New Breakthroughs in Rare Cancers: Developments in Anal Cancer in the Last 12 Months

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Disclosures

• Grants
  • Advaxis
  • Bristol Myers Squibb
  • Forty-seven Inc.
  • Genentech/Roche

• Advisory Boards
  • Advaxis
  • Bayer
  • EMD-Serono
  • Forty-Seven
  • Genentech/Roche
  • Hutchinson
  • LSK
  • Sirtex
  • Taiho
Discussion Points

• Incidence
• Prior treatment guidelines
• New immunotherapeutic developments
• Changes in treatment guidelines
• Ongoing/Developing Clinical Trials
Incidence of Anal Cancer in 2019

- Over 35,000 new cases annually of anal cancer are diagnosed worldwide.
- New anal cancer cases have been rising on average 2.2% each year over the last 10 years. Death rates have been rising on average 2.9% each year over 2006-2015.

Sources:
- www.seer.gov
- St. Laurent et al: Curr Probl Cancer, 2018
- Siegel et al: CA Cancer Clin, 2019
Salient Facts of Anal Cancer

- SCCA is associated with HPV > 90% of all cases
- The majority of patients will present with early stage disease and will be treated with concurrent chemoXRT with sphincter preservation and curative intent.
  - Risk factors for residual or recurrent disease include $T > 4$ cm and $N+$
- Metastatic disease will develop in < 20% of patients
- Historically prior to 2018, no well established chemotherapy regimen for metastatic pts
  - 5-yr OS = 32%

“5-FU/Cisplatin is **recommended** for metastatic disease. No other regimens have been found to be effective.”
# Previously Published Regimens in Metastatic Anal Cancer

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Agents</th>
<th>ORR</th>
<th>Med PFS (months)</th>
<th>Med OS (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilking 1985</td>
<td>15</td>
<td>Vincristine, bleomycin &amp; High-dose methotrexate</td>
<td>3/12 (25%)</td>
<td>2M</td>
<td>NR</td>
</tr>
<tr>
<td>Ajani 1989</td>
<td>3</td>
<td>5-FU/CDDP</td>
<td>NA</td>
<td>17M (2 of 3)</td>
<td>NA</td>
</tr>
<tr>
<td>Faivre 1999</td>
<td>18</td>
<td>5-FU/CDDP</td>
<td>65% (CR=15%)</td>
<td>4M</td>
<td>NA</td>
</tr>
<tr>
<td>Hainsworth 2001</td>
<td>60 (4 with anal cancer)</td>
<td>TPF (max = 4 cycles)</td>
<td>65% (CR = 25%)</td>
<td>26M</td>
<td>NR</td>
</tr>
<tr>
<td>Jhawer 2006</td>
<td>20</td>
<td>Mitomycin C, adriamycin, cisplatin, bleomycin-CCNU</td>
<td>12/20 (60%)</td>
<td>8M</td>
<td>15</td>
</tr>
<tr>
<td>Alcindor 2008</td>
<td>5</td>
<td>Taxol (1st and 2nd line)</td>
<td>60%</td>
<td>Range: 3-8M</td>
<td>Range: 4-20M</td>
</tr>
<tr>
<td>Abbas 2011</td>
<td>7</td>
<td>Taxol (2nd line)</td>
<td>57%</td>
<td>Range: 2-8M</td>
<td>Range: 5-14M</td>
</tr>
<tr>
<td>Kim 2013</td>
<td>8</td>
<td>DCF</td>
<td>CR: 50% (3/4 resected)</td>
<td>19-88M</td>
<td>1 yr: 62.53M%</td>
</tr>
<tr>
<td>Eng, 2014</td>
<td>77</td>
<td>Carbo/Taxol and 5-FU/CDDP</td>
<td>33% - 57%</td>
<td>7M (5M vs. 16M)</td>
<td>22M (17M vs. 53M)</td>
</tr>
<tr>
<td>Kim, 2018</td>
<td>69</td>
<td>Docetaxel, cisplatin, and 5-FU (DCF)</td>
<td>89%</td>
<td>11M</td>
<td>NR</td>
</tr>
</tbody>
</table>
INTERAACT/EA#2133, A MULTICENTER OPEN LABEL RANDOMIZED PHASE II TRIAL OF CISPLATIN (CDDP) PLUS 5 FLUOROURACIL (5FU) VS CARBOPLATIN (C) PLUS WEEKLY PACLITAXEL (P) IN PATIENTS WITH INOPERABLE LOCALLY RECURRENT OR METASTATIC TREATMENT NAÏVE DISEASE: AN INTERNATIONAL RARE CANCERS INITIATIVE (IRCI) TRIAL

