Supplemental Figures

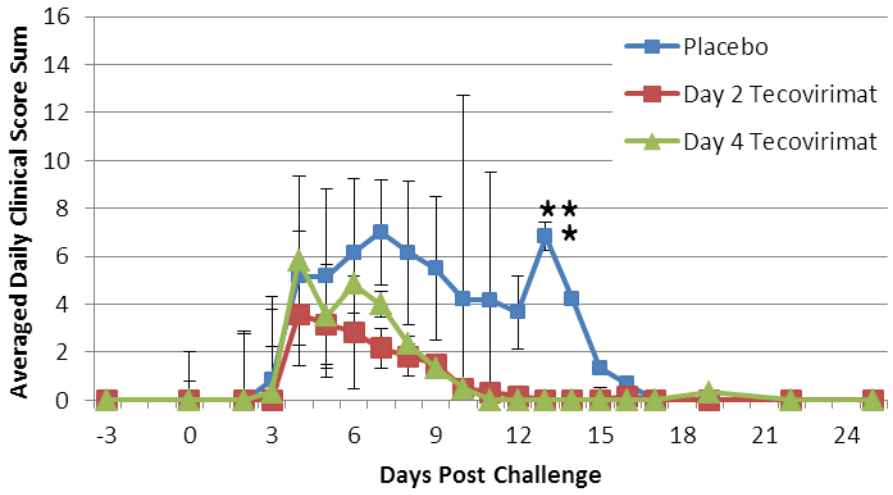


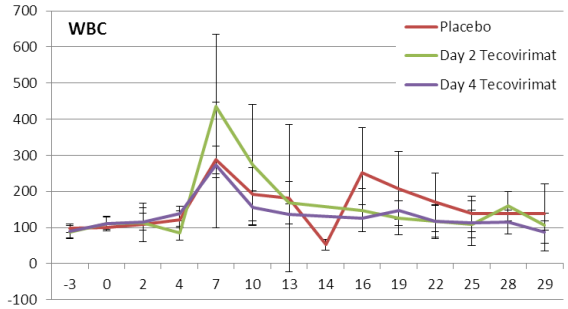
Figure S1. Cumulative daily clinical scores following VARV challenge by treatment group. Cynomolgus macaques were challenged with $1x10^8$ pfu VARV by the intravenous route on Day 0. In a blinded fashion, all animals were assessed daily for clinical signs of disease including but not limited to monitoring of recumbency, unresponsiveness, dyspnea, cough, biscuit and fruit consumption, stool condition, nasal discharge, non-specific rash, edema, bleeding, lymphadenopathy, and dehydration. Each of these is recorded according to the severity of the observation ranking from 0 (absent), to 1 (mild), 2 (moderate), 3 (severe), or 4 (very severe). Scored observations are summed in order to generate a daily "clinical score". Treatment group averages are shown and error bars indicate standard deviations. Unscheduled deaths (euthanasia due to moribund condition) in the placebo group are indicated by asterisks.

Fig. S1 legend continued

Scoring criteria for each observation:

1. Recumbency: 0 = active, 1 = occasional prostration, 2 = persistent prostration but rises when approached, 3 = persistent prostration
2. Unresponsive: 0 = active, 1 = mild unresponsiveness (becomes active when appraoched), 2 = moderate unresponsiveness (withdraws when prodded), 3 = severe unresponsiveness (does not withdraw when prodded), 4 = unresponsive to toe pinch.
3. Dyspnea: 0 = normal breathing, 1 = mildly labored, 2 = labored, 3 = agonal breathing
4. Cough: 0 = none, 1 = ≤ 2 within 5 minutes, 2 = ≥ 3 to 10 within 5 minutes, 3 = > 10 within 5 minutes
5. Biscuit consumption (% of 10 biscuit provided): 0 = ≥ 50%, 1 = > 20 to 40%, 2 = 10%, 3 = 0%
6. Fruit consumption (% of total amount offered): 0 = all, 1 = 50 – 90%, 2 = 10 – 40%, 3 = 0%
7. Condition of stool: 0 = normal feces, 1 = not fully formed, 2 = liquid, 3 = none
8. Nasal discharge: 0 = none, 1 = barely visible, 2 = moderate, 3 = copious
9. Rash (non-specific): 0 = none, 1 = barely visible, 2 = moderate, 3 = copious
10. Edema: 0 = not present, 1 = mild, 2 = moderate, 3 = severe
11. Bleeding: 0 = none, 1 = barely visible, 2 = moderate, 3 = copious
12. Lymphadenopathy (mm maximum dimension): 0 = < 3, 1 = 3 – 9, 2 = ≥ 10 – 19, 3 = ≥ 20
13. Dehydration (observed at the lateral abdomen): 0 = not present, 1 = mild, 2 = moderate, 3 = severe

