SMARTOncology Tumor Insights

Prostate Cancer – Executive Summary

Current Landscape

Long term survival of 3-4 years with approved androgen deprivation therapies in metastatic stages; PSA determines risk to progression after diagnosis

- Prostate cancer -common malignancy diagnosed among US men (~161k, 2017), the second leading cause of their cancer-related deaths (~26K, 2017)
- Median age at diagnosis is 66 years; >95% of mCRPC have adenocarcinoma histology
- PSA screening can identify early stage disease with a better prognosis than an initial diagnosis of metastatic disease (~10-15% of cases), which reduces median overall survival to 3-4 years
- **Treatment options are stratified by disease, stage or risk**
  - Early stage: Surgery/ RT, with (high-risk patients) or without androgen deprivation therapy (ADT)
  - CSPC (local/ distant recurrence OR newly diagnosed metastatic stage): ADT ± docetaxel
  - Asymptomatic mCRPC: Sipuleucel-T (DC therapy)
  - Metastatic CRPC: Next-generation ADT (abiraterone, enzalutamide), chemotherapy (docetaxel, cabazitaxel)
  - Symptomatic mCRPC with bone metastasis: Radium-223
  - Bone metastasis treated with zoledronic acid, denosumab

Key KOL Insights (US)

Sip-T is for CRPC patients, who remain on ADT. They usually are early CRPC, slow-rising PSA and hopefully asymptomatic .

Abiraterone or Enzalutamide are preferred in 1L mCRPC and usually my go-to options because patients are most interested in hormone therapies and pills they can take home. I often reach for Abiraterone because of familiarity. It was FDA-approved first and it's very well tolerated.

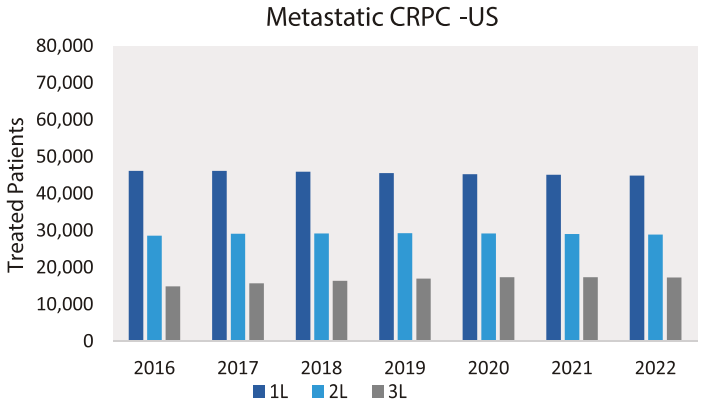
There are patients for whom I reach for Enzalutamide first rather than Abiraterone. These are who may have diabetes and for whom prednisone is not good. Also patients who have recently received Sipuleucel-T (Sip-T) as I'd rather give non-steroid-containing regimen as we're trying to rev up the immune system with Sip-T.

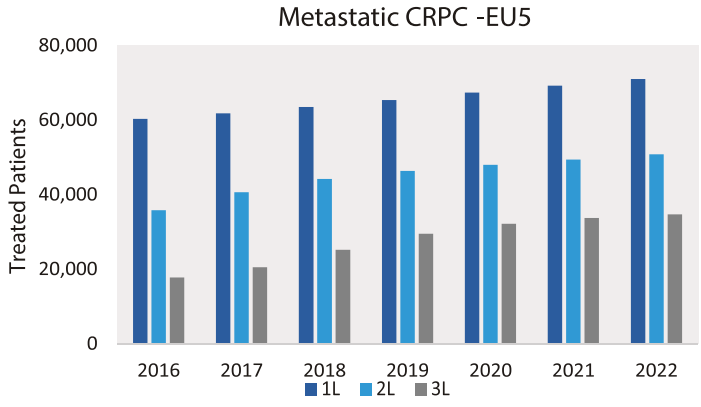
I'll have conversation with patients about Docetaxel's potential for survival benefit, even if they have low disease burden

There's been no proven benefit for Cabazitaxel over Docetaxel in 1L setting. So I only give it to CRPC patients. And it's usually really quite down the line after all the other therapies.

Radium-223 is well-tolerated and it's a good therapy for patients with bone-only mets or bone-dominant disease. I think label's actually for symptomatic patients.

