Insights on Selected Procoagulation markers and Outcomes in Stroke Trial (iSPOT) Primary results

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Neurological Emergencies Treatment Trials

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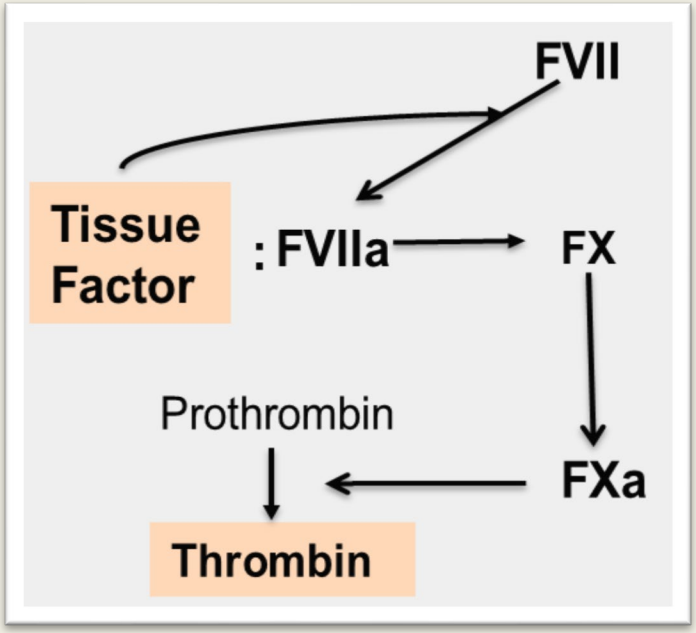
  - ❖NINDS 1U01NS069498 (SHINE)

- No Unlabelled/Unapproved disclosure

Background

- Acute stroke with hyperglycemia is associated with worse functional outcomes
- Tissue factor pathway markers of blood coagulation are elevated in acute ischemic stroke
- These markers are considerably higher in patients with hyperglycemia



- Need for a study of the effects of blood glucose control on blood coagulation markers and their relationship to stroke outcomes.

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Design and Intervention

- Subset of patients enrolled in the SHINE trial
- SHINE treatment arms:
  - ❖Intensive control - target blood glucose 80-130 mg/dL
  - ❖Standard treatment - target blood glucose <180 mg/dL
- SHINE functional outcome – NIHSS adjusted mRS at 90 days
- Compare markers of blood coagulation by treatment, by functional outcome, and the interaction between treatment and outcome

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Main iSPOT Eligibility Criteria

- SHINE Eligible
  - ❖ AIS <12 hours from onset
  - ❖ NIHSS 3-22
  - ❖ BG > 110 mg/dL if history of diabetes or BG ≥150 mg/dL if no history of diabetes

- Exclusions
  - ❖ Systemic anticoagulation
  - ❖ Known hepatic insufficiency (INR>1.5 or hx variceal bleeding or hepatic encephalopathy)
  - ❖ History of thrombotic or hypercoagulable condition

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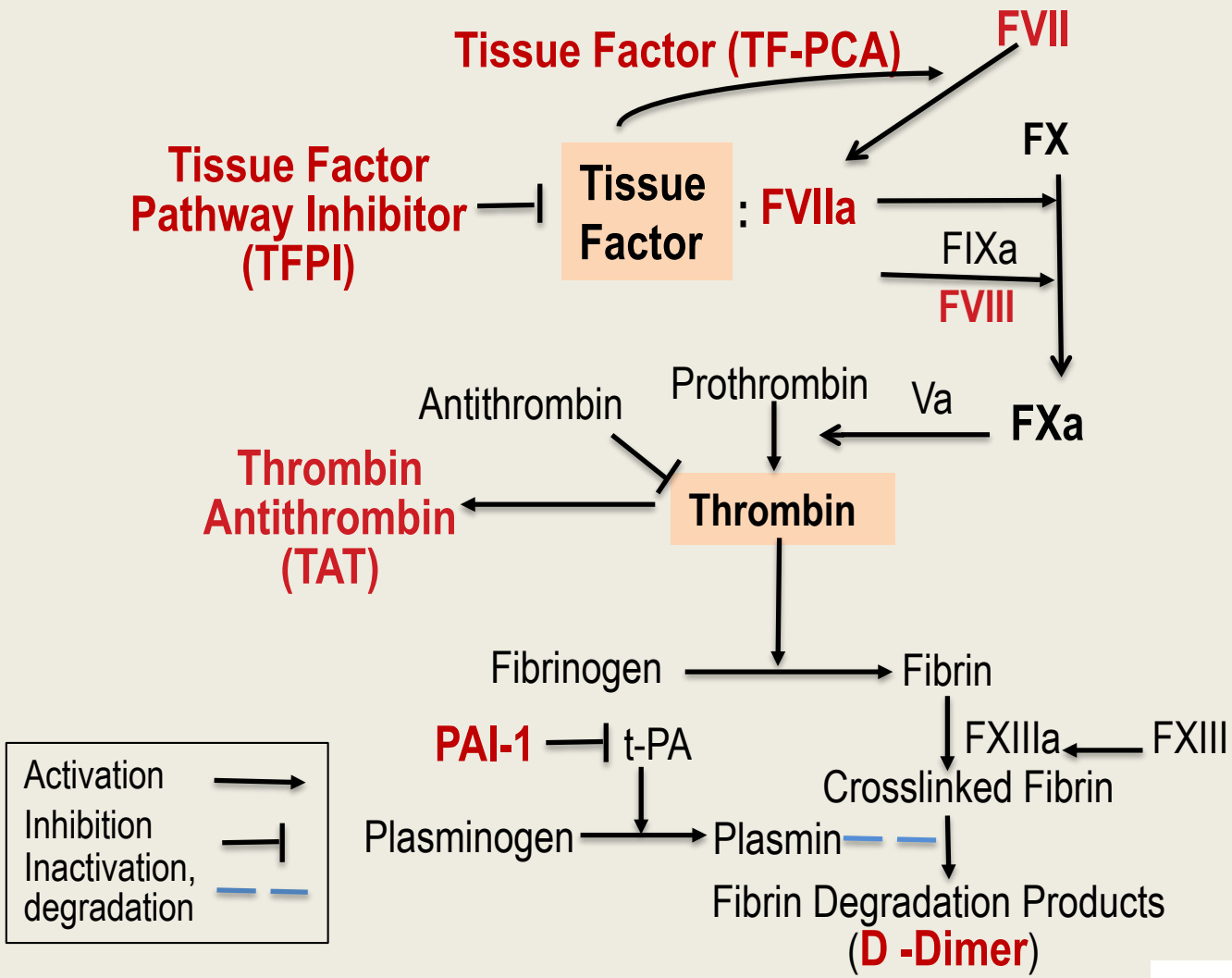
Tissue Factor Pathway of Blood Coagulation
iSPOT measurements