Objective: identify best chemotherapy backbone for development
1) Primary endpoint: RR
2) Secondary endpoints: PFS, OS, correlatives, and QOL, etc.

Arm A
- Cisplatin 75 mg/m2 day 1 + 5FU 1000mg/m2 infusion/24 hours/4 days q28 days
- Treatment for 6M and cont at the discretion of the investigator
- Substratification: HIV+/HIV-, HPV status, and prior XRT
- CT scans: q3M
- N=91

Arm B
- Carboplatin (AUC = 5) + Taxol (weekly) q 28 days

Study PI’s – S Rao, US PI: C Eng

Rao et al: ESMO, 2018
InterAACT/EA#2133 Primary Endpoint

<table>
<thead>
<tr>
<th>Response (RECIST)</th>
<th>Carboplatin-Paclitaxel N=39</th>
<th>Cisplatin-5FU N=35</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%) CI</td>
<td>N (%)</td>
</tr>
<tr>
<td>CR</td>
<td>5 12.8</td>
<td>5 14.3</td>
</tr>
<tr>
<td>PR</td>
<td>18 46.2</td>
<td>15 42.9</td>
</tr>
<tr>
<td>SD</td>
<td>10 25.6</td>
<td>7 20.0</td>
</tr>
<tr>
<td>PD</td>
<td>6 15.4</td>
<td>8 22.9</td>
</tr>
<tr>
<td>CR/PR</td>
<td>23 59</td>
<td>20 57</td>
</tr>
</tbody>
</table>

95% CI: [42.1-74.4] 95% CI: [39.4-73.7]

Rao et al: ESMO, 2018
### InterAACT/EA#2133 Grade ≥ 3 Events

<table>
<thead>
<tr>
<th>Toxicity ≥ Grade 3</th>
<th>Carboplatin Paclitaxel</th>
<th>Cisplatin-5FU</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=42</td>
<td>N=42</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Anaemia</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Fatigue</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Mucositis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Thromboembolism</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Overall</td>
<td>30</td>
<td>71</td>
</tr>
<tr>
<td>SAEs</td>
<td>15</td>
<td>36</td>
</tr>
</tbody>
</table>

Rao et al, ESMO 2018
InterAACT/EA#2133: Secondary Endpoints of PFS and OS

Median PFS
- Carboplatin Paclitaxel: 8.1mths
- Cisplatin/5FU: 5.7mths
p = 0.375

Median OS
- Carboplatin/Paclitaxel: 20M
- Cisplatin/5FU: 12.3M
p = 0.014

Rao et al, ESMO 2018
NCCN Guidelines Version 1.2019
Anal Carcinoma

### CLINICAL PRESENTATION

- Anal canal cancer
  - Biopsy: squamous cell carcinoma

### WORKUP

- Digital rectal examination (DRE)
- Inguinal lymph node evaluation
- Consider biopsy or FNA if suspicious nodes
- Chest/abdominal CT + pelvic CT or MRI
- Consider PET/CT or PET/MRI (if available)
- Anoscopy
- HIV testing (if HIV status unknown)
- Gynecologic exam for women, including screening for cervical cancer

### CLINICAL STAGE

- Locoregional disease

### PRIMARY TREATMENT

- Mitomycin/5-FU + RT
- Mitomycin/capecitabine + RT
- 5-FU/cisplatin + RT (category 2B)

