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Supplementary table 1 – Human papillomavirus (HPV) types detected in penile cancer tumor tissue

| HPV types | N = 41 |
|------------------|---------------|
| 16 | 29 |
| 18 | 3 |
| 33 | 4 |
| 35 | 1 |
| 51 | 3 |
| 52 | 1 |

Supplementary table 2: Patient characteristics stratified by the HPV status

| Characteristic | Overall N = 81¹ | HPV negative N = 40¹ | HPV positive N = 41¹ |
|---------------------------|---------------------------------------|--|--|
| Age group | | | |
| 74 or younger | 61 (75%) | 30 (75%) | 31 (76%) |
| 75 or older | 20 (25%) | 10 (25%) | 10 (24%) |
| Phimosis/balanitis | 48 (59%) | 27 (68%) | 21 (51%) |
| Penile surgery | | | |
| Penile sparing surgery | 48 (59%) | 22 (55%) | 26 (63%) |
| Partial amputation | 26 (32%) | 15 (38%) | 11 (27%) |
| Total amputation | 7 (8.6%) | 3 (7.5%) | 4 (9.8%) |
| Inguinal surgery | | | |
| Active surveillance | 9 (11%) | 7 (18%) | 2 (4.9%) |
| Bilat. DSNB | 34 (42%) | 16 (40%) | 18 (44%) |
| Unilat. DSNB/ILND | 17 (21%) | 6 (15%) | 11 (27%) |
| Bilat. ILND | 21 (26%) | 11 (28%) | 10 (24%) |
| Pelvic surgery | | | |
| Active surveillance | 71 (88%) | 36 (90%) | 35 (85%) |
| Unilat. PLND | 3 (3.7%) | 1 (2.5%) | 2 (4.9%) |
| Bilat. PLND | 7 (8.6%) | 3 (7.5%) | 4 (9.8%) |
| Follow up (months) | 39 (17, 84) | 38 (14, 87) | 39 (19, 74) |

DSNB = Dynamic sentinel node biopsy; HPV = Human papillomavirus; ILND = Inguinal lymph node dissection; PLND = Pelvic lymph node dissection. ¹Median (IQR); n (%).

Supplementary table 3. [¹⁸F]-FDG PET/CT findings stratified by HPV status

| Characteristic | Overall N = 81¹ | HPV negative N = 40¹ | HPV positive N = 41¹ |
|---------------------------------------|---------------------------------------|--|--|
| Inguinal findings | | | |
| Negative | 30 (37%) | 17 (43%) | 13 (32%) |
| Unilateral | 28 (35%) | 11 (28%) | 17 (41%) |
| Bilateral | 23 (28%) | 12 (30%) | 11 (27%) |
| Single/multiple inguinal nodes | | | |
| Negative | 30 (37%) | 17 (43%) | 13 (32%) |
| Unilat. single | 15 (19%) | 4 (10%) | 11 (27%) |
| Unilat. multiple | 13 (16%) | 7 (18%) | 6 (15%) |
| Unilat. single/multiple | 6 (7.4%) | 3 (7.5%) | 3 (7.3%) |
| Bilat. single | 9 (11%) | 5 (13%) | 4 (9.8%) |
| Bilat. multiple | 8 (9.9%) | 4 (10%) | 4 (9.8%) |
| Pelvic findings | | | |
| Negative | 70 (86%) | 35 (88%) | 35 (85%) |
| Unilateral | 8 (9.9%) | 4 (10%) | 4 (9.8%) |
| Bilateral | 3 (3.7%) | 1 (2.5%) | 2 (4.9%) |

HPV = Human papillomavirus; PET/CT = positron emission tomography combined with computed tomography; ¹n (%); Median (IQR).

