Concordance analysis of PD-L1 CPS between different sample types of head and neck squamous cell cancer

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BACKGROUND

For patients with relapsed or metastasized squamous cell cancer of the head and neck (R/M SCCHN), the PD-L1 Combined Positive Score (CPS) is currently the only predictive biomarker for treatment with anti-PD-1 inhibitors. However, ambiguous results have been delivered regarding the overall response rates (ORR) of immunotherapeutic agents based on PD-L1 status. This issue may be attributed to intratumoral, intertumoral and temporal heterogeneity.

METHODS

Concordance of PD-L1 CPS was investigated in and between primary tumors (biopsied and resected tissue) and paired metastatic lesions (lymph node or distant metastasis) at bicategorical CPS cut-off (≥1) and tricategorical CPS cut-offs (<1 / 1-19 / ≥20). A total 147 tissue blocks from 67 SCCHN patients were collected. CPS agreement between specimens was evaluated using $\chi 2$ or Fisher's exact testing

RESULTS

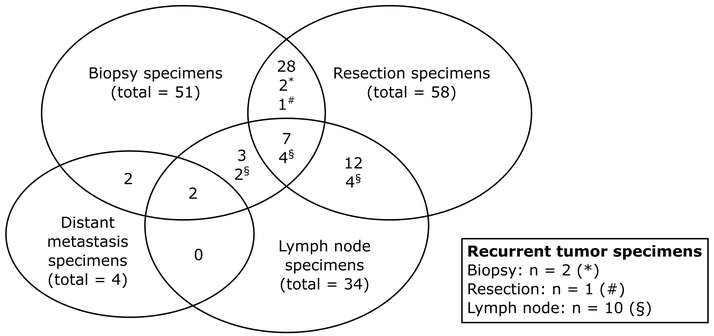

Figure 1. Venn diagram displaying the number of paired tissue specimens

Table 1. PD-L1 CPS concordance between various specimens

CPS n = 42		Biopsy <1	Biopsy ≥1
Resection	<1	1 (2)	4 (10)
	≥1	11 (26)	26 (62)

		Biopsy <1	Biopsy 1-19	Biopsy ≥20
Resection	<1	1 (2)	4 (10)	0
	1-19	10 (24)	17 (41)	1 (2)
	≥20	1 (2)	7 (17)	1 (2)

CPS n = 36		Metastasis <1	Metastasis ≥1
Primary tumor	<1	2 (6)	3 (8)
	≥1	3 (8)	28 (78)

		Metastasis <1	Metastasis 1-19	Metastasis ≥20
Primary tumor	<1	1 (3)	1 (3)	2 (6)
	1-19	4 (11)	16 (44)	2 (6)
	≥20	0	2 (6)	8 (22)

Concordance analysis between paired SCCHN specimens.

Biopsies and paired resection material were severely discordant for 36% and 44% of samples at bicategorical and tricategorical CPS, respectively.

In paired primary tumor – metastatic lesions, disagreement was reached for 16% for bicategorical and 34% for tricategorical CPS and even higher for non-recurrent samples only. Data denote numbers (%).

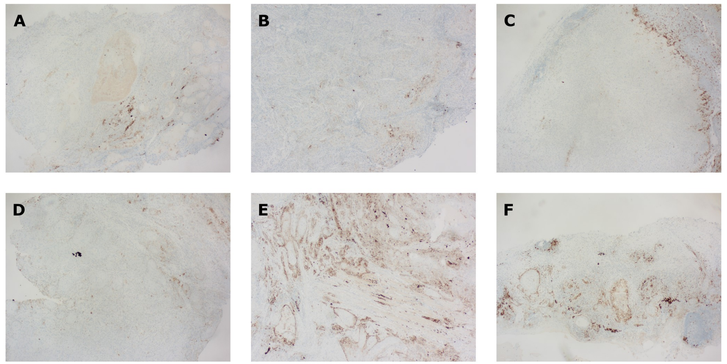

Figure 2. PD-L1 immunohistochemistry stained tissue samples of squamous cell cancer in head and neck.

Each row of images (A, B, C versus D, E, F) represents paired samples retrieved from a different patient: primary tumor biopsies (A,D), resected primary tumors (B,E) and lymph node resections (C, F). In the upper row, all paired tissue samples had concordant PD-L1 CPS (PD-L1 CPS range 1-5).

Paired tissue samples in the lower row had discordant PD-L1 CPS: biopsy (D) = CPS 1-5, resection (E) = CPS 20-40, lymph node (F) = CPS 20

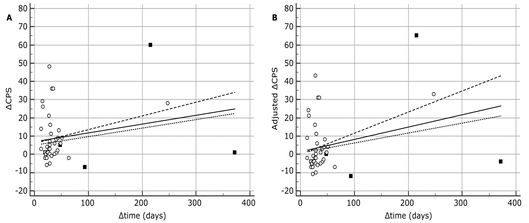

Figure 3. Temporal heterogeneity between biopsy and resection specimens.

Scatter diagram and regression lines for paired biopsy and resection specimens are depicted for A. ΔCPS versus Δtime (all specimens [full line]: n = 42, r = 0.224, *P* = 0.1544; specimens without radiotherapy or chemoradiotherapy prior to resection [dashed line]: n = 37, r = 0.217, P = 0.1974; and specimens with radiotherapy or chemoradiotherapy prior to resection [dotted line]: n = 5, r = 0.250, P = 0.6856); and B. adjusted ΔCPS versus Δtime (all specimens [full line]: n = 42, r = 0.287, P = 0.0651; specimens without radiotherapy or chemoradiotherapy prior to resection [dashed line]: n = 37, r = 0.326, P = 0.0491; and specimens with radiotherapy or chemoradiotherapy prior to resection [dotted line]: n = 5, r = 0.251, P = 0.6843). Dots and rectangles indicate specimens without and with radiotherapy or chemoradiotherapy prior to resection, respectively. CPS, combined positive score

CONCLUSION

INTERTUMORAL, INTRATUMORAL AND TEMPORAL HETEROGENEITY ARE CONFOUNDING FACTORS WHEN DETERMINING PD-L1 CPS ON PAIRED TISSUE SAMPLES. ADDITIONAL RECOMMENDATIONS FOR HIGH-QUALITY SAMPLE SELECTION SHOULD BE PROPOSED AS SPATIOTEMPORAL HETEROGENEITY MAY LEAD TO POTENTIAL UNDER- OR OVERTREATMENT WITH PEMBROLIZUMAB IN PATIENTS WITH R/M SCCHN.

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