- Metastatic disease

- 5-FU/cisplatin ± RT
- Carboplatin/paclitaxel ± RT (preferred)
- FOLFOX ± RT
- FOLFICIS ± RT

- Nivolumab or Pembrolizumab

See Follow-up Therapy and Surveillance (ANAL-3)
Immune Checkpoint Inhibition
HPV and the Role of Immunotherapy

Smola et al: Viruses, 2017
NCI9673 (Part A): Multi-Institutional Phase II ETCTN Study of Nivolumab in Previously Treated Metastatic SCCA

Patients with metastatic squamous cell carcinoma of the anal canal
- Treated with at least one prior therapy for metastatic disease
- No prior immune therapies received as part of cancer treatment

12 patients treated initially with nivolumab 3 mg/kg IV every 2 weeks

Patients will be followed for best response using RECIST criteria 1.1

0 responses
Stop trial

≥1 response
Expand trial to include 25 additional patients with metastatic SCCA

• Simon Optimal, two-stage phase II study, $H_0$: $p \leq 0.05$ and an alternative hypothesis $H_a$: $p \geq 0.20$,
• $\alpha = 0.10$ and $\beta = 0.10$
• *Unmet need and completed enrollment in < 8M

• Diagnostic imaging was completed every 6 wks
• Primary endpoint: RR
• ECOG PS = 0-1
• HIV+ (CD4 > 300) and Hepatitis patients were not excluded
• PD-L1 was not required
• Exploratory correlatives were collected.

Morris et al...Eng: Lanc Onc, 2017
### NCI9673 (Part A): Patient Demographics

<table>
<thead>
<tr>
<th>N=37</th>
<th>Median</th>
<th>Range: 51-64 y/o</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median age</strong></td>
<td>56 y/o</td>
<td></td>
</tr>
<tr>
<td><strong>Race, N (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>34 (87.2)</td>
<td>-</td>
</tr>
<tr>
<td>Black</td>
<td>3 (7.7)</td>
<td>-</td>
</tr>
<tr>
<td>Asian</td>
<td>2 (5.1)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>11 (28)</td>
<td>-</td>
</tr>
<tr>
<td>F</td>
<td>28 (72)</td>
<td>-</td>
</tr>
<tr>
<td><strong>ECOG PS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>10 (27)</td>
<td>-</td>
</tr>
<tr>
<td>1</td>
<td>27 (73)</td>
<td>-</td>
</tr>
<tr>
<td><strong>HIV+</strong></td>
<td>2 (5.1)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Median lines of prior treatments</strong></td>
<td>2</td>
<td>Range: 1-7</td>
</tr>
<tr>
<td><strong>Median # of cycles provided</strong></td>
<td>6</td>
<td>Range: 1-23</td>
</tr>
</tbody>
</table>

Data cutoff date: 5/15/16

Morris et al...Eng: Lanc Onc, 2017
NCI9673 (Part A) Endpoints: RR, PFS and OS

- ORR = 24% (1CR > 2yrs)

Morris et al...Eng: Lanc Onc, 2017
## NCI9673 (Part A): Toxicities of Therapy

<table>
<thead>
<tr>
<th>Toxicity (N=37)</th>
<th>Grade (%)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>17 (46%)</td>
<td>7</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>13 (35%)</td>
<td>11</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>8 (22%)</td>
<td>2</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>1 (3%)</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>8 (22%)</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>8 (22%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anorexia</td>
<td>5 (14%)</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight loss</td>
<td>5 (14%)</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthralgia</td>
<td>3 (8%)</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>3 (8%)</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphedema</td>
<td>1 (3%)</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonitis</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>2 (5%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Morris et al...Eng: Lanc Onc, 2017
NCI9673 (Part A): Baseline Correlatives

MDACC:
- We were able to consent 16 of 18 pts (89%)
- 13 pts (4 responders, 9 NR) with baseline tissue samples
- 9 pts (4 responders, 5 NR) were evaluable for paired sampling
- Findings demonstrated by IHC:
  - Increased CD8 and PD-L1 in responders at baseline
- Findings by flow:
  - Increased dual expression of PD-L1 and LAG-3 and TIM-3 at baseline

Morris et al...Eng: Lanc Onc, 2017
30 patients on the NCI9673 study had pretreatment cfDNA analyzed for mutation profiling on Guardant 70-gene panel.

