with placebo, **bentracimab** **significantly restored platelet function, as measured** by multiple assays, by binding and eliminating free ticagrelor and ticagrelor active metabolite
- **No thrombotic events and no SAEs** reported in volunteers randomized to **bentracimab**, confirming the safety profile
- Based on these data, **bentracimab** **appears to be a very promising option for ticagrelor reversal**
- Assessment of clinical effect of **bentracimab** on patients with bleeding awaits completion of the **REVERSE-IT** study