Supplementary Materials for

# EASIX-guided risk stratification for complications and outcome after CAR T-cell therapy with ide-cel in relapsed/refractory multiple myeloma

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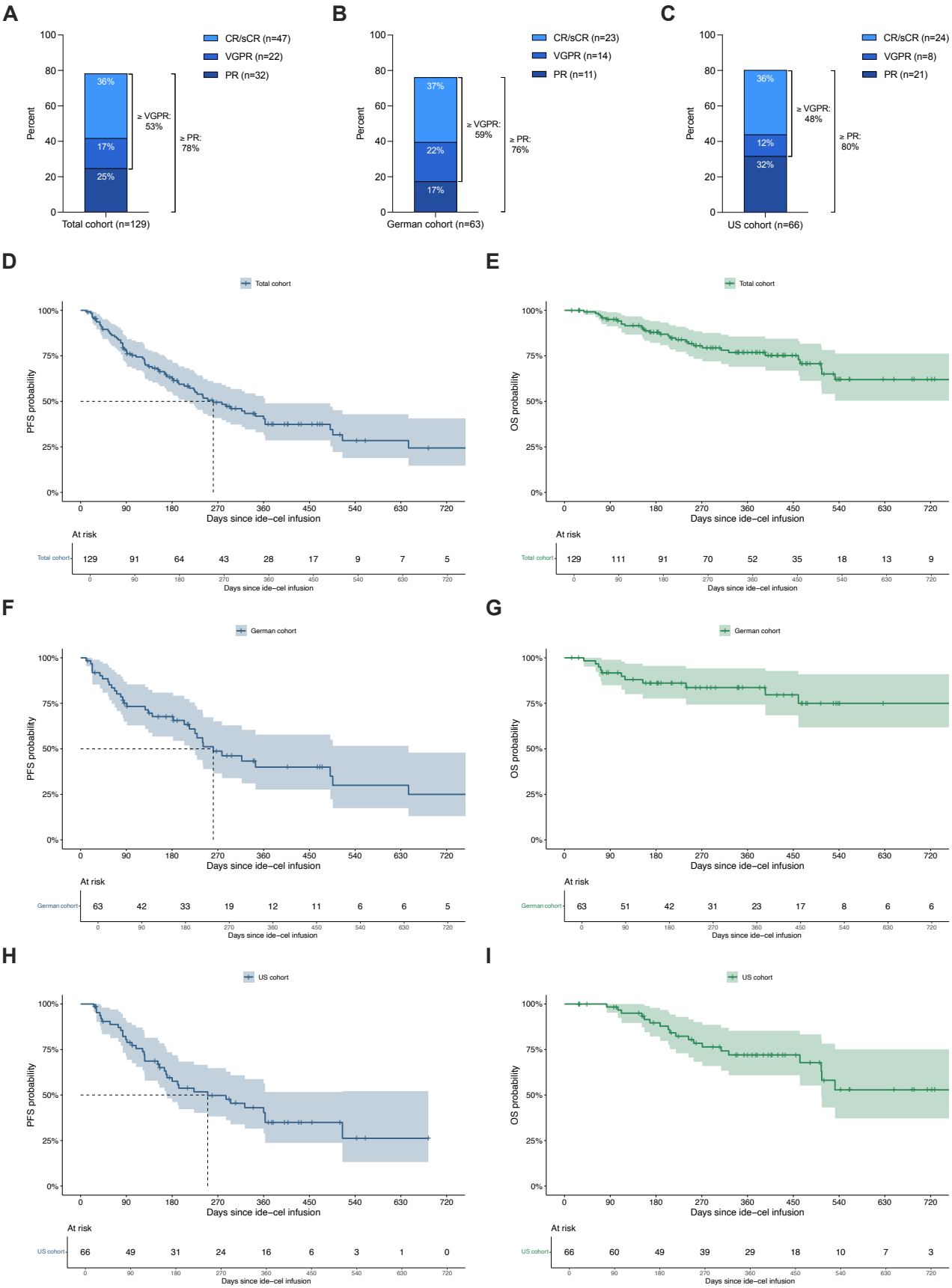
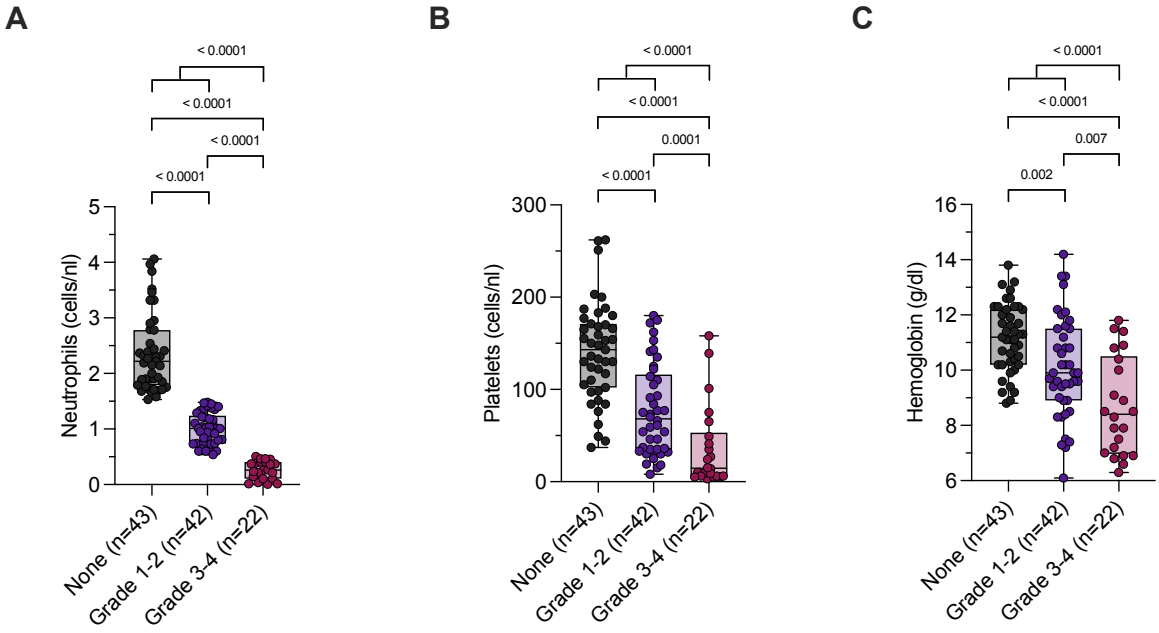
**Supplementary Materials**

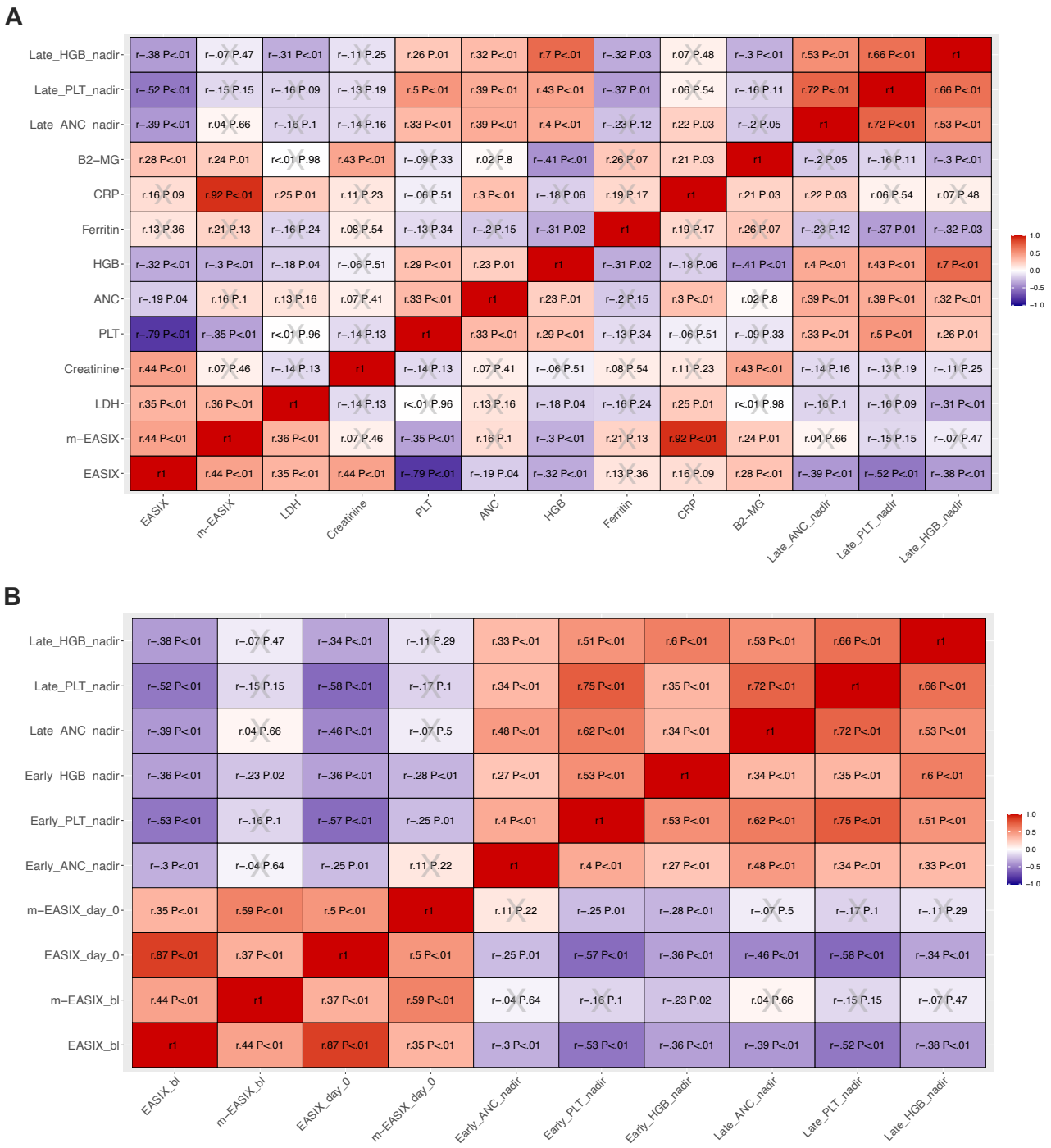
- **Supplementary Figures S1-8**
- **Supplementary Tables S1-18**


A
B
C
CR/sCR (n=47)
VGPR (n=22)
PR (n=32)
CR/sCR (n=23)
VGPR (n=14)
PR (n=11)
CR/sCR (n=24)
VGPR (n=8)
PR (n=21)
Percent
36%
17%
25%
≥ VGPR: 53%
≥ PR: 78%
Total cohort (n=129)
37%
22%
17%
≥ VGPR: 59%
≥ PR: 76%
German cohort (n=63)
36%
12%
32%
≥ VGPR: 48%
≥ PR: 80%
US cohort (n=66)
D
E
F
G
H
I
Total cohort
German cohort
US cohort
PFS probability
OS probability
Days since ide-cel infusion
At risk
Total cohort 129 91 64 43 28 17 9 7 5
Total cohort 129 111 91 70 52 35 18 13 9
German cohort 63 42 33 19 12 11 6 6 5
German cohort 63 51 42 31 23 17 8 6 6
US cohort 66 49 31 24 16 6 3 1 0
US cohort 66 60 49 39 29 18 10 7 3

**Supp. Figure S1 | Efficacy of CAR T-cell therapy. A-C.** Best overall response in the total cohort (**A**), German cohort (**B**) and US cohort (**C**). CR, complete response. PR, partial response. sCR, stringent complete response. VGPR, very good partial response. **D-E.** Kaplan-Meier estimates of the probability of progression-free survival (PFS) (median PFS 261 days; 95% confidence interval [CI] 204-363) (**D**) and overall survival (OS) (median OS not reached [NR]) (**E**) in days since ide-cel infusion for the total cohort. **F-G.** Kaplan-Meier estimates of the probability of PFS (median PFS 261 days; 95% CI 214-645) (**F**) and OS (median OS NR) (**G**) in days since ide-cel infusion for the German cohort. **H-I.** Kaplan-Meier estimates of the probability of PFS (median PFS 250 days; 95% CI 170-NR) (**H**) and OS (median OS NR; 95% CI 505-NR) (**I**) in days since ide-cel infusion for the US cohort.

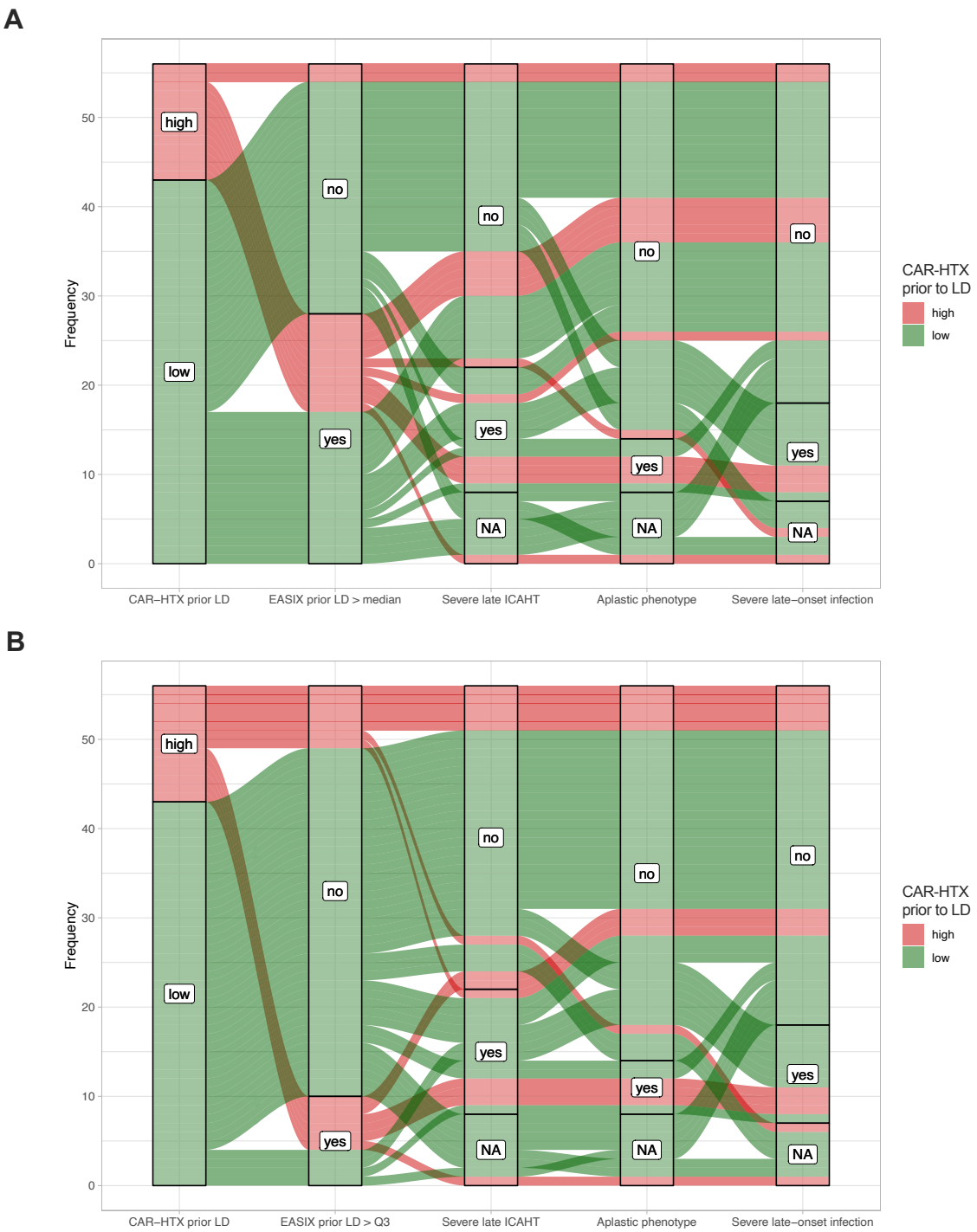



**Supp. Figure S2 | Blood cell count nadir values during the late post-CAR-T period depending on late immune effector cell-associated hematotoxicity (ICAHT) grade.** P-values of the group comparisons are shown at the top. **A.** Late absolute neutrophil count nadir values. Median (left to right): 2.22/nl vs. 1.01/nl vs. 0.26/nl. **B.** Late platelet count nadir values. Median (left to right): 143/nl vs. 68/nl vs. 14.5/nl. **C.** Late hemoglobin nadir values. Median (left to right): 11.20 g/dl vs. 9.90 g/dl vs. 8.40 g/dl.



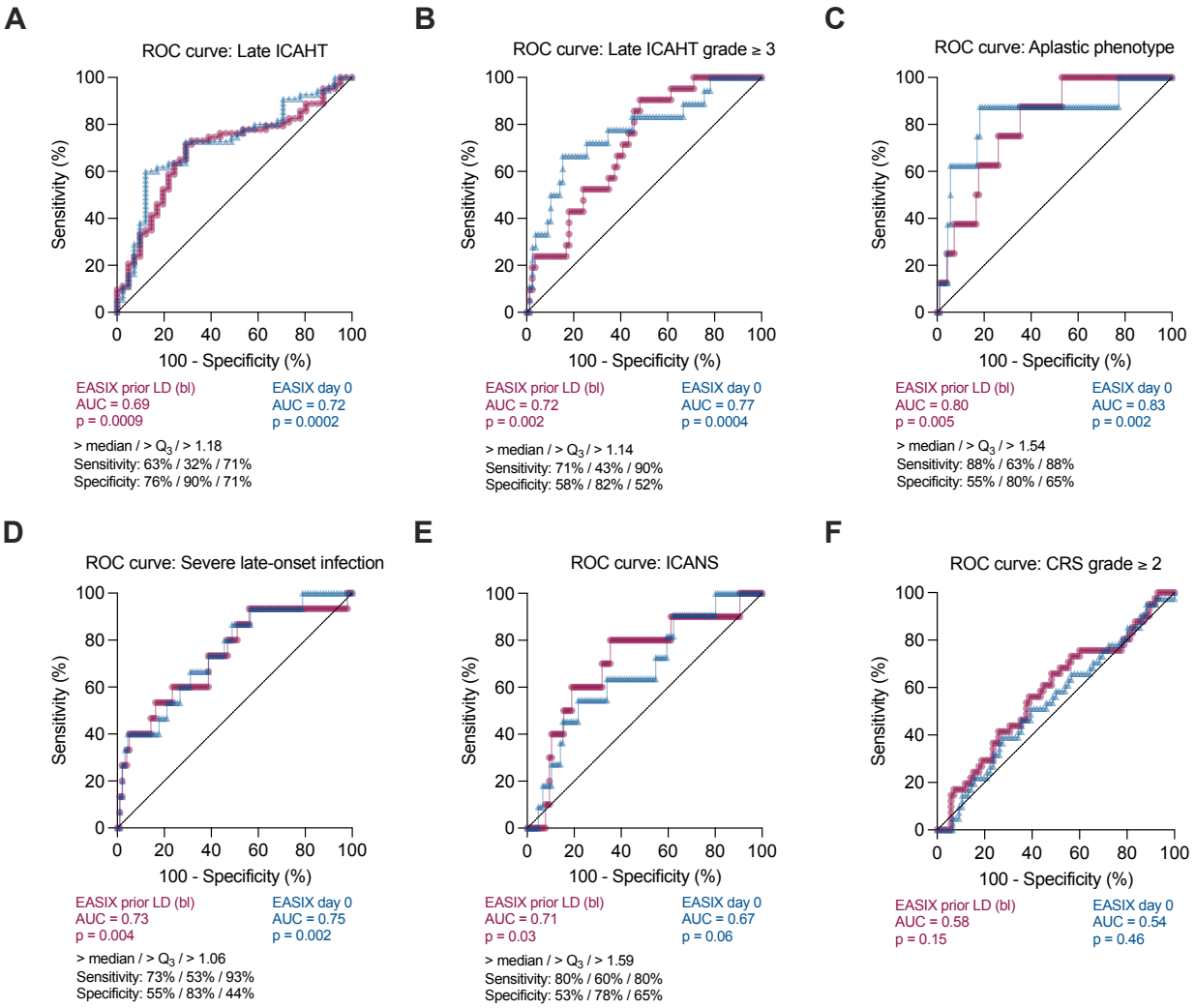

**Supp. Figure S3 | Correlation heatmaps showing associations between laboratory parameters and scores and blood cell count nadir values during the post-CAR-T period in the total cohort.** Coefficient (r) and p-values are based on Spearman correlation analysis and are shown in the individual fields of the heatmaps. Positive r values are shown in red, negative r values in blue. Non-significant associations are marked with a cross. **A.** Correlation heatmap showing associations between laboratory parameters and scores determined prior to lymphodepletion and nadir values during the late post-CAR-T period. Due to missing data for the US cohort, analyses of ferritin were only performed for the German cohort. **B.** Correlation heatmap showing associations between scores determined prior to lymphodepletion (baseline [bl]) or at day 0 (day of CAR T-cell infusion) and nadir values during the early and late post-CAR-T period. ANC, absolute

neutrophil count. EASIX, Endothelial Activation and Stress Index. HGB, hemoglobin. m-EASIX, modified EASIX. PLT, platelet count.



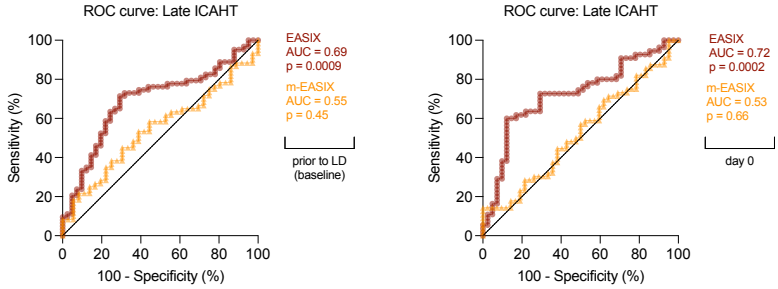

**Supp. Figure S4 | Alluvial plots showing the individual patient distribution and associations between score-based risk groups prior to lymphodepletion (LD) and selected post-CAR-T complications. A.** Associations between CAR-HEMATOTOX (CAR-HTX) groups, median-based EASIX groups and post-CAR-T complications in the German cohort (only patients with available CAR-HTX score shown). Left to right: CAR-HTX prior to LD (high [red] vs. low [green]), EASIX prior to LD > median (> 1.26) (yes vs. no), severe late immune effector cell-associated hematotoxicity (ICAHT) (yes vs. no vs. not available [NA]), aplastic phenotype of neutrophil recovery (yes vs. no vs. NA) and severe late-onset infection (yes vs. no vs. NA). **B.** Associations between CAR-HTX groups, upper quartile ($Q_3$)-based EASIX groups and post-CAR-T

complications in the German cohort (only patients with available CAR-HTX score shown). Left to right: CAR-HTX prior to LD (high [red] vs. low [green]), EASIX prior to LD > $Q_3$ (> 2.15) (yes vs. no), severe late ICAHT (yes vs. no vs. NA), aplastic phenotype of neutrophil recovery (yes vs. no vs. NA) and severe late-onset infection (yes vs. no vs. NA).

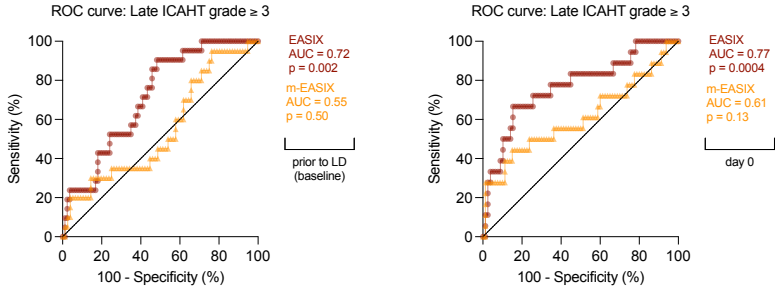



**Supp. Figure S5 | Receiver operating characteristic (ROC) curves to compare the potential of the Endothelial Activation and Stress Index (EASIX) at different time points to identify patients at risk for post-CAR-T complications.** Curves refer to the baseline (bl) EASIX (prior to lymphodepletion [LD]) (red) and the EASIX at day 0 (day of CAR T-cell infusion) (blue). Area under the curve (AUC) values, p-values and sensitivity/specificity for selected baseline EASIX cut-off values (median, upper quartile [$Q_3$], optimal cut-off) are provided below. **A-F.** ROC curves for late immune effector cell-associated hematotoxicity (ICAHT; any grade) (**A**), severe late ICAHT (grade ≥ 3) (**B**), an aplastic phenotype of neutrophil recovery (**C**), severe late-onset infection (**D**), immune effector cell-associated neurotoxicity syndrome (ICANS) (**E**) and cytokine release syndrome (CRS) grade ≥ 2 (**F**) as endpoint.

