Low risk population (non-extirpative therapies)

Drug and device products are being developed for the management of healthy patients with “low risk” prostate cancer (generally Gleason sum 6 or less) and a life expectancy greater than 10 years using a comparator arm of active surveillance. For this indication please consider the following:

Eligibility
1. Trials that evaluate treatments for localized prostate cancer that utilize active surveillance as a comparator arm must balance the potential risk of disease progression if the risk strata are too high versus the potential overtreatment of clinically insignificant disease. Keeping this in mind, please describe the entry criteria that you would recommend for trials for this indication listing the specific risk factors (i.e., PSA, Gleason score, etc.) that you would employ and both the upper and lower limits for each risk factor.

Endpoints
2. The regulatory basis for full approval is demonstration of a clinical benefit, such as increased survival or an improvement in disease-related dysfunction or symptoms. Overall survival is not a practical endpoint for this patient population. What endpoint do you believe measures a clinically meaningful benefit? Please include in your discussion the duration of follow up necessary and magnitude of benefit that would be clinically meaningful for your proposed endpoint.

Focal Therapy

Focal therapy, targeting either an “index” lesion or a portion of the prostate, is being developed for both low risk and intermediate risk prostate cancer patient populations.

Eligibility
3. What should be the eligibility criteria for entry in a focal therapy study? Please include in your discussion your assessment of the scientific basis of focal therapy for either minimal disease or intermediate risk patients.
QUESTIONS

Note: All questions are to be considered in the context of clinical trials to support U.S. regulatory approval.

Definitive Radiation Therapy Failure Population

Patients that have a biochemical failure and/or a positive prostate biopsy following definitive radiation therapy are being entered into clinical trials of local therapies.

Eligibility

4. What should be the eligibility criteria for study entry? Please discuss how you would identify a patient as having failed definitive radiation therapy and the procedure(s) that should be used to rule out metastatic disease. In your discussion of eligibility criteria, also address whether there is a need for intervention for all patients with failure of definitive radiation or would you restrict treatment to a subpopulation based on findings at the time of original diagnosis. For instance, would you exclude patients at either end of the risk strata based on findings at original diagnosis due to either minimal risk of cancer-related morbidity/mortality or a high likelihood of occult metastatic disease?

Comparator

5. What should be the comparator arm for these trials?

Endpoints

6. What endpoint should be employed for radiation failure trials? Discuss the minimum duration of follow up and magnitude of benefit that may be clinically meaningful?

Adjuvant Therapy

Products, both hormonal and non-hormonal, are being developed as adjuvant therapy for patients with high risk prostate cancer undergoing treatments with curative intent.

Endpoints

7. What are the optimal patient population and endpoint that should be used for these trials? Include in your discussion the effect of the primary treatment (surgery versus radiation) and mechanism of action of the adjuvant therapy (hormonal versus non-hormonal) on the choice of endpoint.
Intermediate/High Risk Population undergoing non-extirpative therapy

Products are being developed for the treatment of patients with intermediate to high risk localized prostate cancer that do not remove the entire prostate gland. These include medical therapies and devices that target either the entire prostate gland or a portion of it.

Endpoints

8. What endpoint should be employed to determine the efficacy of treatments that do not remove the prostate? Include in your discussion the effect of the comparator arm (surgery versus radiation therapy) on the choice of endpoint, minimum duration of follow up, and magnitude of benefit that would be clinically meaningful.