

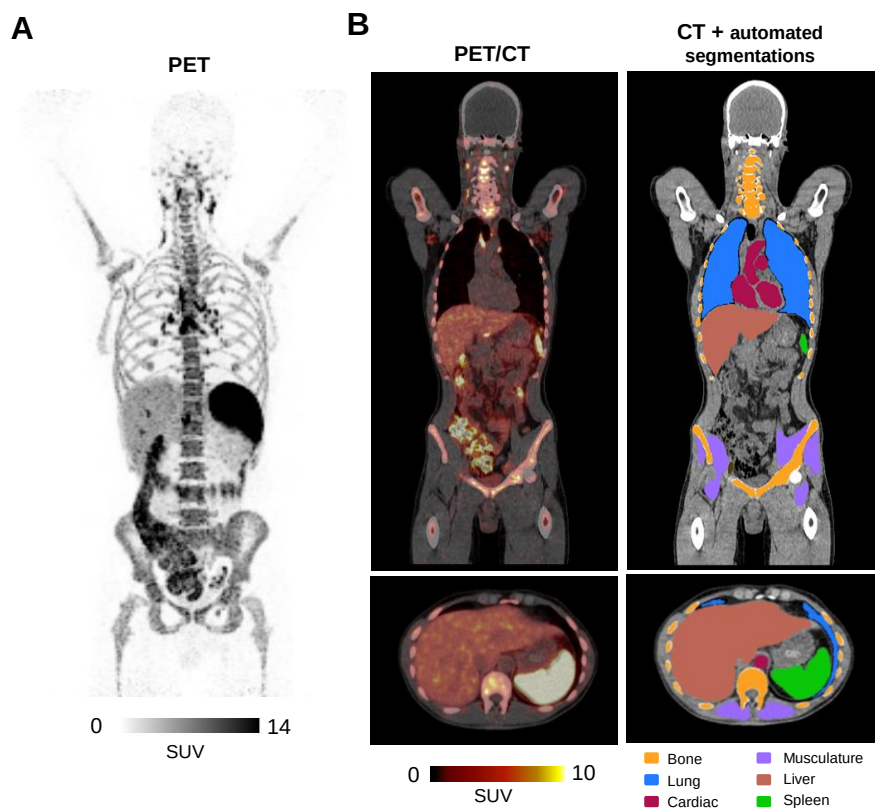


Figure 1 | ^{89}Zr]-Zr-crefmirlimab berdoxam PET imaging allows quantification of whole-body CD8 lymphocyte distribution including spleen, bone marrow and healthy lymph nodes.

A: Maximum intensity projection of a representative baseline ^{89}Zr]-Zr-crefmirlimab berdoxam PET scan with visible uptake in bone marrow, spleen, liver and axillary and mediastinal lymph nodes. **B:** Of the same patient, coronal PET/CT fused image and CT image with projections of automated segmentations used to quantify per-organ uptake values.

