SLFN11 expression in early stage non-small cell lung cancer correlates with benefit from platinum-containing chemotherapy

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Background
- SLFN11 protein is widely reported to sensitize cancer cells to DNA-damaging agents (1).
- Pre-clinical lung cancer models suggest SLFN11 expression may predict response to cisplatin, PARP inhibitors and topoisomerase inhibitors (1-4).
- Tumor expression of SLFN11 is assessed by immunohistochemistry, RNA expression or DNA methylation; no standard method exists (5).
- We used mass spectrometry to quantify SLFN11 protein in archived patient samples of lung cancer treated with adjuvant platinum plus taxane. We correlated proteomic SLFN11 expression with survival.
- Mass spectrometry-based proteomic analysis objectively quantifies SLFN11 protein and other actionable protein biomarkers in formalin-fixed, paraffin-embedded (FFPE) tissue sections (6).

Hypothesis
- A SLFN11 protein cutoff of 100 amol/kg (predefined based on the assay's limit of quantification) is predictive of benefit in lung cancer patients treated with platinum-containing chemotherapy.

Methods

Figure 1. FFPE tissue sections were obtained from 487 patients with lung cancer of multiple subtypes. A pathologist marked the tumor areas, which were microdissected and solubilized. In each tumor sample, multiple protein biomarkers including SLFN11 were quantified with a mass spectrometric assay.

Results

Figure 2. A. Among NSCLC patients treated with platinum-containing chemotherapy (n=77), those with SLFN11 protein levels above the cutoff (n=28) had better disease-free survival (DFS) than patients with SLFN11 levels below the cutoff (HR: 0.43; 95%CI: 0.22-0.88; p=0.042). The association between SLFN11 and DFS remains significant after adjusting for clinical stage. B. There is no association between SLFN11 protein and DFS in the untreated arm (n=410; SLFN11<100 amol/kg) (n=256).

Figure 3. Using the DFS endpoint, the interaction between SLFN11 and platinum is not significant (p=0.158), although the coefficient shows a clear trend. Reference groups are untreated and untreated (p=0.45).

Figure 4. Among NSCLC patients treated with platinum (n=77), there were no statistically significant differences in overall survival (OS) by SLFN11 expression level.