Cervical Cancer has a defined, avoidable etiology, and if caught early is curable.
How Common is Cervical Cancer?

The number of new cervical cancer cases per year increased from 378,000 in 1980 to 454,000 in 2010.

By age 50, at least 80% of women will have acquired HPV

9K-12K new cervical cancers diagnosed in the U.S. per year

Yearly

Over 3,500 preventable deaths from cervical cancer in the U.S. & 200,000 worldwide

Source: Texas department of State Health Services, Texas Cancer Registry October 2010
Cervical cancer is a sexually transmitted disease.

HPV DNA is present in virtually all cases of cervical cancer and precursors.

More than 75% of sexually active women exposed to HPV
Little understanding of why small subset are affected by HPV.

In most cases HPV goes away
Only women with persistent HPV are at risk for cervical cancer
Incidence by Race


In the 50 years following the introduction of pap, US cervical cancer rates decreased by 75% and mortality by 74% 

• Despite this success:
  Imperfect sensitivity of testing: 30% of all cancers
  Error in follow-up of abnormal results: another 10%

Now we enter a new era... the Co Testing ERA
Cytology + HPV DNA
High Grade lesions: 65% HPV 16, 18, 45, and 31.
Low grade lesions: 50% HPV 16, 18, 45, 31; 12% HPV 6 and 11

Up to 40% of patients are infected with more than one HPV type. HPV 16 and HPV 18 are associated with 50% and 20% of cancers.

The first peak of oncogenic HPV infection occurs between the ages of 15 to 25 years, with a secondary peak in the sixth decade of life.
### HPV vaccine types association with diseases

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>HPV</th>
<th>HPV 16/18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical cancer</td>
<td>&gt;99%</td>
<td>70-75%</td>
</tr>
<tr>
<td>Anal cancer</td>
<td>84%</td>
<td>&gt; 80%</td>
</tr>
<tr>
<td>Vaginal cancer</td>
<td>70%</td>
<td>80-90%</td>
</tr>
<tr>
<td>Vulvar cancer</td>
<td>40%</td>
<td>&gt; 90%</td>
</tr>
<tr>
<td>Penile cancer*</td>
<td>47%</td>
<td>&gt; 80%</td>
</tr>
<tr>
<td>Head &amp; Neck cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oropharyngeal cancer</td>
<td>36%</td>
<td>&gt; 95%</td>
</tr>
<tr>
<td>Oral cavity cancer</td>
<td>23%</td>
<td>&gt; 95%</td>
</tr>
</tbody>
</table>

*In addition, 90% of genital warts are caused by HPV 6 and 11 and almost all cases of recurrent respiratory papillomatosis (RRP)*

