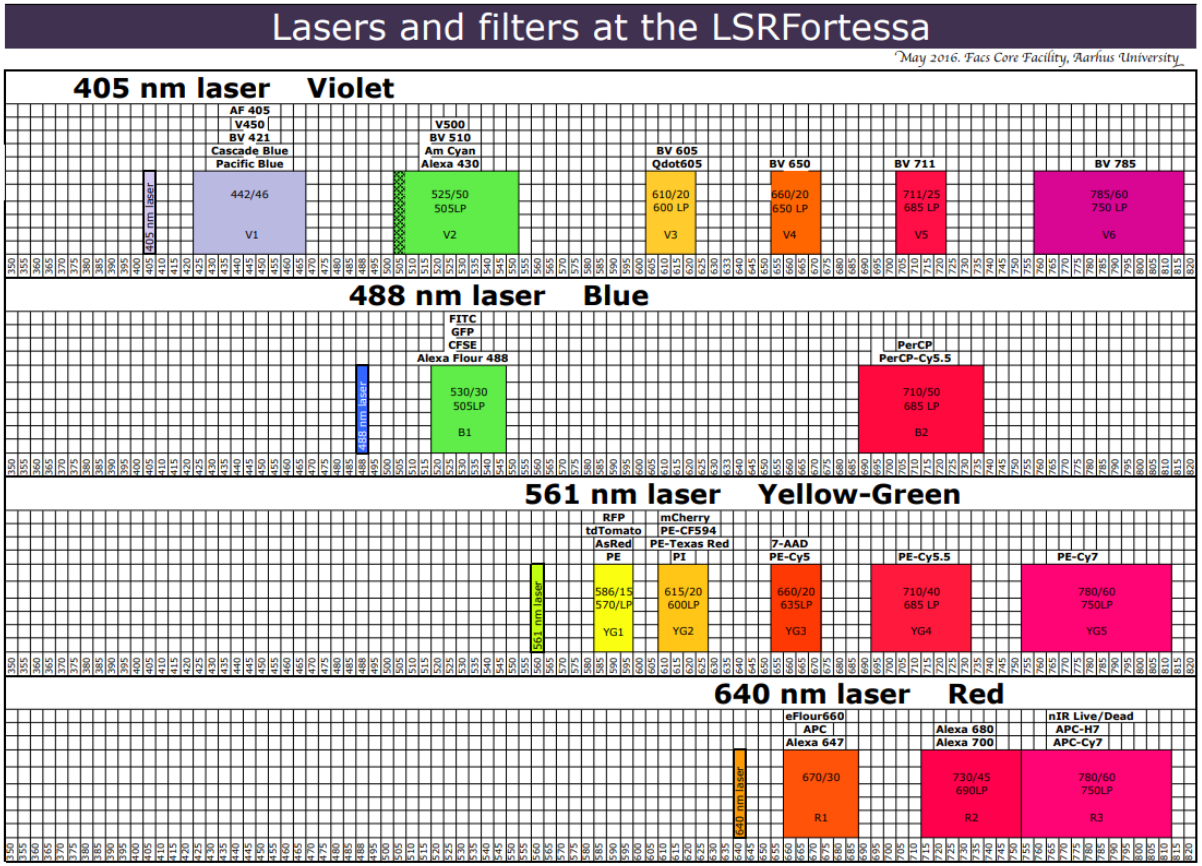
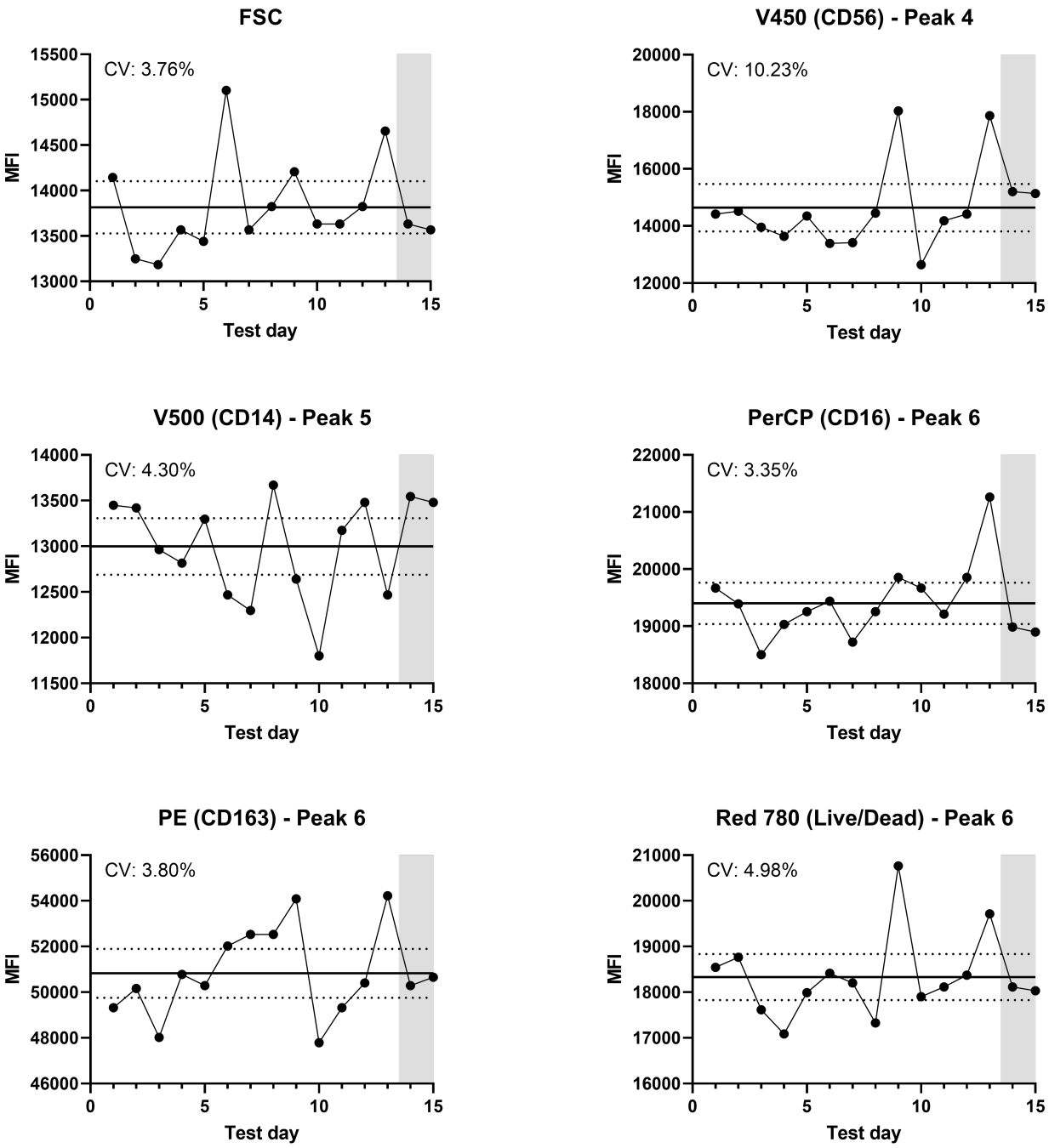
