

## Supplementary information

**Table S1.** Demographic, clinical characteristics and treatment of thrombotic controls and APS patients.

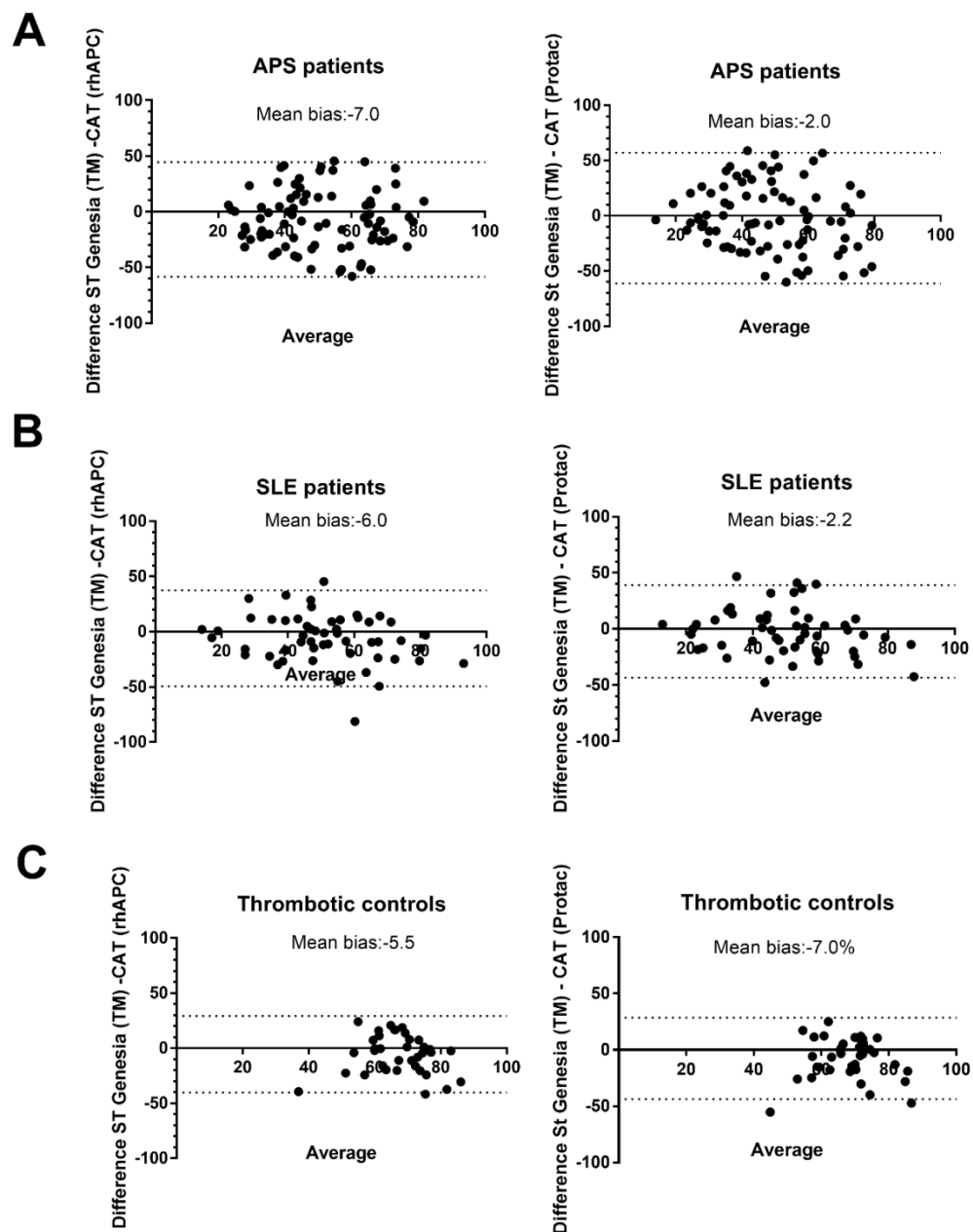
| Diagnosis                                  | Thrombotic controls<br>(n = 36) | All APS<br>(n = 105) | Thrombotic APS<br>Venous or Arterial<br>(n = 83) | Pregnancy morbidity APS<br>(n=22) |
|--|---------------------------------|----------------------|--|-----------------------------------|
| Age, mean years $\pm$ SD                   | 49.1 ( $\pm$ 15.1)              | 47.2 $\pm$ (14.7)    | 51.3 ( $\pm$ 18.4)                               | 44.1 ( $\pm$ 6.8)                 |
| Sex, male/female, n                        | 14/22                           | 25/81                | 25/58  | 0/23                              |
| VTE only (DVT or PE), n (%)                | 32 (88.9)                       | 55 (52.4)            | 51 (61.4)  | 4                                 |
| AT only, n (%)                             | 0 (0)                           | 15 (14.2)            | 13 (15.7)  | 2                                 |
| Severe thrombotic phenotype*, n (%)        | 4(11.1)                         | 21(20)               | 19 (22.9)  | 2 (9.1)                           |
| VTE + AT, n (%)                            | 2 (5.6)                         | 11 (10.5)            | 11 (13.3)  | 2 (9.1)                           |
| Recurrent venous events, n (%)             | 2 (5.6)                         | 10 (9.5)             | 8 (9.6)  |                                   |
| Pregnancy morbidity only (%)               |                                 | 14 (13.2)            |  | 14(63.6)                          |
| Pregnancies                                |                                 | 63                   | 7  | 56                                |
| Life births                                | 12                              | 22                   | 7  | 15                                |
| Total APS-related PM                       | 12                              | 41                   | N/A  | 41                                |
| <10 weeks gestation                        | N/AN/A                          | 33                   |  | 33                                |
| >10 weeks gestation                        |                                 | 8                    |  | 8                                 |
| APS categories ‡, n (%)                    |                                 | 64 (61.0)            | 51 (61.4)  | 13 (59.1)                         |