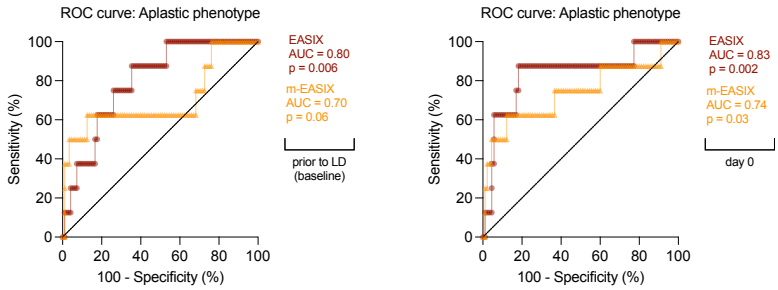
**A**


ROC curve: Late ICAHT
Sensitivity (%)
100 - Specificity (%)
EASIX
AUC = 0.69
p = 0.0009
m-EASIX
AUC = 0.55
p = 0.45
prior to LD (baseline)
ROC curve: Late ICAHT
Sensitivity (%)
100 - Specificity (%)
EASIX
AUC = 0.72
p = 0.0002
m-EASIX
AUC = 0.53
p = 0.66
day 0

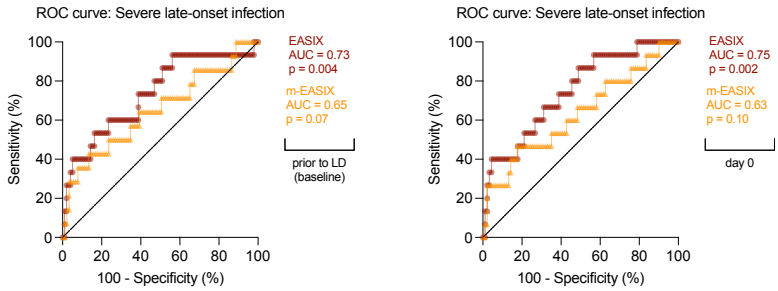
**B**


ROC curve: Late ICAHT grade ≥ 3
Sensitivity (%)
100 - Specificity (%)
EASIX
AUC = 0.72
p = 0.002
m-EASIX
AUC = 0.55
p = 0.50
prior to LD (baseline)
ROC curve: Late ICAHT grade ≥ 3
Sensitivity (%)
100 - Specificity (%)
EASIX
AUC = 0.77
p = 0.0004
m-EASIX
AUC = 0.61
p = 0.13
day 0

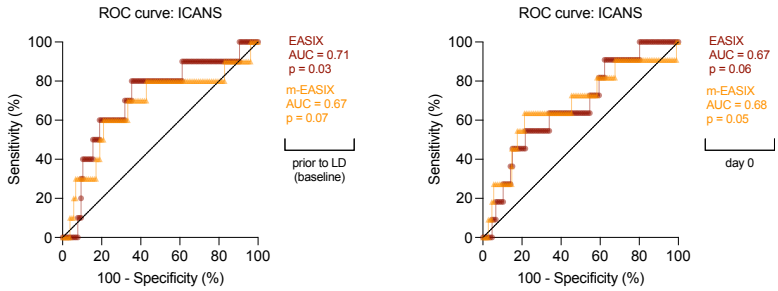
**C**


ROC curve: Aplastic phenotype
Sensitivity (%)
100 - Specificity (%)
EASIX
AUC = 0.80
p = 0.006
m-EASIX
AUC = 0.70
p = 0.06
prior to LD (baseline)
ROC curve: Aplastic phenotype
Sensitivity (%)
100 - Specificity (%)
EASIX
AUC = 0.83
p = 0.002
m-EASIX
AUC = 0.74
p = 0.03
day 0

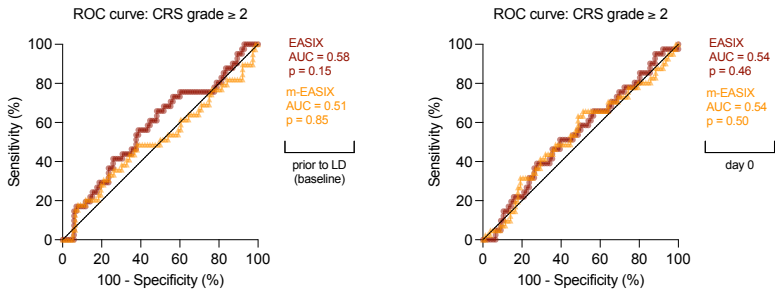
**D**


ROC curve: Severe late-onset infection
Sensitivity (%)
100 - Specificity (%)
EASIX
AUC = 0.73
p = 0.004
m-EASIX
AUC = 0.65
p = 0.07
prior to LD (baseline)
ROC curve: Severe late-onset infection
Sensitivity (%)
100 - Specificity (%)
EASIX
AUC = 0.75
p = 0.002
m-EASIX
AUC = 0.63
p = 0.10
day 0

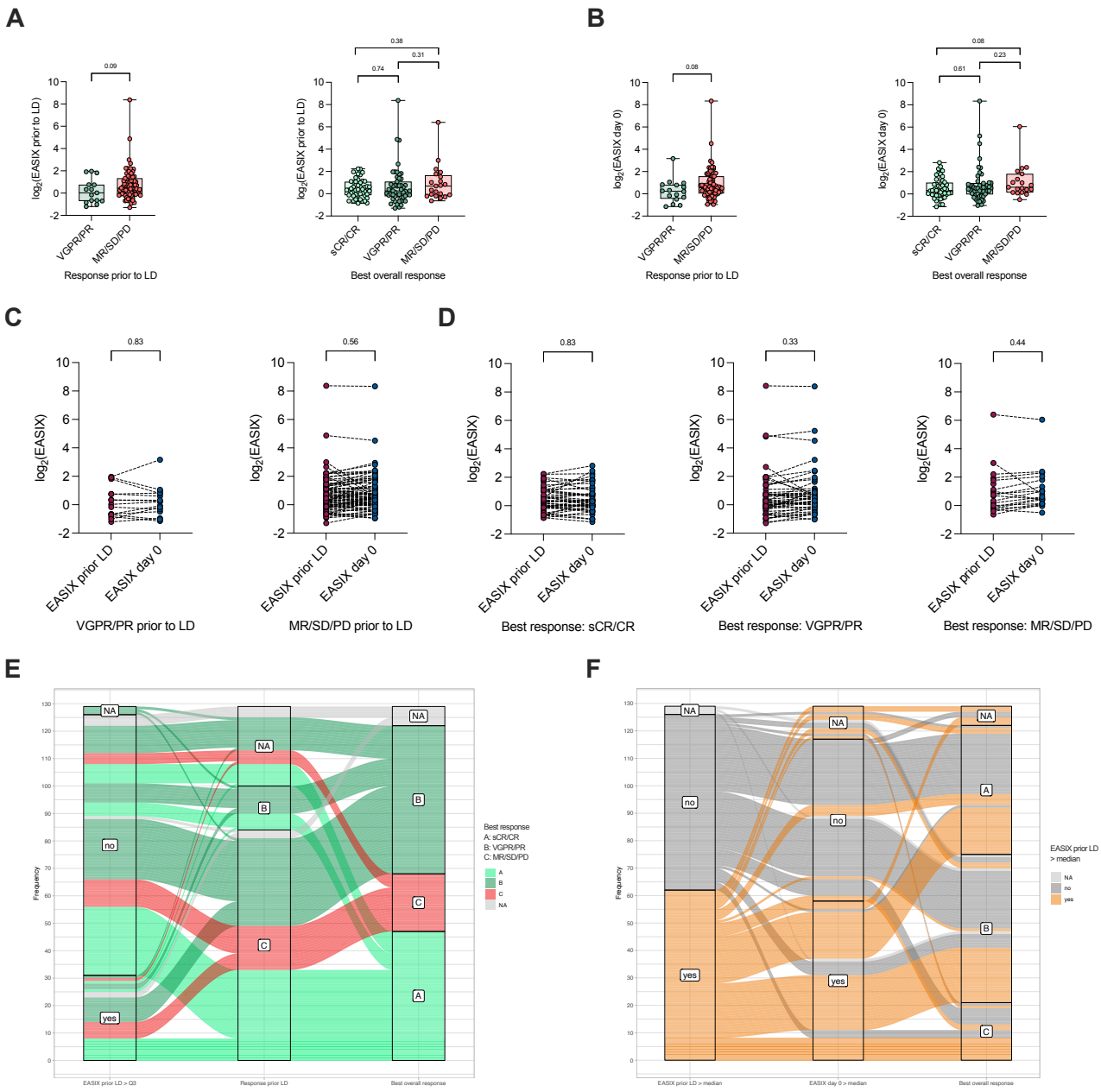
**E**


ROC curve: ICANS
Sensitivity (%)
100 - Specificity (%)
EASIX
AUC = 0.71
p = 0.03
m-EASIX
AUC = 0.67
p = 0.07
prior to LD (baseline)
ROC curve: ICANS
Sensitivity (%)
100 - Specificity (%)
EASIX
AUC = 0.67
p = 0.06
m-EASIX
AUC = 0.68
p = 0.05
day 0

**F**

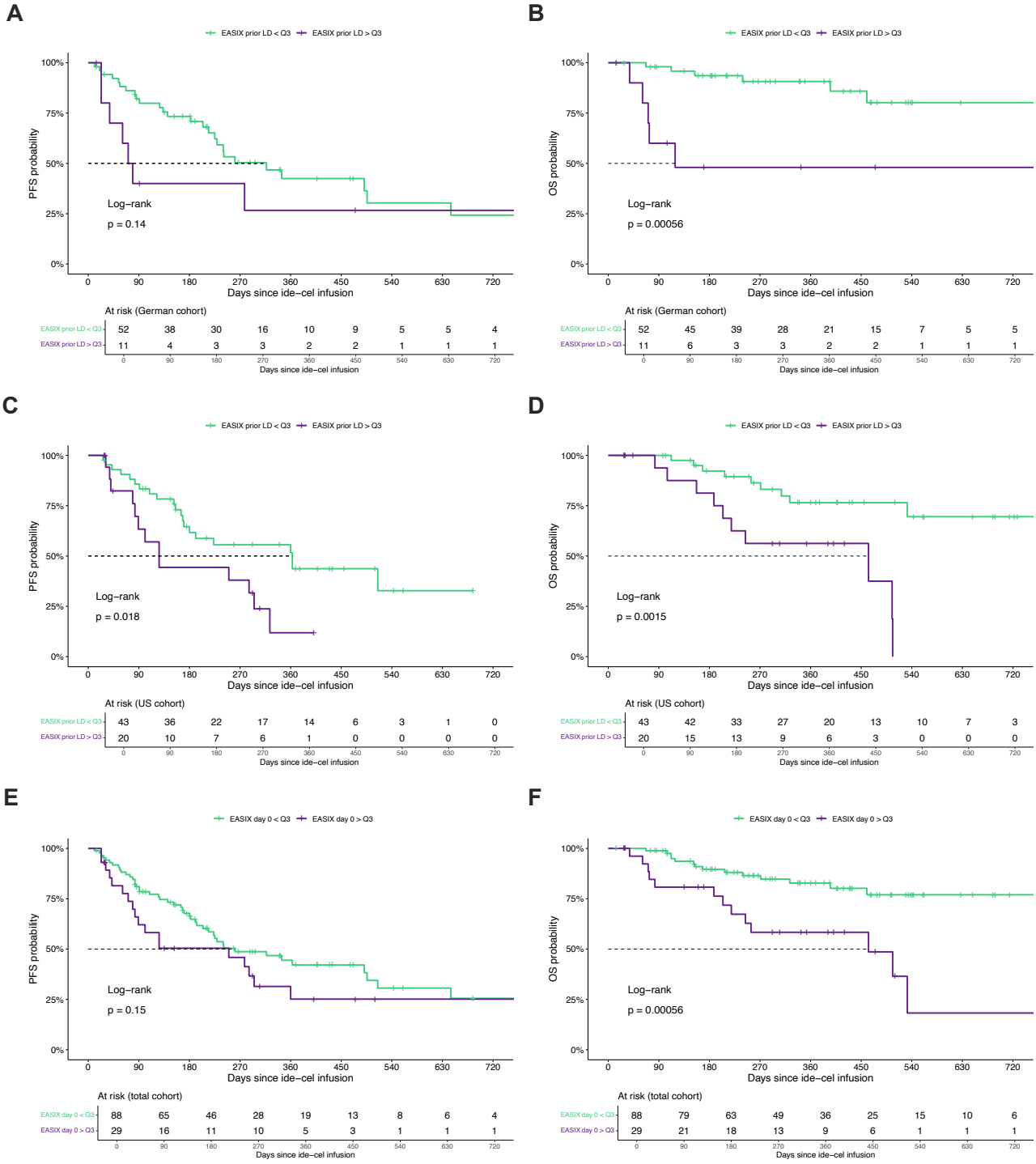

ROC curve: CRS grade ≥ 2
Sensitivity (%)
100 - Specificity (%)
EASIX
AUC = 0.58
p = 0.15
m-EASIX
AUC = 0.51
p = 0.85
prior to LD (baseline)
ROC curve: CRS grade ≥ 2
Sensitivity (%)
100 - Specificity (%)
EASIX
AUC = 0.54
p = 0.46
m-EASIX
AUC = 0.54
p = 0.50
day 0

**Supp. Figure S6 | Receiver operating characteristic (ROC) curves to compare the potential of the Endothelial Activation and Stress Index (EASIX) and the modified EASIX (m-EASIX) at different time points to identify patients at risk for post-CAR-T complications.** Curves refer to the EASIX (red) and the m-EASIX (yellow) determined prior to lymphodepletion (LD; baseline) (left) and at day 0 (day of CAR T-cell infusion) (right). Area under the curve (AUC) values and p-values are provided next to the curves. **A-F.** ROC curves for late immune effector cell-associated hematotoxicity (ICAHT; any grade) (**A**), severe late ICAHT (grade ≥ 3) (**B**), an aplastic phenotype of neutrophil recovery (**C**), severe late-onset infection (**D**), immune effector cell-associated neurotoxicity syndrome (ICANS) (**E**) and cytokine release syndrome (CRS) grade ≥ 2 (**F**) as endpoint.




**Supp. Figure S7 | Associations between Endothelial Activation and Stress Index (EASIX) prior to lymphodepletion (LD) and at day 0 (day of CAR T-cell infusion) and response status before and after CAR T-cell therapy. A.** Baseline $log_2$(EASIX) values (prior to LD) depending on the response status prior to LD (left) (median [left to right]: 0.02 [n=15] vs. 0.46 [n=83]) and best overall response status after CAR T-cell therapy (right) (median [left to right]: 0.34 [n=47] vs. 0.26 [n=51] vs. 0.69 [n=21]). P-values of the group comparisons are shown at the top. CR, complete response. MR, minimal response. PD, progressive disease. PR, partial response. sCR, stringent complete response. SD, stable disease. VGPR, very good partial response. **B.** $Log_2$(EASIX) values at day 0 depending on the response status prior to LD (left) (median [left to right]: 0.23 [n=16] vs. 0.53 [n=75]) and best overall response status after CAR T-cell therapy (right) (median [left to right]: 0.32 [n=44] vs. 0.51 [n=49] vs. 0.61 [n=19]). P-values of the group comparisons are shown at the top. **C**. Individual changes of the $log_2$(EASIX) values between the time point prior to LD and at day 0 among patients with (left; n=15 and

n=16, respectively) and without (right; n=83 and n=75, respectively) treatment response prior to LD. P-values of the group comparisons are shown at the top. **D.** Individual changes of the $log_2$(EASIX) values between the time point prior to LD and at day 0 depending on best overall response after CAR T-cell therapy. Left to right: Patients with a CR or better (n=47 and n=44, respectively), patients with a PR or better (n=51 and n=49, respectively) and patients without treatment response (n=21 and n=19, respectively). P-values of the group comparisons are shown at the top. **E.** Alluvial plot showing the individual patient distribution and associations between the upper quartile ($Q_3$)-based EASIX groups prior to LD and response groups before and after CAR T-cell therapy in the total cohort. Left to right: EASIX prior to LD > $Q_3$ (> 2.15) (yes vs. no vs. not available [NA]), response group prior to LD (B vs. C vs. NA) and best overall response group after CAR T-cell therapy (A [light green] vs. B [dark green] vs. C [red] vs. NA [light grey]). Response groups: A (sCR/CR), B (VGPR/PR), C (MR/SD/PD) and NA (not available/applicable). **F.** Alluvial plot showing the individual patient distribution and associations between the median-based EASIX groups prior to LD, at day 0 and response groups after CAR T-cell therapy in the total cohort. Left to right: EASIX prior to LD > median (> 1.26) (yes [orange] vs. no [dark grey] vs. NA [light grey]), EASIX at day 0 > median (>1.36) (yes vs. no vs. NA) and best overall response group after CAR T-cell therapy (A vs. B vs. C vs. NA). Response groups: A (sCR/CR), B (VGPR/PR), C (MR/SD/PD) and NA (not available/applicable).




**Supp. Figure S8 | Associations between Endothelial Activation and Stress Index (EASIX) and outcomes after CAR T-cell therapy. A.** Kaplan-Meier estimates of the probability of progression-free survival (PFS) in days since ide-cel infusion for the EASIX prior to lymphodepletion [LD] ≤ upper quartile ($Q_3$) (≤ 2.15) group (green) (median PFS 317 days; 95% CI 225-not reached [NR]) and the EASIX prior to LD > $Q_3$ (> 2.15) group (violet) (median PFS 75 days; 95% CI 38-NR) in the German cohort. **B.** Kaplan-Meier estimates of the probability of overall survival (OS) in days since ide-cel infusion for the EASIX prior to LD ≤ $Q_3$ (≤ 2.15) group (green) (median OS NR) and the EASIX prior to LD > $Q_3$ (> 2.15) group (violet)

(median OS 119 days; 95% CI 71-NR) in the German cohort. **C.** Kaplan-Meier estimates of the probability of PFS in days since ide-cel infusion for the EASIX prior to LD ≤ $Q_3$ (≤ 2.15) group (green) (median PFS 363 days; 95% CI 180-NR) and the EASIX prior to LD > $Q_3$ (> 2.15) group (violet) (median PFS 126 days; 95% CI 89-NR) in the US cohort. **D.** Kaplan-Meier estimates of the probability of OS in days since ide-cel infusion for the EASIX prior to LD ≤ $Q_3$ (≤ 2.15) group (green) (median OS NR) and the EASIX prior to LD > $Q_3$ (> 2.15) group (violet) (median OS 463 days; 95% CI 204-NR) in the US cohort. **E.** Kaplan-Meier estimates of the probability of PFS in days since ide-cel infusion for the EASIX at day 0 (day of CAR T-cell infusion) ≤ $Q_3$ (≤ 2.06) group (green) (median PFS 261 days; 95% CI 214-515) and the EASIX at day 0 > $Q_3$ (> 2.06) group (violet) (median PFS 250 days; 95% CI 89-NR) in the total cohort. **F.** Kaplan-Meier estimates of the probability of OS in days since ide-cel infusion for the EASIX at day 0 ≤ $Q_3$ (≤ 2.06) group (green) (median OS NR) and the EASIX at day 0 > $Q_3$ (> 2.06) group (violet) (median OS 463 days; 95% CI 244-NR) in the total cohort.

**Supp. Table S1 | Institutional standard operating procedures for prophylaxes and management of complications**

| | Heidelberg | Würzburg | Boston |
|---|---|---|---|
| **CRS** | | | |
| Tocilizumab | • CRS grade ≥ 2 | • Consideration for CRS grade 1-2<br>• CRS grade ≥ 3 | • Consideration for CRS grade 1<br>• CRS grade ≥ 2 |
| Dexamethasone | • Consideration for CRS grade 2<br>• CRS grade 3 | • Consideration for CRS grade 1-2<br>• CRS grade 3 | • Consideration for CRS grade 1-2<br>• CRS grade 3 |
| Methylprednisolone | • CRS grade 4 | • CRS grade 4 | • CRS grade 4 |
| **ICANS** | | | |
| Dexamethasone | • ICANS grade 2 without improvement within 24 hours<br>• ICANS grade 3 | • Consideration for ICANS grade 1-2 | • Consideration for ICANS grade 1-2 |
| Methylprednisolone | • ICANS grade 3 without improvement within 24 hours<br>• ICANS grade 4 | • ICANS grade ≥ 3 | • Consideration for ICANS grade ≥ 3 |
| **Cytopenias** | | | |
| G-CSF | • Individual decision<br>• Consideration in case of protracted neutropenia (> 10 days after infusion) | • Leukocytopenia CTC grade ≥ 3 | • Individual decision<br>• Consideration in case of protracted or severe neutropenia |
| TPO agonists | | | • Individual decision<br>• Consideration in case of long-lasting or severe thrombocytopenia |
| Red blood cell transfusion | • Individual decision<br>• Therapy-associated anemia with hemoglobin < 8 g/dl and without expected spontaneous reconstitution<br>• Anemia with clinical symptoms | • Hemoglobin < 8 g/dl | • Hemoglobin < 8 g/dl |
| Platelet transfusion | • Relevant bleeding signs<br>• Platelets < 20/nl (outpatient) / < 10/nl (inpatient) | • Bleeding<br>• Platelets < 10/nl | • Bleeding<br>• Platelets < 10/nl |
| **Infection prophylaxis** | | | |
| Antibacterial | • Rifaximin 200 mg p.o. 2x/day until neutrophil recovery | | |
| Antiviral | • Aciclovir 400 mg p.o. 2x/day until $CD4^+$ T cell regeneration | • Aciclovir 400 mg p.o. 2x/day | • Aciclovir 400 mg p.o. 2x/day |
| Antifungal | • Fluconazole 200 mg p.o. 1x/day until neutrophil recovery *or*<br>• Posaconazole 300 mg p.o. 1x/day (after loading dose) according to risk (e.g. steroid administration)<br>• PCP prophylaxis: Cotrimoxazole 960 mg p.o. 1x/day three times per week until $CD4^+$ T cell regeneration | • PCP prophylaxis: Cotrimoxazole 960 mg p.o. 1x/day three times per week | • PCP prophylaxis: Trimethoprim/Sulfametho-xazole ss 1x/day |

| | | | |
|---|---|---|---|
| IVIG substitution | • Infection tendency, IgG < 4 g/l | • Infection tendency, IgG < 4 g/l | • Infection tendency, IgG < 4 g/l |

CRS, cytokine release syndrome. CTC, Common Terminology Criteria for Adverse Events. G-CSF, granulocyte-colony stimulating factor. ICANS, immune effector cell-associated neurotoxicity syndrome. IVIG, intravenous immunoglobulin. PCP, pneumocystis pneumonia. TPO, thrombopoietin receptor.

**Supp. Table S2 | Efficacy of CAR T-cell therapy with ide-cel**

| | **Total cohort** ***n = 129*** | **German cohort** ***n = 63*** | **US cohort** ***n = 66*** | ***p*** |
|---|---|---|---|---|
| **Best overall response** | | | | |
| ≥ PR (ORR) | 101 (78) | 48 (76) | 53 (80) | 0.81 |
| ≥ CR | 47 (36) | 23 (37) | 24 (36) | 0.16 |
| VGPR | 22 (17) | 14 (22) | 8 (12) | |
| PR | 32 (25) | 11 (17) | 21 (32) | |
| MR | 1 (1) | 0 (0) | 1 (2) | |
| SD | 12 (9) | 7 (11) | 5 (8) | |
| PD | 8 (6) | 2 (3) | 6 (9) | |
| Not applicable | 7 (5) | 6 (10) | 1 (2) | |
| **Time to first response**, months, median (range) | 0.9 (0.1-3.8) | 0.6 (0.1-3.8) | 1.0 (0.5-3.0) | **< 0.0001** |
| **Time to best response**, months, median (range) | 1.0 (0.2-15.7) | 0.9 (0.2-15.7) | 1.1 (0.5-12.1) | **0.04** |
| **Progression-free survival**, months, median (95% CI) | 8.6 (6.7-11.9) | 8.6 (7.0-21.2) | 8.2 (5.6-NR) | 0.89 |
| **Overall survival**, months, median (95% CI) | NR | NR | NR | 0.29 |
| **Follow-up**, months, median (95% CI) | 9.6 (7.9-11.6) | 8.8 (6.1-11.5) | 10.8 (8.2-12.9) | 0.38 |

CI, confidence interval. CR, complete response. MR, minimal response. NR, not reached. ORR, overall response rate. PD, progressive disease. PR, partial response. SD, stable disease. VGPR, very good partial response.