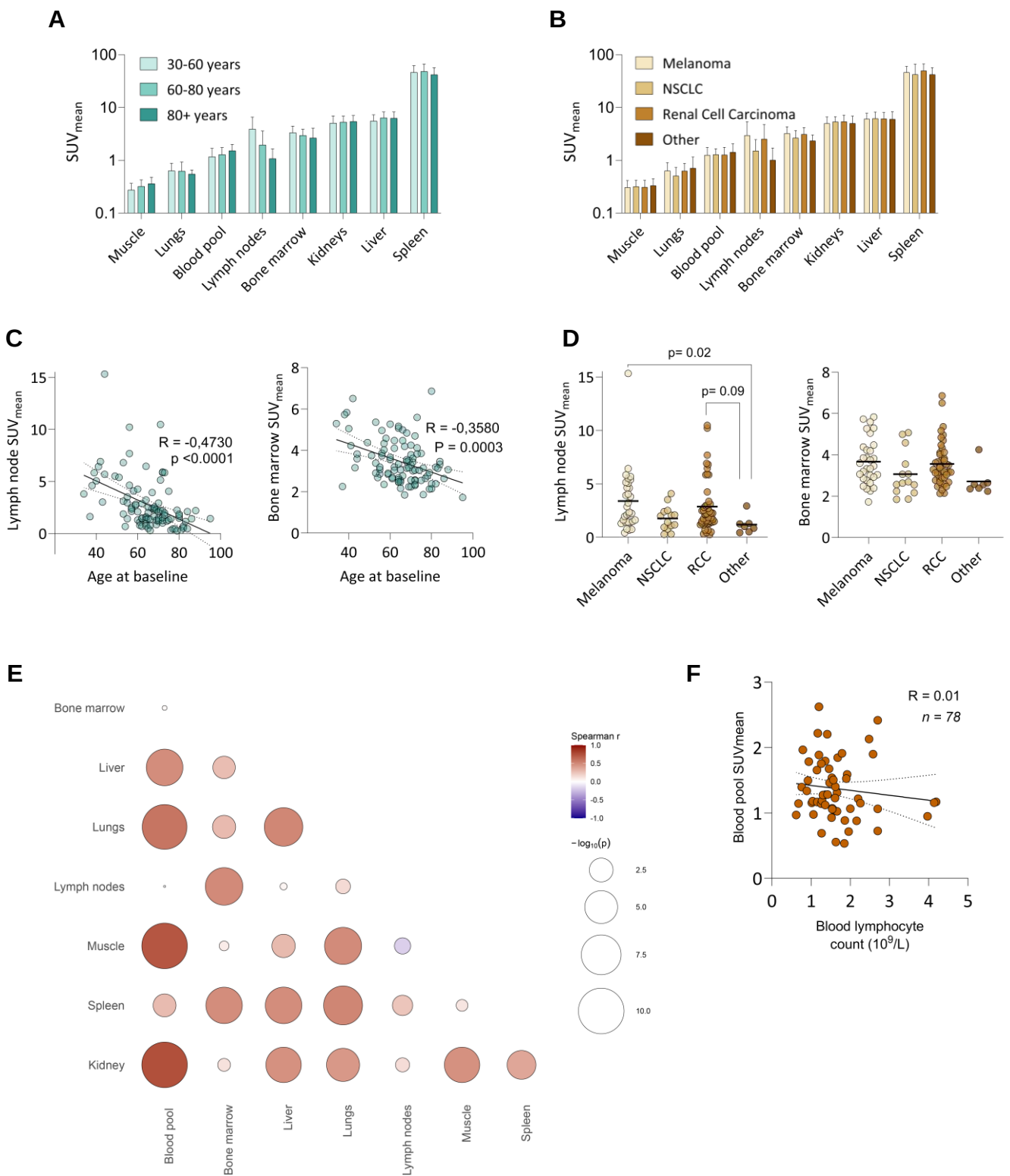


Figure 2 | Baseline uptake of $[^{89}\text{Zr}]\text{Zr}$ -crefmirlimab berdoxam in healthy lymph nodes and bone marrow is correlated with age and blood pool uptake correlates with uptake in muscle and kidney but not with peripheral blood lymphocytes.

A, B: SUV_{mean} in organs of interest for different age groups (**A**) and tumour types (**B**) of the baseline (pre-immunotherapy) PET images of 97 patients, bars indicate group means and error bars standard deviations. **C:** Spearman correlations of baseline lymph node and bone marrow SUV_{mean} against patient age, spearman R and P values of correlations. **D:** Lymph node and bone marrow uptake (SUV_{mean}) per tumour type, black bars indicate group means. **E:** Spearman correlations indicating intercorrelations between organ uptake (SUV_{mean}). Circle size represents $-\log_{10}(p)$ values, color indicating spearman R. **F:** Spearman correlation of blood pool SUV_{mean} and peripheral blood lymphocyte counts of $n = 78$ patients.