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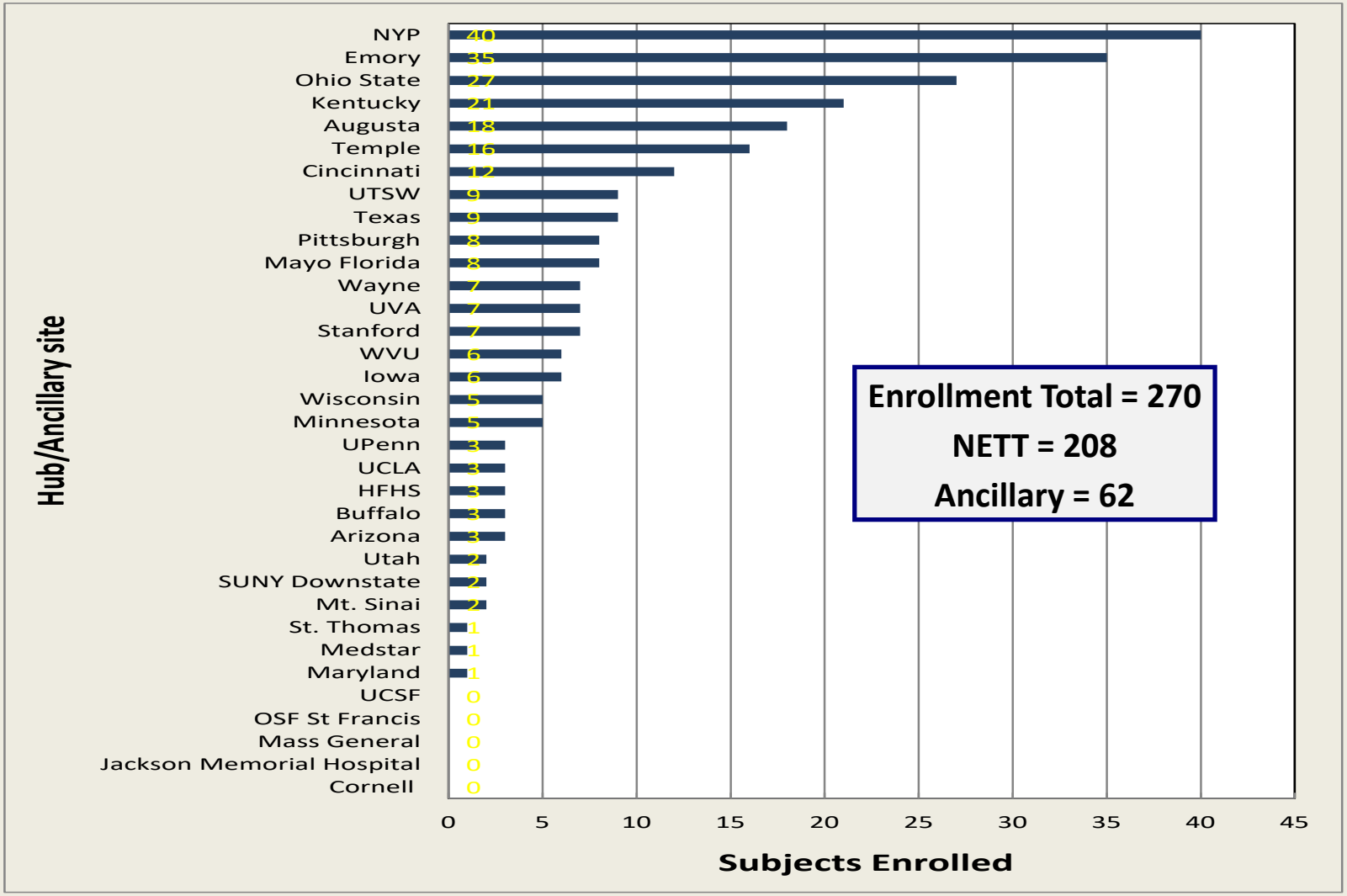
Enrollment by Site



