Background
Downregulated C-type lectin domain family 3 member B (CLEC3B) is observed in NSCLC and is linked with immune cell infiltration. We aimed to analyse the impact of CLEC3B mRNA expression on survival and its molecular link to NSCLC subtypes and to immune cell infiltration.

Methods
19,892 samples were tested at Caris Life Sciences (Phoenix, AZ) with NextGen Sequencing on DNA (592 genes/WES), RNA (WTS) and IHC. Top quartile transcripts per million (TPM) were defined as high (Q4, ≥4.03 TPM) and bottom quartile as low (Q1, ≤0.89 TPM). Cell infiltration was estimated by QuantiSEQ. X

Results
Figure 1: Distribution of CLEC3B mRNA expression in NSCLC

Table 2: Fold change of additional immune marker expression shown upregulated with CLEC3B mRNA expression.

Table: Distribution and demographic information

Distribution of CLEC3B mRNA expression in NSCLC

Figure 2: I/O markers for CLEC3B Q1 vs Q4

Figure 3: Significant alterations for CLEC3B Q1 vs Q4

Conclusions
• High CLEC3B mRNA expression was associated with female sex (55.2% vs 44.8%, p<0.001).
• Adenocarcinoma had higher CLEC3B expression than squamous cell (2.28 vs 1.51, q<0.001).
• CLEC3B correlated negatively with mutations in TP53 (74.7% in Q1 vs 52.4% in Q4), KEAP1 (15.9% vs 11.2%), RB1 (13.5% vs 9.2%), CNOT2A (13.0% vs 8.3%), NF1 (10.3% vs 6.9%) (all q<0.001).
• KRAS (31.8% in Q4 vs 25.6% in Q1), EGFR (17.2% vs 8.1%), STK11 (15.9% vs 11.3%) mutations were more frequently observed in CLEC3B high expressors (all q<0.001).
• High CLEC3B mRNA expression was negatively associated with high TMB (43.0% vs 29.0%) and high PD-L1 expression (62.5% vs 47.7%) (all q<0.05).
• An upregulation of various immunological markers (i.e. LAG3, INF-G, PDCD1) and a higher abundance of several immune cells (i.e. B cells, macrophages, T cells) in the CLEC3B high cohort (all q<0.001).
• Patients with high CLEC3B mRNA expression showed an improved OS when compared to CLEC3B low expression (p<0.001, HR: 1.35); a similar observation was made in patients treated with checkpoint inhibitors (p<0.001, HR: 1.29).
• Our study represents the largest analysis of CLEC3B mRNA expression in NSCLC. High CLEC3B mRNA expression levels are linked to a distinct molecular/immunological profile and to improved survival. Further experiments are now ongoing to unravel functional aspects of CLEC3B biology in NSCLC.

EMAIL: andreas.seeber@tirol-kliniken.at