Perspective on endocrine and chemotherapy agents

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Disclosures

• Dr. Sternberg has received research funding for her department or has consulted with:
  • Janssen, Sanofi-Genzyme, Astellas, Clovis, Bayer, Ferring, Medivation, Roche/Genentech/Ipsen
Hormone Sensitive Advanced Prostate Cancer
Arms of the STAMPEDE trial open to recruitment over time

- Standard-of-care (SOC) = ADT (+/- RT)
- SOC+zoledronic acid
- SOC+docetaxel
- SOC+celecoxib
- SOC+zoledronic acid+docetaxel
- SOC+zoledronic acid+celecoxib

ASCO 2017: No Doce
ASCO 2018: SOC+abi, SOC+M1, RT (M1)

Doce 2-3 yrs: SOC+metformin
SOC+tE2

Include randomisation of tE2 patches for meta-analysis with PATCH
Q1-2017: launch of tE2 comparison
Androgen deprivation therapy (ADT)

Latitude: Phase III Trial of Abiraterone in patients with newly diagnosed metastatic prostate cancer

- Metastatic prostate cancer
- At least 2 poor-risk factors:
  - Visceral mets ≥ 3 bone mets ≥ Gleason 8
- Max: 3 months previous ADT

Co - Primary endpoints:
- OS (HR: 0.80)
- rPFS

N= 1200, Accrual completed 2 yrs ago, Probably at ASCO 2017

Courtesy of K Fizazi
STAMPEDE - OS Primary Endpoint

- 61% M+; 15% N+M0; 24% N0M0; median follow-up: 43 mo

James ND et al. Lancet 2016;387:1163-77
High volume

- HR = 0.63 (95% CI: 0.50-0.79)
- P < 0.0001
- Median 51.2 mo

Low volume

- HR = 0.86 (95% CI: 0.52-1.42)
- P = 0.55
- Median 58.3 mo
Upfront docetaxel in M1
Systematic review and meta-analysis

• Results based on 2,993 men / 1,254 deaths

Trial name

CHAARTED
GETUG 15
STAMPEDE (SOC +/- DOC)
STAMPEDE (SOC + ZA +/- DOC)
Overall

Heterogeneity: $\chi^2 = 4.80$, df=3, $P=0.187$, $I^2 = 37.5\%$

10% absolute improvement in survival (from 40% to 50%) at 4 years

PEACE-1: European Phase III Trial in *de novo* Metastatic Prostate Cancer (revised design)*

- **Patients with newly diagnosed (castration-naïve) metastatic CaP**
- **916 patients planned**

**Randomized**

- Androgen deprivation therapy (ADT) +/- docetaxel
- ADT + Abiraterone 1000 mg Prednisone 5 mg BID +/- docetaxel
- ADT + Local radiotherapy +/- docetaxel
- ADT + Local radiotherapy + Abiraterone-Pred +/- docetaxel

**Co-primary endpoints:**
- OS and PFS (HR: 0.75)

*Protocol was amended in Nov 2015 after the accrual of 276 pts to allow for docetaxel and ADT*

Study sponsor: Unicancer

NCT01957436
# Phase 3 Ongoing Combination Therapy Trials in HSPC

<table>
<thead>
<tr>
<th>Study</th>
<th>Identifier</th>
<th>Study Drugs</th>
<th>Pts (N)</th>
<th>Primary End Point</th>
<th>Status/Read Out</th>
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<tbody>
<tr>
<td>LATITUDE</td>
<td>NCT01715285</td>
<td>ADT ± AA</td>
<td>1209</td>
<td>rPFS, OS</td>
<td>ASCO 2017</td>
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<td>STAMPEDE (Arm G)</td>
<td>NCT00268476</td>
<td>ADT ± AA</td>
<td>1800</td>
<td>OS</td>
<td>LBA ASCO 2017</td>
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<td>PEACE-1</td>
<td>NCT01957436</td>
<td>ADT ± DOC vs ADT + AA ± DOC (± local RT)</td>
<td>916</td>
<td>PFS, OS</td>
<td>Recruiting/2020</td>
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<tr>
<td>STAMPEDE (Arm J)</td>
<td>NCT00268476</td>
<td>ADT ± AA + ENZ*</td>
<td>1800</td>
<td>OS</td>
<td>Closed-will report in 2-3 yrs</td>
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<tr>
<td>SWOG-1216</td>
<td>NCT01809691</td>
<td>ADT + TAK-700 vs ADT + BIC</td>
<td>1304</td>
<td>OS</td>
<td>Recruiting/2027</td>
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<tr>
<td>ENZAMET</td>
<td>NCT02446405</td>
<td>ADT + ENZ vs ADT + antiandrogen</td>
<td>1100</td>
<td>OS</td>
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<td>TITAN</td>
<td>NCT02489318</td>
<td>ADT ± APA (ARN 509)</td>
<td>1000</td>
<td>rPFS, OS</td>
<td>Recruiting/ 2021</td>
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<td>ARCHES</td>
<td>NCT02677896</td>
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<td>1100</td>
<td>rPFS</td>
<td>Recruiting/ 2023</td>
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<td>ARASENS</td>
<td>NCT02799602</td>
<td>ADT + DOC ± ODM-201</td>
<td>1300</td>
<td>OS</td>
<td>Recruiting/2022</td>
</tr>
</tbody>
</table>