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Characteristics of the Patients

Characteristic	Intensive (N=135)		Standard (N=135)	
SHINE functional outcome	Favorable (N=30)	Unfavorable (N=102)	Favorable (N=20)	Unfavorable (N=112)
Age (yr)-median (IQR)	67 (58-71)	64.5 (55-74)	63.5 (57-71)	66 (56-73)
Female sex–no. (%)	9 (30.0)	42 (41.2)	8 (40.0)	47 (42.0)
Previous hx of Diabetes mellitus-no. (%)	23 (76.7)	83 (81.4)	16 (80.0)	92 (82.1)
Blood glucose levels (mg/dL, mean (IQR)				
Initial	167 (148-208)	163 (120-232)	177 (144-215)	184 (145-237)
48-Hr	98 (91-138)	106.5 (94-134)	150 (110-175)	187 (144-235)
IV tPA treated - no. (%)	15 (50.0)	49 (48.0)	9 (45.0)	43 (38.4)
NIHSS at randomization–median (IQR)	7 (3-11)	7 (4-12)	7 (4-10.5)	7(5-11)
Stoke onset to baseline (hr)-median (IQR)	8.3 (6-9.7)	9.0 (7.4-11.5)	9.4 (7.3-11.1)	9.1 (7.0-11.3)

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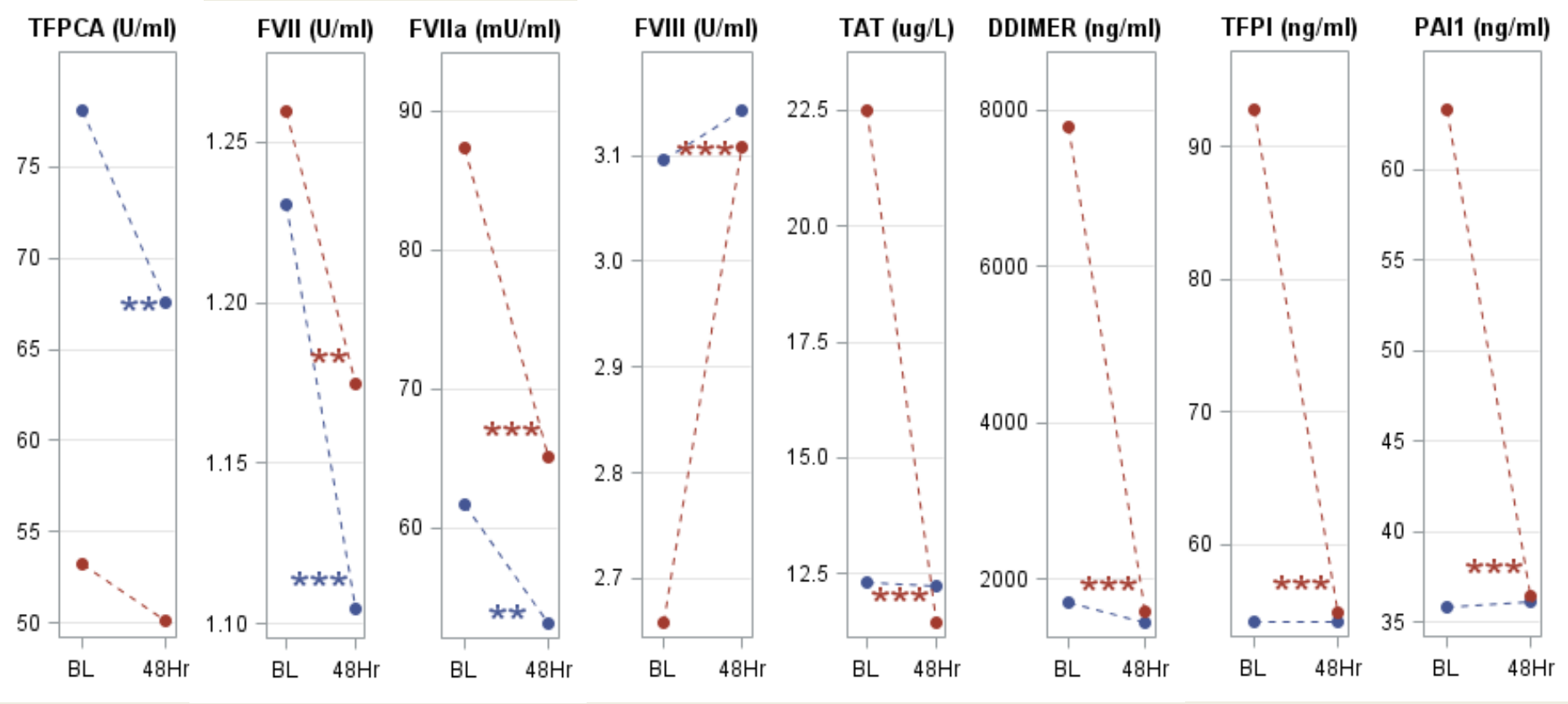
Biomarker levels after stroke by IV tPA administration