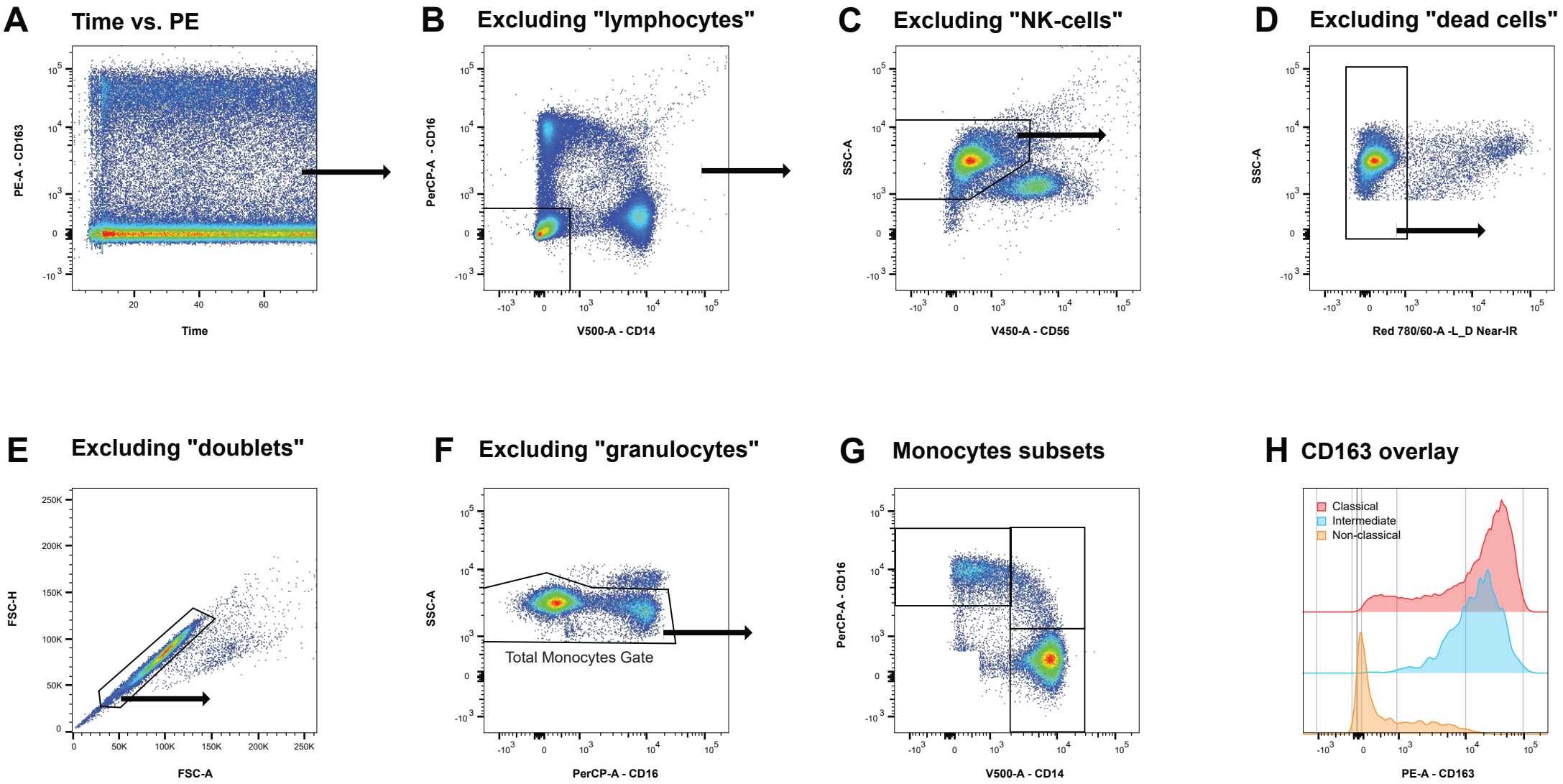