| I  |                                 | 45(42.8)/19 (18.1)   | 36 (43.4)/15 (18.1)                              | 9 (40.9)/4 (18.2)                 |
| /Double aPL +/Triple aPL +                 |                                 |                      |  |                                   |
| IIa  | N/A                             | 16 (15.2)            | 12 (14.5)  | 4 (18.2)                          |
| IIb  |                                 | 11 (10.5)            | 7(8.5)   | 4 (18.2)                          |
| IIc  |                                 | 14 (13.3)            | 13(15.6)   | 2 (9.1)                           |
| Medication                                 |                                 |                      |  |                                   |
| Warfarin                                   |                                 |                      |  |                                   |
| Target INR                                 |                                 |                      |  |                                   |
| 2.0-3.0, n (%)                             | 32 (88.9)                       | 55(52.4)             | 51 (61.4)  | 4 (18.2)                          |
| 3.0-4.0, n (%)                             | 4 (11.1)                        | 36 (34.3)            | 32 (38.6)  | 4 (18.2)                          |
| Aspirin                                    |                                 | 3 (2.9)              |  | 3 (13.6)                          |
| No medication                              |                                 | 12 (10.5)            |  | 12 (50.0)                         |
| a $\beta$ 2GPI IgG (GPU)<br>cut off 20 GPU | N/A                             | 61.3 (14.0-132)      | 69.8 (19.7-132)                                  | 52.7 (14.0-87.4)                  |
| a $\beta$ 2GPI IgM (MPU)<br>cut off 20 MPU | N/A                             | 21.2 (2.1-101)       | 23.1 (2.1-101)                                   | 19.2 (3.2-45.7)                   |
| aCL IgG (GPLU)<br>cut off 20 GPLU          | N/A                             | 44.5 (3.7-144)       | 27.8 (3.7-142)                                   | 61.2 (12.9-144)                   |
| aCL IgM (MPLU)<br>cut off 20 MPLU          | N/A                             | 39.9 (6.0-132)       | 51.3 (14.6-132.2)                                | 28.6 (6.0-98.0)                   |
| LA, n (%)                                  | N/A                             | 90 (85.7)            | 76 (90.5)  | 14 (63.6)                         |