<table>
<thead>
<tr>
<th>POPULATION</th>
<th>PAGE NUMBER</th>
<th>RECOMMENDED SCREENING METHOD&lt;sup&gt;a&lt;/sup&gt;</th>
<th>MANAGEMENT OF SCREEN RESULTS</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aged &lt; 21 y</td>
<td>7</td>
<td>No screening</td>
<td></td>
<td>HPV testing should not be used for screening or management of ASC-US in this age group</td>
</tr>
<tr>
<td>Aged 21-29 y</td>
<td>8-9</td>
<td>Cytology alone every 3 y</td>
<td>HPV-positive ASC-US&lt;sup&gt;b&lt;/sup&gt; or cytology of LSIL or more severe: Refer to ASCCP guidelines</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cytology negative or HPV-negative ASC-US&lt;sup&gt;b&lt;/sup&gt;: Rescreen with cytology in 3 y</td>
<td>HPV testing should not be used for screening in this age group</td>
</tr>
<tr>
<td>Aged 30-65 y</td>
<td>9-16</td>
<td>HPV and cytology &quot;cotesting&quot; every 5 y (preferred)</td>
<td>HPV-positive ASC-US or cytology of LSIL or more severe: Refer to ASCCP guidelines&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Screening by HPV testing alone is not recommended for most clinical settings</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>HPV positive, cytology negative:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Option 1: 12-mo follow-up with cotesting</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Option 2: Test for HPV16 or HPV16/18 genotypes</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• If HPV16 or HPV16/18 positive: refer to colposcopy</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• If HPV16 or HPV16/18 negative: 12-mo follow-up with cotesting</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cotest negative or HPV-negative ASC-US:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Rescreen with cotesting in 5 y</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cytology alone every 3 y (acceptable)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>HPV-positive ASC-US&lt;sup&gt;b&lt;/sup&gt; or cytology of LSIL or more severe: Refer to ASCCP guidelines</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cytology negative or HPV-negative ASC-US&lt;sup&gt;b&lt;/sup&gt;: Rescreen with cytology in 3 y</td>
<td></td>
</tr>
<tr>
<td>Aged &gt; 65 y</td>
<td>16-17</td>
<td>No screening following adequate negative prior screening</td>
<td></td>
<td>Women with a history of CIN2 or a more severe diagnosis should continue routine screening for at least 20 y</td>
</tr>
<tr>
<td>After hysterectomy</td>
<td>17-18</td>
<td>No screening</td>
<td></td>
<td>Applies to women without a cervix and without a history of CIN2 or a more severe diagnosis in the past 20 y or cervical cancer ever</td>
</tr>
<tr>
<td>HPV vaccinated</td>
<td>18-19</td>
<td>Follow age-specific recommendations (same as unvaccinated women)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Placing risk in perspective in making management decisions

* Using risk of CIN3+ to make guidelines that incorporate HPV testing
* Guidelines-recommend co testing
  * 90% HPV-and PAP- so 3-5 yrs
  * 10% HPV+ or PAP + so how do we manage this
Too Much vs Too Little

both can do harm...
CIN 3 - Carcinoma in situ
Cumulative Risk of Cervical cancer in treated or untreated CIN3

<1% vs. 50%

Age

Mean 52.2 yrs
Bimodal distribution - peaks 35-39 yrs and 60-64 yrs

Screening

50% of women diagnosed with cervix have never had a PAP
10% of women diagnosed with cervix cancer have not had a PAP in 5 years
Cervical Cancer: Symptoms

- Often no symptoms
- Post coital bleeding
- Foul vaginal discharge
- Abnormal bleeding
- Pelvic pain
- Unilateral leg swelling or pain
- Pelvic mass/gross cervical lesion
Cervical cancer: What is the chance of survival?

<table>
<thead>
<tr>
<th>FIGO Stage</th>
<th>5-Year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>81-96%</td>
</tr>
<tr>
<td>Stage II</td>
<td>65-87%</td>
</tr>
<tr>
<td>Stage III</td>
<td>35-50%</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>15-20%</td>
</tr>
</tbody>
</table>
Clinical staging of cervical cancer


FIGO 2009 Going Backwards or Forwards?

Updates

- Still clinically staged
- EUA, cystoscopy, proctoscopy, IVP optional
- CT, MRI, PET don’t change clinical stage
- Clinical Staging doesn’t take into account LND
- EUA incorrect in 25% Stage I & 50% Stage II
Staging Options:
FIGO-Basic vs FIGO-Enhanced

Any imaging (PET/MRI/CT) allowed but biopsy/surgery conformation required

* Stage IA
  * IA1-unchanged
  * IA2-based on final pathology P+/P-

* Stage IB
  * P+/P- PA+/PA-

* Stage IIA/IIB
  * P+/P- PA+/PA-

* Stage IIIA/Stage IIIB
  * P+/P- PA+/PA-

* Stage IVA
  * P+/P- PA+/PA-

* Stage IVB-unchanged
Staging Workup

* Examination under anesthesia
* +/- Cystoscopy / proctoscopy
* Chest radiograph
* CT or MRI and PET
* Other tests can be performed for treatment planning but won’t change the stage
Treatment Stage IA1

