Sanofi Response to the Appraisal Consultation Document

Prostate cancer (metastatic, hormone relapsed, not treated with chemotherapy) - abiraterone acetate (with prednisolone)

Please find below Sanofi's response to the Appraisal Consultation Document (ACD) for abiraterone.
Our comments all relate to the question as to whether the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence.

1: Positioning of abiraterone and value of delaying chemotherapy

The ACD notes that delaying the use of chemotherapy is perceived to be one of the major benefits of abiraterone (used prior to docetaxel). However, it is critically important that the potential disadvantages of delaying chemotherapy are also taken into account. If chemotherapy is delayed, patients may experience disease progression and worsening of performance status that may either make them ineligible for chemotherapy or mean that they are less able to tolerate the side effects of chemotherapy if they do receive it. In the abiraterone submission, patients in the abiraterone arm had shorter durations of docetaxel chemotherapy compared to the best supportive care arm (4.13 of the ACD). Docetaxel chemotherapy was unequivocally proven to prolong overall survival in TAX327 – delaying initiation of docetaxel may result in fewer patients receiving the full survival benefit of this drug (Tannock et al 2004, NEJM 351; pp1502 – 1512). This should be viewed in the context of the uncertainty over the overall survival estimates in COU-302. Patient choice is clearly very important and many patients may choose not to undergo chemotherapy, however it is critical that they are able to make an informed choice, and are aware that delaying chemotherapy may mean that they are unable to gain the full survival advantage from the sequence of treatments now available to treat metastatic hormone refractory prostate cancer. Indeed, new evidence suggests that earlier use of chemotherapy in *hormone-sensitive* disease is beneficial, with a 13.6 month survival advantage demonstrated for docetaxel plus androgen deprivation therapy versus androgen deprivation therapy alone (HR 0.61, 95% CI 0.47-0.80, *P*=0.0003 [Sweeney et al, CHAARTED trial, Abstract number LBA2, ASCO 2014]).

It is particularly important not to delay chemotherapy in patients with rapidly progressing disease – as noted in the ACD (section 4.1) clinical experts do not consider it appropriate to use abiraterone to delay chemotherapy in patients who have rapidly progressing disease and who are fit enough to receive chemotherapy. It is important to recognise that the licensed indication for abiraterone is for patients who have no or mild symptoms after androgen deprivation therapy has failed and in whom chemotherapy is not yet clinically indicated and that this indication does not cover the entire population of patients with hormone-refractory metastatic disease who have not received chemotherapy. Indeed, the COU-302 trial was conducted only in patients who were asymptomatic or mildly symptomatic, and also excluded patients with visceral metastases (typically associated with rapidly progressing disease).

2: Evidence for the impact of chemotherapy on Quality of Life

The ACD notes that "The Committee concluded that chemotherapy can reduce a person's quality of life". While chemotherapy is associated with adverse events that may impact on quality of life, it should be noted that in fact the TAX327 trial of docetaxel shows positive effects on quality of life, with a significantly higher proportion of patients recording a response (defined as a 16-point improvement from baseline in the Functional Assessment of Cancer Therapy–Prostate [FACT-P] score on two measurements obtained at least three weeks apart) with docetaxel compared with mitoxantrone, a treatment primarily used for its palliative benefits (22% with docetaxel every 3

weeks, 23% with weekly docetaxel versus 13% with mitoxantrone, p = 0.009, p = 0.005 [Tannock et al 2004, NEJM 351; pp1502 – 1512]). This evidence indicates that the disease control afforded by docetaxel translates to improved, rather than reduced, quality of life.

3: Availability of cabazitaxel in the UK

We agree with the Committee that it is inappropriate to "adjust" post-docetaxel survival estimates from COU302 to exclude the survival benefit associated with cabazitaxel, as this treatment is available on the NHS in England through the Cancer Drugs Fund.