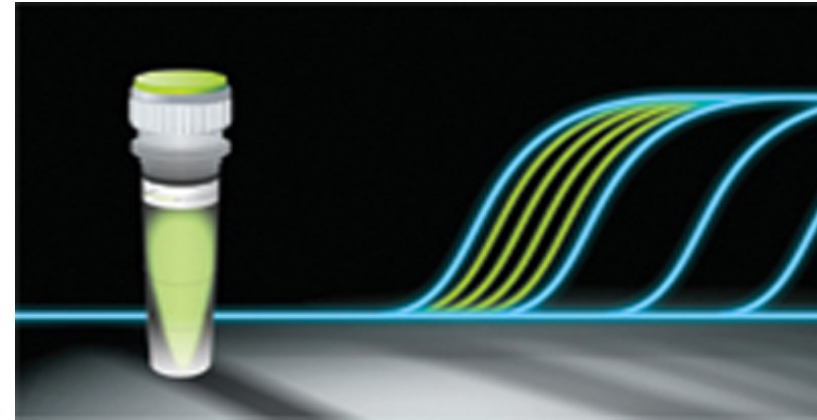
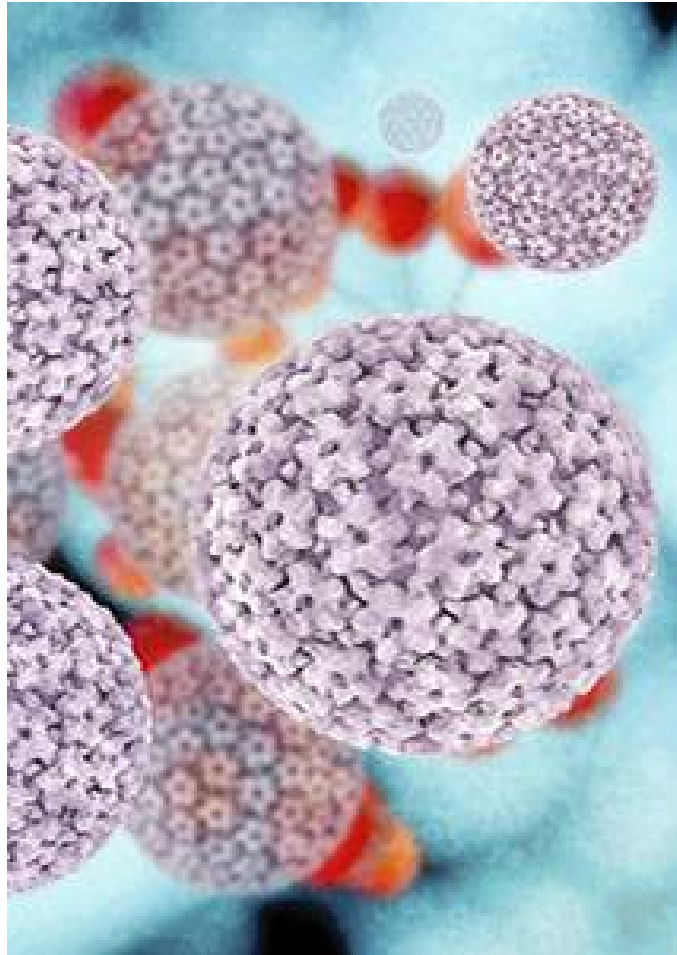
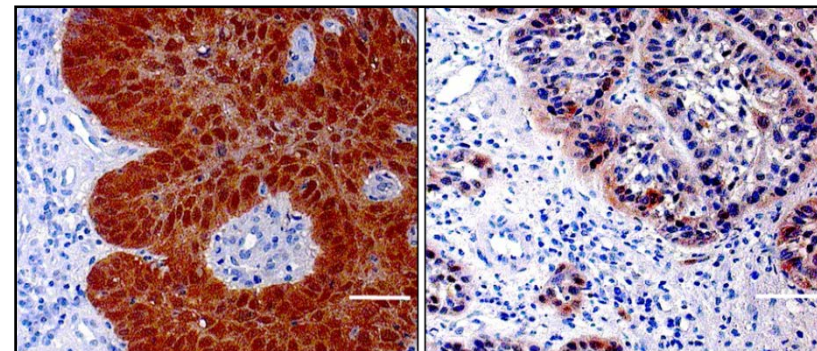


Human papilloma virus in anal
squamous cell carcinoma

Measurement of HPV viral load and HPV16 in anal squamous cell carcinoma (ASCC)



Genotype-specific quantitative PCR



Immunohistochemistry HPV16 (p16)

Human papilloma virus positivity is common and associated with better prognosis in ASCC

Author	Pts (n)	HPV total (%)	HPV16 (%)	Oncological outcome (vs HPV-negative)
Körber	105	83	77	Better local control, PFS, OS
Mai	106	68	n.a.	Better 5 years local control
Rödel	95	96	79	Better local control, CSS and OS
Serup-Hansen	143	88	80	Better DSS and OS
Gilbert	153	n.a.	90	Better local control, OS
Baricevic	110	95	89	Better relapse-free survival and OS

However: HPV is not sufficient as predictive biomarker as it is positive in 80-90%, whereas recurrence occurs in 40% of patients with locally-advanced disease

HPV detection in liquid biopsies

- Detection of circulating tumor HPV DNA (**ctDNA**)
- Detection of HPV16/HPV18 DNA using digital droplet PCR (**ddPCR**)
- Offers possibility for **serial non-invasive monitoring** before, during and after treatment
- Prognostic role of HPV ctDNA **only assessed in few studies** to date

HPV ctDNA after primary chemoradiotherapy in non-metastatic ASCC

- N=33 Patients with **locally advanced ASCC**
- Blood samples taken at **baseline** (n=33) and **post-treatment** (n=18)
- **29/33** patients at baseline had **detectable HPV ctDNA**
- Only 3/18 patients had detectable post-treatment ctDNA that experienced rapid metastatic relapse

Residual HPV ctDNA levels after chemoradiotherapy was associated with poor oncological outcome

HPV ctDNA in liquid biopsies in metastatic ASCC

- Case report in metastatic ASCC, serial liquid biopsies
- 1 patient with sustained partial response with **Nivolumab**

	Baseline	Week 2	Week 4	Week 6	Week 8	Week 10	Week 24
HPV ctDNA (copies/ml)	3731	4074	564	156	77	108	158
Change in tumor size from baseline (%)	0 (Reference)				-75%		-80%

Early and very significant decrease of HPV ctDNA during sustained partial response with Nivolumab from the baseline to week 6 followed by a plateau

HPV ctDNA assessment in the EPITOPES-HPV02 trial in metastatic ASCC

- Phase II single-arm trial assessing DCF chemotherapy in metastatic ASCC, n=57
- HPV ctDNA was detectable in **91% of baseline samples**
- **High baseline HPV ctDNA** associated with **worse PFS** ($p = .04$)
- Detectable ctDNA **after chemotherapy** was associated with **worse PFS** ($p < .001$) and worse OS (OR=7.0, $p=.02$)

Significant prognostic impact of HPV ctDNA level before first-line DCF chemotherapy and HPV ctDNA negativity after chemotherapy completion

Conclusion

- **HPV positivity** in **80-90%** of patients with ASCC
- **HPV16 DNA load** and **HPV16 tumor** expression are significant **prognostic** factors for oncological outcome after chemoradiotherapy in ASCC
- Recent studies highlight the **prognostic** value of **HPV ctDNA** after chemoradiotherapy and palliative systemic treatment in ASCC
- The prognostic significance of HPV will be assessed in the **RADIANCE trial**