- Simple Hysterectomy (Extrrafascial)
- Conization
- Intracavitary radiation

Figure 9-7. Resection margins for extrafascial and radical hysterectomy are significantly different. The extrafascial approach removes the cervix and uterus just at the lateral border of the organ. Radical hysterectomy includes resection of the uterus along with its attached parametrial soft tissue and a margin of upper vagina. The adnexal structures can be incorporated into the resection or preserved, depending on patient age and desire.
Treatment – Microinvasive CA

- Implies minimal risk of nodal involvement
- 3 mm or less invasion and NO LVSI
- Simple hysterectomy
- Cone biopsy
Radical hysterectomy

- Used to treat cervical cancers with invasion > 3mm but confined to the cervix and vagina < 4 cm (Stage IA2 –IB1)

- Removal of parametrium and upper vagina
When is RT or Chemo/RT Indicated After Radical Hysterectomy?

Radiation if **two** of the following:

* deep invasion, large tumor or vascular invasion
  * GOG 92 (Sedlis A Gyn Onc 73:177-183, 1999)

Chemo-RT if **one** of the following:

* Positive margin, parametrial extension, positive node
  * GOG 109 (Peters WA J Clinic Oncol 18:1606-1613, 2000)
Treatment Options Stages IA2- IIA

* Radical Hysterectomy and node dissection
  * Patients with two or more risk factors are candidates for post-op radiation: greater than 1/3 stromal invasion, lymph-vascular space invasion, clinical tumor size ≥4cm

* Fertility sparing surgery
  * Trachelectomy / cryopreservation

* Chemo-Radiation Therapy
  * Number and Level of positive nodes?
Candidates:

* Desire to retain fertility
* Stage IA2 or IB1
* Lesion ≤ 2 - 2.5 cm
* No evidence of lymph node or distant metastases
* Absence of high risk histologies (e.g. neuroendocrine tumors)
Prospective, multi-center, international study

**Objective**: To evaluate the safety and feasibility of performing conservative surgery in women with early stage cervical cancer with favorable pathologic characteristics

**Inclusion Criteria:**
- Stage IA2 or IB1 cervical cancer
- Tumor diameter ≤ 2 cm
- No LVSI
- Squamous cell histology (any grade) or adenocarcinoma (grade 1 or 2 only)
- Cone margins and ECC negative for malignancy or AIS (one repeat cone/ECC permitted)
Radiation – Early stage disease

- Equally effective
- Side effect profile less desirable
- Longer treatment duration
- Obliterates ovarian function
- Decline in sexual function?
Advanced Cervical Cancer

* Advanced disease (Stage IIB-IV)
  * Chemo-radiation Treatment:
    * Radiotherapy to known volume of disease
    * 25 outpatient treatments
    * Chemotherapy, “sensitizers” given along with radiation to improve response
    * Brachytherapy/high dose rate implants
    * Rarely: Surgery
      * Ultra-radical (exenterative) surgery limited to cases of locally invasive disease
  *
* Problem:
  * Distant metastatic failure occurs in 66% of patients in this group
Global Standard Stage IB2 - IVA

- External beam pelvic radiation (40-60 Gy)
- Brachytherapy (80-85 Gy to Point A)
- I.V. Cisplatin chemotherapy
  * Cisplatin 40mg/m² (Max 70mg) IV q wk during RT (6wks)

Reduces risk of pelvic recurrence by 50%
Extends OS by 5-20% c/w XRT alone
Chemoradiation: Risk of Death Decreased by 30-50%

Relative Risk Estimate of Survival from Five Chemoradiation Clinical Trials
<table>
<thead>
<tr>
<th>Side effect profile</th>
<th>Surgery vs. ChemoXRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Surgery-related risk</td>
<td>* 14% risk of major complications (bowel, bladder)</td>
</tr>
<tr>
<td>* Bladder atony 4%</td>
<td>* Stage (5-10 vs 15%)</td>
</tr>
<tr>
<td>* 1-3% fistula rate, half heal spontaneously</td>
<td>* Dose</td>
</tr>
<tr>
<td>* Mortality &lt;1%</td>
<td>* Early &gt; late</td>
</tr>
<tr>
<td></td>
<td>* 26% severe urinary sx</td>
</tr>
</tbody>
</table>
New considerations