P values represent comparisons between baseline and 48-hr levels for each marker by tPA treatment. Value is adjusted using Tukey's method for multiple comparisons. **p < 0.05, ***p < 0.01

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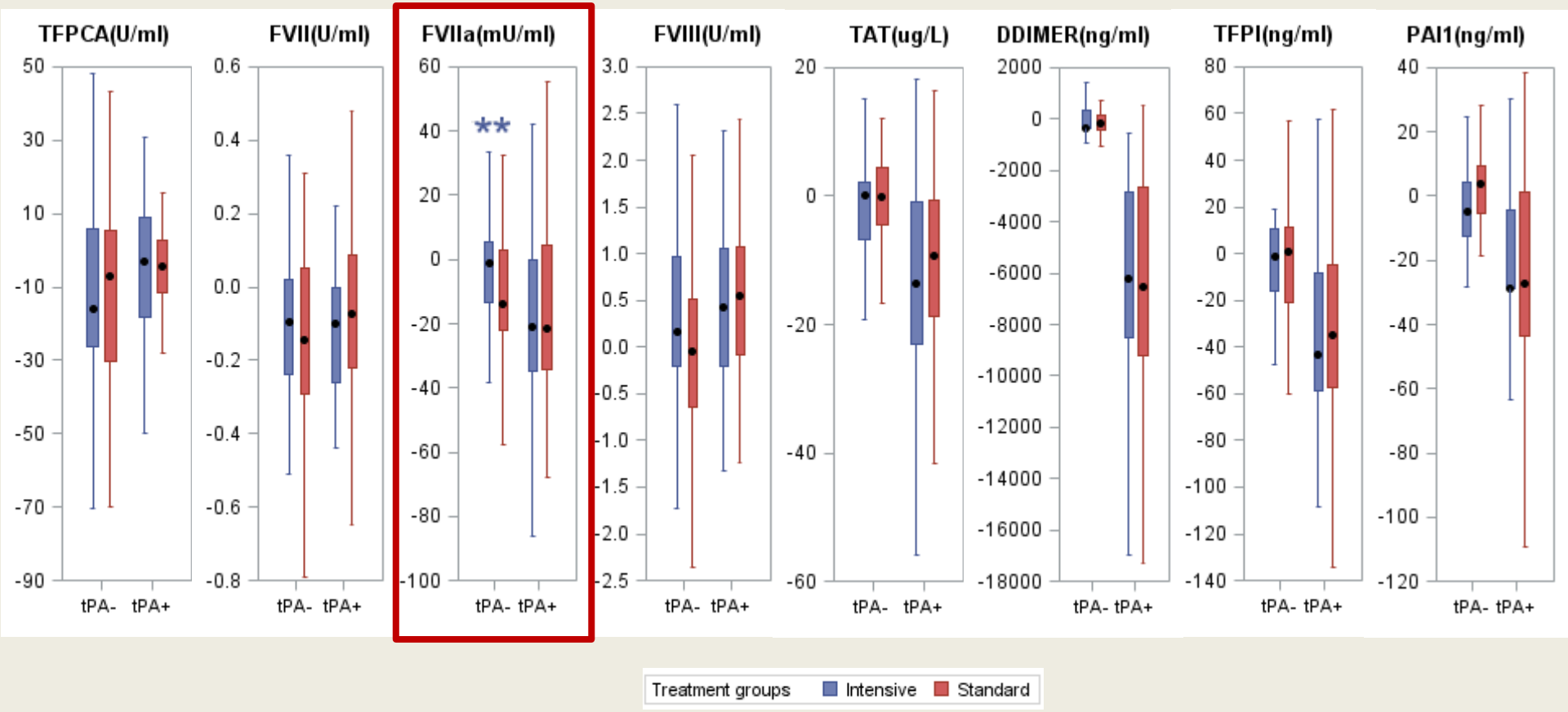
Change in factor levels by SHINE treatment group



P values represent comparisons between Intensive and Standard groups in terms of changes from baseline to 48 hours by tPA treatment regardless functional outcome. **p < 0.05