aB2GPI: anti-beta2 glycoprotein I antibodies; aCL: cardiolipin antibodies, LA: lupus anticoagulant. \*Severe thrombotic phenotype refers to patients with recurrent thromboembolic episodes despite therapeutic anticoagulation or patients with both venous thromboembolism (VTE) and arterial thrombosis (AT). ‡APS categories: I, IIa, IIb, IIc based on [22].

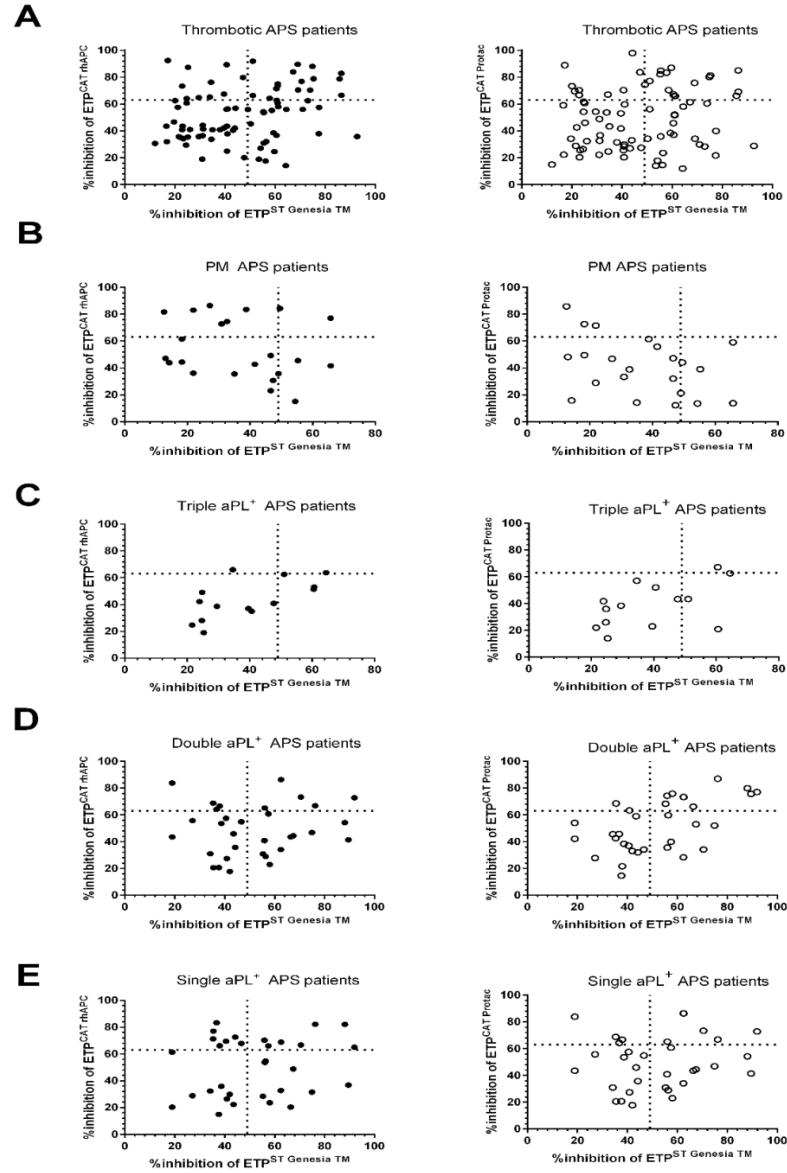
**Table S2.** Demographic, clinical characteristics and treatment of patients with SLE.

