High risk prostate cancer

Steps towards a more patient tailored therapy

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SUMMARY

Long term data show that death from prostate cancer (PCa) is very uncommon among men with low risk PCa, even when untreated. Further reduction of overdiagnosis and overtreatment is therefore warranted. However, PCa does remain the second leading cause of cancer mortality in men in the Western world. Therefore, especially PCa patients who are at high risk to succumb to their disease should be the subject of our attention and further research.

This thesis evaluates in 3 chapters different therapies to achieve a more accurate prognosis for the individual high risk PCa patient and find the treatment strategy having the best survival odds without adding morbidity, thus taking steps towards a more patient tailored therapy.

By looking at the tumor (Chapter I) we show that the androgen receptor (AR) expression profile could provide additional prognostic information on tumor aggressiveness highlighting the importance of the peritumoral

environment and the important link between AR, DNA repair and androgen deprivation especially in the context of therapy. radiotherapy. In Chapter II we show that targeting the disease to its real extent is key in the definitive treatment of locally advanced PCa, highlighting the importance of a full and correct staging. Thinking about the patient (Chapter III), we show that there could be a role for cytoreductive radical prostatectomy (cRP) in de novo metastatic PCa. However, patients receiving cRP will always have more favorable characteristics than those who cannot receive cRP, who are in turn at risk of suffering from early local symptoms.

Refinement of the risk stratification by including the new imaging modalities and prognostic information of positive lymph node spread is proposed as a possible way forward to really start individualizing high risk PCa management. However, critical assessment is needed, also to balance treatment burden against treatment benefit. Providing the appropriate treatment at the right time for the right patient will always remain crucial.

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