**Supp. Table S3 | Safety of CAR T-cell therapy with ide-cel**

| | Total cohort *n = 129* | German cohort *n = 63* | US cohort *n = 66* | *p* |
|---|---|---|---|---|
| **CRS**, No. (%) | | | | |
| Yes | 109 (84) | 57 (90) | 52 (79) | |
| Grade 1 | 67 (52) | 30 (48) | 37 (56) | **0.04** |
| Grade 2 | 41 (32) | 26 (41) | 15 (23) | |
| Grade 3 | 1 (1) | 1 (2) | 0 (0) | |
| No | 20 (16) | 6 (10) | 14 (21) | |
| **ICANS**, No. (%) | | | | |
| Yes | 11 (9) | 4 (6) | 7 (11) | |
| Grade 1 | 4 (3) | 2 (3) | 2 (3) | > 0.99 |
| Grade 2 | 3 (2) | 1 (2) | 2 (3) | |
| Grade 3 | 3 (2) | 1 (2) | 2 (3) | |
| Grade 4 | 1 (1) | 0 (0) | 1 (2) | |
| No | 118 (91) | 59 (94) | 59 (89) | |
| **Supportive measures**, No. (%) | | | | |
| Tocilizumab | 66 (51) | 32 (51) | 34 (52) | > 0.99 |
| Dexamethasone | 57 (44) | 28 (44) | 29 (44) | > 0.99 |
| **Late ICAHT**, No. (%) | | | | |
| Yes | 64 (60) | 35 (64) | 29 (56) | |
| Grade 1 | 22 (21) | 13 (24) | 9 (17) | 0.19 |
| Grade 2 | 20 (19) | 7 (13) | 13 (25) | |
| Grade 3 | 16 (15) | 10 (18) | 6 (12) | |
| Grade 4 | 6 (6) | 5 (9) | 1 (2) | |
| Severe (Grade ≥ 3) | 22 (21) | 15 (27) | 7 (13) | 0.10 |
| No | 43 (40) | 20 (36) | 23 (44) | |
| Unknown | 22 | 8[a] | 14[b] | |
| **Neutrophil recovery phenotype**, No. (%) | | | | |
| Quick | 52 (49) | 22 (40) | 30 (58) | 0.13 |
| Intermittent | 47 (44) | 27 (49) | 20 (38) | |
| Aplastic | 8 (7) | 6 (11) | 2 (4) | 0.27 |
| Unknown | 22 | 8[c] | 14[c] | |
| **Supportive measures**, No. (%) | | | | |
| Red blood cell transfusion | | | | |
| ≤ day 30 | 30 (31), n = 96 | 8 (27), n = 30[d] | 22 (33) | 0.64 |
| > day 30 | 7 (8), n = 92 | 5 (17), n = 30 | 2 (3), n = 62[e] | **0.04** |
| Platelet transfusion | | | | |
| ≤ day 30 | 16 (17), n = 96 | 1 (3), n = 30[d] | 15 (23) | **0.02** |
| > day 30 | 8 (9), n = 92 | 4 (13), n = 30 | 4 (6), n = 62[e] | 0.43 |
| G-CSF | | | | |
| ≤ day 30 | 47 (49), n = 96 | 7 (23), n = 30[d] | 40 (61) | **0.0009** |
| > day 30 | 21 (23), n = 92 | 5 (17), n = 30 | 16 (26), n = 62[e] | 0.43 |
| as prophylaxis | 52 (40) | 0 (0) | 52 (79)[f] | **< 0.0001** |
| TPO agonist | | | | |
| ≤ day 30 | 6 (5) | 0 (0) | 6 (9) | **0.03** |
| > day 30 | 5 (4), n = 122 | 0 (0), n = 60[g] | 5 (8), n = 62[e] | 0.06 |
| Autologous SC boost | 2 (2) | 2 (3)[h] | 0 (0) | 0.24 |

| | | | | |
|---|---|---|---|---|
| **Severe late-onset infection**, No. (%) | | | | |
| Yes | 15 (13) | 11 (20) | 4 (7) | 0.05 |
| No | 101 (87) | 44 (80) | 57 (93) | |
| Unknown | 13 | 8[i] | 5[j] | |
| **Supportive measures**, No. (%) | | | | |
| IVIG substitution, day 0-90 | 34 (26) | 13 (21) | 21 (32) | 0.17 |
| **CAR T-associated parkinsonism**, No. (%) | 1 (1) | 1 (2) | 0 (0) | 0.49 |
| **Cause of death**, No. (%) | | | | |
| MM-dependent | 23 (77) | 9 (82) | 14 (74) | |
| MM progression-related | 19 (63) | 5 (45) | 14 (74) | **0.03** |
| Therapy-related | 4 (13) | 4 (36) | 0 (0) | |
| Not attributable | 0 (0) | 0 (0) | 0 (0) | |
| MM-independent | 0 (0) | 0 (0) | 0 (0) | |
| Not attributable | 1 (3) | 0 (0) | 1 (5) | |
| Unknown | 6 (20) | 2 (18) | 4 (21) | |
| **Non-relapse mortality**, No. (%) | 3[k] (10) | 3 (27) | 0 (0) | **0.02** |
| Others | 25 (83) | 7 (64) | 18 (95) | |
| Unknown | 2 (7) | 1 (9) | 1 (5) | |

a. n=3 patients with a follow-up ≤ 30 days, n=1 patient without available absolute neutrophil count (ANC) values during the late post-CAR-T period and n=4 patients with only one available ANC value during the late post-CAR-T period (evaluable hemoglobin and platelet values were available for two of the four patients). b. n =4 patients with a follow-up ≤ 30 days, n=9 patients without available ANC values during the late post-CAR-T period and n=1 patient with only one available ANC value during the late post-CAR-T period. c. Patients without available data on ANC recovery during the late post-CAR-T period (see above). d. Data available as part of the medical documentation for n=30 patients. e. n=4 patients with a follow-up ≤ 30 days. f. As prophylaxis prior to CAR T-cell infusion (days before CAR T-cell infusion, median [range]: 3 [0-6]). g. n=3 patients with a follow-up ≤ 30 days. h. n=2 patients received an autologous stem cell boost. Both patients had regular need for red blood cell and platelet transfusions and growth factor stimulation during the late post-CAR-T period, without any signs of a spontaneous stabilization around day 60. Patient 1 received $3{,}2 \times 10^6$ $CD34^+$/kg body weight on day 72 after CAR T-cell infusion. Patient 2 received $2{,}37 \times 10^6$ $CD34^+$/kg body weight on day 63. Both patients showed adequate hematopoietic reconstitution after the stem cell boost. i. n=8 patients with a follow-up < 90 days. j. n=5 patients with a follow-up < 90 days. k. In all three cases, death was due to a severe infection.
ANC, absolute neutrophil count. CRS, cytokine release syndrome. G-CSF, granulocyte-colony stimulating factor. ICAHT, immune effector cell-associated hematotoxicity. ICANS, immune effector cell-associated neurotoxicity syndrome. IVIG, intravenous immunoglobulin. MM, multiple myeloma. SC, stem cell. TPO, thrombopoietin receptor.

**Supp. Table S4 | Cytopenias prior to lymphodepletion**

| | **Total cohort** ***n = 129*** | | | **German cohort** ***n = 63*** | | | **US cohort** ***n = 66*** | | | ***p*** |
|---|---|---|---|---|---|---|---|---|---|---|
| | No./Total No. (%) | | | No./Total No. (%) | | | No./Total No. (%) | | | |
| **CTC grade** | **Any** | **1-2** | **3-4** | **Any** | **1-2** | **3-4** | **Any** | **1-2** | **3-4** | |
| **Anemia** | 113/128 (88) | 107/128 (84) | 6/128 (5) | 56/63 (89) | 55/63 (87) | 1/63 (2) | 57/65 (88) | 52/65 (80) | 5/65 (8) | 0.28 |
| **Neutropenia** | 35/126 (28) | 28/126 (22) | 7/126 (6) | 12/60 (20) | 9/60 (15) | 3/60 (5) | 23/66 (35) | 19/66 (29) | 4/66 (6) | 0.16 |
| **Thrombocytopenia** | 55/129 (43) | 47/129 (36) | 8/129 (6) | 24/63 (38) | 21/63 (33) | 3/63 (5) | 31/66 (47) | 26/66 (39) | 5/66 (8) | 0.58 |

CTC, Common Terminology Criteria for Adverse Events.

**Supp. Table S5 | Cytopenias during the early and late post-CAR-T period**

| | **Total cohort** ***n = 129*** | | | **German cohort** ***n = 63*** | | | **US cohort** ***n = 66*** | | | ***p*** |
|---|---|---|---|---|---|---|---|---|---|---|
| | No./Total No. (%) | | | No./Total No. (%) | | | No./Total No. (%) | | | |
| **CTC grade** | **Any** | **1-2** | **3-4** | **Any** | **1-2** | **3-4** | **Any** | **1-2** | **3-4** | |
| **Anemia** | | | | | | | | | | |
| Day 0-30 | 129/129 (100) | 76/129 (59) | 53/129 (41) | 63/63 (100) | 42/63 (67) | 21/63 (33) | 66/66 (100) | 34/66 (52) | 32/66 (48) | 0.11 |
| Day 31-90 | 102/109 (94) | 87/109 (80) | 15/109 (14) | 55/57 (96) | 42/57 (74) | 13/57 (23) | 47/52 (90) | 45/52 (87) | 2/52 (4) | **0.007** |
| **Neutropenia** | | | | | | | | | | |
| Day 0-30 | 120/128 (94) | 20/128 (16) | 100/128 (78) | 61/62 (98) | 4/62 (6) | 57/62 (92) | 59/66 (89) | 16/66 (24) | 43/66 (65) | **0.0006** |
| Day 31-90 | 76/107 (71) | 34/107 (32) | 42/107 (39) | 41/55 (75) | 19/55 (35) | 22/55 (40) | 35/52 (67) | 15/52 (29) | 20/52 (38) | 0.71 |
| **Thrombocytopenia** | | | | | | | | | | |
| Day 0-30 | 126/129 (98) | 61/129 (47) | 65/129 (50) | 62/63 (98) | 34/63 (54) | 28/63 (44) | 64/66 (97) | 27/66 (41) | 37/66 (56) | 0.38 |
| Day 31-90 | 83/109 (76) | 46/109 (42) | 37/109 (34) | 45/57 (79) | 25/57 (44) | 20/57 (35) | 38/52 (73) | 21/52 (40) | 17/52 (33) | 0.78 |

CTC, Common Terminology Criteria for Adverse Events.

**Supp. Table S6 | Comparison of longitudinal neutrophil, platelet and hemoglobin levels between late ICAHT groups**

| **Global comparison of groups across time points** | | | |
|---|---|---|---|
| | **Neutrophils** | **Platelets** | **Hemoglobin** |
| **Contrast** | ***adj. P*** | ***adj. P*** | ***adj. P*** |
| none – (Grade 1-2) | <0.001 | <0.001 | 0.004 |
| none – (Grade 3-4) | <0.001 | <0.001 | <0.001 |
| (Grade 1-2) – (Grade 3-4) | <0.001 | 0.004 | 0.045 |

| **Comparison of groups at individual time points** | | | | |
|---|---|---|---|---|
| | | **Neutrophils** | **Platelets** | **Hemoglobin** |
| **Time point** | **Contrast** | ***adj. P*** | ***adj. P*** | ***adj. P*** |
| Baseline | none – (Grade 1-2) | 0.519 | 0.085 | 0.060 |
| Baseline | none – (Grade 3-4) | 0.078 | 0.061 | 0.003 |
| Baseline | (Grade 1-2) – (Grade 3-4) | 1.000 | 1.000 | 1.000 |
| Day.0 | none – (Grade 1-2) | 0.138 | 0.119 | 0.885 |
| Day.0 | none – (Grade 3-4) | 0.002 | 0.043 | 0.025 |
| Day.0 | (Grade 1-2) – (Grade 3-4) | 1.000 | 1.000 | 1.000 |
| Day..7 | none – (Grade 1-2) | 0.138 | 0.002 | 0.885 |
| Day..7 | none – (Grade 3-4) | <0.001 | <0.001 | 0.178 |
| Day..7 | (Grade 1-2) – (Grade 3-4) | 0.045 | 1.000 | 1.000 |
| Day..14 | none – (Grade 1-2) | 0.737 | <0.001 | 0.204 |
| Day..14 | none – (Grade 3-4) | 0.054 | <0.001 | 0.178 |
| Day..14 | (Grade 1-2) – (Grade 3-4) | 1.000 | 1.000 | 1.000 |
| Day..21 | none – (Grade 1-2) | 0.042 | 0.002 | 0.017 |
| Day..21 | none – (Grade 3-4) | 0.001 | <0.001 | <0.001 |
| Day..21 | (Grade 1-2) – (Grade 3-4) | 1.000 | 0.502 | 1.000 |
| Day..28 | none – (Grade 1-2) | 0.204 | <0.001 | 0.204 |
| Day..28 | none – (Grade 3-4) | <0.001 | <0.001 | <0.001 |
| Day..28 | (Grade 1-2) – (Grade 3-4) | 0.003 | 0.044 | 0.516 |
| Day..35 | none – (Grade 1-2) | 0.138 | 0.046 | 0.107 |
| Day..35 | none – (Grade 3-4) | <0.001 | <0.001 | <0.001 |
| Day..35 | (Grade 1-2) – (Grade 3-4) | 0.005 | <0.001 | 0.516 |
| Day..42 | none – (Grade 1-2) | 0.189 | 0.011 | 0.595 |
| Day..42 | none – (Grade 3-4) | <0.001 | <0.001 | <0.001 |
| Day..42 | (Grade 1-2) – (Grade 3-4) | 0.001 | 0.001 | 0.026 |
| Day..50 | none – (Grade 1-2) | 0.737 | 0.299 | 0.885 |
| Day..50 | none – (Grade 3-4) | <0.001 | <0.001 | 0.007 |
| Day..50 | (Grade 1-2) – (Grade 3-4) | <0.001 | 0.003 | 0.375 |
| Day..63 | none – (Grade 1-2) | 0.097 | 0.050 | 0.041 |
| Day..63 | none – (Grade 3-4) | <0.001 | <0.001 | <0.001 |
| Day..63 | (Grade 1-2) – (Grade 3-4) | 0.547 | 0.027 | 0.049 |
| Day..90 | none – (Grade 1-2) | 0.138 | 0.050 | 0.041 |
| Day..90 | none – (Grade 3-4) | 0.001 | 0.060 | <0.001 |

| | | | | |
|---|---|---|---|---|
| Day..90 | (Grade 1-2) – (Grade 3-4) | 0.929 | 1.000 | 1.000 |

**Analysis of interaction between group and time points**

| | Neutrophils | Platelets | Hemoglobin |
|---|---|---|---|
| **Group** | ***adj. P*** | ***adj. P*** | ***adj. P*** |
| all | 0.007 | <0.001 | <0.001 |
| none/Grade 1-2 | 0.858 | 0.2 | 0.198 |
| none/Grade 3-4 | <0.001 | <0.001 | <0.001 |
| Grade 1-2/Grade 3-4 | 0.009 | <0.001 | 0.005 |

The analyses shown refer to Fig. 1D-F. ICAHT groups: none vs. grade 1-2 vs. grade 3-4. ICAHT, immune effector cell-associated hematotoxicity.

**Supp. Table S7 | Comparison of patient and disease characteristics between baseline EASIX groups (total cohort)**

| | **EASIX ≤ median (≤ 1.26)** ***n = 64*** | **EASIX > median (> 1.26)** ***n = 62*** | ***p*** | **EASIX ≤ $Q_3$ (≤ 2.15)** ***n = 95*** | **EASIX > $Q_3$ (> 2.15)** ***n = 31*** | ***p*** |
|---|---|---|---|---|---|---|
| **Age**, years | | | | | | |
| Median (range) | 65 (35-83) | 64 (34-79) | 0.83 | 65 (34-83) | 63 (48-74) | 0.66 |
| < 70, No. (%) | 45 (70) | 45 (73) | 0.84 | 67 (71) | 23 (74) | 0.82 |
| ≥ 70, No. (%) | 19 (30) | 17 (27) | | 28 (29) | 8 (26) | |
| **Sex**, No. (%) | | | | | | |
| Male | 36 (56) | 49 (79) | **0.008** | 62 (65) | 23 (74) | 0.39 |
| Female | 28 (44) | 13 (21) | | 33 (35) | 8 (26) | |
| **ECOG**[a], No. (%) | | | | | | |
| 0-1 | 55 (96) | 55 (95) | > 0.99 | 83 (97) | 27 (93) | 0.60 |
| 2-3 | 2 (4) | 3 (5) | | 3 (3) | 2 (7) | |
| Unknown | 7 | 4 | | 9 | 2 | |
| **Cytogenetics**, No. (%) | | | | | | |
| Standard risk | 34 (57) | 39 (65) | 0.45 | 53 (59) | 20 (67) | 0.52 |
| High risk | 26 (43) | 21 (35) | | 37 (41) | 10 (33) | |
| Unknown | 4 | 2 | | 5 | 1 | |
| **ISS stage**[a], No. (%) | | | | | | |
| I | 35 (65) | 28 (54) | **0.02** | 54 (68) | 9 (35) | **0.003** |
| II | 18 (33) | 15 (29) | | 22 (28) | 11 (42) | |
| III | 1 (2) | 9 (17) | | 4 (5) | 6 (23) | |
| Unknown | 10 | 10 | | 15 | 5 | |
| **R-ISS stage**[a], No. (%) | | | | | | |
| I | 13 (25) | 11 (22) | **0.04** | 21 (27) | 3 (12) | **0.003** |
| II | 39 (75) | 34 (67) | | 55 (71) | 18 (69) | |
| III | 0 (0) | 6 (12) | | 1 (1) | 5 (19) | |
| Unknown | 12 | 11 | | 18 | 5 | |
| **Extramedullary disease**[a], No. (%) | | | | | | |
| Yes | 24 (38) | 22 (37) | > 0.99 | 35 (37) | 11 (38) | > 0.99 |
| No | 39 (62) | 38 (63) | | 59 (63) | 18 (62) | |
| Unknown | 1 | 2 | | 1 | 2 | |
| **Extraosseous disease**[a], No. (%) | | | | | | |
| Yes | 14 (22) | 16 (27) | 0.68 | 21 (22) | 9 (31) | 0.34 |
| No | 49 (78) | 44 (73) | | 73 (78) | 20 (69) | |
| Unknown | 1 | 2 | | 1 | 2 | |
| **Bone marrow burden**[b] **≥ 50%**, No. (%) | | | | | | |
| Yes | 6 (18) | 8 (23) | 0.77 | 11 (22) | 3 (16) | 0.74 |
| No | 28 (82) | 27 (77) | | 39 (78) | 16 (84) | |
| Unknown | 30 | 27 | | 45 | 12 | |
| **Disease status prior to LD**, No. (%) | | | | | | |
| ≥ CR | 0 (0) | 0 (0) | 0.16 | 0 (0) | 0 (0) | 0.54 |
| VGPR/PR | 10 (21) | 5 (10) | | 12 (17) | 3 (11) | |
| MR/SD/PD | 37 (79) | 46 (90) | | 58 (83) | 25 (89) | |
| Not applicable | 17 | 11 | | 25 | 3 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Cytopenia CTC grade ≥ 3 prior to LD**, No. (%) | | | | | | |
| Yes | 3 (5) | 13 (22) | **0.006** | 7 (8) | 9 (30) | **0.003** |
| No | 61 (95) | 46 (78) | | 86 (92) | 21 (70) | |
| Unknown | 0 | 3 | | 2 | 1 | |
| **eGFR**[a], ml/min, No. (%) | | | | | | |
| > 60 | 52 (81) | 41 (66) | 0.06 | 76 (80) | 17 (55) | **0.002** |
| 30-60 | 12 (19) | 18 (29) | | 19 (20) | 11 (35) | |
| < 30 | 0 | 3 (5) | | 0 | 3 (10) | |
| **Triple-class refractory disease**[c], No. (%) | | | | | | |
| Yes | 52 (81) | 52 (84) | 0.82 | 75 (79) | 29 (94) | 0.10 |
| No | 12 (19) | 10 (16) | | 20 (21) | 2 (6) | |
| **Penta-drug refractory disease**[d], No. (%) | | | | | | |
| Yes | 18 (28) | 22 (35) | 0.45 | 27 (28) | 13 (42) | 0.19 |
| No | 46 (72) | 40 (65) | | 68 (72) | 18 (58) | |
| **Bridging therapy**[e], No. (%) | | | | | | |
| Yes | 49 (77) | 60 (97) | **0.001** | 78 (82) | 31 (100) | **0.01** |
| No | 15 (23) | 2 (3) | | 17 (18) | 0 (0) | |
| **Cytotoxic bridging therapy**[e], No. (%) | | | | | | |
| Yes | 26 (41) | 34 (55) | 0.15 | 45 (47) | 15 (48) | > 0.99 |
| No | 38 (59) | 28 (45) | | 50 (53) | 16 (51) | |
| **Prior BCMA-targeted therapy**, No. (%) | | | | | | |
| Yes | 8 (13) | 13 (21) | 0.24 | 13 (14) | 8 (26) | 0.16 |
| No | 56 (88) | 49 (79) | | 82 (86) | 23 (74) | |
| **Prior therapy lines**, median (95% CI) | 5 (5-6) | 6 (5-6) | 0.15 | 5 (5-6) | 6 (5-7) | 0.19 |
| **Time from initial diagnosis to CAR T-cell therapy**, years, median (range) | 6.1 (1.6-14.4) | 6.4 (0.6-17.6) | 0.94 | 6.2 (1.6-17.6) | 6.4 (0.6-17.2) | 0.92 |
| **EASIX-F prior to LD**, No. (%) [German cohort] | | | | | | |
| Low | 17 (63) | 13 (46) | 0.13 | 27 (60) | 3 (30) | **0.0005** |
| Intermediate | 10 (37) | 11 (39) | | 18 (40) | 3 (30) | |
| High | 0 (0) | 4 (14) | | 0 (0) | 4 (40) | |
| Unknown | 5 | 3 | | 7 | 1 | |
| **EASIX-FC prior to LD**, No. (%) [German cohort] | | | | | | |
| Low | 25 (93) | 15 (54) | **0.003** | 40 (89) | 0 (0) | **<0.0001** |
| Intermediate | 2 (7) | 8 (29) | | 4 (9) | 6 (60) | |
| High | 0 (0) | 5 (18) | | 1 (2) | 4 (40) | |
| Unknown | 5 | 3 | | 7 | 1 | |
| **CAR-HEMATOTOX prior to LD**, No. (%) [German cohort] | | | | | | |
| Low | 26 (93) | 17 (61) | **0.01** | 39 (85) | 4 (40) | **0.007** |
| High | 2 (7) | 11 (39) | | 7 (15) | 6 (60) | |
| Unknown | 4 | 3 | | 6 | 1 | |

a. Determined prior to lymphodepletion (baseline). b. Last bone marrow status determined within 90 days prior to CAR T-cell therapy. c. Refractory to an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 monoclonal antibody. d. Refractory to lenalidomide, pomalidomide, bortezomib, carfilzomib and daratumumab. e. Systemic treatment administered between leukapheresis and lymphodepletion (at least one drug).
BCMA, B-cell maturation antigen. CI, confidence interval. CR, complete response. CTC, Common Terminology Criteria for Adverse Events. EASIX, Endothelial Activation and Stress Index. ECOG, Eastern Cooperative Oncology Group performance status. eGFR, estimated glomerular filtration rate. ISS, International Staging System. LD, lymphodepletion. MR, minimal response. PD, progressive disease. PR, partial response. $Q_3$, third/upper quartile (75$^{th}$ percentile). R-ISS, Revised International Staging System. SD, stable disease. VGPR, very good partial response.

