THE DISEASE LANDSCAPE OF PROSTATE CANCER

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EARLY 1940s
CHICAGO

CASE STUDY 14

An 80 years old, white man was admitted to Hospital on Oct 30, 1940.

For previous 5 months, the patient had pain in the dorsal and lumbar regions of his back.

For two months, he had spent most of his time in bed and was unable to walk without intense pain and fatigue.

Additionally, he presented with a loss of 17 Kg. (37 lbs.) in weight.

"On examination it was found that the patient could not change his position from lying to sitting in bed without agony accompanied by distention of the veins of his neck."

"The prostate was slightly enlarged (2 -[-) and there was a hard nodule (1 cm. in diameter) in the apex of the gland about the membranous urethra."

"Roentgenograms showed diffuse osteolytic lesions in the pelvis with partial collapse of the body of the sixth dorsal and the second lumbar vertebra."

"His weight was 62 Kg." **(136 lbs.)**

Adapted from: Huggins, C., Stephens, R. E. & Hodges, C. V. Studies on prostate cancer II. The effects of castration on advanced carcinoma of the prostate. *Arch. Surg.* 43, 209–223 (1941).

CASE STUDY 14

"The only treatment was orchidectomy, performed on Nov. 12, 1940. "

Adapted from: Huggins, C., Stephens, R. E. & Hodges, C. V. Studies on prostate cancer II. The effects of castration on advanced carcinoma of the prostate. *Arch. Surg.* 43, 209–223 (1941).

CASE STUDY 14

Result 1: Improvement in the mobility of the patient

"Within five days thereafter he was able to raise himself promptly from the lying to the sitting posture."

Result 2: Change in the feel of the prostate itself:

"On November 26 the prostate gland was soft and just palpable."

Result 3:

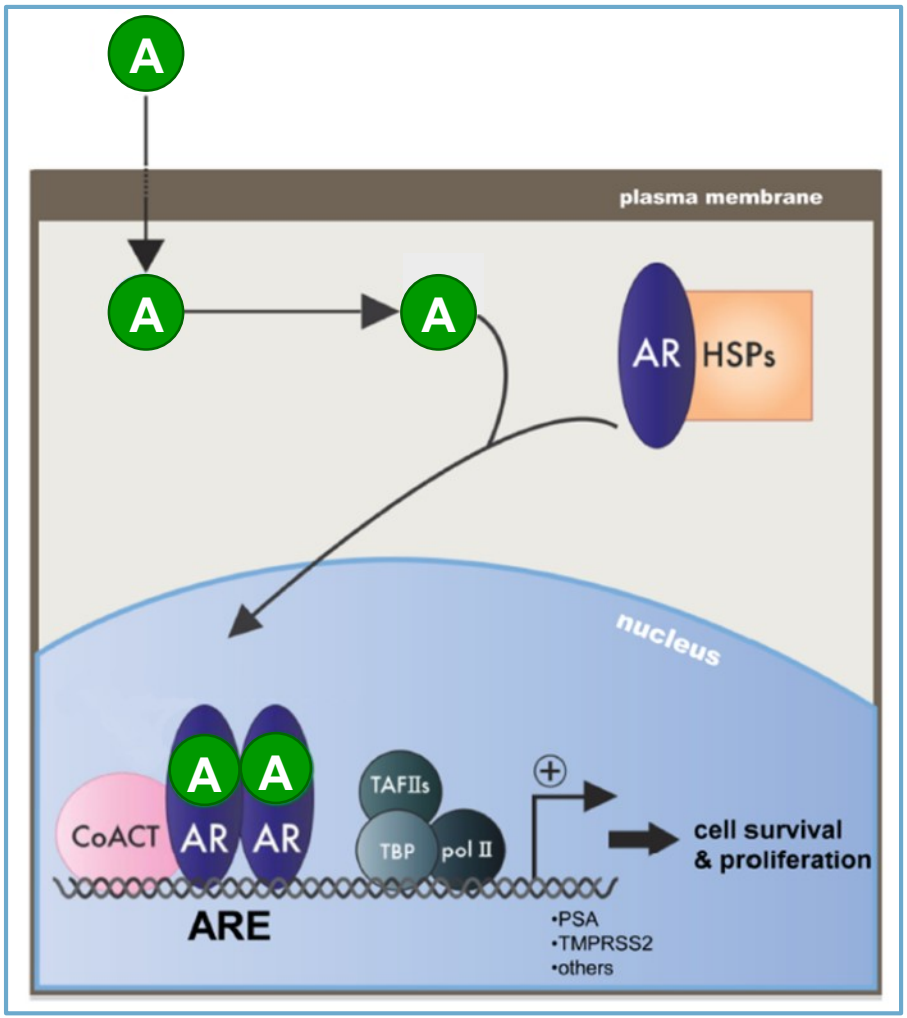
"On April 21, 1941 the patient considered himself well; he had little pain in the lumbar region, and he had just spaded a garden 40 by 50 feet (12.2 by 15.2 meters) without trouble"

Result 4: Improvement in cachexia

"his weight was 74 Kg." (163 lbs)

Adapted from: Huggins, C., Stephens, R. E. & Hodges, C. V. Studies on prostate cancer II. The effects of castration on advanced carcinoma of the prostate. *Arch. Surg.* 43, 209–223 (1941).