Figure S2. Clinical chemistries and hematology by treatment group. Cynomolgus macaques were challenged with $1x10^8$ pfu VARV by the intravenous route on Day 0. All animals were assessed every third day for clinical chemistry and hematology. Values are graphed as group averages (y-axis, error bars indicate standard deviations) as a percentage of the baseline values observed on Days -3 and 0 (averaged) per day post-infection (x-axis). For hematological parameters, the y-axis values indicate as follows: white blood cells (WBC, 10^3/µL), red blood cells (RBC, 10^6/µL), hemoglobin (Hgb, g/dL), hematocrit (Hct, % volume), mean corpuscular volume (MCV, fL), mean corpuscular hemoglobin (MCH, pg), mean corpuscular hemoglobin concentration (MCHC, % volume), platelet count (PLT, 10^3/µL). For clinical chemistry parameters, the y-axis values indicate as follows: albumin (ALB, g/dL), alkaline phosphatase (ALP, IU/L), creatinine (CRE, mg/dL), alanine aminotransferase (ALT, IU/L), aspartate aminotransferase (AST, IU/L), glucose (GLU, mg/dL), amylase (AMY, IU/L), total bilirubin (TBIL, mg/dL), blood urea nitrogen (BUN, mg/dL), total protein (TP, g/dL), calcium (CA, mg/dL), gamma-glutamyl transpepetidase (GGT, IU/L), and uric acid (UA, mg/dL).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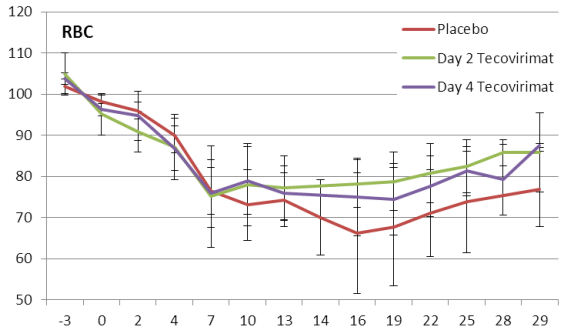
