Objectives

cancer progression and survival, making PD-1/PD-L1 attractive biomarkers for gynecologic malignancies that may benefit from this new class of targeted therapy.

Methods

1995 cases encompassing all gynecologic malignancies (e.g., cervical, uterine, ovarian, vaginal, vulvar) were evaluated at a central laboratory (Caris Life Sciences) for the presence of PD-1 (NAT105 mouse monoclonal antibody, Ventana) positive when 1+ or greater than 5% cells). Intraepithelial PD-1-positive lymphocytes (IEL) and aberrantly expressed PD-L1 on carcinoma cells were considered specific.

Results

Overall, positive PD-1 expression was 67.9% (1086/1599) and PD-L1 expression was 19.6% (313/1599). Analysis showed the highest PD-1 expression in the following tumor types: endometrial cancer (337/450, 74.9%), ovarian cancer (62/930, 6.6%), and cervical cancer (53/94, 56.1%). Furthermore, the highest PD-L1 expression rates were in carcinosarcomas of the endometrium (53/84, 63.1%) and endometrial cancer (39.7%). Amongst the highest PD-1 expression occurred in granulosa cell tumors (77.8%) and endometrioid endometrial cancer (112/450, 24.9%). In terms of histology, the highest PD-1 expression in the following tumor types: endometrial cancer (39.7%), endometrioid endometrial cancer (112/450, 24.9%). However, numbers are low in vaginal and vulvar cancer, so caution is necessary when interpreting those numbers.

Conclusions

• PD-1 expression is found in all gynecologic malignancies independent of histology. By contrast, PD-1/L1 expression to variable across malignancies and histologies independent of the tumor primary showed few statistically significant differences between specific histologic subtypes of endometrial and ovarian cancer. The HPV-associated cancers of the lower genital tract (e.g. carcinoma of the cervix, vagina and vulva), may derive less benefit based on absence of PD-L1.

• Comparison of histologies independent of the tumor primary showed few statistically significant differences between specific histologic subtypes of endometrial and ovarian cancer. However, endometrial carcinoma was noticeably different from endometrioid ovarian carcinoma, again making the case for immunotherapy in this disease.

Background

PD-1 and PD-L1 expression in 1599 gynecological malignancies – implications for immunotherapy

Thomas J. Herbst1, David Arguello2, Sandeep Reddy3, Zoran Gatalica4

1University of Cincinnati College of Medicine, Cincinnati, OH; 2Carys Life Sciences, Phoenix, AZ

Abstract

Objectives: T-cell suppression via PD-1/PD-L1 interactions plays a central role in cancer progression and survival, making PD-1/PD-L1 attractive therapeutic targets. Clinical trials involving PD-1/PD-L1 targeted immunotherapies have demonstrated marked success in solid tumors including melanoma, non-small cell lung carcinoma (NSCLC), and renal cell carcinoma, and studies indicate PD-L1 expression may identify patients who are more likely to benefit from immunotherapies. These agents and biomarkers could revolutionize management of gynecological malignancies that have developed resistance to standard chemotherapies. The purpose of this study is to identify gynecological malignancies that may benefit from this new class of targeted therapy.

Methods: 1995 cases encompassing all gynecologic malignancies (e.g. cervical, uterine, ovarian, vaginal, vulvar) were evaluated at a central laboratory (Caris Life Sciences) for the presence of PD-1 (NAT105 mouse monoclonal antibody, Ventana) and PD-L1 (B7-H1 antibody) expressing cells. Intratumoral PD-1-positive lymphocytes (IEL) and aberrantly expressed PD-L1 on carcinoia cells were considered specific.

Results: Overall, positive PD-1 expression was 67.9% (1086/1599) and PD-L1 expression was 19.6% (313/1599). Analysis showed the highest PD-1 expression in the following tumor types: endometrial cancer (337/450, 74.9%), ovarian cancer (62/930, 6.6%), and cervical cancer (53/94, 56.1%). Furthermore, the highest PD-L1 expression rates were in carcinosarcomas of the endometrium (53/84, 63.1%) and endometrial cancer (39.7%). Amongst the highest PD-1 expression occurred in granulosa cell tumors (77.8%) and endometrioid endometrial cancer (112/450, 24.9%). In terms of histology, the highest PD-1 expression in the following tumor types: endometrial cancer (39.7%), endometrioid endometrial cancer (112/450, 24.9%). However, numbers are low in vaginal and vulvar cancer, so caution is necessary when interpreting those numbers.

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Background (cont.)

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References


Illustration 1: Mechanism of action for PD-1/PD-L1 axis. Our data suggests the HPV-associated cancers of the lower genital tract (e.g. carcinoma of the cervix, vagina and vulva), may derive less benefit based on absence of PD-L1.

Figure 1 – Overall distribution of PD-1, PD-L1 expression in 1599 gynecological malignancies (listed alphabetically). The overall PD-1 expression rate was 31.6% (497/1599); the PD-L1 expression rate was 19.6% (313/1599). The overall co-expression rate was 15.0% (239/1599). The highest co-expression rates of PD-1 and PD-L1 are in sex-conjunctural tumors and endometrioid cancer. Ovarian carcinoma arising from mesothelial tissue, also have high co-expression rates of PD-1/PD-L1. Lower rates are seen in HPV-associated cancers of the data genital female tract (e.g. cervical, vaginal and vulvar cancer). However, numbers are low in vaginal and vulvar cancer, so caution is necessary when interpreting those numbers.

Figure 2 – Overall distribution of PD-1, PD-L1 expression in endometrial cancer (listed alphabetically). Shown are four histologic subtypes where at least ten specimens had been tested for PD-1 and PD-L1. Mucinous endometrial carcinoma, Serous-cystic tumor, dysgerminoma, FNCL and other tumors were tested fewer than five times (each) and, therefore, are not shown.