The SmartAnalyst patient dynamic disease modelling accounts for potential emerging therapies such as PARPi in heavily pre-treated BRCA mut patients





US	2016	2017	2018	2019	2020	2021	2022
1L*	46,191	46,149	45,957	45,585	45,274	45,124	44,913
2L	28,616	29,109	29,230	29,295	29,214	29,035	28,862
3L	14,888	15,689	16,348	16,997	17,343	17,368	17,281

EU5	2016	2017	2018	2019	2020	2021	2022
1L*	60,310	61,811	63,479	65,342	67,325	69,239	71,010
2L	35,822	40,590	44,160	46,364	47,980	49,408	50,787
3L	17,731	20,526	25,158	29,464	32,162	33,715	34,718

Figures above are directional. For in-depth dynamic disease modeling analysis, please contact SmartAnalyst

Note: The above values for 1L of therapy take into account Metastatic Incidence and Recurrent patients from Stages I, II and III. The calculation is based on SmartAnalyst's proprietary model flow; *Around 45-50% patients in 1L are Asymptomatic and the rest are Symptomatic

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INTELLIGENT INSIGHTS. SMART RESULTS.

SMARTOncology Tumor Insights

Prostate Cancer – Emerging Treatment Landscape

Key Insights

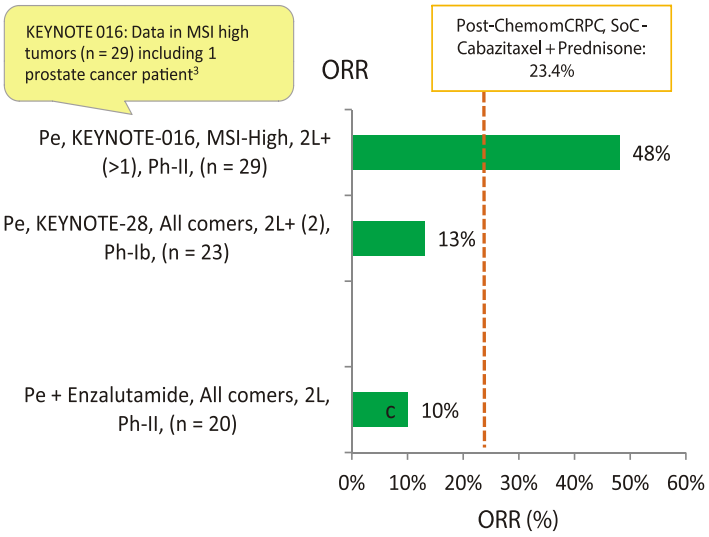
- **Intense pipeline activity in mid-stage clinical development; diverse MoAs, including immunotherapies being positioned across lines and patient segments**

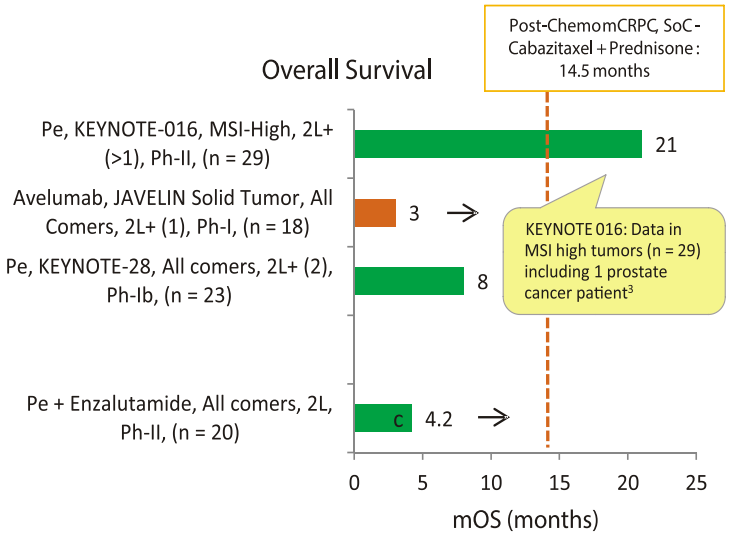
- **Pipeline activity targeting areas of unmet need, driving biomarker based patient segmentation**
  - Diverse MoAs targeting newly diagnosed metastatic prostate cancer patients
  - Agents targeting early-stage prostate cancer also stratifying patients based on risk to recurrence
  - Next-generation ADTs targeting nmCRPC, with 3 agents in Phase III
  - PARP inhibitors targeting BRCA mutants in the post-chemo setting

- **Multiple MoAs being targeted in Phase II and I/II trials**
  - Several immunotherapies targeting early-stage prostate cancer
  - Biomarker-driven strategies are expected to further improve outcomes
  - Vaccine therapy in combination with immune checkpoint inhibitors is emerging

Summary of Clinical Data with PD-1/ PD-L1 inhibitor

Pembrolizumab interim data in prostate cancer cohort shows 13% ORR and 8 months mOS; Sub-group analysis data awaited





Pe – Pembrolizumab[1-3]

Av – Avelumab[4]

NOTE: Number in brackets after the line of therapy depicts number of prior therapies; 'c' refers to combination

→ Depicts median follow up time; mOS – Not reached

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