Supplementary Figure 1: Cytometer laser and filter configurations.
LSRFortessa analyzer from BD Biosciences was used with the shown configurations. Available at the FACS Core unit at Aarhus University.
https://facs.au.dk/equipment/lsrfortessa/

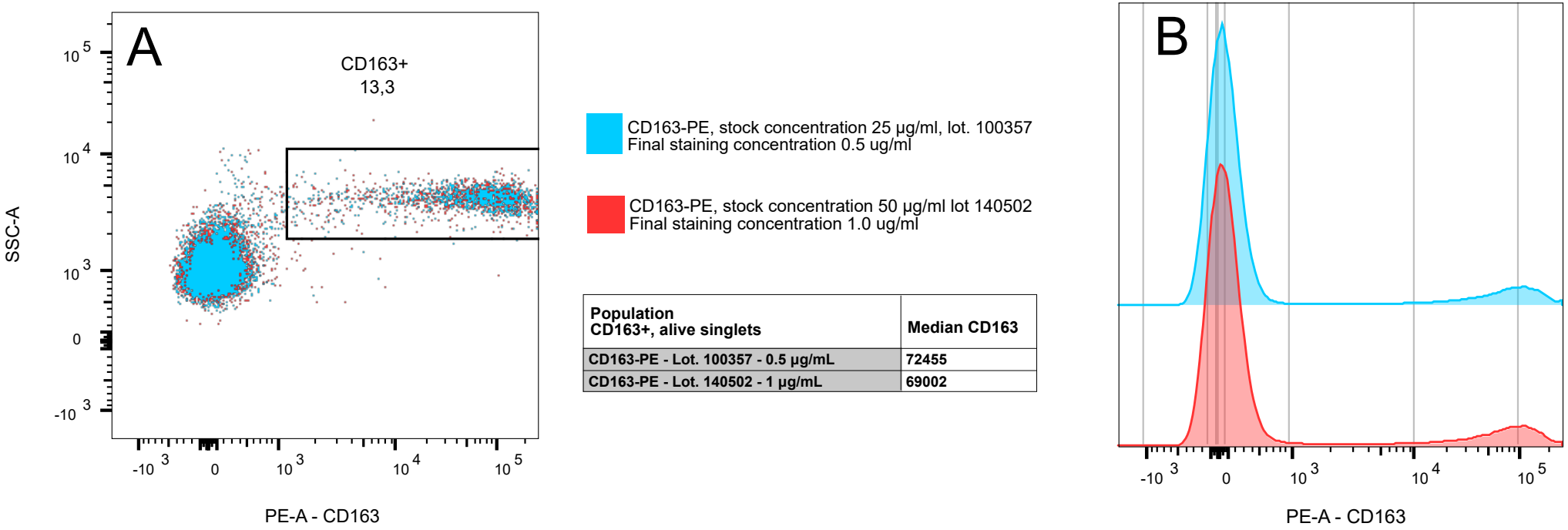


Supplementary Figure 2: Cytometer stability validated by 8-peak rainbow beads.
To verify the stability of the flow cytometer during the study, highly stable 8-peak rainbow beads were run as a control sample on each day of the study. For each parameter (fluorescence detector) the population (peak) of beads with median fluorescense intensity (MFI) level closest to the MFI level of our cells of interest was chosen. Here, we display the MFI values for each parameter over the study period. The solid line and dotted lines show the mean and 95% CI of the mean, respectively. The grey-coloured areas indicate the time healthy controls were analyzed. CV = Coefficient of Variation.