ANDROGEN RECEPTOR SIGNALING IN PROSTATE CANCER



Upon activation by androgen (A) binding

Androgen receptor (AR) is released by chaperones, e.g., heat shock proteins (HSPs), facilitating:

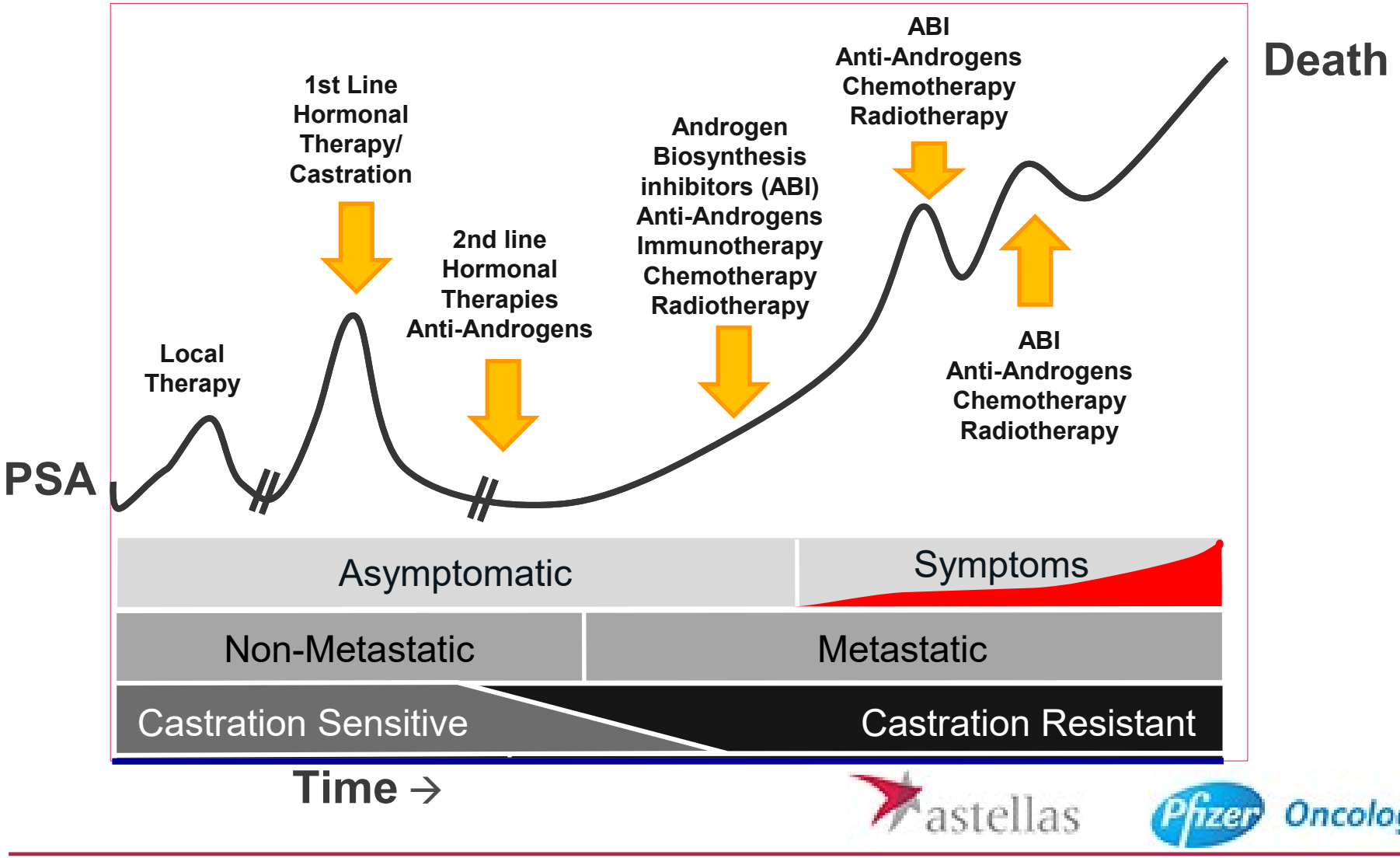
- AR homodimerization
- Rapid nuclear translocation
- Post-translational modification
- Receptor stabilization

Activated AR dimers bind to DNA at androgen response elements (AREs), recruiting a series of coactivators (CoACT) that facilitate formation of active transcription complexes

Gene transcription is initiated

Knudsen KE, Penning TM. *Trends Endocrinol Metab.* 2010;21:315-324.

THE DISEASE CONTINUUM IN PROSTATE CANCER AND CURRENT TREATMENTS BY CLASS



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Zhang T et al. Evolution of clinical states and the castration resistant clinical paradigm. In: Management of Castration Resistant Prostate Cancer. 1st ed. Springer New York, 2014:9-30.
Antonarakis ES et al. Treatment of castration-resistant prostate cancer. In: Campbell-Walsh Urology. 11th ed. Elsevier Philadelphia, 2016:2804-22.

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