| <b>SLE PATIENTS</b>  | <b>All SLE patients (n=53)</b> | <b>SLE aPL with throm-<br/>bosis (n=16)</b> | <b>SLE aPL no throm-<br/>bosis (n=20)</b> | <b>SLE no aPL no thrombosis<br/>(n=17)</b> |
|--|--------------------------------|---|---|--|
| Sex, male/female, n  | 7/47                           | 4/12  | 5/15                                      | 3/14                                       |
| Age, years ( $\pm$ STV)  | 45.6 ( $\pm$ 12.2)             | 48.1 ( $\pm$ 15.9)                          | 46.9( $\pm$ 11.8)                         | 44.5( $\pm$ 8.5)                           |
| <b>SLE manifestations (history)</b>  |                                |   |   |  |
| Rash, n (%)  | 32 (60.4)                      | 9 (56.3)                                    | 12 (60)                                   | 11 (64.7)                                  |
| Photosensitivity, n (%)  | 18 (34)                        | 5 (31.3)                                    | 7 (35)                                    | 6 (35.3)                                   |
| Alopecia, n (%)  | 14 (26.4)                      | 4 (25)                                      | 4 (20)                                    | 6 (35.3)                                   |
| Oral ulcers, n (%)   | 10 (18.9)                      | 5 (31.3)                                    | 3 (15)                                    | 2 (11.8)                                   |
| Joint involvement, n (%)   | 42(79.2)                       | 14 (87.5)                                   | 13 (65)                                   | 15 (88.2)                                  |
| Serositis, n (%)   | 13 (24.5)                      | 4 (25)                                      | 5 (25)                                    | 4 (23.5)                                   |
| Renal involvement, n (%)   | 21 (39.6)                      | 5 (31.3)                                    | 6 (30)                                    | 10 (58.8)                                  |
| NPSLE, n (%)   | 11 (20.8)                      | 5 (31.3)                                    | 3 (15)                                    | 3 (17.6)                                   |
| Low C3 (normal range 0.9-1.8 g/l) and/or C4 (nor-<br>mal range 0.1-0.4 g/l): n (%) | 29 (54.7)                      | 7 (43.8)                                    | 10 (50)                                   | 12 (70.6)                                  |
| aDNA (normal range <50 IU/ml): n (%)   | 37 (69.8)                      | 12 (75)                                     | 12 (60)                                   | 12 (70.6)                                  |
| <b>Patients with thrombosis (history)</b>  |                                |   |   |  |
| Arterial only: n (%)   | 7 (13)                         | 6(37.5)                                     | 0 (0)                                     | 0 (0)                                      |
| Venous only (DVT or PE): n (%)   | 7 (13)                         | 6(37.5)                                     | 0 (0)                                     | 0 (0)                                      |
| Severe thrombotic phenotype**, n (%)   | 4 (7.4)                        | 4 (25)                                      | 0 (0)                                     | 0 (0)                                      |
| Arterial + Venous: n (%)   | 2 (3.7)                        | 2 (12.5)                                    | 0 (0)                                     | 0 (0)                                      |
| Recurrent venous events: n (%)   | 2 (3.7)                        | 2 (12.5)                                    | 0 (0)                                     | 0 (0)                                      |
| <b>Disease activity at sample collection</b>                                       |                                |   |   |  |
| Total BILAG score: median (95% centile)  | 2 (1-4)                        | 2 (1-8)                                     | 3 (1-8)                                   | 1 (1-9)                                    |
| Any BILAG "A", "B" or "C": n (%)   | 45 (83.3)                      | 13 (81.3)                                   | 17 (85)                                   | 15 (83.3)                                  |
| Any BILAG "A" or "B": n (%)  | 19 (35.2)                      | 5 (31.3)                                    | 8 (40)                                    | 6 (33.3)                                   |
| Any BILAG "A" : n (%)  | 3 (5.6)                        | 2 (6.3)                                     | 1 (5)                                     | 0(0)                                       |
| SLEDAI-2K: median (95th centile)   | 2 (1-5)                        | 4 (1-6)                                     | 2 (1-5)                                   | 2 (1-5)                                    |
| <b>Antithrombotic treatment</b>  |                                |   |   |  |
| Anti-platelet therapy, n (%)   | 7 (13.0)                       | 2 (12.5)                                    | 3 (15)                                    | 2 (11.1)                                   |
| Aspirin, n (%)   | 5 (9.3)                        | 1 (6.3)                                     | 3 (6)                                     | 1(5.5)                                     |
| Clopidogrel, n (%)   | 2 (3.7)                        | 1 (6.3)                                     | 0 (0)                                     | 1 (5.5)                                    |
| Anticoagulant therapy, n (%)   | 15 (27.8)                      | 15 (93.8)                                   | 0 (0)                                     | 0 (0)                                      |
| VKA, n (%)   | 15 (27.8)                      | 15 (93.8)                                   | 0 (0)                                     | 0 (0)                                      |
| Target INR   | 5 (9.3)                        | 5 (31.3)                                    | 0 (0)                                     | 0 (0)                                      |
| 2.0-3.0, n (%)   | 10 (18.5)                      | 10 (62.5)                                   | 0 (0)                                     | 0 (0)                                      |
| 3.0-4.0, n (%)   |                                |   |   |  |
| <b>aPL status</b>  |                                |   |   |  |
| a $\beta$ 2GPI IgG (GPU)   | 22.1 (1.0-72.0)                | 35.4 (7.0-72.0)                             | 28.5 (8.0-52.4)                           | 2.5 (1.0-4.3)                              |
| a $\beta$ 2GPI IgM (MPU)   | 15.1 (2.5-69.2)                | 21.2 (4.1-65.7)                             | 19.2(5.0-69.2)                            | 4.2 (2.5-6.1)                              |
| aCL IgG (GPLU)   | 14.9 (0.8-65.4)                | 23.8 (5.2-65.4)                             | 18.9 (6.2-26.2)                           | 2.1 (0.8-5.3)                              |
| aCL IgM (MPLU)   | 13.1 (0.4-81.0)                | 17.6 (5.9-41.0)                             | 20.5 (5.1-81.0)                           | 1.3 (0.4-3.2)                              |
| LA, n (%)  | 30 (55.6)                      | 13 (81.3)                                   | 15 (75)                                   | 0 (0)                                      |
| APS Category I: n (%)  | 29 (53.7)                      | 13 (81.3)                                   | 16 (80)                                   | 0 (0)                                      |
| Double aPL positive: n (%)   | 16 (29.6)                      | 7 (43.8)                                    | 9 (45)                                    | 0 (0)                                      |
| Triple aPL positive: n (%)   | 13 (24.1)                      | 6 (37.5)                                    | 7(35)                                     | 0 (0)                                      |
| Category IIa: n (%)  | 4 (7.4)                        | 2 (12.5)                                    | 2 (10)                                    | 0 (0)                                      |
| Category IIb: n (%)  | 2 (3.7)                        | 1 (6.3)                                     | 1(5)                                      | 0 (0)                                      |
| Category IIc: n (%)  | 1 (1.85)                       | 0 (0)                                       | 1(5)                                      | 0 (0)                                      |