Supplementary Figure 3: Gating strategy

A) Time vs PE plot to verify stable flow/fluidics during data acquisition. B) The majority of lymphocytes were excluded by using a NOT-gate to exclude double negative events for CD14/CD16. C) $CD56^{pos}$ NK cells were excluded. D) Exclusion of dead cells by a L/D vs. SSC plot. E) Exclusion of doublets by a FSC-A vs. FSC-H plot. F) Exclusion of possible granulocyte contamination by exclusion of $CD16^{+}$ and SSC^{high} population. G) Division of monocytes into classical ($CD14^{+}CD16^{-}$), intermediate ($CD14^{+}CD16^{+}$) and non-classical ($CD14^{dim}CD16^{++}$) monocytes. H) Overlayed histograms of the CD163 expression levels of the defined monocyte subsets: classical (orange), intermediate (blue) and non-classical (red) monocytes.

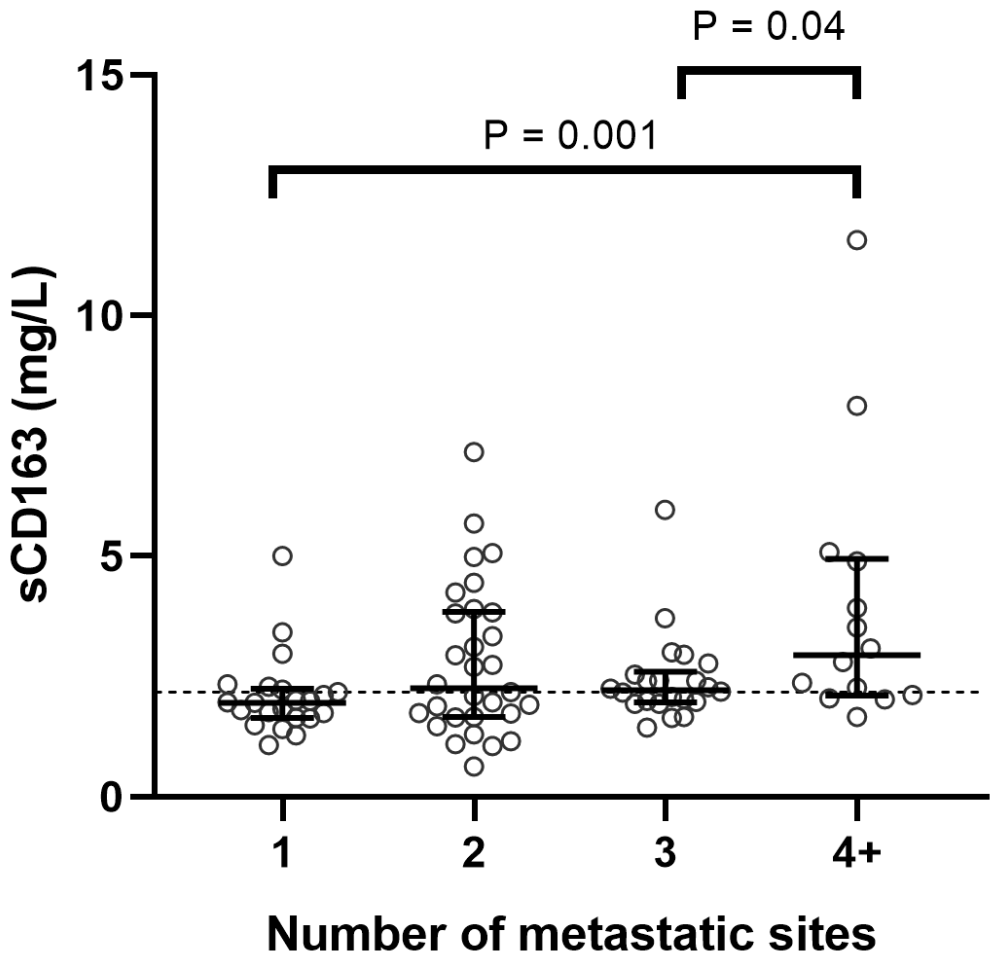


Population CD163+, alive singlets	Median CD163
CD163-PE - Lot. 100357 - 0.5 µg/mL	72455
CD163-PE - Lot. 140502 - 1 µg/mL	69002