While TP53 (29%) and PIK3CA (23%) were the most commonly mutated genes, no associations were noted between response to therapy and the presence/absence of mutations.

Median 1.6 mutations per patient noted in the 30 patients here.

These results are consistent with other reports, with one recent series of SCCA patients using a 255-gene panel showed 3.6 mutations/patient.

Mutation burden does not appear to be a driver for immunogenicity to anti-PD-1 therapy in SCCA.

Pembrolizumab in Metastatic Anal Cancer

- 43 patients screened for PD-L1 expression
- 32 (74%) were PD-L1 positive tumors
- 25 pts were eligible

**Table 3. Best overall response in patients with SCC histology (N = 24)**

<table>
<thead>
<tr>
<th>Best response</th>
<th>n</th>
<th>%</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete response</td>
<td>0</td>
<td>0</td>
<td>0–14</td>
</tr>
<tr>
<td>Partial response</td>
<td>4</td>
<td>17</td>
<td>5–37</td>
</tr>
<tr>
<td>Stable disease</td>
<td>10</td>
<td>42</td>
<td>22–63</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>9</td>
<td>38</td>
<td>19–59</td>
</tr>
<tr>
<td>Not assessed(^b)</td>
<td>1</td>
<td>4</td>
<td>0–21</td>
</tr>
</tbody>
</table>

\(^a\)All responses are confirmed.
\(^b\)Patient discontinued therapy because of toxicity before the first post-baseline response assessment.

CI, confidence interval; SCC, squamous cell carcinoma.

Ott et al: Annals Onc, 2017
Change in 2018 NCCN Guidelines

NCCN Guidelines Version 1.2018
Anal Carcinoma

TREATMENT

Locally recurrent
- APR + groin dissection, if positive inguinal nodes

Metastatic disease
- 5-FU/cisplatin ± RT
  - Nivolumab
  - Pembrolizumab
- Carboplatin/paclitaxel ± RT
- FOLFOX ± RT

SURVEILLANCE

- Inguinal node palpation every 3-6 mo for 5 y
- Chest/abd/pelvic CT with contrast annually for 3 y
- Metastatic disease, see below

Progression on serial exams
- Re-evaluate in 4 wks

Regression or no progression on serial exams
- Complete remission

If progression or persistent disease
- Continue observation and re-evaluate at 3 mo intervals

See Surveillance (ANAL-3)
Ongoing and/or Pending Trials
EA2165: Randomized Phase II Trial of Nivolumab Following ChemoXRT in High-Risk Locally Advanced Anal Cancer (T ≥ 4 cm, N+)

Pre-register

High Risk Anal Cancer

RANDOMIZE

5FU/Capecitabine+ Mitomycin or 5FU+CDDP and concurrent RT

Observation

Nivolumab q4 weeks x 6

Stratification Factors: Nodal status, HIV, RT dose N=73/200

Study PI’s: L. Rajdev Co-PI’s: C. Eng and A. Benson SWOG PI: V. Morris

Primary endpoint: 2-yr DFS (Goal of 62.5% vs. 45%)
Secondary endpoints: CFS, OS, Toxicity
NCI9673 (Part B): Randomized Phase II ETCTN Study of Nivolumab +/- Ipilimumab in Metastatic SCCA of the Anal Canal

Patients with metastatic squamous cell carcinoma of the anal canal
- Treated with at least one prior therapy for metastatic disease
- No prior immune therapies received as part of cancer treatment

N= 40/100

Nivolumab
(480 mg IV q4 weeks)

Nivo + Ipilimumab
(480mg IV q4 weeks) +
1 mg/kg IV q8 weeks)