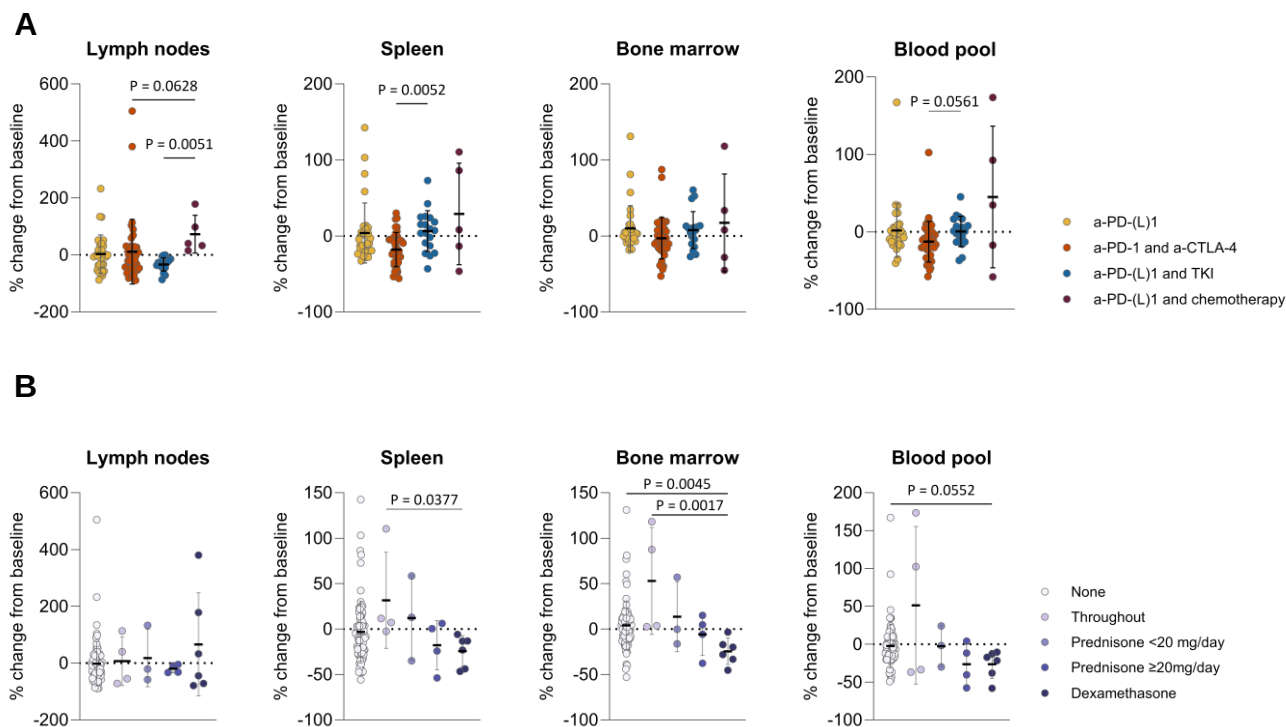


Figure 3 | Upon therapy, patients on combination with TKI and chemotherapy display differential uptake in healthy lymph nodes and dexamethasone use is associates with a decrease in uptake in bone marrow.

A & B: Changes in ^{89}Zr -crefmirlimab berdoxam uptake upon two courses of treatment in a selection of immune relevant organs expressed as percent change in SUV_{mean} in lymph nodes, bone marrow, spleen and blood pool per ICI regimen group (**A**) and corticosteroid treatment group (**B**). Both with two-sided P values from Kruskal-Wallis tests with Dunn's multiple testing correction.

