## Session 5: Urological cancers (Janssen)

### OCPS 22: Management of metastatic castration-refractory prostate cancer: An update in 2014

J. P. Droz

*Claude-Bernard Lyon 1 University and Unit Cancer, Environment, Centre Léon-Bérard, Lyon, France*

Prostate cancer is the first cancer site in incidence and the second in mortality in men worldwide. The median age at diagnosis is 70 years; median age at death is 80 years. Therefore metastatic prostate cancer is a disease of elderly patients. The first-line treatment is androgen deprivation therapy (ADT). However all patients will experience the status of "castration refractory disease" (CRPC). That means that the disease progresses while the patient receives optimal ADT and serum testosterone level is <0.5 ng/ml. The most important prognostic factors in CRPC are: cancer symptoms (pain or not) and metastases sites (bone only vs. visceral metastases). Until the early 2010's the standard treatment of CRPC has been Docetaxel every 3 weeks. This drug was the first to induce significant symptom relief and increased overall survival. In the second line no treatment was available. Therefore the patients had to receive the standard symptomatic treatments: Bone targeted drugs, radiotherapy, radio pharmaceutics (samarium), palliative surgery and pain treatment. Since 2010 new treatments have been developed. Abiraterone acetate is a strong inhibitor of steroids synthesis by blocking CYP 17 enzymes. The most important is that it acts on prostate cancer cells androgen synthesis when castration refractoriness occurs. The drug is given together with low-dose prednisone. It is well tolerated with few side effects. Enzalutamide is a powerful androgen receptor inhibitor. Tolerance is good and side effects minor. In the first line treatment of CRPC Abiraterone Acetate and Prednisone compared to Prednisone only (protocol COU-302) has demonstrated a significant overall survival advantage (HR (95% CI): 0.75 (0.61-0.93) P= 0.0097). Enzalutamide (protocol PREVAIL) has also demonstrated a survival advantage when compared to a placebo (HR: 0.71; 95% CI, 0.60 to 0.84; P < 0.001). Nevertheless patients included in the trials had only bone metastases and had few symptoms. In the second line (after progression on or after docetaxel) the drugs have shown a significant survival advantage: Cabazitaxel (protocol TROPIC), Abiraterone Acetate (protocol COU-301) and enzalutamide (protocol AFFIRM). Finally two treatments have also demonstrated a significant survival advantage, but are not easily accessible: Sipuleucel-T (protocol IMPACT) in asymptomatic patients and radium 223 (protocol ALSYMPCA). Noteworthy all these treatments are as active and tolerable in elderly patients as in younger patients. Tumor heterogeneity and optimal drug sequences will be discussed.

### OCPS 23: Management of testis germ cell tumors

J. P. Droz

*Claude-Bernard Lyon 1 University and Unit Cancer, Environment, Centre Léon-Bérard, Lyon, France*

Testis germ cell tumor is the most frequent cancer in young men. It is a curable disease. Two clinical types, quite equally frequent are described: seminoma and non seminomatous tumors (NSGCT). Seminoma is a unique histological pattern, with normal serum Alpha-Foetoprotein (AFP) level and sometimes slightly elevated serum human chorionic gonadotropin (hCG) level. All other tumors are NSGCT. The initial management of a testis tumor is serum tumor marker (hCG, AFP and LDH) level determination, inguinal orchiectomy, thoraco abdominal and pelvis CT scan and sperm preservation. Stage 1 disease is limited to the testis, based on CT scan and normal serum tumor markers. Stage 1 seminoma is generally managed by surveillance policy because relapse rate is around 15%. Patients with initial tumor size is > 40 mm are at risk of relapse (around 25%) and are candidate to receive one cycle of carboplatin AUC 7. Lombo-aortic radiotherapy is generally not applied due to higher risk of secondary cancers in the irradiation fields. Stage 1 NSGCT of the testis is either surveillance, retroperitoneal lymph node dissection (RPLND) or adjuvant chemotherapy by two cycles of bleomycin – etoposide and cisplatin (BEP regimen). The decision making is based on prognostic factors of relapse and patient preference. Prognostic factor of relapse is small vessel invasion by tumor cells (either vascular or lymphatic). Patients with small vessel invasion are at 50% risk of relapse: They should be proposed to receive chemotherapy. Patients without small vessel invasion should be proposed for surveillance and in some selected cases nerve-sparing RPLND. Patients with RPLN metastases and/or visceral metastases are classified according to the International Classification based on the following prognostic factors - hCG, AFP and LDH levels, presence of non-pulmonary visceral metastases. Patients are assigned to one of the prognostic group: Low, intermediate and poor risk (there is no poor risk group for seminoma patients). The general management is chemotherapy then complete removal of all residual disease. The clinical management for advanced stage seminoma is three cycles of BEP and four cycles of BEP for patients in the good risk and intermediate risk groups respectively. Secondary surgery is limited to patients with residual disease >30 mm and patients with abnormal PET scan. The clinical management for advanced stage NSGCT is three cycles of BEP and four cycles of BEP for patients in the good risk and intermediate/poor risk groups respectively. Secondary surgery is mandatory in patients with initial RPLN >30 mm and patients with any residual disease. PET scan is not valid in the evaluation of these patients. Relapses have poor outcome the standard treatment is chemotherapy (four cycles of paclitaxel, ifosfamide and cisplatin) then complete exeresis of any residual disease.