*Includes upfront Doc

Modified from and courtesy of K. Fizazi
Castration Resistant Advanced Prostate Cancer
Phase III Trial of Enzalutamide +/- Abiraterone (Alliance A031201)
1,311 enrolled

Target deaths=616, 90% power to detect a hazard ratio=0.77
one-sided type I error rate=0.025
Readout expected in December 2019

Stratification Factors: Halabi nomogram, prior docetaxel use

Primary Endpoint
Overall survival

mCRPC
AdenoCa w/o neuroendocrine differentiation or small cell features
No taxanes for M+ disease

ARM A
Enzalutamide 160 mg daily p.o.

ARM B
Enzalutamide 160 mg daily p.o.
Abiraterone 1000 mg daily p.o.
Prednisone 5 mg twice daily p.o.
PLATO, double-blind, placebo-controlled, two-period randomized phase IV trial (n=509)

ENZA Maintenance in Combination With ABI versus ABI
After Disease or confirmed PSA Progression on ENZA in mCRPC

Primary end-point PFS not met
Press release, December 14 2016
PRESIDE: randomized double-blind, phase III trial (n=650)

ENZA Maintenance in Combination With DOC vs DOC After Disease Progression on ENZA in mCRPC

- 650 pts to be enrolled to get 274 patients in period 2
- **Primary outcome**: rPFS
- **Secondary outcomes**: TTPP, PSA response, ORR, TT pain progression, TT opioid use, TTSRE, QoL
- January 2018 (estimated completion)
CHEIRON: randomized double-blind, phase III trial in first-line mCRPC (n=232)

- mCRPC (PCGW2)
- no prior ABI, ENZA or taxane

Stratification by:
- visceral mets
- pain (BPI ≥ 3)

R 1:1

DOC 75 mg/sqm q 21 x 8* plus oral prednisone 10 mg daily
ENZA 160 mg po daily x 24 wks (n = 116)

DOC 75 mg/sqm q 21 x 8* plus oral prednisone 10 mg daily x 24 wks (n = 116)

PRIMARY ENDPOINT
rate of patients without progression (PCWG2) at 6 months after DOC start (50 → 65%)

SECONDARY ENDPOINTS

Orazio Caffo, Italian Study

Results expected at ASCO GU 2018

NCT02453009
## Ongoing Phase III Trials in m0CRPC at high risk with PSA doubling time < 10 months

<table>
<thead>
<tr>
<th>Trial Identifier</th>
<th>Estimated Enrollment</th>
<th>Treatments</th>
<th>Primary Endpoint</th>
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<tbody>
<tr>
<td>SPARTAN (NCT01946204)</td>
<td>1200</td>
<td>Apalutamide 240 mg once daily/placebo</td>
<td>Metastasis free survival</td>
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<td>PROSPER (NCT02003924)</td>
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<td>Enzalutamide 160 mg one daily/placebo</td>
<td>Metastasis free survival</td>
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<td>ARAMIS (NCT01946204)</td>
<td>1500</td>
<td>ODM-201 600 mg twice daily/placebo</td>
<td>Metastasis free survival</td>
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</table>
Perspective on endocrine and chemotherapy agents

HSPC:
• STAMPEDE and CHAARTED: More use of docetaxel in HSPC patients who present with metastatic disease
• Results of ABI arm of Stampede and Latitude Trials (ASCO 2017)

CRPC:
• CABA 20 mg/m² post-DOC supported with level 1 evidence, accepting the risk of a slightly reduced efficacy vs a reduced toxicity
• PLATO Trial ENZA plus ABI results negative, ENZA plus ABI Alliance Trial
• Other combinations under study: novel hormonal agents with Docetaxel Cabazitaxel, Ra 223

M0CRPC: too early
Thank you