Day 4 Tecovirimat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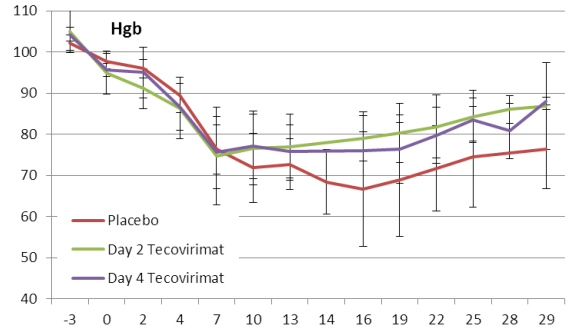
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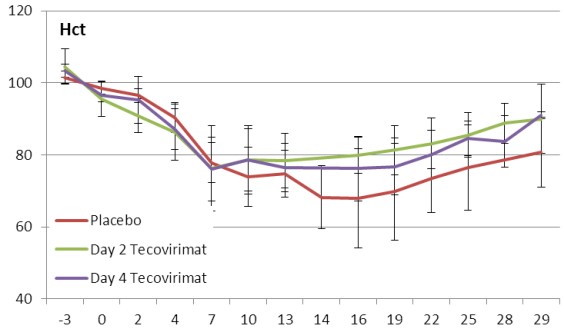
Day 4 Tecovirimat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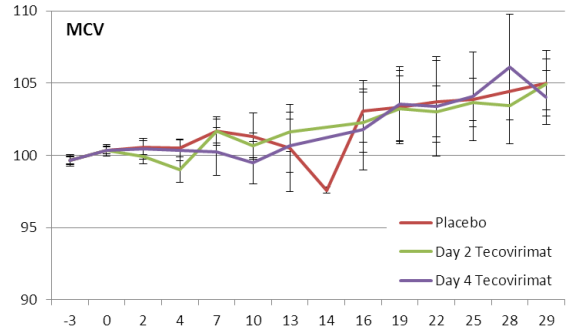
Day 4 Tecovirimat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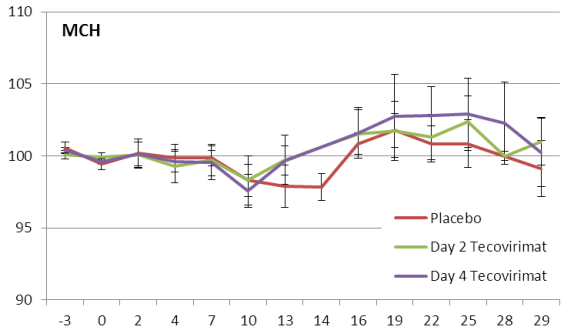
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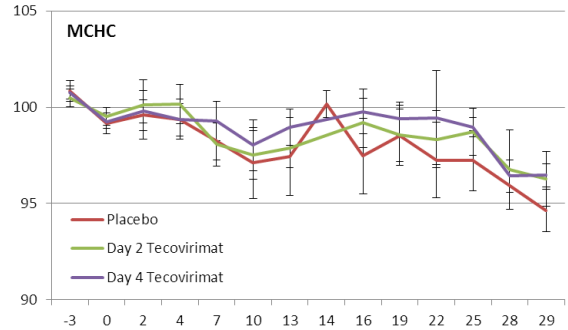
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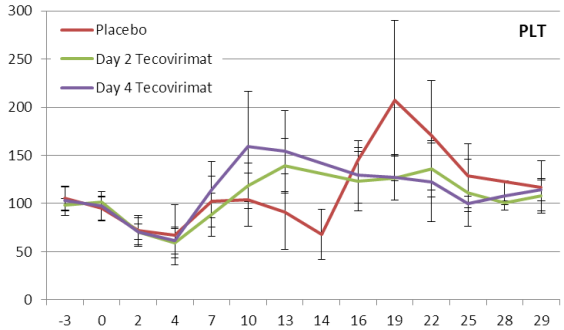
PLT
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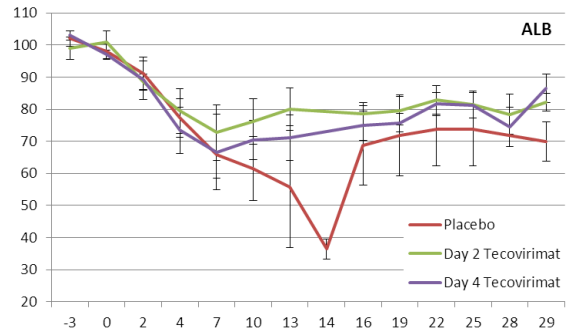
ALB
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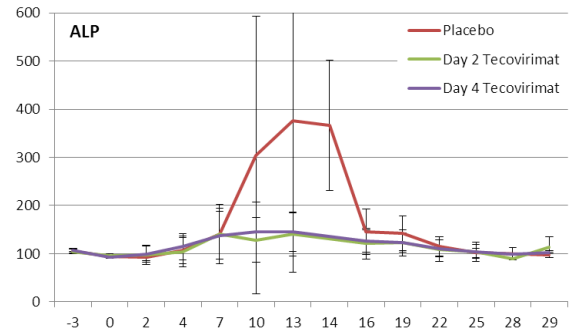
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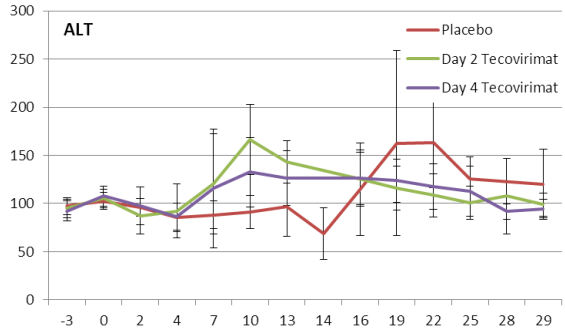
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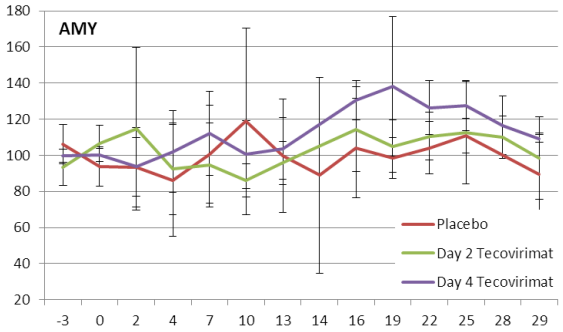
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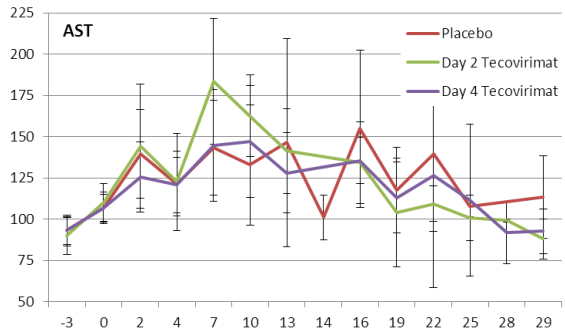
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Day 4 Tecovirimat
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175
150
125
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75
50
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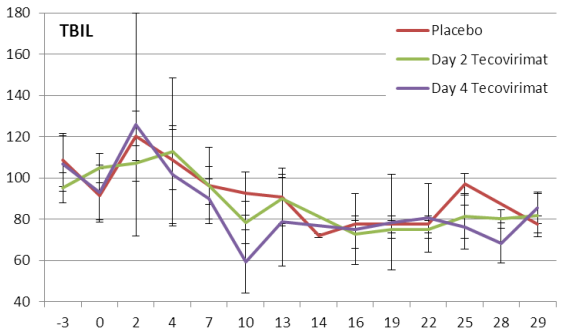