**Supp. Table S8 | Comparison of outcomes, complications and supportive measures between baseline EASIX groups (total cohort)**

| | **EASIX ≤ median (≤ 1.26) *n = 64*** | **EASIX > median (> 1.26) *n = 62*** | ***p*** | **EASIX ≤ $Q_3$ (≤ 2.15) *n = 95*** | **EASIX > $Q_3$ (> 2.15) *n = 31*** | ***p*** |
|---|---|---|---|---|---|---|
| **Best overall response**, No. (%) | | | | | | |
| ≥ CR | 24 (39) | 23 (40) | 0.89 | 37 (41) | 10 (34) | 0.57 |
| VGPR/PR | 28 (45) | 23 (40) | | 39 (43) | 12 (41) | |
| MR/SD/PD | 10 (16) | 11 (19) | | 14 (16) | 7 (24) | |
| Not applicable | 2 | 5 | | 5 | 2 | |
| **CRS**, No. (%) | | | | | | |
| No | 11 (17) | 9 (15) | 0.42 | 15 (16) | 5 (16) | 0.71 |
| Grade 1 | 36 (56) | 29 (47) | | 51 (54) | 14 (45) | |
| Grade 2 | 17 (27) | 23 (37) | | 28 (29) | 12 (39) | |
| Grade 3 | 0 (0) | 1 (2) | | 1 (1) | 0 (0) | |
| **ICANS**, No. (%) | | | | | | |
| No | 62 (97) | 54 (87) | 0.08 | 91 (96) | 25 (81) | **0.02** |
| Grade 1 | 0 (0) | 4 (6) | | 1 (1) | 3 (10) | |
| Grade 2 | 0 (0) | 2 (3) | | 1 (1) | 1 (3) | |
| Grade ≥ 3 | 2 (3) | 2 (3) | | 2 (2) | 2 (6) | |
| **Tocilizumab**, No. (%) | | | | | | |
| No | 39 (61) | 24 (39) | **0.02** | 51 (54) | 12 (39) | 0.21 |
| Yes | 25 (39) | 38 (61) | | 44 (46) | 19 (61) | |
| **Dexamethasone**, No. (%) | | | | | | |
| No | 43 (67) | 29 (47) | **0.03** | 57 (60) | 15 (48) | 0.30 |
| Yes | 21 (33) | 33 (53) | | 38 (40) | 16 (52) | |
| **Late ICAHT**, No. (%) | | | | | | |
| No | 31 (57) | 10 (20) | **0.0008** | 37 (46) | 4 (17) | **0.02** |
| Grade 1 | 8 (15) | 14 (28) | | 17 (21) | 5 (21) | |
| Grade 2 | 9 (17) | 11 (22) | | 14 (18) | 6 (25) | |
| Grade ≥ 3 (severe) | 6 (11) | 15 (30) | **0.03** | 12 (15) | 9 (38) | **0.02** |
| Unknown | 10 | 12 | | 15 | 7 | |
| **Neutrophil recovery phenotype**, No. (%) | | | | | | |
| Quick | 34 (63) | 16 (32) | **0.002** | 43 (54) | 7 (29) | **0.01** |
| Intermittent | 19 (35) | 27 (54) | | 34 (43) | 12 (50) | |
| Aplastic | 1 (2) | 7 (14) | **0.03** | 3 (4) | 5 (21) | **0.02** |
| Unknown | 10 | 12 | | 15 | 7 | |
| **Severe anemia, > day 30**, No. (%) | | | | | | |
| No | 51 (94) | 40 (77) | **0.01** | 75 (91) | 16 (67) | **0.005** |
| Yes | 3 (6) | 12 (23) | | 7 (9) | 8 (33) | |
| Unknown | 10 | 10 | | 13 | 7 | |
| **Severe thrombocytopenia, > day 30**, No. (%) | | | | | | |
| No | 45 (83) | 26 (50) | **0.0004** | 63 (77) | 8 (33) | **0.0001** |
| Yes | 9 (17) | 26 (50) | | 19 (23) | 16 (67) | |
| Unknown | 10 | 10 | | 13 | 7 | |
| **Red blood cell transfusion**, **> day 30**, No. (%) | | | | | | |
| No | 47 (96) | 35 (88) | 0.24 | 63 (94) | 19 (86) | 0.36 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Yes | 2 (4) | 5 (13) | | 4 (6) | 3 (14) | |
| Unknown | 15 | 22 | | 28 | 9 | |
| **Platelet transfusion, > day 30**, No. (%) | | | | | | |
| No | 47 (96) | 34 (85) | 0.13 | 63 (94) | 18 (82) | 0.10 |
| Yes | 2 (4) | 6 (15) | | 4 (6) | 4 (18) | |
| Unknown | 15 | 22 | | 28 | 9 | |
| **G-CSF, > day 30**, No. (%) | | | | | | |
| No | 42 (86) | 27 (68) | **0.05** | 56 (84) | 13 (59) | **0.04** |
| Yes | 7 (14) | 13 (33) | | 11 (16) | 9 (41) | |
| Unknown | 15 | 22 | | 28 | 9 | |
| **G-CSF as prophylaxis**, No. (%) | | | | | | |
| No | 37 (58) | 40 (65) | 0.47 | 59 (62) | 18 (58) | 0.83 |
| Yes | 27 (42) | 22 (35) | | 36 (38) | 13 (42) | |
| **Severe late-onset infection**, No. (%) | | | | | | |
| No | 54 (93) | 44 (80) | 0.05 | 81 (92) | 17 (68) | **0.005** |
| Yes | 4 (7) | 11 (20) | | 7 (8) | 8 (32) | |
| Unknown | 6 | 7 | | 7 | 6 | |
| **IVIG substitution, day 0-90**, No. (%) | | | | | | |
| No | 50 (78) | 42 (68) | 0.23 | 69 (73) | 23 (74) | > 0.99 |
| Yes | 14 (22) | 20 (32) | | 26 (27) | 8 (26) | |
| **Cause of death**, No. (%) | | | | | | |
| MM-dependent | 7 (70) | 16 (80) | | 11 (73) | 12 (80) | |
| MM progression-related | 7 (70) | 12 (60) | 0.31 | 9 (60) | 10 (67) | > 0.99 |
| Therapy-related | 0 (0) | 4 (20) | | 2 (13) | 2 (13) | |
| MM-independent | 0 (0) | 0 (0) | | 0 (0) | 0 (0) | |
| Not attributable | 1 (10) | 0 (0) | | 1 (7) | 0 (0) | |
| Unknown | 2 (20) | 4 (20) | | 3 (20) | 3 (20) | |
| **Non-relapse mortality**, No. (%) | 0 (0) | 3 (15) | 0.44 | 1 (7) | 2 (13) | 0.40 |
| Others | 10 (10) | 15 (75) | | 14 (93) | 11 (73) | |
| Unknown | 0 (0) | 2 (10) | | 0 (0) | 2 (13) | |

CR, complete response. CRS, cytokine release syndrome. EASIX, Endothelial Activation and Stress Index. G-CSF, granulocyte-colony stimulating factor. ICAHT, immune effector cell-associated hematotoxicity. ICANS, immune effector cell-associated neurotoxicity syndrome. IVIG, intravenous immunoglobulin. MM, multiple myeloma. MR, minimal response. PD, progressive disease. PR, partial response. $Q_3$, third/upper quartile ($75^{th}$ percentile). SD, stable disease. VGPR, very good partial response.

**Supp. Table S9 | Laboratory parameters and scores at day 0 (day of CAR T-cell infusion)**

| | Total cohort *n = 129* | German cohort *n = 63* | US cohort *n = 66* | *p* |
|---|---|---|---|---|
| **Laboratory parameters at day 0 (day of CAR T-cell infusion)**, median (range) | | | | |
| LDH, U/l | 193 (108-1436), n = 119 | 191 (108-770), n = 60 | 202 (118-1436), n = 59 | 0.39 |
| Creatinine, mg/dl | 0.84 (0.45-4.82), n = 127 | 0.91 (0.45-1.68) | 0.79 (0.47-4.82), n = 64 | **0.003** |
| Platelet count, cells/nl | 130 (7-369) | 142 (14-369) | 107 (7-253) | **0.001** |
| Absolute neutrophil count, cells/nl | 1.83 (0.14-17.06), n = 112 | 1.11 (0.18-3.37), n = 46 | 3.29 (0.14-17.06) | **< 0.0001** |
| Hemoglobin, g/dl | 9.8 (7.2-14.0) | 10.2 (7.4-14.0) | 9.2 (7.2-12.6) | **0.0003** |
| CRP, mg/dl | 0.7 (0.1-29.49), n = 127 | 0.43 (0.1-29.49), n = 62 | 0.89 (0.1-12.55), n = 65 | **0.007** |
| Ferritin, ng/ml | 287 (18-4752), n = 105 | 261 (18-4752), n = 43 | 293 (68-3655), n = 62 | 0.61 |
| **Scores at day 0 (day of CAR T-cell infusion)** | | | | |
| EASIX, median ($Q_1$-$Q_3$) | 1.36 (1.00-2.06), n = 117 | 1.33 (0.98-1.72), n = 60 | 1.43 (1.05-3.16), n = 57 | 0.17 |
| > median (> 1.36), No. (%) | 58 (50) | 27 (45) | 31 (54) | 0.36 |
| > $Q_3$ (> 2.06), No. (%) | 29 (25) | 10 (17) | 19 (33) | 0.05 |
| Modified EASIX, median ($Q_1$-$Q_3$) | 1.19 (0.43-3.96), n = 119 | 0.55 (0.33-2.11), n = 60 | 1.87 (0.65-7.87), n = 59 | **0.0002** |
| > 6.2, No. (%) | 24 (20) | 8 (13) | 16 (27) | 0.07 |
| EASIX-F, No. (%) | | | | |
| Low | 50 (51) | 23 (52) | 27 (50) | 0.92 |
| Intermediate | 35 (36) | 16 (36) | 19 (35) | |
| High | 13 (13) | 5 (11) | 8 (15) | |
| Unknown | 31 | 19 | 12 | |
| EASIX-FC, No. (%) | | | | |
| Low | 59 (60) | 32 (74) | 27 (48) | **0.002** |
| Intermediate | 32 (32) | 6 (14) | 26 (46) | |
| High | 8 (8) | 5 (12) | 3 (5) | |
| Unknown | 30 | 20 | 10 | |
| CAR-HEMATOTOX, No. (%) | | | | |
| Low | 38 (34) | 17 (35) | 21 (33) | 0.84 |
| High | 73 (66) | 31 (65) | 42 (67) | |
| Unknown | 18 | 15 | 3 | |

CRP, C-reactive protein. EASIX, Endothelial Activation and Stress Index. LDH, lactate dehydrogenase. $Q_1$, first/lower quartile (25$^{th}$ percentile). $Q_3$, third/upper quartile (75$^{th}$ percentile).

## Supp. Table S10 | Logistic regression analysis of late ICAHT

| | Univariate analysis: Late ICAHT | | | | |
|---|---|---|---|---|---|
| **Characteristic** | **N** | **Event N** | **OR** | **95% CI** | **p-value** |
| **Age [cont.]** | 107 | 64 | 1 | 0.96, 1.04 | 0,96 |
| **Age ≥ 70 years** | | | | | |
| No | 76 | 44 | — | — | |
| Yes | 31 | 20 | 1,32 | 0.56, 3.22 | 0,53 |
| **Sex** | | | | | |
| M | 76 | 42 | — | — | |
| W | 31 | 22 | 1,98 | 0.83, 5.05 | 0,14 |
| **High risk cytogenetics** | | | | | |
| No | 63 | 39 | — | — | |
| Yes | 39 | 24 | 0,98 | 0.43, 2.26 | 0,97 |
| **ISS 3**[a] | | | | | |
| No | 87 | 54 | — | — | |
| Yes | 8 | 5 | 1,02 | 0.23, 5.23 | 0,98 |
| **R-ISS 3**[a] | | | | | |
| No | 91 | 57 | — | — | |
| Yes | 4 | 2 | 0,6 | 0.07, 5.16 | 0,61 |
| **Extramedullary disease**[a] | | | | | |
| No | 63 | 36 | — | — | |
| Yes | 41 | 25 | 1,17 | 0.53, 2.64 | 0,7 |
| **Extraosseous disease**[a] | | | | | |
| No | 77 | 42 | — | — | |
| Yes | 27 | 19 | 1,98 | 0.79, 5.30 | 0,15 |
| **BM burden ≥ 50%**[b] | | | | | |
| No | 47 | 31 | — | — | |
| Yes | 11 | 8 | 1,38 | 0.34, 6.94 | 0,67 |
| **PD prior to LD** | | | | | |
| No | 45 | 23 | — | — | |
| Yes | 42 | 29 | 2,13 | 0.90, 5.23 | 0,09 |
| **Gr. 3-4 cytopenia prior to LD** | | | | | |
| No | 90 | 49 | — | — | |
| Yes | 14 | 13 | 10,9 | 2.03, 202 | **0,024** |
| **eGFR < 60 ml/min**[a] | | | | | |
| No | 80 | 47 | — | — | |
| Yes | 27 | 17 | 1,19 | 0.49, 3.01 | 0,7 |
| **Triple-class refractory**[c] | | | | | |
| No | 18 | 13 | — | — | |
| Yes | 89 | 51 | 0,52 | 0.15, 1.50 | 0,24 |
| **Penta-drug refractory**[d] | | | | | |
| No | 74 | 44 | — | — | |
| Yes | 33 | 20 | 1,05 | 0.46, 2.46 | 0,91 |
| **Prior BCMA-TT** | | | | | |
| No | 90 | 54 | — | — | |
| Yes | 17 | 10 | 0,95 | 0.33, 2.84 | 0,93 |
| **Bridging therapy**[e] | | | | | |
| No | 17 | 7 | — | — | |
| Yes | 90 | 57 | 2,47 | 0.87, 7.39 | 0,094 |
| **CRS ≥ °2** | | | | | |
| No | 73 | 40 | — | — | |
| Yes | 34 | 24 | 1,98 | 0.85, 4.88 | 0,12 |
| **Tocilizumab** | | | | | |
| No | 54 | 27 | — | — | |
| Yes | 53 | 37 | 2,31 | 1.06, 5.19 | **0,038** |
| **Dexamethasone** | | | | | |
| No | 63 | 33 | — | — | |
| Yes | 44 | 31 | 2,17 | 0.97, 5.00 | 0,063 |
| **log2(LDH) [bl]** | 104 | 63 | 2,12 | 1.00, 5.31 | 0,075 |
| **LDH > ULN [bl]** | | | | | |
| No | 78 | 44 | — | — | |
| Yes | 26 | 19 | 2,1 | 0.82, 5.89 | 0,14 |
| **log2(PLT) [bl]** | 107 | 64 | 0,31 | 0.14, 0.60 | **0,001** |
| **PLT < LLN [bl]** | | | | | |
| No | 63 | 28 | — | — | |
| Yes | 44 | 36 | 5,63 | 2.34, 14.8 | **<0.001** |
| **log2(creatinine) [bl]** | 107 | 64 | 0,95 | 0.40, 2.26 | 0,9 |

| | | | | | |
|---|---|---|---|---|---|
| **creatinine > ULN [bl]** | | | | | |
| No | 84 | 46 | — | — | |
| Yes | 23 | 18 | 2,97 | 1.07, 9.68 | **0,048** |
| **log2(CRP) [bl]** | 97 | 60 | 0,82 | 0.64, 1.03 | 0,093 |
| **CRP > ULN [bl]** | | | | | |
| No | 60 | 41 | — | — | |
| Yes | 37 | 19 | 0,49 | 0.21, 1.13 | 0,1 |
| **log2(ferritin) [bl][f]** | 47 | 32 | 1,15 | 0.88, 1.56 | 0,32 |
| **Ferritin > ULN [bl][f]** | | | | | |
| No | 29 | 20 | — | — | |
| Yes | 18 | 12 | 0,9 | 0.26, 3.27 | 0,87 |
| **log2(ANC) [bl]** | 104 | 62 | 0,34 | 0.17, 0.64 | **0,001** |
| **ANC < LLN [bl]** | | | | | |
| No | 74 | 38 | — | — | |
| Yes | 30 | 24 | 3,79 | 1.46, 11.2 | **0,009** |
| **log2(HGB) [bl]** | 106 | 63 | 0,03 | 0.00, 0.19 | **<0.001** |
| **HGB < LLN [bl]** | | | | | |
| No | 13 | 7 | — | — | |
| Yes | 93 | 56 | 1,3 | 0.39, 4.21 | 0,66 |
| **log2(B2-MG) [bl]** | 95 | 59 | 1,66 | 0.82, 3.54 | 0,17 |
| **log2(LDH x creatinine) [bl]** | 104 | 63 | 1,53 | 0.90, 2.90 | 0,15 |
| **log2(EASIX) [bl]** | 104 | 63 | 2,11 | 1.33, 3.65 | **0,004** |
| **EASIX > median (> 1.26) [bl]** | | | | | |
| No | 54 | 23 | — | — | |
| Yes | 50 | 40 | 5,39 | 2.30, 13.5 | **<0.001** |
| **EASIX > Q3 (> 2.15) [bl]** | | | | | |
| No | 80 | 43 | — | — | |
| Yes | 24 | 20 | 4,3 | 1.47, 15.8 | **0,014** |
| **log2(m-EASIX) [bl]** | 96 | 60 | 1 | 0.84, 1.20 | >0.99 |
| **m-EASIX > 6.2 [bl]** | | | | | |
| No | 87 | 53 | — | — | |
| Yes | 9 | 7 | 2,25 | 0.51, 15.7 | 0,33 |
| **EASIX-F high [bl][f]** | | | | | |
| No | 52 | 32 | — | — | |
| Yes | 3 | 3 | — | — | — |
| **EASIX-F inter/high [bl][f]** | | | | | |
| No | 26 | 17 | — | — | |
| Yes | 21 | 15 | 1,32 | 0.38, 4.78 | 0,66 |
| **EASIX-FC high [bl][f]** | | | | | |
| No | 42 | 27 | — | — | |
| Yes | 5 | 5 | — | — | — |
| **EASIX-FC inter/high [bl][f]** | | | | | |
| No | 35 | 22 | — | — | |
| Yes | 14 | 11 | 2,17 | 0.55, 10.9 | 0,3 |
| **CAR-HTX high [bl][f]** | | | | | |
| No | 36 | 22 | — | — | |
| Yes | 12 | 12 | — | — | — |
| **log2(EASIX) [d0]** | 96 | 55 | 2,22 | 1.37, 3.99 | **0,003** |
| **EASIX > median (> 1.36) [d0]** | | | | | |
| No | 49 | 20 | — | — | |
| Yes | 47 | 35 | 4,23 | 1.81, 10.4 | **0,001** |
| **EASIX > Q3 (> 2.06) [d0]** | | | | | |
| No | 74 | 37 | — | — | |
| Yes | 22 | 18 | 4,5 | 1.51, 16.7 | **0,012** |
| **log2(m-EASIX) [d0]** | 98 | 56 | 1,09 | 0.92, 1.30 | 0,35 |
| **m-EASIX > 6.2 [d0]** | | | | | |
| No | 78 | 44 | — | — | |
| Yes | 20 | 12 | 1,16 | 0.43, 3.26 | 0,77 |
| **EASIX-F high [d0]** | | | | | |
| No | 86 | 47 | — | — | |
| Yes | 10 | 8 | 3,32 | 0.78, 22.9 | 0,14 |
| **EASIX-F inter/high [d0]** | | | | | |
| No | 41 | 23 | — | — | |
| Yes | 40 | 28 | 1,83 | 0.74, 4.65 | 0,2 |
| **EASIX-FC high [d0]** | | | | | |
| No | 77 | 47 | — | — | |
| Yes | 7 | 7 | — | — | — |
| **EASIX-FC inter/high [d0]** | | | | | |
| No | 47 | 30 | — | — | |
| Yes | 38 | 23 | 0,87 | 0.36, 2.11 | 0,75 |

| | | | | | |
|---|---|---|---|---|---|
| **CAR-HTX high [d0]** | | | | | |
| No | 30 | 15 | — | — | |
| Yes | 61 | 44 | 2,59 | 1.05, 6.51 | **0,04** |
| | | | **Multivariate analysis: Late ICAHT** | | |
| **Characteristic** | | | **OR** | **95% CI** | **p-value** |
| PD prior to LD | | | 1,66 | 0.60, 4.66 | 0,33 |
| Gr. 3-4 cytopenia prior to LD | | | 8,36 | 1.28, 168 | 0,061 |
| Bridging therapy | | | 0,79 | 0.12, 5.45 | 0,8 |
| Tocilizumab | | | 1,36 | 0.37, 5.08 | 0,64 |
| Dexamethasone | | | 1,52 | 0.38, 6.07 | 0,55 |
| EASIX > median (> 1.26) [bl] | | | 3,59 | 1.30, 10.5 | **0,016** |
| Age ≥ 70 years | | | 1,77 | 0.54, 6.26 | 0,35 |
| Sex [W] | | | 6,01 | 1.64, 26.4 | **0,011** |
| PD prior to LD | | | 2,16 | 0.70, 6.92 | 0,18 |
| Gr. 3-4 cytopenia prior to LD | | | 8,7 | 1.16, 191 | 0,072 |
| Bridging therapy | | | 0,41 | 0.05, 3.23 | 0,39 |
| Tocilizumab | | | 1,52 | 0.51, 4.56 | 0,45 |
| EASIX > median (> 1.26) [bl] | | | 6,18 | 1.96, 22.2 | **0,003** |
| log2(LDH) [bl] | | | 2,15 | 0.81, 6.53 | 0,15 |
| log2(PLT) [bl] | | | 0,34 | 0.15, 0.66 | **0,004** |
| log2(creatinine) [bl] | | | 1,02 | 0.38, 2.70 | 0,97 |
| log2(LDH) [bl] | | | 3,63 | 1.06, 15.0 | 0,052 |
| log2(PLT) [bl] | | | 0,58 | 0.23, 1.35 | 0,23 |
| log2(creatinine) [bl] | | | 1,17 | 0.38, 3.62 | 0,78 |
| log2(ANC) [bl] | | | 0,57 | 0.23, 1.29 | 0,19 |
| log2(HGB) [bl] | | | 0,03 | 0.00, 0.45 | **0,015** |
| log2(CRP) [bl] | | | 0,68 | 0.48, 0.93 | **0,019** |
| LDH > ULN [bl] | | | 2,16 | 0.66, 7.80 | 0,21 |
| PLT < LLN [bl] | | | 4,55 | 1.61, 14.5 | **0,006** |
| creatinine > ULN [bl] | | | 4,93 | 1.32, 22.9 | **0,026** |
| ANC < LLN [bl] | | | 2,77 | 0.92, 9.36 | 0,081 |
| HGB < LLN [bl] | | | 0,76 | 0.16, 3.41 | 0,72 |
| CRP > ULN [bl] | | | 0,29 | 0.09, 0.83 | **0,026** |
| CAR-HTX high [d0] | | | 1,63 | 0.56, 4.68 | 0,37 |
| EASIX > median (> 1.36) [d0] | | | 3,82 | 1.37, 11.3 | **0,012** |

a. Determined prior to lymphodepletion (baseline). b. Last bone marrow status determined within 90 days prior to CAR T-cell therapy. c. Refractory to an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 monoclonal antibody. d. Refractory to lenalidomide, pomalidomide, bortezomib, carfilzomib and daratumumab. e. Systemic treatment administered between leukapheresis and lymphodepletion (at least one drug). f. Due to missing data for the US cohort, analyses of ferritin and ferritin-based scores prior to lymphodepletion were only performed for the German cohort.
ANC, absolute neutrophil count. B2-MG, beta-2-microglobulin. BCMA, B-cell maturation antigen. bl, baseline. BM, bone marrow. CAR-HTX, CAR-HEMATOTOX score. CI, confidence interval. CRP, C-reactive protein. CRS, cytokine release syndrome. d0, day 0 (day of CAR T-cell infusion). EASIX, Endothelial Activation and Stress Index. eGFR, estimated glomerular filtration rate. HGB, hemoglobin. ICAHT, immune effector cell-associated hematotoxicity. ICANS, immune effector cell-associated neurotoxicity syndrome. ISS, International Staging System. LD, lymphodepletion. LDH, lactate dehydrogenase. LLN, lower limit of normal. m-EASIX, modified EASIX. OR, odds ratio. PD, progressive disease. PLT, platelet count. $Q_3$, third/upper quartile (75$^{th}$ percentile). R-ISS, Revised International Staging System. ULN, upper limit of normal.

