Cancer de la prostate: best of 2016

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Disclosure

• Participation to advisory boards, speaker or investigator for: Amgen, Astellas, Astra Zeneca, Bayer, Celgene, Genentech, Ipsen, Jansen, Lilly, Novartis, Pfizer, Roche, Sanofi, Orion, MedImmune, New Oncology, DebioPharm
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I am a PI of Eli Lilly and Company trial with NOTCH inhibitor.

I will not discuss off label use in my presentation.

I will discuss investigational use in my presentation.
Patient case 1: Presentation

• Age 48 years; Performance status 0
• Presenting PSA 89.3 ng/ml
  – RTUP; Gleason 8 (4+4)
  – No symptoms
Be careful...!!!
Some patients with metastatic hormone-sensitive prostate cancer may not be willing/are too frail to receive docetaxel
Patient case 1: Presentation

• Age 48 years; Performance status 0

• Presenting PSA 89.3 ng/ml
  – RTUP; Gleason 8 (4+4) with metastases
  – LHRHa for 6 months; PSA nadir 5 ng/ml
  – Bicalutamide added for PSA progression and no response

• Now PSA progression 16.2 ng/ml

• Bone metastase and liver metastases
Patient case 1: best option?

- ADT+docetaxal
- ADT+Cabazitexal
- ADT+Arinhibitors (ABI/ENZA)
- ADT+RAD223
General recommendations in CRPC

• Check serum Testosterone (should be < 0.50 ng/mL)
• Imaging check up (bone scan + CT scan)
• Continue castration
• If prescribed, stop a androgen receptor antagonist (« Withdrawal syndrome »)
• Treat symptoms (bone RXT, TURP, anemia, etc)
• Discuss a new line of anti-cancer treatment
BE careful...!!!

Patient < 50 ans
Castration <6 mois
Liver metastases
= NO ENZA/ABI
Patient case 1: Presentation

• Age 48 years; Performance status 0

• Presenting PSA 89.3 ng/ml
  – RTUP; Gleason 8 (4+4)
  – LHRHa for 6 months; PSA nadir 5 ng/ml
  – Bicalutamide added for PSA progression and no response

• Now PSA progression 16.2 ng/ml
  – Bone metastase and liver metastases
  – Treatment with abiraterone
  – And Palliative radiation to lumbar spine
Patient case 1: how to monitor?

• Blood test

• Physical examination every months

• Physical examination every 3 month

• Bone scan and CT scan
Patient case 1: Presentation

- Age 48 years; Performance status 0
- Presenting PSA 89.3 ng/ml
  - RTUP; Gleason 8 (4+4)
  - LHRHa for 6 months; PSA nadir 5 ng/ml
  - Bicalutamide added for PSA progression and no response
- Now PSA progression 16.2 ng/ml
  - Bone metastase and liver metastases
  - Treatment with abiraterone
  - At 3 months, PSA decrease after starting treatment with abiraterone
    - PSA 2 ng/ml
Patient case 1: Presentation

- Age 48 years; Performance status 0
- Presenting PSA 89.3 ng/ml
  - RTUP; Gleason 8 (4+4)
  - LHRHa for 6 months; PSA nadir 5 ng/ml
  - Bicalutamide added for PSA progression and no response
- Now PSA progression 16.2 ng/ml
  - Bone metastase and liver metastases
  - Treatment with abiraterone
  - At 3 months, PSA decrease after starting treatment with abiraterone
    - PSA 2 ng/ml
    - And then INCREASE at 4 months...10ng/ml
Patient case 1: best option?

- ADT+docetaxal
- ADT+Cabazitexal
- ADT+Arinhbitors (switch to ENZA)
- ADT+RAD223
FIRSTANA: Study Design

Hypothesis: cabazitaxel is more effective than docetaxel in 1L mCRPC
FIRSTANA: Overall Survival

Docetaxel remains the standard for 1L chemotherapy
Hypothesis: Cabazitaxel 20 mg/m² is non inferior to cabazitaxel 25 mg/m²
Proselica study

CBZ 20 mg/m² is non inferior to CBZ 25 mg/m² and safer (and cheaper)
Que peut-on cibler ?
Que peut-on cibler ?

Bar chart titled "Actionable mutations in CRPC" showing percentages for various categories including:
- Informative aberration
- AR amp/mut
- Actionable non-AR
- PI3K
- DNA repair
- BRAF RAF1
- CDK inhibition
- WNT
- Germline

Robinson et al. Cell 2015
DNA-Repair Defects and Olaparib in Metastatic Prostate Cancer

Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer

CRPC post docetaxel trated with Ipilimumab+RTE
Ipilimumab in prostate cancer

A trend but no evidence for better OS with ipi
PD-1 Blockade in Tumors with Mismatch-Repair Deficiency

Study Design

Colorectal Cancers

Cohort A
Deficient in Mismatch Repair
(n=25)

Cohort B
Proficient in Mismatch Repair
(n=25)

Non-Colorectal Cancers

Cohort C
Deficient in Mismatch Repair
(n=21)

- Anti-PD1 (Pembrolizumab) – 10 mg/kg every 2 weeks
- Mismatch repair testing was performed locally using standard IHC for MMR deficiency or PCR-based test for microsatellite instability

Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MMR-deficient non CRC n=30 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age (range) – years</td>
<td>56 (36-92)</td>
</tr>
<tr>
<td>Gender-female no. (%)</td>
<td>14 (47)</td>
</tr>
<tr>
<td>ECOG PS-zero</td>
<td>6 (20)</td>
</tr>
<tr>
<td>Primary-location</td>
<td></td>
</tr>
<tr>
<td>Endometrial</td>
<td>9 (30)</td>
</tr>
<tr>
<td>Ampullary/biliary</td>
<td>7 (23)</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Small bowel</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Gastric</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Other (prostate, thyroid, sarcoma)</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Metastatic</td>
<td>30 (100)</td>
</tr>
<tr>
<td>Liver Mets</td>
<td>16 (53)</td>
</tr>
<tr>
<td>Median Prior Regimens</td>
<td>2</td>
</tr>
<tr>
<td>Germline mutation or Lynch Syndrome</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5 (17)</td>
</tr>
<tr>
<td>No</td>
<td>7 (23)</td>
</tr>
<tr>
<td>Unknown</td>
<td>18 (60)</td>
</tr>
</tbody>
</table>
Study Design

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Cohort A
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(n=25)

Cohort B
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Baseline Characteristics
MSI-H prostate cancer are not so rare (5%)
And progression?
Hyperprogressive disease (HPD): a new pattern of progression

Champiat et al, Clin Cancer Res 2016
Hyperprogressive disease (HPD): a new pattern of progression

Champiat et al, Clin Cancer Res 2016
Thank you...
Thank you...and discussion