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120
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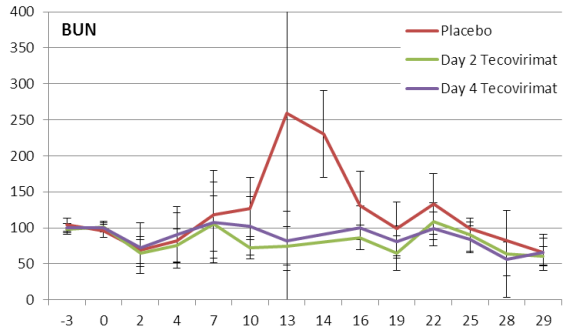
BUN
Placebo
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200
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100
50
0
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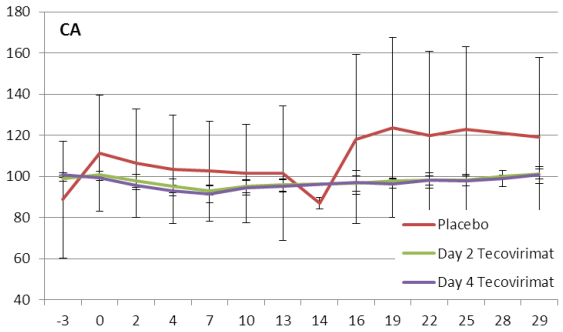
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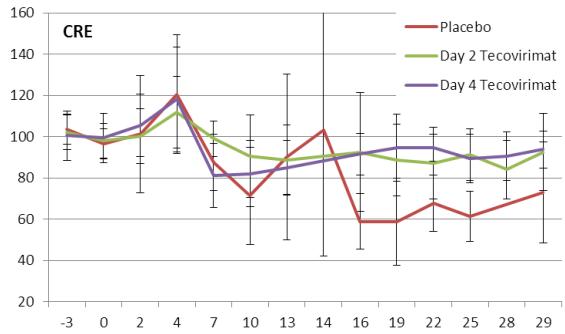
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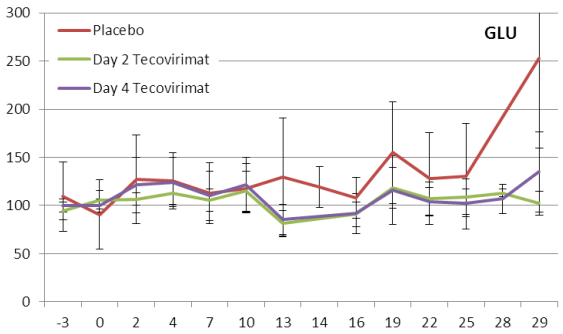
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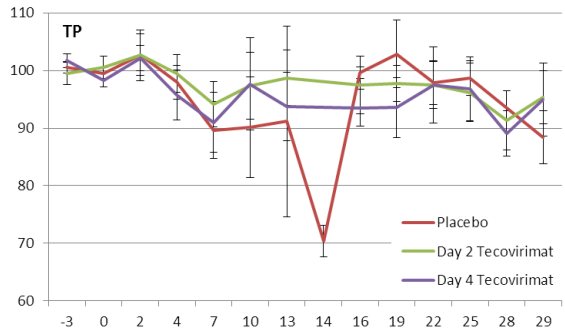
TP
Placebo
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Day 4 Tecovirimat
110
100
90
80
70
60
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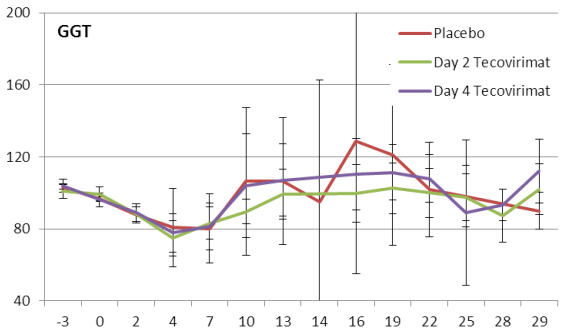
GGT
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120
80
40
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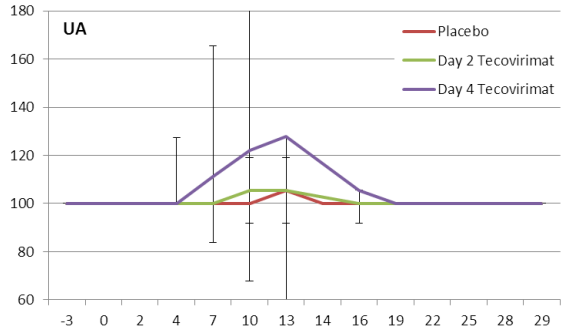
UA
Placebo
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140
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100
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60
-3
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2
4
7
10
13
14
16
19
22
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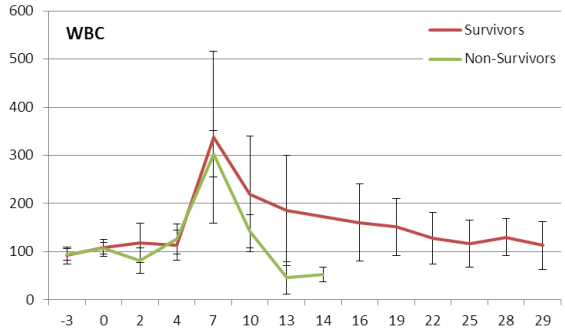
28
29