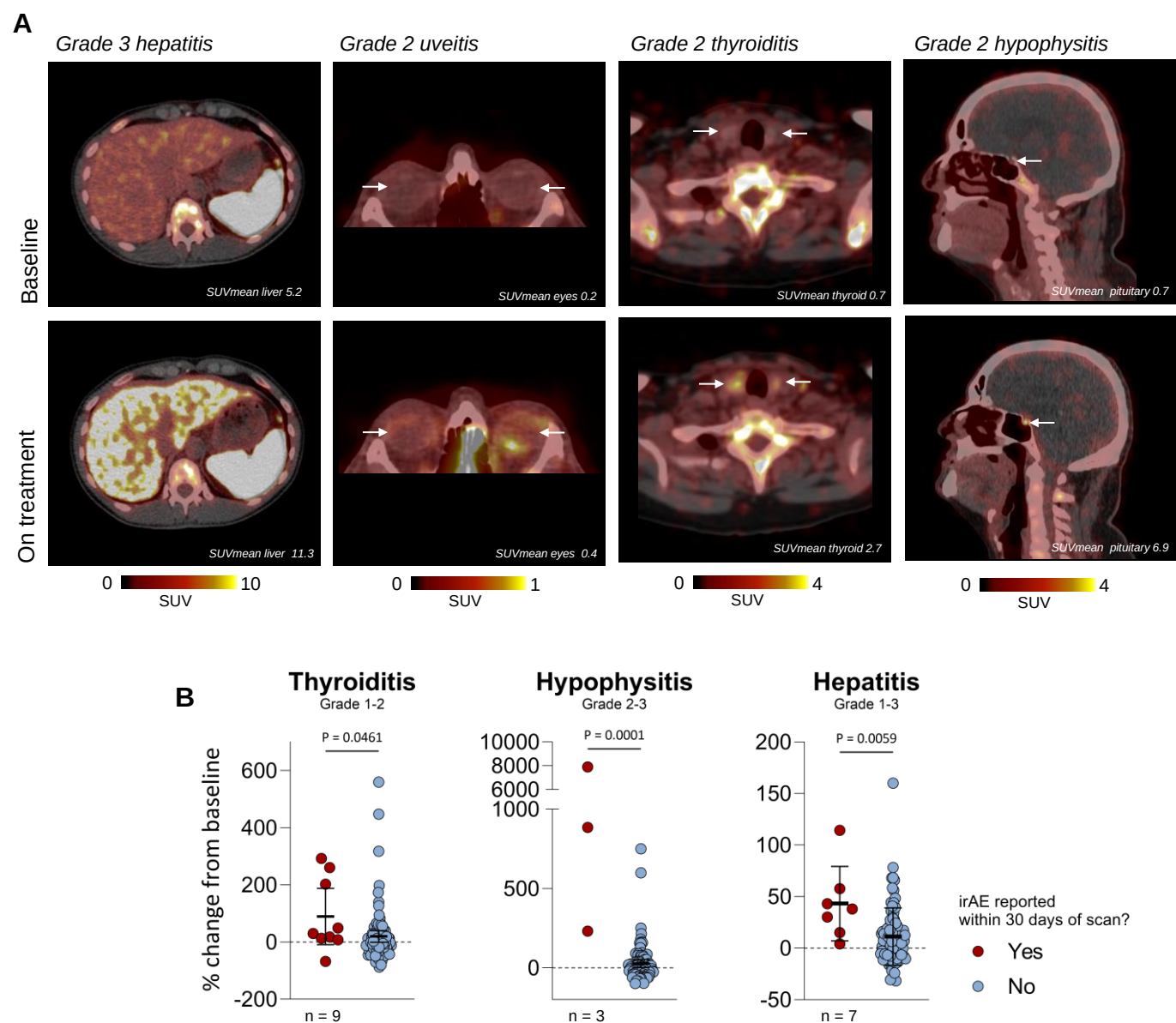


Figure 4 | Increased uptake of $[^{89}\text{Zr}]\text{Zr}$ -crefmirlimab berdoxam in irAE affected organs was observed in most cases.

A: PET/CT fusion images of organs affected by irAEs with visible increase in uptake compared to baseline image, SUVmean was quantified using either automated (liver, thyroid) or manual segmentation methods (eyes, pituitary). **B:** Quantification of percent increase in SUV_{mean} in affected and non-affected thyroid, pituitary and liver, respectively. P values from Mann-Whitney U tests.

