

			Gene expression of adenocarcinoma related markers			Gene expression of squamous cell carcinoma related markers					Gene expression of neuroendocrine related markers			SSP classification. Total number of rules for each class N=5							
Case	Specimen for pathology review	Specimen for SSP	NAPSA	SFTPG	TTF-1	KRT40	KRT6A	TP73L	KRT5	KRT16	SYP	CHGA	CD56	No of adenocarcinoma class rules fulfilled	No of squamous cell carcinoma class rules fulfilled	No of neuroendocrine class rules fulfilled	SSP histology prediction outcome (bronchoscopy specimen)	Pathology department outcome (bronchoscopy specimen)	Pathology department final diagnosis	Pathology department review	PATHOLOGY department review
1	BB RUL	BB RUL	High	High	Low	Low	Low	Low	Low	Low	Low	Low	Low	5	0	0	Adenocarcinoma	Benign bronchial biopsy	Squamous cell carcinoma (dg later on bronchoscopic rebiopsy)	Squamous cell carcinoma	BB essentially benign with a lot of macrophages and some type II pneumocytes (Napsin A and TTF-1 positive)
2	BB LUL	BB LUL	Low	Low	High	Low	Low	High	High	Low	Low	Low	Low	3	2	3	Neuroendocrine	Benign bronchial biopsy	Adenocarcinoma (on cytology sample from bronchial brush)	NSCLC NOS	BB with benign tissue (some inflammation) NSCLC in cytology (bronchial brush) but insufficient for further analysis (it was suggested that "adenocarcinoma cannot be ruled out")
3	BB LUL	BB LUL	High	Low	Low	Low	High	Low	Low	Low	Low	Low	Low	2	3	3	Squamous cell carcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	BB with adenocarcinoma with typical IHC profile, quite a lot of tumor, practically no bronchial epithelium (no metaplasia)
4	BB LUL	BB LUL	Low	High	Low	Low	High	Low	Low	High	Low	Low	Low	1	3	0	Squamous cell carcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	BB with adenocarcinoma with typical IHC profile, moderate amount of tumor, practically no bronchial epithelium (no metaplasia), inflammation is present
5	SB RUL	BB RUL	Low	Low	High	Low	Low	High	High	Low	High	Low	Low	3	3	2	Squamous cell carcinoma	Benign bronchial biopsy	Adenocarcinoma (dg later on surgical lung biopsy)	Adenocarcinoma	Initial BB without malignancy but a lot of epithelium (no metaplasia). SB later with adenocarcinoma (with signet ring morphology, only CK7 pos, p40 neg, CK5 not stained)
6	FNA EBUS LN 7	FNA lymph node 7	High	High	High	Low	Low	Low	High	High	Low	Low	Low	2	3	1	Squamous cell carcinoma	Lymph node FNA cytology insufficient for diagnosis	Adenocarcinoma (dg later on skin met)	Adenocarcinoma	FNA mostly necrosis and some atypical cells (insufficient for diagnosis). Skin excision metastasis of adenocarcinoma positive for TTF-1
7	BB RLL	BB RLL	High	High	Low	Low	High	Low	High	High	Low	Low	Low	1	3	0	Squamous cell carcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	BB with adenocarcinoma with typical IHC profile, quite a lot of tumor, there is benign bronchial epithelium (no metaplasia)
8	BB LLL	BB LLL	Low	Low	Low	Low	High	High	High	High	Low	Low	Low	1	4	0	Squamous cell carcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	BB with adenocarcinoma with typical IHC profile, a lot of tumor, practically no bronchial epithelium (no metaplasia)
9	BB RUL	BB RUL	Low	Low	High	Low	Low	High	High	Low	High	Low	Low	3	3	2	Squamous cell carcinoma	Bronchial biopsy insufficient for definite diagnosis	Adenocarcinoma (dg later on TTP lung biopsy)	Adenocarcinoma	BB with scant tumor cells suggests NSCLC morphology without definite metaplasia, insufficient for IHC. TTP biopsy later confirms adenocarcinoma with typical IHC profile
10	FNA EBUS LN 4R	FNA lymph node 4R	Low	Low	High	Low	Low	High	High	Low	High	Low	Low	3	3	2	Squamous cell carcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	FNA with adenocarcinoma with typical IHC profile (EGFR L858R)
11	BB LUL	BB LUL	Low	Low	Low	Low	High	High	High	High	Low	Low	Low	1	4	2	Squamous cell carcinoma	Benign bronchial biopsy with cell metaplasia	Adenocarcinoma (dg later on TTP lung biopsy)	NSCLC NOS	BB without malignancy, metaplasia is seen. TTP later with NSCLC only CK7+ (KRAS G12V)
12	BB RLL	BB RLL	Low	Low	Low	Low	High	High	High	High	Low	Low	Low	0	5	1	Squamous cell carcinoma	Malignancy	Adenocarcinoma (dg later on bone met)	NSCLC of unclear type	BB with NSCLC of unclear type, CK5, p40, and TTF-1 in all cells, spindle shaped; handling as adenocarcinoma recommended, but not definite subtyping
13	BB RLL	BB RLL	High	Low	High	Low	Low	High	Low	High	Low	Low	Low	3	3	1	Squamous cell carcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma with typical IHC profile (and known EGFR del19), CK5 not stained as not deemed necessary, one biopsy with tumor, one benign with normal epithelium (no

Supplementary table 2. Review of the cases where the pathology department and SSP predictor outcomes differ.

BB - Bronchial (forceps) biopsy provided by bronchoscopy

SB - Surgical biopsy

FNA - Fine needle aspiration by EBUS

TTP - Transthoracic lung biopsy

LN - Lymph node

RUL - Right upper lobe

RLL - Right lower lobe

LUL - Left upper lobe

LLL - left lower lobe

NSCLC NOS- Non-small cell lung cancer not otherwise specified