NAPi2b (SCL34A2) is a sodium-dependent phosphate transporter expressed in lung, ovarian, and thyroid cancers. Prior studies and publicly available expression data have suggested an enrichment of expression in lung adenocarcinomas (1, 2, Figure 1).

Introduction

XMT-1536 is a NaPi2b targeting ADC (Antibody Drug Conjugate) composed of a humanized antibody (XMT1533) conjugated to a human/mouse chimeric antibody derived from XMT-1535. MERS67 is a novel anti-NaPi2b antibody and demonstrates differential expression patterns in lung cancer histologic subtypes.

Methods

An IHC assay for MERS67 was established on a Leica BondRx instrument. The assay was performed on a tissue microarray (TMA) of NSCLC tumor tissues. Tumors in the NSCLC array had previously been classified based on morphologic features only. All arrays were scored based on the H-score method. (H= [1 x (% cells 1+) + 2 x (% cells 2+) + 3 x (% cells 3+) ])

Figure 1 (RTK array) data was extracted from dChipSuite (3.4. data of July 27, 2018) and demonstrates differential expression of SLC34A2/NaPi2b between lung squamous and adenocarcinoma. Data from ovarian cancer samples is also shown as a comparison.

Figure 2 (Graphical Rendering of XMT-1536, a NaPi2b Targeting Antibody Drug Conjugate. MERS67 is a human/rabbit chimeric antibody derived from XMT-1535. MERS67 is a human/rabbit chimeric antibody derived from XMT-1535.

Within the tumor tissue microarray, 99 individual cases were evaluable. By morphologic classification 63 cases were SqCC, and 23 cases were ACA. Using an arbitrary cut point of 0.2, 34/63 cases were positive for NaPi2b in SqCC (Figure 4a) and 19/23 cases were positive in ACA (Figure 4b). Immunoreactivity with NaPi2b/MERS67 was noted in ACA (p40 negative/TTF-1 positive) samples (Figure 4a). In comparison lung SCC (p40 positive/TTF-1 negative) were not immunoreactive for NaPi2b/MERS67 (Figure 4b).

Figure 3A NaPi2b H-scores entire set

Figure 3B NaPi2b H scores in samples with tumor differentiation confirmed

Figure 5a NaPi2b in scores in samples with tumor differentiation confirmed

Figure 5b NaPi2b RNA in a high expressing cell line following media change

Figure 5c NaPi2b RNA in a low expressing cell line following media change

Within the tumor tissue microarray, 99 individual cases were evaluable. By morphologic classification 63 cases were SqCC, and 23 cases were ACA. Using an arbitrary cut point of 0.2, 34/63 cases were positive for NaPi2b in SqCC (Figure 4a) and 19/23 cases were positive in ACA (Figure 4b).

Immunoreactivity with NaPi2b/MERS67 was noted in ACA (p40 negative/TTF-1 positive) samples (Figure 4a). In comparison lung SCC (p40 positive/TTF-1 negative) were not immunoreactive for NaPi2b/MERS67 (Figure 4b).

Figure 4a Lung Adenocarcinoma

Figure 4b Lung Squamous Cell Carcinoma

Summary

- MERS67 is an IHC reagent that is a ribonucleotide of XMT-1535, the humanized antibody component of the ADC XMT-1536.
- MERS67 shows differential expression between squamous cell and adenocarcinoma tumor tissues and the effect is accentuated when the tumors are classified by TTF-1 and p40 antibodies, rather than by morphology alone.
- NaPi2b expression in cell lines tends to be low and expression may be impacted by media composition although additional experiments, including analysis at the protein level, are needed to confirm this hypothesis.

2) Lin et al, Clinical Cancer Research, 2015
3) Cerami et al, Cancer Discov, 2012

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