Supplementary table 4: Histopathological characteristics stratified by the HPV status

| Characteristic | Overall N = 81¹ | HPV negative N = 40¹ | HPV positive N = 41¹ |
|------------------------------------|---------------------------------------|--|--|
| pT stage | | | |
| T1 | 45 (56%) | 24 (60%) | 21 (51%) |
| T2 | 21 (26%) | 10 (25%) | 11 (27%) |
| T3 | 14 (17%) | 5 (13%) | 9 (22%) |
| T4 | 1 (1.2%) | 1 (2.5%) | 0 (0%) |
| WHO Grade | | | |
| 1 | 7 (8.6%) | 6 (15%) | 1 (2.4%) |
| 2 | 35 (43%) | 20 (50%) | 15 (37%) |
| 3 | 39 (48%) | 14 (35%) | 25 (61%) |
| LVI | 20 (25%) | 5 (13%) | 15 (37%) |
| pN stage | | | |
| pN0 | 51 (63%) | 28 (70%) | 23 (56%) |
| pN1 | 5 (6.2%) | 2 (5.0%) | 3 (7.3%) |
| pN2 | 11 (14%) | 3 (7.5%) | 8 (20%) |
| pN3 | 14 (17%) | 7 (18%) | 7 (17%) |
| No. positive inguinal nodes | | | |
| 0 | 51 (63%) | 28 (70%) | 23 (56%) |
| 1 | 11 (14%) | 5 (13%) | 6 (15%) |
| 2 | 8 (9.9%) | 3 (7.5%) | 5 (12%) |
| 3 or more | 11 (14%) | 4 (10%) | 7 (17%) |

HPV = Human papillomavirus; LVI = Lymphovascular invasion; pN = Pathological N stage; pT = Pathological T stage; WHO = World Health Organization. ¹n (%).

Supplementary Table 5. Diagnostic accuracy of [¹⁸F]-FDG PET/CT for detection of inguinal lymph node metastasis stratified by HPV status

| Characteristic | Overall¹ | HPV negative¹ | HPV positive¹ |
|-----------------------|----------------------------|---------------------------------|---------------------------------|
| All patients | | | |
| No. pts/groins | 81/162 | 40/80 | 41/82 |
| False negative | 7 (4.3%) | 3 (3.8%) | 4 (4.9%) |
| False positive | 39 (24%) | 21 (26%) | 18 (22%) |
| True Negative | 81 (50%) | 42 (53%) | 39 (48%) |
| True positive | 35 (22%) | 14 (18%) | 21 (26%) |
| cN0 patients | | | |
| No. pts/groins | 42/84 | 20/40 | 22/44 |
| False negative | 3 (3.6%) | 2 (5.0%) | 1 (2.3%) |
| False positive | 24 (29%) | 10 (25%) | 14 (32%) |
| True Negative | 56 (67%) | 28 (70%) | 28 (64%) |
| True positive | 1 (1.2%) | 0 (0%) | 1 (2.3%) |
| cN+ patients | | | |
| No. pts/groins | 39/78 | 20/40 | 19/38 |
| False negative | 4 (5.1%) | 1 (2.5%) | 3 (7.9%) |
| False positive | 15 (19%) | 11 (28%) | 4 (11%) |
| True Negative | 25 (32%) | 14 (35%) | 11 (29%) |
| True positive | 34 (44%) | 14 (35%) | 20 (53%) |

cN0 = clinically node negative; cN+ = clinically node positive; HPV = Human papillomavirus.
¹n (%).

Supplementary Table 6. Diagnostic accuracy of [¹⁸F]-FDG PET/CT for detection of a pelvic lymph node metastasis stratified by HPV status

| Characteristic | Overall N = 17¹ | HPV negative N = 7¹ | HPV positive N = 10¹ |
|-----------------------|---------------------------------------|---|--|
| Status | | | |
| False negative | 4 (24%) | 1 (14%) | 3 (30%) |
| False positive | 3 (18%) | 2 (29%) | 1 (10%) |
| True Negative | 7 (41%) | 3 (43%) | 4 (40%) |
| True positive | 3 (18%) | 1 (14%) | 2 (20%) |

HPV = Human papillomavirus. ¹n (%).