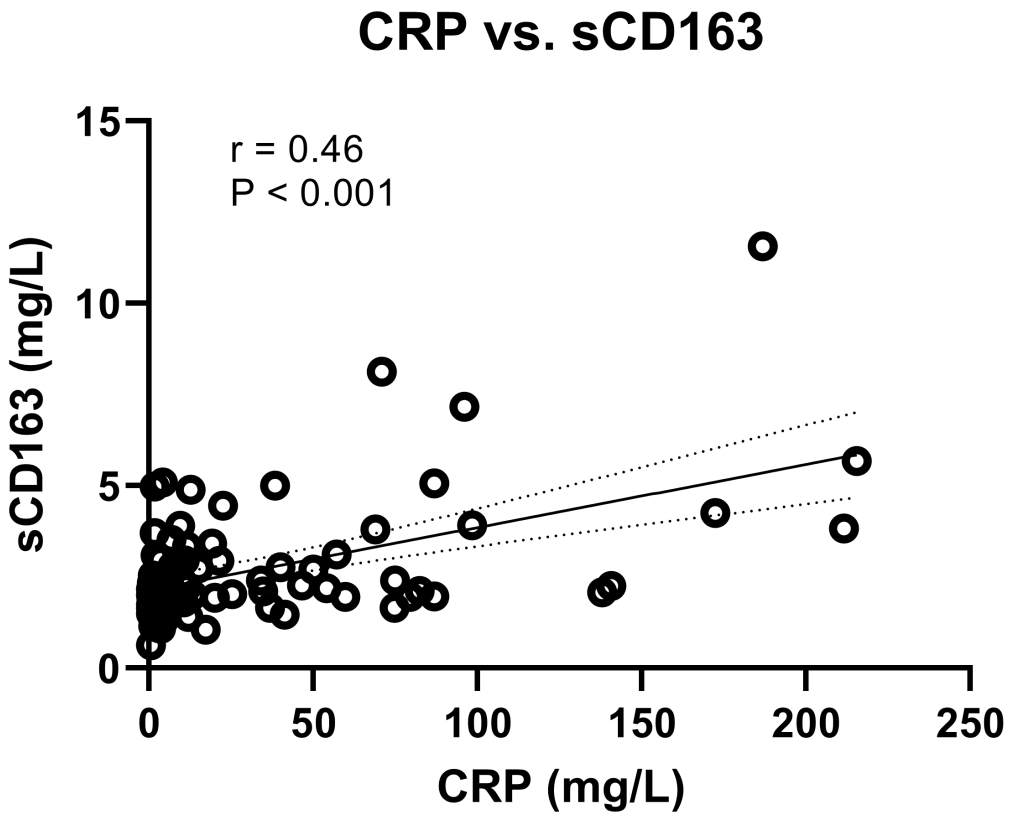
Supplementary Figure 4: Control of CD163 PE staining

Two different lots of the CD163 PE antibody were available in the laboratory during the study period.
All patient samples were stained with the 100357 lot. no. (25 µg/mL).
Retrospectively, there was uncertainty about the lot no. of CD163 PE antibody used for staining the healthy control samples.
We do believe the same lot no. (100357) was used for staining of patient and control samples,
but it could not be completely ruled out that the lot no. 140502 (50 µg/mL) had been used.
Further, during the analysis of patient samples, due to minor changes in the staining protocol,
the staining concentration of anti-CD163 PE varied between 0.5 and 0.9 µg/mL.
To investigate any potential impact of variations in anti-CD163 PE staining concentrations,
a control experiment was performed to evaluate the median fluorescense intensity (MFI)
of CD163 PE on monocytes using the titrated 0.5 µg/mL vs. the double amount of antibody; 1.0 µg/mL.

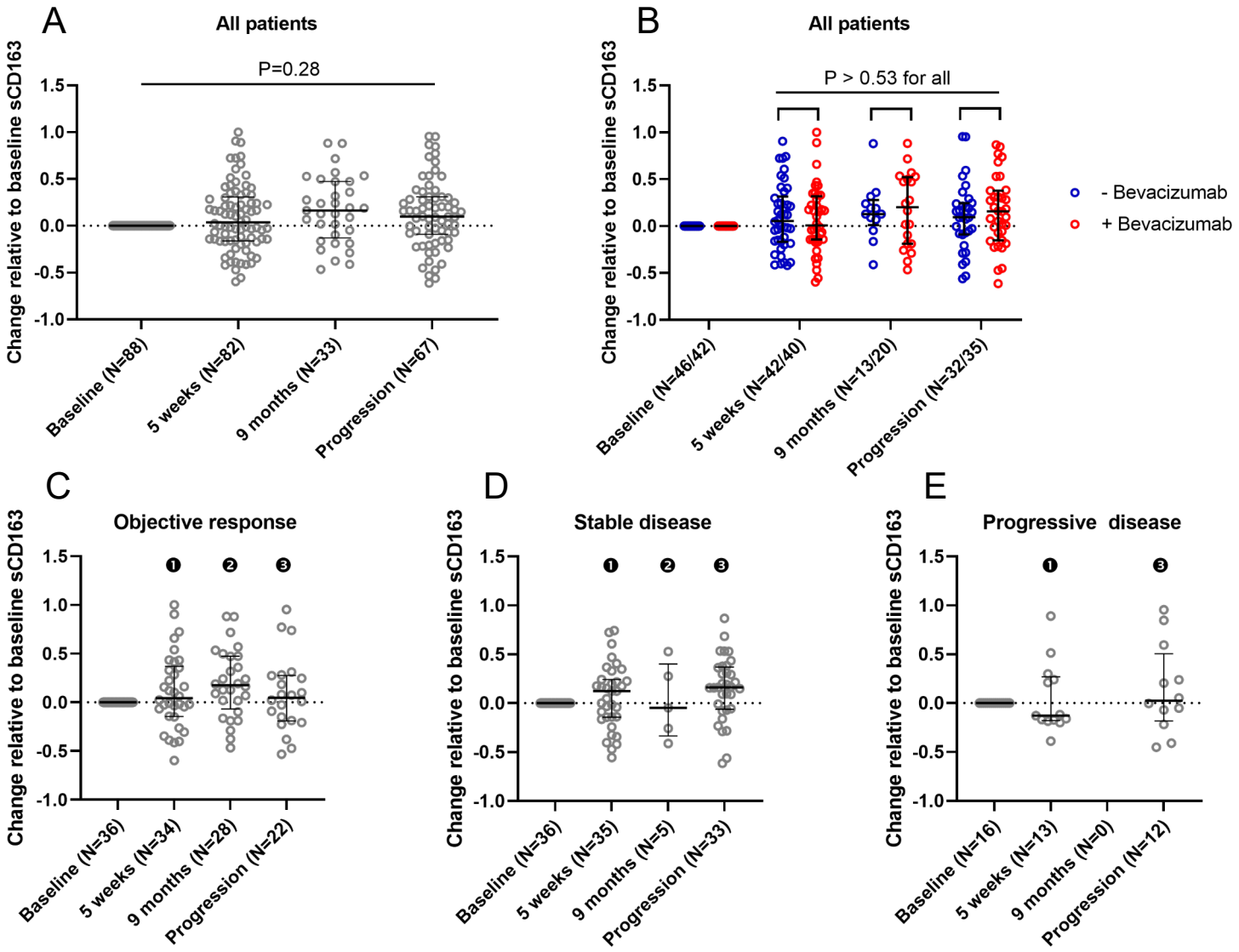
Here, PBMCs that were Fc-blocked and stained with Live/Dead Near-IR before incubating with either 0.5 µg/mL (lot. 100357)
or 1.0 µg/mL (lot 140502) of CD163-PE antibody.
It is seen that the MFI of live, single cell monocytes (SSC-A high and $CD163^{pos}$) showed similar MFI results.
Further, overlaid dot plots (**A**) and histograms (**B**) of the two staining concentrations showed highly similar staining patterns and intensities.
Thus, we conclude that using the CD163 PE antibody at either 0.5 or 1.0 µg/mL did not impact the staining intensity,
which is in agreement with our expectations, and our antibody titrations.