## Supp. Table S11 | Logistic regression analysis of severe late ICAHT

| | Univariate analysis: Severe late ICAHT | | | | |
|---|---|---|---|---|---|
| **Characteristic** | **N** | **Event N** | **OR** | **95% CI** | **p-value** |
| **Age [cont.]** | 107 | 22 | 0,98 | 0.93, 1.03 | 0,38 |
| **Age ≥ 70 years** | | | | | |
| No | 76 | 17 | — | — | |
| Yes | 31 | 5 | 0,67 | 0.20, 1.90 | 0,47 |
| **Sex** | | | | | |
| M | 76 | 13 | — | — | |
| W | 31 | 9 | 1,98 | 0.73, 5.26 | 0,17 |
| **High risk cytogenetics** | | | | | |
| No | 63 | 11 | — | — | |
| Yes | 39 | 11 | 1,86 | 0.71, 4.87 | 0,2 |
| **ISS 3**[a] | | | | | |
| No | 87 | 18 | — | — | |
| Yes | 8 | 2 | 1,28 | 0.18, 6.10 | 0,78 |
| **R-ISS 3**[a] | | | | | |
| No | 91 | 19 | — | — | |
| Yes | 4 | 1 | 1,26 | 0.06, 10.5 | 0,84 |
| **Extramedullary disease**[a] | | | | | |
| No | 63 | 14 | — | — | |
| Yes | 41 | 7 | 0,72 | 0.25, 1.93 | 0,52 |
| **Extraosseous disease**[a] | | | | | |
| No | 77 | 16 | — | — | |
| Yes | 27 | 5 | 0,87 | 0.26, 2.52 | 0,8 |
| **BM burden ≥ 50%**[b] | | | | | |
| No | 47 | 13 | — | — | |
| Yes | 11 | 1 | 0,26 | 0.01, 1.58 | 0,22 |
| **PD prior to LD** | | | | | |
| No | 45 | 8 | — | — | |
| Yes | 42 | 10 | 1,45 | 0.51, 4.21 | 0,49 |
| **Gr. 3-4 cytopenia prior to LD** | | | | | |
| No | 90 | 15 | — | — | |
| Yes | 14 | 6 | 3,75 | 1.10, 12.4 | **0,03** |
| **eGFR < 60 ml/min**[a] | | | | | |
| No | 80 | 15 | — | — | |
| Yes | 27 | 7 | 1,52 | 0.52, 4.15 | 0,43 |
| **Triple-class refractory**[c] | | | | | |
| No | 18 | 6 | — | — | |
| Yes | 89 | 16 | 0,44 | 0.15, 1.41 | 0,15 |
| **Penta-drug refractory**[d] | | | | | |
| No | 74 | 17 | — | — | |
| Yes | 33 | 5 | 0,6 | 0.18, 1.69 | 0,36 |
| **Prior BCMA-TT** | | | | | |
| No | 90 | 18 | — | — | |
| Yes | 17 | 4 | 1,23 | 0.32, 3.97 | 0,74 |
| **Bridging therapy**[e] | | | | | |
| No | 17 | 1 | — | — | |
| Yes | 90 | 21 | 4,87 | 0.91, 90.4 | 0,14 |
| **CRS ≥ °2** | | | | | |
| No | 73 | 14 | — | — | |
| Yes | 34 | 8 | 1,3 | 0.47, 3.42 | 0,6 |
| **Tocilizumab** | | | | | |
| No | 54 | 10 | — | — | |
| Yes | 53 | 12 | 1,29 | 0.50, 3.36 | 0,6 |
| **Dexamethasone** | | | | | |
| No | 63 | 12 | — | — | |
| Yes | 44 | 10 | 1,25 | 0.48, 3.22 | 0,64 |
| **log2(LDH) [bl]** | 104 | 21 | 3,5 | 1.60, 9.14 | **0,004** |
| **LDH > ULN [bl]** | | | | | |
| No | 78 | 11 | — | — | |
| Yes | 26 | 10 | 3,81 | 1.37, 10.6 | **0,01** |
| **log2(PLT) [bl]** | 107 | 22 | 0,76 | 0.47, 1.25 | 0,25 |
| **PLT < LLN [bl]** | | | | | |
| No | 63 | 9 | — | — | |
| Yes | 44 | 13 | 2,52 | 0.98, 6.75 | 0,059 |
| **log2(creatinine) [bl]** | 107 | 22 | 2,02 | 0.73, 5.93 | 0,18 |

| | | | | | |
|---|---|---|---|---|---|
| **creatinine > ULN [bl]** | | | | | |
| No | 84 | 11 | — | — | |
| Yes | 23 | 11 | 6,08 | 2.18, 17.5 | **<0.001** |
| **log2(CRP) [bl]** | 97 | 20 | 0,98 | 0.73, 1.29 | 0,89 |
| **CRP > ULN [bl]** | | | | | |
| No | 60 | 14 | — | — | |
| Yes | 37 | 6 | 0,64 | 0.21, 1.77 | 0,4 |
| **log2(ferritin) [bl]**[f] | 47 | 14 | 1,19 | 0.90, 1.59 | 0,23 |
| **Ferritin > ULN [bl]**[f] | | | | | |
| No | 29 | 9 | — | — | |
| Yes | 18 | 5 | 0,85 | 0.22, 3.07 | 0,81 |
| **log2(ANC) [bl]** | 104 | 20 | 0,5 | 0.25, 0.97 | **0,045** |
| **ANC < LLN [bl]** | | | | | |
| No | 74 | 12 | — | — | |
| Yes | 30 | 8 | 1,88 | 0.66, 5.17 | 0,22 |
| **log2(HGB) [bl]** | 106 | 22 | 0,08 | 0.01, 0.63 | **0,02** |
| **HGB < LLN [bl]** | | | | | |
| No | 13 | 0 | — | — | |
| Yes | 93 | 22 | — | — | — |
| **log2(B2-MG) [bl]** | 95 | 20 | 1,6 | 0.71, 3.64 | 0,25 |
| **log2(LDH x creatinine) [bl]** | 104 | 21 | 2,69 | 1.48, 5.57 | **0,003** |
| **log2(EASIX) [bl]** | 104 | 21 | 1,51 | 1.09, 2.26 | **0,022** |
| **EASIX > median (> 1.26) [bl]** | | | | | |
| No | 54 | 6 | — | — | |
| Yes | 50 | 15 | 3,43 | 1.26, 10.4 | **0,02** |
| **EASIX > Q3 (> 2.15) [bl]** | | | | | |
| No | 80 | 12 | — | — | |
| Yes | 24 | 9 | 3,4 | 1.20, 9.58 | **0,02** |
| **log2(m-EASIX) [bl]** | 96 | 20 | 1,09 | 0.89, 1.33 | 0,37 |
| **m-EASIX > 6.2 [bl]** | | | | | |
| No | 87 | 16 | — | — | |
| Yes | 9 | 4 | 3,55 | 0.80, 14.9 | 0,081 |
| **EASIX-F high [bl]**[f] | | | | | |
| No | 52 | 12 | — | — | |
| Yes | 3 | 3 | — | — | — |
| **EASIX-F inter/high [bl]**[f] | | | | | |
| No | 26 | 7 | — | — | |
| Yes | 21 | 7 | 1,36 | 0.38, 4.85 | 0,63 |
| **EASIX-FC high [bl]**[f] | | | | | |
| No | 42 | 11 | — | — | |
| Yes | 5 | 3 | 4,23 | 0.62, 35.5 | 0,14 |
| **EASIX-FC inter/high [bl]**[f] | | | | | |
| No | 35 | 8 | — | — | |
| Yes | 14 | 7 | 3,38 | 0.91, 13.0 | 0,069 |
| **CAR-HTX high [bl]**[f] | | | | | |
| No | 36 | 10 | — | — | |
| Yes | 12 | 4 | 1,3 | 0.29, 5.18 | 0,71 |
| **log2(EASIX) [d0]** | 96 | 18 | 1,79 | 1.24, 2.87 | **0,006** |
| **EASIX > median (> 1.36) [d0]** | | | | | |
| No | 49 | 4 | — | — | |
| Yes | 47 | 14 | 4,77 | 1.55, 18.0 | **0,011** |
| **EASIX > Q3 (> 2.06) [d0]** | | | | | |
| No | 74 | 8 | — | — | |
| Yes | 22 | 10 | 6,87 | 2.28, 21.7 | **<0.001** |
| **log2(m-EASIX) [d0]** | 98 | 18 | 1,25 | 1.02, 1.55 | **0,031** |
| **m-EASIX > 6.2 [d0]** | | | | | |
| No | 78 | 10 | — | — | |
| Yes | 20 | 8 | 4,53 | 1.47, 14.0 | **0,008** |
| **EASIX-F high [d0]** | | | | | |
| No | 86 | 12 | — | — | |
| Yes | 10 | 6 | 9,25 | 2.32, 41.1 | **0,002** |
| **EASIX-F inter/high [d0]** | | | | | |
| No | 41 | 6 | — | — | |
| Yes | 40 | 10 | 1,94 | 0.64, 6.31 | 0,25 |
| **EASIX-FC high [d0]** | | | | | |
| No | 77 | 13 | — | — | |
| Yes | 7 | 4 | 6,56 | 1.30, 36.8 | **0,022** |

| | | | | | |
|---|---|---|---|---|---|
| **EASIX-FC inter/high [d0]** | | | | | |
| No | 47 | 8 | — | — | |
| Yes | 38 | 11 | 1,99 | 0.71, 5.76 | 0,19 |
| **CAR-HTX high [d0]** | | | | | |
| No | 30 | 6 | — | — | |
| Yes | 61 | 15 | 1,3 | 0.46, 4.05 | 0,63 |
| **Multivariate analysis: Severe late ICAHT** | | | | | |
| **Characteristic** | | | **OR** | **95% CI** | **p-value** |
| Bridging therapy | | | 2,78 | 0.46, 53.5 | 0,35 |
| EASIX > median (> 1.26) [bl] | | | 2,91 | 1.04, 9.14 | 0,051 |
| Gr. 3-4 cytopenia prior to LD | | | 2,86 | 0.79, 10.0 | 0,1 |
| EASIX > median (> 1.26) [bl] | | | 2,79 | 0.96, 8.83 | 0,066 |
| Age ≥ 70 years | | | 0,88 | 0.25, 2.76 | 0,83 |
| Sex [W] | | | 2,42 | 0.75, 8.09 | 0,14 |
| Bridging therapy | | | 2,96 | 0.44, 60.9 | 0,34 |
| Gr. 3-4 cytopenia prior to LD | | | 2,39 | 0.63, 8.60 | 0,18 |
| EASIX > median (> 1.26) [bl] | | | 3,16 | 0.99, 11.3 | 0,06 |
| log2(LDH) [bl] | | | 3,78 | 1.55, 10.3 | **0,005** |
| log2(PLT) [bl] | | | 1,26 | 0.65, 2.58 | 0,51 |
| log2(creatinine) [bl] | | | 1,97 | 0.66, 6.38 | 0,23 |
| log2(LDH) [bl] | | | 4,14 | 1.55, 12.8 | **0,007** |
| log2(PLT) [bl] | | | 2,25 | 0.99, 5.55 | 0,064 |
| log2(creatinine) [bl] | | | 2,01 | 0.62, 6.68 | 0,23 |
| log2(ANC) [bl] | | | 0,49 | 0.20, 1.09 | 0,093 |
| log2(HGB) [bl] | | | 0,21 | 0.01, 4.24 | 0,31 |
| LDH > ULN [bl] | | | 2,84 | 0.88, 8.98 | 0,075 |
| PLT < LLN [bl] | | | 1,96 | 0.62, 6.48 | 0,25 |
| creatinine > ULN [bl] | | | 5,56 | 1.71, 18.6 | **0,004** |
| ANC < LLN [bl] | | | 1,14 | 0.31, 3.84 | 0,83 |
| CAR-HTX high [bl] | | | 0,66 | 0.13, 3.04 | 0,6 |
| EASIX > median (> 1.26) [bl] | | | 4,69 | 1.14, 22.5 | **0,039** |
| CAR-HTX high [d0] | | | 0,66 | 0.16, 2.66 | 0,55 |
| EASIX > median (> 1.36) [d0] | | | 5,22 | 1.44, 23.9 | **0,019** |

a. Determined prior to lymphodepletion (baseline). b. Last bone marrow status determined within 90 days prior to CAR T-cell therapy. c. Refractory to an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 monoclonal antibody. d. Refractory to lenalidomide, pomalidomide, bortezomib, carfilzomib and daratumumab. e. Systemic treatment administered between leukapheresis and lymphodepletion (at least one drug). f. Due to missing data for the US cohort, analyses of ferritin and ferritin-based scores prior to lymphodepletion were only performed for the German cohort.
ANC, absolute neutrophil count. B2-MG, beta-2-microglobulin. BCMA, B-cell maturation antigen. bl, baseline. BM, bone marrow. CAR-HTX, CAR-HEMATOTOX score. CI, confidence interval. CRP, C-reactive protein. CRS, cytokine release syndrome. d0, day 0 (day of CAR T-cell infusion). EASIX, Endothelial Activation and Stress Index. eGFR, estimated glomerular filtration rate. HGB, hemoglobin. ICAHT, immune effector cell-associated hematotoxicity. ICANS, immune effector cell-associated neurotoxicity syndrome. ISS, International Staging System. LD, lymphodepletion. LDH, lactate dehydrogenase. LLN, lower limit of normal. m-EASIX, modified EASIX. OR, odds ratio. PD, progressive disease. PLT, platelet count. $Q_3$, third/upper quartile (75$^{th}$ percentile). R-ISS, Revised International Staging System. ULN, upper limit of normal.

**Supp. Table S12 | Logistic regression analysis of an aplastic phenotype of neutrophil recovery**

| | Univariate analysis: Aplastic phenotype | | | | |
|---|---|---|---|---|---|
| **Characteristic** | **N** | **Event N** | **OR** | **95% CI** | **p-value** |
| **Age [cont.]** | 107 | 8 | 0,98 | 0.91, 1.06 | 0,64 |
| **Age ≥ 70 years** | | | | | |
| No | 76 | 6 | — | — | |
| Yes | 31 | 2 | 0,8 | 0.11, 3.73 | 0,8 |
| **Sex** | | | | | |
| M | 76 | 5 | — | — | |
| W | 31 | 3 | 1,52 | 0.30, 6.63 | 0,58 |
| **High risk cytogenetics** | | | | | |
| No | 63 | 3 | — | — | |
| Yes | 39 | 5 | 2,94 | 0.68, 15.1 | 0,16 |
| **ISS 3**[a] | | | | | |
| No | 87 | 7 | — | — | |
| Yes | 8 | 1 | 1,63 | 0.08, 11.3 | 0,67 |
| **R-ISS 3**[a] | | | | | |
| No | 91 | 7 | — | — | |
| Yes | 4 | 1 | 4 | 0.18, 36.4 | 0,26 |
| **Extramedullary disease**[a] | | | | | |
| No | 63 | 4 | — | — | |
| Yes | 41 | 3 | 1,16 | 0.22, 5.56 | 0,85 |
| **Extraosseous disease**[a] | | | | | |
| No | 77 | 4 | — | — | |
| Yes | 27 | 3 | 2,28 | 0.42, 11.1 | 0,3 |
| **BM burden ≥ 50%**[b] | | | | | |
| No | 47 | 5 | — | — | |
| Yes | 11 | 0 | — | — | — |
| **PD prior to LD** | | | | | |
| No | 45 | 1 | — | — | |
| Yes | 42 | 5 | 5,95 | 0.91, 117 | 0,11 |
| **Gr. 3-4 cytopenia prior to LD** | | | | | |
| No | 90 | 4 | — | — | |
| Yes | 14 | 3 | 5,86 | 1.04, 30.2 | **0,033** |
| **eGFR < 60 ml/min**[a] | | | | | |
| No | 80 | 6 | — | — | |
| Yes | 27 | 2 | 0,99 | 0.14, 4.61 | 0,99 |
| **Triple-class refractory**[c] | | | | | |
| No | 18 | 2 | — | — | |
| Yes | 89 | 6 | 0,58 | 0.12, 4.19 | 0,52 |
| **Penta-drug refractory**[d] | | | | | |
| No | 74 | 6 | — | — | |
| Yes | 33 | 2 | 0,73 | 0.10, 3.38 | 0,71 |
| **Prior BCMA-TT** | | | | | |
| No | 90 | 5 | — | — | |
| Yes | 17 | 3 | 3,64 | 0.69, 16.6 | 0,1 |
| **Bridging therapy**[e] | | | | | |
| No | 17 | 1 | — | — | |
| Yes | 90 | 7 | 1,35 | 0.22, 26.1 | 0,79 |
| **CRS ≥ °2** | | | | | |
| No | 73 | 4 | — | — | |
| Yes | 34 | 4 | 2,3 | 0.51, 10.3 | 0,26 |
| **Tocilizumab** | | | | | |
| No | 54 | 1 | — | — | |
| Yes | 53 | 7 | 8,07 | 1.36, 154 | 0,055 |
| **Dexamethasone** | | | | | |
| No | 63 | 2 | — | — | |
| Yes | 44 | 6 | 4,82 | 1.05, 34.0 | 0,062 |
| **log2(LDH) [bl]** | 104 | 8 | 3,36 | 1.39, 9.00 | **0,008** |
| **LDH > ULN [bl]** | | | | | |
| No | 78 | 3 | — | — | |
| Yes | 26 | 5 | 5,95 | 1.35, 31.0 | **0,021** |
| **log2(PLT) [bl]** | 107 | 8 | 0,63 | 0.35, 1.26 | 0,15 |
| **PLT < LLN [bl]** | | | | | |
| No | 63 | 3 | — | — | |
| Yes | 44 | 5 | 2,56 | 0.60, 13.1 | 0,21 |
| **log2(creatinine) [bl]** | 107 | 8 | 1,98 | 0.42, 8.33 | 0,35 |

| | | | | | |
|---|---|---|---|---|---|
| **creatinine > ULN [bl]** | | | | | |
| No | 84 | 3 | — | — | |
| Yes | 23 | 5 | 7,5 | 1.69, 39.4 | **0,009** |
| **log2(CRP) [bl]** | 97 | 8 | 1,53 | 1.04, 2.29 | **0,031** |
| **CRP > ULN [bl]** | | | | | |
| No | 60 | 3 | — | — | |
| Yes | 37 | 5 | 2,97 | 0.68, 15.2 | 0,15 |
| **log2(ferritin) [bl][f]** | 47 | 6 | 1,44 | 0.97, 2.27 | 0,084 |
| **Ferritin > ULN [bl][f]** | | | | | |
| No | 29 | 3 | — | — | |
| Yes | 18 | 3 | 1,73 | 0.29, 10.4 | 0,53 |
| **log2(ANC) [bl]** | 104 | 6 | 1,01 | 0.34, 3.34 | 0,99 |
| **ANC < LLN [bl]** | | | | | |
| No | 74 | 5 | — | — | |
| Yes | 30 | 1 | 0,48 | 0.02, 3.12 | 0,51 |
| **log2(HGB) [bl]** | 106 | 8 | 0,17 | 0.01, 3.88 | 0,26 |
| **HGB < LLN [bl]** | | | | | |
| No | 13 | 0 | — | — | |
| Yes | 93 | 8 | — | — | — |
| **log2(B2-MG) [bl]** | 95 | 8 | 1,58 | 0.48, 4.90 | 0,43 |
| **log2(LDH x creatinine) [bl]** | 104 | 8 | 2,44 | 1.23, 5.04 | **0,01** |
| **log2(EASIX) [bl]** | 104 | 8 | 1,53 | 1.05, 2.30 | **0,026** |
| **EASIX > median (> 1.26) [bl]** | | | | | |
| No | 54 | 1 | — | — | |
| Yes | 50 | 7 | 8,63 | 1.46, 165 | **0,048** |
| **EASIX > Q3 (> 2.15) [bl]** | | | | | |
| No | 80 | 3 | — | — | |
| Yes | 24 | 5 | 6,75 | 1.53, 35.3 | **0,014** |
| **log2(m-EASIX) [bl]** | 96 | 8 | 1,42 | 1.11, 1.90 | **0,008** |
| **m-EASIX > 6.2 [bl]** | | | | | |
| No | 87 | 4 | — | — | |
| Yes | 9 | 4 | 16,6 | 3.15, 93.4 | **<0.001** |
| **EASIX-F high [bl][f]** | | | | | |
| No | 52 | 4 | — | — | |
| Yes | 3 | 2 | 24 | 1.92, 591 | **0,017** |
| **EASIX-F inter/high [bl][f]** | | | | | |
| No | 26 | 3 | — | — | |
| Yes | 21 | 3 | 1,28 | 0.21, 7.64 | 0,78 |
| **EASIX-FC high [bl][f]** | | | | | |
| No | 42 | 3 | — | — | |
| Yes | 5 | 3 | 19,5 | 2.42, 206 | **0,007** |
| **EASIX-FC inter/high [bl][f]** | | | | | |
| No | 35 | 2 | — | — | |
| Yes | 14 | 4 | 6,6 | 1.12, 53.0 | **0,044** |
| **CAR-HTX high [bl][f]** | | | | | |
| No | 36 | 3 | — | — | |
| Yes | 12 | 3 | 3,67 | 0.59, 23.0 | 0,15 |
| **log2(EASIX) [d0]** | 96 | 8 | 1,67 | 1.14, 2.63 | **0,011** |
| **EASIX > median (> 1.36) [d0]** | | | | | |
| No | 49 | 1 | — | — | |
| Yes | 47 | 7 | 8,4 | 1.41, 160 | 0,051 |
| **EASIX > Q3 (> 2.06) [d0]** | | | | | |
| No | 74 | 2 | — | — | |
| Yes | 22 | 6 | 13,5 | 2.82, 98.2 | **0,003** |
| **log2(m-EASIX) [d0]** | 98 | 8 | 1,47 | 1.12, 1.99 | **0,007** |
| **m-EASIX > 6.2 [d0]** | | | | | |
| No | 78 | 3 | — | — | |
| Yes | 20 | 5 | 8,33 | 1.85, 44.3 | **0,007** |
| **EASIX-F high [d0]** | | | | | |
| No | 86 | 3 | — | — | |
| Yes | 10 | 5 | 27,7 | 5.38, 173 | **<0.001** |
| **EASIX-F inter/high [d0]** | | | | | |
| No | 41 | 3 | — | — | |
| Yes | 40 | 5 | 1,81 | 0.41, 9.35 | 0,44 |
| **EASIX-FC high [d0]** | | | | | |
| No | 77 | 5 | — | — | |
| Yes | 7 | 3 | 10,8 | 1.75, 64.8 | **0,008** |
| **EASIX-FC inter/high [d0]** | | | | | |
| No | 47 | 2 | — | — | |
| Yes | 38 | 6 | 4,22 | 0.91, 30.1 | 0,09 |

| | | | | | |
|---|---|---|---|---|---|
| **CAR-HTX high [d0]** | | | | | |
| No | 30 | 2 | — | — | |
| Yes | 61 | 6 | 1,53 | 0.33, 10.9 | 0,62 |

a. Determined prior to lymphodepletion (baseline). b. Last bone marrow status determined within 90 days prior to CAR T-cell therapy. c. Refractory to an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 monoclonal antibody. d. Refractory to lenalidomide, pomalidomide, bortezomib, carfilzomib and daratumumab. e. Systemic treatment administered between leukapheresis and lymphodepletion (at least one drug). f. Due to missing data for the US cohort, analyses of ferritin and ferritin-based scores prior to lymphodepletion were only performed for the German cohort.
ANC, absolute neutrophil count. B2-MG, beta-2-microglobulin. BCMA, B-cell maturation antigen. bl, baseline. BM, bone marrow. CAR-HTX, CAR-HEMATOTOX score. CI, confidence interval. CRP, C-reactive protein. CRS, cytokine release syndrome. d0, day 0 (day of CAR T-cell infusion). EASIX, Endothelial Activation and Stress Index. eGFR, estimated glomerular filtration rate. HGB, hemoglobin. ICANS, immune effector cell-associated neurotoxicity syndrome. ISS, International Staging System. LD, lymphodepletion. LDH, lactate dehydrogenase. LLN, lower limit of normal. m-EASIX, modified EASIX. OR, odds ratio. PD, progressive disease. PLT, platelet count. $Q_3$, third/upper quartile ($75^{th}$ percentile). R-ISS, Revised International Staging System. ULN, upper limit of normal.