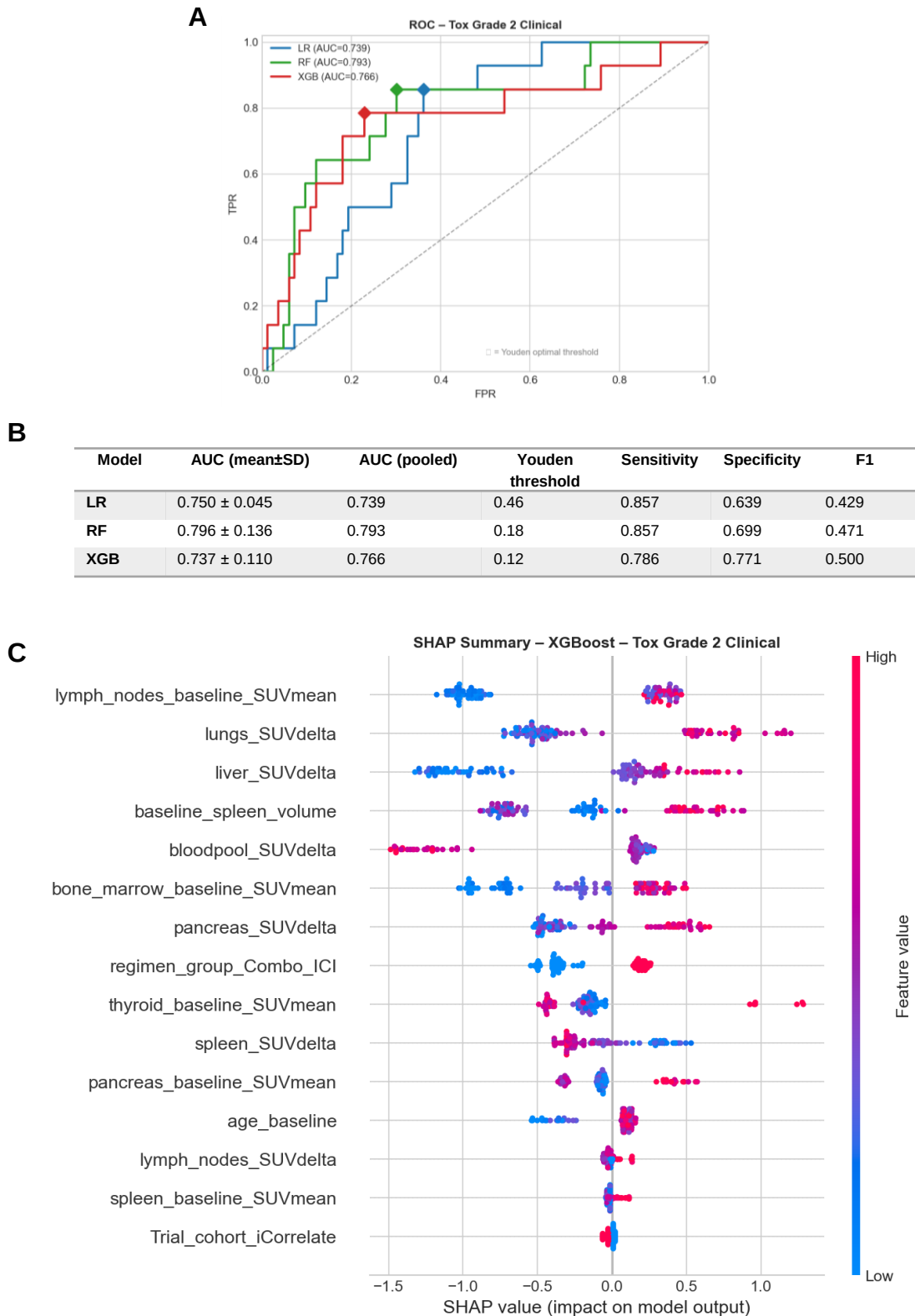
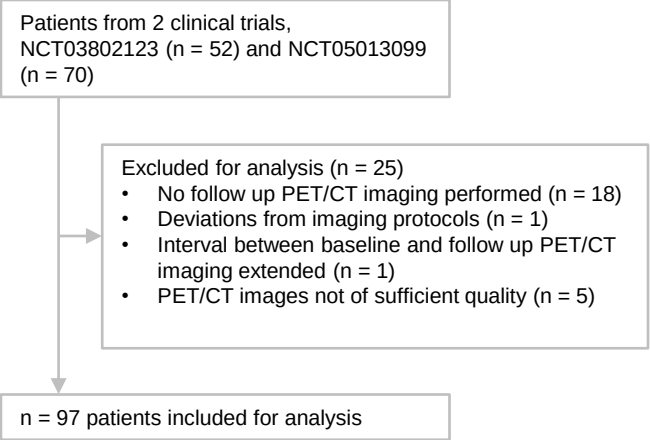


Figure 5 | Three machine learning prediction models predict grade ≥ 2 irAE clinically relevant with high accuracy, revealing baseline lymph node SUVmean and Δ SUVmean of lungs and liver as predictive features.

A: Area Under the Curve (AUC) of the Receiver Operating Characteristic (ROC) for the three models. **B:** performance of the three models employing the optimized Youden threshold. **C:** SHAP values for the top 15 predictive features indicating the impact of high and low feature values on model output. LR = Linear Regression, RF = Random Forest, XGB = XGBoost.

A



B

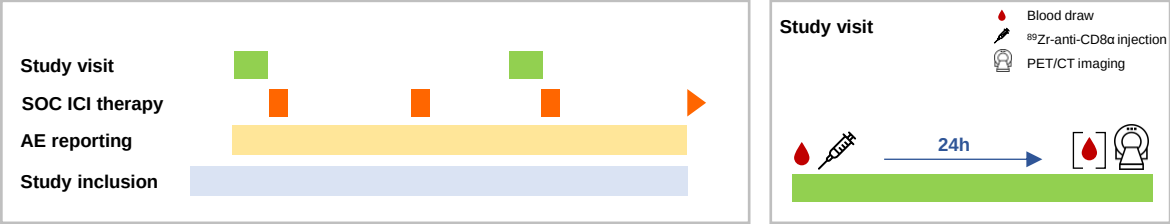


Figure S1 | CONSORT flowchart and study design

A: Flowchart indicating selection of patients for analysis based on availability and quality of data. **B:** Study design indicating order and duration of events during study and schematic overview of a study visit.



Figure S2 | Systematic and manual corrections of original automated segmentations

Lung and kidney automated segmentations underwent systematic corrections to account for overestimation of spill over from high activity in lung and liver. Where needed, all automated segmentations were adapted to remove tumor volumes from the normal organ volumes.