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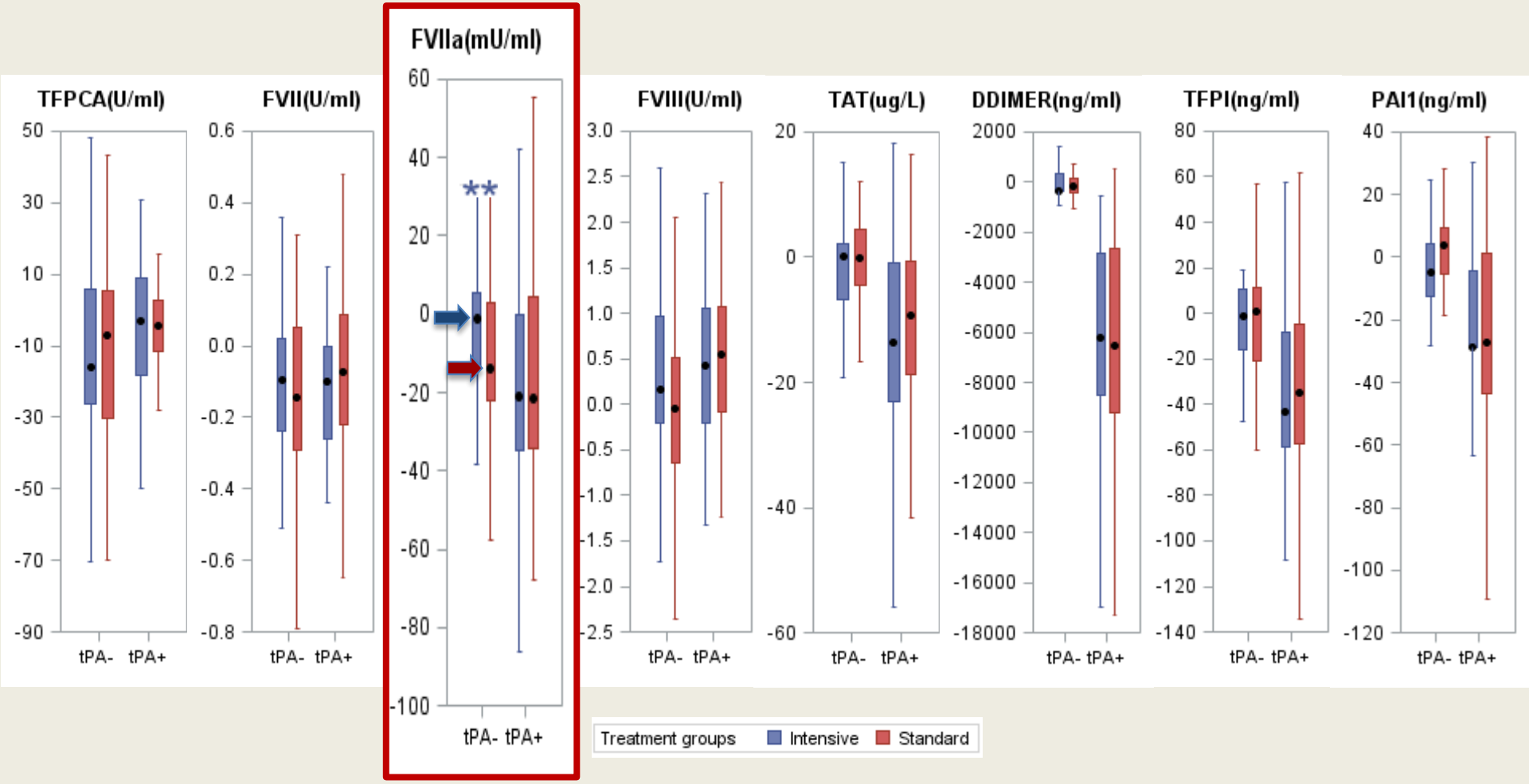
Change in factor levels by SHINE treatment group



P values represent comparisons between Intensive and Standard groups in terms of changes from baseline to 48 hours by tPA treatment regardless functional outcome. **p < 0.05