**Supp. Table S13 | Logistic regression analysis of severe late-onset infections**

| | Univariate analysis: Severe late-onset infection | | | | |
|---|---|---|---|---|---|
| **Characteristic** | **N** | **Event N** | **OR** | **95% CI** | **p-value** |
| **Age [cont.]** | 116 | 15 | 0,97 | 0.91, 1.02 | 0,23 |
| **Age ≥ 70 years** | | | | | |
| No | 84 | 13 | — | — | |
| Yes | 32 | 2 | 0,36 | 0.05, 1.43 | 0,2 |
| **Sex** | | | | | |
| No | 80 | 12 | — | — | |
| Yes | 36 | 3 | 0,52 | 0.11, 1.76 | 0,33 |
| **High risk cytogenetics** | | | | | |
| No | 71 | 7 | — | — | |
| Yes | 41 | 8 | 2,22 | 0.73, 6.84 | 0,16 |
| **ISS 3**[a] | | | | | |
| No | 97 | 13 | — | — | |
| Yes | 8 | 2 | 2,15 | 0.29, 10.6 | 0,38 |
| **R-ISS 3**[a] | | | | | |
| No | 101 | 14 | — | — | |
| Yes | 4 | 1 | 2,07 | 0.10, 17.5 | 0,54 |
| **Extramedullary disease**[a] | | | | | |
| No | 70 | 6 | — | — | |
| Yes | 44 | 8 | 2,37 | 0.77, 7.72 | 0,14 |
| **Extraosseous disease**[a] | | | | | |
| No | 85 | 9 | — | — | |
| Yes | 29 | 5 | 1,76 | 0.50, 5.62 | 0,35 |
| **BM burden ≥ 50%**[b] | | | | | |
| No | 54 | 5 | — | — | |
| Yes | 13 | 2 | 1,78 | 0.23, 9.55 | 0,52 |
| **PD prior to LD** | | | | | |
| No | 50 | 4 | — | — | |
| Yes | 44 | 7 | 2,18 | 0.61, 8.84 | 0,24 |
| **Gr. 3-4 cytopenia prior to LD** | | | | | |
| No | 99 | 11 | — | — | |
| Yes | 14 | 3 | 2,18 | 0.44, 8.37 | 0,28 |
| **eGFR < 60 ml/min**[a] | | | | | |
| No | 85 | 8 | — | — | |
| Yes | 31 | 7 | 2,81 | 0.90, 8.63 | 0,069 |
| **Triple-class refractory**[c] | | | | | |
| No | 16 | 3 | — | — | |
| Yes | 100 | 12 | 0,59 | 0.16, 2.84 | 0,46 |
| **Penta-drug refractory**[d] | | | | | |
| No | 79 | 9 | — | — | |
| Yes | 37 | 6 | 1,51 | 0.47, 4.55 | 0,47 |
| **Prior BCMA-TT** | | | | | |
| No | 97 | 13 | — | — | |
| Yes | 19 | 2 | 0,76 | 0.11, 3.10 | 0,73 |
| **Bridging therapy**[e] | | | | | |
| No | 16 | 0 | — | — | |
| Yes | 100 | 15 | — | — | — |
| **CRS ≥ °2** | | | | | |
| No | 78 | 8 | — | — | |
| Yes | 38 | 7 | 1,98 | 0.64, 5.98 | 0,22 |
| **Tocilizumab** | | | | | |
| No | 57 | 6 | — | — | |
| Yes | 59 | 9 | 1,53 | 0.51, 4.86 | 0,45 |
| **Dexamethasone** | | | | | |
| No | 66 | 6 | — | — | |
| Yes | 50 | 9 | 2,2 | 0.74, 6.99 | 0,16 |
| **log2(LDH) [bl]** | 113 | 15 | 2,32 | 1.09, 5.11 | **0,027** |
| **LDH > ULN [bl]** | | | | | |
| No | 79 | 9 | — | — | |
| Yes | 34 | 6 | 1,67 | 0.52, 5.07 | 0,37 |
| **log2(PLT) [bl]** | 116 | 15 | 0,58 | 0.34, 0.99 | **0,04** |
| **PLT < LLN [bl]** | | | | | |
| No | 67 | 5 | — | — | |
| Yes | 49 | 10 | 3,18 | 1.05, 10.9 | **0,048** |
| **log2(creatinine) [bl]** | 116 | 15 | 3,1 | 1.00, 10.7 | 0,054 |

| | | | | | |
|---|---|---|---|---|---|
| **creatinine > ULN [bl]** | | | | | |
| No | 90 | 7 | — | — | |
| Yes | 26 | 8 | 5,27 | 1.69, 16.9 | **0,004** |
| **log2(CRP) [bl]** | 104 | 14 | 1,22 | 0.91, 1.65 | 0,18 |
| **CRP > ULN [bl]** | | | | | |
| No | 63 | 7 | — | — | |
| Yes | 41 | 7 | 1,65 | 0.52, 5.21 | 0,39 |
| **log2(ferritin) [bl][f]** | 48 | 11 | 1,1 | 0.80, 1.51 | 0,55 |
| **Ferritin > ULN [bl][f]** | | | | | |
| No | 30 | 8 | — | — | |
| Yes | 18 | 3 | 0,55 | 0.11, 2.26 | 0,43 |
| **log2(ANC) [bl]** | 113 | 13 | 1,02 | 0.47, 2.33 | 0,97 |
| **ANC < LLN [bl]** | | | | | |
| No | 81 | 10 | — | — | |
| Yes | 32 | 3 | 0,73 | 0.16, 2.61 | 0,66 |
| **log2(HGB) [bl]** | 115 | 15 | 0,05 | 0.00, 0.59 | **0,021** |
| **HGB < LLN [bl]** | | | | | |
| No | 13 | 0 | — | — | |
| Yes | 102 | 15 | — | — | — |
| **log2(B2-MG) [bl]** | 105 | 15 | 2,59 | 1.09, 6.56 | **0,035** |
| **log2(LDH x creatinine) [bl]** | 113 | 15 | 2,3 | 1.28, 4.40 | **0,007** |
| **log2(EASIX) [bl]** | 113 | 15 | 1,63 | 1.15, 2.51 | **0,011** |
| **EASIX > median (> 1.26) [bl]** | | | | | |
| No | 58 | 4 | — | — | |
| Yes | 55 | 11 | 3,38 | 1.07, 12.9 | **0,049** |
| **EASIX > Q3 (> 2.15) [bl]** | | | | | |
| No | 88 | 7 | — | — | |
| Yes | 25 | 8 | 5,45 | 1.74, 17.6 | **0,004** |
| **log2(m-EASIX) [bl]** | 103 | 14 | 1,24 | 1.00, 1.54 | **0,043** |
| **m-EASIX > 6.2 [bl]** | | | | | |
| No | 94 | 10 | — | — | |
| Yes | 9 | 4 | 6,72 | 1.46, 29.8 | **0,011** |
| **EASIX-F high [bl][f]** | | | | | |
| No | 51 | 8 | — | — | |
| Yes | 4 | 3 | 16,1 | 1.82, 350 | **0,022** |
| **EASIX-F inter/high [bl][f]** | | | | | |
| No | 26 | 6 | — | — | |
| Yes | 22 | 5 | 0,98 | 0.24, 3.82 | 0,98 |
| **EASIX-FC high [bl][f]** | | | | | |
| No | 43 | 8 | — | — | |
| Yes | 5 | 3 | 6,56 | 0.94, 56.6 | 0,058 |
| **EASIX-FC inter/high [bl][f]** | | | | | |
| No | 34 | 4 | — | — | |
| Yes | 15 | 7 | 6,56 | 1.60, 30.9 | **0,011** |
| **CAR-HTX high [bl][f]** | | | | | |
| No | 38 | 8 | — | — | |
| Yes | 11 | 3 | 1,41 | 0.26, 6.26 | 0,66 |
| **log2(EASIX) [d0]** | 105 | 15 | 1,67 | 1.18, 2.58 | **0,008** |
| **EASIX > median (> 1.36) [d0]** | | | | | |
| No | 54 | 4 | — | — | |
| Yes | 51 | 11 | 3,44 | 1.08, 13.2 | **0,047** |
| **EASIX > Q3 (> 2.06) [d0]** | | | | | |
| No | 80 | 8 | — | — | |
| Yes | 25 | 7 | 3,5 | 1.10, 11.1 | **0,031** |
| **log2(m-EASIX) [d0]** | 106 | 15 | 1,25 | 1.01, 1.56 | **0,038** |
| **m-EASIX > 6.2 [d0]** | | | | | |
| No | 85 | 9 | — | — | |
| Yes | 21 | 6 | 3,38 | 1.01, 10.9 | **0,042** |
| **EASIX-F high [d0]** | | | | | |
| No | 93 | 9 | — | — | |
| Yes | 12 | 6 | 9,33 | 2.47, 36.4 | **<0.001** |
| **EASIX-F inter/high [d0]** | | | | | |
| No | 45 | 6 | — | — | |
| Yes | 44 | 8 | 1,44 | 0.46, 4.77 | 0,53 |
| **EASIX-FC high [d0]** | | | | | |
| No | 86 | 9 | — | — | |
| Yes | 7 | 4 | 11,4 | 2.20, 66.4 | **0,004** |
| **EASIX-FC inter/high [d0]** | | | | | |
| No | 51 | 7 | — | — | |
| Yes | 43 | 8 | 1,44 | 0.47, 4.47 | 0,52 |

| | | | | | |
|---|---|---|---|---|---|
| **CAR-HTX high [d0]** | | | | | |
| No | 34 | 1 | — | — | |
| Yes | 64 | 14 | 9,24 | 1.73, 171 | **0,036** |
| **Multivariate analysis: Severe late-onset infection** | | | | | |
| **Characteristic** | | | **OR** | **95% CI** | **p-value** |
| Age ≥ 70 years | | | 0,3 | 0.04, 1.28 | 0,15 |
| Sex [W] | | | 0,52 | 0.10, 1.94 | 0,36 |
| EASIX > Q3 (> 2.15) [bl] | | | 5,7 | 1.77, 19.1 | **0,004** |
| log2(LDH) [bl] | | | 1,44 | 0.58, 3.63 | 0,43 |
| log2(creatinine) [bl] | | | 2,94 | 0.92, 9.75 | 0,066 |
| log2(PLT) [bl] | | | 0,87 | 0.43, 1.79 | 0,7 |
| log2(HGB) [bl] | | | 0,07 | 0.00, 1.43 | 0,088 |
| LDH > ULN [bl] | | | 1,36 | 0.38, 4.54 | 0,62 |
| PLT < LLN [bl] | | | 3,79 | 1.15, 14.3 | **0,035** |
| creatinine > ULN [bl] | | | 5,93 | 1.79, 20.9 | **0,004** |

a. Determined prior to lymphodepletion (baseline). b. Last bone marrow status determined within 90 days prior to CAR T-cell therapy. c. Refractory to an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 monoclonal antibody. d. Refractory to lenalidomide, pomalidomide, bortezomib, carfilzomib and daratumumab. e. Systemic treatment administered between leukapheresis and lymphodepletion (at least one drug). f. Due to missing data for the US cohort, analyses of ferritin and ferritin-based scores prior to lymphodepletion were only performed for the German cohort.
ANC, absolute neutrophil count. B2-MG, beta-2-microglobulin. BCMA, B-cell maturation antigen. bl, baseline. BM, bone marrow. CAR-HTX, CAR-HEMATOTOX score. CI, confidence interval. CRP, C-reactive protein. CRS, cytokine release syndrome. d0, day 0 (day of CAR T-cell infusion). EASIX, Endothelial Activation and Stress Index. eGFR, estimated glomerular filtration rate. HGB, hemoglobin. ICANS, immune effector cell-associated neurotoxicity syndrome. ISS, International Staging System. LD, lymphodepletion. LDH, lactate dehydrogenase. LLN, lower limit of normal. m-EASIX, modified EASIX. OR, odds ratio. PD, progressive disease. PLT, platelet count. $Q_3$, third/upper quartile ($75^{th}$ percentile). R-ISS, Revised International Staging System. ULN, upper limit of normal.

## Supp. Table S14 | Logistic regression analysis of CRS grade ≥ 2

| | Univariate analysis: CRS grade ≥ 2 | | | | |
|---|---|---|---|---|---|
| **Characteristic** | **N** | **Event N** | **OR** | **95% CI** | **p-value** |
| **Age [cont.]** | 129 | 42 | 1,02 | 0.98, 1.06 | 0,39 |
| **Age ≥ 70 years** | | | | | |
| No | 93 | 27 | — | — | |
| Yes | 36 | 15 | 1,75 | 0.78, 3.88 | 0,17 |
| **Sex** | | | | | |
| M | 87 | 28 | — | — | |
| W | 42 | 14 | 1,05 | 0.47, 2.29 | 0,9 |
| **High risk cytogenetics** | | | | | |
| No | 74 | 23 | — | — | |
| Yes | 49 | 16 | 1,08 | 0.49, 2.32 | 0,85 |
| **ISS 3**[a] | | | | | |
| No | 107 | 37 | — | — | |
| Yes | 10 | 4 | 1,26 | 0.31, 4.70 | 0,73 |
| **R-ISS 3**[a] | | | | | |
| No | 111 | 39 | — | — | |
| Yes | 6 | 2 | 0,92 | 0.12, 4.95 | 0,93 |
| **Extramedullary disease**[a] | | | | | |
| No | 78 | 22 | — | — | |
| Yes | 48 | 18 | 1,53 | 0.71, 3.29 | 0,28 |
| **Extraosseous disease**[a] | | | | | |
| No | 94 | 30 | — | — | |
| Yes | 32 | 10 | 0,97 | 0.40, 2.26 | 0,94 |
| **BM burden ≥ 50%**[b] | | | | | |
| No | 57 | 13 | — | — | |
| Yes | 14 | 6 | 2,54 | 0.72, 8.70 | 0,14 |
| **PD prior to LD** | | | | | |
| No | 51 | 16 | — | — | |
| Yes | 53 | 20 | 1,33 | 0.59, 3.01 | 0,5 |
| **Gr. 3-4 cytopenia prior to LD** | | | | | |
| No | 110 | 37 | — | — | |
| Yes | 16 | 3 | 0,46 | 0.10, 1.52 | 0,24 |
| **eGFR < 60 ml/min**[a] | | | | | |
| No | 95 | 26 | — | — | |
| Yes | 34 | 16 | 2,36 | 1.05, 5.34 | **0,038** |
| **Triple-class refractory**[c] | | | | | |
| No | 22 | 9 | — | — | |
| Yes | 107 | 33 | 0,64 | 0.25, 1.70 | 0,36 |
| **Penta-drug refractory**[d] | | | | | |
| No | 88 | 34 | — | — | |
| Yes | 41 | 8 | 0,39 | 0.15, 0.90 | **0,034** |
| **Prior BCMA-TT** | | | | | |
| No | 107 | 35 | — | — | |
| Yes | 22 | 7 | 0,96 | 0.34, 2.50 | 0,94 |
| **Bridging therapy**[e] | | | | | |
| No | 18 | 1 | — | — | |
| Yes | 111 | 41 | 9,96 | 1.93, 183 | **0,028** |
| **CRS ≥ °2** | | | | | |
| No | 87 | 0 | — | — | |
| Yes | 42 | 42 | — | — | — |
| **Tocilizumab** | | | | | |
| No | 63 | 3 | — | — | |
| Yes | 66 | 39 | 28,9 | 9.43, 127 | **<0.001** |
| **Dexamethasone** | | | | | |
| No | 72 | 6 | — | — | |
| Yes | 57 | 36 | 18,9 | 7.42, 55.6 | **<0.001** |
| **log2(LDH) [bl]** | 126 | 41 | 0,88 | 0.43, 1.65 | 0,69 |
| **LDH > ULN [bl]** | | | | | |
| No | 87 | 31 | — | — | |
| Yes | 39 | 10 | 0,62 | 0.26, 1.41 | 0,27 |
| **log2(PLT) [bl]** | 129 | 42 | 0,98 | 0.65, 1.51 | 0,91 |

| | | | | | |
|---|---|---|---|---|---|
| **PLT < LLN [bl]** | | | | | |
| No | 73 | 22 | — | — | |
| Yes | 56 | 20 | 1,29 | 0.61, 2.71 | 0,5 |
| **log2(creatinine) [bl]** | 129 | 42 | 1,6 | 0.75, 3.53 | 0,23 |
| **creatinine > ULN [bl]** | | | | | |
| No | 100 | 26 | — | — | |
| Yes | 29 | 16 | 3,5 | 1.49, 8.40 | **0,004** |
| **log2(CRP) [bl]** | 116 | 39 | 1 | 0.81, 1.22 | 0,98 |
| **CRP > ULN [bl]** | | | | | |
| No | 73 | 25 | — | — | |
| Yes | 43 | 14 | 0,93 | 0.41, 2.05 | 0,85 |
| **log2(ferritin) [bl]**[f] | 55 | 26 | 1,1 | 0.86, 1.42 | 0,45 |
| **Ferritin > ULN [bl]**[f] | | | | | |
| No | 34 | 14 | — | — | |
| Yes | 21 | 12 | 1,9 | 0.64, 5.87 | 0,25 |
| **log2(ANC) [bl]** | 126 | 40 | 0,98 | 0.58, 1.68 | 0,95 |
| **ANC < LLN [bl]** | | | | | |
| No | 91 | 30 | — | — | |
| Yes | 35 | 10 | 0,81 | 0.34, 1.87 | 0,64 |
| **log2(HGB) [bl]** | 128 | 42 | 0,55 | 0.11, 2.75 | 0,46 |
| **HGB < LLN [bl]** | | | | | |
| No | 15 | 6 | — | — | |
| Yes | 113 | 36 | 0,7 | 0.23, 2.23 | 0,53 |
| **log2(B2-MG) [bl]** | 117 | 41 | 1,25 | 0.71, 2.21 | 0,44 |
| **log2(LDH x creatinine) [bl]** | 126 | 41 | 1,1 | 0.67, 1.76 | 0,71 |
| **log2(EASIX) [bl]** | 126 | 41 | 1,05 | 0.79, 1.38 | 0,72 |
| **EASIX > median (> 1.26) [bl]** | | | | | |
| No | 64 | 17 | — | — | |
| Yes | 62 | 24 | 1,75 | 0.83, 3.76 | 0,15 |
| **EASIX > Q3 (> 2.15) [bl]** | | | | | |
| No | 95 | 29 | — | — | |
| Yes | 31 | 12 | 1,44 | 0.61, 3.33 | 0,4 |
| **log2(m-EASIX) [bl]** | 115 | 39 | 1,01 | 0.86, 1.18 | 0,87 |
| **m-EASIX > 6.2 [bl]** | | | | | |
| No | 104 | 33 | — | — | |
| Yes | 11 | 6 | 2,58 | 0.73, 9.55 | 0,14 |
| **EASIX-F high [bl]**[f] | | | | | |
| No | 59 | 24 | — | — | |
| Yes | 4 | 3 | 4,38 | 0.52, 91.4 | 0,21 |
| **EASIX-F inter/high [bl]**[f] | | | | | |
| No | 30 | 13 | — | — | |
| Yes | 25 | 13 | 1,42 | 0.49, 4.17 | 0,52 |
| **EASIX-FC high [bl]**[f] | | | | | |
| No | 50 | 23 | — | — | |
| Yes | 5 | 3 | 1,76 | 0.27, 14.3 | 0,55 |
| **EASIX-FC inter/high [bl]**[f] | | | | | |
| No | 40 | 16 | — | — | |
| Yes | 17 | 10 | 2,14 | 0.68, 7.05 | 0,2 |
| **CAR-HTX high [bl]**[f] | | | | | |
| No | 43 | 18 | — | — | |
| Yes | 13 | 7 | 1,62 | 0.46, 5.83 | 0,45 |
| **log2(EASIX) [d0]** | 117 | 41 | 0,98 | 0.72, 1.28 | 0,86 |
| **EASIX > median (> 1.36) [d0]** | | | | | |
| No | 59 | 19 | — | — | |
| Yes | 58 | 22 | 1,29 | 0.60, 2.77 | 0,52 |
| **EASIX > Q3 (> 2.06) [d0]** | | | | | |
| No | 88 | 30 | — | — | |
| Yes | 29 | 11 | 1,18 | 0.48, 2.80 | 0,71 |
| **log2(m-EASIX) [d0]** | 119 | 41 | 0,97 | 0.82, 1.14 | 0,73 |
| **m-EASIX > 6.2 [d0]** | | | | | |
| No | 95 | 33 | — | — | |
| Yes | 24 | 8 | 0,94 | 0.35, 2.37 | 0,9 |
| **EASIX-F high [d0]** | | | | | |
| No | 104 | 36 | — | — | |
| Yes | 13 | 5 | 1,18 | 0.34, 3.81 | 0,78 |

| | | | | | |
|---|---|---|---|---|---|
| **EASIX-F inter/high [d0]** | | | | | |
| No | 50 | 19 | — | — | |
| Yes | 51 | 20 | 1,05 | 0.47, 2.36 | 0,9 |
| **EASIX-FC high [d0]** | | | | | |
| No | 97 | 35 | — | — | |
| Yes | 8 | 3 | 1,06 | 0.21, 4.60 | 0,94 |
| **EASIX-FC inter/high [d0]** | | | | | |
| No | 59 | 25 | — | — | |
| Yes | 47 | 14 | 0,58 | 0.25, 1.29 | 0,18 |
| **CAR-HTX high [d0]** | | | | | |
| No | 38 | 12 | — | — | |
| Yes | 73 | 27 | 1,27 | 0.56, 2.99 | 0,57 |

| **Multivariate analysis: CRS grade ≥ 2** | | | |
|---|---|---|---|
| **Characteristic** | **OR** | **95% CI** | **p-value** |
| Age ≥ 70 years | 1,94 | 0.65, 5.84 | 0,23 |
| Sex [W] | 1,86 | 0.67, 5.28 | 0,23 |
| Extramedullary disease | 1,32 | 0.51, 3.47 | 0,57 |
| ISS 3 | 0,34 | 0.06, 1.72 | 0,21 |
| PD prior to LD | 1,69 | 0.64, 4.64 | 0,3 |
| eGFR < 60 ml/min | 5,53 | 1.59, 22.3 | **0,01** |
| Pentra-drug refractory | 0,39 | 0.12, 1.15 | 0,1 |

a. Determined prior to lymphodepletion (baseline). b. Last bone marrow status determined within 90 days prior to CAR T-cell therapy. c. Refractory to an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 monoclonal antibody. d. Refractory to lenalidomide, pomalidomide, bortezomib, carfilzomib and daratumumab. e. Systemic treatment administered between leukapheresis and lymphodepletion (at least one drug). f. Due to missing data for the US cohort, analyses of ferritin and ferritin-based scores prior to lymphodepletion were only performed for the German cohort.
ANC, absolute neutrophil count. B2-MG, beta-2-microglobulin. BCMA, B-cell maturation antigen. bl, baseline. BM, bone marrow. CAR-HTX, CAR-HEMATOTOX score. CI, confidence interval. CRP, C-reactive protein. CRS, cytokine release syndrome. d0, day 0 (day of CAR T-cell infusion). EASIX, Endothelial Activation and Stress Index. eGFR, estimated glomerular filtration rate. HGB, hemoglobin. ICANS, immune effector cell-associated neurotoxicity syndrome. ISS, International Staging System. LD, lymphodepletion. LDH, lactate dehydrogenase. LLN, lower limit of normal. m-EASIX, modified EASIX. OR, odds ratio. PD, progressive disease. PLT, platelet count. $Q_3$, third/upper quartile ($75^{th}$ percentile). R-ISS, Revised International Staging System. ULN, upper limit of normal.