- MIS?
- Lymphatic mapping
- Retroperitoneal lymphadenectomy
- Additional chemotherapy
- New radiation sensitizers/IMRT
Primary Objective

To compare disease-free survival amongst patients who undergo a Minimally Invasive Radical Hysterectomy (TLRH, TRRH) versus Abdominal Radical Hysterectomy (TARH)
Patterns of Spread
Sentinel node, Right side: 
Lymphazurin

Ombel. artery
New considerations

- MIS?
- Lymphatic mapping
- Retroperitoneal lymphadenectomy
- Additional chemotherapy
- New radiation sensitizers/IMRT
Surgical Staging Options

Complication rates:
- Transperitoneal laparotomy: 10-16%
- Extraperitoneal laparotomy: 5-10%
- Laparoscopy extraperitoneal: 1-3%

Survival advantage:
- Surgical vs Radiogr.: 4yr PFS 49 vs 36%
  \[N=555/130 \text{ GOG studies} \quad \text{HR 1.46 (1.08-1.99)}\]
  \[\text{Gold MA et al Cancer 2008; 112:1954-63} \quad *p=0.01\]
- Surgical vs Clinical: 29 vs 19 months
  \[N=274 \text{ Stage IIIB-IVA} \quad \text{Holcomb et al. Eur J Gynecol Oncol 1999;20:90-3}\]
Laparoscopic RPLND in locally advanced cervical cancer

* Of the 26 patients with negative pelvic and para-aortic nodes on PET/CT
  * 3 (12%) had histopathologically positive para-aortic nodes.
* Of the 27 patients with positive pelvic but negative para-aortic nodes on PET/CT, 6 (22%) had histopathologically positive para-aortic nodes.
* Eleven (18.3%) patients had a treatment modification based on surgical findings.

_Cancer_. 2011 May 1;117(9):1928-34.
New considerations

- MIS?
- Lymphatic mapping
- Retroperitoneal lymphadenectomy
- Additional chemotherapy
- New radiation sensitizers/IMRT
C-xrt followed by Chemo

* Meta analysis showed increased OS of 19% at 5 yrs

* Included early trials but did not include GOG 120 or RTOG 90-01 which set standard for C-xrt

* Lorvidhaya 4 arm trial
  * Increased OS in C-xrt but no further increase in C-xrt and adj chemo

Klopp Curr Oncol Rep DOI 10.1007 Nov 2010
Lorvidhaya Radiat Oncol Biol Phys 2003
RTOG-0724 (GOG):

* Early stage cervical cancer s/p RH
  * Stage IA2-IB2:
    * Positive nodes
    * Parametrial extension
    * Positive margins after radical hysterectomy

* Patients had positive nodes or parametrial involvement and disposition to C-XRT
* Randomized to adjuvant T/C or none
THE OUTBACK TRIAL: Phase III trial of adjuvant chemo following chemoradiation for locally advanced cervical cancer VS chemoradiation

Stage IB$_2$-IVa
Cervical cancer: Stratify for
- FIGO stage
- Pelvic nodal involvement
- Uterine +ve on MRI

4 cycles Carboplatin + Paclitaxel

Standard chemoXRT

Standard chemoXRT
New considerations

- MIS?
- Lymphatic mapping
- Retroperitoneal lymphadenectomy
- Additional chemotherapy
- New radiation sensitizers/IMRT
GOG Phase I Trials of CRT

* GOG 9803 CDDP-Paclitaxel-Pelvic RT (PALN-neg)
  * MTD = CDDP 40 mg/m² (maximum 70 mg) and paclitaxel 40 mg/m² weekly × 6 cycles