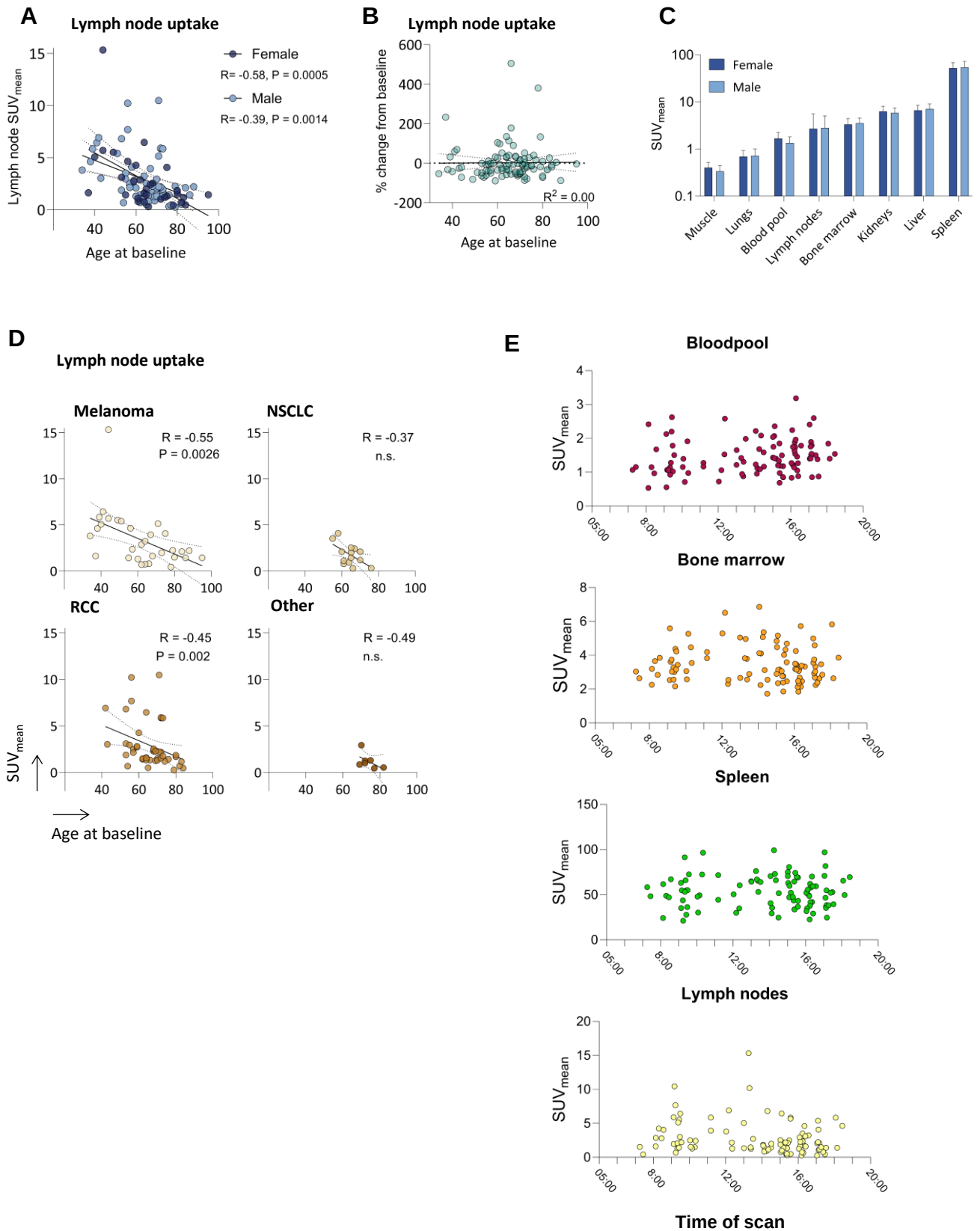
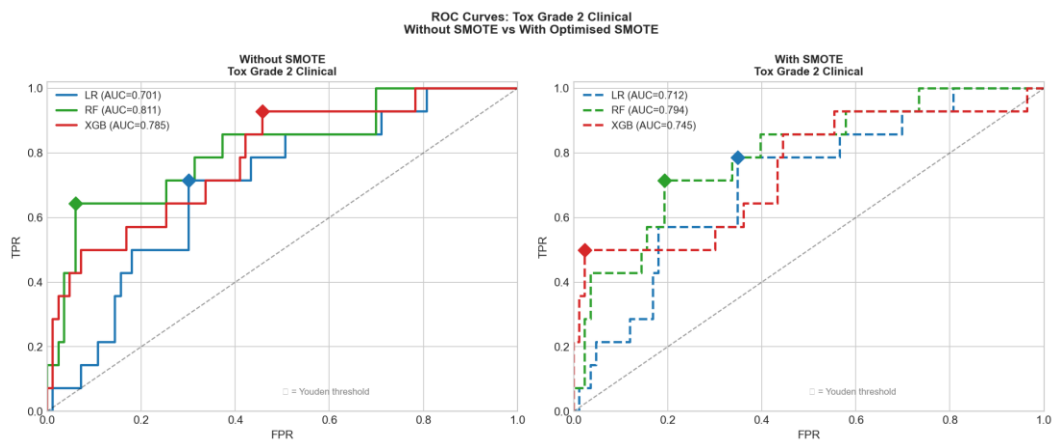