aPL: antiphospholipid antibodies, a $\beta$ 2GPI: anti-beta2 glycoprotein I antibodies; anti-DNA: anti-DNA antibodies, aCL: cardiolipin antibodies, LA: lupus anticoagulant, SLE: systemic lupus erythematosus.



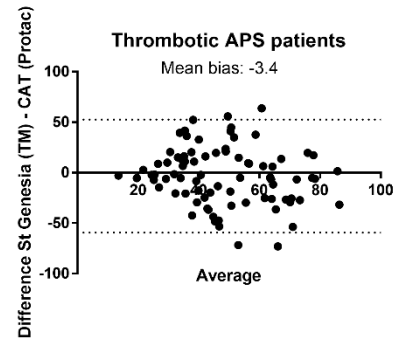
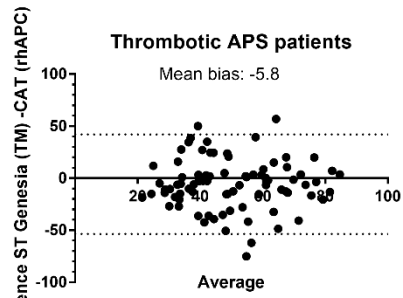
**Figure S1.** Bland-Altman graphs for the agreement in APCr between ST-Genesia® with and the CAT analyser with rhAPC (left panel) and Protac® (right panel) in **A.** APS patients **B.** SLE patients and **C.** thrombotic controls. Horizontal broken lines indicate the 95% limits of agreement.



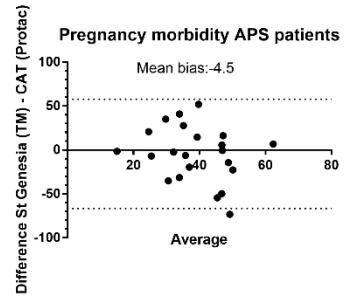
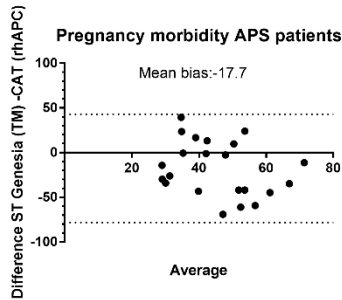
**Figure S2.** Agreement in APCr between the ST-Genesia® in the presence of TM and the CAT analyser with rhAPC (left panel) and Protac® (right panel) in APS patients stratified according to clinical phenotype and aPL status. A. thrombotic, B. pregnancy morbidity (PM), C. triple aPL positive (+), D. double aPL + and E. single aPL+ APS patients,