* GOG 9804 CDDP-Paclitaxel-EFRT (PALN-pos)
  * MTD = CDDP 40 mg/m² (maximum 70 mg) and paclitaxel 40 mg/m² weekly × 6 cycles

* GOG 9912 CDDP-Gemcitabine-RT (PALN-neg)
  * Closed due to toxicity

* GOG 9918 CDDP-Cetuximab-RT (PALN-any)
  * Active for accrual

* GOG 9913 CDDP-Topo (weekly)-RT (PALN-neg)
  * Active for accrual

• PFS at 3 yrs: 74.4% Gem/cis/rad vs 65.0% Cis/rad (p=0.029)

OS at 3 years: 78.2% in Gem/cis/rad vs 69.1% Cis/rad

Abbreviations: CI = confidence interval; cis = cisplatin; Gem = gemcitabine; OS = overall survival; Rad = radiation.

Log-rank p = 0.022
Hazard ratio = 0.68
95% CI = 0.49-0.95
RTOG 0417 Phase II Study of Bevacizumab with Radiotherapy and Cisplatin Chemotherapy in Locally Advanced Cervical Carcinoma

N=57

SCHEMA

Pelvic RT:
45 Gy given in 25 once-daily fractions (1.8 Gy/fraction) Monday-Friday over 5 weeks
down
LDR x 2 or HDR x 5
down
Parametrial boost (if indicated)

Bevacizumab (Avastin®): IV Q2 weeks (Days 1, 15 and 29) during chemoradiation, given before cisplatin, on the same day as cisplatin

Cisplatin: Weekly infusion x 6 weeks

Bulky IB-IIIB
Weekly CDDP
Avastin10mg/kg

Schefter T
Case Presentation: Recurrent Disease

- 41 y.o. G$_3$P$_2$ - Principal
  - Previous Stage IB$_2$ SCC
  - Standard CDDP-XRT
    - Complete response
  - LLE swelling, pelvic ache, cough
- Exam:
  - Pelvic mass
  - Nodes
  - Lung nodules
Signs and Symptoms of Recurrent Disease

- Weight loss
- Leg edema
- Pelvic and/or thigh-buttock pain
- Serosanguinious vaginal discharge
- Progressive ureteral obstruction
- Supraclavicular adenopathy
- Cough
- Chest pain
“What if it comes back?”

* **Bottom line: Bad news**

* **Isolated central pelvic recurrence:**
  * Total pelvic exenteration → 50% cure

* **Multiple metastases**
  * Chemotherapy → limited success
Total Pelvic Exenteration

* Removal of gynecologic organs and vagina
* Removal of bladder and rectosigmoid
* Colostomy
* Urinary conduit
* Neovagina
Prognostic Variables

- Pathologic Subtype
- Tumor Size
- Depth of Invasion
- Lymphvascular Invasion
- Lymph Node Metastases
  - Early stage negative nodes
    - 86-92% 5 yr survival
  - Early stage positive nodes
    - 50-60% 5 yr survival
Predictors of Response to Chemotherapy in Recurrent Cervical Cancer

- Previous radio-sensitizing chemotherapy
- Platinum free interval
- Quality of life / Pain / Performance Status
- Site of recurrence
  - Response more frequent in non-irradiated sites (70% vs 23%, \(P = .008\), GOG 76X, Rose PG et al J Clin Oncol 17:2676, 1999)
Recurrent Cervical Cancer: Current GOG Studies (Phase II)

- 76 series (limited access), untreated
- 227 biologic series
- 127 series, prior therapy, squamous
- 128 series, prior therapy, non-squamous
  - No further studies planned
Extrapelvic Non-Isolated and Pelvic Sidewall Recurrence following XRT

