LATEST ONCOLOGY UPDATES

Title: Multinational, Double-Blind, Phase III Study of Prednisone and Either Satraplatin or Placebo in Patients with Castrate-Refractory Prostate Cancer Progressing After Chemotherapy: The SPARC Trial

Background:

- Single agent Docetaxel is the standard of care for first line management of castrate-refractory prostate cancer (CRPC); there is currently no standard second line therapy:
  - In Canada, many patients receive second line Mitoxantrone for palliative benefit based on phase II data
- Satraplatin is a novel oral platinum compound:
  - Forms platinum-DNA adducts and cross links, but is not susceptible to some cisplatin resistance mechanisms
- Satraplatin has previously demonstrated activity in CRPC in II/III trials:
  - Phase II: Latif et al, Invest New Drugs 23: 79-84, 2005
    - Dose limiting toxicity: myelosuppression
  - Phase III: Sternberg et al, Oncology 68: 2-9, 2005:
    - Similar design as this trial with prednisone as comparative arm
    - Closed prematurely by sponsoring company after 50 patients accrued
    - Illustrated a progression free survival (PFS) advantage of 5.2 months vs 2.5 months - hazard ratio (HR) 0.50, 95% CI: 0.28-0.92, p=0.023; Non significant OS benefit

Study design:

- International, double-blind, randomized, placebo controlled phase III
- Population:
  - TxNxM1 metastatic prostate adenocarcinoma:
    - Stage D2 – visceral, bone or distant lymph node involvement
  - Had evidence of disease progression after ≥ 2 cycles of prior chemotherapy:
    - Radiographic evidence of progressive disease OR
    - Increasing PSA
- Inclusion Criteria:
  - ECOG performance status ≤ 2
  - Life expectancy > 3 months
  - Medical or surgical castrate hormonal levels (< 50 ng/dL)
  - Adequate bone marrow, hepatic and renal function
- Exclusion Criteria:

- > 1 prior chemotherapy regimen
- Prior platinum therapy
- Additional malignancy
- "Significant" radiotherapy

- Intervention:
  - Patients were randomized in a 2:1 ratio to one of two arms:
    - **Treatment A**: Satraplatin + Prednisone:
      - Satraplatin 80 mg/m^2 po days 1-5 q35days + Prednisone 5 mg po bid
    - **Treatment B**: Placebo + Prednisone
  - Patients were stratified by:
    - ECOG PS: 0-1 vs 2
    - Mean baseline Present Pain Intensity (PPI) score: 0-1 vs 2-5
    - Type of disease progression: tumour vs PSA progression
- Endpoints:
  - Primary: intention to treat population
    - Progression Free Survival (PFS):
      - Composite endpt: tumour progression, skeletal related event, symptomatic progression or death from any cause
      - PSA progression alone was NOT a component of PFS
    - Overall Survival (OS)
  - Secondary:
    - Time To Pain Progression (TTPP)
  - Exploratory:
    - Tumour response (RR) RECIST
    - PSA response (PSA)
    - Pain response (PR)

Study Results:

- Study groups:
  - 950 patients randomized at 170 sites in 16 countries
    - 635 were randomized to Satraplatin – received median 4 cycles
    - 325 were randomized to placebo
- Patient Characteristics:
  - Patient were well balanced with respect to baseline characteristics
  - 89% were ECOG 0-1
  - 62% had pain index scores of 0-1 (no or mild pain)
  - 44% of patients had PSA progression only on study entry
  - 51% of patients had received first line Docetaxel
  - 61.7% of Satraplatin patients and 68.6% of placebo patients received post-study treatments

- Endpoints:

	Treatment A	Treatment B	Hazard Ratio	p-value
1º OS (median)	61.3 weeks	61.4 weeks	0.98 (0.74-1.15)	0.80
1º PFS	11.1 weeks	9.7 weeks	0.67 (0.57-0.77)	**<0.001**
2º TTPP	66.1 weeks	22.3 weeks	0.64 (0.51-0.79)	**<0.001**
Exploratory: RR	8.0%	0.7%		**0.002**
Exploratory: PSA	24.2%	13.8%		**0.005**
Exploratory: PR	25.4%	12.4%		**<0.001**

- Toxicities:
    - Hematologic toxicities were the most common dose-limiting toxicity in the Satraplatin group (significantly more common than with placebo, $p<0.05$)
    - GI toxicities were the second most common Satraplatin toxicity (significantly more common than with placebo, $p<0.001$)
    - 14.9% of the Satraplatin group discontinued study treatment because of adverse effects compared to 10.2% of the placebo group

Conclusions:

- While this study showed an improvement in PFS, it did not show a survival benefit
- Satraplatin did show efficacy in palliative endpoints
- Treatment was generally well tolerated

Study commentary:

- The study population differed from the general Canadian castration resistant population in that only 51% received first line Docetaxel
- While this study showed a palliative benefit, the subjects were generally well (89% performance status 0-1, 62% no or mild pain, 44% PSA progression only on study entry)
- Based on this study's modest PFS improvement and palliative benefit alone, Satraplatin is unlikely to be adopted in Canada as "standard" second line chemotherapy in castration resistant Prostate Cancer

Website link to source: http://jco.ascopubs.org/cgi/content/short/27/32/5431