Figure S3. Select Clinical Chemistries and Hematology by Survival. Cynomolgus macaques were challenged with $1x10^8$ pfu VARV by the intravenous route on Day 0. All animals were assessed every third day for clinical chemistry and hematology. Values are graphed as group averages (y-axis, error bars indicate standard deviations) as a percentage of the baseline values observed on Days -3 and 0 (averaged) per day post-infection (x-axis). The y-axis values are the same as described in the legend to Figure S2. Survivors include all animals in both tecovirimat treatment groups as well as survivors in the placebo treatment group.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Non-Survivors
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100
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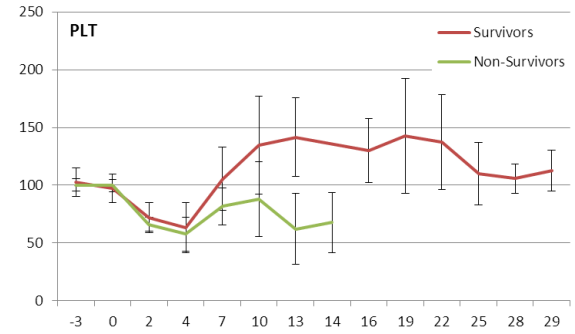
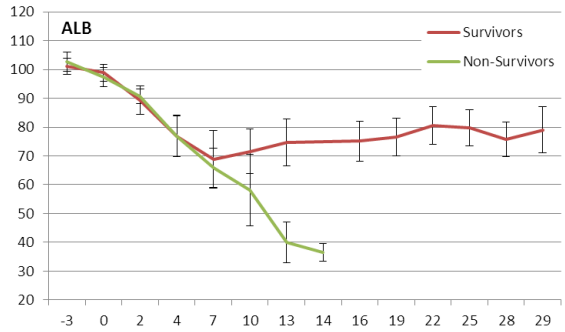
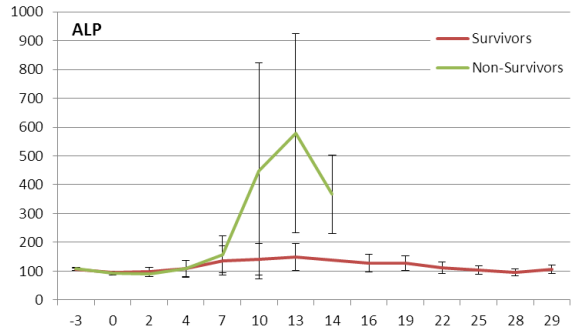