Primary endpoint: PFS
Secondary endpoints: OS, RR, and SAE’s
Exploratory correlatives to be collected.
NCI9673 (Part B)– Biomarker Analysis (PI’s: Wistuba and Eng)

Enrollment

N= 100 Patients

3 X Biopsy
3 X Blood

3 X Biopsy
3 X Blood

Baseline

Treatment

Week 9

Tx Discontinuation

Biopsy (→) Optional

Core 1 FFPE

Histology
IHC
mIF

Core 2 Fresh

Flow cytometry (TILs)

Core 3 FFPE

mRNA (Nanostring, HTG Edge-Seq)
TBD

Core 4-5 Fresh Frozen

RNA-seq
DNA (WES, targeted, TCR/B)

Blood (→) Mandatory

1 x 10 ml Red Top Tubes
9 x 10 ml Sodium Heparin Green Top Tubes

• Plasma (cfDNA)
• Cytokines (MSD)
• PBMCs (Germline DNA)
• Flow Cytometry Panels (2 Panels)
• Functional T cell assays
• TCR sequencing

Supported by NCI IMT Supplemental Grant: 3P30CA016672-41S9 and BMS
A Phase I Study of Ipilimumab and Nivolumab in Advanced HIV-Associated Solid Tumors With Expansion Cohorts in HIV-Associated Solid Tumors and a Cohort of HIV-Associated Classical Hodgkin Lymphoma

• Patients receive nivolumab IV q2 weeks.
• Patients in dose level 2 also receive ipilimumab IV over 90 minutes on day 1 of every third course of nivolumab, and patients in dose level -2 also receive ipilimumab IV over 90 minutes on day 1 of every sixth course of nivolumab.
• For Stratum 1: CD4+ cell count >200 cells/mm^3
• For Stratum 2: CD4 cell count between 100-200 cells/mm^3
• N=84
MDACC Genentech Rare Cancers Alliance:
Phase II Study of Atezolizumab/Bevacizumab in Metastatic SCCA

Patients with metastatic squamous cell carcinoma of the anal canal
- Treated with at least one prior therapy for metastatic disease
- No prior immune therapies received as part of cancer treatment

- Clopper and Pearson Method phase II study
- $H_0$: $p \leq 0.05$ and an alternative hypothesis $H_a$: $p \geq 0.30$,
- $\alpha = 0.10$ and $\beta = 0.10$

20 patients treated initially with Atezo 1200 mg IV and bev 15 mg/kg q 3 weeks

Patients will be followed for best response using RECIST criteria 1.1

Primary endpoint: RR

NCT03074513
Key Eligibility Criteria:
- Surgically unresectable, locally advanced/recurrent or metastatic squamous cell carcinoma patients of the anal canal

Arm 1:
Docetaxel 40 mg/m² day 1, Cisplatin 40 mg/m² day 1 and 5-FU at 1200 mg/m²/day for 2 days + Atezolizumab (800 mg q2 weeks x 12M)

Arm 2:
mDCF

2:1 Randomization (N=99)
N=99

Primary Endpoint: 12M PFS
Secondary Endpoints: 3-yr PFS, RR, OS, QOL

Study PI: S. Kim
HIV+ CD4 > 400

A Study of mDCF +/- Atezolizumab in Treatment-Naïve Metastatic Squamous Cell Anal Carcinoma (SCARCE)

NCT03519295

A Study of mDCF +/- Atezolizumab in Treatment-Naïve Metastatic Squamous Cell Anal Carcinoma (SCARCE)
Randomized Phase 2 Trial of Avelumab +/- Cetuximab for Unresectable, Locally Advanced or Metastatic Squamous Cell Anal Carcinoma (SCCAC)

Key Eligibility Criteria:
- Surgically unresectable, locally advanced/recurrent or metastatic squamous cell carcinoma patients of the anal canal
  > 1 Prior Therapy