## Supp. Table S15 | Logistic regression analysis of ICANS

| | Univariate analysis: ICANS | | | | |
|---|---|---|---|---|---|
| **Characteristic** | **N** | **Event N** | **OR** | **95% CI** | **p-value** |
| **Age [cont.]** | 129 | 11 | 1,03 | 0.96, 1.10 | 0,44 |
| **Age ≥ 70 years** | | | | | |
| No | 93 | 8 | — | — | |
| Yes | 36 | 3 | 0,97 | 0.20, 3.57 | 0,96 |
| **Sex** | | | | | |
| M | 87 | 8 | — | — | |
| W | 42 | 3 | 0,76 | 0.16, 2.79 | 0,7 |
| **High risk cytogenetics** | | | | | |
| No | 74 | 6 | — | — | |
| Yes | 49 | 5 | 1,29 | 0.35, 4.53 | 0,69 |
| **ISS 3**[a] | | | | | |
| No | 107 | 9 | — | — | |
| Yes | 10 | 1 | 1,21 | 0.06, 7.62 | 0,86 |
| **R-ISS 3**[a] | | | | | |
| No | 111 | 10 | — | — | |
| Yes | 6 | 0 | — | — | — |
| **Extramedullary disease**[a] | | | | | |
| No | 78 | 7 | — | — | |
| Yes | 48 | 4 | 0,92 | 0.23, 3.24 | 0,9 |
| **Extraosseous disease**[a] | | | | | |
| No | 94 | 9 | — | — | |
| Yes | 32 | 2 | 0,63 | 0.09, 2.62 | 0,57 |
| **BM burden ≥ 50%**[a] | | | | | |
| No | 57 | 3 | — | — | |
| Yes | 14 | 3 | 4,91 | 0.82, 29.8 | 0,071 |
| **PD prior to LD** | | | | | |
| No | 51 | 3 | — | — | |
| Yes | 53 | 6 | 2,04 | 0.51, 10.1 | 0,33 |
| **Gr. 3-4 cytopenia prior to LD** | | | | | |
| No | 110 | 10 | — | — | |
| Yes | 16 | 1 | 0,67 | 0.04, 3.87 | 0,71 |
| **eGFR < 60 ml/min**[a] | | | | | |
| No | 95 | 8 | — | — | |
| Yes | 34 | 3 | 1,05 | 0.22, 3.90 | 0,94 |
| **Triple-class refractory**[c] | | | | | |
| No | 22 | 1 | — | — | |
| Yes | 107 | 10 | 2,16 | 0.38, 40.8 | 0,47 |
| **Penta-drug refractory**[d] | | | | | |
| No | 88 | 7 | — | — | |
| Yes | 41 | 4 | 1,25 | 0.31, 4.41 | 0,73 |
| **Prior BCMA-TT** | | | | | |
| No | 107 | 9 | — | — | |
| Yes | 22 | 2 | 1,09 | 0.16, 4.64 | 0,92 |
| **Bridging therapy**[e] | | | | | |
| No | 18 | 1 | — | — | |
| Yes | 111 | 10 | 1,68 | 0.29, 31.9 | 0,63 |
| **CRS ≥ °2** | | | | | |
| No | 87 | 4 | — | — | |
| Yes | 42 | 7 | 4,15 | 1.18, 16.7 | **0,031** |
| **Tocilizumab** | | | | | |
| No | 63 | 3 | — | — | |
| Yes | 66 | 8 | 2,76 | 0.76, 13.1 | 0,15 |
| **Dexamethasone** | | | | | |
| No | 72 | 0 | — | — | |
| Yes | 57 | 11 | — | — | — |
| **log2(LDH) [bl]** | 126 | 10 | 1,02 | 0.28, 2.63 | 0,97 |
| **LDH > ULN [bl]** | | | | | |
| No | 87 | 8 | — | — | |
| Yes | 39 | 2 | 0,53 | 0.08, 2.26 | 0,44 |
| **log2(PLT) [bl]** | 129 | 11 | 0,65 | 0.38, 1.19 | 0,13 |
| **PLT < LLN [bl]** | | | | | |
| No | 73 | 5 | — | — | |
| Yes | 56 | 6 | 1,63 | 0.47, 5.95 | 0,44 |
| **log2(creatinine) [bl]** | 129 | 11 | 1,13 | 0.29, 3.65 | 0,85 |

| | | | | | |
|---|---|---|---|---|---|
| **creatinine > ULN [bl]** | | | | | |
| No | 100 | 9 | — | — | |
| Yes | 29 | 2 | 0,75 | 0.11, 3.13 | 0,72 |
| **log2(CRP) [bl]** | 116 | 11 | 1,25 | 0.91, 1.70 | 0,16 |
| **CRP > ULN [bl]** | | | | | |
| No | 73 | 5 | — | — | |
| Yes | 43 | 6 | 2,21 | 0.62, 8.12 | 0,22 |
| **log2(ferritin) [bl][f]** | 55 | 4 | 0,77 | 0.42, 1.25 | 0,33 |
| **Ferritin > ULN [bl][f]** | | | | | |
| No | 34 | 4 | — | — | |
| Yes | 21 | 0 | — | — | — |
| **log2(ANC) [bl]** | 126 | 11 | 1,22 | 0.52, 3.13 | 0,66 |
| **ANC < LLN [bl]** | | | | | |
| No | 91 | 8 | — | — | |
| Yes | 35 | 3 | 0,97 | 0.20, 3.60 | 0,97 |
| **log2(HGB) [bl]** | 128 | 11 | 0,22 | 0.02, 2.98 | 0,24 |
| **HGB < LLN [bl]** | | | | | |
| No | 15 | 0 | — | — | |
| Yes | 113 | 11 | — | — | — |
| **log2(B2-MG) [bl]** | 117 | 10 | 0,89 | 0.30, 2.20 | 0,82 |
| **log2(LDH x creatinine) [bl]** | 126 | 10 | 1,02 | 0.39, 2.11 | 0,96 |
| **log2(EASIX) [bl]** | 126 | 10 | 1,25 | 0.82, 1.77 | 0,22 |
| **EASIX > median (> 1.26) [bl]** | | | | | |
| No | 64 | 2 | — | — | |
| Yes | 62 | 8 | 4,59 | 1.09, 31.3 | 0,061 |
| **EASIX > Q3 (> 2.15) [bl]** | | | | | |
| No | 95 | 4 | — | — | |
| Yes | 31 | 6 | 5,46 | 1.45, 22.8 | **0,013** |
| **log2(m-EASIX) [bl]** | 115 | 10 | 1,2 | 0.95, 1.49 | 0,1 |
| **m-EASIX > 6.2 [bl]** | | | | | |
| No | 104 | 7 | — | — | |
| Yes | 11 | 3 | 5,2 | 0.98, 23.2 | **0,035** |
| **EASIX-F high [bl][f]** | | | | | |
| No | 59 | 4 | — | — | |
| Yes | 4 | 0 | — | — | — |
| **EASIX-F inter/high [bl][f]** | | | | | |
| No | 30 | 4 | — | — | |
| Yes | 25 | 0 | — | — | — |
| **EASIX-FC high [bl][f]** | | | | | |
| No | 50 | 4 | — | — | |
| Yes | 5 | 0 | — | — | — |
| **EASIX-FC inter/high [bl][f]** | | | | | |
| No | 40 | 2 | — | — | |
| Yes | 17 | 2 | 2,53 | 0.28, 22.7 | 0,37 |
| **CAR-HTX high [bl][f]** | | | | | |
| No | 43 | 3 | — | — | |
| Yes | 13 | 1 | 1,11 | 0.05, 9.63 | 0,93 |
| **log2(EASIX) [d0]** | 117 | 11 | 1,24 | 0.82, 1.75 | 0,24 |
| **EASIX > median (> 1.36) [d0]** | | | | | |
| No | 59 | 4 | — | — | |
| Yes | 58 | 7 | 1,89 | 0.54, 7.56 | 0,33 |
| **EASIX > Q3 (> 2.06) [d0]** | | | | | |
| No | 88 | 5 | — | — | |
| Yes | 29 | 6 | 4,33 | 1.20, 16.3 | **0,024** |
| **log2(m-EASIX) [d0]** | 119 | 11 | 1,25 | 0.99, 1.59 | 0,053 |
| **m-EASIX > 6.2 [d0]** | | | | | |
| No | 95 | 6 | — | — | |
| Yes | 24 | 5 | 3,9 | 1.03, 14.3 | **0,038** |
| **EASIX-F high [d0]** | | | | | |
| No | 104 | 9 | — | — | |
| Yes | 13 | 2 | 1,92 | 0.27, 8.73 | 0,44 |
| **EASIX-F inter/high [d0]** | | | | | |
| No | 50 | 4 | — | — | |
| Yes | 51 | 5 | 1,25 | 0.31, 5.33 | 0,75 |
| **EASIX-FC high [d0]** | | | | | |
| No | 97 | 8 | — | — | |
| Yes | 8 | 0 | — | — | — |
| **EASIX-FC inter/high [d0]** | | | | | |
| No | 59 | 3 | — | — | |
| Yes | 47 | 7 | 3,27 | 0.85, 15.9 | 0,1 |

| | | | | | |
|---|---|---|---|---|---|
| **CAR-HTX high [d0]** | | | | | |
| No | 38 | 1 | — | — | |
| Yes | 73 | 9 | 5,2 | 0.92, 97.9 | 0,12 |
| | | **Multivariate analysis: ICANS** | | | |
| **Characteristic** | | | **OR** | **95% CI** | **p-value** |
| CRS ≥ °2 | | | 5,42 | 1.36, 27.2 | **0,022** |
| EASIX > Q3 (> 2.15) [bl] | | | 5,24 | 1.33, 22.9 | **0,019** |

a. Determined prior to lymphodepletion (baseline). b. Last bone marrow status determined within 90 days prior to CAR T-cell therapy. c. Refractory to an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 monoclonal antibody. d. Refractory to lenalidomide, pomalidomide, bortezomib, carfilzomib and daratumumab. e. Systemic treatment administered between leukapheresis and lymphodepletion (at least one drug). f. Due to missing data for the US cohort, analyses of ferritin and ferritin-based scores prior to lymphodepletion were only performed for the German cohort.
ANC, absolute neutrophil count. B2-MG, beta-2-microglobulin. BCMA, B-cell maturation antigen. bl, baseline. BM, bone marrow. CAR-HTX, CAR-HEMATOTOX score. CI, confidence interval. CRP, C-reactive protein. CRS, cytokine release syndrome. d0, day 0 (day of CAR T-cell infusion). EASIX, Endothelial Activation and Stress Index. eGFR, estimated glomerular filtration rate. HGB, hemoglobin. ICANS, immune effector cell-associated neurotoxicity syndrome. ISS, International Staging System. LD, lymphodepletion. LDH, lactate dehydrogenase. LLN, lower limit of normal. m-EASIX, modified EASIX. OR, odds ratio. PD, progressive disease. PLT, platelet count. $Q_3$, third/upper quartile ($75^{th}$ percentile). R-ISS, Revised International Staging System. ULN, upper limit of normal.

## Supp. Table S16 | Logistic regression analysis of treatment response

| | Univariate analysis: Treatment response (≥ PR) | | | | |
|---|---|---|---|---|---|
| **Characteristic** | **N** | **Event N** | **OR** | **95% CI** | **p-value** |
| **Age [cont.]** | 122 | 101 | 1,01 | 0.96, 1.06 | 0,65 |
| **Age ≥ 70 years** | | | | | |
| No | 89 | 74 | — | — | |
| Yes | 33 | 27 | 0,91 | 0.33, 2.77 | 0,86 |
| **Sex** | | | | | |
| No | 83 | 67 | — | — | |
| Yes | 39 | 34 | 1,62 | 0.58, 5.30 | 0,38 |
| **High risk cytogenetics** | | | | | |
| No | 68 | 54 | — | — | |
| Yes | 48 | 43 | 2,23 | 0.78, 7.34 | 0,15 |
| **High risk cytogenetics with 1q** | | | | | |
| No | 46 | 34 | — | — | |
| Yes | 70 | 63 | 3,18 | 1.17, 9.25 | **0,027** |
| **ISS 3**[a] | | | | | |
| No | 103 | 88 | — | — | |
| Yes | 9 | 6 | 0,34 | 0.08, 1.75 | 0,16 |
| **R-ISS 3**[a] | | | | | |
| No | 106 | 90 | — | — | |
| Yes | 6 | 4 | 0,36 | 0.06, 2.72 | 0,25 |
| **Extramedullary disease**[a] | | | | | |
| No | 77 | 63 | — | — | |
| Yes | 42 | 36 | 1,33 | 0.49, 4.04 | 0,59 |
| **Extraosseous disease**[a] | | | | | |
| No | 92 | 78 | — | — | |
| Yes | 27 | 21 | 0,63 | 0.22, 1.95 | 0,39 |
| **BM burden ≥ 50%**[b] | | | | | |
| No | 53 | 41 | — | — | |
| Yes | 14 | 14 | — | — | — |
| **PD prior to LD** | | | | | |
| No | 46 | 37 | — | — | |
| Yes | 51 | 44 | 1,53 | 0.52, 4.66 | 0,44 |
| **Gr. 3-4 cytopenia prior to LD** | | | | | |
| No | 104 | 86 | — | — | |
| Yes | 15 | 12 | 0,84 | 0.24, 3.94 | 0,8 |
| **eGFR < 60 ml/min**[a] | | | | | |
| No | 89 | 73 | — | — | |
| Yes | 33 | 28 | 1,23 | 0.43, 4.03 | 0,71 |
| **Triple-class refractory**[c] | | | | | |
| No | 20 | 15 | — | — | |
| Yes | 102 | 86 | 1,79 | 0.52, 5.40 | 0,32 |
| **Penta-drug refractory**[d] | | | | | |
| No | 84 | 71 | — | — | |
| Yes | 38 | 30 | 0,69 | 0.26, 1.89 | 0,45 |
| **Prior BCMA-TT** | | | | | |
| No | 101 | 86 | — | — | |
| Yes | 21 | 15 | 0,44 | 0.15, 1.38 | 0,14 |
| **Bridging therapy**[e] | | | | | |
| No | 18 | 15 | — | — | |
| Yes | 104 | 86 | 0,96 | 0.21, 3.28 | 0,95 |
| **CRS ≥ °2** | | | | | |
| No | 81 | 66 | — | — | |
| Yes | 41 | 35 | 1,33 | 0.49, 3.99 | 0,59 |
| **Tocilizumab** | | | | | |
| No | 57 | 43 | — | — | |
| Yes | 65 | 58 | 2,7 | 1.03, 7.65 | **0,049** |
| **Dexamethasone** | | | | | |
| No | 67 | 52 | — | — | |
| Yes | 55 | 49 | 2,36 | 0.88, 7.05 | 0,1 |
| **log2(LDH) [bl]** | 119 | 98 | 0,85 | 0.42, 1.94 | 0,66 |
| **LDH > ULN [bl]** | | | | | |
| No | 83 | 69 | — | — | |
| Yes | 36 | 29 | 0,84 | 0.31, 2.41 | 0,74 |
| **log2(PLT) [bl]** | 122 | 101 | 1,39 | 0.85, 2.21 | 0,17 |
| **PLT < LLN [bl]** | | | | | |
| No | 68 | 59 | — | — | |
| Yes | 54 | 42 | 0,53 | 0.20, 1.37 | 0,2 |

| | | | | | |
|---|---|---|---|---|---|
| **log2(creatinine) [bl]** | 122 | 101 | 0,88 | 0.35, 2.39 | 0,8 |
| **creatinine > ULN [bl]** | | | | | |
| No | 94 | 79 | — | — | |
| Yes | 28 | 22 | 0,7 | 0.25, 2.14 | 0,5 |
| **log2(CRP) [bl]** | 110 | 91 | 0,95 | 0.74, 1.23 | 0,68 |
| **CRP > ULN [bl]** | | | | | |
| No | 68 | 56 | — | — | |
| Yes | 42 | 35 | 1,07 | 0.39, 3.12 | 0,89 |
| **log2(ferritin) [bl]**[f] | 50 | 42 | 0,89 | 0.62, 1.27 | 0,52 |
| **Ferritin > ULN [bl]**[f] | | | | | |
| No | 31 | 27 | — | — | |
| Yes | 19 | 15 | 0,56 | 0.12, 2.65 | 0,45 |
| **log2(ANC) [bl]** | 119 | 99 | 1,98 | 1.03, 3.94 | **0,044** |
| **ANC < LLN [bl]** | | | | | |
| No | 86 | 73 | — | — | |
| Yes | 33 | 26 | 0,66 | 0.24, 1.92 | 0,43 |
| **log2(HGB) [bl]** | 121 | 100 | 0,64 | 0.07, 4.73 | 0,67 |
| **HGB < LLN [bl]** | | | | | |
| No | 15 | 12 | — | — | |
| Yes | 106 | 88 | 1,22 | 0.26, 4.34 | 0,77 |
| **log2(B2-MG) [bl]** | 112 | 94 | 1,05 | 0.51, 2.39 | 0,91 |
| **log2(LDH x creatinine) [bl]** | 119 | 98 | 0,86 | 0.50, 1.60 | 0,61 |
| **log2(EASIX) [bl]** | 119 | 98 | 0,84 | 0.62, 1.16 | 0,25 |
| **EASIX > median (> 1.26) [bl]** | | | | | |
| No | 62 | 52 | — | — | |
| Yes | 57 | 46 | 0,8 | 0.31, 2.08 | 0,65 |
| **EASIX > Q3 (> 2.15) [bl]** | | | | | |
| No | 90 | 76 | — | — | |
| Yes | 29 | 22 | 0,58 | 0.21, 1.69 | 0,3 |
| **log2(m-EASIX) [bl]** | 109 | 90 | 0,94 | 0.78, 1.14 | 0,49 |
| **m-EASIX > 6.2 [bl]** | | | | | |
| No | 99 | 83 | — | — | |
| Yes | 10 | 7 | 0,45 | 0.11, 2.25 | 0,28 |
| **EASIX-F high [bl]**[f] | | | | | |
| No | 53 | 45 | — | — | |
| Yes | 4 | 3 | 0,53 | 0.06, 11.5 | 0,61 |
| **EASIX-F inter/high [bl]**[f] | | | | | |
| No | 27 | 23 | — | — | |
| Yes | 23 | 19 | 0,83 | 0.17, 3.92 | 0,8 |
| **EASIX-FC high [bl]**[f] | | | | | |
| No | 45 | 38 | — | — | |
| Yes | 5 | 4 | 0,74 | 0.09, 15.6 | 0,8 |
| **EASIX-FC inter/high [bl]**[f] | | | | | |
| No | 36 | 29 | — | — | |
| Yes | 16 | 14 | 1,69 | 0.35, 12.3 | 0,54 |
| **CAR-HTX high [bl]**[f] | | | | | |
| No | 39 | 32 | — | — | |
| Yes | 11 | 10 | 2,19 | 0.33, 43.5 | 0,49 |
| **log2(EASIX) [d0]** | 112 | 93 | 0,83 | 0.60, 1.15 | 0,23 |
| **EASIX > median (> 1.36) [d0]** | | | | | |
| No | 57 | 49 | — | — | |
| Yes | 55 | 44 | 0,65 | 0.23, 1.76 | 0,4 |
| **EASIX > Q3 (> 2.06) [d0]** | | | | | |
| No | 85 | 72 | — | — | |
| Yes | 27 | 21 | 0,63 | 0.22, 1.98 | 0,41 |
| **log2(m-EASIX) [d0]** | 114 | 94 | 0,94 | 0.77, 1.15 | 0,52 |
| **m-EASIX > 6.2 [d0]** | | | | | |
| No | 91 | 77 | — | — | |
| Yes | 23 | 17 | 0,52 | 0.18, 1.63 | 0,23 |
| **EASIX-F high [d0]** | | | | | |
| No | 100 | 84 | — | — | |
| Yes | 12 | 9 | 0,57 | 0.15, 2.78 | 0,44 |
| **EASIX-F inter/high [d0]** | | | | | |
| No | 48 | 42 | — | — | |
| Yes | 50 | 41 | 0,65 | 0.20, 1.97 | 0,45 |
| **EASIX-FC high [d0]** | | | | | |
| No | 95 | 81 | — | — | |
| Yes | 8 | 7 | 1,21 | 0.19, 23.5 | 0,86 |

| | | | | | |
|---|---|---|---|---|---|
| **EASIX-FC inter/high [d0]** | | | | | |
| No | 58 | 50 | — | — | |
| Yes | 45 | 36 | 0,64 | 0.22, 1.83 | 0,4 |
| **CAR-HTX high [d0]** | | | | | |
| No | 36 | 31 | — | — | |
| Yes | 71 | 59 | 0,79 | 0.23, 2.35 | 0,69 |

a. Determined prior to lymphodepletion (baseline). b. Last bone marrow status determined within 90 days prior to CAR T-cell therapy. c. Refractory to an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 monoclonal antibody. d. Refractory to lenalidomide, pomalidomide, bortezomib, carfilzomib and daratumumab. e. Systemic treatment administered between leukapheresis and lymphodepletion (at least one drug). f. Baseline ferritin and ferritin-based scores were only analyzed in the German cohort.

ANC, absolute neutrophil count. B2-MG, beta-2-microglobulin. BCMA, B-cell maturation antigen. bl, baseline. BM, bone marrow. CAR-HTX, CAR-HEMATOTOX score. CI, confidence interval. CRP, C-reactive protein. CRS, cytokine release syndrome. d0, day 0 (day of CAR T-cell infusion). EASIX, Endothelial Activation and Stress Index. eGFR, estimated glomerular filtration rate. HGB, hemoglobin. ICANS, immune effector cell-associated neurotoxicity syndrome. ISS, International Staging System. LD, lymphodepletion. LDH, lactate dehydrogenase. LLN, lower limit of normal. m-EASIX, modified EASIX. OR, odds ratio. PD, progressive disease. PLT, platelet count. $Q_3$, third/upper quartile ($75^{th}$ percentile). R-ISS, Revised International Staging System. ULN, upper limit of normal.

**Supp. Table S17 | Cox regression analysis of progression-free survival (PFS)**

| | Univariate analysis: PFS | | | | |
|---|---|---|---|---|---|
| **Characteristic** | **N** | **Event N** | **HR** | **95% CI** | **p-value** |
| **Age [cont.]** | 129 | 70 | 0,98 | 0.96, 1.00 | 0,11 |
| **Age ≥ 70 years** | | | | | |
| No | 93 | 53 | — | — | |
| Yes | 36 | 17 | 0,69 | 0.40, 1.19 | 0,18 |
| **Sex** | | | | | |
| M | 87 | 53 | — | — | |
| W | 42 | 17 | 0,71 | 0.41, 1.23 | 0,23 |
| **High risk cytogenetics** | | | | | |
| No | 74 | 43 | — | — | |
| Yes | 49 | 25 | 0,97 | 0.59, 1.60 | 0,92 |
| **High risk cytogenetics with 1q** | | | | | |
| No | 49 | 27 | — | — | |
| Yes | 74 | 41 | 1,13 | 0.69, 1.85 | 0,63 |
| **ISS 3**[a] | | | | | |
| No | 107 | 52 | — | — | |
| Yes | 10 | 9 | 2,56 | 1.25, 5.23 | **0,01** |
| **R-ISS 3**[a] | | | | | |
| No | 111 | 56 | — | — | |
| Yes | 6 | 5 | 4,22 | 1.65, 10.8 | **0,003** |
| **Extramedullary disease**[a] | | | | | |
| No | 78 | 36 | — | — | |
| Yes | 48 | 33 | 1,91 | 1.18, 3.08 | **0,008** |
| **Extraosseous disease**[a] | | | | | |
| No | 94 | 45 | — | — | |
| Yes | 32 | 24 | 2,46 | 1.48, 4.09 | **<0.001** |
| **BM burden ≥ 50%**[b] | | | | | |
| No | 57 | 35 | — | — | |
| Yes | 14 | 6 | 0,65 | 0.27, 1.54 | 0,33 |
| **PD prior to LD** | | | | | |
| No | 51 | 31 | — | — | |
| Yes | 53 | 26 | 0,99 | 0.58, 1.67 | 0,96 |
| **Gr. 3-4 cytopenia prior to LD** | | | | | |
| No | 110 | 57 | — | — | |
| Yes | 16 | 10 | 1,35 | 0.69, 2.65 | 0,39 |
| **eGFR < 60 ml/min**[a] | | | | | |
| No | 95 | 51 | — | — | |
| Yes | 34 | 19 | 1 | 0.59, 1.69 | 0,99 |
| **Triple-class refractory**[c] | | | | | |
| No | 22 | 9 | — | — | |
| Yes | 107 | 61 | 1,12 | 0.55, 2.25 | 0,76 |
| **Penta-drug refractory**[d] | | | | | |
| No | 88 | 47 | — | — | |
| Yes | 41 | 23 | 1,01 | 0.61, 1.67 | 0,97 |
| **Prior BCMA-TT** | | | | | |
| No | 107 | 56 | — | — | |
| Yes | 22 | 14 | 1,27 | 0.71, 2.30 | 0,42 |
| **Bridging therapy**[e] | | | | | |
| No | 18 | 7 | — | — | |
| Yes | 111 | 63 | 2,14 | 0.97, 4.70 | 0,059 |
| **CRS ≥ °2** | | | | | |
| No | 87 | 45 | — | — | |
| Yes | 42 | 25 | 1,26 | 0.77, 2.06 | 0,36 |
| **Tocilizumab** | | | | | |
| No | 63 | 37 | — | — | |
| Yes | 66 | 33 | 0,83 | 0.52, 1.34 | 0,45 |
| **Dexamethasone** | | | | | |
| No | 72 | 41 | — | — | |
| Yes | 57 | 29 | 0,89 | 0.55, 1.44 | 0,64 |
| **log2(LDH) [bl]** | 126 | 68 | 1,52 | 1.04, 2.22 | **0,032** |
| **LDH > ULN [bl]** | | | | | |
| No | 87 | 46 | — | — | |
| Yes | 39 | 22 | 1,53 | 0.91, 2.55 | 0,11 |
| **log2(PLT) [bl]** | 129 | 70 | 0,77 | 0.60, 0.98 | **0,037** |
| **PLT < LLN [bl]** | | | | | |
| No | 73 | 35 | — | — | |
| Yes | 56 | 35 | 1,77 | 1.10, 2.85 | **0,018** |