Horizontal broken line represents the cut off value for APCr with the ST-Genesia® (49%) and vertical dotted line in the left panel represents the APCr cut off value of 56% for the CAT with rhAPC and in the right panel the APCr cut off value of 63% for the CAT with Protac®. All cut off values were defined as below the 99<sup>th</sup> centile of NC. PM: pregnancy morbidity, aPL: antiphospholipid antibody

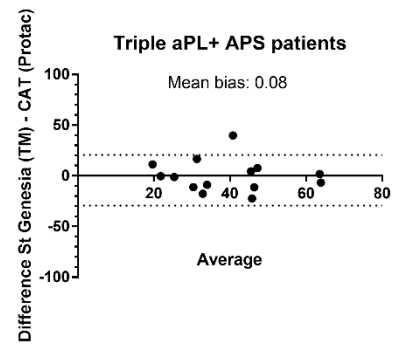
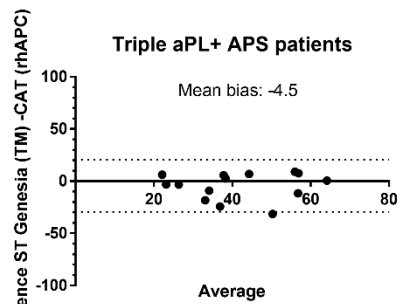
**A**



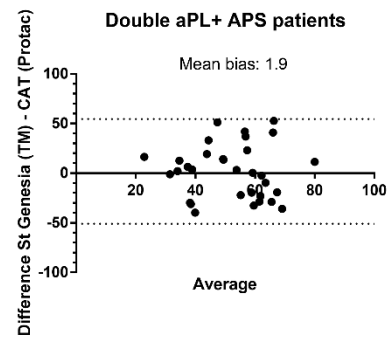
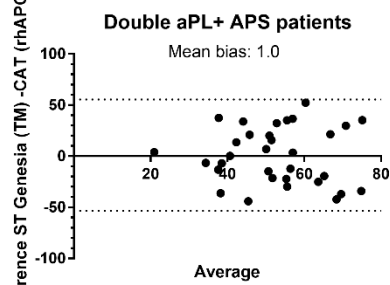
**B**



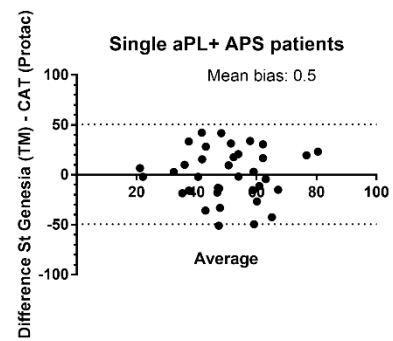
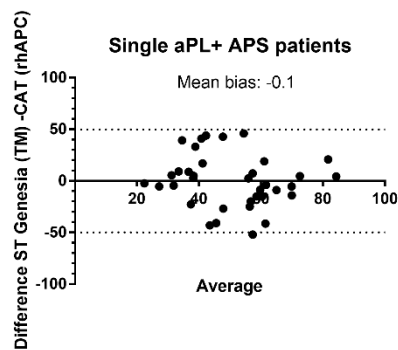
**C**