Figure S3 | Baseline uptake values correlations with sex, age and time of scan

A: Lymph node uptake against age for female (dark blue dots) and male (blue dots) patients. Spearman R and two-sided P values. **B:** Percent change in lymph node uptake expressed as % change in SUV_{mean} against patient age at baseline. **C:** SUV_{mean} group means for a selection of organs for male and female patients, error bars represent standard deviation of the mean. **D:** Baseline lymph node uptake (SUV_{mean}) against age for the four different tumour type groups. **E:** baseline uptake in four organs, against the time of the PET image acquisition.

A



B

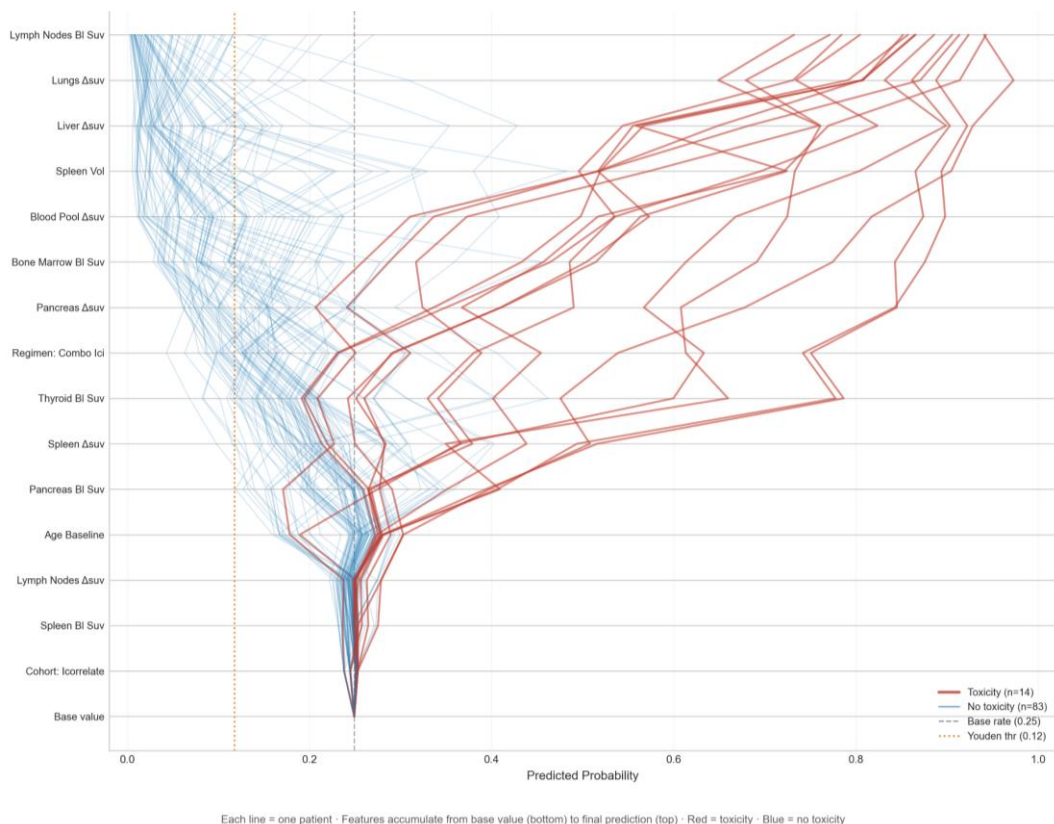


Figure S4 | ROC-AUC with and without SMOTE artificial data augmentation and decision plot.