- Cisplatin + Taxol- 43%
- Cisplatin + Topotecan- 27%
- Cisplatin + Gemzar- 22%
- Cisplatin + Navelbine- 30%
- Cisplatin- 15-23%
- Ifosfamide- 15%
- 5-FU- 18%
- Navelbine- 18%
- CPT-11- 18%
- Bleomycin- 10%
- Vincristine- 18%
nab-paclitaxel in advanced cervix cancer

* 28.6% had a partial response
* 42.9% had stable disease

* Median progression-free and overall survival were 5.0 and 9.4 months, respectively
Treatment of Recurrence Phase III

- **GOG 204** TP vs VP vs GP vs TP
  - closed, unable to show superiority over TP

- **GOG 169** CDDP vs CDDP/Taxol
  - RR superior with combination
  - *JCO* 22(15) 3113 2004 Moore

- **GOG 179** CDDP vs CDDP/Topo
  - RR, OS, PFS superior with combination
  - *JCO* 23(21) 4626, 2005 Long
Bevacizumab

* Phase II n=6
  * median 3 priors
  * 1CR, 1PR, 2 SD TTP 4 mos
    * Wright eg al Gyn Onc 2006

* GOG Phase II 227-C
  * 1-2 priors
  * Bev 15mg/kg q 3 weeks
  * 23.9% progression free >6 months
  * 10.9% PR
    * MRD 6.21 months (range, 2.83 to 8.28 months)
    * Median PFS and OS: 3.40 mos and 7.29 mos respectively.
      * J Clin Oncol. 2009 Mar 1;27(7):1069-74
240-Randomized 4 arm study
Non platinum doublets

Topotecan/Paclitaxel or Platinum/Paclitaxel +/- Bevacizumab

Results pending

Non superiority of Topotecan/Paclitaxel over Platinum/Paclitaxel
Targeted Therapies for Recurrent Cervical Cancer

* Therapeutic HPV Vaccines
* Anti-EGFR
  Anti-angiogenesis
  * Important in cervical cancer growth, invasion, and metastasis
  * E6 mediated inactivation of wild-type p53 up-regulates VEGF
* Oncolytic viruses
**Cetuximab in Combination with Cisplatin in Advanced Carcinoma Of The Cervix 76-DD**

<table>
<thead>
<tr>
<th>Tumor Response</th>
<th>CIS-RT</th>
<th></th>
<th>No CIS-RT</th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Complete Response</td>
<td>0</td>
<td>0.0</td>
<td>1</td>
<td>3.4</td>
<td>1</td>
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<tr>
<td>Partial Response</td>
<td>3</td>
<td>7.5</td>
<td>4</td>
<td>13.8</td>
<td>7</td>
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<tr>
<td>Non-Response*</td>
<td>37</td>
<td>92.5</td>
<td>24</td>
<td>82.8</td>
<td>61</td>
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<tr>
<td><strong>Total</strong></td>
<td>40</td>
<td></td>
<td>29</td>
<td></td>
<td>69</td>
</tr>
</tbody>
</table>

RR=11.6%
pemetrexed (Alimta, LY231514) as second line chemotherapy carcinoma of the cervix

- 15% had partial responses with a median response duration of 4.4 months
- The response rate for non-radiated or radiated disease sites was 25% and 7% respectively.
- 59% had stable disease and 26% patients had increasing disease.
- Median progression free survival (PFS) was 3.1 months and overall survival (OS) was 7.4 months.
A Phase II Trial of Erlotinib In Recurrent Carcinoma of The Cervix: A Gynecologic Oncology Group Study

- PO erlotinib 150 mg daily until progressive disease or adverse effects
- 28 enrolled 25 evaluable
- No objective responses
- 1 patient had a progression-free survival (PFS) ≥ 6 months (4%)
Study VEG105281 GSK

- FIGO Stage IVB or recurrent or persistent cervical cancer
- Zero or one prior chemo regimen for advanced/recurrent disease