PLT
Survivors
Non-Survivors
250
200
150
100
50
0
-3 0 2 4 7 10 13 14 16 19 22 25 28 29


ALB
Survivors
Non-Survivors
120
110
100
90
80
70
60
50
40
30
20
-3 0 2 4 7 10 13 14 16 19 22 25 28 29


ALP
Survivors
Non-Survivors
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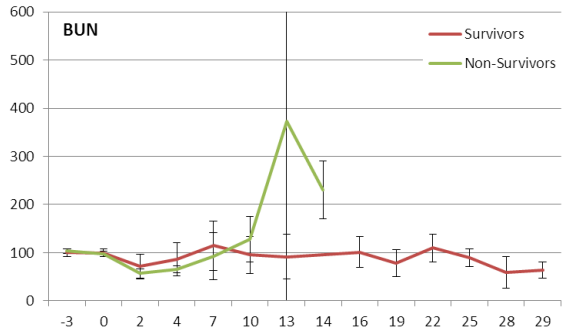
900
800
700
600
500
400
300
200
100
0
-3 0 2 4 7 10 13 14 16 19 22 25 28 29


BUN
Survivors
Non-Survivors
600
500
400
300
200
100
0
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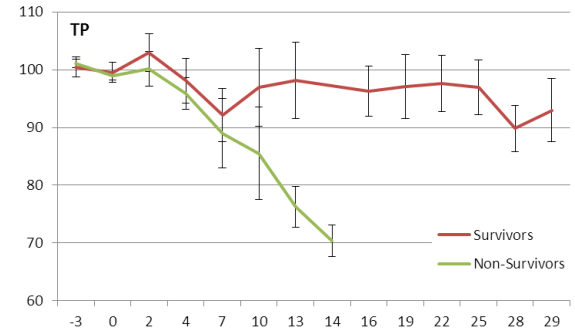
TP
Survivors
Non-Survivors
110
100
90
80
70
60
-3 0 2 4 7 10 13 14 16 19 22 25 28 29