A: ROC-AUC with (right) and without (left) SMOTE data augmentation. Diamond shape indicates Youden optimized threshold. **B:** Decision plot indicating contribution of features to the prediction decision, each line represents one patient, indicating the accumulating effect of features from the base value to the final prediction. Red lines indicate patients with clinically relevant toxicity, blue lines indicate no toxicity.

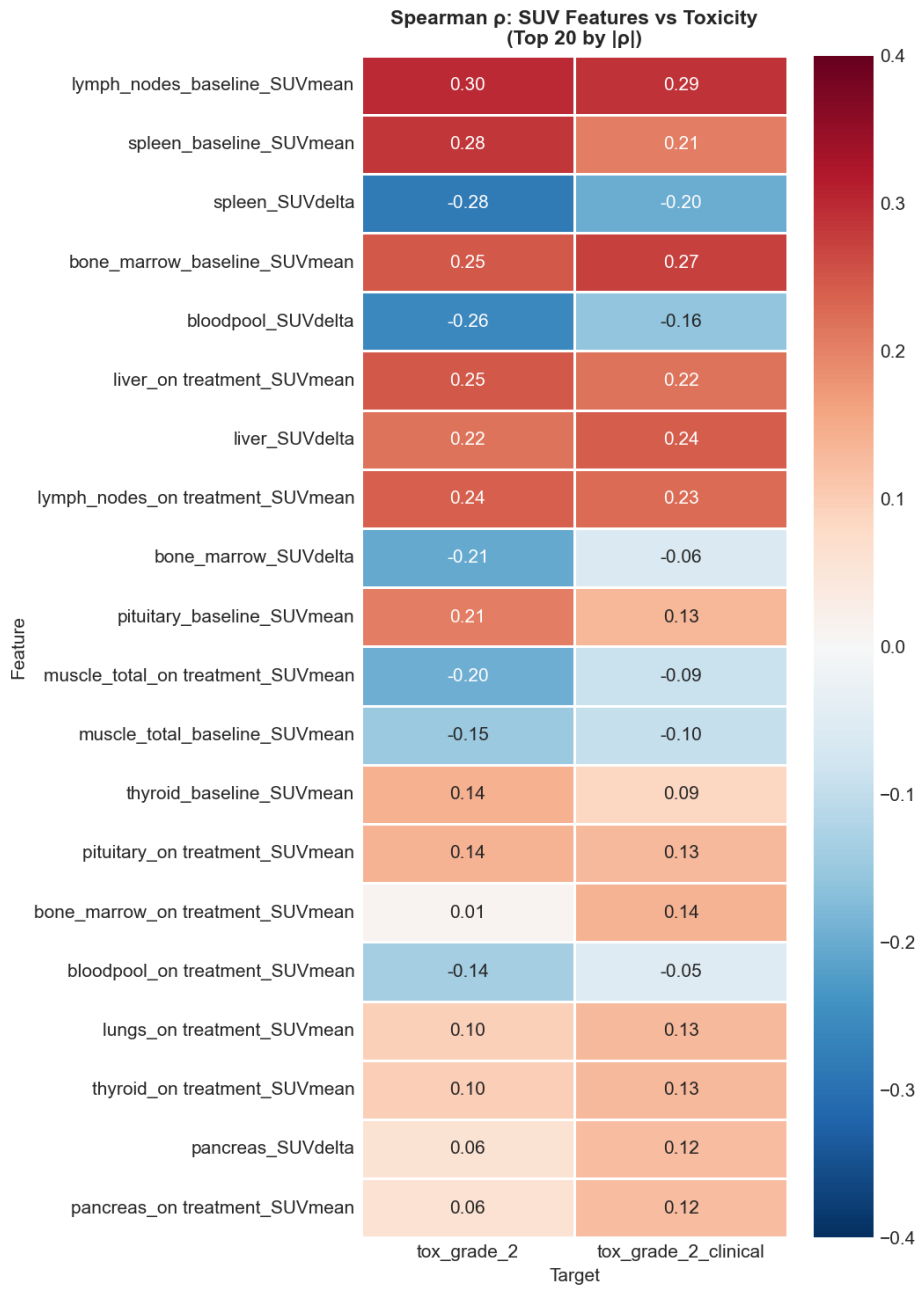


Figure S5 | Correlation of features with two training outcomes: 1) irAEs grade ≥ 2 and 2) clinically relevant grade ≥ 2 irAEs.