Arm 1: Avelumab (10 mg/kg) q2 wks

Arm 2:
Avelumab + Cetuximab q 2 wks

Primary Endpoint: RR

Secondary Endpoints: PFS, OS

Study PI's: Lonardi, Buggin

NCT03944252

HIV+ CD4 > 300

N=54
Key Eligibility Criteria:
- Surgically unresectable, recurrent or metastatic squamous cell carcinoma patients of the anal canal

Arm 1:
Carboplatin (AUC = 5) + Taxol 80 mg/m2 (weekly) q28 days + Nivolumab (max x 6) followed by maintenance Nivolumab

Arm 2:
Carbo/Weekly Taxol (max x 6M)

2:1 Randomization (N=205)

Substratify: HIV+ and prior XRT

Primary Endpoint: PFS

Secondary Endpoints: RR, OS, and exploratory correlatives

Study PI: C. Eng
Phase II Study of MEDI0457 (INO-3112) and Durvalumab (MEDI4736) in Patients with Recurrent/Metastatic HPV Associated Cancers

• VGX-3100 plus DNA-based immune activator encoded for IL-12
  • DNA plasmid vaccine
  • Target E6 and E7 oncogenes of HPV-16 and HPV-18

• Electroporation via Cellectra 5P
  • Electric field pulse
  • Increases expression of E6/E7 antigens and IL-12
  • Improves T-cell response

Courtesy of M. Frumovitz
A Phase 2, MEDI0457 (INO-3112) and Durvalumab (MEDI4736) in Patients With Recurrent/Metastatic HPV-Associated Cancers

Cervical Cancer Lead-in (n=6)

Cohort A:
Cervical Cancer

Cohort B:
Rare Tumors
(Anal, Penile, Vulvar, Vaginal)

Cohort C:
HIV(+) Cancers
(Any Site)

N=77

PI: M Frumovitz
DECREASE:
De-Intensified ChemoRadiation for Early-Stage Anal Squamous Cell Cancer:

Jennifer Dorth, MD
Joshua Meyer, MD
Paul Catalano, ScD
Cathy Eng, MD
Prajnan Das, MD
James Murphy, MD
Craig Messick, MD
Sheetal Kircher, MD
Terry Wong, MD
Marc Gollub, MD
Mark Rosen, MD, PhD
Inclusion:
- T1-T2 N0 M0 ≤ 4cm
- N0 based on PET/CT and CT
- SCC of anal canal or margin
- HIV negative or positive (CD4 ≥300)

Design:
- Stratified by T1 vs. T2 and HIV status

Primary endpoint: 2-year disease control ≥ 85%
Prognostic Impact of Residual HPV ctDNA after chemoXRT in Locally Advanced Anal Cancer

FIG 1

33 patients with Stage II-III ASCC undergoing chemoradiotherapy

33 patients with blood samples at baseline

18 patients with matched blood samples before and after chemoradiotherapy

15 patients with blood samples only before chemoradiotherapy

3 metastatic relapses
1 loco-regional relapse

1 metastatic relapse
3 loco-regional relapses

FIG 3

HPV ctDNA copies/ml

Baseline
After CRT

Cabel et al: CCR, 2018
Postchemotherapy (Post-CT) PFS according to residual HPV ctDNA in metastatic anal CA patients after 5 months of chemotherapy.

HR = 5.5 (95% CI = 2.1–14.3, $P < 0.001$)
Conclusions:

• InterAACT/EA2133 indicates carbo/weekly paclitaxel is the new SOC
• Single agent immune checkpoint inhibition provides durable and prolonged responses with excellent tolerability.
• Pending:
  • NCI9673 (Part B): Randomized phase II ETCTN study of nivolumab +/- ipilimumab is open for enrollment.
  • Pilot trial of Atezo/Bev (MDACC)
  • MEDI0457/Durvalumab (MDACC)
  • mDCF +/- Atezo (France)
  • Avelumab +/- Cetux (Italy)
  • EA#2182 DECREASE to be open shortly early Fall 2019
  • EA#2176 for tx naïve patients will be open Fall/Winter 2019
• *Always encourage clinical trial enrollment
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