Virchows Arch (2016) 468:509–510
DOI 10.1007/s00428-016-1942-9

EDITORIAL

In this issue

Fred T. Bosman [1]

This issue opens with a review paper by Hofman et al. (DOI 10.1007/s00428-016-1910-4), who discuss potential and pitfalls of immunohistochemical staining of PD-L1 in the context of immunotherapy targeting the PD-L1/PD-1 axis. This new approach towards immunotherapy has revolutionized treatment approaches for some tumor types, notably for patients with metastatic lung cancer. However, not all patients respond. As a consequence, there is a need for a biomarker that allows better selection of patients, to improve treatment efficacy and to manage cost. Assessment of PD-L1 expression through immunohistochemical staining has been advocated as one such potential biomarker, as clinical trials targeting the PD-1/PDL1 axis have shown a tendency towards higher efficacy for cases with high expression by immunohistochemistry of PD-L1. This raises several questions, in particular regarding reliability of the test results and the definition of a threshold for positive PD-L1 labelling on biopsy tissue samples. This is a frequent problem for immunohistochemical markers as such, but a burning issue for PD-L1 staining, as some patients respond to treatment targeting PD-L1/PD-1 even though staining is weak or even absent. The authors discuss the main challenges related to detection of PD-L1 by immunohistochemistry as a companion diagnostic test. Time will tell if this test is an efficient approach towards selection of lung cancer (and other) patients for immune checkpoint blockade treatment.

Freudenthaler et al. (DOI 10.1007/s00428-016-1916-y) revisit classical pathology in their retrospective observational study of histopathological and demographic characteristics of amyloid in gastrointestinal biopsies. They identified amyloid in biopsies by Congo red staining in combination with polarization microscopy and, when positive, further classification was undertaken by immunohistochemistry. Amyloid, vascular as well as interstitial, was present in gastrointestinal biopsies mainly in elderly male patients. One third of the amyloid positive biopsies came from the colon, one fourth from the stomach and the rest in decreasing order of frequency from the rectum, duodenum and jejunum/ileum. Over half of the cases were of ALλ amyloid type. Of note, only one out of four of patients with ATTR amyloidosis carried a TTR mutation. Different amyloid types showed differences in age, anatomical distribution and the pattern of deposition.

Brauswetter et al. (DOI 10.1007/s00428-016-1905-1) report on gene copy number alterations of MET and PIK3CA in head and neck cancer, notably in terms of associations with pathological characteristics and prognostic significance of copy number changes of these genes. For MET and PIK3CA copy number analysis was performed by fluorescence in situ, in combination with assessment of expression of EGFR, p16 and Ki-67 by immunohistochemistry. Polysomy of PIK3CA was found in 20 % of cases but amplification in only about 5 %, both associated with shorter disease-specific survival. Cases with a PIK3CA abnormality also had larger tumor volume and downregulated p16 expression. One third of cases had polysomy of chromosome 7, which carries the MET gene, but MET amplification was not found. MET polysomic cases expressed low levels of EGFR. The authors conclude that PIK3CA and MET abnormalities are involved in oncogenesis of certain cancers of head and neck and that these data might serve to develop novel targeted therapies for tumors, which continue to carry a poor prognosis. The cover image is taken from this paper and illustrates PIK3CA amplification by FISH.

Finally, Picanço-Albuquerque et al. (DOI 10.1007/s00428-016-1904-2) assess the association of PTEN loss in a prostate cancer biopsy with the likelihood of increased Gleason grade

✉ Fred T. Bosman
fred.bosman@citycable.ch

[1] Institute of Pathology, University Medical Center (CHUV) of Lausanne, Lausanne, Switzerland

in a subsequent prostatectomy specimen. This had previously been done by immunohistochemistry, which led to the finding that when in a Gleason 3 + 3 biopsy PTEN is not expressed, there is an increased risk that the tumor in the prostatectomy specimen will be graded as Gleason 3 + 4. This is revisited in this paper using a highly sensitive FISH assay. In addition, concordance of PTEN loss by IHC and *PTEN* deletion by FISH were compared. Over a quarter of cases with a *PTEN* deletion were upgraded but only one in ten of control cases. A high level of concordance was found between PTEN immunohistochemistry and *PTEN* deletion by FISH. Only few discordant cases were found, which might be explained by variations in immunoreactivity. Immunohistochemistry and FISH are therefore complementary and PTEN loss in a biopsy consistently predicts higher Gleason grade in a subsequent prostatectomy specimen.