| | | | | | |
|---|---|---|---|---|---|
| **log2(creatinine) [bl]** | 129 | 70 | 1,31 | 0.79, 2.19 | 0,3 |
| **creatinine > ULN [bl]** | | | | | |
| No | 100 | 52 | — | — | |
| Yes | 29 | 18 | 1,28 | 0.74, 2.18 | 0,38 |
| **log2(CRP) [bl]** | 116 | 64 | 1,2 | 1.06, 1.37 | **0,005** |
| **CRP > ULN [bl]** | | | | | |
| No | 73 | 31 | — | — | |
| Yes | 43 | 33 | 2,19 | 1.33, 3.60 | **0,002** |
| **log2(ferritin) [bl]**[f] | 55 | 27 | 1,2 | 1.02, 1.41 | **0,032** |
| **Ferritin > ULN [bl]**[f] | | | | | |
| No | 34 | 14 | — | — | |
| Yes | 21 | 13 | 1,75 | 0.82, 3.76 | 0,15 |
| **log2(ANC) [bl]** | 126 | 67 | 0,87 | 0.63, 1.20 | 0,38 |
| **ANC < LLN [bl]** | | | | | |
| No | 91 | 47 | — | — | |
| Yes | 35 | 20 | 1,1 | 0.65, 1.85 | 0,73 |
| **log2(HGB) [bl]** | 128 | 69 | 0,46 | 0.15, 1.37 | 0,16 |
| **HGB < LLN [bl]** | | | | | |
| No | 15 | 8 | — | — | |
| Yes | 113 | 61 | 0,87 | 0.42, 1.83 | 0,72 |
| **log2(B2-MG) [bl]** | 117 | 61 | 1,31 | 0.91, 1.89 | 0,15 |
| **log2(LDH x creatinine) [bl]** | 126 | 68 | 1,38 | 1.03, 1.85 | **0,032** |
| **log2(EASIX) [bl]** | 126 | 68 | 1,24 | 1.07, 1.43 | **0,004** |
| **EASIX > median (> 1.26) [bl]** | | | | | |
| No | 64 | 30 | — | — | |
| Yes | 62 | 38 | 1,73 | 1.07, 2.82 | **0,026** |
| **EASIX > Q3 (> 2.15) [bl]** | | | | | |
| No | 95 | 48 | — | — | |
| Yes | 31 | 20 | 2,05 | 1.21, 3.48 | **0,008** |
| **log2(m-EASIX) [bl]** | 115 | 63 | 1,18 | 1.07, 1.29 | **<0.001** |
| **m-EASIX > 6.2 [bl]** | | | | | |
| No | 104 | 55 | — | — | |
| Yes | 11 | 8 | 2,51 | 1.19, 5.30 | **0,016** |
| **EASIX-F high [bl]**[f] | | | | | |
| No | 59 | 32 | — | — | |
| Yes | 4 | 2 | 0,98 | 0.23, 4.13 | 0,98 |
| **EASIX-F inter/high [bl]**[f] | | | | | |
| No | 30 | 13 | — | — | |
| Yes | 25 | 14 | 1,47 | 0.69, 3.14 | 0,32 |
| **EASIX-FC high [bl]**[f] | | | | | |
| No | 50 | 22 | — | — | |
| Yes | 5 | 5 | 3,35 | 1.24, 9.00 | **0,017** |
| **EASIX-FC inter/high [bl]**[f] | | | | | |
| No | 40 | 19 | — | — | |
| Yes | 17 | 10 | 1,67 | 0.77, 3.62 | 0,2 |
| **CAR-HTX high [bl]**[f] | | | | | |
| No | 43 | 20 | — | — | |
| Yes | 13 | 8 | 1,68 | 0.73, 3.85 | 0,22 |
| **log2(EASIX) [d0]** | 117 | 64 | 1,23 | 1.06, 1.42 | **0,005** |
| **EASIX > median (> 1.36) [d0]** | | | | | |
| No | 59 | 30 | — | — | |
| Yes | 58 | 34 | 1,61 | 0.97, 2.65 | 0,063 |
| **EASIX > Q3 (> 2.06) [d0]** | | | | | |
| No | 88 | 46 | — | — | |
| Yes | 29 | 18 | 1,5 | 0.87, 2.60 | 0,15 |
| **log2(m-EASIX) [d0]** | 119 | 65 | 1,09 | 0.99, 1.20 | 0,069 |
| **m-EASIX > 6.2 [d0]** | | | | | |
| No | 95 | 51 | — | — | |
| Yes | 24 | 14 | 1,61 | 0.89, 2.93 | 0,12 |
| **EASIX-F high [d0]** | | | | | |
| No | 104 | 54 | — | — | |
| Yes | 13 | 10 | 2,15 | 1.09, 4.25 | **0,027** |
| **EASIX-F inter/high [d0]** | | | | | |
| No | 50 | 19 | — | — | |
| Yes | 51 | 33 | 2,51 | 1.41, 4.45 | **0,002** |
| **EASIX-FC high [d0]** | | | | | |
| No | 97 | 45 | — | — | |
| Yes | 8 | 8 | 3,49 | 1.62, 7.54 | **0,001** |

| | | | | | |
|---|---|---|---|---|---|
| **EASIX-FC inter/high [d0]** | | | | | |
| No | 59 | 26 | — | — | |
| Yes | 47 | 28 | 1,64 | 0.95, 2.83 | 0,075 |
| **CAR-HTX high [d0]** | | | | | |
| No | 38 | 20 | — | — | |
| Yes | 73 | 37 | 1,22 | 0.70, 2.11 | 0,48 |

| **Multivariate analysis: PFS** | | | |
|---|---|---|---|
| **Characteristic** | **HR** | **95% CI** | **p-value** |
| ISS 3 | 2,76 | 1.32, 5.77 | **0,007** |
| Extraosseous disease | 2,34 | 1.31, 4.19 | **0,004** |
| EASIX > Q3 (> 2.15) [bl] | 2,03 | 1.13, 3.64 | **0,017** |
| ISS 3 | 2,56 | 1.21, 5.41 | **0,014** |
| Extraosseous disease | 2,27 | 1.27, 4.06 | **0,006** |
| Bridging therapy | 1,61 | 0.66, 3.91 | 0,29 |
| EASIX > Q3 (> 2.15) [bl] | 1,89 | 1.05, 3.41 | **0,035** |
| ISS 3 | 2,86 | 1.24, 6.57 | **0,013** |
| Extraosseous disease | 2,1 | 1.15, 3.85 | **0,016** |
| Bridging therapy | 1,64 | 0.67, 3.99 | 0,28 |
| Gr. 3-4 cytopenia prior to LD | 1,06 | 0.50, 2.26 | 0,87 |
| EASIX > Q3 (> 2.15) [bl] | 1,73 | 0.93, 3.24 | 0,086 |
| Age ≥ 70 years | 0,8 | 0.44, 1.45 | 0,45 |
| Sex [W] | 0,67 | 0.36, 1.24 | 0,2 |
| ISS 3 | 3,09 | 1.43, 6.68 | **0,004** |
| Extraosseous disease | 2,32 | 1.29, 4.16 | **0,005** |
| EASIX > Q3 (> 2.15) [bl] | 1,89 | 1.04, 3.43 | **0,037** |
| log2(LDH) [bl] | 1,34 | 0.84, 2.15 | 0,22 |
| log2(PLT) [bl] | 1,01 | 0.71, 1.45 | 0,94 |
| log2(creatinine) [bl] | 1,21 | 0.69, 2.14 | 0,51 |
| log2(ANC) [bl] | 0,72 | 0.48, 1.08 | 0,11 |
| log2(HGB) [bl] | 1,59 | 0.36, 7.02 | 0,54 |
| log2(CRP) [bl] | 1,21 | 1.04, 1.41 | **0,013** |
| LDH > ULN [bl] | 1,35 | 0.75, 2.42 | 0,31 |
| PLT < LLN [bl] | 1,53 | 0.89, 2.63 | 0,13 |
| creatinine > ULN [bl] | 1 | 0.54, 1.85 | >0.99 |
| ANC < LLN [bl] | 1,02 | 0.56, 1.85 | 0,95 |
| HGB < LLN [bl] | 0,52 | 0.24, 1.14 | 0,1 |
| CRP > ULN [bl] | 2,11 | 1.22, 3.66 | **0,008** |
| log2(EASIX) [bl] | 1,17 | 0.99, 1.38 | 0,059 |
| log2(CRP) [bl] | 1,17 | 1.02, 1.33 | **0,025** |
| EASIX > Q3 (> 2.15) [bl] | 1,74 | 0.98, 3.09 | 0,058 |
| CRP > ULN [bl] | 2,02 | 1.21, 3.35 | **0,007** |
| EASIX > Q3 (> 2.15) [bl] | 1,4 | 0.50, 3.89 | 0,52 |
| CAR-HTX high [bl] | 1,48 | 0.58, 3.73 | 0,41 |
| EASIX > Q3 (> 2.06) [d0] | 1,7 | 0.92, 3.11 | 0,088 |
| CAR-HTX high [d0] | 0,98 | 0.54, 1.78 | 0,94 |

a. Determined prior to lymphodepletion (baseline). b. Last bone marrow status determined within 90 days prior to CAR T-cell therapy. c. Refractory to an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 monoclonal antibody. d. Refractory to lenalidomide, pomalidomide, bortezomib, carfilzomib and daratumumab. e. Systemic treatment administered between leukapheresis and lymphodepletion (at least one drug). f. Due to missing data for the US cohort, analyses of ferritin and ferritin-based scores prior to lymphodepletion were only performed for the German cohort.
ANC, absolute neutrophil count. B2-MG, beta-2-microglobulin. BCMA, B-cell maturation antigen. bl, baseline. BM, bone marrow. CAR-HTX, CAR-HEMATOTOX score. CI, confidence interval. CRP, C-reactive protein. CRS, cytokine release syndrome. d0, day 0 (day of CAR T-cell infusion). EASIX, Endothelial Activation and Stress Index. eGFR, estimated glomerular filtration rate. HGB, hemoglobin. HR, hazard ratio. ICANS, immune effector cell-associated neurotoxicity syndrome. ISS, International Staging System. LD, lymphodepletion. LDH, lactate dehydrogenase. LLN, lower limit of normal. m-EASIX, modified EASIX. PD, progressive disease. PLT, platelet count. $Q_3$, third/upper quartile ($75^{th}$ percentile). R-ISS, Revised International Staging System. ULN, upper limit of normal.

## Supp. Table S18 | Cox regression analysis of overall survival (OS)

| | Univariate analysis: OS | | | | |
|---|---|---|---|---|---|
| **Characteristic** | **N** | **Event N** | **HR** | **95% CI** | **p-value** |
| **Age [cont.]** | 129 | 30 | 1 | 0.96, 1.04 | 0,93 |
| **Age ≥ 70 years** | | | | | |
| No | 93 | 24 | — | — | |
| Yes | 36 | 6 | 0,66 | 0.27, 1.63 | 0,37 |
| **Sex** | | | | | |
| M | 87 | 23 | — | — | |
| W | 42 | 7 | 0,8 | 0.34, 1.88 | 0,61 |
| **High risk cytogenetics** | | | | | |
| No | 74 | 18 | — | — | |
| Yes | 49 | 11 | 1,08 | 0.51, 2.30 | 0,83 |
| **High risk cytogenetics with 1q** | | | | | |
| No | 49 | 13 | — | — | |
| Yes | 74 | 16 | 0,88 | 0.43, 1.84 | 0,74 |
| **ISS 3**[a] | | | | | |
| No | 107 | 21 | — | — | |
| Yes | 10 | 6 | 3,51 | 1.41, 8.73 | **0,007** |
| **R-ISS 3**[a] | | | | | |
| No | 111 | 23 | — | — | |
| Yes | 6 | 4 | 5,75 | 1.96, 16.9 | **0,001** |
| **Extramedullary disease**[a] | | | | | |
| No | 78 | 16 | — | — | |
| Yes | 48 | 13 | 1,41 | 0.68, 2.92 | 0,36 |
| **Extraosseous disease**[a] | | | | | |
| No | 94 | 17 | — | — | |
| Yes | 32 | 12 | 2,3 | 1.10, 4.83 | **0,027** |
| **BM burden ≥ 50%**[b] | | | | | |
| No | 57 | 16 | — | — | |
| Yes | 14 | 1 | 0,26 | 0.03, 1.94 | 0,19 |
| **PD prior to LD** | | | | | |
| No | 51 | 14 | — | — | |
| Yes | 53 | 14 | 1,29 | 0.61, 2.71 | 0,5 |
| **Gr. 3-4 cytopenia prior to LD** | | | | | |
| No | 110 | 23 | — | — | |
| Yes | 16 | 6 | 2,24 | 0.91, 5.53 | 0,08 |
| **eGFR < 60 ml/min**[a] | | | | | |
| No | 95 | 21 | — | — | |
| Yes | 34 | 9 | 1,11 | 0.51, 2.44 | 0,79 |
| **Triple-class refractory**[c] | | | | | |
| No | 22 | 5 | — | — | |
| Yes | 107 | 25 | 0,75 | 0.29, 1.98 | 0,56 |
| **Penta-drug refractory**[d] | | | | | |
| No | 88 | 18 | — | — | |
| Yes | 41 | 12 | 1,43 | 0.69, 2.97 | 0,34 |
| **Prior BCMA-TT** | | | | | |
| No | 107 | 25 | — | — | |
| Yes | 22 | 5 | 0,9 | 0.34, 2.34 | 0,82 |
| **Bridging therapy**[e] | | | | | |
| No | 18 | 1 | — | — | |
| Yes | 111 | 29 | 6,44 | 0.87, 47.4 | 0,068 |
| **CRS ≥ °2** | | | | | |
| No | 87 | 19 | — | — | |
| Yes | 42 | 11 | 1,31 | 0.62, 2.75 | 0,48 |
| **Tocilizumab** | | | | | |
| No | 63 | 17 | — | — | |
| Yes | 66 | 13 | 0,77 | 0.37, 1.58 | 0,47 |
| **Dexamethasone** | | | | | |
| No | 72 | 17 | — | — | |
| Yes | 57 | 13 | 1,08 | 0.52, 2.22 | 0,84 |
| **log2(LDH) [bl]** | 126 | 30 | 1,65 | 0.99, 2.77 | 0,055 |
| **LDH > ULN [bl]** | | | | | |
| No | 87 | 18 | — | — | |
| Yes | 39 | 12 | 1,98 | 0.95, 4.15 | 0,068 |
| **log2(PLT) [bl]** | 129 | 30 | 0,62 | 0.45, 0.85 | **0,003** |
| **PLT < LLN [bl]** | | | | | |
| No | 73 | 12 | — | — | |
| Yes | 56 | 18 | 2,25 | 1.08, 4.68 | **0,029** |

| | | | | | |
|---|---|---|---|---|---|
| **log2(creatinine) [bl]** | 129 | 30 | 1,6 | 0.82, 3.14 | 0,17 |
| **creatinine > ULN [bl]** | | | | | |
| No | 100 | 22 | — | — | |
| Yes | 29 | 8 | 1,4 | 0.62, 3.14 | 0,42 |
| **log2(CRP) [bl]** | 116 | 29 | 1,38 | 1.15, 1.66 | **<0.001** |
| **CRP > ULN [bl]** | | | | | |
| No | 73 | 10 | — | — | |
| Yes | 43 | 19 | 3,25 | 1.51, 7.00 | **0,003** |
| **log2(ferritin) [bl]**[f] | 55 | 9 | 1,2 | 0.88, 1.62 | 0,25 |
| **Ferritin > ULN [bl]**[f] | | | | | |
| No | 34 | 6 | — | — | |
| Yes | 21 | 3 | 0,98 | 0.24, 3.96 | 0,97 |
| **log2(ANC) [bl]** | 126 | 29 | 0,85 | 0.52, 1.39 | 0,52 |
| **ANC < LLN [bl]** | | | | | |
| No | 91 | 22 | — | — | |
| Yes | 35 | 7 | 0,76 | 0.32, 1.77 | 0,52 |
| **log2(HGB) [bl]** | 128 | 30 | 0,05 | 0.01, 0.23 | **<0.001** |
| **HGB < LLN [bl]** | | | | | |
| No | 15 | 0 | — | — | |
| Yes | 113 | 30 | — | — | — |
| **log2(B2-MG) [bl]** | 117 | 27 | 2,03 | 1.27, 3.24 | **0,003** |
| **log2(LDH x creatinine) [bl]** | 126 | 30 | 1,55 | 1.07, 2.26 | **0,02** |
| **log2(EASIX) [bl]** | 126 | 30 | 1,34 | 1.12, 1.60 | **0,001** |
| **EASIX > median (> 1.26) [bl]** | | | | | |
| No | 64 | 10 | — | — | |
| Yes | 62 | 20 | 2,27 | 1.06, 4.86 | **0,034** |
| **EASIX > Q3 (> 2.15) [bl]** | | | | | |
| No | 95 | 15 | — | — | |
| Yes | 31 | 15 | 4,85 | 2.35, 10.0 | **<0.001** |
| **log2(m-EASIX) [bl]** | 115 | 29 | 1,28 | 1.13, 1.44 | **<0.001** |
| **m-EASIX > 6.2 [bl]** | | | | | |
| No | 104 | 23 | — | — | |
| Yes | 11 | 6 | 4,23 | 1.70, 10.5 | **0,002** |
| **EASIX-F high [bl]**[f] | | | | | |
| No | 59 | 11 | — | — | |
| Yes | 4 | 0 | — | — | — |
| **EASIX-F inter/high [bl]**[f] | | | | | |
| No | 30 | 5 | — | — | |
| Yes | 25 | 4 | 1,02 | 0.27, 3.80 | 0,98 |
| **EASIX-FC high [bl]**[f] | | | | | |
| No | 50 | 7 | — | — | |
| Yes | 5 | 2 | 3,91 | 0.79, 19.5 | 0,1 |
| **EASIX-FC inter/high [bl]**[f] | | | | | |
| No | 40 | 5 | — | — | |
| Yes | 17 | 5 | 3,29 | 0.94, 11.5 | 0,062 |
| **CAR-HTX high [bl]**[f] | | | | | |
| No | 43 | 7 | — | — | |
| Yes | 13 | 3 | 1,83 | 0.47, 7.16 | 0,39 |
| **log2(EASIX) [d0]** | 117 | 27 | 1,35 | 1.13, 1.62 | **<0.001** |
| **EASIX > median (> 1.36) [d0]** | | | | | |
| No | 59 | 9 | — | — | |
| Yes | 58 | 18 | 2,47 | 1.11, 5.50 | **0,027** |
| **EASIX > Q3 (> 2.06) [d0]** | | | | | |
| No | 88 | 14 | — | — | |
| Yes | 29 | 13 | 3,49 | 1.64, 7.44 | **0,001** |
| **log2(m-EASIX) [d0]** | 119 | 28 | 1,18 | 1.04, 1.35 | **0,013** |
| **m-EASIX > 6.2 [d0]** | | | | | |
| No | 95 | 19 | — | — | |
| Yes | 24 | 9 | 2,61 | 1.16, 5.84 | **0,02** |
| **EASIX-F high [d0]** | | | | | |
| No | 104 | 20 | — | — | |
| Yes | 13 | 7 | 3,61 | 1.51, 8.60 | **0,004** |
| **EASIX-F inter/high [d0]** | | | | | |
| No | 50 | 6 | — | — | |
| Yes | 51 | 17 | 3,6 | 1.40, 9.24 | **0,008** |
| **EASIX-FC high [d0]** | | | | | |
| No | 97 | 18 | — | — | |
| Yes | 8 | 4 | 4,57 | 1.50, 14.0 | **0,008** |

| | | | | | |
|---|---|---|---|---|---|
| **EASIX-FC inter/high [d0]** | | | | | |
| No | 59 | 8 | — | — | |
| Yes | 47 | 16 | 2,84 | 1.21, 6.67 | **0,017** |
| **CAR-HTX high [d0]** | | | | | |
| No | 38 | 5 | — | — | |
| Yes | 73 | 20 | 2,88 | 1.07, 7.72 | **0,036** |
| | | | **Multivariate analysis: OS** | | |
| **Characteristic** | | | **HR** | **95% CI** | **p-value** |
| ISS 3 | | | 4,42 | 1.62, 12.1 | **0,004** |
| Extraosseous disease | | | 3,42 | 1.44, 8.17 | **0,006** |
| EASIX > Q3 (> 2.15) [bl] | | | 3,89 | 1.71, 8.83 | **0,001** |
| ISS 3 | | | 3,94 | 1.43, 10.8 | **0,008** |
| Extraosseous disease | | | 3,31 | 1.38, 7.91 | **0,007** |
| Bridging therapy | | | 3,13 | 0.40, 24.7 | 0,28 |
| EASIX > Q3 (> 2.15) [bl] | | | 3,44 | 1.51, 7.84 | **0,003** |
| ISS 3 | | | 4,06 | 1.38, 11.9 | **0,011** |
| Extraosseous disease | | | 3,13 | 1.28, 7.63 | **0,012** |
| Bridging therapy | | | 3,57 | 0.45, 28.1 | 0,23 |
| Gr. 3-4 cytopenia prior to LD | | | 1,39 | 0.51, 3.83 | 0,52 |
| EASIX > Q3 (> 2.15) [bl] | | | 2,82 | 1.20, 6.61 | **0,017** |
| Age ≥ 70 years | | | 0,71 | 0.28, 1.81 | 0,48 |
| Sex [W] | | | 0,68 | 0.25, 1.85 | 0,45 |
| ISS 3 | | | 4,69 | 1.67, 13.2 | **0,003** |
| Extraosseous disease | | | 3,41 | 1.42, 8.18 | **0,006** |
| EASIX > Q3 (> 2.15) [bl] | | | 3,52 | 1.51, 8.19 | **0,004** |
| log2(LDH) [bl] | | | 1,3 | 0.72, 2.34 | 0,38 |
| log2(PLT) [bl] | | | 1,03 | 0.63, 1.69 | 0,9 |
| log2(creatinine) [bl] | | | 1,38 | 0.64, 2.97 | 0,41 |
| log2(ANC) [bl] | | | 0,89 | 0.51, 1.56 | 0,69 |
| log2(HGB) [bl] | | | 0,17 | 0.02, 1.39 | 0,1 |
| log2(CRP) [bl] | | | 1,22 | 0.99, 1.51 | 0,062 |
| LDH > ULN [bl] | | | 1,75 | 0.79, 3.89 | 0,17 |
| PLT < LLN [bl] | | | 2,05 | 0.95, 4.43 | 0,067 |
| creatinine > ULN [bl] | | | 1,13 | 0.47, 2.71 | 0,79 |
| ANC < LLN [bl] | | | 0,8 | 0.33, 1.96 | 0,63 |
| CRP > ULN [bl] | | | 2,79 | 1.23, 6.32 | **0,014** |
| log2(EASIX) [bl] | | | 1,22 | 1.00, 1.48 | 0,053 |
| log2(CRP) [bl] | | | 1,32 | 1.09, 1.60 | **0,005** |
| EASIX > Q3 (> 2.15) [bl] | | | 3,74 | 1.73, 8.08 | **<0.001** |
| CRP > ULN [bl] | | | 2,46 | 1.11, 5.47 | **0,027** |
| EASIX > Q3 (> 2.15) [bl] | | | 4,9 | 1.12, 21.3 | **0,034** |
| CAR-HTX high [bl] | | | 0,86 | 0.18, 4.17 | 0,86 |
| EASIX > Q3 (> 2.06) [d0] | | | 3,95 | 1.62, 9.64 | **0,003** |
| CAR-HTX high [d0] | | | 1,59 | 0.55, 4.56 | 0,39 |

a. Determined prior to lymphodepletion (baseline). b. Last bone marrow status determined within 90 days prior to CAR T-cell therapy. c. Refractory to an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 monoclonal antibody. d. Refractory to lenalidomide, pomalidomide, bortezomib, carfilzomib and daratumumab. e. Systemic treatment administered between leukapheresis and lymphodepletion (at least one drug). f. Due to missing data for the US cohort, analyses of ferritin and ferritin-based scores prior to lymphodepletion were only performed for the German cohort.
ANC, absolute neutrophil count. B2-MG, beta-2-microglobulin. BCMA, B-cell maturation antigen. bl, baseline. BM, bone marrow. CAR-HTX, CAR-HEMATOTOX score. CI, confidence interval. CRP, C-reactive protein. CRS, cytokine release syndrome. d0, day 0 (day of CAR T-cell infusion). EASIX, Endothelial Activation and Stress Index. eGFR, estimated glomerular filtration rate. HGB, hemoglobin. HR, hazard ratio. ICANS, immune effector cell-associated neurotoxicity syndrome. ISS, International Staging System. LD, lymphodepletion. LDH, lactate dehydrogenase. LLN, lower limit of normal. m-EASIX, modified EASIX. PD, progressive disease. PLT, platelet count. $Q_3$, third/upper quartile (75$^{th}$ percentile). R-ISS, Revised International Staging System. ULN, upper limit of normal.