Supplementary Figure 5: Baseline serum sCD163 and number of metastatic sites.
Number of metastatic sites were calculated as the sum of the dichotomized values of metastases in relation to lungs, mediastinal lymph nodes, retroperitoneal lymph nodes, liver, bones, soft tissues and adrenal glands. Bars show median and inter-quartile range. Comparisons were performed by Kruskal-Wallis test followed by Student's t-test or Wilcoxon rank-sum test as appropriate. Only P-values <0.05 are shown.



Supplementary Figure 6: Correlaton of sCD163 and CRP.
Correlaton of sCD163 (mg/L) and CRP (mg/L) for all mRCC patents.
P and r-values are by Pearson correlaton using ln(sCD163) and ln(CRP) transformed values. Best fitted line is shown (with 95% CI as dotted lines).



Supplementary Figure 7: Dynamics of serum sCD163 during treatment.

Data is shown as relative changes of sCD163 compared to baseline values. Thus, a value of 0.5 indicates an increase in sCD163 of 50% from the baseline level.

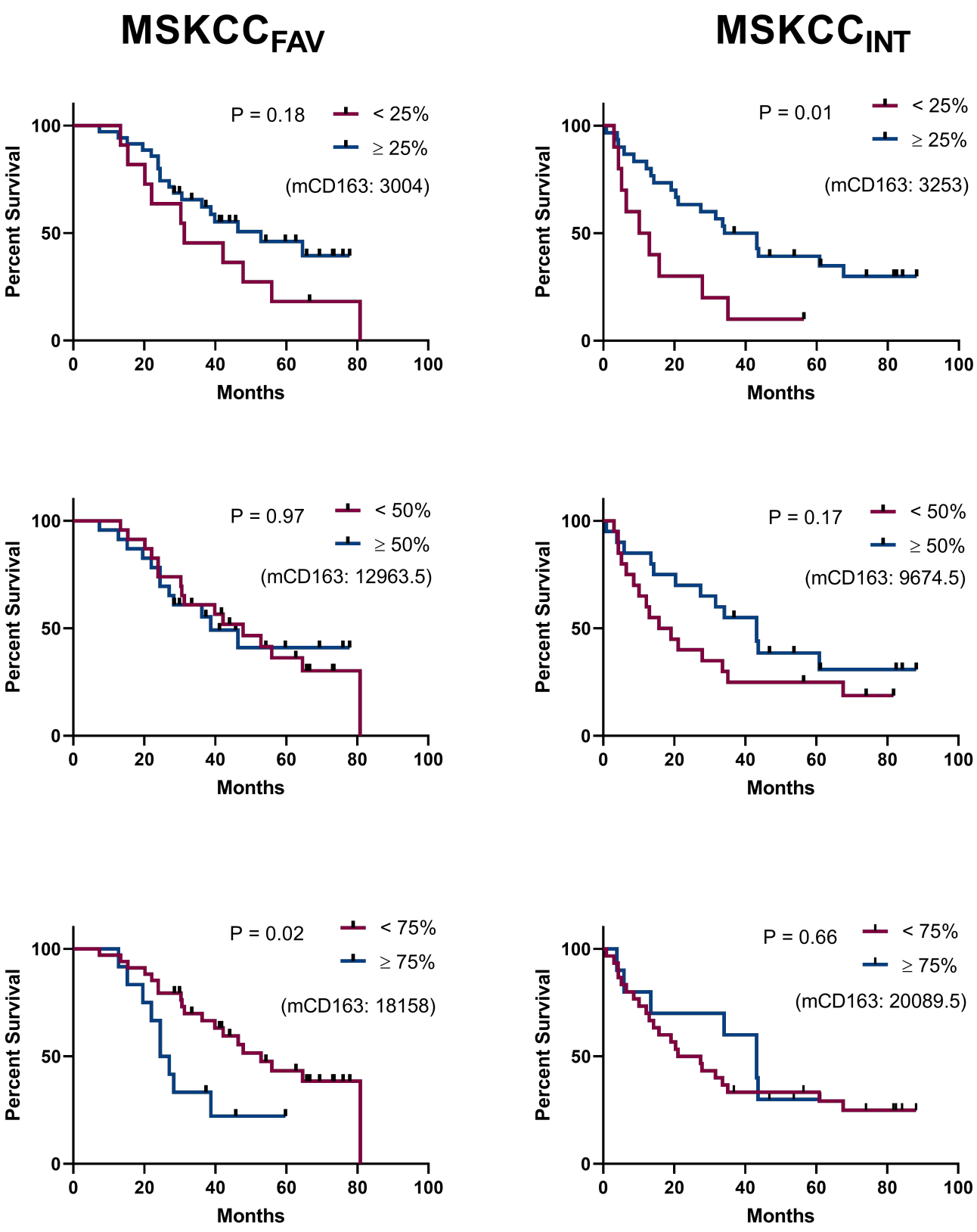
A) Levels of sCD163 during treatment for all patients. P-value is from mixed-effect analysis of ln-transformed absolute values.

B) Data as shown in A) but with stratification by randomization to +/- bevacizumab.

C-E) Data as shown in A) but with stratification treatment response: Objective response (either complete or partial response), stable disease, or progressive disease. Numbers indicate groups compared to each other. P-values were > 0.32 for all comparisons.

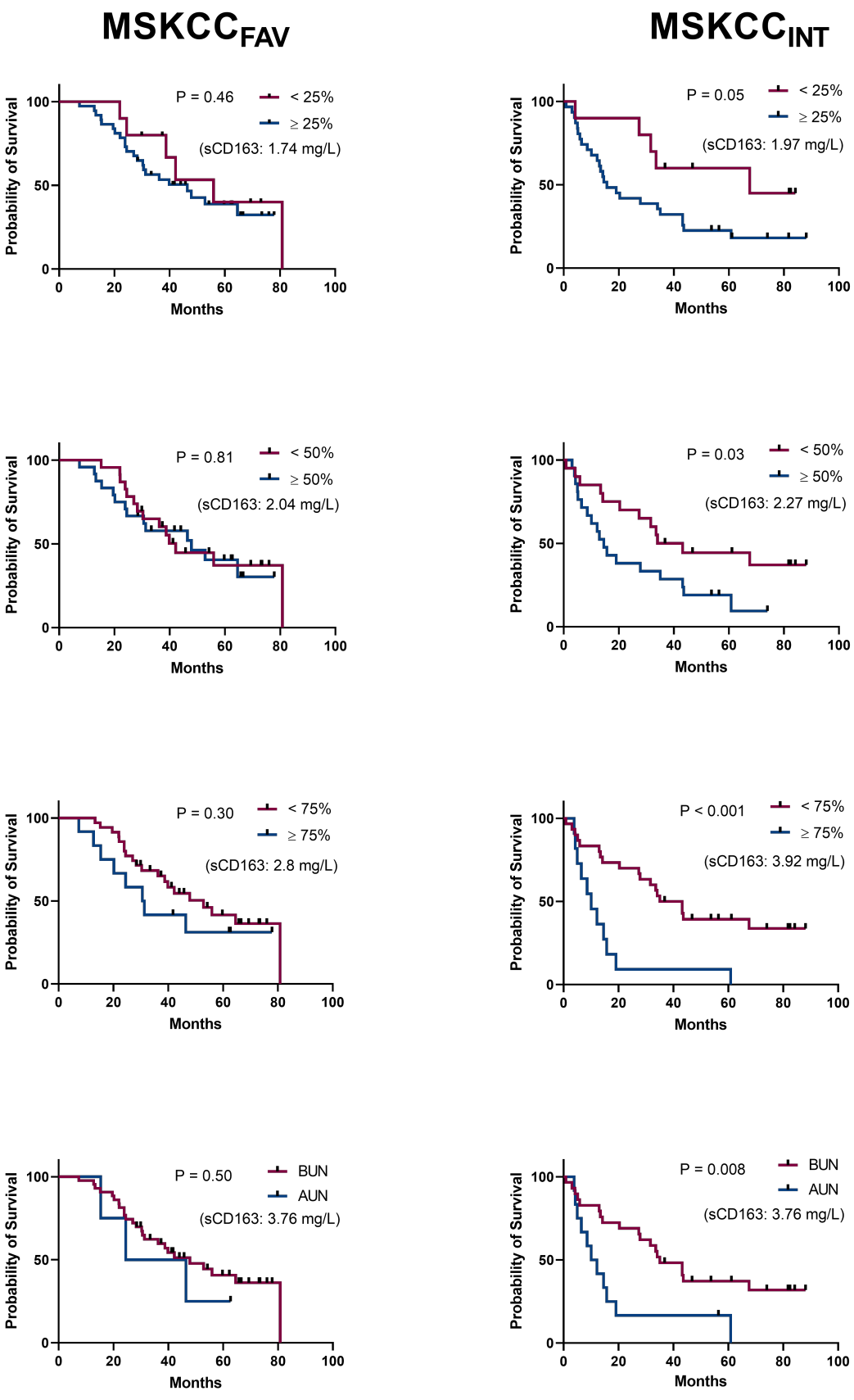
Bars show median and inter-quartile range. Statistical comparisons were done by mixed-effect analysis, one-way ANOVA, and Student's t-test, as appropriate.

