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APPENDIX S1

Supplementary materials

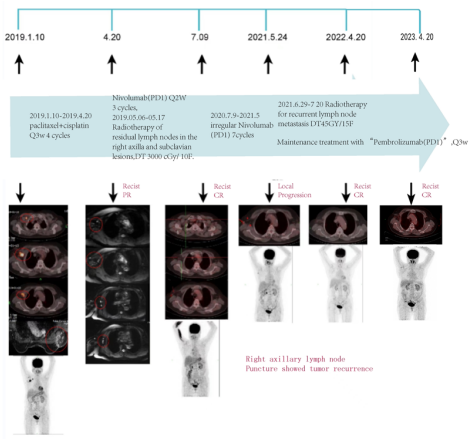
A detailed treatment history of the 3 patients with hidradenocarcinoma treated with PD1 inhibitors in this study is presented below.

Patient No.1 was a 70-year-old female. After a biopsy of the right axillary mass at the local hospital, a pathological diagnosis of hidradenocarcinoma with 4 lymph node metastases (lymph node sizes of 1.1 * 1 * 0.7 cm, 2 * 1.6 * 1 cm, 3 * 2.5 * 1.5 cm, and 4 * 2.5 * 2.5 cm) was made. The patient was then referred to our hospital, and the pathology consultation showed the following: CK5/6+, EMA 2+, TTF-1-, NapsinA-, PAX-8-, GCDFP-15-, GATA-3-, CerbB2 2+, KI67 95%, ER-, PR-, AR-, PDL1 CPS = 1. NGS analysis revealed the following: microsatellite stable (MSS) and TMB-L (TMB =5.0). PET-CT showed the following: multiple lymph node metastases in the right subclavian and right axilla. MRI of breast and gastrointestinal endoscopy excluded tumors originating from other sources. The diagnosis was multiple lymph node metastases of right axillary hidradenocarcinoma. There was no indication for radical surgery after the surgical consultation. The internal medicine department administered the TP scheme for 6 cycles, and there was more than 50% tumor regression after 4 cycles. After multidisciplinary consultation and discussion, PET imaging of the residual lesions in the right axillary and subclavian lymph nodes was used to administer radiotherapy at a dose of 30 Gy/10 F. Chemotherapy was combined with nivolumab immunotherapy beginning in the 5th cycle of chemotherapy. After 3 cycles of immunotherapy, PET-CT was performed to evaluate efficacy. After 27.9 months of follow-up irregular immunotherapy and continuous tumor-free status, PET-CT and pathological puncture analyses confirmed the recurrence of the right axillary lymph node metastasis, and the imaging-visible lesion (irradiation dose 45 Gy/15 F) and the lymph node drainage area of group I and group II (irradiation dose 36.75 Gy/15 F) were again treated with radiotherapy. At the same time, the patient was also treated with pembrolizumab immunotherapy. Subsequent PET-CT confirmed maintenance of the CR status (Fig. S1A).

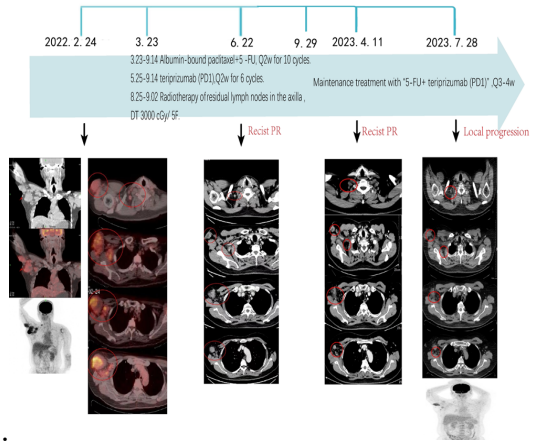
Patient No.2 was a 52-year-old male. He underwent right axillary skin biopsy at a local hospital and was pathologically diagnosed with hidradenocarcinoma. He was referred to our hospital, and the pathological consultations showed the following: CK5/6 (−), CK7(+), EGFR (−), S-100 (−), HMB45 (−), P120 (membrane+), ER (−), PR (−), CerbB-2 (2+), Ki-67 (approximately 30%+), SOX-10 (−), mammaglobin(+),