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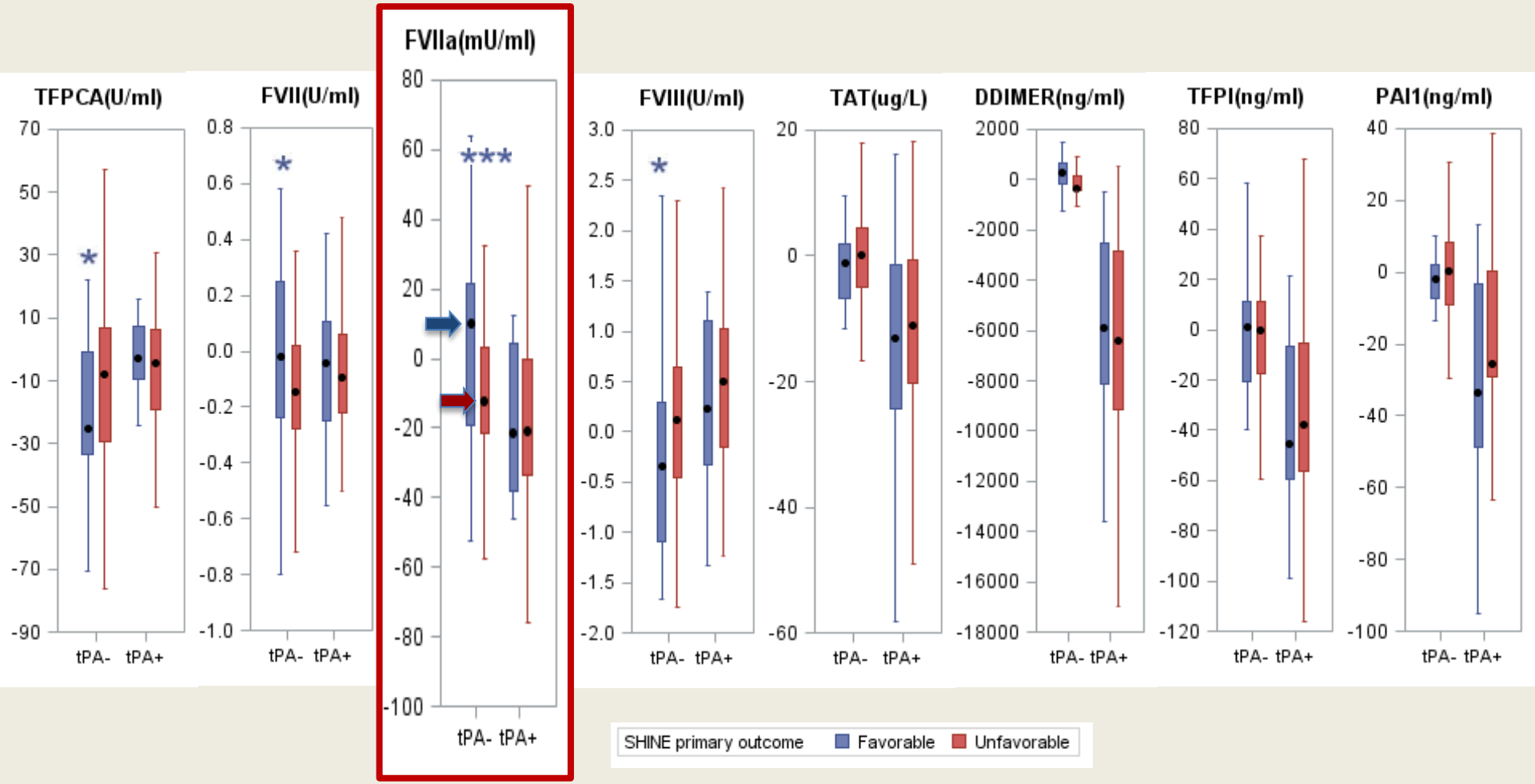
Change in factor levels by functional outcome



P values represent comparisons between Favorable and Unfavorable groups in terms of changes from baseline) to 48 hours by tPA treatment regardless of treatment group. * $p < 0.1$, ***$p < 0.01$

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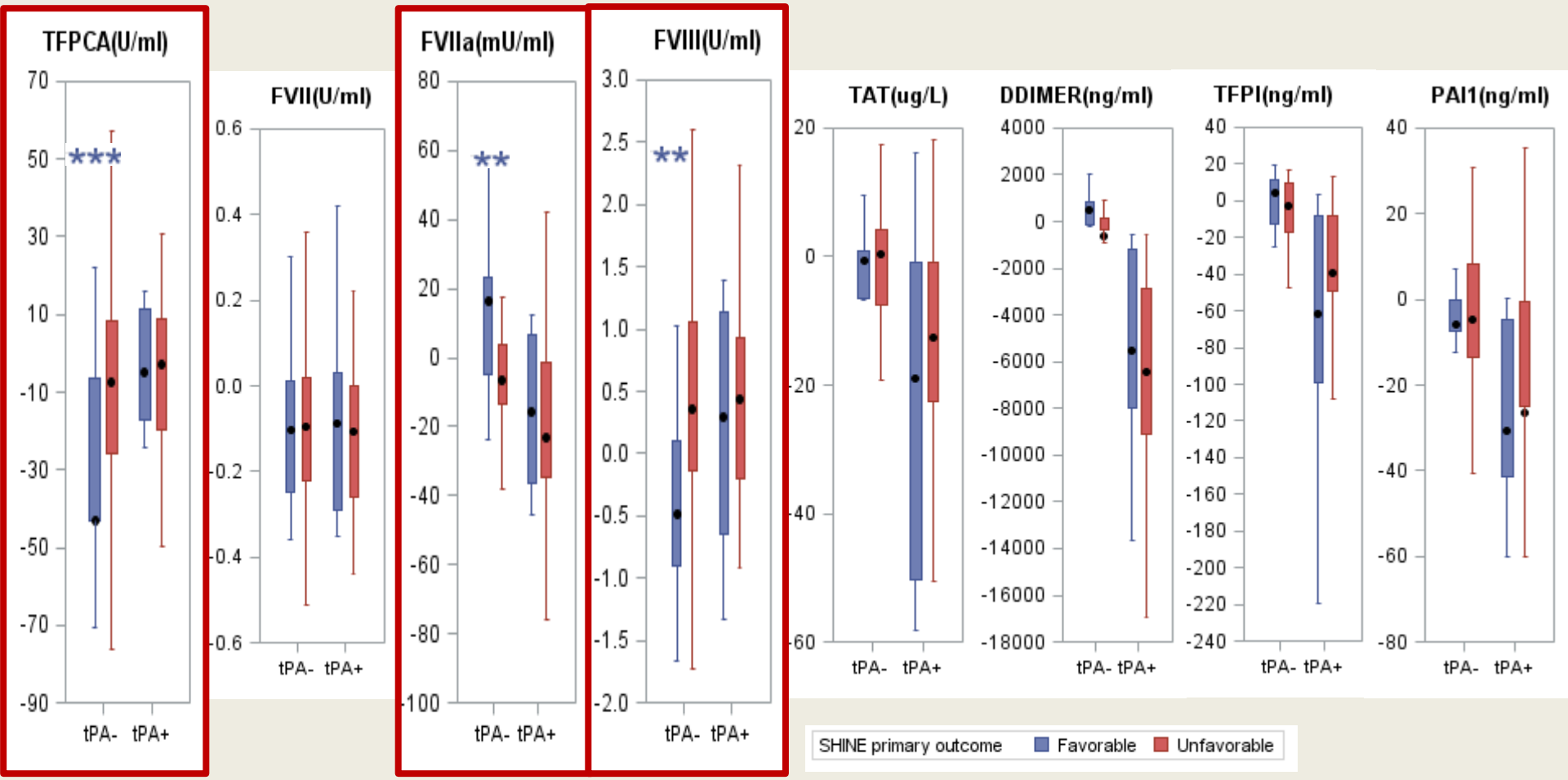
Relationship of change in factor levels and functional outcome: intensive BG control



