High-risk prostate cancer treatment: Integrating chemotherapy?

Karim Fizazi, MD, PhD
Department of Cancer Medicine
Institut Gustave Roussy
Villejuif, France
Disclosure slide

• Participation to advisory boards or speaker for: Amgen, Astellas-Medivation, Astrazeneca, Bayer, BMS, Celgene, Dendreon, Exelixis, Ipsen, Janssen-Cougar, Keocyt, Millennium-Takeda, Novartis, Sanofi-Aventis
A patient with high-risk prostate cancer

What to do?

You should have a prostatectomy!

No! Radiation therapy!

Yes, but they also talk about hormones
Rationale for chemotherapy in localized CaP

- Docetaxel: established standard in metastatic prostate cancer

![Survival Graph]

HR = 0.81, p = 0.02

- In Oncology, minor OS benefit in the metastatic setting usually transfers in higher benefit in localized disease (breast, colon, etc)

Tannock IF: NEJM 351:1502-12, 2004
Fizazi K: Lancet Oncol 2007; 8: 994-1000
## Phase III trials of Docetaxel in Localized prostate cancer

<table>
<thead>
<tr>
<th>Study name</th>
<th>PI</th>
<th>Local treatment</th>
<th># patients (enrolled/planned)</th>
<th>Status</th>
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<tbody>
<tr>
<td>GETUG 12</td>
<td>K. Fizazi (France)</td>
<td>XRT</td>
<td>413</td>
<td>Accrual completed</td>
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<tr>
<td>RTOG 0521</td>
<td>H. Sandler (USA)</td>
<td>XRT</td>
<td>600</td>
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<td>TAX 3501</td>
<td>M. Eisenberger (USA)</td>
<td>RP</td>
<td>228 /1700</td>
<td>Early accrual termination</td>
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<td>AdPro</td>
<td>Ahlgren (Sweden)</td>
<td>RP</td>
<td>396</td>
<td>Accrual completed</td>
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<td>DANA FARBER</td>
<td>A. D’Amico (USA)</td>
<td>XRT</td>
<td>350</td>
<td>Ongoing</td>
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<td>Mc Kenzie (Can)</td>
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</tr>
</tbody>
</table>
ADJUVANT

Docetaxel given after prostatectomy
Sanofi-Aventis 3501 Study
P.I. Mario Eisenberger

- Primary endpoint: PFS
- N= 228/1696 (high-risk localized disease, )
- Stratification: Age (> 65 vs < 65) / Predicted prob. of 5-y FFP / Country
SPCG-12 AdPro
PI: G. Algren (Sweden)

Prostatectomy and post-op PSA<0.5

High risk:
- pT2 GS 4+3
- G 8-10 & SM +
- pT3 and GS ≥ 7

- if pre op PSA ≥ 10,
- LN Dissection

Randomize

Docetaxel x 6 cycles

Observation

N = 396
Primary Endpoint: PSA Progression
ADJUVANT

Docetaxel given after Radiotherapy
RTOG 0521 study
(H.M.Sandler)

Androgen Suppression (2 y) + Radiotherapy* (72 - 75.6 Gy)

Androgen Suppression (2 y) + Radiotherapy* * (72 - 75.6 Gy)

Docetaxel 75 q3w x 6 + Prednisone

- Primary endpoint: OS
- N= 600 planned pts
- Stratification:
  - 1: Gleason ≥ 9, PSA ≤ 150, and any T-stage
  - 2: Gleason 8, PSA < 20, and any ≥ T2
  - 3: Gleason 8, PSA ≥ 20-150, and any T-stage
  - 4: Gleason 7, PSA ≥ 20-150, and any T-stage

* LHRH A + AA
* * 3DCRT/IMRT
NEO-ADJUVANT

Docetaxel before Radiotherapy
High risk prostate cancer
GETUG 12 trial

Stratification
- Gleason $\geq 8$
- PSA>20
- T3
- pN+ / pN-

Randomize

Primary endpoint: Progression-free survival
$n = 413$ pts (Accrual: 2002-2006)
GETUG 12 trial: Population

- T3 63%
- PSA > 20 ng/mL 61%
- Gleason score ≥ 8 42%
- pN+ 28%

# Adverse factors
- 1 36%
- 2 39%
- 3 18%
- 4 6%
PSA response (assessed at 3 months)

PSA ≤ 0.2 ng/mL
p < 0.0001

GETUG 12

Fizazi et al., Eur J Cancer 2012
Progression-Free Survival: Preliminary results

Median f/u: 4.5 years

Adjusted HR: 0.79 [0.53-1.18], (p=0.26)

Fizazi et al, ASCO 2011, Abstr 4513
GETUG 12: Overall Survival

94% [91% – 96%]

IDMC recommendation (Dec 2010): Second analysis of PFS (and first analysis of OS) when median follow-up is ~7 years

Fizazi et al, ASCO 2011, Abstr 4513
A multi-arm trial: STAMPEDE
Prostate Cancer: STAMPEDE

PI: Nick James

Key endpoints:

**Primary:** Failure free survival

**Secondary:** QOL, cost effectiveness, toxicity, SREs, overall survival

Androgen suppression (AD)

- AD + Taxotere (T)
- AD + zoledronic acid (Z)
- AD + celecoxib
- AD + celecoxib + Z
- AD + T + Z

Pilot

- Efficacy
- Safety in 210 patients on trial for min 18 weeks

Confirm stages I - IV

Reject arms not improving Failure Free Survival at each stage

Follow-up until death

n = 3300

Prostate Cancer

- High risk newly diagnosed
- or PSA relapse after RP/RXT
- or metastases

N= 3300-6000
PEACE-2: European Phase III Trial of Cabazitaxel and Pelvic irradiation in patients with high-risk localized prostate cancer

Primary end point:
- cPFS (HR: 070)

Secondary endpoints:
- PSA response at 3 months
- bPFS
- Metastases-free survival
- CaP-specific survival
- OS
- Acute/Lg term tolerance
- QoL
- Biomarkers (biopsy)

Androgen deprivation therapy (ADT) x 3 years + RXT (prostate)

ADT + RXT (Pelvis)

ADT + Cabazitaxel x 4 cycles + RXT (prostate)

ADT + Cabazitaxel x 4 cycles + RXT (Pelvis)

Patients with high-risk localized prostate cancer: at least 2 of the following criteria:
- Gleason≥8
- ≥ T3
- PSA>20 ng/mL

1050 patients planned

Study sponsor: Unicancer
Planned accrual duration: 4 years
Conclusion: Chemotherapy in high-risk localized prostate cancer

- Not to be used outside clinical trial
- Docetaxel: 10 phase III trials ongoing
- Phase III trials to get mature in 2013-15:
  - GETUG 12 - Stampede
  - RTOG 0521 - SWOG Mitoxantrone
  - Adpro (SPCG 12)
- Peace-2 European trial to start soon