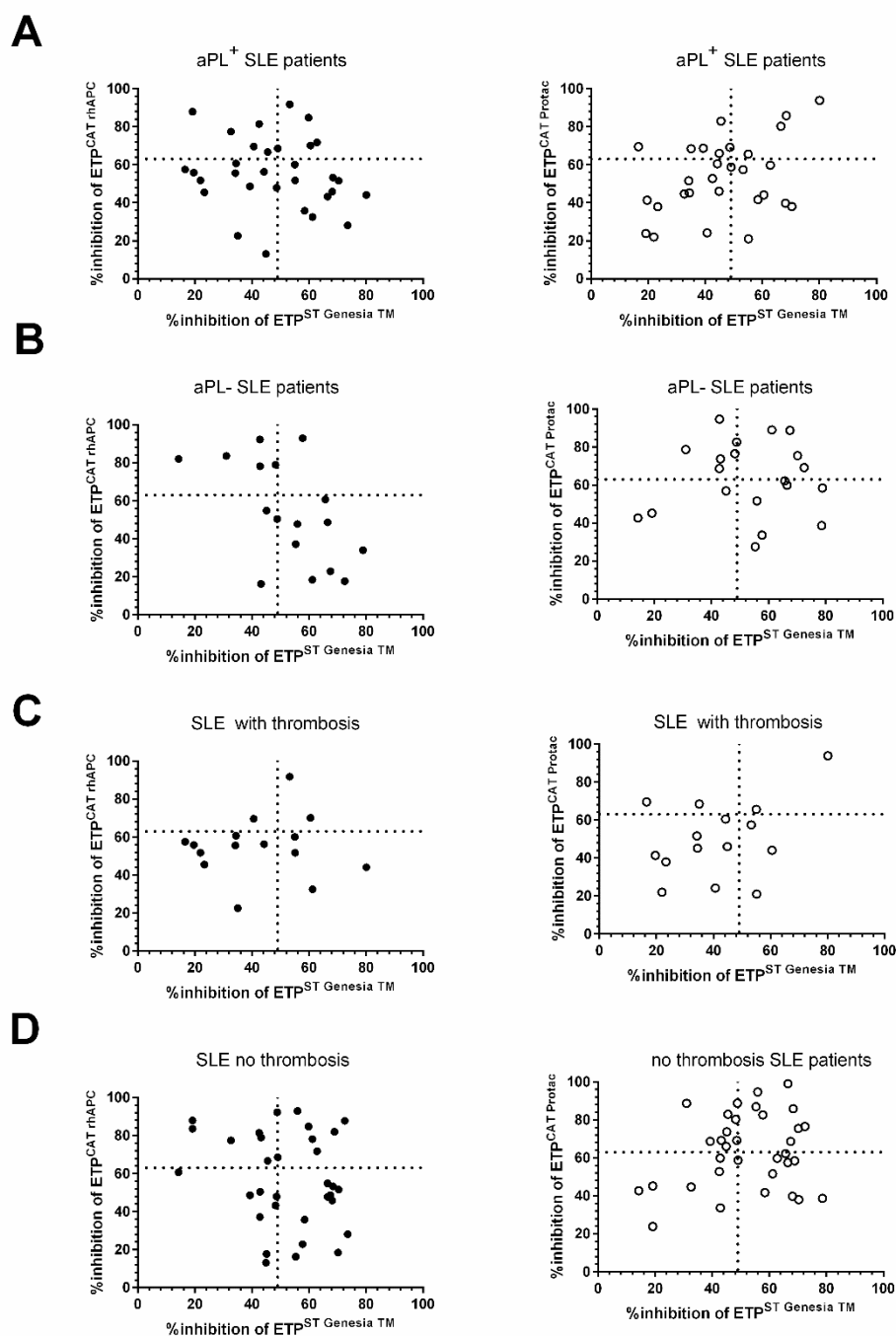
**D**



**E**



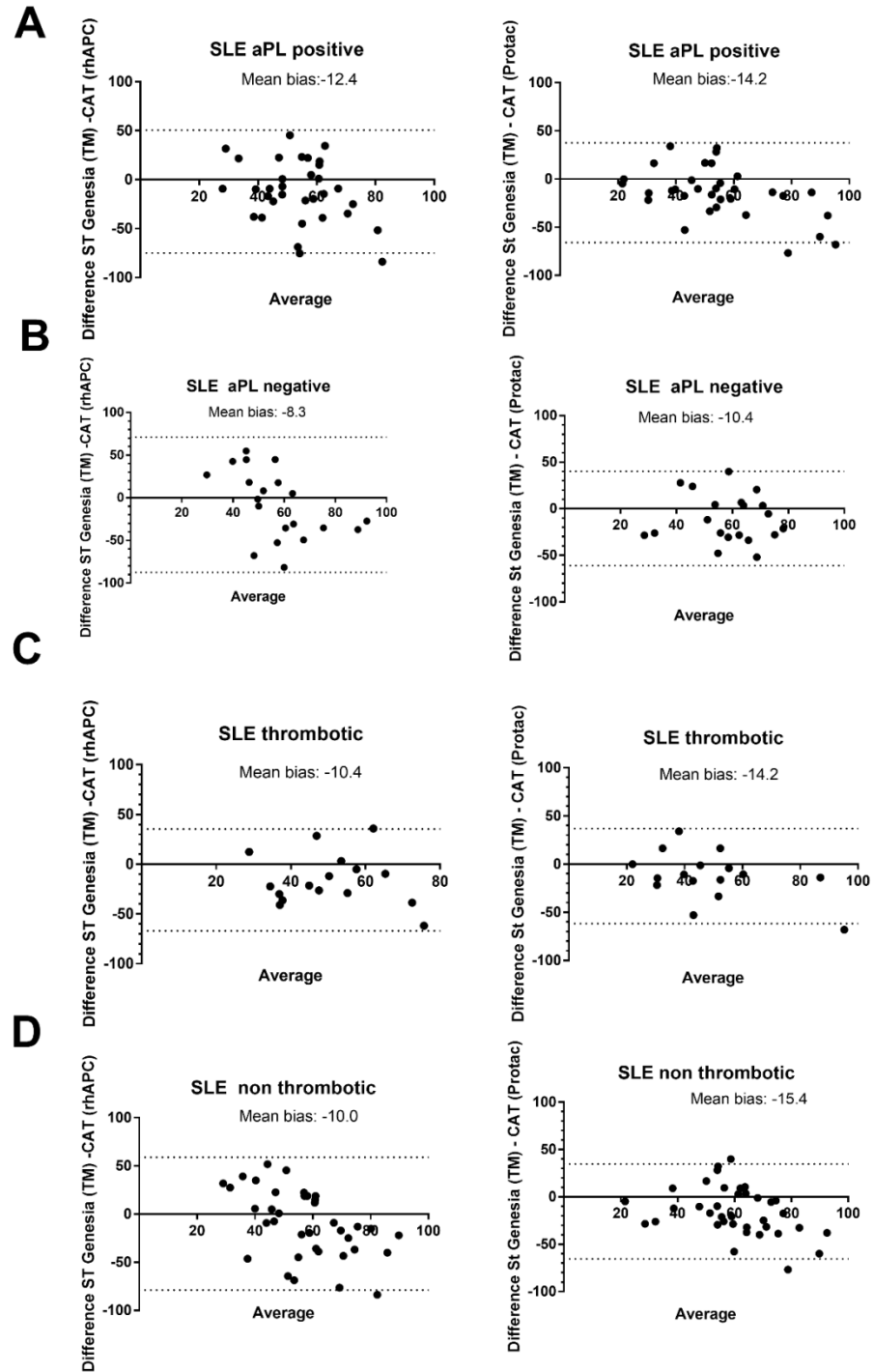
**Figure S3.** Bland-Altman graphs for the agreement in APCr values between ST-Genesia® with TM and the CAT analyser with rhAPC or Protac® in APS patients stratified according to clinical phenotype and aPL status: A. thrombotic and B. pregnancy morbidity C. triple D. double E. single aPL positive. Horizontal broken lines indicate the 95% limits of agreement.



**Figure S4.**

Agreement in APCr between the ST-Genesia® and the CAT analyser with rhAPC (left panel) and Protac® (right panel) in SLE patients stratified according to aPL status and thrombotic history: A. aPL positive, B. aPL negative (-) and according to into C. thrombotic and D. non thrombotic.

Horizontal broken line represents the cut off value for APCr with the ST-Genesia® (49%) and vertical dotted line in the left panel represents the APCr cut off value of 56% for the CAT with rhAPC and in the right panel the APCr cut off value of 63% for the CAT with Protac®. All cut off values were defined as below the 99<sup>th</sup> centile of NC.



**Figure S5.** Bland-Altman graphs for the agreement in APCr values between ST-Genesia® with TM and the CAT analyser with rhAPC and Protac® in patients with SLE stratified according to aPL status and thrombotic history A. aPL positive B. aPL negative C. thrombotic and D. non thrombotic SLE. Horizontal broken lines indicate the 95% limits of agreement.