GATA3(+), GCOFP-15 (partial+), and P40 (−). The PDL1 CPS was 5. NGS analysis revealed the following: MSS and TMB-H (TMB =17.28). Her-2 amplification was not found (no amplification of the Her-2 gene). PET-CT showed multiple lymph node metastases in the right subclavian and right axilla lymph nodes. MRI of the prostate and the skull excluded tumors originating from other sources. The diagnosis was multiple lymph node metastases of right axillary hidradenocarcinoma. After surgical consultation, there was no indication of the need for radical surgery. The patient was treated with TF for 10 cycles and with 6 cycles of immunotherapy with toripalimab from the 5th cycle. In addition, the patient received radiation therapy of residual lymph nodes in the axilla (irradiation dose 3000 cGy/5F). He was subsequently treated with 5FU combined with toripalimab, and follow-up chest CT confirmed maintenance of the PR status. Local progression occurred after 16.4 months. (Fig. S1B).

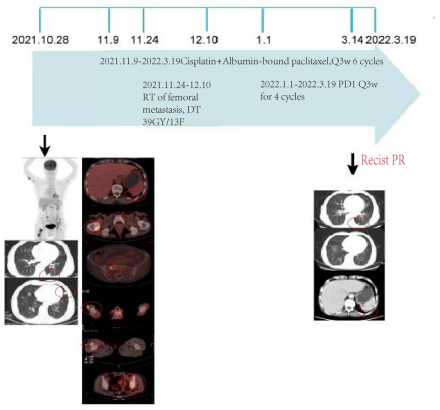
Patient No.3 was a 65-year-old male who underwent right upper arm mass excision at a local hospital with a pathological diagnosis of hidradenocarcinoma. A right upper arm mass was found again 2 months later at a local hospital. Chest CT and bone ECT showed lung metastasis and bone metastasis. One cycle of treatment with an AI regimen was performed, and the mass did not shrink. He was referred to our hospital later for pathological consultation, which showed the following: CK19(+), CK7(+), CK(+), CK8/18(+), EMA(+), CD34(-), Bcl-2(-), CAM5 2(+), vimentin (-), S-100(-), desmin(-), SMA(-), TLE1(-), calponin (-), INI-1 (+), TTF-1 (-), NapsinA (-)VILLIN (-)CDX-2 (-), and CK20 (−). The molecular test results showed the following: negative SYT gene isolation test. The NGS analysis showed the following: MSS and TMB-H (TMB =32.64). PET-CT showed recurrence of hidradenocarcinoma with metastasis to bones, both lungs, perispleen, mediastinum, and multiple lymph nodes in bilateral pulmonary siphons. The diagnosis was hidradenocarcinoma of the right upper arm. After surgical consultation, there was no indication for the need for radical surgery, and TP was given for 6 cycles by the internal medicine department. After multidisciplinary consultation, PET imaging of femoral metastasis was used to administer palliative analgesic radiotherapy at a dose of 39 Gy/13F, and the procedure went well. TP was combined with toripalimab immunotherapy beginning in the 3rd cycle, and chest CT review after 4 cycles of immunotherapy revealed PR (Fig. S1C).



A.



B.



C.

Figure S1

A-C .Three typical cases who achieved complete responses or partial responses after Chemotherapy ± radiotherapy combined with PD-1 inhibitors.(A) Patient 1; (B) Patient 2; (C) Patient 3.

