Reference	Case	Previous therapies	Anti-HER2 therapy	Treatment responses
Vulvar PD				
Karam et al.[4]	Vulvar and perianal PD	8 surgical excisions + local imiquimod cream	Monthly trastuzumab: 300 mg iv for 12 doses + 260 mg iv for two doses	Almost complete disappearance of vulvar pruritus and pain by the second dose; significant reduction in the extension of vulvar lesions and of the expansive area of associated erythema. After about 12 months of trastuzumab treatment, gradual recurrence of pruritus and pain. After the 14th dose of trastuzumab, stability with recurrent but tolerable flares of PD.
Hanawa et al.[5]	Vulvar EMPD and multiple metastatic lymph nodes	None	Weekly trastuzumab (2 mg/kg) + paclitaxel (80 mg/m2)	No objective response with trastuzumab as single agent. After 4 courses of combination therapy, disappearance of vulvar granulomatous lesions and regression of the pararenal artery lymph node metastasis. Histopathologically, disappearance of most tumor cells in epidermal nests and lymph nodes, almost no remaining Paget cells overexpressing the HER2 protein. Recurrence 1 year after the end of treatment.
Wakabayashi et al.[6]	VPD extending to the urethra, vaginal wall and uterine	Wide local excision and radical hysterectomy + excision of a 24 x 17 mm tumor	Three-weekly trastuzumab (loading dose of 8 mg/kg, 6 mg/kg maintenance dose)	After three courses, partial response with decrease in the pelvic, para-aortic and mesenteric lymph nodes, in the left lung and liver metastasis. After ten courses, near-complete response with the only 3mm residual disease being, scar-like

	cervix	in the right pelvic floor after 5 years		shadow in the left lung. 17 infusions with no disease progression.
Hsieh GL. et al.[7]	VPD with liver lesions, retroperitoneal lymph nodes, spreading to the cervix and upper vagina.	6 surgical excision, 3 laser ablations, topical imiquimod treatment, external beam vulvar radiation and interstitial brachytherapy	Carboplatin (5AUC) + paclitaxel 175mg/m2 every 21 days plus trastuzumab (from cycle 2) for six cycles; _____ TDM1 3.6 mg/kg every 21 days	Complete response to treatment on PET/CT scan after six cycles (PFS of 7 months). _____ Decreased size and metabolic activity of the primary pelvic lesion after cycle 3 and complete response on imaging after cycle 6 (PFS of 6 months).
Non-vulvar PD				
Takahagi et al.[10]	Man with scrotal and inguinal PD relapsed with cutaneous and nodal metastasis	Local excision + lymph node dissection and adjuvant chemotherapy	Weekly trastuzumab (2 mg/kg) + paclitaxel (80 mg/m2)	No objective response with trastuzumab + monthly docetaxel, then changed to weekly paclitaxel. In 3 months almost complete disappearance of the cutaneous lesions. Histopathologically, no residual HER2 positive cells. Recurrence with brain metastasis 6 months after the start of the combination therapy.
Vornicova et al.[11]	Man with perineal PD with	Local excision	Lapatinib + capecitabine	Partial response to chemotherapy combination treatment with doxorubicin and cyclophosphamide (6 cycles), then

	adnexal adenocarcinoma relapsed with bone metastasis			maintenance with letrozole. Progression after 4 months with HER2 positive disease, treated with lapatinib + capecitabine with partial response. After 6 weeks of combination treatment, lapatinib single agent was continued for more than 1 year.
Yu et al.[12]	Two male brothers: A. Scrotal PD with inguinal nodal metastasis, relapsed with abdominal nodal metastasis B - one with genital PD	A - Local excision + bilateral inguinal lymphadenectomy B - Local excision + sentinel lymph node biopsy	Three- weekly trastuzumab (600mg iv)	Trastuzumab therapy was started after lack of response of lymph node metastases to chemotherapy combination treatment with cisplatin + 5-fluorouracil + docetaxel. Partial response after 4 cycles of trastuzumab, with regression of retroperitoneal and iliac artery metastatic lymph nodes.
Watanabe et al.[13]	Man with scrotal and axillary PD and lymph node metastasis, relapsed with iliac nodal metastasis	Local excision	Three-weekly trastuzumab (6 mg/kg iv)	Partial response after 7 weeks. Progression 5 months after the start of trastuzumab.
Shin et al.[14]	Man with	Local	Maintenance	Progression after the interruption of

	scrotal PD with repeated relapses of disease with nodal metastasis	excision and adjuvant combination therapy with trastuzumab + docetaxel + carboplatin	with trastuzumab single agent, then lapatinib and capecitabine after first progression, then T-DM1.	maintenance therapy with trastuzumab single agent. Partial response to lapatinib, maintained for several months. After progression, partial response with lapatinib + capecitabine. After progression, treatment with T-DM1 with radiologic complete response for almost 1 year.
Nordmann et al.[15]	Man with scrotal PD and nodal metastasis	Radiotherapy	Three- weekly trastuzumab (6 mg/kg iv) + carboplatin 300 mg after progression during lapatinib	Local and pulmonary relapse 6 months after radiotherapy, treated with lapatinib (activating ERBB2 point mutation) with no response. Then, treatment with trastuzumab + carboplatin was started after immunohistochemical confirmation of HER2 positivity, with complete clinical response and partial nodal and pulmonary response. Progression of disease after 10 cycles.

Case reports of HER2-positive Paget's disease (PD) treated with anti-HER2 agents.T-DM1, trastuzumab emtansine.