P values represent comparisons between Favorable and Unfavorable groups in terms of changes from baseline to 48 hours by tPA treatment in intensive group. ** p < 0.05, ***p < 0.01

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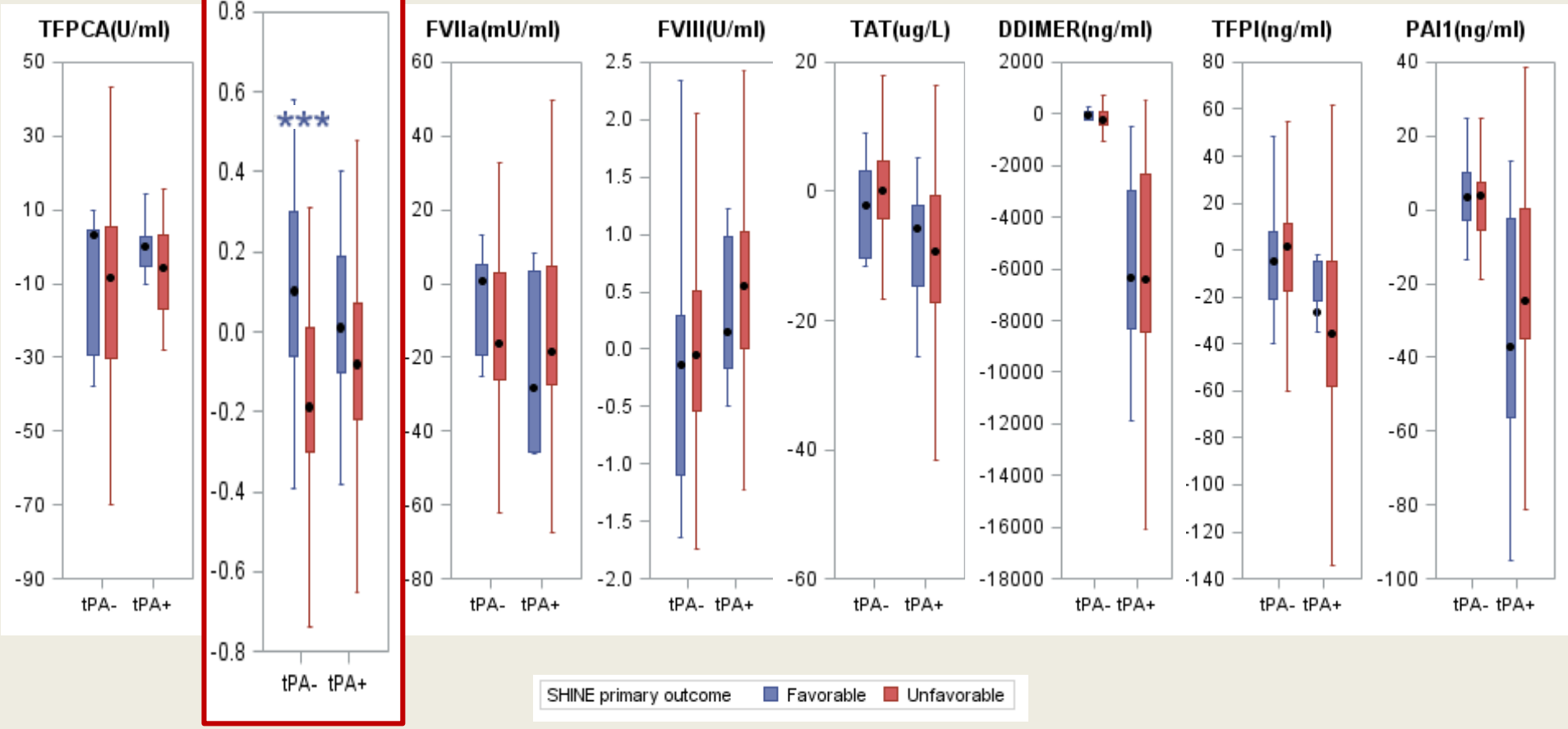
Relationship of change in factor levels and functional outcome: standard BG control