Overall Survival: mCD163

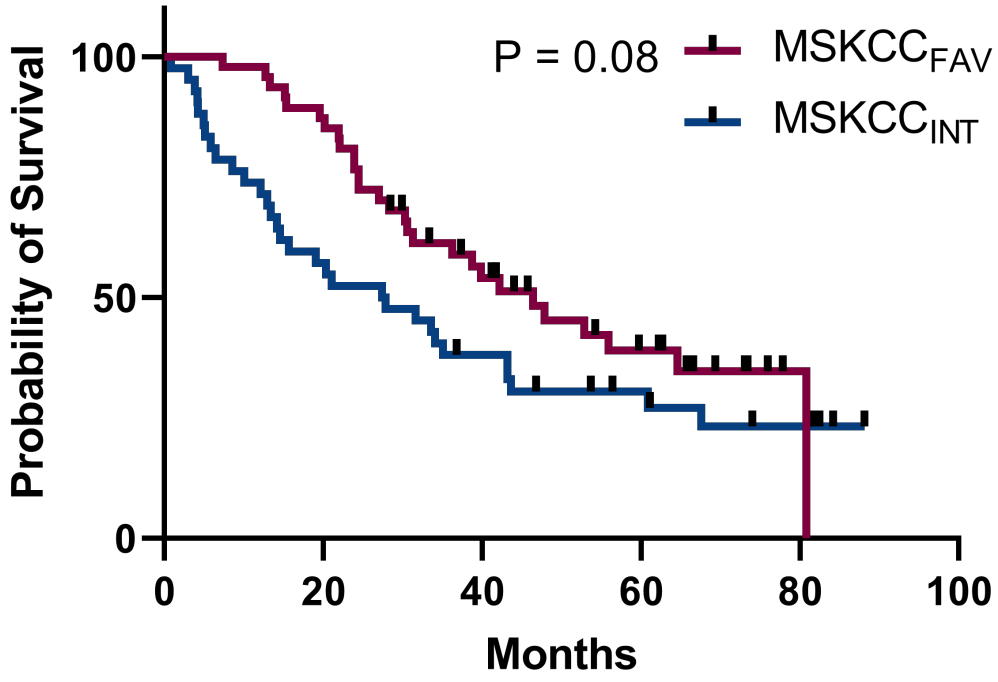


Supplementary Figure 8:
Overall survival by monocyte mCD163 after stratification based on MSKCC prognosis group.
Left and right columns show patients with MSKCCFAV and MSKCCINT risk, respectively. Overall survival is depicted as months on the X-axes. The separator value of monocyte mCD163 MFI used for the binomial categorization is shown in parentheses on each graph. P-values by log-rank test. Censored patients are annotated with a rectangle on top of the line.

Overall survival: sCD163



Supplementary Figure 9:
Overall survival by serum sCD163 after stratification based on MSKCC prognosis group.
Left and right columns show patients with MSKCCFAV and MSKCCINT risk, respectively.
Overall survival is depicted as months on the X-axes. The separator value of serum sCD163 (in mg/L) used for the binomial categorization is shown in parentheses on each graph. P-values by log-rank test. Censored patients are annotated with a rectangle on top of the line. AUN = Above upper normal. BUN = Below upper normal.



Supplementary Figure 10:
Overall survival by MSKCC prognosis group.
Overall survival is depicted as months on the x-axis. P-value by log-rank test. Censored patients are annotated with a rectangle on top of the line.