**Randomized Phase II**

**Endpoint: PFS**

**TR Analyses**
* ERbB1, ERbB2, and the combined ERbB1/ERbB2 overexpressed and gene-amplified (FISH+) populations

- **Oral Lapatinib 1500mg qd**
- **Oral Pazopanib 800mg qd**
- **Oral Lapatinib 1000mg + Pazopanib 400mg qd**

Lapatinib: oral dual EGFR/HER2/neu TK inhibitor
Pazopanib: oral TK inhibitor in VEGF pathway

Monk BJ et al J Clin Oncol 27:15s, 2009 (suppl; abstr 5520)
Kaplan-Meier Curve OS
Monk BJ et al J Clin Oncol 27:15s, 2009 (suppl; abstr 5520)

Median OS (weeks)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lapatinib</td>
<td>39.1</td>
</tr>
<tr>
<td>Pazopanib</td>
<td>50.7</td>
</tr>
</tbody>
</table>

HR (90% CI)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>HR</th>
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<tbody>
<tr>
<td>(90% CI)</td>
<td>(0.67, 0.99)</td>
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</table>

p-value

<table>
<thead>
<tr>
<th>Treatment</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p=0.045</td>
</tr>
</tbody>
</table>

Subjects At Risk

<table>
<thead>
<tr>
<th>Treatment</th>
<th>At Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lapatinib</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>69</td>
</tr>
<tr>
<td></td>
<td>59</td>
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<tr>
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<td>Pazopanib</td>
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** The CI are 90% (alpha=10%) naïve CIs.
*** Wald normal approximation is used to calculate the p-value

* One-sided p-value due to study design. Two-sided would be p=.09.

**** Stratified log-rank p-value and hazard ratio (Pike) adjusted only for one of the stratification factors – prior chemotherapy.
A PHASE II EVALUATION OF BRIVANIB (BMS582664, IND#) IN THE TREATMENT OF PERSISTENT OR RECURRENT CARCINOMA OF THE CERVIX (BMS Study CA182-048)
GOG 265

A PHASE II EVALUATION OF ADXS11-001 (NSC 752718, IND#13,712) IN PERSISTENT OR RECURRENT CARCINOMA OF THE CERVIX

- 6 patient safety lead in
- Two stage phase II
- The primary measure of efficacy will be overall survival at 12 months.
- Study Chair: W Huh
Summary of Treatment for Recurrent Disease

* Only pelvic exenteration curative for central pelvic recurrences
* Palliative radiation of painful metastases
* Cisplatin doublets standard in treating metastatic disease
* Anti-vascular compounds emerging as new systemic agents for advanced and recurrent cancer
* Quality of life and honesty needs to be emphasized
Beta-adrenergic blockers, Stress, and QOL

Clinical trial using beta blockade and stress reduction techniques

Outcomes- 1-Overall Survival
2-Improved QOL

Translational outcomes- biologic stress markers
SAVE THE DATE:
Tuesday, January 29, 2013 8:00 a.m. – 4:00 p.m.
United Way of Greater Houston

50 Waugh Drive
Houston, Texas 77007
Registration opens in December.
Registration Fee: $25
Cervical Cancer Survivors attend for FREE.
Linda Leach at: lileach@mdanderson.org or (713) 563-1218.
Known cause... HPV
  ▪ Belief barriers

Screening test... Pap smear (HPV test)
  ▪ Barriers to screening and follow up

A preventative vaccine
  ▪ Barriers to access and acceptability

Long preinvasive development stage... 3-10 years
  ▪ Barriers to follow up

Curable preinvasive stage... leep, cone, hysterectomy
  ▪ Missed opportunities

Curable early stage... radical hysterectomy
  ▪ Missed opportunities
Unite!

Have a voice! Be heard!

Lobby for vaccination and education in schools

Lobby for money

Know sources for help-

* http://www.foundationforwomenscancer.org/
* http://www.gog.org/
* http://www.cervicalcancerfreeamerica.org/
* http://clinicaltrials.gov/

Raise awareness and funding

* “disease of the developing world”
* “its only 4000 women” Are they serious????