P values represent comparisons between Favorable and Unfavorable groups in terms of changes from baseline to 48 hours by tPA treatment in standard group. ***p < 0.01

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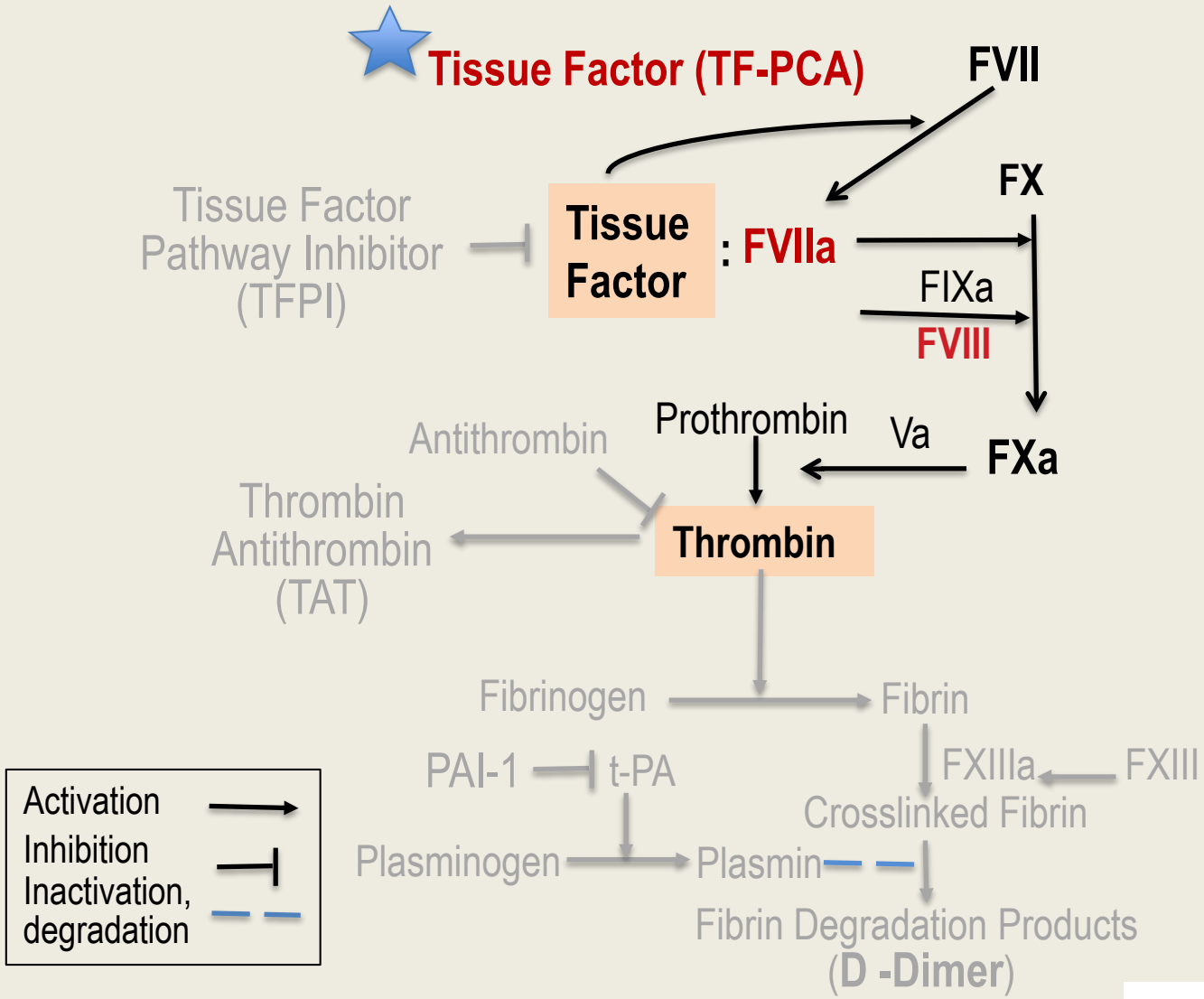
Summary and significance



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The SHINE-iSPOT Team!

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