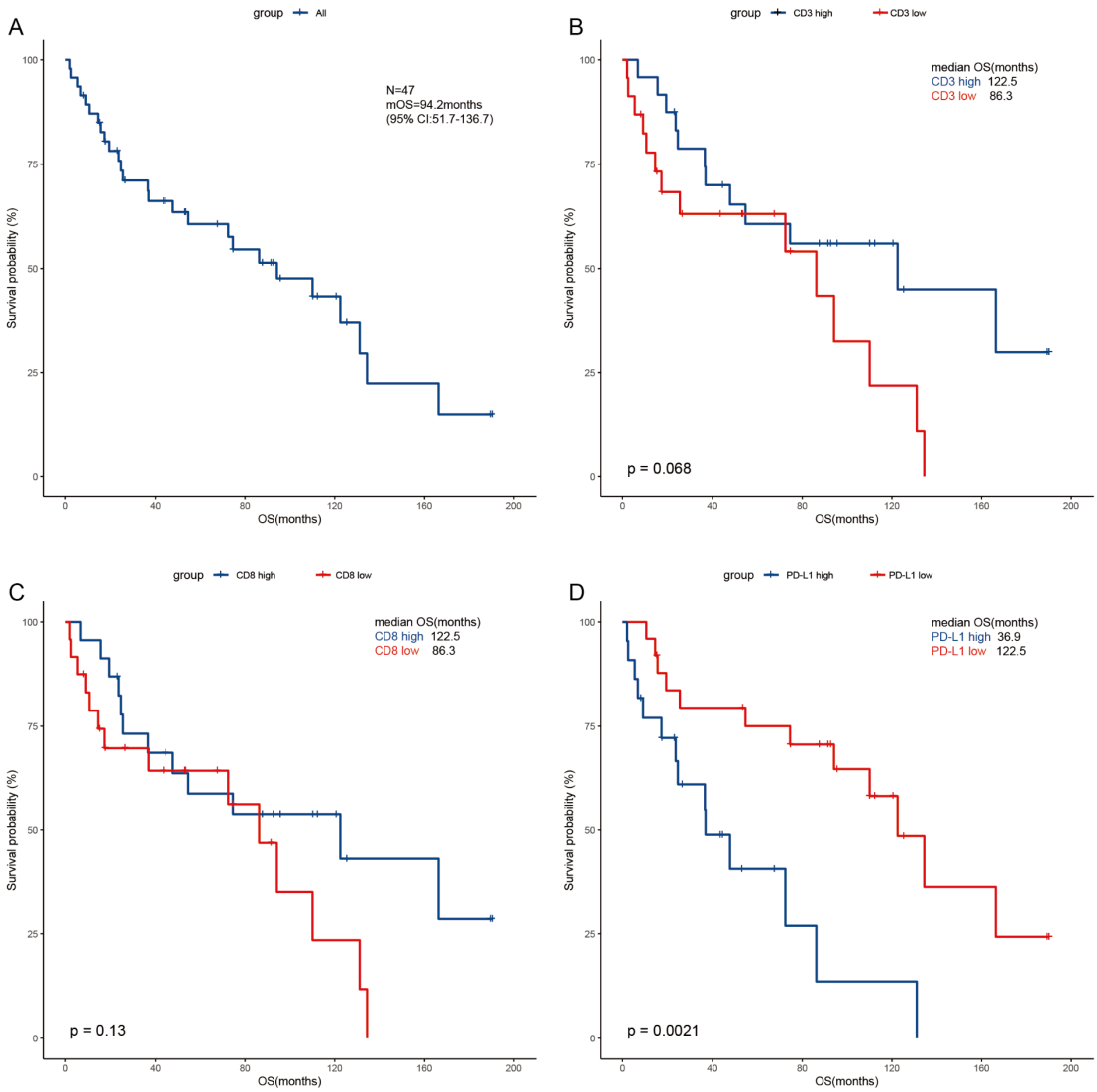


Figure S2 Correlation of biomarker expression between survival

(A) The median overall survival (mOS) in the whole cohort of 47 patients. (B) The median OS in patients with CD3 high VS low. (C)The median OS in patients with CD8 high VS low. (D) The median OS in patients with PD-L1 high VS low.

Table SI Association of biomarker status with clinic features

	CD3 status			CD8 status			PD-L1 status		
	High	**Low**	**P.overall**	**High**	**Low**	**P.overall**	**High**	**Low**	**P.overall**
TNM stage									
I-II	14	9	0.036	14	9	0.190	15	8	0.185
III-IV	10	14		9	15		10	14	
Gender									
Male	16	13	0.678	16	13	0.432	13	16	0.247
Female	8	10		7	11		12	6	
Age(years)									
≤60	11	12	0.886	10	13	0.659	14	9	0.459
＞60	13	11		13	11		11	13	
CD3 status									
High	-	-	-	22	2	**<0.001**	16	8	0.110
Low	-	-	-	1	22		9	14	
CD8 status									
High	-	-	-	-	-	-	16	7	0.056
Low	-	-	-	-	-	-	9	15	
PD-L1 status									
High	-	-	-	-	-	-	-	-	-
Low	-	-	-	-	-	-	-	-	-